Published in : Disability and Rehabilitation (2022), vol. 44, n°01, pp. 13–23
DOI: 10.1080/09638288.2020.1759703
Status : Postprint (Author's version)

EVALUATING THE EFFECTS OF TDCS IN STROKE PATIENTS USING FUNCTIONAL OUTCOMES: A SYSTEMATIC REVIEW

Stephen Bornheim[a,b], Aurore Thibaut[c], Charlotte Beaudart[d], Pierre Maquet[e], Jean-Louis Croisier[a,b] and Jean-François Kaux[a,b]

[a]Department of Physical Medicine and Rehabilitation, Liege University Hospital Center, Liege, Belgium; [b]Department of Sport and Rehabilitation Sciences, University of Liege, Liege, Belgium; [c]Coma science group, GIGA-Research, University and University hospital of Liege, Liege, Belgium; [d]Department of Public Health, Epidemiology and Health Economics, University of Liege, Liege, Belgium; [e]Department of Neurology, Liege University Hospital Center, Liege, Belgium

Keywords:

tDCS; stroke; functional outcomes; rehabilitation; physical therapy

Abstract

Background and purpose: Transcranial direct current stimulation (tDCS) has been extensively studied over the past 20 years to promote functional motor recovery after stroke. However, tDCS clinical relevance still needs to be determined. The present systematic review aims to determine whether tDCS applied to the primary motor cortex (M1) in stroke patients can have a positive effect on functional motor outcomes.

Materials and methods: Two databases (Medline & Scopus) were searched for randomized, double-blinded, sham-controlled trials pertaining to the use of M1 tDCS on cerebral stroke patients, and its effects on validated functional motor outcomes. When data were provided, effect sizes were calculated. PROSPERO registration number: CRD42018108157

Results: 46 studies (*n* = 1291 patients) met inclusion criteria. Overall study quality was good (7.69/10 on the PEDro scale). Over half (56.5%) the studies were on chronic stroke patients. There seemed to be a certain pattern of recurring parameters, but tDCS protocols still remain heterogeneous. Overall results were positive (71.7% of studies found that tDCS has positive results on functional motor outcomes). Effect-sizes ranged from 0 to 1.33. No severe adverse events were reported.

Conclusion: Despite heterogeneous stimulation parameters, outcomes and patient demographics, tDCS seems to be complementary to classical and novel rehabilitation approaches. With minimal adverse effects (if screening parameters are respected), none of which were serious, and a high potential to improve recovery when using optimal parameters (i.e.: 20min of stimulation, at 2mA with 25 or 35cm2 electrodes that are regularly humidified), tDCS could potentially be ready for clinical applications.

Published in : Disability and Rehabilitation (2022), vol. 44, n°01, pp. 13–23
DOI: 10.1080/09638288.2020.1759703
Status : Postprint (Author's version)

➢ **IMPLICATIONS FOR REHABILITATION**

- tDCS could potentially be ready for clinical application.
- Evidence of very low to very high quality is available on the effectiveness of tDCS to improve motor control following stroke.
- This should with caution be focused on the primary motor cortex.

Introduction

Motor recovery after stroke is often incomplete and is the 3rd most common cause of global disability [1]. The first three months in stroke recovery are extremely important, as most of the functional recovery happens in this period [2]. There are numerous approaches for stroke neurorehabilitation, and Transcranial Direct Current Stimulation (tDCS) seems to be an interesting adjuvant. Despite the technique having been used sporadically since the 1880s [3], as a treatment method, tDCS has been exponentially gaining popularity in the last 20 years [4]. Not only does it improve local blood circulation to ischemic areas [5], change interhemispheric inhibition (IHI) to a more balanced state [6], but studies are also showing potential neurogenesis [7]. tDCS also seems to be beneficial for certain complications of strokes, such as aphasia [8], dysphagia [9], and neglect [10].

It seems that the technique is getting close to transitioning from clinical trials to being potentially used in clinical practice [11]. However, to date, there is a vast amount of differences in settings (such as electrode placement, size and number as well as stimulation duration and intensity) and outcome measures (functional, analytical, upper or lower limb, motor or sensitive, etc.) making it extremely difficult for clinicians to make a well-considered decision. A recent survey has also found that questionable research practices and poor reproducibility are present in a large proportion of non-invasive brain stimulation studies [12].

Previous systematic literature reviews conclude that despite the heterogenous parameters (such as electrode placement, size and number as well as stimulation duration and intensity), tDCS seems to be beneficial for motor recovery after stroke [13], though, most studies are done on specifically selected patients (mainly mild to moderate deficits, and mostly in the subacute or chronic phase) [14].

There are significant modifications in functional and structural connectivity in the primary motor cortex following strokes [15] that can impact functional recovery. The primary motor cortex is subjected to a high level of reorganization in order to recover motor control [16] which could be potentiated by non-invasive brain stimulation [17].

Therefore, the scope of this systematic literature review was the effects of tDCS stimulating the primary motor cortex (M1), in randomized, double-blinded, sham-controlled trials, measured by validated, functional outcomes, useful for neuro-rehabilitation specialists working with stroke patients.

Published in : Disability and Rehabilitation (2022), vol. 44, n°01, pp. 13–23
DOI: 10.1080/09638288.2020.1759703
Status : Postprint (Author's version)

Methods

The following systematic literature adhered to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (see **Supplementary Annex 1**), and the protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO, registration number: CRD42018108157) database.

LITERATURE SEARCH

Our literature search was conducted through electronic searches of MEDLINE and SCOPUS. We searched for articles on MEDLINE up to the last week of September 2019, and SCOPUS up to the last week of September 2019. This study was subsequently updated to include studies published between the last week of September 2019 and the last week of March 2020. The search strategy and search terms used in this review can be found in **Supplementary Annex 2**.

The articles were exported to the COVIDENCE website (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia. Available at www.covidence.org).

SELECTION CRITERIA

Articles were selected using the COVIDENCE software. Two investigators (SB & AT) independently read through the titles and abstracts, selecting articles that initially fulfilled inclusion criteria (see **Table 1**). If there were discrepancies, a discussion to either include or exclude the article helped make the decision. If the issue remained unresolved, a third evaluator (JFK) had the final decision. Then both authors separately read all remaining articles full texts following the same decision-making process (**Figure 1**).

We did not restrict our inclusion studies based on the mode of stimulation, nor the stroke phase.

