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Review

Transcranial Direct Current Stimulation in the Treatment of Gait Disturbance in Post-stroke Patients: An Overview of Systematic Reviews

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Reviews

Transcranial Direct Current Stimulation in the Treatment of Gait Disturbance in Post-Stroke Patients: An Overview of Systematic Reviews

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Abstract: Introduction: The transcranial direct current stimulation (tDCS) is a promising technique for brain modulation after cerebrovascular accident (CVA). This treatment modality has been previously studied in the recovery of patients. The aim of this review is to analyze the evidence in the application of tDCS in the recovery of gait disturbance in stroke patients. Methods: This review was conducted according to the recommendations of the PRISMA statement. Three different electronic databases were searched for relevant results: PubMed, Scopus, and Cochrane. We included reviews and meta-analyses that only considered randomized controlled trials (RCTs) that investigated the effects of transcranial direct electrical stimulation, in combination or not with other physiotherapy treatment, on gait recovery. Results: Thirteen studies with a total of 195 RCTs were included. Data on population, outcome measures, protocols and outcomes were extracted. The Amstar-2 scale and the GRADE system of certainty of evidence were used. Only one study received high certainty of evidence, 5 received low certainty of evidence and 7 received critically low certainty of evidence. Conclusions: Although the tDCS produces positive changes in gait recovery in spatio-temporal parameters, mobility, endurance, strength and motor function, there is insufficient evidence to recommend this treatment.

Keywords: Physiotherapy; neurorehabilitation; transcranial electrical stimulation; stroke; gait; non-invasive stimulation techniques

1. Introduction

Stroke is one of the leading causes of disability in the world and most survivors have limitations in mobility and gait [1]. Gait performance is considered an indicator of health and quality of life in people who have suffered a stroke [2], because gait performance is linked to the development of activities of daily living and community participation. Therefore, it is considered one of the most important objectives in the recovery of stroke survivors [3,4].

In recent years, numerous techniques have attempted to address gait impairments in stroke survivors from different approaches. Some of these techniques, such as percutaneous nerve electrostimulation, virtual reality, biofeedback using electromyography, neurophysiological approaches, or the use of auditory signals during gait re-education, have been classified by The America Stroke Association as level IIb-B evidence, indicating an unestablished recommendation and conflicts in evidence [5].

Non-invasive brain stimulation (NIBS) includes several techniques developed to achieve neuromodulation of the brain. It has its origins in the 1980s with the application of current to healthy subjects, which was a revolution compared to direct brain stimulation [6]. Two main techniques are described: magnetic fields and electrical stimulation. Transcranial electrical stimulation (TES) involves the application of a weak electrical current to the scalp, powered by batteries and connected to an anode and a cathode. Its effect lies in the modulation of the polarization of cell membranes, and it is voltage dependent [7,8]. The most popular type of TES is the tDCS [8]. The long-term effects of

transcranial electrical stimulation are commonly defined by two concepts: long-term potentiation (LTP), related to neural excitation, and long-term depression (LTD), related to neural inhibition [9]. Both, which are a synaptic mechanism of plasticity, are related to the stimulation protocol; thus, the anode is more related to LTP effects, while the cathode is more related to LTD effects [10]. Their application is usually 1-2 mA and the duration of the treatment is between 10-30 minutes [11].

The key to the application of these techniques is the durability of the effects after treatment, which are associated with repeated stimulation in short periods of time, increasing the benefits and prolonging neuroplasticity. However, although the application of tDCS has a modulating effect at the cortical level that seems to favour the patient's recovery and is associated with benefits in certain pathologies, there is a lack of evidence to support the use of these techniques for the recovery of gait in neurological patients [5]. This could be due to possible differences in application protocols, as factors such as electrode size, connector position and the conductivity of the different electrode materials, including saline concentration and conductive gel, could affect the results obtained [7].

