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Review

Transcranial Direct Current Stimulation in the Treatment of Chronic Knee Pain: A Scoping Review

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Abstract: Background: Chronic knee pain in older adults is a prevalent condition that significantly impacts quality of life. Transcranial Direct Current Stimulation (tDCS) has emerged as a potential non-invasive treatment option. This scoping review aims to evaluate the efficacy of tDCS in treating chronic knee pain among older adults. Methods: A comprehensive search of peer-reviewed articles was conducted, focusing on randomized controlled trials and pilot studies. Studies were included if they met specific Population, Concept, and Context (PCC) criteria. The primary outcomes assessed were pain reduction and functional improvement. Results: Eleven studies met the inclusion criteria, with a total of 779 participants. However, the results varied across studies, with some showing minimal differences between active tDCS and sham treatments. Advanced neuroimaging techniques, such as functional near-infrared spectroscopy (fNIRS), provided insights into the neuromodulatory effects of tDCS, revealing changes in brain activity related to pain perception. Conclusions: Transcranial Direct Current Stimulation (tDCS) presents a promising avenue for treating chronic knee pain in elderly individuals. However, the current body of research offers mixed results, emphasizing the need for more extensive and standardized studies. Future research should focus on understanding the underlying mechanisms, optimizing treatment protocols, and exploring the long-term effects and safety of tDCS.

Keywords: transcranial direct current stimulation (tDCS); chronic knee pain; non-pharmacological treatment; neuromodulation; pain management

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1. Introduction

Chronic knee pain is a pervasive and debilitating medical condition that affects a significant portion of the global population, particularly among older adults and those with underlying health conditions such as osteoarthritis and rheumatoid arthritis [1–3]. The impact of chronic knee pain extends beyond physical discomfort, often leading to reduced mobility [4], psychological distress, and a diminished quality of life [5]. A wide choice of therapeutic options is available for chronic knee pain ranging from conservative (e.g., patients' education, physical therapy, topical and systemic non-steroidal anti-inflammatory drugs, opioids, and intra-articular treatments) [6] to surgical interventions like knee replacement, with varying degrees of success [7–9]. The impact of chronic knee pain extends beyond individual suffering; it imposes substantial burdens on healthcare systems worldwide, including increased healthcare costs, frequent medical consultations, and the necessity for long-term management strategies. Given the widespread prevalence and the profound personal and societal impacts of chronic knee pain, there is an urgent need for effective and accessible treatment options. This scoping review aims to evaluate the efficacy of Transcranial Direct Current Stimulation (tDCS) as a potential non-invasive treatment for chronic knee pain in older adults. By systematically examining existing research, we seek to provide a comprehensive overview of tDCS's effectiveness, safety, and underlying mechanisms. This review will address critical gaps in current research and offer insights to guide future studies and clinical practices. To underline the importance of this review, it is crucial to highlight the limitations of conventional treatments for chronic knee pain, such as potential side effects, high costs, and limited long-term efficacy. Therefore, exploring alternative modalities like tDCS, which promises a favorable safety profile and potential neuromodulatory benefits, is of paramount importance. Our goal is to contribute to the ongoing discussion on innovative, non-invasive treatments for chronic knee pain, ultimately aiming to enhance patient outcomes and reduce the overall burden on healthcare systems [10]. However, these treatments often come with their own set of limitations, including:

1. Potential side effects, such as gastrointestinal issues from NSAIDs or addiction risks from opioids.
2. High costs associated with long-term medication use or surgical interventions.
3. Limited long-term efficacy, as some treatments may only provide temporary relief.