Table 1. Study characteristics

	Inclusion criteria	Exclusion criteria
Population	Cerebral strokes Adults	Other stroke locations (e.g., sedullary strokes) or other pathologies Healthy subjects Children
Intervention	tDCS M1 Stimulated	Other forms of transcranial brain stimulation (tACS, tRNS, TMS, rTMS) Other areas than M1 stimulated
Design	Randomized double-blinded (or pseudo-blinded) sham-controlled studies	Studies without a control group Single blinded
Outcomes	Validated functional motor, strength, gait, balance or sensory outcomes, spasticity measurements	Non-functional outcomes / non-validated outcomes: (e.g. pain, deglutition disorders, memory, speech disorders, neglect)
Language	English	Other than English studies

Published in : Disability and Rehabilitation (2022), vol. 44, n°01, pp. 13–23
DOI: 10.1080/09638288.2020.1759703
Status : Postprint (Author's version)

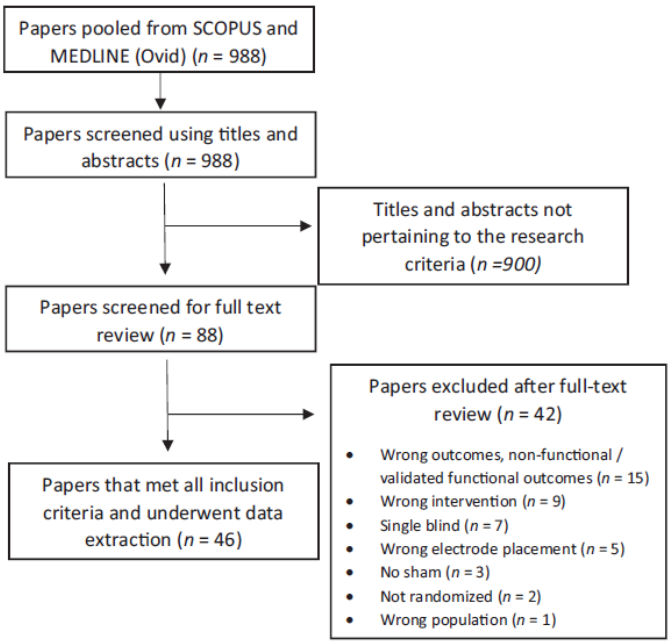

Figure 1. Flow chart of the selection of articles in our review.

DATA EXTRACTION

Data was extracted using a structured table (**Supplementary Annex 3**, summarized in **Table 2**) to include the following data: (1) Author and study information, (2) total number of participants (*n*), (3) mean age (range if available), (4) gender of participants, (5) handedness of participants, (6) stroke phase, (7) stroke type (ischemic/hemorrhagic), (8) stroke location (side and depth), (9) mean time since injury (range if available), (10) inclusion criteria, (11) exclusion criteria, (12) the trial design and blinding, (13) group distribution, (14) time of the evaluations and follow-ups, (15) the rehabilitation intervention, (16) the validated functional outcomes, (17) other eventual outcomes, (18) electrode location, (19) stimulation intensity, (20) duration of stimulation, (21) number of sessions, (22) sponge size and density (if available), (23) motor function results, (24) author-reported study limitations.

Published in : Disability and Rehabilitation (2022), vol. 44, n°01, pp. 13–23
DOI: 10.1080/09638288.2020.1759703
Status : Postprint (Author's version)

Table 2. Summary of included study data.

Study	*n*	Stroke phase	Stimulation type	Stimulation intensity (mA)	Stimulation duration (min)	Number of sessions	Electrode size (cm^2)	Outcomes measured	Effect of tDCS	Cohen's d
Alisar et al. [18]	32	Subacute & Chronic	Bilateral	2	30	15	22	FIM, UEFM	↑	0,31
Allman et al. [19]	24	Chronic	Anodal	1	20	9	35	ARAT, UEFM, WMFT	↑	0,25
Andrade et al. [20]	40	Subacute	Anodal	0,7	*N/A*	10	16	BBT, BI, mAS, MRC, UEFM	↑	Insufficient Data
Andrade et al. [21]	60	Acute	Anodal, Bilateral & Cathodal	2	*N/A*	10	35	6MWT, BBS, FES, FSST, STS	↑	Insufficient Data
Ang et al. [22]	19	Chronic	Bilateral	1	20	10	*N/A*	UEFM	–	0,08
Au-Yeung et al. [23]	10	Chronic	Anodal & Cathodal	1	20	3*1	35	PF, PPT	–	0
Beaulieu et al. [24]	14	Chronic	Bilateral	2	20	12	35	BBT, MALS, mAS, UEFM, WMFT	–	1,29
Bornheim et al. [25]	50	Acute	Anodal	2	20	20	25	BI, FMMA, SIS, SWMT, TS, WMFT	↑	1,1
Bolognini et al. [6]	14	Chronic	Bilateral	2	40	10	35	HGS, JTT, MALS, UEFM	↑	Insufficient Data
Chang et al. [26]	24	Subacute	Anodal	2	10	10	Anode: 7.07; Cathode: 28.26	BBS, FAC, LEFM,	↑	0,04
Danzl et al. [27]	8	Chronic	Anodal	2	20	12	Anode: 25; Cathode: 35	10mWT, BBS, FAC, TUG	↑	0,85
Dehem et al. [28]	21	Chronic	Bilateral	1	20	1	35	BBT, PPT	↑	0,02
Del Felice et al. [29]	10	Chronic	Bilateral & Cathodal	1	20	5	25	ARAT, BI, ESS, mAS, MRC, PASS	↑	Insufficient Data
Di Lazzaro et al., [30]	34	Acute	Bilateral	2	40	5	35	9HPT, ARAT, HGS, MALS, MRS,	–	Insufficient Data
Edwards et al. [31]	82	Chronic	Anodal	2	20	36	35	BI, MRC, WMFT	–	0,02
Figlewski et al. [32]	44	Chronic	Anodal	1,5	30	9	35	WMFT	↑	0,14
Fusco et al. [33]	11	Subacute	Extracephalic Cathodal	1,5	10	10	35	10mWT, 6MWT, 9HPT, BT, FAC, HGS, PF, RMI, TUG, UEFM	–	1,23
Fusco et al. [34]	8	Subacute	Anodal	1,5	15	2*1	35	9HPT, HGS, PF	↑	0,10
Geroin et al. [35]	20	Chronic	Anodal	1,5	7	10	35	10mWT, 6MWT, FAC, mAS, Mi-LE, RMI	–	0,35
Goodwill et al. [36]	15	Chronic	Bilateral	1,5	20	9	25	HGS, MAS, TS	–	1,06
Hesse et al. [37]	96	Subacute	Anodal & Cathodal	2	20	30	35	BBT, BI, FMMA, mAS, MRC	–	0,01
Hummel et al. [38]	11	Chronic	Anodal	1	20	2*1	25	PF	↑	0,62
Ilic et al. [39]	26	Chronic	Anodal	2	20	10	25	JTT, UEFM	↑	Insufficient Data
Khedr et al. [40]	40	Subacute	Anodal & Cathodal	2	25	6	35	BI, HGS, MRC, OMCASS	↑	Insufficient Data
Kim et al. [41]	18	Subacute	Anodal & Cathodal	2	20	10	25	BI, UEFM	↑	Insufficient Data
Klomjai et al. [42]	19	Subacute	Bilateral	2	20	1	35	STS, TUG	↑	0,43

(*continued*)

QUALITY ASSESSMENT

For the quality assessment, we used the Physiotherapy Evidence Database Scale (PEDro) to assess the methodological quality of included articles [63]. The scale uses 10 "yes"/"no" questions, rating internal validity of a clinical trial (the 11^{th} item is not considered for calculating the score, therefore scores range between 0 and 10). Studies are considered to be of excellent quality if scores are equal to or higher than 9/10, of good quality if between 6 and 8/10, fair quality if between 4 and 5/10 and poor quality if lower or equal to 3/10. As for data selection criteria, two investigators (SB & AT) independently read through the full text articles, evaluating each one individually. If there were discrepancies, a discussion took place to resolve the issue. If the issue remained unresolved, a third evaluator (JFK) had the final decision. As this scale uses the same questions as the Cochrane Risk of Bias tool, the PEDro score gives us insight into potential biases in the papers that we analyzed.

