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The influence of a single transcranial direct current stimulation session on physical fitness in healthy subjects: a systematic review

Nastasia Marinus, PhD[a,b;1]; Sybren Van Hoornweder (SVH), MSc[a;1,]; Marthe Aarts, MSc[a]; Jessie Vanbilsen, MSc[a]; Dominique Hansen, PhD, FESC[a,b,c;2], Raf Meesen, PhD[a,d;2]

[a]REVAL - Rehabilitation Research Center, Faculty of Rehabilitation Sciences, Hasselt University, Diepenbeek, Belgium
[b]BIOMED - Biomedical Research Center, Hasselt University, Diepenbeek, Belgium
[c]Heart Centre Hasselt, Jessa Hospital, Hasselt, Belgium
[d]Movement Control and Neuroplasticity Research Group, Department of Movement Sciences, Group Biomedical Sciences, KU Leuven, Leuven, Belgium

[1] These authors share first authorship
[2] These authors share last authorship

Address for correspondence:
Nastasia Marinus
Hasselt University, Faculty of Rehabilitation Sciences
Agoralaan, Building A, 3590 Diepenbeek, Belgium
E-mail author: Nastasia.marinus@uhasselt.be
ORCID-ID: 0000-0002-4903-2439
Tel +3211269318

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Abstract

The current PRISMA-adherent review, therefore, aimed to examine the effect of tDCS on the three core components of physical fitness: muscle strength, -endurance and cardiopulmonary endurance. Randomized controlled- or cross-over trials evaluating the effect of a single tDCS session (vs. sham) in healthy individuals were included. Hereby, a wide array of tDCS-related factors was taken into account.

Thirty-five studies (540 participants) were included. In general, a large heterogeneity (age, activity level, experimental tDCS protocol, testing procedure, outcome measures) was found between studies which was reflected in the results of the individual studies. However, muscle endurance seemed most susceptible to improvements after tDCS. Also, stimulation of the primary motor cortex and the dorsolateral prefrontal cortex yielded positive results on muscle and cardiopulmonary endurance. Furthermore, anodal tDCS (AtDCS) yielded the greatest results and online tDCS seemed most beneficial. Finally, no relationship between tDCS and dose-related parameters was present.

These findings can contribute to optimizing rehabilitation in patients with a variety of (chronic) diseases such as cardiovascular disease. Therefore, future studies should focus on further unravelling the potential of AtDCS on physical fitness and, more specifically, muscle endurance in both healthy subjects and patients suffering from (chronic) diseases.

Keywords: tDCS, transcranial direct current stimulation, physical fitness, muscle endurance, muscle strength, cardiopulmonary endurance

1. Introduction

Physical fitness, entailing muscle strength, muscle endurance, and cardiorespiratory endurance, amongst others, is of indisputable importance for both health, prognosis and sports performance (Chen et al., 2018;McLeod et al., 2016;Roshanravan et al., 2016;Ruegsegger and Booth 2018;Tomas-Carus et al., 2016;Wang et al., 2020). In particular, in an ageing and sedentary society, and with the steady increase in the prevalence of chronic diseases or disabilities, the preservation or improvement of these factors has become top priority. Moreover, numerous researchers have increasingly recognized the potential of medically safe ergogenic aids (Machado et al., 2019;Stecker et al., 2019;Vicente-Salar et al., 2020).

Physical fitness is traditionally often believed to be related to the collective function of the skeletal muscle, cardiovascular and pulmonary system. However, various studies suggest that the brain might also be a key contributor and that the brain is targeted indirectly by exercise-based rehabilitation or sports training programs (Iodice et al., 2019;Noakes 2012;Pires et al., 2016;Stevinson and Biddle 1998;Taylor et al., 2016). Therefore, the question arises whether direct stimulation of the brain via noninvasive brain stimulation, and specifically via transcranial direct current stimulation (tDCS), is be a promising ergogenic tool.

Through the application of a weak electric current (typically 1 – 2mA) to the scalp, tDCS can modulate the underlying cortex and function as a neuromodulatory ergogenic resource to change physical performance (Machado et al., 2019;Nitsche et al., 2008). Specifically, tDCS modulates the excitability of neuronal membranes in the vicinity of stimulation electrodes (10.1177/1559325816685467, 10.1113/jphysiol.2003.055772). Although various tDCS montages, that incorporate different amounts of electrodes, are present, two surface electrodes are generally used (an anode and a cathode) and two forms of tDCS are distinguished. In anodal tDCS (AtDCS), the anode is positioned over the region of interest and the cathode is used as a reference electrode. Although AtDCS generally leads to increased brain excitability, large interindividual variability has been observed. For instance, Wiethoff et al. (2014) found that approximately 50% of participants did not respond to anodal tDCS (10.1016/j.brs.2014.02.003), with other work reporting similar findings and even noting that factors such as stimulation duration can reverse the effects of AtDCS (10.1016/j.brs.2014.02.004, 10.1016/j.brs.2020.02.027). Likely, this variability stems from interindividual differences in factors such as anatomy (10.1111/ner.13342). In cathodal tDCS

(CtDCS), the reversed procedure is performed which typically results in decreased brain excitability, although here as well, large interindividual variations are present (Nitsche and Paulus 2000) (10.1016/j.brs.2014.02.003).

In the past, multiple reviews investigated the effectiveness of tDCS on various components of physical fitness and found (task-dependent) improvements in muscle strength, time to exhaustion and reaction time (Angius et al., 2017;Machado et al., 2019;Shyamali Kaushalya et al., 2021;Wang et al., 2021). However, there is currently a lack of a comprehensive overview of the effects of tDCS on all three core components of physical fitness. Moreover, the field continues to evolve rapidly. As such, various studies have recently been published that have not yet been discussed in the aforementioned reviews (Alix-Fages et al., 2019;Byrne and Flood 2019;Kamali et al., 2019;Lattari et al., 2018c;Oki et al., 2019;Vargas et al., 2018;Wrightson et al., 2020). In addition, the influence of tDCS dose-related parameters [i.e., duration, current and charge density] on physical fitness remains unclear (Caulfield et al., 2020;Kasten et al., 2019). A more thorough understanding is of utmost scientific importance, as previous reviews in other scientific domains underscore the significance of these parameters (Caulfield et al., 2020;Chhatbar et al., 2016;Lefebvre and Liew 2017;Marquez et al., 2015;Van Hoornweder et al., 2021). In the current systematic review, the three core components of physical fitness (i.e., muscle strength, muscle endurance and cardiopulmonary endurance) will be examined to provide a comprehensive overview of the effectiveness of tDCS as an ergogenic tool. These results could be relevant for healthy subjects and could potentially provide a starting point for interventions in subjects with chronic diseases.

2. Methods

2.1. Literature search

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Moher et al., 2009). Two electronic databases (PubMed and Web of Science) were searched (up to July 2022) to address the impact of tDCS versus sham on the three core components of physical fitness: muscle strength, muscle endurance and/or cardiopulmonary endurance (cf. Table 1). Two researchers (MA and JV) independently conducted the literature search. First, duplicate studies were removed. Subsequently, articles were screened based on title and abstract. Finally, the full-text of studies was read to screen them for eligibility. Disagreements were resolved via a consensus-based discussion.

