TRANSCRANIAL DIRECT-CURRENT STIMULATION IN COMBINATION WITH EXERCISE: A SYSTEMATIC REVIEW

REVIEW ARTICLE
ARTIGO DE REVISÃO
ARTÍCULO DE REVISIÓN

ESTIMULAÇÃO TRANSCRANIANA POR CORRENTE CONTÍNUA EM COMBINAÇÃO COM O EXERCÍCIO: UMA REVISÃO SISTEMÁTICA

ESTIMULACIÓN TRANSCRANEANA POR CORRIENTE CONTINUA EN COMBINACIÓN CON EL EJERCICIO: UNA REVISIÓN SISTEMÁTICA

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ABSTRACT

Introduction: Transcranial direct-current stimulation (tDCS) is a noninvasive technique that allows the modulation of cortical excitability and can produce changes in neuronal plasticity. The application of tDCS has recently been associated with physical activity. Objectives: To verify the effect of Transcranial Direct-Current Stimulation (tDCS) in combination with physical exercise, characterizing methodological aspects of the technique. Methods: In the database search, studies with animals, other neuromodulation techniques and opinion and review articles were excluded. Publications up to 2016 were selected and the methodological quality of the articles was verified through the PEDro scale. Results: The majority of studies (86%) used tDCS on the motor cortex area, with anodal current and the allocation of monocephalic electrodes (46.5%). The prevalent current intensity was 2mA (72%), with duration of 20min (55.8%). The profile of the research participants was predominantly of subjects aged up to 60 years (72.1%). The outcomes were favorable for the use of anodal tDCS in combination with physical exercise. Conclusion: Transcranial Direct-Current Stimulation is a promising technique when used in combination with aerobic and anaerobic exercises; however, it is necessary to investigate concurrent exercise. ***Level of Evidence II; Therapeutic Studies Investigating the Results of Treatment (systematic review of Level II studies or Level I studies with inconsistent results).***

Keywords: Electrical stimulation; Transcranial direct current stimulation; Physical activity.

RESUMO

Introdução: A estimulação transcraniana por corrente contínua (ETCC) é uma técnica não invasiva que permite a modulação da excitabilidade cortical e pode produzir alterações na plasticidade neuronal. A aplicação da ETCC tem sido recentemente associada à atividade física. Objetivos: Verificar o efeito da Estimulação Transcraniana por Corrente Contínua (ETCC) em combinação com o exercício físico, caracterizando os aspectos metodológicos da técnica. Métodos: Na busca em base de dados, excluíram-se estudos com animais e outras técnicas de neuromodulação, além de artigos de revisão e opinião. Foram selecionadas publicações até 2016 e a qualidade metodológica dos artigos foi verificada através da escala PEDRo. Resultados: A maioria dos estudos (86%) utilizou a ETCC na área do córtex motor, com corrente anódica e montagem monocefálica (unipolar) (46,5%). A intensidade da corrente dominante foi 2mA (72%) com duração de 20 min (55,8%). O perfil dos participantes da pesquisa foi predominantemente de indivíduos com até 60 anos de idade (72,1%). Os desfechos foram favoráveis ao uso da ETCC anódica em combinação com o exercício físico. Conclusão: A Estimulação Transcraniana por Corrente Contínua é uma técnica promissora quando utilizada em combinação com os os exercícios aeróbicos e anaeróbicos; entretanto, é necessário investigar o exercício concomitante. **Nível de evidência II; Estudos terapêuticos investigando os resultados do tratamento (revisão sistemática dos estudos de nível II ou estudos de nível I com resultados inconsistentes).**

Descritores: *Estimulação Elétrica; Estimulação transcraniana por corrente contínua; Exercício físico.*

RESUMEN

Introducción: La estimulación transcraneana por corriente continua (ETCC) es una técnica no invasiva que permite la modulación de la excitabilidad cortical y puede producir alteraciones en la plasticidad neuronal. La aplicación de la ETCC ha sido recientemente asociada a la actividad física. Objetivos: Verificar el efecto de la Estimulación Transcraneana por Corriente Continua (ETCC) en combinación con el ejercicio físico, caracterizando los aspectos metodológicos de la técnica. Métodos: En la búsqueda en base de datos, se excluyeron estudios con animales y otras técnicas de neuromodulación, además de artículos de revisión y opinión. Fueron seleccionadas publicaciones hasta 2016 y la calidad metodológica de los artículos fue verificada a través de la escala PEDRo. Resultados: La mayoría de los estudios (86%) utilizó la ETCC en el área del córtex motor, con corriente anódica y montaje monocefálico (unipolar) (46,5%). La intensidad de la corriente dominante fue 2mA (72%) con duración de 20 min (55,8%). El perfil de los participantes de la investigación fue predominantemente de individuos con hasta 60 años de edad (72,1%). Los desenlaces fueron favorables al uso de la ETCC anódica en combinación con el ejercicio físico. Conclusión: La Estimulación Transcraneana *por Corriente Continua es una técnica alentadora cuando utilizada en combinación con los ejercicios aeróbicos y anaeróbicos; entretanto, es necesario investigar el ejercicio concomitante.* ***Nivel de evidencia II; Estudios terapéuticos investigando los resultados del tratamiento (revisión sistemática de los estudios de nivel II o estudios de nivel I con resultados inconsistentes).***

