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# Transcranial Direct Current Stimulation (tDCS) in chronic low back pain: Systematic review with meta-analysis

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## ABSTRACT

**Background and objective.** Changes in grey matter of cortex and other parts of brain leads to increased pain perception in chronic low back pain (CLBP) patients which could be reduced by electrical application on these areas. The objective of the present review was to evaluate the efficacy of transcranial direct current stimulation (tDCS) alone as well as tDCS in combination with other interventions on pain in chronic low back pain patients.

**Method.** PubMed and Cochrane search engines was used to locate the literature. The eligibility criterion for the study includes articles published in English language, published till March 2020 and the application of tDCS alone as well as in combination with other interventions on CLBP patients.

Pain intensity was measured by visual analogue scale (VAS), numeric rating scale (NRS) or defense and veteran pain rating scale (DVPRS). Mean difference with 95% CI for the active tDCS, sham tDCS and tDCS in combination with other interventions was calculated.

**Result.** 7 articles, with 427 patients, were included in the quantitative meta-analysis. The result showed statistically significant reduction in pain in tDCS alone as compared to sham tDCS Z= 1.93. P= 0.05 and insignificant reduction in pain in tDCS when used in combination with other intervention as compared to sham tDCS, Z= 0.72, P= 0.47 with heterogeneity of 84 % in the included studies.

**Conclusion.** It can be concluded that there is significant reduction of pain in patients of chronic low back pain when tDCS is applied in isolation.

**Keywords:** chronic low back pain, meta-analysis, pain, Transcranial Direct Current Stimulation

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## INTRODUCTION

Chronic low back pain (CLBP) is fourth leading cause of disability worldwide with one year prevalence of about 10-14%,affecting mainly women of age group 40 to 80 years putting a huge burden on individual as well as community (1,2,3). CLBP is can be managed by pharmacological and non-pharmacological methods (4). Physiotherapy plays an integral role in pain management in CLBP by using techniques such as activity modification (ergonomics) , exercises including walking, manual therapy techniques like manipulation and electrotherapy modalities particularly the use of TENS (5,6,7,8).

Transcranial direct current stimulation (tDCS), is a non invasive brain stimulation technique having a potential to alter the plasticity of brain. Recent studies have shown the potential of tDCS in various areas such as enhancement of limb function in stroke condition, spinal cord injury, psychological conditions like depression, Bipolar disorders, Schizophrenia, Parkinson's disease, memory deficits in Alzheimer's and cognitive augmentation and has proved neuro modulatory effect of tDCS. The analgesic effect of tDCS has also been explored in neuropathic pain, fibromyalgia and Phantom limb pain.

The application of tDCS is primarily used to treat psychological disorders, stroke, and musculoskeletal conditions (9-18). It helps to decrease depression (9,10,19) pain (20-22) and increase functions (23-26). The application of tDCS is experimented in both iso-

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lated as well as in combination with other interventions for its priming effect. Recent evidences have suggested alteration in the homeostatic plasticity in people with CLBP. This impaired homeostatic control and maladaptive synaptic plasticity leads to pain persistence in CLBP patients (27). It was also suggested that there is decrease in grey matter in the dorsolateral prefrontal cortices bilaterally and in the right thalamus in CLBP patients (28). Reorganization of primary somatosensory cortex has also been reported in CLBP (29). These changes in cortical grey matter are correlated with chronic increasing unpleasantness and intensity of pain in patients with CLBP (30). Therefore, therapeutic techniques that can target the brain structures involved in pain processing can be the best approach for effective management of pain by reducing or blocking the pain signals. tDCS can be seen as a potential intervention for modulating the pain and can be used in CLBP. The primary objective of this review was to summarize the literature available till date on effectiveness of tDCS in CLBP. The secondary objective was to compare the efficacy of tDCS alone or in combination with other intervention on pain management in CLBP patients. Hence, this systematic review will give an insight about the role of tDCS on pain management in CLBP patients.

## METHODOLOGY

### Eligibility criteria

This meta-analysis and systematic review was done in accordance with the PRISMA guidelines. Articles comparing the effectiveness of tDCS with sham tDCS on pain in CLBP were included. All English language published articles till March 2020 was included in this review.

### Information sources

The information was collected from two electronic databases Pubmed (MEDLINE) and Cochrane (CENTRAL) from inception to March 2020. The search was restricted to Randomized controlled trials (RCT's), done on human and in English language.