Therefore, there is growing interest in exploring alternative non-invasive treatment modalities that can offer effective pain relief without the associated drawbacks of conventional therapies. One such promising avenue is the use of Transcranial Direct Current Stimulation (tDCS) [11–13]. tDCS is considered promising because it is non-invasive, has a favorable safety profile, and has shown potential in modulating neural pathways involved in pain perception and modulation. Additionally, preliminary studies indicate that tDCS can improve pain and functional outcomes in various neurological and psychiatric conditions [14]. Transcranial Direct Current Stimulation involves the application of a low electrical current to the scalp through electrodes to modulate neuronal activity [15]. The technique has been explored in a range of medical conditions, from depression and anxiety to chronic pain syndromes. Preliminary studies suggest that tDCS could offer a novel approach to managing chronic knee pain by targeting the neural pathways involved in pain perception and modulation [16–24]. This review aims to identify and address specific gaps in current research on tDCS for chronic knee pain, including its efficacy, safety, and mechanisms of action, to guide future research directions. Moreover, we seek to offer valuable insights into the current state of research in this emerging field, identify gaps in our understanding, and highlight opportunities for future investigations. By doing so, we hope to contribute to the ongoing discussion on alternative, non-invasive treatments for chronic knee pain and potentially pave the way for more effective and patient-centered therapeutic options.

2. Methods

This scoping review was conducted following the JBI [25] methodology for scoping reviews. The PRISMA-ScR [26] (Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews) Checklist was used for reporting.

2.1. Review Question

We aimed to answer the following research question: "What is the current evidence on the efficacy, safety, and mechanisms of action of Transcranial Direct Current Stimulation (tDCS) as a treatment for chronic knee pain"?

2.2. Eligibility Criteria

Studies were eligible for inclusion if they met the following Population, Concept, and Context (PCC) criteria.

2.3. Population

Adults aged 18 years and older with chronic knee pain or knee osteoarthritis.

2.4. Concept

Investigating the efficacy, safety, and mechanisms of action of tDCS.

2.5. Context

Outpatient and inpatient settings, studies from any geographical location, published in peer-reviewed journals in English.

2.6. Exclusion Criteria

Studies not meeting the specified PCC criteria were excluded from this review.

2.7. Search Strategy

An initial limited search of MEDLINE was conducted via the PubMed interface to identify relevant articles on the topic. The search strategy included specific keywords, MeSH terms, and Boolean operators to ensure comprehensive coverage. The following search strings were used:

MEDLINE: ((“transcranial direct current stimulation”[MeSH Terms] OR “tDCS”[Title/Abstract]) AND (“chronic knee pain”[Title/Abstract] OR “knee osteoarthritis”[Title/Abstract] OR “OA”[Title/Abstract]) AND (“efficacy”[Title/Abstract] OR “safety”[Title/Abstract] OR “mechanisms of action”[Title/Abstract])).

Cochrane Central: ((“transcranial direct current stimulation” OR “tDCS”) AND (“chronic knee pain” OR “knee osteoarthritis” OR “OA”) AND (“efficacy” OR “safety” OR “mechanisms of action”)).

Scopus: TITLE-ABS-KEY((“transcranial direct current stimulation” OR “tDCS”) AND (“chronic knee pain” OR “knee osteoarthritis” OR “OA”) AND (“efficacy” OR “safety” OR “mechanisms of action”)).

PEDro: (“transcranial direct current stimulation” OR “tDCS”) AND (“chronic knee pain” OR “knee osteoarthritis” OR “OA”) AND (“efficacy” OR “safety” OR “mechanisms of action”).

The searches were performed on 31 August 2023, without any date restrictions. Full-text availability was required for inclusion.

2.8. Study Selection

After developing the search strategy, the results were imported into EndNote V.X9 (Clarivate Analytics), where duplicates were removed to create a unique set of records. These records were then processed using Rayyan QCRI online software in two screening phases. In the first phase, “title and abstract screening”, two authors independently reviewed the articles based on their titles and abstracts. Discrepancies were resolved by a third author to determine their relevance to the research question. In the second phase, “full-text selection”, the same independent review process was applied to the full texts of the selected articles. Any conflicts were resolved through discussion or consultation with a third author. This structured approach ensured a thorough and systematic selection of articles for the scoping review.

2.9. Data Extraction and Data Synthesis

Data extraction utilized a pre-designed form based on the Joanna Briggs Institute (JBI) data extraction tool, customized for this review. Extracted details included authors, publication country and year, study design, patient characteristics, outcomes, type of intervention, related procedures, and additional relevant information. Descriptive analyses summarized the characteristics of the included studies using frequencies and percentages. The search decision process, detailing the number of articles identified, screened, assessed for eligibility, and included, was systematically mapped for transparency. The extracted data were summarized in tabular form, providing an organized overview of the key information from each study, facilitating comparison and analysis. This concise presentation ensured a clear and structured depiction of the main characteristics and results of the included studies.