Several reviews have attempted to answer the evidence of tDCS application for gait recovery in stroke patients [4,12–24]. However, the variability of the protocols and the heterogeneity of the outcome measures make it difficult to interpret the results. Other authors have attempted to synthesise and address the evidence for these protocols for the recovery of upper limb function [25] , however, no review of systematic reviews and meta-analyses for gait recovery has been conducted to allow the generation of evidence based tables and clinical recommendations. Therefore, an onverview of systematic reviews and meta-analyses is needed to summarise the effect of the application of tDCS in post-stroke patients for gait recovery, through the description of evidence based tables that facilitate the clinical recommendation of the different applications of this technique, using the GRADE method.

2. Materials and Methods

2.1 Database Search Strategy

The following databases were searched on 21 March 2023: PubMed, Scopus, and Cochrane Database of Systematic Reviews. The search terms used were: "stroke", "cerebrovascular accident", "apraxia of gait", "gait disorder", "gait dysfunction". A combination of these and similar terms was performed using the Boolean operators AND and OR. We did not search the grey literature, as we aimed for studies that had been previously screened by reviewers. We also did not consult with experts in the field, conference abstracts, dissertations or reports not published on personal websites. The review protocol was registered with PROSPERO (CRD42021237915).

2.2. Eligibility Criteria

- Type of studies: This study only includes systematic reviews (with or without meta-analysis) that analysed randomised controlled trials due to their methodological quality. Published from 2015 to 2022. Only titles written in English and Spanish were considered.
- Type of participants:
  o Subjects diagnosed with an ischaemich or haemorrahagic stroke.
  o Adults, over 18 years of age.
  o Acute, sub-acute or chronic stroke.
- Type of intervention: we included studies in which the interventions involved tDCS, whether administered alone or in combination with another form of treatment and compared to another form of physical therapy, or placebo. We excluded papers that did not define interventions or multi-therapies and also any pharmacological treatment (e.g., botulinum toxin).
- Type of outcome measures: studies quantitatively assessing gait pattern (three-dimensional instrumental analysis systems), gait speed, functional mobility, endurance, motor function and muscle strength.

Table 1. Full search strategy.

PubMed Search
2,(((stroke) AND (NIBS)) OR (tDCS)) AND (gait),Most Recent,"Meta-Analysis, Systematic Review, from 2016 - 2022","(((((""stroke""[MeSH Terms] OR ""stroke""[All Fields] OR ""strokes""[All Fields] OR ""stroke s""[All Fields]) AND ""NIBS""[All Fields]) OR (""transcranial direct current stimulation""[MeSH Terms] OR (""transcranial""[All Fields] AND ""direct""[All Fields] AND ""current""[All Fields] AND ""stimulation""[All Fields]) OR ""transcranial direct current stimulation""[All Fields] OR ""tdcs""[All Fields])) AND (""gait""[MeSH Terms] OR ""gait""[All Fields])) AND ((meta-analysis[Filter] OR systematicreview[Filter]) AND (2016:2022[pdat]))"
Cochrane Search
"transcranial direct current stimulation":ti,ab,kw AND "stroke":ti,ab,kw
Scopus Search
stroke AND tdcs AND gait AND PUBYEAR > 2014 AND PUBYEAR < 2023 AND (LIMIT-TO (DOCTYPE , "re")) AND (LIMIT-TO (SUBJAREA, "HEAL"))

2.3. Study Selection and Data Extraction

The method of data collection was based on the Cochrane Handbook of Systematic Reviews of Interventions. Review Manager 5 software (RevMan 2020) was used for review writing [26].

Two reviewers screened the title, abstract and full texts independently for the inclusion of all systematic reviews potentially identified in the search. Differences were resolved by discussion, or, if necessary, consultation of a third team member.

Two authors independently extracted data from the reviews using a predefined data extraction form. Where outcome information was unclear or missing, the individual published file was accessed for further details.

2.4. Methodological Assessment and Evaluation of the Quality of Evidence

No reassessment was performed on the studies included in the reviews; however, the quality of the studies was reported according to the assessment of the author of each review. This information was subtracted during data collection and extraction.