2.2 Selection criteria

The main aim of this review was to evaluate the impact of tDCS on exercise performance. Therefore, only (1) prospective randomized controlled trials (RCT) or cross-over trials were included which (2) evaluated the effect of a single tDCS session in comparison to sham stimulation on (3) an objective measure of muscle strength, muscle endurance and/or cardiopulmonary endurance in (4) healthy individuals.

Only English-written articles were included. Studies were not excluded based on sex or age. Studies were not included when a) information was missing (i.e., tDCS stimulation intensity, electrode positioning), which was essential for a complete and correct overview in this systematic review, and b) when it could not be retrieved after contacting the corresponding author (or another co-author of that specific paper).

2.3 Quality assessment

Two researchers (MA and JV) independently evaluated the internal and external validity of the included RCTs via the PEDro scale (Blobaum 2006). In case of disparities, a third reviewer (NM) was consulted. This scale consists of 11 questions that have to be answered with ‘yes’ (score 1) or ‘no’ (score 0). In accordance to its intended use, item 1 was withheld during calculation of the final score, resulting in a maximal score of 10. A score of 9-10 was considered to indicate excellent quality, 6-8 as good quality, 4-5 as moderate quality and 0-3 as poor quality.

2.4 Data extraction

Participant-, tDCS-, and physical fitness data were extracted from the included studies (cf. Figure 1). To minimize the risk of bias, data extraction was performed by two independent researchers (MA and JV) and validated by two different researchers (NM and SVH). In case of disparities, a fifth reviewer (DH) was consulted.

To increase between-study comparability, tDCS intensity, duration and electrode size were used to calculate current density (mA/cm^2) and electric charge density (coulomb $(\text{A*s})/\text{cm}^2$). Current density was categorized as low (0.029-0.043 mA/cm^2), mild (0.044-0.057 mA/cm^2), moderate (0.058-0.083 mA/cm^2) or high (0.084-0.429 mA/cm^2). Charge density was categorized as low (0.017-0.045 C/cm^2), moderate (0.046-0.096 C/cm^2) or high (0.097-0.514 C/cm^2). tDCS duration was divided into three subgroups: ≤15 minutes, 20 minutes and ≥30 minutes of tDCS.

Moreover, to be able to make conclusions regarding the impact of tDCS on the whole spectrum of physical fitness, the available physical fitness outcomes were grouped into three different categories: muscle strength, muscle endurance and physical endurance. After the data extraction process, two reviewers (NM and SVH) assigned the physical outcome measures to any of the categories based on their (clinical) experience. However, in case of disparities, a third reviewer (DH) was consulted.

Data which were not related to the tDCS procedure or to physical fitness (muscle strength, muscle endurance and physical endurance) were not included in the systematic review.

3. Results

3.1 Study selection

The complete study selection procedure is displayed in Figure 2. In total, 449 publications were retained. Removal of duplicates resulted in 406 studies. Based on the abstract, 57 full-text articles were found to be eligible. Twenty-two studies were excluded (e.g., because of not fulfilling the inclusion criteria or because of lack of detailed information regarding tDCS stimulation intensity or electrode positioning). Finally, 35 studies were included.

3.2 Quality assessment

The internal and external validity of the included studies, evaluated with the PEDro scale, is shown in Table 2 (Blobaum 2006). PEDro scores ranged between 4/10 to 9/10. Notably, 29% of the studies did not specify eligibility criteria. Furthermore, in 66% of studies, allocation was not concealed. Also, although possible with tDCS, only 9% of the studies blinded the therapists (who administered the therapy) and solely 45% of the studies blinded the assessors (who measured key outcomes). Finally, three studies (9%) were of excellent quality, 21 (60%) were of good quality, and 11 (31%) were of moderate quality.

3.3 Data extraction

3.3.1 Participant and study characteristics

Thirty-five studies were included in this systematic review, resulting in 540 participants (344 ♂ and 181 ♀ (Lattari et al. 2018 did not describe the sex-distribution (Lattari et al., 2018b)) with a mean age of 27.3 ± 3.8 years (Table 3). The impact of tDCS on muscle strength was examined in sixteen studies, resulting in 256 participants (mean age 28.1 ± 3.8 years, 166 ♂ and 90 ♀) (cf. Table 3 and 4). Similarly, the impact of tDCS on muscle endurance was also examined in sixteen studies, resulting in 265 participants (mean age 27.3 ± 4.0 years, 158 ♂ and 92 ♀). Finally, the impact of tDCS on cardiopulmonary endurance was examined in thirteen studies, resulting in 169 participants (mean age 24.3 ± 3.8 years, 151 ♂ and 18 ♀) (cf. Table 3 and 4).

3. 4. General impact of tDCS

Table 5 provides a general overview of the effects of tDCS on the different core components of physical fitness. Overall, it seems that AtDCS yields greater effects than CtDCS, and AtDCS seems to be particularly effective as an ergogenic aid to improve muscle endurance. Also, online tDCS seems to be superior over offline tDCS. In general, a clear dose-response relationship is absent, although all protocols that used a high current density yielded positive effects on muscle endurance.

3. 5. Impact of tDCS on muscle strength

Sixteen studies reported an increase in muscle strength in at least one key outcome measure (increase in 1 Repetition Maximum (RM) or Maximum Voluntary Isometric Contraction (MVIC)) in the tDCS vs. sham group (Alix-Fages et al., 2020;Barwood et al., 2016;Ciccone et al., 2019;Esteves et al., 2019;Frazer et al., 2017;Giboin and Gruber 2018;Hazime et al., 2017;Holgado et al., 2019;Kamali et al., 2019;Lampropoulou and Nowicky 2013;Montenegro et al., 2015;Oki et al., 2019;Vargas et al., 2018;Washabaugh et al., 2016;Workman et al., 2020a;Workman et al., 2020c) examined the impact of tDCS on muscle strength. Five studies (31%) (Frazer et al., 2017;Hazime et al., 2017;Kamali et al., 2019;Vargas et al., 2018;Washabaugh et al., 2016).

Two studies (13%) reported a decrease in muscle strength in at least one key outcome measure (decrease in torque or in MVIC amplitude) in the tDCS vs. sham group. (Giboin and Gruber 2018;Workman et al., 2020a). Nine studies (56%) reported no differences in any of the key muscle strength outcome measures between the tDCS and sham group (1 RM, (non-fatigued) MVIC, (mean) torque, mean power output, torque integral or total work (per set)) (Alix-Fages et al., 2020;Barwood et al., 2016;Ciccone et al., 2019;Esteves et al., 2019;Holgado et al., 2019;Lampropoulou and Nowicky 2013;Montenegro et al., 2015;Oki et al., 2019;Workman et al., 2020c). The protocols and results of each study are shown in Table 4. A summary of the influence of tDCS on muscle strength according to tDCS type, -timing, -duration, -current density, - charge density, targeted brain region and RPE is displayed in Table 5. Overall, the impact of tDCS on muscle strength is inconclusive, and the most optimal tDCS modalities remain to be established.