3. Results

Below is the PRISMA 2020 flow diagram (Figure 1); from 135 records identified in the initial literature search, 124 were excluded and 11 articles were included (Tables 1 and 2).

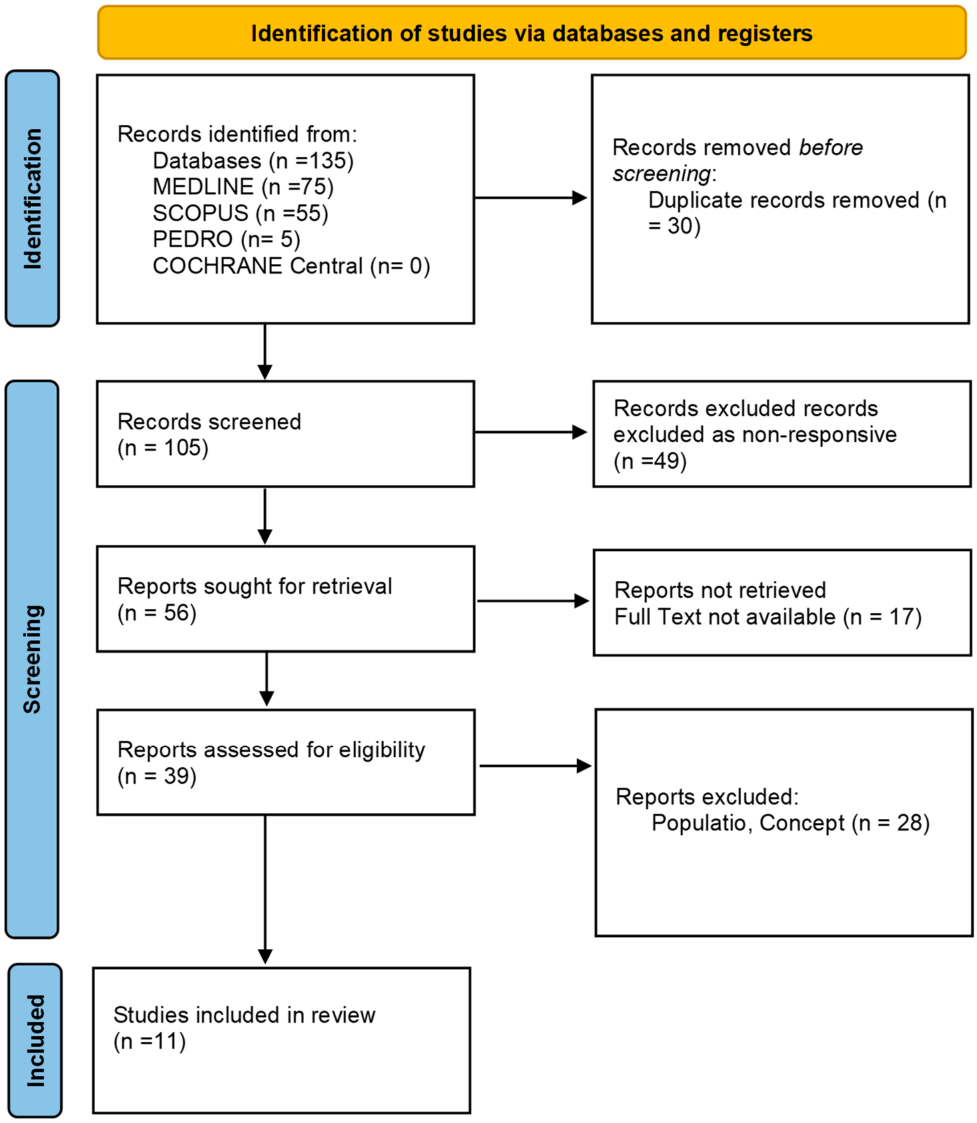

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 (PRISMA) flow diagram.