Descriptores: *Estimulación eléctrica; Estimulación transcraneal de corriente directa; Ejercicio físico.*

DOI: http://dx.doi.org/10.1590/1517-869220192506215836 Article received on 10/26/2018 accepted on 04/22/2019

INTRODUCTION

Transcranial direct-current stimulation (tDCS) is a noninvasive technique that allows the modulation of cortical excitability and can produce changes in neuronal plasticity. Through an electric current with a low amperage, positive (anodal) polarity increases cortical excitability and negative (cathodal) decreases it.[1,2] Basically, the application of tDCS is performed using two silicone electrodes, 5cmx7cm in size, surrounded by a sponge soaked in saline solution and a device that provides low amperage current (0.4-2.0mA) continuously (3-20min).[3]

Regarding electrode positioning, one possibility is the bi-cephalic montage, in which an anodal[4] or cathodal current electrode[4] is positioned over a cerebral region (for example, over the area of the motor cortex) and the other, called the 'reference', is positioned over another cerebral region (example, over the prefrontal cortex). In the uni-cephalic montage, an electrode with anodal or cathodal current stimulates a certain brain region, while the other electrode is placed over an extracephalic region.[5] In the bi-hemispherical technique,[6] the two electrodes stimulate the same brain region, however, in antagonistic positions, that is, one electrode can be located on the left temporal cortex and another on the right temporal cortex.

To define the brain region to be stimulated is also something that lacks agreement in the scientific literature. This is because there are several brain areas that can exert control over a particular physiological or motor reaction as a result of physical exercise. It is hypothesized, then, that the excitatory or inhibitory action of the tDCS may be in part related to the brain region stimulated and the type of physical exercise proposed.[7-10] The intensity of the current also seems to influence the study results, with intensities of 1.0mA,[11] 1.5mA,[12] and 2.0mA[13] possibly presenting different results. The time of exposure to the stimulation has also not been standardized, and may vary from 10 to 40 min.[14,15]

Exercise, in turn, when associated with tDCS, may present optimized performance with improved oxygen consumption,[16] in the case of aerobic exercises, and increased strength,[17] in the case of resistance exercises. Finally, the profile of individuals submitted to tDCS, such as young people and older adults, seems to influence the results: due to the anatofunctional alterations of the older adult brain,[18] allowing greater conduction when compared to a younger individuals.

This systematic review aimed to map the methodological aspects of tDCS associated with exercise. The following were considered as the variables of analysis, the type, time and intensity of the current tested, location of the cortex for current application, type of electrode montage, profile of individuals studied, type of physical exercise associated with the use of tDCS and the methodological design of the study.

METHOD

Initially, this review was registered on the PROSPERO database (International Prospective Register of Systematic Reviews),[19] under ID number=CRD42017060270, with the PRISMA recommendations followed.[20]

Search for material

The search for articles occurred in the MEDLINE, CAPES periodicals, Cochrane and SciELO databases. For the selection of key terms, the Medical Subject Headings (MeSH) list was consulted. The terms used to search, in Portuguese and English, were: Electric Cerebral Stimulation, Aerobic Exercise, tDCS, Transcranial direct-current stimulation, Exercise, Concurrent Training, Anaerobic Exercise. These terms were combined with the Boolean connectors OR between the synonyms and to establish the relationship between tDCS and exercise.

Inclusion criteria for the articles

The articles were included in the study when they presented, as an independent variable, tDCS associated with physical exercise, which could be aerobic, anaerobic or concurrent. As a dependent variable, physiological and/or biomechanical changes were considered as the effect of the physical exercise. Studies with animals and neuromodulation techniques other than tDCS and opinion and review articles were excluded.

