Review Article

Effectiveness of atDCS versus ctDCS on hand function in stroke - A Systematic Review

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Abstract:

Stroke is the leading cause of long-term disability among adults in industrialized countries. More than 60% of Stroke survivors suffer from persistent neurological deficits that impair their activities of daily living (i.e. dressing, eating, self-care and personal hygiene). This present systematic review is aimed to explore the literature-related to studies conducted on patients with Stroke concerning of specific study design, recovery stage of patient, patient distribution in the study, intensity of current used in treatment, duration of treatment intervention, frequency of treatment intervention, outcome measures used in the study, mechanism of improvement and conclusion. **Methodology:** PubMed databases were searched to identify eligible studies using the keywords Cathodal transcranial direct current stimulation, stroke and hand function. Only Randomized Clinical trial published in the last 10 years (2013-2023) were included in this review. **Results:** Eight studies were included in the review conducted on the effect of transcranial direct current stimulation (tDCS) on hand function in stroke patients. All studies investigated Functional recovery over a longer period using different outcome measures like Action Research Arm Test, Fugl-Meyer assessment scale, 9hole pegboard test with different follow-up times from 1day to 2 weeks It was found that there was significant improvement in tDCS group in most of the studies. **Conclusion:** This review concludes that in 2 out of 8 randomized clinical trial anodal transcranial direct current stimulation (atDCS) showed more improvement than other groups and 5 out of 8 studies conclude that cathodal transcranial direct current stimulation (ctDCS) is more effective than other group.

Key words: Transcranial direct current stimulation, Hand function, Stroke

Introduction:

Stroke is the leading cause of long-term disability among adults in industrialized countries. More than 60% of Stroke survivors suffer from persistent neurological deficits that impair their activities of daily living (i.e dressing, eating, self-care and personal hygiene).[1] Neurological recovery from Stroke takes place in the arms and legs during the first 8 weeks, but improvement in the upper limbs is more limited than recovery of gait, even with neurorehabilitation.[2] Clearly, additional therapeutic approaches are required to enhance recovery of upper limb function after Stroke.[2]

Among the recovery treatment measures, transcranial direct current stimulation (tDCS) provides a new way for the modulation of brain activity by improving local blood circulation to ischemic areas[3], change interhemispheric inhibition (IHI) to a more balanced state[4], and showing potential neurogenesis and promotion of motor rehabilitation.[5] Three different types of stimulation can be distinguished. In anodal stimulation, the anodal electrode (+) usually is placed over the lesioned brain area and the reference electrode over the contralateral orbit. This leads to subthreshold depolarization, hence promoting neural excitation.[6] In cathodal stimulation, the cathode (−) usually is placed over the non-lesioned brain area and the reference electrode over the contralateral orbit, leading to subthreshold polarization and hence inhibiting neural activity.[6]

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Dual tDCS means the simultaneous application of anodal and cathodal stimulation.[6] According to studies tDCS promotes neuroplasticity post Stroke through either increasing ipsilesional excitability or decreasing contralesional excitability or both at the same time via bihemispheric tDCS.[7]

This present systematic review is aimed to explore the literature-related to studies conducted on patients with Stroke concerning of specific study design, recovery stage of patient, patient distribution in the study, intensity of current used in treatment, duration of treatment intervention, frequency of treatment intervention, outcome measures used in the study, mechanism and conclusion

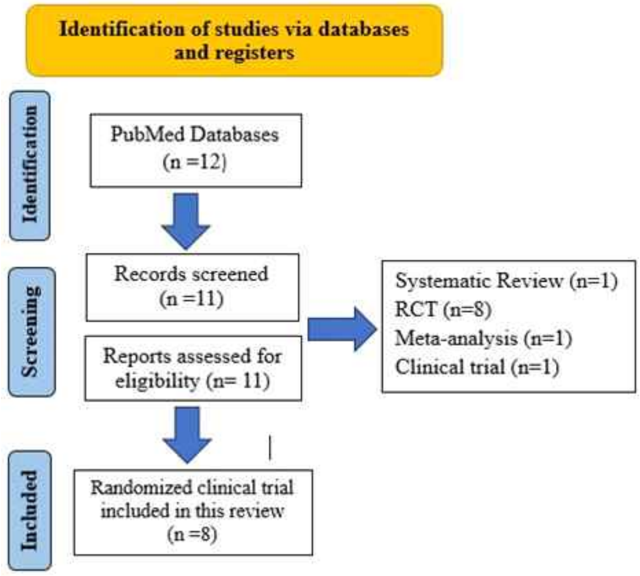
Methodology:

Systematic search was undertaken in commonly used search engine (PubMed) for the period of 2013 to 2023 with the key words like Cathodal transcranial direct current stimulation, Hand function, Stroke.