MONTAGE NOMENCLATURE

The following montages were used in the studies analyzed: anodal stimulation corresponds to the montage where the anode (active electrode) was placed over the affected primary motor cortex area (C3 or C4 position, according to the electroencephalogram 10/20 system) and the cathode (reference electrode) was placed in the contralateral supra-orbital region (respectively Fp2 or FP1). Cathodal stimulation corresponds to the montage where the cathode (active electrode) was placed over the unaffected primary motor cortex area and the anode (reference electrode) was placed in the

Published in : Disability and Rehabilitation (2022), vol. 44, n°01, pp. 13–23
DOI: 10.1080/09638288.2020.1759703
Status : Postprint (Author's version)

contralateral supra-orbital region. For bilateral stimulation, the anode (active electrode) was placed over the affected primary motor cortex area and the cathode (also an active electrode) was placed over the unaffected primary motor cortex area. For extracephalic cathodal montages, the cathode (active electrode) was placed over the unaffected primary motor cortex area and the anode (reference electrode) was placed above the right shoulder (non-cephalic). One article [57] used a combined anodal and cathodal montage.

STROKE PHASES

For clarity, strokes are considered acute if time post onset is less than 1 month, subacute if between 1 and 6 months, and chronic if over 6 months.

PRINCIPAL SUMMARY MEASURES

Effect sizes and the Spearman's rank-order correlations were calculated with TIBCO Software Inc. (2017). Statistica (version 13. http://statistica.io).

Results

Our study includes data pertaining from the last 20 years. In total, 46 randomized, controlled, double blinded (of which 10 crossover) trials were included, totaling 1291 patients. A preliminary analysis portrays the literature as being over diverse in terms of population, parameters studied (stimulation frequency, duration, intensity) and functional outcomes evaluating efficiency.

IDENTIFICATION AND SELECTION OF STUDIES

Searches on MEDLINE yielded 404 citations, while those on SCOPUS yielded 919. After the COVIDENCE software initially scanned for duplicates, 988 articles were included for title and abstract screening. Following that, 88 articles were retained to undergo a manual screening for duplicates and then a full-text review. 46 articles met our inclusion criteria. 42 were excluded for the following reasons: wrong outcomes, nonfunctional/validated functional outcomes (*n* = 15), wrong intervention (*n* = 9), single blind (n¼ 7), wrong electrode placement (*n* = 5), no sham (*n* = 3), not randomized (*n* = 2), wrong population (*n* = 1).

PATIENTS

A total of 1291 patients were analyzed, averaging 27.47 (± 19.86) 95%CI [21.7; 33.21] (min 8; max 96) per study. The average age of patients was 60.53 (±6.05) 95%CI [58.79; 62.28] years, with subjects ranging from 15 (only one of the 1291 patients was a minor) to 86 years old. 841 were male (65.14%), and 414 (92%) were right-handed, 34 (7.56%) left-handed and 2 (0.44%) ambidextrous (however only 23 articles (50%) reported patient handedness).

Published in : Disability and Rehabilitation (2022), vol. 44, n°01, pp. 13–23
DOI: 10.1080/09638288.2020.1759703
Status : Postprint (Author's version)

TDCS

Type of montage: as seen in **Table 2**, montages vary greatly. The articles included in this study however used anodal, bilateral or cathodal stimulations. While all of them are based on rebalancing interhemispheric inhibition (anodal tDCS increases IHI towards the contralateral side, cathodal tDCS decreases IHI towards the contralateral side, and bilateral combines both) [64], their mechanism is opposite.

Intensity of stimulation: Intensity varies between 0,7 and 2 mA, but most intensities are either 1 mA (30.43% of studies), 1,5mA (17.39% of studies) or 2 mA (45.65% of studies).

Duration of stimulation: Durations vary from 7 to 40 min, but most (56.52%) last 20 min.

Number of sessions: The number of sessions varies greatly, some studies stimulate every weekday for 4 weeks, some only stimulate once. Overall, most studies stimulate 5 times a week for two weeks, crossover studies usually have a single session of stimulation, and a washout period of a few days to a few weeks.

Current density: Sponge size is important, as the focalization of stimulations and current density increase as the size decreases [65]. However, none of the articles used in our review used HD-tDCS electrodes (despite this not being an exclusion criteria). Sponge sizes here varied between 7,07cm^2 and 35cm^2, most being 25cm^2 (19.57%) or 35cm^2 (58.7%). Very few studies supplied readers with current density (even if the calculation is easy). Available densities ranged from 0,04 to 0,08 A/m^2. The parameters remain there for heterogeneous without any justification of why.

PATHOLOGY

In agreement with other literature reviews, we find that the vast majority of our articles (26 (56.5%)) relate to work on chronic stroke patients, 6 (13%) on subacute patients, and 10 (21.7%) acute. 4 (8.7%) studies looked at two populations (chronic and subacute) and one study was counted twice as there were two experiments in the same publication [30].

Of the 1291 subjects, 1202 (93.1%) had their stroke type described (ischemic or hemorrhagic). 1063 (88.43%) were ischemic, 139 (11.56%) were hemorrhagic.

1168 (90.47%) patients had their stroke location's side described (518 right, 649 left, 1 bilateral). 682 (52.8%) had their stroke location's depth described: 198 (29.03%) were pure cortical strokes, 294 (43.12%) subcortical and 190 (27.85%) were mixed cortical subcortical.

Published in : Disability and Rehabilitation (2022), vol. 44, n°01, pp. 13–23
DOI: 10.1080/09638288.2020.1759703
Status : Postprint (Author's version)

Table 2. Continued.