Eligibility criteria

Articles in Portuguese or English published up to 9/22/2016. In order to select the articles of the search, the titles and abstracts were read, with the aim of analyzing whether the article met the inclusion and exclusion criteria, using the Skimming reading technique.[21] If, however, doubts remained about the need to include the article in this study, a full reading of the studies found was performed. In the process of searching for articles, there was no type of delimitation for the population studied. Also, all forms of tDCS application, types of physical training, duration of electrostimulation, current intensity and brain regions stimulated were accepted.

Analysis of the articles

The articles were submitted to a descriptive analysis, carried out by two researchers who evaluated the methodological quality of the articles through the PEDro scale.[22] Figure 1 shows the selection process of the articles.

The studies were summarized through descriptive statistics, with absolute and relative frequency of the items: study design, gender of the individuals investigated, mean age of the volunteers, tDCS techniques, brain areas stimulated, current intensity and duration of stimulation.

RESULTS

A total of 43 articles that met the inclusion criteria were retrieved. The first article was published in 2007 and the majority of the articles were published between 2013 and 2016.

Design of the studies

The majority of the studies were experimental (97.7%), with a cross-over design being the most used (61%), followed by a parallel design (37%), and one case report design (2%). Most of the experimental studies were double-blind (60%); with the tDCS being the blind experimental part in all the studies.

Area of stimulation, intensity, duration of the current

The majority of the studies aimed to use exercise as a potentiator of the tDCS in the motor cortex, thus, 86% of the studies used this area as a stimulation area; with the anodal current being the most used for this.

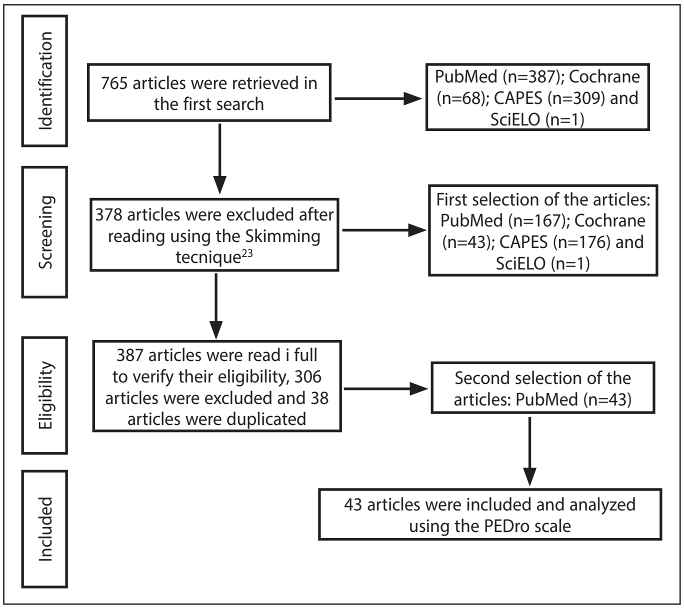

Figure 1. Stages of selection of the articles.

Regarding the intensity of the current, the majority of the studies applied 2mA (72%). The duration of the tDCS application was 20 minutes (55.8%) and 15 minutes (25.7%). Table 1 shows the methodological characterization of tDCS used in the studies analyzed.

Table 2 presents information related to authors, methodological classification through the PEDro scale, methods, year of publication, protocol and the main results of the studies analyzed.

DISCUSSION

This systematic review showed that there are a relatively high number of clinical studies on this topic (43 articles with a total of 909 subjects tested). Although the clinical methodology of the studies tested was evaluated with the PEDRo scale, these studies are still few and have heterogeneity in the outcomes and population studied. There were also few mechanistic studies.

As shown in Table 1, all the studies presented the clinical study method and were randomized, and of these, 7 presented more robust methods in the description of what was performed in the study. The fact that these studies were carried out in a double-blind manner minimized possible bias. However, a large number of studies were not performed in a randomized double-blind manner, which may have led to biases in the quantification of the results. This assumption is based on the need for double-blind randomized methodological control, as this is able to minimize biases with greater efficiency.[41] However, blinding is not always possible, as sometimes studies present techniques that are not automated, which makes the study blinding difficult. Thus, in these cases, the orientation for researchers is to minimize the possible influences of other techniques or treatments that may impact on the results[41] or to use more objective clinical outcomes.[49-51]

There are other methodological issues that need to be carefully observed regarding the use of tDCS and stimulation parameters. The first is related to the type of stimulation the individuals are to be submitted to, such as anodal, cathodal or bicephalic montage.[43] Some studies used parameters that have been studied little, such as temporal cortex stimulation. Montenegro et al.,[48] when stimulating the temporal cortex of athletes by anodal tDCS, expected to find a greater participation of the parasympathetic activity and a reduction of the sympathetic activity, thus modulating the heart rate. Based on this study, it would be possible to state that, in these situations, anodal tDCS also shows an efficient method to modulate the cardiorespiratory variables during physical exercise.