The methodological quality of each systematic review was assessed using AMSTAR 2 (A Messurement Tool to Assess Systematic Review). Based in 16 items, this tool assesses the methodology used in a systematic review. Each item is rated as "yes" (clearly done), "no" (clearly not done), "cannot be answered", or "not applicable". Finally, the studies are classified according to their confidence. "High", the SR has no weaknesses. "Medium", no critical weaknesses, but some non-critical weaknesses. "Low", some critical weaknesses. "Critically Low", more than one critical weakness.

We assessed the quality of evidence for our primary endpoint, the evidence for the use of tDCS for gait training in stroke patients, using GRADE. We used the recommendation methods described in chapter 12, section 8.a of the Cochrane handbook [27], using GRADEproGDT software. All decisions to downgrade the quality of studies were justified by comments, so that the reader can understand the decisions and agree or disagree.

3. Results

3.1. Selection of Studies

A total of 47 studies were found, duplicates were removed leaving a total of 21 articles. Studies were screened by title and abstract to check that they met the previously established inclusion criteria. Finally, 13 reviews were included [4,12–15,18–24,28] with a total of 195 randomised controlled trials (RCT) included. The selection process is shown in the flow chart (Figure 1) with a list of excluded studies, reasons, and funding (Table S1).
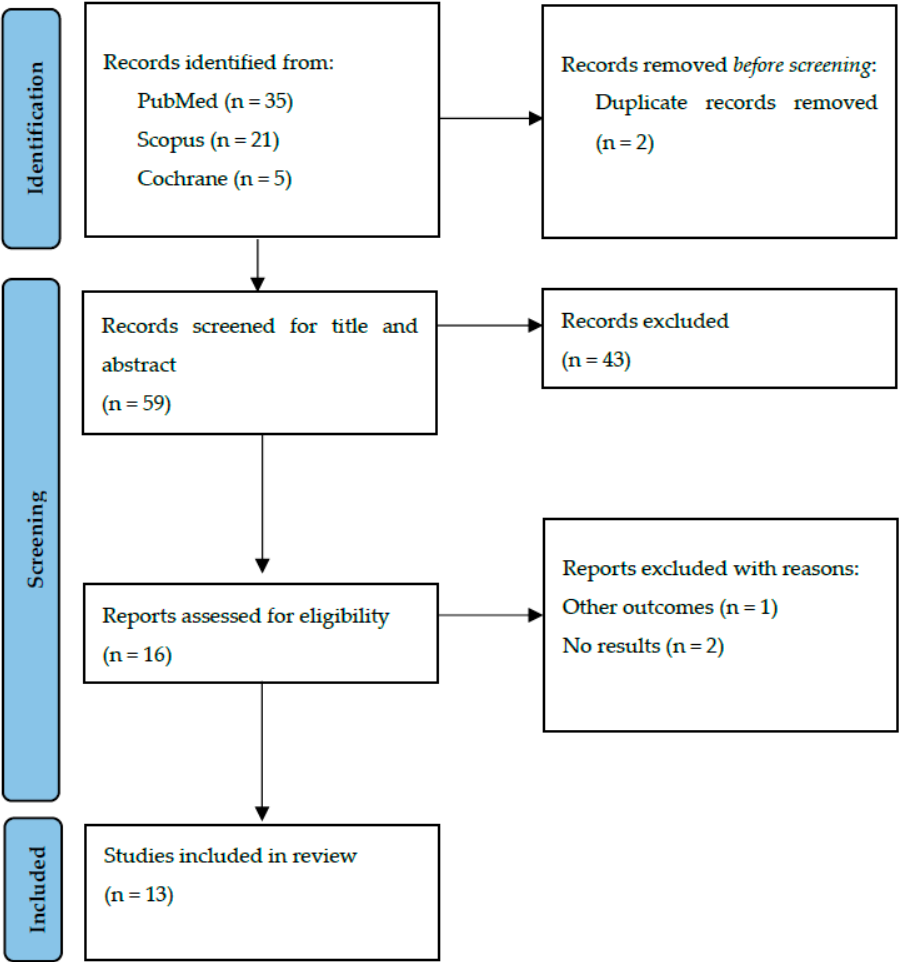
Figure 1. Flow chart (PRISMA).