Study	*n*	Stroke phase	Stimulation type	Stimulation intensity (mA)	Stimulation duration (min)	Number of sessions	Electrode size (cm^2)	Outcomes measured	Effect of tDCS	Cohen's d
Lefebvre et al. [43]	19	Chronic	Bilateral	1	20	2*1	35	PPT	↑	Insufficient Data
Lindenberg et al. [44]	20	Chronic	Bilateral	1,5	30	5	16,3	UEFM, WMFT	↑	0,29
Marquez et al. [45]	25	Chronic	Anodal & Cathodal	1	20	3*1	35	HGS, JTT, PF	–	Insufficient Data
Menezes et al. [46]	20	Chronic	Anodal	1	20	4*1	***N/A***	Active ROM, HGS, PF	–	0,02
Mortensen et al. [47]	15	Chronic	Anodal	1,5	20	5	35	HGS, JTT	↑	Insufficient Data
Nair et al. [48]	14	Chronic	Cathodal	1	30	5	***N/A***	Active ROM, UEFM	↑	1,01
Rabadi et al. [49]	16	Acute	Cathodal	1	30	10	35	ARAT	–	0,88
Rocha et al. [50]	21	Chronic	Anodal & Cathodal	1	anodal: 13; cathodal: 9	12	35	HGS, MALS, UEFM	↑	0,22
Rossi et al. [51]	50	Acute	Anodal	2	20	5	35	BI, FMMA, MRS	–	0,16
Saeys et al. [52]	31	Subacute	Bilateral	1,5	20	2*16	35	POMA, RMI, TIS	↑	0,94
Salazar et al. [53]	30	Chronic	Bilateral	2	30	10	25	HGS, UEFM	↑	0,79
Sattler et al. [54]	20	Acute	Anodal	1,2	13	5	35	9HPT, HTap, HGS, JTT, UEFM	↑	0,65
Seo et al. [55]	21	Chronic	Anodal	2	20	10	35	10mWT, 6MWT, BBS, FAC, LEFM, MRC	↑	1,33
Shaheiwola et al. [56]	30	Chronic	Bilateral	2	20	20	25	mAS, UEFM, WMFT	↑	0,28
Sik et al. [57]	31	Chronic	Anodal and Anodal + Cathodal	2	20	15	16	JTT, WMFT	↑	Insufficient Data
Straudi et al. [58]	23	Subacute and Chronic	Bilateral	1	30	10	35	BBT, MALS, UEFM	↑	0,04
Tahtis et al. [59]	14	Subacute	Bilateral	2	15	1	25	POMA, TUG	↑	1,21
Triccas et al. [60]	22	Subacute and Chronic	Anodal	1	20	18	35	ARAT, MALS, UEFM	–	0,70
Viana et al. [61]	20	Chronic	Anodal	2	13	15	35	HGS, mAS, UEFM, WMFT	↑	0,29
Wu et al. [62]	90	Subacute and Chronic	Extracephalic Cathodal	1,2	20	20	24,75	BI, mAS, UEFM	↑	Insufficient Data

n: number of subjects who received motor cortical stimulation; 10mWT: 10 m Walking Test; 6MWT: 6 min Walk Test; 9HPT: Nine-hole peg test; Active ROM: active range of motion; ARAT: Action Research Arm Test; BBS: Berg Balance Scale; BBT: Box block test; BI: Barthel Index or modified Barthel Index; ESS: European Stroke Scale; FAC: Functional Ambulatory Category; FES: Fall Efficacy Scale; FIM: Functional Independence Measure; FMMA: Fugl-Meyer Motor Assessment; FSST: Four Square Step Test; HTap: Hand Tapping Test) , HGS: Handgrip Strength; JTT: Jebsen-Taylor Hand Function Test; LEFM: Lower Extremity Fugl-Meyer; MALS: Motor Activity Log Scale; mAS: Modified Ashworth Scale; MAS: Motor Assessment Scale; MFT: Manual Function Test; MI: Motricity Index; Mi-LE: Lower Limb Motricity Index; MRC: Medical Research Council Scale) = Lovett=Manual Muscle Test, MRS: Modified Rankin Scale; OMCASS: Orgogozo Stroke Scale; PASS: Postural Assessment Scale for Stroke; PF: Pinch Force; POMA: Performance-Oriented Mobility Assessment) =Tinetti, PPT: Purdue Pegboard Test; RMI: Rivermead Mobility Index; SIS: Stroke Imact Scale; STS: Sit to Stand; SWMT: Semmes Weinstein Monofilament Test; TIS: Trunk Impairment Scale; TS: Tardieu Scale; TUG: Time Up and Go; UEFM: Upper Extremity Fugl-Meyer; WMFT: Wolf Motor Function Test.

INTERVENTIONS

Rehabilitation protocols were heterogeneous in terms of types (1 study used GRASP (Graded Repetitive Arm Supplementary Program) (2.1%), 1 MI-BCI (Brain-computer interface-assisted motor imagery) (2.1%), 1 VRT (Virtual Reality Treatment) (2.1%), 1 PRT (Progressive Resistance Training) (2.1%), 2 RPNSS (Repetitive Peripheral Nerve Sensory Stimulation) (4.3%), 2 FES (Functional Electrical Stimulation) (4.3%), 5 CIMT (Constraint Induced Motor Therapy) (10.6%), 8 RAT (Robot Assisted Therapy) (17%), 19 conventional rehabilitation (43.12%), and 7 (14.9%) studies did not use any intervention).

EVALUATIONS

As seen in **Table 2**, there is a considerable heterogeneity of evaluations (40 validated different ones used in the 46 articles retained). The time of evaluations was also heterogeneous, varying from a single post-stimulation assessment, to follow-ups to evaluations at six months post intervention. Most data (71.7%) pertains to upper limbs, there is a huge lack of data on lower extremities and balance (17.4% of studies), and most upper extremity evaluations are subjective and not really functional (i.e.: Upper Extremity Fugl-Meyer). 10.9% of studies looked at both upper and lower extremities.

Published in : Disability and Rehabilitation (2022), vol. 44, n°01, pp. 13–23
DOI: 10.1080/09638288.2020.1759703
Status : Postprint (Author's version)

EFFECTS ON MOTOR OUTCOMES

The effects of tDCS on functional outcomes in stroke patients has been, and still is, very controversial. 13 of the 46 studies (28.3%) found that tDCS had no effect on functional motor improvement and 71.7% found some form of improvement after tDCS. More specifically, 7 out the 10 acute patient studies showed improvements after tDCS, 5 out of 6 subacute patient studies, 19 out of 26 chronic patient studies and 2 out of 4 studies that looked at both chronic and subacute phases. Tests and improvements are summarized in **Table 2**.

EFFECT SIZE

Effect sizes are summarized in **Table 2**. The average effect size was 0.51 (±0.45) 95% CI [0.35; 0.66] and ranged from 0 to 1.33. The effect sizes were considered as very small (between 0.01 and 0.2), small (between 0.2 and 0.5), medium (between 0.5 and 0.8), large (between 0.8 and 1.2), very large (between 1.2 and 2) [66,67]. Overall, 11 articles had very small effect sizes, 8 had small effect sizes, 4 had medium effect sizes, 6 had large effect sizes, and 4 had very large effect sizes. The Spearman's rank-order correlation between number of sessions and effect size (R = 0,03, p = 0.85), between intensity and effect size (R = 0.23, p = 0.21), and duration and effect size (R = 0.0004, p = 0.99) was calculated. The Kruskal–Wallis test was used to compare stroke phases and effect sizes (p = 0.49). We also looked at the effect of montage types on effect sizes (p = 0.06). There is insufficient data to compare effect sizes between hemorrhagic and ischemic strokes, as well as by the location of strokes.