### Search Strategy

For searching the relevant literature in Pubmed, the following keywords were used: "Low back pain" OR "LBP" AND "Transcranial direct current stimulation" OR "tDCS" (all in title and/or abstract) in advanced search options were used to search relevant articles and during the search Filter: Clinical Trial and Humans was used to scrutinize the articles. For searching in Cochrane ("Transcranial direct current stimulation"): ti, ab, kw OR ("tDCS"): ti, ab, kw AND ("Low back pain"): ti, ab, kw was used.

### Study selection

We used the PICO strategy where the population was chronic low back pain patients; the intervention was transcranial direct current stimulation (tDCS); the comparator group was either active tDCS or sham tDCS or control group; outcome measure was pain measured by visual analogue scale (VAS), numeric rating scale (NRS), Defense and veteran pain rating scale (DVPRS). The key words used are mentioned above. Only Randomized controlled trials published in English language were selected for this review. Studies which included both the active tDCS in combination with other interventions or in isolation and sham tDCS on patients of chronic low back pain were selected.

### Data collection process

Two authors (RC and SJ) autonomously searched and extracted the data according to the MeSH term and related keywords. Extracted information was cross checked for any disparity. Any disagreement was resolved through discussion with MM and the choice of majority was selected.

### Study selection

Eligible relevant studies were scrutinized by two reviewers (SJ and RC) first by title and then by the title and abstract and lastly by the availability of the full text. Studies that were not experimental; if values not available for the study variable, i.e. pain (VAS, NRS DVPRS); and studies with unavailability of data in terms of mean and standard deviation (SD) were excluded from meta-analysis.

### Data Extraction

To find out the effectiveness of the intervention, mean and standard deviation (SD) of pain (VAS or NRS) along with other sample characteristics like age, height, weight, body mass index (BMI) was extracted from both the experimental and control group. Data for author/year, continent/country, total number of subjects for both the experimental and control group were also extracted and compared.

### Risk Bias in individual studies

Methodological study quality was assessed with PEDro (The Physiotherapy Evidence Database). Studies were considered of higher quality if they met the criteria for randomization and allocation concealment, assessor blinding and intention-to-treat analysis. Quality assessment was done independently by two investigators (RC, MM).

### Synthesis of results

This was done using Review Manager (RevMan 5) which is Cochrane collaborations software for

systematic reviews and meta-analysis. Mean difference, 95% CI was computed by entering the data for mean, SD and total number of subjects for both the active tDCS and sham tDCS group. Forest plots for pain were also produced using Rev Man 5.3. The significance level was 0.05. Analysis was performed by two independent investigators (RC, SJ). Table 1 shows the risk of bias by Cochrane collaboration modified tool.

### Study selection

785 articles were retrieved from PubMed and 41 articles from Cochrane. All the articles were screened first by the title and then by the abstract. After screening and following the inclusion criteria and removal of duplicates, 7 articles were selected for this systematic review. Figure 1 showing the PRISMA flow chart for study selection process. There was no conflict between two authors.

### Study characteristics

*A*uthors of all the included studies were from different countries (i.e) Brazil (31), Iran (32), China (33), Boston (34), Australia (35), Italy (36) and Germany (37). All the studies included in this review have used either tDCS alone or in combination with other interventions. Two studies have exclusively used tDCS alone for treating the CLBP (33,34). Jiang et al., 2019 used dry needle based tDCS alone and Mariano et al., 2018 used tDCS alone for treating the CLBP. Hazime et al., 2017 and Schabrun et al., 2014 used tDCS alone and as well as in combination with peripheral electrical stimulation (31,35). Jafarzadeh et al., 2019 used tDCS in combination with postural training (32) and Straudi et al., 2019 used tDCS along with group exercises (36). Luedtke et al., 2015 used tDCS alone as well as along with cognitive behavioral therapy in chronic low back pain patients (37). 6 studies used anodal tDCS at primary motor cortex area C3/C4 position (using the international 10/20 electroencephalography system (31-33,35-37). Only one study has used cathode over FC1 and anode over contralateral mastoid process for stimulation targeting the dorsal anterior cingulated cortex (34). 5 studies used multiple session of tDCS application (31,32,34,36,37) whereas, 2 studies used single session of tDCS application (33,35). Dosimetry used in the included studies was 2mA intensity for 20 minutes duration except one study which used 1 mA intensity for 30 minute (35). Number of sessions varied from one session (33,35) to 12 sessions (31) over the period of one day and upto 10 sessions of tDCS application. Pain intensity was measured using either VAS or NRS in 6 studies (31-33,35-37) and only one study used DVPRS for assessing pain (34). Table 2 shows the details of the study characteristics of the included studies.