3.2. Methodological Quality Assessment

The results of the methodological assessment of the included systematic reviews/meta-analyses are shown in Table 2. Only one study was rated with "High" confidence [12], although, it did not justify the study design decision. While 7 studies were rated with "Critically Low" confidence [4,14,18,20–22,28], the remaining 5 studies were classified with "Low" confidence. [13,15,19,23,24].

3.3. Assessing the Quality of Evidence

The results of the evidence assessment of the included systematic reviews/meta-analyses are shown in Table S1. The following outcomes of interest were broken down: gait speed, functional mobility, endurance, motor function and muscle strength.

Table 2. AMSTAR checklist.

AMSTAR Checklist	Li et al.	De Paz et al.	Vaz et al.	Elsner et al.	Tien et al.	Santos et al.	Mitsutake et al.	Dong et al.	Navarro-López et al.	Veldema et al.	Corominas-Teruel et al.	Bressi et al.
1	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y
2	N	N	Y	Y	N	Y	Y	Y	N	N	Y	Y
3	N	N	N	N	N	N	N	N	N	N	N	N
4	PY	PY	PY	Y	N	PY	PY	PY	Y	PY	PY	PY
5	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y
6	Y	N	Y	Y	Y	Y	Y	N	Y	Y	Y	Y
7	N	N	N	Y	N	N	N	N	PY	N	N	N
8	Y	Y	Y	Y	Y	Y	Y	PY	Y	Y	Y	Y
9	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
10	N	N	N	Y	N	N	N	N	N	N	N	N
11	Y	NA	Y	Y	Y	NA	Y	Y	NA	Y	NA	NA
12	Y	NA	N	Y	Y	NA	Y	Y	NA	Y	NA	NA
13	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
14	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
15	N	NA	N	Y	N	NA	N	N	NA	N	NA	NA
16	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Overall assessment	Critically low	Low	Critically low	High	Critically low	Low	Critically low	Critically low	Low	Critically low	Low	Low

1= Question PICO; 2= Protocol registered prior to review; 3= Justification of the design of the studies included; 4= adequate literature search; 5= Selection of duplicate studies; 6= Duplicate data extraction; 7= Justification of excluded studies; 8= Adequate description of the studies included; 9=Risk of bias of individual included studies; 10= source of funding for the studies included; 11= Appropriate meta-analytical methods; 12= Risk of bias assessment on meta-analysis; 13= Consideration of the risk of bias in the interpretation of the results of the review; 14= Explanation of heterogeneity in results; 15= Assessment of the presence and impact of publication bias; 16= Conflict of interest.

3.4. Summary of Results

The characteristics of the included studies are summarised in Table 3. Of the 13 included studies, we found 8 meta-analyses [4,12,14,18,20–22,28] and 5 systematic reviews [13,15,19,23,24]. All articles defined the intervention as applying tDCS in combination with another physiotherapy treatment (treadmill, walking assistance robot, conventional physiotherapy, etc.) or alone. The control group received a placebo stimulation treatment in combination or not with physiotherapy, or a different stimulation protocol.

The outcome measures described by the reviews were organised as follows: spatiotemporal parameters of gait [4,13–15,18–21,23,24,28] functional mobility [4,13–15,18–21,23,24] gait endurance [4,13,15,18–21,23,24] motor function [17,19,24,28] muscle strength [4,12–14,24] and lower limb functionality [12,22].

3.4.1. Effect of tDCS in Combination with Physiotherapy on Spatiotemporal Parameters.

The outcome measures described for this outcome were 10MWT (10 Meter walk test), quantitative analysis using technological systems and gait cadence. For gait speed, the meta-analyses by Li et al. [4], Vaz et al. [14], Tien et al. [18] and Dong et al. [21] found no significant improvements in their meta-analyses.

Mitsutake et al. [20] included both online and offline stimulation in their analysis. Only the online application showed a significant improvement over offline.

According to GRADE, the certainty of the evidence for these studies was classified as "low" and "very low".

As for systematic reviews, Paz et al. [13] and Santos et al. [19] expressed significant improvements in walking speed (9.09%, p=0.046). For Navarro-López et al. [15] and Bressi et al**.** [24] there were no significant improvements in any of the included studies. For the review by Corominas-Teruel et al. [23] the results were presented as effect size. Only one study showed a large effect in this respect.