Selection criteria for randomized clinical studies: Only Randomized Clinical Trial published in the English language in which ctDCS was used for hand function Recovery in patients with stroke were included. The Exclusion criteria were systematic review, meta-analysis and clinical trial.

Data extraction: The Data Analysis was done through Pub med Electronic Database searched by SC. The Title and Abstract of all the retrieved results were then screened for eligibility by SC & SG. The Screening process was aimed at narrowing down the volume of articles by rejecting the studies that are not relevant or appropriate according to previously stated criteria, Full text versions of all relevant articles were evaluated by SC and SG.

Data analysis: The selected studies were analyzed in terms of specific study design, recovery stage of patient, patient distribution in the study, intensity of current used in treatment, duration of treatment intervention, frequency of treatment intervention, outcome measures used in the study, mechanism and conclusion



Results:

Table no 1: Quality assessment of included articles using PedRo scale[8]

Article	Pedro item 1	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
Kim DY *et al* [2]	+	+	+	+	+	+	+	+	-	-	+	9
Au-Yeung SS *et al*[9]	+	+	+	+	+	+	+	+	+	-	+	10
Rabadi MH & Aston CE[10]	+	+	+	+	+	+	+	+	+	-	+	10
Khedr EM *et al* [11]	+	+	+	+	+	-	+	+	+	+	+	10
Rocha S *et al* [12]	+	+	+	+	+	-	+	+	+	+	+	10
Zimerman M *et al* [13]	+	+	+	+	+	-	+	+	+	+	+	10
Yao X *et al* [14]	+	+	+	+	+	-	-	+	+	+	+	9
Fusco A *et al*[15]	+	+	+	+	+	-	+	+	+	+	+	10

Table no 2: Summary of Randomized trial studies included in this review

Author name	No pf patients	Type of patients	Type of study	Intervention	Result	Interpretation	Outcome measures
Kim D Y *et al*[2]	20 atDCS7 ctDCS6 sham tdCS 7	Subacute Stroke	Randomized controlled trial	Group1: atDCS+ conventional occupational therapy. Group2: ctDCS+ conventional occupational therapy. Group3: Sham treatment+ conventional occupational therapy. 10sessions 5times/week for 2week. Duration 20 min Intensity 2mA	ctDCS> atDCS> Sham treatment ctDCS> sham (P 0.05)	tDCS induces changes in cortical excitability by hyperpolarization or depolarization of the resting potentials of neuronal membranes.	FMA, modified Barthel Index.
Au-Yeung SS *et al*[9]	10	chronic stroke	Double-blind, placebo-controlled, randomized crossover trial	All of the subjects received a-tDCS, c-tDCS, and sham tDCS (sham), period of at least 5 days between sessions Duration 20 min Intensity 1mA.	Ctdcs showed more significant improvement by **1.1** point on pegboard test. (p=0.014)	CtDCS is more effective. Because ctDCS maintain balance between the hemisphere.	Purdue pegboard test, color-word Stroop test.
Rabadi MH & Aston CE [10]	16 (c-tDCS plus OT; n=8) control (s-tDCS plus OT; n=8).	acute ischemic stroke	Randomized, double-blinded, sham-controlled	groupA(c-tDCS plus OT), group B(sham tdcs plus OT) duration 30 min intensity 1 mA 5 days/week For 2week	c-tDCS showed clinically relevant 10-point improvement on ARAT total score (P = 0.18)	30-min of c-tDCS showed improvement. Because intact cortex is essential for motor recovery	Action Research Arm Test
Khedr EM *et al*[11]	40 (atDCS14) (ctDCS13) (sham tdcs13)	Subacute ischemic stroke	Randomized Clinical Trial.	Group A(atdcs) Group B(ctdcs) Group c(sham tdcs) intensity 2mA duration 25 min for 6 days	atDCS= ctDCS (P = .002)	atDCS, ctDCS are superior to sham tdcs because they increased cortical excitability	National Institutes of Health Stroke Scale, Orgogozo's MCA scale, Barthel index, Medical Research Council
Rocha S *et al*[12]	21 atDCS7 ctDCS 7 shamtdCS7	Chronic stroke	Pilot double-blind sham-controlled randomized trial	Group A (atdcs + cimt) Group B (ctdcs+ cimt) Group C (sham tdcs + cimt) 12 sessions atDCS for 13 min ctDCS for 9 min	Atdcs >Ctdcs>sham tdcs	Atdcs >Ctdcs>sham tdcs Because anodal tDCS upregulated of the activity of the damaged motor cortex	Fugl-Meyer assessment, motor activity log scale, handgrip strength
Zimerman M *et al*[13]	12	Chronic stroke	Double-blind, crossover study	Group A (ctdcs) Group B (sham tdcs duration 20 min intensity 1mA	tDCS facilitated the acquisition of a new motor skill compared with sham stimulation (P=0.04)	tDCS is a promising tool to improve not only motor behaviour, but also procedural learning	3-minute block