### Quality assessment

Table 2 summarizes the quality of the studies included in this review. One study has score of 11/11 (37). Two studies have score of 10/11 (31,36). Three studies had a score of 9/11(32-34) and one study has score of 7/11(35) on the PEDro (Physiotherapy Evidence Database) depicting the high quality of the included studies.

### Risk bias within studies

The risk of bias is explained in Figure 1. All the included studies showed low risk in Random sequence generation (Selection bias), allocation concealment, Blinding of participants and personnel (Performance bias), Blinding of outcome assessment (Detection bias), incomplete outcome data (Attrition

**TABLE 1.** Risk of Bias by Cochrane collaboration modified tool

| | Hazime et al. 2017 | Jafarzadeh et al. 2019 | Jiang et al. 2019 | Mariano et al. 2018 | Schabrun et al. 2014 | Straudi et al. 2019 | Luedtke et al. 2015 |
|---|---|---|---|---|---|---|---|
| **1. Random sequence generation (Selection bias)** | Low Risk | Low Risk | Low Risk | Low Risk | Low Risk | Low Risk | Low Risk |
| **2. Allocation concealment (Selection bias)** | Low Risk | High Risk | Low Risk | High Risk | High Risk | High Risk | Low Risk |
| **3. Blinding of participants and personnel (Performance bias)** | Low Risk | Low Risk | Low Risk | Low Risk | Low Risk | Low Risk | Low Risk |
| **4. Blinding of outcome assessment (Detection bias)** | Low Risk | Low Risk | Low Risk | Low Risk | High Risk | Low Risk | Low Risk |
| **5. Incomplete outcome data (Attrition bias)** | Low Risk | Low Risk | Low Risk | Low Risk | Low Risk | Low Risk | High Risk |
| **6. Selective reporting (Reporting bias)** | Low Risk | Low Risk | Low Risk | Low Risk | Low Risk | Low Risk | Low Risk |
| **7. Other bias** | Low Risk | Unclear Risk | Unclear Risk | Unclear Risk | High Risk | Unclear Risk | Unclear Risk |