3.6. Impact of tDCS on muscle endurance

The impact of tDCS on muscle endurance was examined by 16 studies (Abdelmoula et al., 2016;Alix-Fages et al., 2020;Angius et al., 2016;Byrne and Flood 2019;Ciccone et al., 2019;Kamali et al., 2019;Lattari et al., 2018b;Montenegro et al., 2015;Muthalib et al., 2013;Oki et al., 2016;Vieira et al., 2020;Williams et al., 2013;Workman et al., 2020b;Workman et al., 2020c, d;Wrightson et al., 2020). A positive impact of tDCS on at least one key outcome measure of muscle endurance (increase in number of repetitions, time to exhaustion (TTE), short-term endurance index (SEI) or fatigability, fatigue index (FI) or a smaller decrease in movement velocity or TTE) was reported by 11 studies (69%) (Abdelmoula et al., 2016;Alix-Fages et al., 2020;Angius et al., 2016;Kamali et al., 2019;Lattari et al., 2018b;Oki et al., 2016;Vieira et al., 2020;Williams et al., 2013;Workman et al., 2020b;Workman et al., 2020c, d). However, five studies (31%) did not report any significant difference in at least one key muscle endurance parameter (fatigability, TTE, number of repetitions, FI) in the tDCS vs sham group (Byrne and Flood 2019;Ciccone et al., 2019;Montenegro et al., 2015;Muthalib et al., 2013;Wrightson et al., 2020). The protocols and results of each study are shown in Table 4. A summary of the influence of tDCS on muscle strength according to tDCS type, -timing, -duration, -current density, -charge density, targeted brain region and RPE is displayed in Table 5. To conclude, the impact of tDCS on muscle endurance seems to be promising, but the most optimal tDCS modalities remain to be established.

3.7. Impact of tDCS on cardiopulmonary endurance

The impact of tDCS on cardiopulmonary endurance was examined by 13 studies (Angius et al., 2015;Angius et al., 2018;Angius et al., 2016;Angius et al., 2019;Baldari et al., 2018;Barwood et al., 2016;Esteves et al., 2019;Holgado et al., 2019;Kamali et al., 2019;Lattari et al., 2018a;Park et al., 2019;Valenzuela et al., 2018;Vitor-Costa et al., 2015). Seven studies (54%) reported a positive impact of tDCS on at least one key outcome measure of whole-body endurance (decrease in HR, increase in TTE) (Angius et al., 2018;Angius et al., 2016;Angius et al., 2019;Kamali et al., 2019;Lattari et al., 2018a;Park et al., 2019;Vitor-Costa et al., 2015). However, six studies (46%) reported no differences in cardiopulmonary endurance-related parameters (FI, heart rate (HR), respiratory exchange ratio (RER), TTE, expiratory volume (VE), maximal oxygen consumption (VO2peak), ventilatory threshold (VT) or peak velocity (Vpeak)) in the tDCS vs. sham group (Angius et al., 2015;Baldari et al., 2018;Barwood et al., 2016;Esteves et al., 2019;Holgado et al., 2019;Valenzuela et al., 2018). The protocols and results of each study are shown in Table 4. A summary of the influence of tDCS on muscle strength according to tDCS type, -timing, -duration, -current density, - charge density, targeted brain region and RPE is displayed in Table 5. To summarize, the impact of tDCS on cardiopulmonary endurance is highly variable and the impact of specific tDCS modalities remains to be studied in more detail.

4. Discussion

The current systematic review aimed to evaluate the effect of tDCS on the three core components of physical fitness (muscle strength, muscle endurance and cardiopulmonary endurance), providing the most comprehensive overview of this topic, to this date. Data from 35 sham-controlled studies (540 participants), with moderate to excellent methodological quality were pooled. Based on this systematic review, tDCS as an ergogenic tool in the context of physical fitness seems to be the most effective to improve muscle endurance in contrast to muscle strength and cardiopulmonary endurance. Moreover, AtDCS (in contrast to CtDCS) and online tDCS (in contrast to offline tDCS) seem to be the most effective. Surprisingly, there seemed to be no relationship between tDCS effectiveness and dose-related parameters (tDCS duration and current/charge density). Regarding electrode positioning, stimulation of M1 and DLPFC yielded positive results in the context of muscle- and cardiopulmonary endurance.

The most distinct effect of tDCS seemed to be on muscle endurance. Indeed, 11 studies (69%) reported a positive impact, while 5 studies (31%) indicated no significant effect. In contrast, tDCS did not seem to influence muscle strength. Only 5 studies (31%) reported a positive impact, while 9 studies (56%) did not find any significant effect and 2 studies (13%) reported a negative impact. The discrepancy between muscle strength vs. muscle endurance is somewhat unexpected, given the results of a previous review indicating that tDCS yielded positive results on muscle strength (Machado et al., 2019). A potential explanation for this peculiar finding might relate to the temporal characteristics of strength vs. endurance tasks. Muscle endurance tasks require prolonged periods of muscle activity (and neural activity), relative to muscle strength tasks. tDCS might be better-suited to influence the prolonged central (neural) mechanisms related to prolonged muscle performance (i.e., muscle endurance).

Nevertheless, this hypothesis remains entirely speculative, as research concerning this topic is, to the best of our knowledge, non-existent. Therefore, future research should investigate the differences between muscle strength and endurance performance on a central, neural level and how this relates to tDCS. Concerning cardiopulmonary endurance, tDCS yielded variable results, as 7 studies (54%) reported a positive impact on at least one key outcome measure, and 6 studies (46%) reported non-significant results. The limited impact of tDCS on cardiopulmonary endurance may be potentially explained by the extensiveness of systems contributing to cardiopulmonary endurance (i.e., the muscular-, neural-, cardiovascular-, pulmonary- and metabolic system) (Hansen et al., 2019). Influencing only one system (i.e., the neural system) may yield small, difficult to perceive, effects when using the general performance as an outcome measure. Measuring brain activity after tDCS during cardiopulmonary task performance may prove to be a better-suited outcome measure. Reassuringly, tDCS did not seem to induce negative effects on the core components of physical fitness, as only three studies (9%) reported negative results.

AtDCS yielded the most promising results in the context of muscle endurance. An explanation for this might be that AtDCS can counteract the reduced motor neuron excitability associated with physical (muscle endurance) performance (Machado et al., 2019;Taylor et al., 2016;Taylor and Gandevia 2008). A second hypothesis that might explain the current findings is that AtDCS can blunt the perception of muscle exertion (Oki et al., 2016). This latter hypothesis is substantiated by 3 included studies, who reported a decreased RPE during muscle endurance tasks (Alix-Fages et al., 2020;Kamali et al., 2019;Oki et al., 2016). One could state that the work of Williams et al. (2013) contradicts the latter hypothesis, as an increased RPE was noted. However, as AtDCS in this study also increased TTE, it seems plausible that RPE increased due to higher muscle exertion (as evidenced by increased TTE) (Williams et al., 2013).

Literature regarding the impact of tDCS on muscle endurance is scarce and conflicting (Cogiamanian et al., 2007;Kan et al., 2013). Potentially, these conflicting results can be partially explained through the (arbitrary) classification of the three core concepts of physical fitness. Numerous studies use outcome measurements that entail multiple components of physical fitness, as such, the choice of how to define muscle strength, muscle endurance and cardiopulmonary endurance can be arbitrary, and operationalization of these terms can form a source of conflict.

Noteworthy, all of the included studies applied AtDCS. Eight studies (23%) used CtDCS in addition to AtDCS. This disbalance is most likely attributable to the hypothesis that AtDCS counteracts reduced motor neuron excitability associated with physical exercise performance (Machado et al., 2019;Taylor et al., 2016;Taylor and Gandevia 2008). In line with this hypothesis, CtDCS, which decreases neuronal excitability in most instances (Das et al., 2016), would yield negative results on physical exercise performance. The current results seem to corroborate this hypothesis, as all the CtDCS studies either yielded no significant results (Alix-Fages et al., 2020;Angius et al., 2018;Baldari et al., 2018;Holgado et al., 2019;Lampropoulou and Nowicky 2013;Vitor-Costa et al., 2015) or negative results (Giboin and Gruber 2018;Lattari et al., 2018b) on the included (core) components of physical fitness.