ADVERSE EFFECTS

Similarly to Brunoni's systematic review [68], there seems to be a lack of assessing and reporting adverse effects of tDCS in the literature. We found that 32 studies (=69.57%) of our articles reported if there were adverse effects or not, compared to 56% in Brunoni's review. Of these 32 studies 17 (53.13%) reported at least one adverse effect (compared to 63% in Brunoni's review). The adverse effects (and number of studies in which the occurred) were: dizziness (1), warmth (1), trouble concentrating (1), light flashes (2), discomfort (3), sleepiness (4), mild itching (5), burning sensation (6), redness (6), headaches (7), tingling (12).

QUALITY ASSESSMENT

The overall quality of the studies was good. The average score for articles analyzed was 7.69/10 (±1.19) (min 6; max 10) 95% CI [7.35; 8.04] (**Table 3**). The Mann-Whitney U test did not show any significant (p¼ 0.81) differences between the quality of studies that found that tDCS improved performances, and those that did not.

Published in : Disability and Rehabilitation (2022), vol. 44, n°01, pp. 13–23
DOI: 10.1080/09638288.2020.1759703
Status : Postprint (Author's version)

Table 3. Pedro Scores. All studies included specified eligibility criteria.

Study	Pedro item 2	Pedro item 3	Pedro item 4	Pedro item 5	Pedro item 6	Pedro item 7	Pedro item 8	Pedro item 9	Pedro item 10	Pedro item 11	Total PEDro Score (/10)
Alisar et al. [18]	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	7
Allman et al. [19]	Yes	Yes	No	Yes	No	Yes	Yes	No	Yes	Yes	7
Andrade et al. [20]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	8
Andrade et al. [21]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Ang et al. [22]	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes	7
Au-Yeung et al. [23]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Beaulieu et al. [24]	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes	7
Bornheim et al. [25]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Bolognini et al. [6]	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
Chang et al. [26]	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	7
Danzl et al. [27]	Yes	No	Yes	Yes	No	Yes	No	Yes	Yes	No	6
Dehem et al. [28]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Del Felice et al. [29]	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	7
Di Lazzaro et al., [30]	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
Edwards et al. [31]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Figlewski et al. [32]	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
Fusco et al. [33]	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	7
Fusco et al. [34]	Yes	Yes	No	Yes	No	Yes	Yes	No	No	Yes	6
Geroin et al. [35]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	9
Goodwill et al. [36]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	9
Hesse et al. [37]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	9
Hummel et al. [38]	No	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	6
Ilic et al. [39]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	9
Khedr et al. [40]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	8
Kim et al. [41]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	9
Klomjai et al. [42]	Yes	No	Yes	Yes	Yes	Yes	No	No	Yes	Yes	7
Lefebvre et al. [43]	No	No	Yes	Yes	Yes	No	Yes	No	Yes	Yes	6
Lindenberg et al. [44]	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	7
Marquez et al. [45]	Yes	Yes	No	Yes	No	Yes	Yes	No	Yes	Yes	7
Menezes et al. [46]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	9
Mortensen et al. [47]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	9
Nair et al. [48]	Yes	No	Yes	Yes	No	Yes	No	No	Yes	Yes	6
Rabadi et al. [49]	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	8
Rocha et al. [50]	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	8

(continued)

Table 3. Continued.

Study	Pedro item 2	Pedro item 3	Pedro item 4	Pedro item 5	Pedro item 6	Pedro item 7	Pedro item 8	Pedro item 9	Pedro item 10	Pedro item 11	Total PEDro Score (/10)
Rossi et al. [51]	Yes	No	Yes	Yes	No	No	Yes	No	Yes	Yes	6
Saeys et al. [52]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	9
Salazar et al. [53]	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	8
Sattler et al. [54]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	9
Seo et al. [55]	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	8
Shaheiwola et al. [56]	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	7
Sik et al. [57]	Yes	No	Yes	Yes	No	Yes	No	No	Yes	Yes	6
Straudi et al. [58]	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	8
Tahtis et al. [59]	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	7
Triccas et al. [60]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	9
Viana et al. [61]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	9
Wu et al. [62]	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	8

Discussion

The results of this systematic literature review bring together evidence from 46 different randomized, double-blinded, sham-controlled trials of overall good quality. We can cautiously conclude that motor cortical tDCS seems to be an effective tool for functional stroke rehabilitation, but because of heterogeneity of stimulation parameters, evaluation tools and patient demographics, results remain inconsistent. Based on these results, there does not seem to be a superior montage, or other parameters, nor an optimal amount of sessions.

Published in : Disability and Rehabilitation (2022), vol. 44, n°01, pp. 13–23
DOI: 10.1080/09638288.2020.1759703
Status : Postprint (Author's version)

14 of the 33 studies with available effect sizes, had medium to very large effect sizes (the average being considered as a medium effect size). This is encouraging, despite the variability in parameters and outcomes.

One of the main factors lacking in half of the studies was patient handedness. This is an important factor to take into account when talking about brain modulation techniques, as there are cortical and subcortical asymmetries between left and right-handed people [69].

Concerning electrode locations, 31/46 studies used the international 10-20 EEG system as a standardized measure of placing electrodes. However, placement remains vague and not tailored to individual variability of cortical mapping. 8 studies used TMS (which is proven to have much higher precision that the 10-20 system [70]) and 2 MRI to place electrodes. 5 studies did not specify how they placed electrodes.

Most studies are conducted on chronic stroke patients, most probably due to the easier recruitment and screening, but also due to the fact that as stroke recovery significantly slows down after 6 months [2], by implementing a new rehabilitation technique (such as tDCS), if significant improvements are observed, they are much more likely to be due to the technique than spontaneous recovery.

Another analysis lacking in studies was the comparison between the effects of tDCS on ischemic and hemorrhagic strokes. Ischemic strokes seem to cause less impairment than hemorrhagic strokes, however recovery is slower [71]. Despite over half the patients having the location or depth of their stroke described, only 4 studies compared outcomes based on this. Overall, responsiveness to tDCS seems to be better with subcortical strokes (despite being anatomically further away from the stimulation site than cortical strokes). However, it has been shown that subcortical lesions recover much faster than cortical lesions [72].

For outcomes, it is important to distinguish strength and dexterity measures. The vast majority of the tests measure complex tasks that require a certain degree of coordination, others measure simple movements, and others objectively measure strength with precision tools.

This review finds that tDCS is well supported by patients, and secondary effects are very limited (the majority of patients only feel a slight tingling or mild burning sensation). But it is important to keep in mind that even if increasing densities increases the depth of the penetration of the electrical field, it also increases discomfort [73].

Despite the relative controversial results, with no serious adverse effects, on the basis of this literature, tDCS seems to be ready to be used in a clinical setting, as long as patients are correctly screened [74] and ideal parameters are used (in accordance with safety standards [4]).