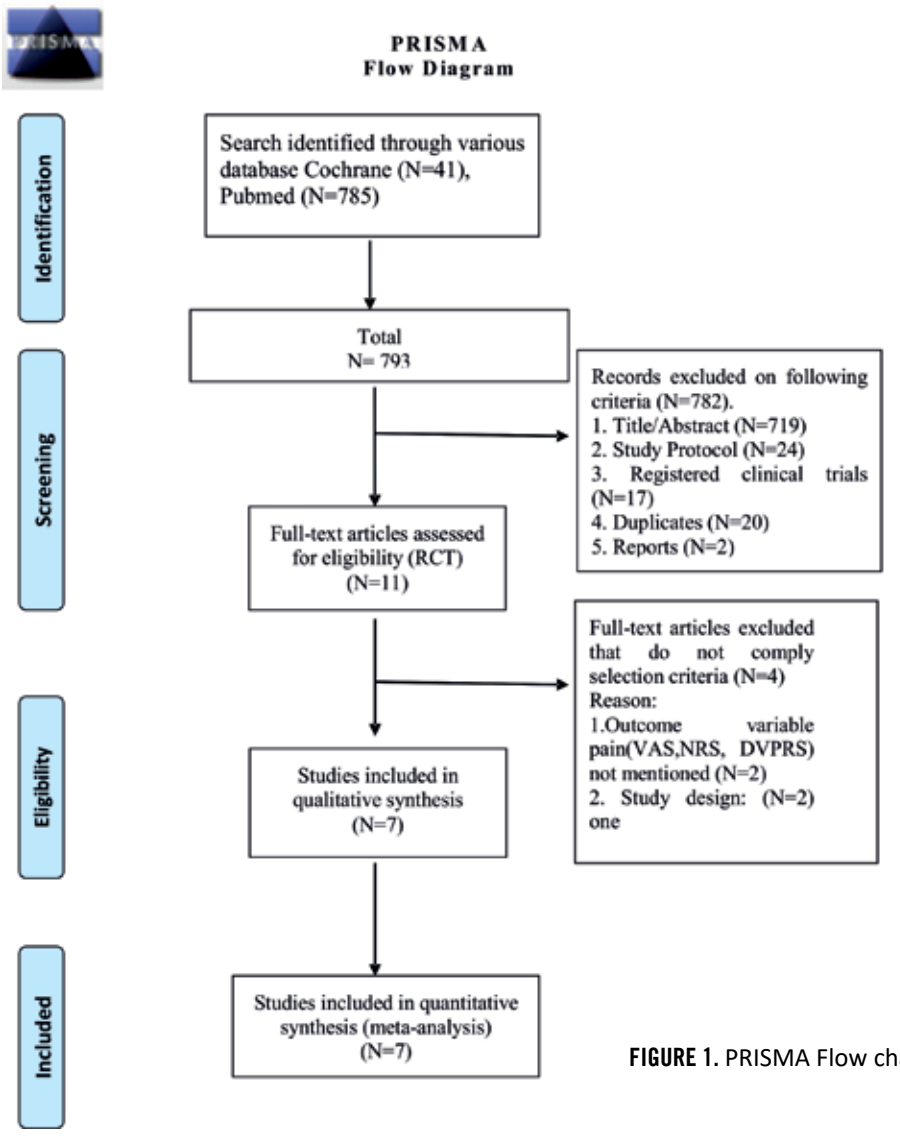


**FIGURE 1.** PRISMA Flow chart of study selection process

bias), Selective reporting (Reporting bias) and high risk in other bias. The overall risk of bias was low in all the included studies.

## RESULTS

The result of the meta-analysis showed that the there is significant reduction in pain (VAS) in active tDCS alone group as compared to the sham group Z=1.91, P=0.05 with a heterogeneity of 51% in the included studies (Figure 2). The meta-analysis also showed that the combination of tDCS with other interventions when compared to sham tDCS was statistically insignificant. The studies included for this meta-analysis shows high heterogeneity with $I^2$ 84% in the included studies (Figure 3).

## DISCUSSION

This systematic review summarizes the utilization of tDCS in reducing pain in chronic low back pain patients whether used alone or in combination with other interventions. The result of the meta-analysis suggests that the tDCS alone when compared to sham tDCS was effective in reducing pain in chronic low back pain patients. The analgesic effect produced by the tDCS in CLBP is consistent with the finding of previous studies reporting similar analgesic effects in patients with fibromyalgia, multiple sclerosis and osteoarthritis (16,17,38,39,40). The results also showed that the combination of tDCS with other interventions was not favoring the use of tDCS as combination when compared to sham stimulation and had statistically insignificant results and have high heterogeneity of 82% in the studies included in this review. These studies were using tDCS along with postural training, group exercises, cognitive behavior therapy, peripheral electrical stimulation as combination for treating chronic low back pain patients which are divergent from one another and their effects cannot be compared. Only two studies in the present review have used tDCS