Table 1. Characterization of the tDCS in the 43 articles analyzed.

	Absolute Frequency	Relative frequency
Study design		
Randomized crossover	26	60,5%
Randomized parallel	16	37,2%
Case study	1	2,3%
Blinding of the study		
Double-blind (volunteers and evaluators)	26	60,5%
Blind (volunteers)	17	39,5%
Stimulation techniques		
Anodal and cathodal (bi-cephalic)	3	7,0%
Anodal and placebo (uni-cephalic)	20	46,5%
Cathodal and placebo (uni-cephalic)	2	4,7%
Anodal, cathodal or placebo (uni-cephalic)	7	16,3%
Anodal and cathodal (bi-cephalic) or Placebo	11	25,6%
Cerebral areas stimulated		
Motor córtex	37	86,0%
Prefrontal córtex	3	7,0%
Temporal córtex	2	4,7%
Ipsiolateral córtex	1	2,3%
Current intensity		
1mA	10	23,3%
1,5 mA	2	4,7%
2 mA	31	72,1%
Duration of stimulation		
10 minutes	5	11,6%
13 minutes	1	2,3%
15 minutes	11	25,6%
17 minutes	1	2,3%
20 minutes	24	55,8%
40 minutes	1	2,3%
Profile of the sample		
Gender		
Men	14	32,6%
Women	0	0,0%
Both	29	67,4%
Mean of the age group of the volunteers		
60 years or less	31	72,1%
60 years or more	7	16,3%
Both ages (more and less than 60 years)	5	11,6%

The use of cathodal stimulation had its beneficial effect diagnosed in the improvement of the motor control in people affected by stroke.[24] In this study, cathodal tDCS was used associated with muscular control of the elbow flexors in post-stroke subjects, classified as having a moderate level of impairment. The study showed that the subjects presented significant results in the increase of the control of the effort of the muscle group related to the brain region injured by the stroke.

In addition to these two forms of stimulation, the third way of stimulating the subjects was through bi-cephalic montage. This stimulation has been performed more in studies with hemiparetic post-stroke subjects. In this situation, the aim is to stimulate, by anodal current, the injured brain region, to excite a region that normally has diminished cortical activity. With the cathodal current, the focus is to decrease the excitability of the region opposite the lesion that may already be excited.[22, 11, 24]

Regarding the intensity and duration of the stimulations, the studies presented three types of stimulation, with a current of 2mA for 40, 20, 15 or 10 minutes,[17, 12, 8, 15, 4] with 1mA for 20, 15 and 10 minutes[16, 10, 27, 7] and with 1.5mA for 20 minutes.[14] Despite the discrepancies, Nitsche and Paulus[3] affirm that, after one hour of tDCS for 20 minutes at 2mA, it is possible to verify changes in cortical excitability. This may be the reason that the majority of the studies opted for this experimental schema.

Table 2. Authors, methodological quality, year of publication, study protocol, main results of articles analyzed.