Table no 2: Summary of Randomized trial studies included in this review (Contd..)

Author name	No pf patients	Type of patients	Type of study	Intervention	Result	Interpretation	Outcome measures
Yao X *et al* [14]	40 Ctdcs 20 ShamtdCS 20	Sub-acute and chronic	Single-blind randomized control trial	Experimental group: receiving c-tDCS and VR. Control group: receiving sham stimulation and VR. Duration 20 min Intensity 2mA 10 session for 2 week.	ctDCS> sham tdCS FM-UE (P = 0.003) ARAT (P = 0.026) BI (P = 0.043)	tDCS induces changes in cortical excitability by regulating the conductivity of sodium and calcium channels	FM-UE, ARAT, Barthel Index
Fusco A *et al*[15]	14 ctDCS 7 sham tdCS 7	Acute stroke	Experimental Trial	experimental group (cathodal tDCS plus rehabilitation) control group (sham tDCS plus rehabilitation) 10 sesssion 5days/week for 2week Duration 10 min Intensity 1.5mA	BI-score (??= 0.931) FAC-score (??= 0.931) RMI score (??= 0.537) Fugl-Meyer-score (??= 0.444)	Cathodal tDCS, provided in an early phase of stroke, does not lead to a functional improvement.	10MWT, TUG, 6MWT, 9HPT, Barthel index, Functional ambulation classification, Fugl-Meyer, Rivermed mobility index

Discussion:

The results of this systematic literature review bring together evidence from different double-blind, sham-controlled, randomized crossover trial, pilot study, double-blind, crossover study, randomized controlled trial, single-blind randomized control trial. All these patients were treated with conventional rehabilitation techniques along with tDCS for improving hand function. In 1 study they have used constraint-induced movement therapy (CIMT) as an additional therapy along with tDCS and in 1 study they have used Virtual Reality (VR) as an additional therapy.

Chronic stroke patients were included in 3out of 8 studies, in 2 studies acute patients were included, in 1 study subacute patients were included and in only 1 study both subacute and chronic patients were included.

In the current systematic review number of patients included in the study varied from a minimum of 10 patients to a maximum of 40patients. In 3 out of 8 studies patients were divided into atDCS, ctDCS or sham tDCS. In 4 studies patients were divided into ctDCS or sham tDCS and in 1 study all the patient underwent all the 3 interventions.

Concerning electrode locations 4 out of 8 studies have used International 10/20 Electroencephalogram System as a standardized measure of placing electrodes and in 4 studies they have used Transcranial Magnetic Stimulation (TMS) System as a standardized measure of placing electrodes.

In the current systematic review, the intensity of current included in the study varied from a minimum of 1mA to a maximum of 2mA. In 4 out of 8 studies the frequency of treatment was 5 days per week for 2 weeks, in 1 study frequency of treatment was for 12 days, in 1 study frequency of treatment was for 6days, in one study there were only 2 session of treatment and in one study there was only single session but of different intervention.