It is important to remember that tDCS has never been intended to replace physical therapy, on the contrary, through this literature review, tDCS seems to be a good adjuvant to classical and novel rehabilitation protocols.

Our study does contain certain limitations. One limitation is that grey literature was not analyzed. This systematic literature review was based on the results of two databases. Increasing the number of databases could have made this review more exhaustive but according to the new version of AMSTAR2, a minimum of 2 bibliographic databases is necessary for the search strategy. Another

Published in : Disability and Rehabilitation (2022), vol. 44, n°01, pp. 13–23
DOI: 10.1080/09638288.2020.1759703
Status : Postprint (Author's version)

limitation is that only motor cortex stimulation studies were included. Obviously, there is a wide variety of regions, other that M1 that can be damaged by strokes (**Table 2**).

Conclusion

Despite being around for 20 years, there is still a huge variability in stimulation parameters and outcomes measured, which needs to be addressed. Despite the lack of consensus, tDCS is a safe and useful method in potentializing and improving upon classical and novel neuro-rehabilitation techniques.

Supplementary Data

ANNEX 1

doi.org/10.1080/09638288.2020.1759703

ANNEX 2 : SCOPUS AND MEDLINE SEARCH STRATEGY

Scopus:

(((TITLE-ABS-KEY (transcranial AND direct AND current AND stimulation) OR TITLE-ABS-KEY (tdcs) OR TITLE-ABS-KEY (transcranial W/4 stimulation))) AND ((TITLE-ABS-KEY (stroke*) OR TITLE-ABS-KEY (cerebrovascular AND accident*) OR TITLE-ABS-KEY (cva) OR TITLE-ABS-KEY (brain W/5 vascular AND accident)))) AND ((TITLE-ABS-KEY (random* AND controlled AND trial) OR TITLE-ABS-KEY (random* AND clinical AND trial) OR TITLE-ABS-KEY (controlled AND clinical AND trial) OR TITLE-ABS-KEY (placebo W/2 controlled) OR TITLE-ABS-KEY (sham W/2 controlled) OR TITLE-ABS-KEY (random* W/2 double-blind*) OR TITLE-ABS-KEY (random* W/2 allocation) OR TITLE-ABS-KEY (rct))) AND (LIMIT-TO (LANGUAGE , "English ")) AND (LIMIT-TO (EXACTKEYWORD , "Human ")).

MEDLINE:

(transcranial direct current stimulation/ OR tdcs*.ti,ab,kf OR (transcranial adj4 stimulation*).ti,ab,kf) AND (exp Stroke/ OR stroke*.ti,ab,kf OR cerebrovascular accident*.ti,ab,kf OR CVA*.ti,ab,kf OR (Brain adj5 vascular accident).ti,ab,kf) AND limit to (english language and humans) AND (Randomized Controlled Trials as Topic/ OR Controlled Clinical Trials as Topic/ OR ("Randomized controlled trial*" or "Randomized clinical trial*" or "Controlled clinical trial*" or Placebo-controlled or Sham-controlled or "Randomized double-blind*" or (Random* adj2 allocat*) or RCT).ti,ab,kw,pt)

Published in : Disability and Rehabilitation (2022), vol. 44, n°01, pp. 13–23
DOI: 10.1080/09638288.2020.1759703
Status : Postprint (Author's version)

ANNEX 3: PRISMA 2009 CHECKLIST

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4 & 5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	4
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5 & 6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5 & 6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	N/A

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	N/A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	5
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Annexe 2
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Annexe 3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Annexe 2
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	10& 11
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	11 & 12
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	13
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	14

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

Published in : Disability and Rehabilitation (2022), vol. 44, n°01, pp. 13–23
DOI: 10.1080/09638288.2020.1759703
Status : Postprint (Author's version)

Disclosure statement

No potential conflict of interest was reported by the author(s).

References

[1] Feigin VL, Norrving B, Mensah GA. Global burden of stroke. Circ Res. 2017;120(3):439–448.
[2] Lee KB, Lim SH, Kim KH, et al. Six-month functional recovery of stroke patients: a multi-time-point study. Int J Rehabil Res. 2015;38(2):173–180.
[3] Zago S, Ferrucci R, Fregni F, et al. Bartholow, Sciamanna, Alberti: pioneers in the electrical stimulation of the exposed human cerebral cortex. Neuroscientist. 2008;14(5): 521–528.
[4] Bikson M, Grossman P, Thomas C, et al. Safety of transcranial direct current stimulation: evidence based update 2016. Brain Stimul. 2016;9(5):641–661.
[5] Zheng X, Alsop DC, Schlaug G. Effects of transcranial direct current stimulation (tDCS) on human regional cerebral blood flow. Neuroimage. 2011;58(1):26–33.
[6] Bolognini N, Vallar G, Casati C, et al. Neurophysiological and behavioral effects of tDCS combined with constraint-induced movement therapy in poststroke patients. Neurorehabil Neural Repair. 2011;25(9):819–829.
[7] Braun R, Klein R, Walter HL, et al. Transcranial direct current stimulation accelerates recovery of function, induces neurogenesis and recruits oligodendrocyte precursors in a rat model of stroke. Exp Neurol. 2016;279:127–136.
[8] Galletta EE, Conner P, Vogel-Eyny A, et al. Use of tDCS in aphasia rehabilitation: a systematic review of the behavioral interventions implemented with noninvasive brain stimulation for language recovery. Am J Speech-Language Pathol. 2016;25:S854.
[9] Pisegna JM, Kaneoka A, Pearson WG, et al. Effects of noninvasive brain stimulation on post-stroke dysphagia: a systematic review and meta-analysis of randomized controlled trials HHS Public Access. Clin Neurophysiol. 2016;127(1): 956–968.
[10] Bornheim S, Maquet P, Croisier JL, et al. Motor cortex transcranial Direct Current Stimulation (tDCS) improves acute stroke visuo-spatial neglect: a series of four case reports. Brain Stimul. 2018;11(2):459–461.
[11] Page SJ, Cunningham DA, Plow E, et al. It takes two: noninvasive brain stimulation combined with neurorehabilitation. Arch Phys Med Rehabil. 2015;96(4):S89–S93.
[12] Heroux ME, Loo CK, Taylor JL, et al. Questionable science and reproducibility in electrical brain stimulation research. 2017;12(4):e0175635.
[13] Adeyemo BO, Simis M, Macea DD, et al. Systematic review of parameters of stimulation, clinical trial design characteristics, and motor outcomes in non-invasive brain stimulation in stroke. Front Psychiatry. 2012;3:88.
[14] Marquez J, van Vliet P, McElduff P, et al. Transcranial direct current stimulation (tDCS): does it have merit in stroke rehabilitation? A systematic review. Int J Stroke. 2015;10(3): 306–316.
[15] Li Y, Wang D, Zhang H, et al. Changes of brain connectivity in the primary motor cortex after subcortical stroke. Med (United States). 2016;95(6):e2579.
[16] Dancause N. Vicarious function of remote cortex following stroke: recent Evidence from human and animal studies. Neuroscientist. 2006;12(6):489–499.