According to GRADE, they were classified as "low" and "very low" certainty (Table S2).

As for gait cadence, which was recorded as steps per minute (p/m). Vaz et al. [14] and Mitsutake et al. [20] showed no significant differences. According to GRADE, they were classified with "very low" certainty of evidence (Table S2).

3.4.2. Effect of tDCS in Combination with Physiotherapy on Functional Mobility

The outcome measures were the TUG (Time up and go), the FAC (Functional ambulatory category), the RMI (Rivermead mobility index) and the Tinetti test. In the studies by Vaz et al. [14], Mitsutake et al. [20] and Dong et al. [21] found no significant improvements in their meta-analysis evaluated by FAC and TUG. Whereas Tien et al. [18], who found significant improvements describing FAC, RMI and TUG, found no significant differences with the Tinetti test. According to GRADE, the certainty of evidence was classified as "low" and "very low". However, Li et al. [4] who were the only ones with a "moderate" certainty of evidence, showed significant improvements for functional mobility.

In terms of systematic reviews, studies find controversial results depending on the outcome measures used. It is noted that Paz et al. [13] Navarro-López et al. [15] Bressi et al. [24] and Santos et al. [19] do not provide sufficient evidence to recommend the use of tDCS for functional mobility.

For the review by Corominas-Teruel et al. [23], who evaluated the results using cohen's d, also did not consider there was insufficient evidence for a treatment recommendation.

According to GRADE, except for Paz et al. [13], which classified the certainty of the evidence as moderate, the rest were classified as "low" and "very low" (Table S2).

3.4.3. Effect of tDCS in Combination with Physiotherapy on Endurance

The outcome measure for this outcome was the 6MWT (6 Minute walking test). Li et al. [4], Tien et al. [18] and Dong et al. [21] reported no significant improvements in their meta-analyses.

Mitsutake et al. [20] included both online and offline application in their analysis. Only the online application showed significant improvements over the offline application. According to GRADE, the certainty of the evidence was classified as "low" and "very low".

In terms of systematic reviews, the included studies show controversial results. Paz et al. [13], Navarro-López et al. [15], Santos et al. [19] and Bressi et al. [24] were not considered to show significant improvements in gait endurance. Corominas-Teruel et al. [23], who evaluated the results using cohen's d, also did not have enough evidence to make a treatment recommendation. According to GRADE, the certainty of the evidence was classified as "low" and "very low" (Table S2).

3.4.4. Effect of tDCS in Combination with placebo On Motor Function

The outcome measure used for this outcome was the FMA-LE (Fugl-Meyer assessment lower extremity). Dong et al. [21] and Li et al. [16] reported no significant improvement. According to GRADE, the certainty of the evidence was classified as "low".

The systematic review by Paz et al. [13], Navarro-López et al. [15], Santos et al. [19] and Bressi et al. [24] were not considered to have enough evidence to recommend the use of tDCS to improve motor function. According to GRADE, the certainty of the evidence was classified as "very low" (Table S2).

3.4.5. Effect of tDCS in Combination with Physiotherapy on Muscle strength

The outcome measures for this outcome were the MRC (Medical research council) and MI-LE (Motricity index lower extremity). Although Li et al. [4] reported significant improvements, Vaz et al. [14] did not report significant improvements for muscle strength. According to GRADE, the certainty of the evidence was classified as "low" and "very low".

In terms of systematic reviews, only Paz et al. [13] and Bressi et al. [24] reported insufficient evidence to recommend tDCS treatment for muscle strength. The certainty of the evidence was classified as "low" (Table S2).

3.4.6. Effect of tDCS in Combination with Placebo on Lower Limb Function

Outcome measures for this outcome were spatiotemporal parameters (10MWT and cadence), endurance (6MWT), functional mobility (FAC, Tinetti and MI-LE), motor function (FMA) and balance (BBS). Elsner et al. [12], showed no significant improvements in either statistical analysis. Veldema et al. [22], performed a comparative meta-analysis of different stimulation protocols. They described a large effect in the application of tDCS in contralateral and bilateral hemispheres.