In 4 out of 8 studies the duration of treatment session was for 20 minute. In 3 studies duration of treatment varied from a minimum 10minutes to a maximum of 30 minutes. In one study duration of treatment session was different for atDCS(13minutes) and ctDCS (9minutes).

9 hole pegboard test and Action Research Arm Test was a common outcome measure in 2 out of 8 studies, Barthal Index and Fugl-Meyer assessment scale was a common outcome measure in 4 out of 8 studies.

Apart from this there were few other scales and tests which were used as outcome measure in the studies those are colour word stroop test, motor activity log scale, 10 Minute Walk Test (10MWT), 6Minute Walk Test(6MWT), Time Up and Go Test(TUG), Rivermed Mobility Index, hand dynamometer.

ARAT is used to evaluates the person's ability to use their upper limb in the handling of objects through grip, pressure and gross motor movements, which are essential for performing ADLs.[16] The ICQ for the total score was 0.98 indicating very high inter-rater reliability.[17] In 2 out of 8 studies they have seen the improvement in the score of ARAT which shows that the patient have improved in handling of objects through grip, pressure and gross motor movements.

Studies in which ctDCS was more effective as compared to another group. Rabadi MH and Aston CE's work demonstrated that because intact cortex is necessary for motor recovery, 30-min of c-tDCS improved motor recovery compared to sham tDCS[10]. According to research done by [Kim DY et al, Zimerman M et al, Fusco A et al] showed that ctDCS showed more improvement as compared to atDCS and sham tDCS because ctDCS induces changes in cortical excitability by hyperpolarization or depolarization of the resting potentials of neuronal membranes of the unaffected hemisphere. [2, 13, 15] An observation by Au-Yeung SS et al in their study on 10 patients who underwent all the 3 intervention with a period of 5 days in between each session showed that single session of ctDCS showed more improvement as compared to atDCS and sham tDCS because c-tDCS help correct the overriding influence of nonlesioned over the lesioned hemisphere and maintain balance between the hemisphere.[9] Park E et al[18] in their study showed that the application of cathodal tDCS to the dominant motor cortex modulated the interhemispheric interaction between the two hemispheres by releasing the contralateral motor cortex from suppression, which led to the increased excitability of the nondominant motor cortex.

Studies where the effectiveness of atDCS was higher than that of other groups. According to a study by (Kherd EM et al. and Rocha S et al.), atDCS increased the cortical excitability of injured motor cortex, resulting in greater improvement than ctDCS and sham tDCS.[11–12] In research conducted by (Allman C et al).found that in ipsilesional motor cortex regions, atDCS increases gray matter volume and activation.

Transcranial direct current stimulation (tDCS) provides a new way for the modulation of brain activity by following studies. Kim DY et al[2] tDCS induces changes in cortical excitability by hyperpolarization or depolarization of the resting potentials of neuronal membranes. This effect is mediated by activation of sodium- and calcium-dependent membrane channels and NMDA receptors. A study done by (Hummel F et al)[20] showed that tDCS influences motor cortical excitability, and can facilitate cortical plasticity elicited by motor training. tDCS enhances regional cerebral blood flow, alters local cortical excitability, and boosts activation of supplementary cerebral regions and even neurogenesis, according to research by Bornheim S et al.[21]

Tyrosine receptor kinase B (TrkB) activation and brain-derived neurotrophic factor (BDNF) production were shown to be enhanced by tDCS in vitro research conducted by Kim DY et al[2]; this suggests that tDCS may facilitate the acquisition of motor skills by increasing synaptic plasticity.

A research by Kim J. et al[22], tDCS stimulation increases calcium transport in astrocytes, which may accelerate the process of brain plasticity. By stimulating astrocytes, it has aided in the restoration of damaged neurons.

Research indicating that tDCS did not yield statistically significant improvement (Fusco A et al)[15] concluded that, in the absence of intact tracts of the pyramidal system, tDCS was not particularly successful in stroke rehabilitation, regardless of the type of stimulation used.

Conclusion:

This review concludes that in 2 out of 8 randomized clinical trial atDCS showed more improvement than other groups and 5 out of 8 studies conclude that ctDCS is more effective than other group.

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