Authors	Pedro scale	Year	Méthods	Main results
barwood et al.[23]	9	2016	The researchers conducted two independent studies and a third to evaluate the data of the subjective perception of effort in the combination of the two studies. In the two independent studies, anodal current and placebo of 2mA for 20 minutes was used, with the first study being associated with a 20 Km counter-clock cycling test, which 6 men completed. The second was performed with 8 men with a fixed intensity cycling test at 55% of maximum power and at thermal conditions of 33°C.	(anodal in the first study) Heart Rate ↔ Subjective perception of effort ↔ (anodal in the second study) Heart Rate ↔ Subjective perception of effort ↔ (anodal data combined) Subjective perception of effort ↔
Montenegro et al.[24]	8	2016	The study was performed with two groups, one with post-stroke subjects, the other with 9 healthy subjects, both submitted to the same knee extension and knee flexion evaluation procedure with two sets of 10 repetitions at 50% of maximal force, after the application of the bi-cephalic tDCS and the placebo situation on the motor cortex for 20 minutes with 2mA.	(bi-cephalic post-stroke individuals) Muscle torque ↔ Force steadiness (both) ↑ (bi-cephalic healthy individuals) Muscle torque ↔ Force steadiness (extensors) ↑ Force steadiness (flexors) ↔
Mendonça et al.[25]	8	2016	The study was carried out with 45 individuals with fibromyalgia who were divided into 3 intervention groups (tDCS + aerobic exercise, aerobic exercise and tDCS only). the tDCS was applied for 20 minutes at 2mA. The tDCS plus aerobic exercise group was compared to the other two groups.	((Bi-cephalic tDCS + aerobic exercise) Pain Questionnaire ↓
Lattari et al.[18]	8	2016	The study involved 10 subjects who underwent tDCS at 2mA for 20 minutes of the alternating anodal, cathodal and placebo techniques, associated with elbow flexion exercises on the bar with measured load for 10 maximal repetitions, the anodal technique being compared to the other two situations.	(Anodal tDCS) Range of movement ↑ Subjective perception of effort ↓
Oki et al.[26]	6	2016	The study was performed with 13 older adults submitted to anodal tDCS or placebo situation over the motor cortex for 15 minutes at 2mA, and was associated with isometric exercise of elbow flexion until the moment of muscle contraction failure.	(Anodal) Time to muscle failure ↑ Subjective perception of effort ↓
Ojardias et al.[27]	1	2016	The case study was performed with 1 post-stroke individual, who underwent bi-cephalic tDCS with the anodal current electrode over the injured primary motor cortex and the other over the region opposite the lesion, at 2mA for 20 minutes, in association with exercise to verify cardiorespiratory fitness.	(bi-cephalic) 6-minute walk test ↑
Panouilleres et al.[28]	9	2015	The study was carried out with 38 healthy older adults and 42 young people, all of whom underwent bi-cephalic tDCS at 2mA for 17 minutes, with the anodal technique applied over the motor cortex region responsible for motor task control, associated with a visual motor test for hands	(bi-cephalic) Visual motor coordination of hands in young people ↑ (bi-cephalic)Visual motor coordination of hands in older adults ↑
Uehara et al.[12]	9	2015	The study was performed with 20 healthy young subjects undergoing tDCS and placebo over the motor cortex, at 1mA for 15 minutes, associated with muscle contraction exercises.	(cathodal) Selective muscle activation ↑
Murray et al.[7]	9	2015	The study involved 9 individuals with chronic spinal cord injury who underwent bi-cephalic tDCS and placebo, with two different stimulations (1mA and 2mA) over the motor cortex, both for 20 minutes, associated with muscle excitability and sensory perception.	(bi-cephalic at 2mA) Muscle excitability ↑ (bi-cephalic with 1mA and 2mA) sensory perception ↑