The certainty of the evidence was classified as "low" and "very low" (Table S2).

Table 3. Summary of included studies.

Review	Data assessed as up to date	Population	Interventions	Comparison interventions	Outcomes for which data were reported	Review limitations
Li et al. (2018) [4]	April 2017 (English)	Post-stroke patients over 18 years of age	**tDCS:** 1. Transcranial direct current stimulation applying anode in ipsilateral (affected) hemisphere (n=6). Combined therapy with physiotherapy, robotic-assisted therapy and task-oriented training. 2. Applying cathode on contralateral hemisphere (n=2). Rehabilitation treatment. 3. Bihemispheric application (n=3). Rehabilitation treatment.	Simulated treatment (complementary robot-assisted treatments, task-related training, robotic orthoses and conventional rehabilitation)	• Gait speed (10MWT and quantitative gait analysis (GAITRite and Eagle digital System)) • Functional mobility (TUG, Tinetti and FAC) • Running resistance (6MWT) • Strength of MMII (Medical Research Council and MI-LE)	1. It only included studies in one language (English). 2. Heterogeneity in outcome measures and tDCS application parameters. 3. Low number of studies. 4. Low sample size. 5. Some authors did not cooperate in the data request and the data may be biased.
De Paz et al. (2019) [13]	2018	Patients diagnosed with a pathology of the central nervous system	**tDCS** applying anode in ipsilateral (affected) hemisphere (n=4).	1. Simulated treatment of tDCS 2. No intervention 3. Conventional motor rehabilitation treatment.	• Walking speed (10MWT) • Functional mobility (TUG, FAC and FMA) • Resistance (6MWT) • MMII strength (MI-LE and MRC)	1. Heterogeneity in tDCS application parameters. 2. Low number of studies. 3. Low sample size. 4. Only articles in English and Spanish. 5. It does not include data on comparator groups. 6. Misquoted references.
Vaz et al. (2019) [14]	December 2018	Subjects who have suffered an acute/subacute (less than six months) or chronic (more than six months) stroke.	**tDCS:** 1. Transcranial direct current stimulation applying anode in ipsilateral (affected) hemisphere (n=6). 2. Applying cathode on contralateral hemisphere (n=1). **rTMS (**n=3)	1. Simulated treatment of tDCS 2. rTMS combined or not with other types of therapy (conventional, robotic, treadmill, motor imagery)	• Walking speed (10MWT) • Functional mobility (FAC) • MMII strength (MI) • Cadence	1. Heterogeneity in tDCS application parameters. 2. Low number of studies. 3. Low sample size of included studies. 4. Heterogeneity in the exercises described as "conventional therapy" in the control group.
Elsner et al. (2020) [12]	January 2019 (all languages)	Post-stroke patients over 18 years of age	**tDCS:** 1. Transcranial direct current stimulation applying anode in ipsilateral (affected) hemisphere (n=7). 2. Applying cathode on contralateral hemisphere (n=2). 3. Bihemispheric application (n=2).	1. Simulated treatment of tDCS 2. No intervention 3. Conventional motor rehabilitation treatment	• MMII function (gait speed, FAC) • Muscular strength	1. Heterogeneity in the pooling of results in meta-analysis. 2. Heterogeneity in comparison therapy. 3. Low sample size.
Tien et al. (2020) [18]	January 2019	Post-stroke patients over 18 years of age	**tDCS:** 1. tDCS applying cathode on affected hemisphere (n=1)	Simulated treatment of tDCS.	• Walking speed (10MWT) • Functional gait mobility (FAC, Tinetti, TUG and RMI)	1. Low sample size. 2. Heterogeneity in application protocols.