Online tDCS yielded the greatest results in the context of muscle endurance and strength. The effect of online tDCS on cardiopulmonary endurance remain uninvestigated, most likely due to methodological considerations (i.e., excessive body movements present during whole body exercise hinder online tDCS). Two studies directly compared online tDCS to offline tDCS (Giboin and Gruber 2018;Washabaugh et al., 2016). Giboin et al. (2018) concluded that both AtDCS and CtDCS yielded detrimental effects on muscle strength, with this detrimental effect being more pronounced during online tDCS. In contrast, Washabaugh et al. (2016) concluded that online tDCS yielded greater knee extension strength improvements. Moreover, they found that this improvement was not present in the knee flexors, which were not trained during tDCS. In contrast to the field of motor learning (Ziemann and Siebner 2008), the rationale underlying the effectiveness of online tDCS remains unaddressed by the field.

No clear demarcated effect of tDCS duration seemed to be present (Table 4). Concerning muscle strength and -endurance, a duration of ≤15 and 20 minutes of tDCS yielded similar results (Table 4). In the context of cardiopulmonary endurance, 100% of the studies applying tDCS for 30 minutes yielded positive results. Nevertheless, this group only consisted of one study and therefore, this finding warrants careful interpretation. Both for current- and charge density, over all three core components of physical fitness, no clear relationship between tDCS effectiveness and tDCS dose seemed to be present. This was not in line with our initial hypothesis, and contrasts previous meta-analyses focusing on different clinical populations (i.e., stroke survivors) and motor function (Chhatbar et al., 2016;Van Hoornweder et al., 2021). A possible explanation for this unexpected result might be that the current study population was too variable. In addition, a meta-regression analysis or the use of electric field modelling might be better-suited to investigate the relationship between tDCS dose and tDCS effect (Chhatbar et al., 2016;Wischnewski et al., 2021).

Studies aiming to increase muscle strength mainly targeted M1, with 4 studies finding positive results, 4 studies finding non-significant results, and 2 studies reporting negative effects. Due to these variable results, it remains impossible to conclude whether tDCS over M1 yields positive results on muscle strength. Concerning both muscle- and cardiopulmonary endurance, stimulation over M1 (n=7 and n=4 respectively) or DLPFC (n=4 and n=2 respectively) seemed to be most effective (respectively 70% & 75%, and 57% & 60% of the studies reported a positive effect on respectively muscle endurance and cardiopulmonary endurance). As aforementioned, stimulation over M1 is hypothesized to predominantly counteract reduced motor neuron excitability associated with physical exercise performance (Machado et al., 2019;Taylor et al., 2016;Taylor and Gandevia 2008). Concerning tDCS over DLPFC, two hypotheses can be identified. First, research has demonstrated that activity in the prefrontal cortex increases due to fatigue-induced activity decrease in M1 (Berchicci et al., 2013;Menotti et al., 2014). As such, AtDCS might potentially support increased prefrontal cortex activity. Second, AtDCS over DLPFC has previously demonstrated the ability to alleviate pain affect (Boggio et al., 2008;Byrne and Flood 2019;Maeoka et al., 2012). As such, AtDCS during physical task performance might be capable of diminishing sensations of muscle exertion (Oki et al., 2016).

4.1. Limitations and future directions

The interpretability of the current systematic review suffers from several limitations.

First, between-study heterogeneity was large. Various age groups were included, ranging from younger (mean age of 20 years) to older (mean age of 85 years) adults. As research indicates that the excitatory effect of AtDCS diminishes as a result of ageing (Ghasemian-Shirvan et al., 2020), this might form a source of between-study variability. Nevertheless, only two studies included participants of 65 years and older and even these two studies reported contrasting results (Oki et al., 2019;Oki et al., 2016). As such, it seems likely that other factors contribute to the large between-study variability. Indeed, participants also differed in regard to activity level. Moreover, experimental protocols (i.e., electrode placement, investigated muscle group, wash-out period, outcome measure, tDCS dose-related parameters) also varied across studies. Another, non-mutually exclusive, explanation for the substantial between-study heterogeneity might be related to tDCS itself. As tDCS induces significantly different electric fields in participants as a result of differences in head anatomy and tissue conductivity, and electric field strength is a key physical agent of tDCS, using tDCS at a fixed, non-personalized, stimulation intensity likely also strongly contributes to the observed variability across studies (10.1038/s41598-018-37226-x, 10.1016/j.neuroimage.2018.12.053, 10.1016/j.brs.2022.07.049). A potential solution for this might be dose-controlled tDCS, although factors such as requiring the magnetic resonance imaging scans of the entire population currently limit feasibility of this approach (10.1016/j.brs.2019.10.004, 10.1016/j.brs.2020.04.007). Notably, variable tDCS induced electric fields become even more important in the context of stimulating the cortical representation of the leg muscles, which lie deeper in the cortex than the upper limb muscle representations. In participants where tDCS only induces a weak electric field, the electric field strength that reaches the leg muscle representations might be too low to elicit neuromodulatory effects.

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Second, conducting a meta-analysis was unwarranted, as the included studies encompassed a wide array of outcome measures. While these outcome measures could, in theory, be bundled via standardized effect measures, the lack of knowledge concerning the degree of correlation or similarity in responsiveness across outcome measures, poses an insurmountable barrier that would likely lead to biased meta-analyses (Puhan et al., 2006). Furthermore, even studies using similar outcome measures often used different testing procedures (e.g., body weight exercise vs. open-chain weightlifting vs. closed-chain weightlifting), which hindered the creation of a single, unbiased outcome measure. Therefore, to advance the field, it is of critical importance that future work uses more comparable task designs and outcome measures, basing itself on previous literature. By doing so, meta-(regression) analyses will become possible, and our understanding of tDCS and its impact on physical performance will incrementally advance.

Third, it was not possible to take the interaction between the different outcome variables into account. As a consequence, interaction-effects may have been missed.

Fourth and finally, the sample size of the included studies was rather small, ranging from 6 up to maximally 36 participants. As tDCS demonstrates intra-individual variability, with responders and non-responders (López-Alonso et al., 2015), future studies should strive for greater sample sizes, counteracting the inherent variability of tDCS. It might also be worthwhile to differentiate between responders and non-responders through the application of transcranial magnetic stimulation (Nejadgholi et al., 2015).

Given the variable results reported in this systematic review, it is clear that more research is required, especially in larger sample sizes. Moreover, given the potential of tDCS, specifically on muscle endurance, further insight into the different tDCS parameters (i.e.., type, timing, duration, current/charge densities and brain region) is essential to fully unravel the potential of tDCS as an ergogenic aid. In this regard, future work should better address the neural effects of tDCS during performance of physical fitness related activities. Also, it may be worthwhile to further explore the potential of high-density tDCS, given that evidence indicates that scalp-applied currents should exceed 4–6 mA to achieve 1 mV/mm voltage gradient in postmortem brain tissue and that even higher currents may be needed in vivo (Vöröslakos et al., 2018). However, an important side note regarding this is that higher current intensities are associated with a higher risk of skin burns, phosphenes, and other side effects (Bikson et al., 2009;Vöröslakos et al., 2018). Finally, given our inconclusive results of tDCS in healthy populations, it seems interesting to further explore the potentially greater benefits of tDCS in several disabled populations. Based on our results, it may be worthwhile to further examine the potential of tDCS in patients with an affected muscle endurance performance such as postsurgery patients (for example in case of extended immobilization), COPD (Gea et al., 2013) or heart failure patients (Philippou et al., 2020). As this population suffers from decreased physical fitness, there might be more room for tDCS-induced improvements.