**TABLE 2.** Baseline characteristics of included studies

| Reference article | Participants characteristics | Origin of Study | Study design | Treatment group | Control group | Outcome measures | Findings |
|---|---|---|---|---|---|---|---|
| 1. Hazime et al. 2017 | 92 patients with chronic low back pain | Brazil | Randomized double blind placebo controlled | tDCS+PES, tDCS alone, 2 mA for 20 min, 12 non consecutive sessions in 4 weeks (3 session per week), follow up at 3 and 6 month. Anode at PMC(C3-C4 EEG system) | Sham tDCS | Pain-NRS, Short form Mc-gill pain questionnaire (SF-MPQ), Roland Morris disability questionnaire | tDCS + PES and only PES group showed significant reduction in pain., tDCS + PES group showed maintained reduction in pain at 3 month follow up and no effect at 6 month follow up. Secondary variable sensory and affective aspect of pain clinically important improvement at 3 month in tDCS only group. No improvement in disability |
| 2. Jafarzadeh et al. 2019 | 36 participants with CLBP | Iran | Randomized double blind sham controlled | Active anodal tDCS+ postural training, sham tDCS+ postural training, 2 mA for 20 min for 2 weeks (3 session per week). Anode at PMC(C3-C4 EEG system) | Only postural training | Pain-VAS, Berg balance scale (BBS), Antero-postero stability index(APSI), Mediolateral stability index(MLSI) and Overall stability index (OSI) | Significant reduction in VAS and BBS in tDCS group post treatment and at 1 month follow up, Antero-postero stability index(APS)I, Mediolateral stability index(MLSI) and Overall stability index (OSI) also showed significant improvement in tDCS group as compared to sham |
| 3. Jiang et al. 2019 | 60 patients with CLBP | China | Prospective double blind sham controlled randomized controlled trial | Dry needle based active tDCS on PMC(C3-C4 EEG system) single session, 2 mA for 20 min | Sham tDCS | Pain-NRS, low back muscle activity measured by surface electromyographic topography | Significant pain reduction in active tDCS group as compared to sham tDCS, No change in the low back muscle activity measured by sEMG topography |
| 4. Mariano et al. 2018 | 21 participants with CLBP | Boston, Massechusettes | Double blind randomized placebo controlled-pilot study | Active tDCS at left dorsal anterior cingulated cortex (dACC) and cathode over FC1(10-20 EEG system), 2 mA for 20 min, 10 consecutive sessions(one session per day) | Sham tDCS | Pain-Defense and veteran pain rating scale(DVPRS), West Haven-Yale Multidimensional Pain Inventory's General Activity Subscale (WHY-MPI-C), Roland Morris Disability Questionnaire (RMDQ), Chronic Pain Acceptance Questionnaire (CPAQ-8), Pain Anxiety Symptoms Scale (PASS-20) | No significant change in DVPRS score, significant increase in WHY-MPI-C scores at 6 week follow-up, significant reduction in RMDQ scores at six-week follow-up, no significant change CPAQ-8 scores and PASS-20 scores and GAD-7 scores ,PHQ-9 scores were significantly reduced at sixweek follow-up |
| 5. Schabrun et al. 2014 | 14 participant with CLBP | Brisbane, Australia | Placebo controlled crossover design with participant blinding | tDCS+PES, tDCS alone, PES alone, single session, 1 mA on PMC(C3-C4 EEG system) for 30 min | Sham tDCS | NRS, motor cortical organization (TMS map parameters), sensitization (local and remote PPTs, Schober test), Higher sensory function (TPD) | tDCS+PES showed significant reduction in pain and sensitization. Motor cortical organization were normalized and sensory function improved in the tDCS+PES group. Pain reduction were more in individuals with greater sensitization. Pain reduction was also seen in tDCS only and PES only group. PES only group also showed improved sensory function and reduced map volume as compared to sham group. |

| Reference article | Participants characteristics | Origin of Study | Study design | Treatment group | Control group | Outcome measures | Findings |
|---|---|---|---|---|---|---|---|
| 6. Straudi et al. 2019 | 35 patients with CLBP | Italy | Double blind randomized controlled trial-pilot study | Real tDCS, real tDCS +group exercises, 5 consecutive sessions (1 session daily), 2 mA for 20 min before the exercise | Sham tDCS | Pain –VAS, Roland Morris Disability Questionnaire, EuroQuol-5 Dimension for quality of life, Patient Health Questionnaire-9 for psychological well being | Significant between group difference in pain reduction and Patient Health Questionnaire-9 in real tDCS+exercise group at 1 month follow up. No significant improvement in disability and quality of life. |
| 7. Luedtke et al. 2015 | 135 patients of non specific chronic low back pain | Germany | Double blind parallel group randomized controlled trial | Anodal tDCS, Anodal tDCS +cognitive behavioral therapy | Sham tDCS | Pain (VAS), disability (Oswestry disability index) | No significant difference in the reduction of pain as well as disability between the groups. The reduction in pain was insignificant when tDCS was applied preceding the cognitive behavioral therapy (CBT). |

**TABLE 3.** Quality assessment of selected Randomized Controlled Trials using Physiotherapy Evidence Database (PEDro scoring). Higher score implies higher quality

| | | Hazime et al. 2017 | Jafazadeh et al. 2019 | Jiang et al. 2019 | Mariano et al. 2018 | Schabrun et al. 2014 | Luedtke et al. 2015 | Straudi et al. 2019 |
|---|---|---|---|---|---|---|---|---|
| 1 | **Specified eligibility criteria** | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| 2 | **Random allocation** | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| 3 | **Concealed allocation** | Yes | No | Yes | No | No | Yes | No |
| 4 | **Similar baseline** | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| 5 | **Subjects blinding** | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| 6 | **Therapists blinding** | No | No | No | No | No | Yes | Yes |
| 7 | **Assessors blinding** | Yes | Yes | Yes | Yes | No | Yes | Yes |
| 8 | **Measures of key outcomes from more than 85% of subjects** | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| 9 | **Intention to treat analysis of one key outcome** | Yes | No | No | No | No | Yes | Yes |
| 10 | **Statistical comparisons between-group of at least one key outcome** | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| 11 | **Variability for at least one key outcome** | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| | **Total** | 10/11 | 9/11 | 9/11 | 9/11 | 7/11 | 11/11 | 10/11 |