Legends: BPI: Brief Pain Inventory, DPIS: Descending Pain Inhibitory System, fNIRS: Functional Near-Infrared Spectroscopy, IL-6, IL-10, TNF-α: Interleukin-6, Interleukin-10, Tumor Necrosis Factor-alpha, KOA: Knee Osteoarthritis, QST: Quantitative Sensory Testing, RCT: Randomized Controlled Trial, tDCS: Transcranial Direct Current Stimulation, TENS: Transcutaneous Electrical Nerve Stimulation.

Table 1. Summary of studies on transcranial direct current stimulation (tDCS) for chronic knee pain.

Author and Title	Population (Number, Gender, Age)	Methods (Protocol/Brain Area)	Outcomes/Results
Ahn H et al. [16]: Anodal Bayesian analysis of the effect of transcranial direct current stimulation on experimental pain sensitivity in older adults with knee osteoarthritis: randomized sham-controlled pilot clinical study	40 participants aged 50–70 years	2 mA tDCS for 20 min; anode over C3/C4; cathode on the contralateral supraorbital area	Improved pain thresholds and reduced clinical pain symptoms
Ahn H et al. [17]: Efficacy of combining home-based transcranial direct current stimulation with mindfulness-based meditation for pain in older adults with knee osteoarthritis: A randomized controlled pilot study	120 participants; average age 59.47 ± 6.91 years	Home-based tDCS and mindfulness meditation; anode over the primary motor cortex; cathode over the supraorbital region	Reduced experimental pain sensitivity
Pollonini L et al. [18]: Longitudinal effect of transcranial direct current stimulation on knee osteoarthritis patients measured by functional infrared spectroscopy: a pilot study	10 participants; average age 62.4 ± 6.9 years	Self-treatment with 2 mA tDCS for 20 min; anode over the primary motor cortex (M1); cathode on the supraorbital area	Increased cortical activity and reduced pain
Suchting R et al. [27]: The Effect of Transcranial Direct Current Stimulation on Inflammation in Older Adults With Knee Osteoarthritis: A Bayesian Residual Change Analysis	40 participants aged 50–70 years	tDCS for 20 min daily for 5 days; anode over the primary motor cortex; cathode on the supraorbital área	Reduced inflammation markers
Sajadi S et al. [28]: Randomized clinical trial comparing of transcranial direct current stimulation (tDCS) and transcutaneous electrical nerve stimulation (TENS) in knee osteoarthritis	40 participants aged 51–71 years	tDCS vs. TENS; 2 mA for 20 min; electrodes over M1 and SO areas	tDCS showed a slight advantage in improving quality of life
Tavares DRB et al. [20]: Motor cortex transcranial direct current stimulation effects on knee osteoarthritis pain in elderly subjects with dysfunctional descending pain inhibitory system: A randomized controlled trial	104 elderly subjects; mean age 73.9 ± 8.01 years	15 daily sessions of 2 mA tDCS; anode over M1 (C3/C4); cathode over SO	Significant pain relief
Rahimi F et al. [29]: The effect of transcranial direct stimulation as an add-on treatment to conventional physical therapy on pain intensity and functional ability in individuals with knee osteoarthritis: A randomized controlled trial	80 participants aged 50–65 years	tDCS combined with physical therapy; 2 mA for 20 min over 5 sessions	Reduced pain intensity and improved functional ability
Azizi S et al. [30]: Transcranial direct current stimulation for knee osteoarthritis: a single-blind randomized sham-controlled trial	54 participants aged 30–70 years	tDCS for 20 min over 5 sessions; anode over the primary motor cortex (C3/C4); cathode on the supraorbital region	No significant difference between active and sham groups