In this context, to gain a more thorough understanding of the potential of tDCS, it is of utmost importance to focus more on the theoretical principles of tDCS, (a) hereby comparing and analyzing different tDCS protocols, and (b) monitoring brain activity to better understand the neurophysiological principles of tDCS in the context of physical fitness.

5. Conclusion

Overall, tDCS in the context of physical fitness seems to be most suited to improve muscle endurance. However, given the current heterogeneous results, future studies should focus on further unraveling the ergogenic effect of anodal tDCS on physical fitness in general and, more specifically, on muscle endurance. In the same vein, future research should, when constructing their study design, be attentive to previous studies to improve between-study comparability.

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Author contribution:

Nastasia Marinus and Sybren Van Hoornweder performed data interpretation, and drafted and revised the article. Marthe Aarts and Jessie Vanbilsen carried out data extraction. Dominique Hansen and Raf Meesen critically revised the article and conceptualized the idea.

Ethics approval

This is a systematic review. No ethical approval is required.

Declarations

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Figure captions

Fig. 1 Overview of data extraction. Regarding Time To Exhaustion (TTE) and Rating of Perceived Exertion (RPE), the nature of the experimental protocol was used to determine whether the outcome variable related to muscle strength, muscle endurance or cardiopulmonary endurance. FI = fatigue index; HR = heart rate; MVC = maximum voluntary contraction; RER = respiratory exchange ratio; RM = repetition maximum; SEI = strength endurance index; tDCS = transcranial direct current stimulation; TI = torque integral; VE = expiratory volume; VO2 = peak oxygen consumption; VT = ventilatory threshold.

Fig. 2 Flow diagram of the study selection procedure

Tables

Table 1 Search terms with Boolean operators

PICO	Search terms	Hits
Participants	Healthy individuals OR Humans OR Individuals	
Intervention	tDCS OR transcranial direct current stimulation OR direct current stimulation	
Comparison	Sham-tDCS OR placebo-tDCs	
Outcomes	Exercise capacity OR Peak oxygen uptake OR Endurance OR Fatigue OR Rate of perceived exertion OR Perception of effort OR exercise tolerance OR Muscle strength	
Participants AND Intervention AND Comparison AND Outcomes		Pubmed: 45 WoS: 404

Last search: 27/08/2021

Table 2 Quality assessment of the included studies based on the PEDro scale (n=35)

		PEDro items											
		1	2	3	4	5	6	7	8	9	10	11	/10
Study	Abdelmoula et al. (2016)	✖	✖	✖	✓	✓	✖	✖	✖	✖	✓	✓	4
	Alix-Fages et al. (2020)	✖	✓	✓	✓	✓	✖	✓	✖	✖	✓	✓	7
	Angius et al. (2015)	✖	✓	✓	✓	✓	✖	✖	✓	✓	✓	✓	8
	Angius et al. (2016)	✖	✓	✖	✓	✓	✖	✖	✖	✖	✓	✓	5
	Angius et al. (2018)	✓	✓	✓	✓	✓	✖	✓	✓	✓	✓	✓	9
	Angius et al. (2019)	✖	✓	✓	✓	✖	✖	✖	✓	✓	✓	✓	7
	Baldari et al. (2018)	✓	✓	✓	✖	✓	✖	✖	✓	✓	✓	✓	7
	Barwood et al. (2016)	✖	✓	✓	✓	✓	✖	✖	✖	✖	✓	✓	6
	Byrne and Flood (2019)	✓	✓	✖	✓	✓	✖	✖	✖	✖	✓	✓	5

Ciccone et al. (2019)	✓	✓	✖	✖	✓	✖	✖	✖	✖	✓	✓	4
Esteves et al. (2019)	✓	✓	✖	✓	✓	✖	✖	✖	✖	✓	✓	5
Frazer et al. (2017)	✖	✓	✖	✓	✓	✓	✖	✖	✖	✓	✓	6
Giboin and Gruber (2018)	✓	✓	✖	✖	✓	✖	✓	✖	✖	✓	✓	5
Hazime et al. (2017)	✓	✓	✓	✓	✓	✖	✓	✖	✖	✓	✓	7
Holgado et al. (2019)	✓	✓	✖	✓	✓	✖	✖	✖	✖	✓	✓	5
Kamali et al. (2019)	✓	✓	✓	✖	✓	✖	✓	✖	✖	✓	✓	6
Lampropoulou and Nowicky (2013)	✖	✓	✖	✓	✓	✖	✓	✖	✓	✓	✓	7
Lattari et al. (2018a)	✓	✓	✖	✓	✓	✖	✓	✖	✖	✓	✓	6
Lattari et al. (2018b)	✓	✓	✓	✓	✓	✖	✖	✓	✓	✓	✓	8
Montenegro et al. (2015)	✓	✓	✖	✖	✓	✓	✓	✖	✖	✓	✓	6
Muthalib et al. (2013)	✖	✓	✖	✓	✖	✖	✖	✖	✖	✓	✓	4
Oki et al. (2016)	✓	✓	✖	✖	✓	✖	✓	✓	✓	✓	✓	7
Oki et al. (2019)	✓	✓	✖	✓	✓	✖	✓	✖	✖	✓	✓	6
Park et al. (2019)	✖	✓	✖	✖	✓	✖	✖	✖	✖	✓	✓	4
Valenzuela et al. (2018)	✓	✖	✖	✓	✓	✖	✓	✖	✖	✓	✓	5
Vargas et al. (2018)	✓	✓	✓	✓	✓	✖	✓	✓	✓	✓	✓	9
Vieira et al. (2020)	✓	✓	✖	✓	✓	✖	✖	✓	✓	✓	✓	7
Vitor-Costa et al. (2015)	✓	✓	✓	✓	✖	✖	✖	✓	✓	✓	✓	7
Washabaugh et al. (2016)	✓	✓	✖	✓	✖	✖	✖	✖	✖	✓	✓	4

Williams et al. (2013)	✓	✓	✖	✓	✓	✖	✓	✖	✖	✓	✓	6
Workman et al. (2020a)	✓	✓	✖	✖	✓	✖	✓	✓	✓	✓	✓	7
Workman et al. (2020b)	✓	✓	✖	✓	✓	✖	✓	✓	✓	✓	✓	8
Workman et al. (2020d)	✓	✓	✖	✓	✓	✖	✖	✖	✓	✓	✓	6
Workman et al. (2020c)	✓	✓	✖	✓	✓	✖	✖	✓	✓	✓	✓	7
Wrightson et al. (2020)	✓	✓	✓	✖	✓	✓	✓	✓	✓	✓	✓	9

When a criterion was not explicitly addressed, it was scored as ‘No’. ✓ = fulfilled, ✖ = not fulfilled, 1 = Eligibility criteria specified, 2 = Randomization, 3 = Concealed allocation, 4 = Baseline characteristics, 5 = Blinding subjects, 6 = Blinding therapists, 7 = Blinding researchers, 8 = >85% Follow-up, 9 = Intention-to-treat analysis, 10 = between group comparisons, 11 = Point measures and variability measures.