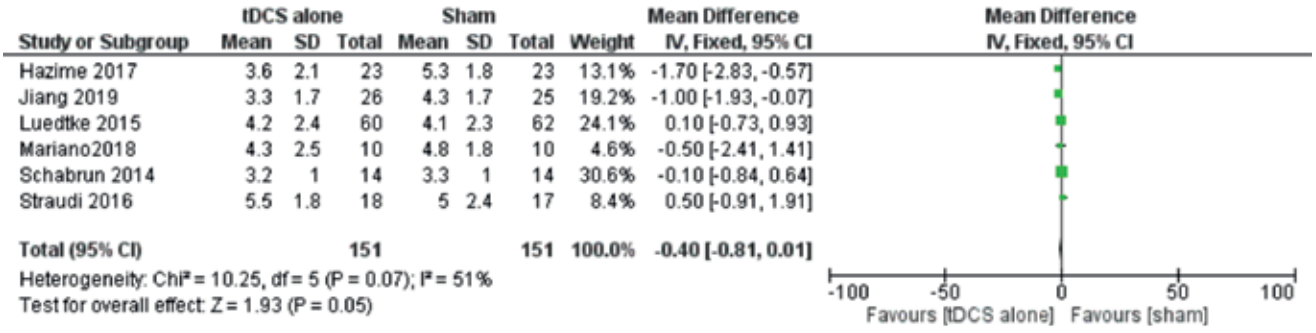


**FIGURE 2.** Forest plot for pain in tDCS alone vs Sham in patients with chronic low back pain

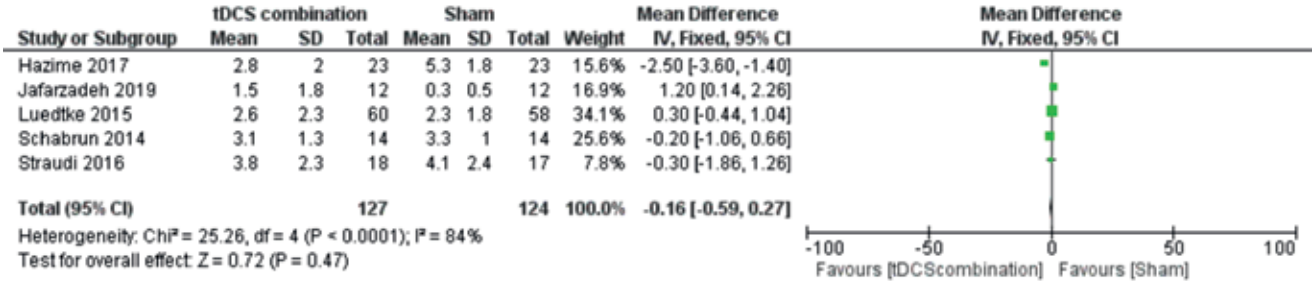


**FIGURE 3.** Forest plot for pain in tDCS in combination with other interventions vs Sham in patients with chronic low back pain


**FIGURE 4.** Risk of bias summary for the included studies

along with peripheral electrical stimulation and have reported significant reduction in pain in CLBP (31,35). The reduction in pain achieved by application of tDCS can be due to modulating the areas involved in pain processing system of the brain. Previous studies have demonstrated increase in motor cortical excitability with anodal stimulation and decrease in the cortical excitability with cathodal stimulation (41). The increased motor cortical excitability is thought to modulate the corticostriato-thalamic system (42) that inhibits the pain impulses at spinal cord (43) and the thalamic nuclei activation also leads to alteration in the other pain related structures like anterior cingulate and periaqueductal grey matter and thereby modulating the affective components of pain (44,45). In view of the encouraging results achieved by application of tDCS in various conditions like fibromyalgia, bipolar disorder, depression and osteoarthritis; tDCS can also be seen as a potential method for reducing pain in chronic low back pain patients. However, tDCS to be used as a priming intervention needs to be further explored in chronic low back pain patients. This systematic review included seven moderate to high quality studies with low risk of bias. However, this systematic review addresses some limitations that includes small number of studies (n=7) with around 427 patients. There was high heterogeneity in the included studies for meta-analysis of tDCS in combination with other interventions vs sham with $I^2$ 84%. So, in order to generalize the effectiveness of tDCS more

high-quality studies with large sample size are needed to confirm our conclusion.

## CONCLUSION

It can be concluded that application of tDCS alone can be an effective method for reducing pain in CLBP. However, the use of tDCS in combination with other treatment approaches needs to be explored further.

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