Table 1. *Cont.*

Author and Title	Population (Number, Gender, Age)	Methods (Protocol/Brain Area)	Outcomes/Results
Teixeira PEP et al. [19]: Development of a Clinical Prediction Rule for Treatment Success with Transcranial Direct Current Stimulation for Knee Osteoarthritis Pain: A Secondary Analysis of a Double-Blind Randomized Controlled Trial	51 participants with knee osteoarthritis; average age 74.8 ± 7.44 years	tDCS applied to motor cortex (M1) or pre-frontal areas	Development of Clinical Prediction Rule
Martorella G et al. [31]: Self-administered transcranial direct current stimulation for pain in older adults with knee osteoarthritis: A randomized controlled study	120 older adults with knee osteoarthritis; aged 50–85 years	Self-administered tDCS at home for 15 sessions; anode over the primary motor cortex (M1); cathode over the supraorbital region (SO)	Significant pain reduction
Montero-Hernandez S et al. [32]: Self-administered transcranial direct current stimulation treatment of knee osteoarthritis alters pain-related fNIRS connectivity networks	120 subjects aged 66 ± 8.3 years	3-week course of self-administered tDCS monitored with fNIRS; anode over the primary motor cortex (M1); cathode over supraorbital area	Significant changes in brain connectivity related to pain

This table provides a comprehensive overview of the included studies on the use of Transcranial Direct Current Stimulation (tDCS) for treating chronic knee pain in elderly individuals. It includes details on the authors, study population, methods, and key outcomes, highlighting the various protocols and results across different trials.

Table 2. Summary of preliminary studies on tDCS for chronic knee pain.

Study	Year	Population	Method	Key Findings
Ahn et al. [16]	2018	Older adults with OA	RCT, 5 days tDCS	Significant improvement in pain thresholds
Ahn et al. [17]	2019	Older adults with OA	RCT, tDCS + meditation	Significant reduction in experimental pain sensitivity
Pollonini et al. [18]	2020	Knee OA patients	Pilot, 2 weeks tDCS	Decreased clinical pain and increased cortical activity
Suchting et al. [27]	2020	Older adults with knee OA	RCT, 5 days tDCS	Reduced inflammation markers
Sajadi et al. [28]	2020	Knee OA patients	RCT, tDCS vs. TENS	tDCS showed a slight advantage in quality-of-life improvement
Tavares et al. [20]	2021	Elderly individuals with dysfunctional pain inhibition	RCT, 15 days tDCS	Significant pain relief and short-term effects
Rahimi et al. [29]	2021	Individuals with knee OA	RCT, tDCS + physical therapy	Significant reduction in pain intensity and improved function
Azizi et al. [30]	2021	Patients with knee OA	RCT, sham-controlled	No significant difference between active and sham groups
Teixeira et al. [19]	2022	Patients with knee OA	RCT, prediction rule analysis	Development of a Clinical Prediction Rule
Martorella et al. [31]	2022	Older adults with knee OA	RCT, self-administered tDCS	Marked reduction in osteoarthritis-induced knee pain
Montero-Hernandez et al. [32]	2023	Older adults with knee OA	RCT, self-administered tDCS	Significant changes in brain connectivity related to pain

Summary of preliminary studies investigating the use of Transcranial Direct Current Stimulation (tDCS) for chronic knee pain. The table includes information about the study, year, population, method, and key findings.

3.1. Direct Comparison: tDCS vs. Sham Control

A pivotal aspect of understanding the efficacy of any treatment is comparing it with a control, often a sham procedure. In the context of tDCS, the majority of studies have reported favorable outcomes. Ahn H et al., 2018 [16]: This study stands out for its meticulous observation of pain thresholds. The research authors found notable increases in heat and pressure pain thresholds, as well as conditioned pain modulation, suggesting a direct impact of tDCS on pain perception mechanisms. Tavares DRB et al., 2021 [20]: Targeting elderly subjects, this study delved into the effects of tDCS on individuals with a dysfunctional descending pain inhibitory system. The results were promising in the short term, with significant pain reduction, but these effects waned during follow-up, indicating the need for sustained treatments or complementary therapies. Azizi S et al., 2021 [30]: In a broader age range of 30 to 70 years, this study uniquely combined tDCS with acetaminophen administration. While knee pain reduction was evident post treatment and at a three-month follow-up, the lack of significant difference between active and sham groups calls for further investigation.