Review	Data assessed as up to date	Population	Interventions	Comparison interventions	Outcomes for which data were reported	Review limitations
			2. tDCS applying anode on affected hemisphere (n=9) 3. Bihemispheric application (n=3)		• Resistance (6MWT)	3. Heterogeneity in comparison therapy. 4. Only articles in English and Chinese.
Santos et al. (2020) [19]	October 2018	Children, adolescents, adults and older people who do not have a progressive central nervous system disease.	**tDCS** in combination with motor training.	Simulated treatment in combination with motor training.	• Walking speed (10MWT) • Functional mobility (TUG) • Resistance (6MWT) • Motor function (FMA)	1. Low sample size. 2. Heterogeneity in application protocols. 3. Articles in English and Portuguese only.
Matsutake et al. (2021) [20]	19 March 2021	Patients diagnosed with haemorrhagic or ischaemic stroke with unilateral hemiplegia. They can walk without support and can maintain their weight and balance.	**tDCS**: 1. Anode in affected hemisphere + combined therapy simultaneously (online) (n=4) 2. Anode in affected hemisphere followed by combined therapy (not simultaneously) (offline) (n=2)	Simulated tDCS treatment in combination with robot-assisted gait therapy or neuromuscular stimulation.	• Walking speed (10MWT) • Functional Gait Mobility (FAC and TUG) • Resistance (6MWT) • Cadence (gait analysis)	1. Low sample size. 2. Heterogeneity in application protocols. 3. Heterogeneity in comparison therapy. 4. Studies published in English only.
Dong et al. (2021) [21]	August 2020	Patients who have been diagnosed with a stroke.	**tDCS** applying anode in ipsilateral hemisphere.	Simulated treatment of tDCS.	• Walking speed (10MWT) • Functional gait mobility (FAC, TUG and FMA-LE) • Resistance (6MWT)	1. Low sample size. 2. Heterogeneity in application protocols. 3. Heterogeneity in comparison therapy. 4. Studies published in English only.
Navarro-López et al. (2021) [15]	March 2020	Patients who have been diagnosed with a stroke.	**tDCS**: 1. tDCS applying cathode on affected hemisphere (n=2) 2. tDCS applying anode on affected hemisphere (n=6) 3. Bihemispheric application (n=4)	Simulated treatment of tDCS.	• Walking speed (10MWT) • Functional gait mobility (FAC, TUG and Tinetti) • Resistance (6MWT)	1. Low sample size. 2. Heterogeneity in application protocols. 3. Heterogeneity in comparison therapy. 4. Studies published only in English and Spanish.
Veldema et al. (2022) [22]	31 March 2021	Patients diagnosed with stroke	**NIBS**: • tDCS • rTMS • iTBS • tACS • tsDCS	Simulated stimulation	Lower limb functionality (combining outcome measures of balance, gait and motor function).	1. Low sample size 2. Low number of studies 3. Only included studies in English or German.
Corominas-Teruel et al. (2022) [23]	7 February 2022	Patients who have suffered a stroke aged 18 years or older	**tDCS**.	Simulated stimulation alone or in combination with other therapies.	• Walking speed • Functional mobility (TUG) • Resistance (6MWT)	1. Heterogeneity in application parameters 2. Only includes studies in English

Review	Data assessed as up to date	Population	Interventions	Comparison interventions	Outcomes for which data were reported	Review limitations
Bressi et al. (2022) [24]	15 March 2021	Patients over 18 years of age who have suffered a stroke in a chronic process (>6 months).	**tDCS** in combination with gait-assisted robot	Simulated stimulation	• Walking speed (10MWT) • Functional mobility (TUG, RMI and FAC) • Resistance (6MWT) • Motor function (FMA) • Muscle strength (MRC)	1. Heterogeneity in application parameters 2. Low number of studies 3. Low sample size 4. Only included studies in English 5. Includes all types of studio designs

tDCS= Transcranial Direct-Current Stimulation; rTMS= repetitive transcranial magnetic stimulation; NIBS= Non-invasive brain stimulation; iTBS= intermitent transcranial brain stimulation; tACS= transcranial alterning current stimulation; tsDCS= transcranial spinal direct current stimulation ; FAC= Functional Ambulatory Category; TUG= Time Up and Go; FMA= Fugl Meyer Assessment; mEFAP= modified Emory Functional Ambulatory Profile; 6MWT= 6 minutes walking test; 10MWT= 10 meters walking test; MAS= Modified Ashworth Scale; RMI= Rivermead Mobility Index; CT= conventional therapy; MI-LE= Lower limb Motricity Index.