Table 3 Baseline characteristics of the included studies

Study	N (♂)	Characteristics	Age (years)	Height (cm)	Weight (kg)
Abdelmoula et al. (2016)	11 (8)	Healthy subjects	25.0 ± 1.8	/	/
Alix-Fages et al. (2020)	14 (14)	Recreationally active resistance trained subjects	22.8 ± 3.0	180.0 ± 5.7	81.7 ± 6.7
Angius et al. (2015)	9 (9)	Recreationally active subjects	23.0 ± 4.0	179.7 ± 8.2	75.4 ± 9.9
	7 (7)	Recreationally active subjects	23.0 ± 4.0	179.7 ± 6.8	75.1 ± 9.9
Angius et al. (2016)	9 (9)	Recreationally active subjects	23.0 ± 2.0	179.0 ± 7.0	76.0 ± 9.0
Angius et al. (2019)	12 (9)	Recreationally active subjects	23.0 ± 3.0	179.0 ± 10.0	74.9 ± 16.5
Angius et al. (2018)	12 (8)	Recreationally active subjects	24.0 ± 5.0	175.0 ± 12.0	74.0 ± 17.0
Baldari et al. (2018)	13 (13)	Recreational endurance runners	27.0 ± 5.0	176.0 ± 7.0	70.0 ± 7.0
Barwood et al. (2016)	6 (6)	Regularly exercised subjects	21.0 ± 2.0	185.0 ± 6.0	80.3 ± 10.4
Byrne and Flood (2019)	23 (11)	Healthy pain-free subjects	26.0 ± 5.0	174.8 ± 9.0	76.4 ± 15.0
Ciccone et al. (2019)	20 (10)	Recreationally active subjects	21.0 ± 1.5	173.6 ± 11.8	71.2 ± 14.2
Esteves et al. (2019)	11 (11)	Recreational cyclists	26.8 ± 4.6	/	78.9 ± 7.1

Frazer et al. (2017)	13 (8)	Right-handed subjects	18-35	/	/
Giboin and Gruber (2018)	14 (14)	Healthy subjects	26.0 ± 3.0	182.0 ± 6.0	80.0 ± 6.0
Hazime et al. (2017)	8 (0)	Handball players	19.7 ± 2.3	166.0 ± 50.0	64.9 ± 7.9
Holgado et al. (2019)	36 (36)	Trained cyclists and triathletes	27.0 ± 6.8	/	70.1 ± 9.5
Kamali et al. (2019)	12 (12)	Experienced bodybuilders	25.6 ± 6.0	/	60 – 120
Lampropoulou and Nowicky (2013)	12 (4)	Active, right-handed subjects	32.0 ± 6.0	/	/
Lattari et al. (2018a)	11 (0)	Physically active subjects	24.0 ± 2.2	175.0 ± 5.9	75.4 ± 6.1
Lattari et al. (2018b)	15 (?)	Subjects with advanced expertise in strength training	24.5 ± 3.3	163.7 ± 6.7	62.6 ± 7.7
Montenegro et al. (2015)	14 (14)	Healthy, right-handed subjects	26.0 ± 4.0	177.1 ± 6.0	77.8 ± 17.9
Muthalib et al. (2013)	15 (15)	Healthy subjects	27.7 ± 8.4	176.4 ± 7.4	72.7 ± 8.7
Oki et al. (2016)	13 (5)	Subjects who did not perform resistance training in min. three months	68.3 ± 2.0	165.0 ± 3.0	74.5 ± 3.0
Oki et al. (2019)	11 (4)	Right-handed community-dwelling subjects	85.8 ± 4.3	161.1 ± 15.1	66.4 ± 17.6
Park et al. (2019)	12 (12)	Trained subjects	27.4 ± 2.4	174.1 ± 3.6	71.5 ± 7.5
Valenzuela et al. (2018)	8 (8)	Elite triathletes	20.0 ± 2.0	/	/
Vargas et al. (2018)	20 (0)	Soccer players	16.2 ± 0.9	167.0 ± 8.0	59.8 ± 9.0
Vieira et al. (2020)	11 (11)	Intermediately resistance-trained subjects	25.5 ± 4.4	180.4 ± 5.2	81.8 ± 7.6
Vitor-Costa et al. (2015)	11 (11)	Physically active subjects	26.0 ± 4.0	177.0 ± 3.0	77.0 ± 15.0
Washabaugh et al. (2016)	22 (15)	Right-leg dominant subjects	22.8 ± 5.7	/	/
Williams et al. (2013)	18 (9)	Right-handed subjects	25.0 ± 6.0	/	/
Workman et al. (2020a)	27 (11)	Right-dominant, recreationally active subjects	24.8 ± 3.3	169.2 ± 10.5	72.1 ± 13.4

Workman et al. (2020b)	20 (10)	Right-dominant, recreationally active subjects	24.6 ± 3.8	171.1 ± 11.1	71.7 ± 14.0
Workman et al. (2020c)	16 (7)	Right-dominant, recreationally active subjects	24.5 ± 3.8	170.0 ± 11.7	71.1 ± 14.4
Workman et al. (2020d)	34 (12)	Right-dominant, recreationally active subjects	24.0 ± 3.6	169.2 ± 9.9	71.2 ± 13.3
Wrightson et al. (2020)	20 (11)	Active subjects	23.8 + 4.7	168.2 ± 6.8	64.8 ± 9.8

Table 4 Data extraction

Study	Physical fitness modality	Length (min) & timing & type	tDCS placement	Current (mA) - density (mA/cm²)	Charge (C) - density (C/cm²)	Protocol	Findings (tDCS vs. sham)
Abdelmoula et al. (2016)	ME	10 Offline AtDCS	A: HS R biceps brachii C: R shoulder	1.5 - 0.043	0.9 - 0.026	Isometric TTE at 35% MVC torque with R elbow flexor before and after AtDCS/Sham	• Less ↓ in TTE during contraction after AtDCS vs. sham • RPE: NSD
Alix-Fages et al. (2020)	MS & ME	15 Online AtDCS & CtDCS	AtDCS) A: L DLPFC C: R OFC CtDCS) vice versa	2 - 0.035	1.8 - 0.031	Performance of 1RM bench press and sets of 5 reps at 75% 1RM with 1-minute inter-set rest until failure	• AtDCS: ↑ reps, less ↓ in movement velocity across sets, ↓ RPE • CtDCS: NSD (RPE, reps) • 1 RM: NSD
Angius et al. (2015)	CPE	10 Offline AtDCS	A: L M1 C: R DLPFC	2 - 0.167	1.2 - 0.1	Cycling TTE at 70% W_{max} at min. 60 rpm	• TTE & RPE: NSD
Angius et al. (2016)	ME & CPE	10 Offline AtDCS	Cephalic tDCS) A: L M1, C: R DLPFC Extracephalic tDCS) A: L M1, C: R shoulder	2 - 0.167	1.2 - 0.1	Isometric TTE of R knee extensors at 20% MVIC	• Cephalic tDCS: NSD (TTE, RPE, HR) • Extracephalic tDCS: ↑ TTE, ↓RPE • HR: NSD
Angius et al. (2018)	CPE	10 Offline AtDCS & CtDCS	AtDCS) A1 & A2: L & R M1 C1 & C2: L & R shoulder CtDCS) vice versa	2 - 0.057	1.2 - 0.034	Cycling TTE at 70% W_{peak} at min. 60 rpm	• AtDCS: ↑ TTE, ↓ RPE • CtDCS: NSD • HR: NSD