Park et al.[29]	7	2015	The study was carried out with 24 post-stroke subjects who underwent bi-cephalic tDCS and placebo over the motor cortex for 15 minutes at 2mA, associated with strength exercises of the muscle groups involved in the gait.	(bi-cephalic) Gait symmetry ↑ (bi-cephalic) Gait speed ↑
Angius et al.[30]	6	2015	The study was performed with 9 healthy subjects, who underwent anodal tDCS, cathodal tDCS and placebo on the motor cortex for 10 minutes at 2mA, associated with aerobic exhaustion exercises.	(anodal and cathodal) Maximum O2 consumption capacity ↔ (anodal) Pain resistance ↑
Hoff et al.[31]	6	2015	The study was performed with 16 healthy older adults who underwent anodal tDCS and placebo over the motor cortex, at 2mA for 15 minutes, associated with visual feedback motor test for the trained right hand and untrained left hand.	(anodal) Motor coordination by visual feedback in trained hand ↑ (anodal) Motor coordination by visual feedback in untrained hand ↔
Von Rein et al.[32]	6	2015	The study presented 20 healthy young people who underwent anodal tDCS over the motor cortex. at 2mA for 20 minutes, associated with visual feedback motor test.	(anodal) Motor coordination by visual feedback with tDCS ↑
Wrightson et al.[33]	6	2015	The study was carried out with 10 healthy young people who underwent anodal and cathodal tDCS on the prefrontal cortex at 2mA for 20 minutes, associated with gait test.	(cathodal) Balance (time of gait variation) ↓ (anodal) Balance (time of gait variation) ↑
Hendy & Kidgel.[34]	9	2014	The study was conducted with 10 subjects who underwent anodal tDCS and placebo over the right motor cortex for 20 minutes at 2mA associated with upper limb strength training.	(anodal) Strength in the untrained limb ↑ Evoked Motor Potential ↑
Duarte et al.[35]	9	2014	The study was performed with 24 children with cerebral palsy, who underwent anodal tDCS and a placebo situation over the motor cortex for 20 minutes at 1mA, associated with treadmill training.	(anodal) Static and dynamic balance ↑
Valentino et al.[36]	9	2014	The study included 10 subjects with Parkinson's disease who underwent an anodal tDCS and placebo over the motor cortex for 20 minutes at 1mA, associated with walk tests.	(anodal) Motor control during walking ↑
Zimerman et al.[5]	8	2014	The study involved 10 young people and 13 older adults, all of whom underwent bi-cephalic tDCS and placebo over the motor cortex for 20 minutes at 1mA, associated with visual motor training.	(bi-cephalic with cathode on the cerebral region responsible for the training) Motor visual coordination ↓
Kaski et al.[14]	7	2014	The study was performed with 16 individuals divided into 2 groups that underwent anodal tDCS and the placebo situation, one over the pre-motor cortex and the other with motor cortex stimulation for 15 minutes at 2mA, associated with walking exercises and balance training.	(anodal) Gait speed ↑ Gait balance ↑
Sriraman et al.[37]	6	2014	The study was performed with 12 healthy subjects who underwent anodal tDCS and placebo over motor cortex for 15 minutes at 1mA, associated with visual motor training of the knee.	(anodal) Visual motor coordination of the knee ↑
KIM et al.[9]	5	2014	The study was performed with 30 subjects divided into two groups (healthy or stroke patients), who underwent anodal tDCS over the motor cortex for 20 minutes at 1mA, associated with wrist flexion and extension exercises.	(anodal) Evoked Motor Potential ↑
Middleton et al.[38]	2	2014	The study was carried out with 5 individuals who suffered cranial trauma or were post-stroke, all of whom were submitted to bicephalic tDCS for 24 sessions over the motor cortex at 1.5mA for 15 minutes, associated with strength training.	(bi-cephalic) Strength ↑