3.2. The Modern Approach: Self-Administered tDCS and Telehealth

Martorella G et al., 2022 [31]: Embracing the digital age, this study introduced a novel approach where older adults were trained to self-administer tDCS. The telehealth component ensured adherence and correct technique, and the results were encouraging, with a marked reduction in osteoarthritis-induced knee pain. Pollonini L et al., 2020 [18]: A shorter two-week protocol was the focus here, with older adults self-administering tDCS. The dual outcomes of decreased clinical pain measures and increased cortical hemodynamics, as gauged by fNIRS, highlight the potential of tDCS in modulating brain activity related to pain. Montero-Hernandez S et al., 2023 [32]: This study further emphasizes the role of brain connectivity in pain management. After a 3-week tDCS course, fNIRS neuroimaging showcased significant shifts in brain connectivity patterns, underscoring the profound neural changes tDCS can induce.

3.3. Beyond Pain: Metabolic, Inflammatory, and Neuromodulatory Impacts

Suchting R et al., 2020 [27]: Diving deeper into the physiological effects of tDCS, the authors of this study observed that short tDCS sessions could modulate inflammatory markers in the blood. The intriguing observation of increased β-endorphin levels, potentially linked to the placebo effect, adds another layer to the complex interplay of tDCS and pain perception.

3.4. Synergistic Approaches: tDCS in Conjunction with Other Techniques

Ahn H et al., 2019 [17]: Merging mindfulness meditation with tDCS, this study ventured into the realm of holistic pain management. The combined approach yielded a significant reduction in experimental pain sensitivity, suggesting a potential synergistic effect. Sajadi S et al., 2020 [28]: In a direct comparison, tDCS was pitted against the established Transcutaneous Electrical Nerve Stimulation (TENS) technique. While both modalities reduced pain, tDCS had a slight edge in enhancing life quality, indicating its potential superiority or complementary role alongside TENS. Rahimi F et al., 2021 [29]: This study took a comprehensive approach, combining tDCS with a gamut of physical therapy techniques. The results were promising in the short term, but the lack of sustained benefits at follow-up suggests the need for ongoing or supplementary treatments.

3.5. Predictive Analysis and Future Directions

Teixeira PEP et al., 2022 [19]: In a bid to optimize tDCS treatments, the authors of this study aimed to develop a Clinical Prediction Rule. Such endeavors are crucial in tailoring treatments to individual patient profiles, ensuring maximum efficacy and minimizing potential side effects.

4. Discussion

Transcranial Direct Current Stimulation (tDCS) has emerged as a potential non-invasive neuromodulatory technique for chronic pain management, offering an alternative to conventional therapies. The surge in research focusing on its application for knee osteoarthritis in elderly individuals has yielded a spectrum of results, ranging from promising to inconclusive. This review synthesizes findings from 11 pivotal studies, providing a comprehensive overview of the multifaceted landscape of tDCS research [30,33,34].

Initial studies, such as those by Ahn H et al., 2018 [16] and Pollonini L et al., 2020 [18], have demonstrated tDCS's potential as an alternative or complementary treatment for knee osteoarthritis pain. Their rigorous methodologies and significant outcomes in pain measures have strengthened the case for tDCS. Particularly noteworthy are the advancements in neuroimaging, especially studies employing functional near-infrared spectroscopy (fNIRS). The study by Pollonini L et al., 2020 [18] is exemplary in this context, providing compelling evidence of the neuromodulatory effects of tDCS through fNIRS. These studies offer valuable insights into the brain's response to tDCS, revealing alterations in cortical hemodynamics and connectivity patterns associated with pain perception. Such neuroimaging findings are crucial, as they lend physiological credibility to the subjective pain relief reported by patients, thereby bridging the gap between subjective experiences and objective measures. The study by Suchting R et al., 2020 [27] further complements this narrative by demonstrating reductions in inflammatory markers, suggesting a potential physiological basis for the analgesic effects of tDCS.

Nevertheless, the study by Azizi S et al., 2021 [30] highlights the complexities involved, raising pertinent questions about the placebo effect and the genuine efficacy of tDCS. The heterogeneity in study designs, population sizes, and treatment protocols poses significant challenges in synthesizing these findings. This variability, particularly in treatment duration and intensity, complicates the interpretation of results.