Published in : Disability and Rehabilitation (2022), vol. 44, n°01, pp. 13–23
DOI: 10.1080/09638288.2020.1759703
Status : Postprint (Author's version)

[17] Polanıa R, Paulus W, Nitsche MA. Modulating cortico-striatal and thalamo-cortical functional connectivity with transcranial direct current stimulation. Hum Brain Mapp. 2012; 33(10):2499–2508.

[18] Alisar DC, Ozen S, Sozay S. Effects of bihemispheric transcranial direct current stimulation on upper extremity function in stroke patients: a randomized double-blind sham-controlled study. J Stroke Cerebrovasc Dis. 2020;29(1): 104454.

[19] Allman C, Amadi U, Winkler AM, et al. Ipsilesional anodal tDCS enhances the functional benefits of rehabilitation in patients after stroke. Sci Transl Med. 2016;8(330): 330re1–330re1.

[20] Andrade SM, Batista LM, Nogueira L, et al. Constraintinduced movement therapy combined with transcranial direct current stimulation over premotor cortex improves motor function in severe stroke: A pilot randomized controlled trial. Rehabil Res Pract. 2017;2017:1–9.

[21] Andrade SM, Ferreira JJ, de A, Rufino TS, Medeiros G, et al. Effects of different montages of transcranial direct current stimulation on the risk of falls and lower limb function after stroke. Neurol Res. 2017;39(12):1037–1043.

[22] Ang KK, Guan C, Phua KS, et al. Facilitating effects of transcranial direct current stimulation on motor imagery brain-computer interface with robotic feedback for stroke rehabilitation. Arch Phys Med Rehabil. 2015;96(3):S79–S87.

[23] Au-Yeung SSY, Wang J, Chen Y, et al. Transcranial direct current stimulation to primary motor area improves hand dexterity and selective attention in chronic stroke. Am J Phys Med Rehabil. 2014;93(12):1057–1064.

[24] Beaulieu LD, Blanchette AK, Mercier C, et al. Efficacy, safety, and tolerability of bilateral transcranial direct current stimulation combined to a resistance training program in chronic stroke survivors: A double-blind, randomized, placebo-controlled pilot study. RNN. 2019;37(4):333–346.

[25] Bornheim S, Croisier JL, Maquet P, et al. Transcranial direct current stimulation associated with physical-therapy in acute stroke patients - A randomized, triple blind, sham-controlled study. Brain Stimul. 2020;13(2):329–336.

[26] Chang MC, Kim DY, Park DH. Enhancement of cortical excitability and lower limb motor function in patients with stroke by transcranial direct current stimulation. Brain Stimul. 2015;8(3):561–566.

[27] Danzl MM, Chelette KC, Lee K, et al. Brain stimulation paired with novel locomotor training with robotic gait orthosis in chronic stroke: a feasibility study. NRE. 2013; 33(1):67–76.

[28] Dehem S, Gilliaux M, Lejeune T, et al. Effectiveness of a single session of dual-transcranial direct current stimulation in combination with upper limb robotic-assisted rehabilitation in chronic stroke patients. Int J Rehabil Res. 2018;41(2): 138–145.

[29] Del Felice A, Daloli V, Masiero S, et al. Contralesional cathodal versus dual transcranial direct current stimulation for decreasing upper limb spasticity in chronic Stroke individuals: a clinical and neurophysiological study. J Stroke Cerebrovasc Dis. 2016;25(12):2932–2941.

[30] Di Lazzaro V, Dileone M, Capone F, et al. Immediate and late modulation of interhemipheric imbalance with bilateral transcranial direct current stimulation in acute stroke. Brain Stimul. 2014;7(6):841–848.

[31] Edwards DJ, Cortes M, Rykman-Peltz A, et al. Clinical improvement with intensive robot-assisted arm training in chronic stroke is unchanged by supplementary tDCS. RNN. 2019;37(2):167–180.

[32] Figlewski K, Blicher JU, Mortensen J, et al. Transcranial direct current stimulation potentiates improvements in functional ability in patients with chronic stroke receiving constraint-induced movement therapy. Stroke. 2017;48(1): 229–232.

Published in : Disability and Rehabilitation (2022), vol. 44, n°01, pp. 13–23
DOI: 10.1080/09638288.2020.1759703
Status : Postprint (Author's version)

[33] Fusco A, Assenza F, Iosa M, et al. The ineffective role of cathodal tDCS in enhancing the functional motor outcomes in early phase of stroke rehabilitation: an experimental trial. Biomed Res Int. 2014;2014:547290.

[34] Fusco A, Iosa M, Venturiero V, et al. After vs. priming effects of anodal transcranial direct current stimulation on upper extremity motor recovery in patients with subacute stroke. Restor Neurol Neurosci. 2014;32(2):301–312.

[35] Geroin C, Picelli A, Munari D, et al. Combined transcranial direct current stimulation and robot-assisted gait training in patients with chronic stroke: a preliminary comparison. Clin Rehabil. 2011;25(6):537–548.

[36] Goodwill AM, Teo W-P, Morgan P, et al. Bihemispheric-tDCS and upper limb rehabilitation improves retention of motor function in chronic stroke: a pilot study. Front Hum Neurosci. 2016;10:258.

[37] Hesse S, Waldner A, Mehrholz J, et al. Combined transcranial direct current stimulation and robot-assisted arm training in subacute stroke patients: an exploratory, randomized multicenter trial. Neurorehabil Neural Repair. 2011;25(9): 838–846.

[38] Hummel FC, Voller B, Celnik P, et al. Effects of brain polarization on reaction times and pinch force in chronic stroke. BMC Neurosci. 2006;7(1):73.

[39] Ilic NV, Dubljanin-Raspopovic E, Nedeljkovic U, et al. Effects of anodal tDCS and occupational therapy on fine motor skill deficits in patients with chronic stroke. RNN. 2016; 34(6):935–945.

[40] Khedr EM, Shawky OA, El-Hammady DH, et al. Effect of anodal versus cathodal transcranial direct current stimulation on stroke rehabilitation: a pilot randomized controlled trial. Neurorehabil Neural Repair. 2013;27(7):592–601.

[41] Kim DY, Lim J-Y, Kang EK, et al. Effect of transcranial direct current stimulation on motor recovery in patients with subacute stroke. Am J Phys Med Rehabil. 2010;89:879–886.

[42] Klomjai W, Aneksan B, Pheungphrarattanatrai A, et al. Effect of single-session dual-tDCS before physical therapy on lower-limb performance in sub-acute stroke patients: A randomized sham-controlled crossover study. Ann Phys Rehabil Med. 2018;61(5):286–291.

[43] Lefebvre S, Thonnard J-L, Laloux P, et al. Single session of dual-tDCS transiently improves precision grip and dexterity of the paretic hand after stroke. Neurorehabil Neural Repair. 2014;28(2):100–110.