Table 2. Authors, methodological quality, year of publication, study protocol, main results of articles analyzed.

Authors	Pedro scale	Year	Méthods	Main results
Ochi et al.[15]	9	2013	The study was performed with 18 subjects hemiparetic due to stroke who underwent bi-cephalic tDCS and placebo over the motor cortex for 10 minutes at 1mA, being performed with anodal and cathodal montage on the injured cortex and that opposite the injury, both applied for 5 days, associated with arm strength training.	(bi-cephalic) Force control ↑
Kaski et al.[39]	9	2013	The study was carried out with 9 individuals who underwent the anodal tDCS and placebo on the Cz area so that the motor cortex was stimulated bilaterally at 2mA for 15 minutes, associated with gait training.	(bilateral anodal) Gait speed ↑ Gait motor coordination ↑ Gait balance ↑
Zimerman et al.[40]	8	2013	The study involved 29 older adults and 24 young people that underwent bi-cephalic tDCS and placebo over the motor cortex for 20 minutes at 1mA, associated with visual motor training.	(bi-cephalic with anode on the cerebral region responsible for the training) Motor coordination and attention ↑
Kim & Ko.[6]	7	2013	The study was carried out with 44 subjects who underwent anodal tDCS and placebo over the motor cortex for 20 minutes at 2mA, associated with voluntary exercises for upper limbs.	(anodal) Evoked motor potential ↑
Williams et al.[13]	6	2013	The study was performed with 18 healthy volunteers who underwent anodal tDCS and placebo, over the motor cortex for 20 minutes at 1.5mA, associated with two contractions of 20% of the maximal effort of the elbow flexors.	(anodal) Evoked Motor Potential ↑ Muscle Fatigue ↓
Khan et al.[41]	6	2013	The study was performed with 9 subjects who underwent bi-cephalic tDCS and placebo over the motor cortex for 15 minutes at 2mA, associated with wrist flexion exercises.	(bi-cephalic) Blood flow in the musculature ↑ Motor coordination ↑
Kan et al.[42]	6	2013	The study was carried out with 15 subjects who underwent anodal tDCS and placebo over the motor cortex for 10 minutes at 2mA, associated with isometric exercises for elbow flexors.	(anodal) Muscle Fatigue ↔ Isometric strength ↔
Montenegro et al.[17]	6	2013	The study was conducted with 11 subjects, who underwent anodal tDCS and placebo over the prefrontal cortex for 20-minute at 2mA, associated with isocaloric aerobic physical exercise session.	(anodal) Post exercise O2 consumption ↑
Hendy & Kidgell.[43]	6	2013	The study was performed with 30 subjects who underwent anodal tDCS and placebo over the motor cortex for 20 minutes at 2mA, associated with strength training of the wrist extensors.	(anodal) Dynamic strength ↔
Okano et al.[11]	6	2013	The study was performed with 10 athletes who underwent anodal tDCS and placebo over the temporal cortex for 20 minutes at 2mA, associated with maximal exercise on a cycle ergometer.	(anodal) SNA activity ↑ Subjective perception of effort ↓
Miyaguchi et al.[44]	2	2013	The study was performed with 9 healthy subjects that underwent anodal tDCS and placebo over the motor cortex at 2mA for 10 minutes, associated with finger abduction and adduction exercises.	(anodal) Evoked Motor Potential ↑
Montenegro et al.[8]	7	2012	The study was conducted with 9 healthy subjects submitted to bicephalic tDCS and placebo over the lateral dorsal prefrontal cortex for 20 minutes at 2mA associated with aerobic exercise.	(bi-cephalic) Aerobic capacity ↔
Jayaram et al.[10]	6	2012	The study was performed with 40 individuals who underwent anodal and cathodal tDCS and placebo over the insular cortex for 15 minutes at 2mA, associated with gait adaptation training.	(anodal) Gait speed adaptation ↑ (cathodal) Gait speed adaptation ↓
Bradnam et al.[45]	6	2012	The study was performed with 12 post-stroke subjects divided into two groups (one group of patients with mild impairment, the other group with moderate and severe impairment) that underwent bicephalic tDCS and placebo, over the motor cortex for 20 minutes at 1mA , associated with brachial bicep exercises.	(bi-cephalic with cathodal on the injured region) Coefficient of variation of force in moderate and severe patients ↑ Coefficient of variation of force in mild patients ↓
*COSTA.[46]	6	2012	The study was carried out with 11 healthy subjects, who underwent anodal and cathodal tDCS and placebo over the motor cortex for 13 minutes at 2mA, associated with resistance training with submaximal loads on an exercise bike.	(anodal) Aerobic resistance ↑ (cathodal) Aerobic resistance ↔ (anodal and cathodal) Heart Rate ↔ (anodal and cathodal) Surface electromyography ↔
Bolognini et al.[16]	9	2011	The study was carried out with 14 post-stroke subjects who underwent bi-cephalic tDCS and placebo, over the motor cortex for 40 minutes at 2mA, associated with upper limb motor coordination training.	(bi-cephalic with anodal on the injured region) Motor coordination of the upper limbs ↑
Hesse et al.[47]	9	2011	The study included 96 post-stroke patients who underwent bicephalic tDCS over the motor cortex for 20 minutes at 2mA, associated with strength training for upper limbs.	(bi-cephalic) Upper limb strength ↔
Montenegro et al[7].	6	2011	The study was conducted with two groups, one with 10 healthy subjects and the other with 10 athletes, both of whom were submitted to anodal tDCS and the placebo situation over the temporal cortex for 20 minutes at 2mA, associated with autonomic nervous control during rest.	(anodal) Athletes' heart rate variability ↔ Healthy individuals' heart rate variability ↑
Madhavan et al.[49]	6	2011	The study was performed with 9 post-stroke subjects who underwent bi-cephalic tDCS and placebo over the motor cortex for 15 minutes at 2mA, associated with dorsiflexion and plantar flexion exercises.	(bi-cephalic with anodal on the injured region) Motor coordination ↑ Coefficient of variation of force ↓
Geroin et al.[50]	6	2011	The study was carried out with 30 post-stroke subjects who underwent bi-cephalic tDCS and placebo, over the motor cortex for 20 minutes at 2mA, associated with gait training.	(bi-cephalic) Motor control on the gait ↔
Cogiamanian et al.[51]	7	2007	The study was performed with 24 healthy subjects who underwent anodal and cathode tDCS and placebo over the primary motor cortex for 10 minutes at 1.5mA, associated with isometric strength training of the elbow flexors, with the anodal condition compared to the other two situations.	(anodal) Muscle fatigue ↓

Legend: The symbols in the main results refer to: did not present significant differences in the parameters investigated (↔); increase in the parameters investigated significantly (↑); decrease in parameters investigated significantly (↓). * Masters dissertation.

