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BACKGROUND

Mental health disorders have emerged as a pressing global concern, with the World Health Organization (WHO) estimating that such conditions account for a substantial portion of the worldwide burden of disease. Mental disorders accounted for 654.8 million estimated cases in 1990 and 970.1 million cases in 2019, corresponding to an increase of 48.1% between 1990 and 2019 with mood disorders such as depression also contributing significantly to the overall disease burden.

In the context of Malaysia, mental health disorders have likewise gained increasing recognition and attention. According to the National Health and Morbidity Survey conducted in 2015, the prevalence of mental health disorders among Malaysian adults was estimated to be 29% which was a threefold increase in comparison with the 10% prevalence rate identified in 1996. A review of depression studies in Malaysia showed the prevalence of MDD in Malaysia to be between 8 to 12%. At the same time, for schizophrenia, the expected incidence rate was 100 cases/100,000 population/year and possible reasons for low reported incidence were delayed or underreporting and administrative reasons.

Although numerous advanced medications and psychotherapeutic interventions are available for the management of depression and schizophrenia, a significant proportion of patients either do not respond adequately or experience debilitating side effects. Treatment-resistant depression and schizophrenia remain significant challenges, highlighting the need for innovative treatment approaches. One such intervention that has garnered increasing interest is transcranial direct current stimulation (tDCS). This technique involves the application of a weak electrical current to specific regions of the brain, with the aim of modulating neural activity and potentially improving the symptoms associated with these mental health conditions.

Emerging evidence suggests that tDCS may offer a novel and effective adjunctive therapy for individuals struggling with treatment-resistant depression, potentially addressing a critical unmet need in the management of this debilitating condition. Similarly, research has also explored the potential of tDCS in the treatment of schizophrenia, with studies indicating that this non-invasive brain stimulation technique may have a positive impact on cognitive functioning, negative symptoms, and even auditory hallucinations in individuals living with this complex mental disorder.

Hence, this review was requested to assess the evidence on the use of tDCS as a therapeutic modality for patients with depression and schizophrenia focusing on its potential application in the Malaysian context before its introduction in health facilities in Ministry of Health.

OBJECTIVE

The objective of this technology review was to assess the effectiveness, safety, and cost-effectiveness of transcranial direct current stimulation (tDCS) for depression and schizophrenia.

METHODS

A systematic search was conducted on the following databases without any restriction on publication language and publication status. The Ovid interface: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily 1946 to Dec 1st, 2023. Searches were also run in Cochrane Embase, PubMed, and INAHTA databases. Google was used to search for additional web-based materials and information. Additional articles were identified by reviewing the references of retrieved articles. The last search was conducted on 17th July 2024.

RESULTS AND CONCLUSION:

A total of **410** records were identified through the Ovid interface, Pubmed and other sources. After screening, 46 articles were assessed for eligibility and 344 records were excluded. After reading, appraising, and applying the inclusion and exclusion criteria to the full-text articles, 20 were included while the other 26 were excluded since the studies had irrelevant populations and few were narrative reviews. Twenty full-text articles finally selected for this review were one umbrella review, 12 systematic reviews and meta-analyses, five randomised controlled trials, one cross-sectional study, and one cost analysis.

Efficacy/ effectiveness

Transcranial direct current stimulation (TDCS) for depression

Multiple meta-analyses and systematic reviews demonstrated that transcranial direct current stimulation (tDCS) appeared as an effective treatment for major depressive disorder (MDD), showing significant improvements in depressive symptoms, with moderate evidence for improved response rates and, to a lesser extent, remission rates when compared to sham treatments. The effectiveness of tDCS appears to be enhanced when combined with medication, while evidence of its standalone efficacy remains limited. However, the quality of evidence is mixed, and the long-term effectiveness of tDCS is still uncertain.

Transcranial direct current stimulation (TDCS) for schizophrenia

Limited retrievable evidence suggests that tDCS has shown limited ability to reduce positive symptoms, improve executive function, working memory, attention, and auditory hallucinations. Some studies reported significant improvements in negative symptoms particularly with higher frequency stimulation, improvement in self-awareness, and psychological domain of life quality, however, the effects were short-term. The overall effectiveness of tDCS in treating schizophrenia appears inconsistent with mixed results across different studies.

Safety

Evidence consistently shows that transcranial direct current stimulation (tDCS) appears safe and well-tolerated intervention for both depression and schizophrenia. Multiple systematic reviews, meta-analyses, and randomized controlled trials report no significant differences in dropout rates or adverse events between active tDCS and sham groups. Common mild side effects include itching, tingling,

and local discomfort, with no serious or irreversible adverse effects documented across numerous studies.

Economic implication

Limited retrievable evidence suggests that the cost of a tDCS treatment program for depression is [redacted] per patient for a 15-session program. In Norway, tDCS treatment costs vary significantly between home-based and outpatient settings, with prices ranging from [redacted] depending on the setting. The estimated cost of tDCS devices ranges from a few hundred to several thousand dollars, depending on their features and research-grade capabilities.

Organisational Issues

Training

Training for tDCS focuses on proper device use and safety. Researchers and technicians must learn equipment setup, correct electrode placement, and dosage accuracy. Physicians should oversee higher-risk procedures, but no specific professional qualifications are required for operators. Training includes managing adverse effects like skin burns and cognitive changes, with competency assessments after instruction. Future certification for trainers may be required.

Guidelines

Clinical practice guidelines on transcranial direct current stimulation (tDCS) for depression and schizophrenia generally acknowledge its potential but fall short of making specific recommendations. For depression, some guidelines note the efficacy of tDCS, especially in non-drug-resistant cases, but no formal recommendation is provided. In schizophrenia, the evidence is mixed, with meta-analyses showing limited or no significant effects on symptoms, leading to a lack of endorsement for its use. Overall, while tDCS is recognized as a promising treatment, particularly for depression, more research is needed to support its broader clinical application, and its use should be carefully supervised by trained psychiatrists.

Ethical Issues

Ethical concerns in transcranial stimulation research focus on informed consent, risk-benefit analysis, and the fair distribution of outcomes. Using tDCS for neuroenhancement raises ethical issues, such as widening social inequalities and risks related to unknown long-term behavioral effects. An international survey among tDCS researchers found tDCS to be seen as partly effective in research and clinical contexts, but with greater ethical concerns for enhancement use. Most researchers opposed public availability due to safety risks, emphasizing the need for stricter regulations and more clinical trials. Woodham et al. (2021) also stressed the importance of regulation, particularly with the rise of DIY use, and highlighted concerns over maladaptive long-term neuroplastic changes, calling for professional oversight to ensure safety.

CONCLUSION

In conclusion, transcranial direct current stimulation (tDCS) shows potential as a treatment for depression, particularly in reducing depressive symptoms and improving response rates compared to

sham treatments. While tDCS appears effective, its benefits may not surpass those of traditional antidepressants, and its effectiveness as a standalone treatment remains limited. The combination of tDCS with medication shows more significant improvements, suggesting that tDCS might be best used as an adjunctive therapy. However, its effectiveness for schizophrenia is less clear, with limited and inconclusive evidence regarding its impact on negative and cognitive symptoms. In terms of safety, tDCS is generally well-tolerated, with a relatively low incidence of adverse effects. Economically, limited evidence suggests that the cost of a tDCS treatment program for depression is approximately [redacted] per patient for a 15-session program. The use of tDCS for MDD is acknowledged though it is not specifically recommended in many guidelines.