One of the key strengths of this review is its comprehensive scope, covering a wide range of studies and providing a holistic view of the current state of research on tDCS for knee osteoarthritis in elderly individuals. Many included studies employed rigorous methodologies, such as randomized controlled trials, enhancing the reliability of their findings. Additionally, the review includes studies utilizing different tDCS protocols, offering insights into various effective approaches. Furthermore, some studies, like that by Suchting R et al., 2020 [27], extend beyond subjective measures to include objective markers such as inflammatory cytokines, adding depth to the understanding of tDCS effects. The review focuses on a prevalent condition that is often inadequately managed, making the findings highly relevant to both clinicians and patients [18,31].

Despite these strengths, the review also has several limitations. The diversity in methodologies, while a strength in some respects, also makes it challenging to draw overarching conclusions. Some studies had relatively small sample sizes, limiting the generalizability of the findings. Most studies had short follow-up periods, making it difficult to assess the long-term efficacy and safety of tDCS. The lack of standardized protocols for tDCS application complicates the comparison of results across studies. The presence of studies with no significant differences between active and sham tDCS raises questions about placebo effects and the actual efficacy of the treatment. Few studies comprehensively addressed the potential adverse effects of tDCS, leaving gaps in understanding its safety profile [20,29].

In light of these findings, it is evident that while tDCS holds promise, there is a pressing need for more standardized and extensive research. Future endeavors should prioritize standardization, possibly through multicenter trials, and delve deeper into the long-term effects and safety of tDCS. Additionally, the potential synergy of tDCS with other treatments, such as physical therapy or medications, warrants further exploration.

The findings of this review have several implications for clinical practice in the management of knee osteoarthritis pain in elderly individuals. The review suggests that tDCS could be a viable alternative or adjunctive treatment for pain management. Clinicians should consider incorporating tDCS into their treatment protocols, particularly for patients who have not responded well to conventional therapies. The study by Teixeira PEP et al., 2022 [19] indicates the potential for developing a Clinical Prediction Rule for identifying patients who are more likely to benefit from tDCS, paving the way for more personalized treatment plans. Some studies, like Rahimi F et al., 2021 [29], demonstrate that combining tDCS with other treatments such as physical therapy can yield better outcomes. Given that most studies reported minimal adverse effects, tDCS appears to have a favorable safety profile. However, clinicians should exercise caution and monitor patients for any potential side effects, especially when used in combination with other treatments. Incorporating objective measures such as inflammatory markers, as carried out in Suchting R et al., 2020 [27], could provide a more comprehensive understanding of treatment efficacy. Given the self-administered nature of some tDCS protocols, clinicians should ensure that patients are adequately educated on how to safely and effectively administer the treatment at home.

Clinicians should stay updated on ongoing and future research in this area, as more studies are needed to confirm the long-term efficacy and safety of tDCS for knee osteoarthritis pain in elderly individuals. By integrating these insights into clinical practice, healthcare providers can offer a more nuanced and effective approach to managing knee osteoarthritis pain in the aging population.

5. Clinical Implications

The findings of this review suggest that Transcranial Direct Current Stimulation (tDCS) could be a viable alternative or adjunctive treatment for managing knee osteoarthritis pain in elderly individuals. Clinicians should consider incorporating tDCS into their treatment protocols, particularly for patients who have not responded well to conventional therapies. The development of Clinical Prediction Rules can help tailor tDCS treatments to individual patient profiles, enhancing personalized medicine approaches. Furthermore, combining tDCS with other treatments, such as physical therapy, may provide more comprehensive pain management solutions. Ensuring proper patient education on the self-administration of tDCS is crucial to maximizing its efficacy and safety. Continued research and adherence to emerging evidence will be essential to optimize tDCS application in clinical practice.

6. Conclusions

This scoping review underscores the emerging potential of Transcranial Direct Current Stimulation (tDCS) in addressing chronic knee pain among older adults. While the prevailing research on tDCS for knee osteoarthritis in this demographic is encouraging, it is the advancements in neuroimaging, especially those employing spectroscopy, that truly pave the way for deeper insights. These cutting-edge studies reinforce the concept of neuromodulation in chronic pain management. As the field progresses, there is a pressing need to amplify research efforts in this domain, aiming to elucidate the underlying mechanisms and optimize the therapeutic potential of tDCS.

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