Angius et al. (2019)	CPE	30 Offline AtDCS	A: L DLPFC, C: R SOA	2 - 0.057	3.6 - 0.103	Cycling TTE at 70% W_{peak} at min. 60 rpm	• ↓ RPE & HR • ↑ TTE
Baldari et al. (2018)	CPE	20 Offline AtDCS & CtDCS	AtDCS) A: L & R M1 (leg area) C: occipital protuberance CtDCS) vice versa	2 - 0.056	2.4 - 0.067	TTE during incremental treadmill ramp exercise, 1% gradient	• TTE, Vpeak, HR & VO2peak: NSD
Barwood et al. (2016)	CPE & MS	20 Offline AtDCS	A: L TC C: R SOA	1.5 - 0.429	1.8 - 0.514	20km cycling time trial	• MPO, HR & RPE: NSD
Byrne et al. (2019)	ME	20 Offline AtDCS	A: L DLPFC C: R SOA	2 - 0.057	2.4 - 0.069	Isometric TTE of D knee extensors at 25% MVIC	• TTE: NSD
Ciccone et al. (2019)	ME & MS	30 Online AtDCS	AtDCS 1) A: L TC C: R SOA AtDCS 2) A: R TC C: L SOA	2 - 0.08	3.6 - 0.144	50 isokinetic reps of R knee extensors at 180°/sec	• FI & mean TI: NSD
Esteves et al. (2019)	CPE & MS	20 Offline AtDCS	A: L TC, C: R SOA	2 - 0.057	2.4 - 0.069	Four Wingate trials: 4 x 30s cycling trial at highest speed	• MPO, FI & RPE: NSD
Frazer et al. (2017)	MS	20 Offline AtDCS	A: HS L biceps brachi C: L SOA	2 - 0.035	2.4 - 0.096	1RM of L & R biceps brachii with dumbbell, training of R biceps brachii (4 sets of 6-8 reps) after tDCS/sham stimulation	• ↑ 1RM in L biceps brachii
Giboin and Gruber (2018)	MS	10 Online & Offline AtDCS &	AtDCS) A: HS R vastus lateralis, C: contralateral orbit	2 - 0.08	1.2 - 0.034	35 x 5 sec. MVIC of knee extensors	• Online AtDCS & CtDCS: ↓ MVIC amplitude throughout 35 reps

		CtDCS	CtDCS) vice versa				• Offline AtDCS: ↓ MVIC amplitude throughout 35 reps • Online & Offline: non-fatigued MVIC: NSD
Hazime et al. (2017)	MS	20 Online AtDCS	A: M1 (ND side) C: SOA (D side)	2 - 0.057	2.4 - 0.069	MVIC of D shoulder endo- & exorotators	• ↑ MVIC endorotators during AtDCS & 60 min. post AtDCS • ↑ MVIC exorotators during AtDCS & 30- & 60-min. post AtDCS • MVIC endorotators 30 min post AtDCS: NSD
Holgado et al. (2019)	CPE & MS	20 Offline AtDCS & CtDCS	AtDCS) A: L DLPFC C: R shoulder CtDCS) vice versa	2 - 0.08	2.4 - 0.096	Average W during 20 min self-paced cycling time trial	• MPO, HR & RPE: NSD
Kamali et al. (2019)	MS & ME & CPE	13 Offline AtDCS	A1: L & R M1 leg area C1: R shoulder A2: L TC C2: L shoulder	C1: 2 - 0.057 C2: 2 - 0.125	C1: 1.56 - 0.045 C2: 1.56 - 0.096	Isotonic 1RM during knee extension task, max. number of reps at 30% 1RM	• AtDCS: ↑ 1RM & SEI • ↓ RPE & HR (during endurance task)
Lampropoulou and Nowicky (2013)	MS	10 Offline AtDCS & CtDCS	A/C: HS R elbow flexors C/A: L shoulder	1.5 - 0.083	0.9 - 0.037	MVIC of R elbow flexors, 15min blocks of 3 trials (3-5sec) of 30, 50, 70 or 100% MVIC with 30sec rest periods (non-fatiguing bouts)	• RPE: NSD at 5, 25 & 45min post tDCS • MVIC: NSD
Lattari et al. (2018a)	CPE	20 Offline AtDCS	A: L DLPFC C: R SOA	2 - 0.057	2.4 - 0.069	Cycling TTE at 100% W_{peak} at min. 60 rpm	• ↑ TTE • RPE: NSD

Lattari et al. (2018b)	ME	20 Offline AtDCS & CtDCS	A/C: L DLPFC C/A: R OFC	2 - 0.057	2.4 - 0.069	Total amount of reps at 10RM load on leg press	• AtDCS: ↑ reps • CtDCS: ↑ RPE
Montenegro et al. (2015)	MS & ME	20 Offline AtDCS	A: L M1 C: R SOA	2 - 0.057	2.4 - 0.069	3 sets of 10 reps of isokinetic concentric force production of D knee flexors & extensors	• FI, mean torque, total work per set: NSD
Muthalib et al. (2013)	ME	10 Offline AtDCS	A: R M1 C: R shoulder	2 - 0.083	1.2 - 0.05	Isometric TTE at 30% MVIC L elbow flexors	• TTE, TI: NSD
Oki et al. (2016)	ME	20 Online AtDCS	A: HS Biceps Brachii C: L SOA	1.5 - 0.043	1.8 - 0.051	Isometric TTE at 20% MVIC biceps brachii	• ↑ TTE • ↓ RPE
Oki et al. (2019)	MS	20 Offline AtDCS	A: HS L biceps brachii C: L SOA	1.5 - 0.043	1.8 - 0.051	MVIC of L elbow flexors	• MVIC: NSD
Park et al. (2019)	CPE	20 Offline AtDCS	A: vertex C: C5 & C6	1.98 - 0.071	2.27 - 0.081	Running TTE at speed equivalent to 80% of VO_{2max}	• ↑ TTE • RPE, HR, VE, RER, VT: NSD
Valenzuela et al. (2018)	CPE	20 Offline AtDCS	A: L M1 C: R SOA	2 - 0.08	2.4 - 0.096	800m freestyle swimming test	• ↑ vigor self-perception • Swimming time, FI: NSD
Vargas et al. (2018)	MS	20 Online AtDCS	A= M1 (ND side) C= SOA (D side)	2 - 0.057	2.4 - 0.069	ND & D knee extensors 5 MVIC of D & ND knee extensors (with 1 min rest)	• ↑ MVIC (D side) during tDCS & 30- & 60-min post tDCS • MVIC ND side: NSD
Vieira et al.	ME	20 Offline AtDCS	A: L DLPFC	2 - 0.057	2.4 - 0.069	Total amount of reps during 3 sets	• ↑ total reps & ↑ reps in 1st block