[44] Lindenberg R, Renga V, Zhu LL, et al. Bihemispheric brain stimulation facilitates motor recovery in chronic stroke patients. Neurology. 2010;75(24):2176–2184.

[45] Marquez JL, Conley AC, Karayanidis F, et al. Determining the benefits of transcranial direct current stimulation on functional upper limb movement in chronic stroke. Int J Rehabil Res. 2017;40(2):138–145.

[46] Menezes IS, Cohen LG, Mello EA, et al. Combined brain and peripheral nerve stimulation in chronic stroke patients with moderate to severe motor impairment. Neuromodulation Technol Neural Interface. 2018;21(2):176–183.

[47] Mortensen J, Figlewski K, Andersen H. Combined transcranial direct current stimulation and home-based occupational therapy for upper limb motor impairment following intracerebral hemorrhage: a double-blind randomized controlled trial. Disabil Rehabil. 2016;38(7):637–643.

[48] Nair D, Renga V, Lindenberg R, et al. Optimizing recovery potential through simultaneous occupational therapy and non-invasive brain-stimulation using tDCS. Restor Neurol Neurosci. 2011;29(6):411–420.

Published in : Disability and Rehabilitation (2022), vol. 44, n°01, pp. 13–23
DOI: 10.1080/09638288.2020.1759703
Status : Postprint (Author's version)

[49] Rabadi MH, Aston CE. Effect of transcranial direct current stimulation on severely affected arm-hand motor function in patients after an acute ischemic stroke. Am J Phys Med Rehabil. 2017;96:S178–S84.

[50] Rocha S, Silva E, Foerster A, et al. The impact of transcranial direct current stimulation (tDCS) combined with modified constraint-induced movement therapy (mCIMT) on upper limb function in chronic stroke: a double-blind randomized controlled trial. Disabil Rehabil. 2016;38(7): 653–660.

[51] Rossi C, Sallustio F, Di Legge S, et al. Transcranial direct current stimulation of the affected hemisphere does not accelerate recovery of acute stroke patients. Eur J Neurol. 2013;20(1):202–204.

[52] Saeys W, Vereeck L, Lafosse C, et al. Transcranial direct current stimulation in the recovery of postural control after stroke: a pilot study. Disabil Rehabil. 2015;37(20): 1857–1863.

[53] Salazar AP, Cimolin V, Schifino GP, et al. Bi-cephalic transcranial direct current stimulation combined with functional electrical stimulation for upper-limb stroke rehabilitation: A double-blind randomized controlled trial. Ann Phys Rehabil Med. 2020;63(1):4–11.

[54] Sattler V, Acket B, Raposo N, et al. Anodal tDCS combined with radial nerve stimulation promotes hand motor recovery in the acute phase after ischemic stroke. Neurorehabil Neural Repair. 2015;29(8):743–754.

[55] Seo HG, Lee WH, Lee SH, et al. Robotic-assisted gait training combined with transcranial direct current stimulation in chronic stroke patients: A pilot double-blind, randomized controlled trial. RNN. 2017;35(5):527–536.

[56] Shaheiwola N, Zhang B, Jia J, et al. Using tDCS as an add-on treatment prior to FES therapy in improving upper limb function in severe chronic stroke patients: a randomized controlled study. Front Hum Neurosci. 2018;12:233.

[57] Şik BY, Dursun N, Dursun E, et al. Transcranial direct current stimulation: the effects on plegic upper extremity motor function of patients with stroke. J Neurol Sci. 2015; 32:320–334.

[58] Straudi S, Fregni F, Martinuzzi C, et al. tDCS and robotics on upper limb stroke rehabilitation: effect modification by stroke duration and type of stroke. Biomed Res Int. 2016; 2016:5068127.

[59] Tahtis V, Kaski D, Seemungal BM. The effect of single session bi-cephalic transcranial direct current stimulation on gait performance in sub-acute stroke: A pilot study. Restor Neurol Neurosci. 2014;32(4):527–532.

[60] Triccas LT, Burridge JH, Hughes A, et al. A double-blinded randomised controlled trial exploring the effect of anodal transcranial direct current stimulation and uni-lateral robot therapy for the impaired upper limb in sub-acute and chronic stroke. NRE. 2015;37(2):181–191.

[61] Viana RT, Laurentino GEC, Souza RJP, et al. Effects of the addition of transcranial direct current stimulation to virtual reality therapy after stroke: a pilot randomized controlled trial. NRE. 2014;34(3):437–446.

[62] Wu D, Qian L, Zorowitz RD, et al. Effects on decreasing upper-limb poststroke muscle tone using transcranial direct current stimulation: a randomized sham-controlled study. Arch Phys Med Rehabil. 2013;94(1):1–8.

[63] Maher CG, Sherrington C, Herbert RD, et al. Reliability of the PEDro Scale for Rating Quality of Randomized Controlled Trials. Phys Ther. 2003;83(8):713–721.

[64] Tazoe T, Endoh T, Kitamura T, et al. Polarity specific effects of transcranial direct current stimulation on interhemispheric inhibition. PLoS One. 2014;9(12): e114244.

[65] Nitsche MA, Doemkes S, Karakose T, et al. Shaping the effects of transcranial direct current stimulation of the human motor cortex. J Neurophysiol. 2007;97(4):3109–3117.

Published in : Disability and Rehabilitation (2022), vol. 44, n°01, pp. 13–23
DOI: 10.1080/09638288.2020.1759703
Status : Postprint (Author's version)

[66] Sawilowsky SS. New effect size rules of thumb. J Mod App Stat Meth. 2009;8(2):597–599.
[67] Cohen J. Statistical power analysis for the behavioral sciences. Routledge; 1988.
[68] Brunoni AR, Amadera J, Berbel B, et al. A systematic review on reporting and assessment of adverse effects associated with transcranial direct current stimulation. Int J Neuropsychopharmacol. 2011;14(8):1133–1145.
[69] Toga AW, Thompson PM. Mapping brain asymmetry. NatRev Neurosci. 2003;4(1):37–48.
[70] Rich TL, Menk JS, Rudser KD, et al. Determining electrode placement for transcranial direct current stimulation: a comparison of EEG- Versus TMS-guided methods. Clin EEG Neurosci. 2017;48(6):367–375.
[71] Kelly PJ, Furie KL, Shafqat S, et al. Functional recovery following rehabilitation after hemorrhagic and ischemic stroke. Arch Phys Med Rehabil. 2003;84(7):968–972.
[72] Renner CIE, Schubert M, Jahn M, et al. Intracortical excitability after repetitive hand movements is differentially affected in cortical versus subcortical strokes. J Clin Neurophysiol. 2009;26(5):348–357.
[73] Nitsche MA, Cohen LG, Wassermann EM, et al. Transcranial direct current stimulation: State of the art 2008. Brain Stimul. 2008;1(3):206–223.
[74] Bornheim S, Croisier JL, Maquet P, et al. Proposal of a New Transcranial Direct Current Stimulation Safety Screening Tool. Am J Phys Med Rehabil. 2019;98(7):e77–e78.