Regarding the area of stimulation, Machado[52] stated that brain regions are responsible for controlling one or several areas and functions of the body. Therefore, there was difficulty in exactly defining which area to stimulate. These differences in brain controls related to body functions tended to be reflected in the studies of tDCS associated with exercise. The stimulated brain region seen in most of the studies investigating the effect of tDCS on physical activity was the motor cortex.[6, 18, 26] The temporal cortex,[12, 53] dorsolateral prefrontal cortex[54] and ipsilateral hemisphere[11] were other regions studied. A possible explanation for different regions being stimulated in the studies of tDCS associated with physical exercise may be, in the case of subjects with some brain injury, stimulation of the areas corresponding to the location of these lesions.[10, 24]

The gender of the participants is another point to be discussed, as, of the 43 studies included in the review, only 9 were performed with male-only volunteers, that is, the majority of the studies investigated the effects of tDCS on both genders. Therefore, it is important to emphasize that the participation of individuals of both sexes in the same study should be interpreted carefully, due to the biological differences between the male and female genders, especially in strength patterns.[3] The studies indicated significant results when men and women underwent tDCS, which may suggest that anyone may be susceptible to the effects of anodal or cathodal stimulation.[52, 27, 8]

It is also possible to observe that 28 studies were performed with individuals categorized as young adults, thus indicating a possible uniformity in the age group submitted to the tDCS technique. Despite this, five studies[10,25,17,7,52] showed large differences between the ages of the volunteers and, perhaps, because of this age dispersion, highlighted antagonistic results. Among the five studies with differences in the age range, the one carried out by Zimerman et al.[5] can be cited, as it presented a population with a large age difference among the participants. In this study young people and older adults underwent cathodal stimulation associated with the motor task, with antagonistic results found. It was possible to verify that only the older adult group presented a significant improvement in the motor behavior.

The study by Bolognini et al,[17] when distributing stroke patients with different age groups (age 26-75 years) into two groups, found that both groups presented significant changes when submitted to tDCS associated with motor work, that is, regardless of the difference in the age groups, it is possible that tDCS causes significant changes. In the investigation by Madhavan et al.[25] it is possible to identify that young people and older adults with hemiparesis, when submitted to anodal and cathodal tDCS presented significant changes in the control of lower limb movements. Similarly, healthy and post-stroke individuals who underwent anodal stimulation associated with wrist flexion and extension exercises through videogames and a writing test presented significant changes when compared to similar situations without the use of tDCS.[10]

Although some of the studies discussed in this review are of low intensity physical activity, this does not imply the impoverishment of the tDCS technique when associated with physical exercises of higher intensities. Physical exercises will mostly require a range of less complex motor skills with fewer muscles involved than more complex activities involving a greater variety of musculature worked on in the same session of physical activity. Therefore, it is possible to comprehend, regardless of the muscle group worked on, the importance will be in the physical activity.[45, 46] In addition, Kaski et al.[14] and Montenegro et al.[24] presented good perspectives in the association of tDCS and performance of physical valences at higher intensities allowing speculation of a promising future, however, there is a need for further studies regarding these relationships.

CONCLUSION

Transcranial direct-current stimulation seems to be a promising technique when associated with aerobic and anaerobic exercises, however, more research is needed regarding this association with concurrent physical activity. This is relevant as these two forms of exercise play an important role in physical and mental rehabilitation, disease prevention and maintenance of health, therefore, configure a great opportunity to optimize benefits in health promotion.

ACKNOWLEDGMENT

Fundação Carlos Chagas Filho de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ). Dr. Felipe Fregni is supported by a NIH grant 1R01AT009491-01A1.

All authors declare no potential conflict of interest related to this article

AUTHORS' CONTRIBUTIONS: Each author made significant individual contributions to this manuscript. LVDC (0000-0003-2076-4019)*: Substantial contribution in the conception or design of the study, or the acquisition, analysis, or interpretation of the study; writing or critical review of the article and its intellectual content; agreeing to take responsibility for all aspects of the study, in the sense of guaranteeing that any issues related to the integrity or precision of any portion of the study were duly studied and resolved. FP (0000-0002-3811-3188)*: Substantial contribution in the conception or design of the study, or the acquisition, analysis, or interpretation of the study; writing or critical review of the article and its intellectual content; agreeing to take responsibility for all aspects of the study, in the sense of guaranteeing that any issues related to the integrity or precision of any portion of the study were duly studied and resolved. FF (0000-0002-1703-7526)*: Writing or critical review of the article and its intellectual content; agreeing to take responsibility for all aspects of the study, in the sense of guaranteeing that any issues related to the integrity or precision of any portion of the study were duly studied and resolved. JLG (0000-0002-9355-7793)*: Substantial contribution in the conception or design of the study, or the acquisition, analysis, or interpretation of the study; final approval of the version of the manuscript to be published. *ORCID (Open Researcher and Contributor ID).

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