(2020)			C: R OFC			of back squats at 80% MVC load	• Reps in 2th and 3th block: NSD
Vitor-Costa et al. (2015)	CPE	13 Offline AtDCS & CtDCS	AtDCS) A: L & R M1 (leg area) C: occipital protuberance CtDCS) vice versa	2 - 0.056	1.56 - 0.043	Cycling at 80% W_{peak} at min. 60 rpm	• AtDCS: ↑ TTE • CtDCS: NSD • RPE, HR: NSD
Washabaugh et al. (2016)	MS	12 Online & Offline AtDCS	A: HS R knee extensor C: R SOA	2 - 0.057	1.44 - 0.041	MVIC of R & L knee flexors & extensors	• Online AtDCS (during extension MVIC): ↑ MVIC of extensors • Offline AtDCS: NSD
Williams et al. (2013)	ME	20 Online AtDCS	A: HS L Biceps Brachii C: L SOA	1.5 - 0.043	1.8 - 0.051	ND elbow flexors Isometric TTE of ND elbow flexors at 20% MVC, FI	• ↑ TTE and ↑ RPE & FI when tDCS duration exceeded TTE • TTE extending tDCS: NSD
Workman et al. (2020a)	MS	20 Online AtDCS	A: L M1 C: R SOA	2 - 0.057, 4 - 0.114	2.4 - 0.069, 4.8 - 0.137	Isokinetic fatigue task (40 reps, 120◦/sec) of D knee flexors & extensors	• 2mA tDCS: ↓ torque of D knee extensors • 4mA tDCS: NSD
Workman et al. (2020b)	ME	20 Online AtDCS	A: L M1 C: R SOA	2 - 0.057, 4 - 0.114	2.4 - 0.069, 4.8 - 0.137	Isokinetic fatigue task (40 reps, 120◦/sec) of D & ND knee flexors & extensors	• 4mA: ↑ R knee extensor fatigability in ♀ vs. ♂ • R knee flexors: NSD (results L flexors & extensors were not analyzed)
Workman et al. (2020c)	ME & MS	20 Online AtDCS	A: L M1 C: R SOA	2 - 0.057, 4 - 0.114	2.4 - 0.069, 4.8 - 0.137	Isokinetic fatigue task (40 reps, 120◦/sec) of D & ND knee flexors	• 2mA & 4mA: ↑ FI-torque & FI-work in R knee extensors (↑ fatigability)

							& extensors	- L knee extensors & L & R Knee flexors: NSD - Wtotal: NSD
Workman et al. (2020d)	ME	20	Online AtDCS	A: L M1 C: R SOA	4 - 0.114	4.8 - 0.137	Isokinetic fatigue task (40 reps, 120°/sec) of D knee flexors & extensors	- ↑ L knee flexor FI - R & L knee extensors, and R knee flexors: NSD
Wrightson et al. (2020)	ME	10	Offline AtDCS	A: HS R vastus lateralis C: L deltoid region	1 - 0.029, 2 - 0.029	0.6 - 0.017, 1.2 - 0.034	Isometric TTE of knee extensors at 20% MVIC	- 1mAtDCS: TTE & RPE: NSD - 2mA tDCS: TTE & RPE: NSD

Green, red and orange colors indicate a positive, negative, or and non-significant change respectively. A = anode; aMVC = amplitude of maximal voluntary contraction; AtDCS = anodal transcranial direct current stimulation; C = cathode; C = coulombs; cm = centimetres; CPE = cardiopulmonary endurance; CtDCS = cathodal transcranial direct current stimulation; D = dominant side; DLPFC = dorsolateral prefrontal cortex; FI = fatigue index; HR = heart rate; HS = hotspot; L = left; M1 = primary motor cortex; mA = milli-ampere; ME = muscle endurance; MPO = Mean power output; MS = muscle strength; MVC = maximal voluntary contraction; MVIC = maximal voluntary isometric contraction; ND = non-dominant side; NSD = not significant difference; OFC = orbitofrontal cortex; R = right; reps = repetitions; RER = respiratory exchange ratio; RM = repetition maximum; RPE = rating of perceived exertion; sec = seconds; SEI = short-term endurance index; SOA = supra-orbital area; TC = temporal cortex; tDCS = transcranial direct current stimulation; TI = torque integral; TTE = time to exhaustion; TI = torque integral; VA = voluntary activation; VE = expiratory volume; VO2 = oxygen consumption; Vpeak = peak velocity; VT = Ventilatory threshold; Wpeak = maximal power output.

Table 5 Overview of number of studies reporting a positive, negative or non-significant impact on muscle strength (n=16), muscle endurance (n=16) and cardiopulmonary endurance (n=13) according to different tDCS characteristics

	Muscle strength			Muscle endurance			Cardiopulmonary endurance		
	+	-	NSD	+	-	NSD	+	-	NSD
tDCS type									
AtDCS	5 (31%)	2 (13%)	9 (56%)	11 (69%)	0	5 (31%)	7 (54%)	0	6 (46%)
CtDCS	0	1 (25%)	3 (75%)	0	0	1 (100%)	0	0	4 (100%)
tDCS timing									
Online tDCS	3 (38%)	2 (25%)	3 (38%)	6 (86%)	0	1 (14%)	0	0	0
Offline tDCS	4 (36%)	1 (9%)	6 (55%)	5 (56%)	0	4 (44%)	7 (54%)	0	6 (46%)
tDCS duration									
≤15 minutes	2 (40%)	1 (20%)	2 (40%)	4 (67%)	0	2 (33%)	4 (80%)	0	1 (20%)
20 minutes	3 (30%)	1 (10%)	6 (60%)	7 (78%)	0	2 (22%)	2 (29%)	0	5 (71%)
30 minutes	0	0	1 (100%)	0	0	1 (100%)	1 (100%)	0	0
Current density									
Low	1 (33%)	0	2 (67%)	4 (80%)	0	1 (20%)	0	0	0
Mild	4 (50%)	1 (13%)	3 (38%)	5 (71%)	0	2 (29%)	5 (71%)	0	2 (29%)
Moderate	0	1 (25%)	3 (75%)	0	0	2 (100%)	1 (33%)	0	2 (67%)
High	1 (25%)	1 (25%)	2 (50%)	5 (100%)	0	0	2 (50%)	0	2 (50%)
Charge density									
Low	2 (40%)	1 (20%)	2 (40%)	3 (75%)	0	1 (25%)	3 (100%)	0	0
Moderate	4 (40%)	1 (10%)	5 (50%)	7 (70%)	0	3 (30%)	3 (43%)	0	4 (57%)
High	0	1 (25%)	3 (75%)	4 (80%)	0	1 (20%)	2 (50%)	0	2 (50%)
Brain region									
M1/HS	4 (40%)	2 (20%)	4 (40%)	7 (70%)	0	3 (30%)	3 (50%)	0	3 (50%)
DLPFC	0	0	2 (100%)	3 (75%)	0	1 (25%)	2 (67%)	0	1 (33%)
TC	1 (25%)	0	3 (75%)	1 (50%)	0	1 (50%)	1 (33%)	0	2 (67%)
RPE	2 (33%)	0	4 (67%)	5 (63%)	1 (13%)	2 (25%)	2 (22%)	0	7 (78%)

Some studies investigated both online and offline tDCS and/or both anodal tDCS (AtDCS) and cathodal tDCS (CtDCS) or used two different current/charge densities. Therefore, some studies are mentioned twice in this table, once per protocol. Color scale accentuates the size of the percentage, relative to percentages of the same category (i.e., positive effect (+), negative effect (-) or non-significant difference (NSD)), with harsher colors being linked to higher percentages. DLPFC = dorsolateral prefrontal cortex; HS = hotspot; M1 = left motor cortex; NSD = non-significant difference; RPE = ratings of perceived exertion; TC = temporal cortex; tDCS = transcranial direct current stimulation.