4. Discussion

This review has included 8 meta-analyses and 5 systematic reviews with the aim of assessing the quality of evidence regarding the application of tDCS in the recovery of gait in post-ACV patients. The evidence has been assessed using the AMSTAR-2 tools for risk of bias and GRADEpro for certainty of evidence. Outcome measures for lower limb recovery were extracted and classified as follows: spatiotemporal parameters (gait speed and cadence), functional mobility, endurance, muscular strength, motor function and lower limb functionality.

Although some studies have shown that tDCS improves significantly gait speed [20], functional mobility [4,13,18], muscle strength [4], endurance [20] and functionality of the lower limbs [22] compared to sham stimulation, and to the control group, the certainty of the evidence does not seem homogeneous to recommend the benefits of the application of tDCS.

Brain reorganisation after stroke seems to be crucial to patient recovery [29], however, it has been observed that the healthy hemisphere may influence this reorganisation during the recovery period. Abnormalities are observed in the interhemispheric relationship to produce voluntary movement [30] and the reduced excitability of the injured hemisphere, particularly the primary motor cortex (M1), compared to the intact hemisphere. [31]. Also, some theories point to the influence of the intact hemisphere on affect, although this cannot be confirmed. Therefore, although tDCS techniques appear to be a useful tool for influencing factors related to corticospinal excitability of the injured hemisphere and recovery, the results seem to be inconclusive.

Previous authors have reviewed the evidence for these techniques in upper limb recovery [32,33], but there does not seem to be clear evidence of their influence on functional recovery. Whereas other authors have shown significant results in the application of tDCS for the prevention of falls and recovery of the lower limb [34]. This may be due to differences in the brain representation of the upper limbs compared to the lower limbs. It has been observed that the activation of mechanically similar joints does not follow the same patterns as would be expected, in fact, it is related to the task being performed. For example, in a brain image we can see that the contraction of the elbow follows a more lateralised pattern, while the contraction of the knee follows a more medial pattern. [35]. Therefore, tDCS techniques may give different results depending on the task targeted for recovery, as reflected in this gait study.

In this review, we found a large heterogeneity of findings suggesting that the application of tDCS could lead to improvements in gait, but not all results seem to be conclusive. This could be explained by differences in application protocols or sample size, as most of them include a small number of participants, even in combination with several studies. As for the outcome measures, there is a high heterogeneity in the management and statistical analysis of these data.

On the other hand, it is important to mention the differences in the application protocols for the different techniques. Regarding the application of tDCS, the intensity applied in the included studies ranges between 1-2.5 mA, although other authors have previously set the threshold for corticospinal excitation at 2 mA for the anode [36]. Another important factor is the application of unilateral or bilateral tDCS. Most of the included reviews involve studies where unilateral application (anode or cathode) is predominant for excitatory or inhibitory purposes. Although the benefit of unilateral application in post-ACV patients has been demonstrated [37], some reviews continue to include RCTs that perform bilateral application [4,15,18]. Finally, some studies differentiate between online delivery, which combines stimulation and some targeted activity simultaneously, and offline delivery, which performs pre-treatment stimulation. No direct benefits are observed for offline stimulation. [20].

This overview of systematic reviews and meta-analyses presents an update of the evidence on the application of tDCS for gait recovery. However, these results should be interpreted with caution due to some limitations in the review process. First, only studies published in any journal that were in English and/or Spanish were included. Second, an exhaustive search of the grey literature was not conducted. Third, the sample size in the included studies is too small to draw robust conclusions. Fourth, some reviews include studies with a high risk of bias, especially in randomisation and blinding of patients, therapists, and assessors.

5. Conclusions

This paper suggests that tDCS, in combination with other therapies, may help improve gait recovery in stroke patients. However, the results appear inconclusive, and the certainty of the evidence was classified as low and very low for most outcomes. Thus, the application of tDCS is classified as inconclusive, indicating that the review found low, very low or insufficient quality evidence for the effectiveness of the treatment.

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