

# Efficacy and prognosis of different interventional psychiatric treatments for patients with severe depression

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**Abstract.** This review examines the efficacy and prognosis of various interventional psychiatric treatments for patients with severe depression. Major depressive disorder (MDD), characterized by persistent low mood and loss of interest, is a significant global health issue, particularly prevalent among younger populations and exacerbated by the COVID-19 pandemic. Despite the availability of multiple pharmacological, psychotherapeutic, and specialized physical treatments for MDD, the overall prognosis remains poor. Consequently, physical treatments such as electroconvulsive therapy (ECT), transcranial magnetic stimulation (TMS), vagus nerve stimulation (VNS), and deep brain stimulation (DBS) have emerged as interventional psychiatric therapies for recurrent and treatment-resistant depression. Studies indicate that ECT is the preferred treatment for severe and refractory depression due to its rapid onset of action; rTMS is more suitable for long-term management of mild to moderate refractory depression because of its non-invasive nature; and tDCS, with its portability and safety, is often used as an adjunct to pharmacotherapy or psychotherapy. These interventional treatments have complementary value in treating treatment-resistant depression and are expected to improve efficacy and expand clinical applications in the future with the optimization of nutreregulation techniques and the advancement of interdisciplinary research.

**Keywords:** Major depressive disorder; Interventional psychiatry; therapy.

## 1. Introduction

What is Major Depressive Disorder, defined by persistent dejected and loss of interest, poses a significant global health on younger populations, exacerbated by psychosocial stressors such as the COVID-19 pandemic. In the meantime, the morbidity and illness bear of MDD have increased significantly after the COVID-19 pandemic, and the prevalence of MDD is likely to increase more in younger groups than in older groups [1]. In the context of the continuous increase in the prevalence of MDD and its increasing harm to society, countless scholars are researching and looking for treatment methods for MDD patients. Building upon the foundational work of previous researchers., various drugs that can effectively treat MDD, psychotherapies that can be used to improve the mood of patients, and special physical therapy methods have appeared, giving MDD patients the possibility of cure.

## 2. Interventional Psychiatry

With the application of various treatments to the treatment of MDD patients over the years, countless patients have been cured, but the overall situation is still not optimistic. After a two-, four-, or six-year follow-up evaluation of the two groups of cured patients in the Netherlands, the cure rate continues to decline. 55% of patients have experienced chronic attacks, and most MDD patients have a poor prognosis [2]. As a result, physical therapy for recurrent and refractory depression, like Electronic Toll Collection (ECT), has been discovered or improved. With the exploration of physical therapy methods for MDD and the continuous development of neuromodulation techniques, the term interventional psychiatry was established. It refers to therapies like ECT, TMS, VNS, and DBS, as well as protocols for implants, administration, use of risk assessment, and mitigation strategies. At present, the relevant research is mainly on the promotion of interventional psychiatric treatment



methods and the training of relevant medical technicians, and there is a lack of summary and comparison of the treatment methods they contain, and more research on a single method. The majority of the studies is about a single of these treatments. Some of these treatments are used only for major or treatment-resistant depressive disorder, while others are used as an adjunct to medication. Several of them are briefly described in the following sections.

### **2.1. Electric Convulsive Therapy (ECT)**

The earliest interventional psychiatric treatments must have been Electric Convulsive Therapy (ECT). ECT works roughly by placing unilateral or bilateral electrodes in the temporal region of the head in the human body to induce seizures, changing the content and distribution of neurotransmitters in the patient's brain. There are three main ways in which ECT is used in modern times, which are bilateral, right unilateral, and bifrontal placement. The whole methods are highly efficient when used appropriately. The most widely accepted of these is bilateral electrode placement. Instead of its unignorable cognitive side effects, it is used as a standard of care method in many countries, and it is characterized by high efficacy and fast onset. For some patients, right unilateral ECT has the same efficacy as bilateral ECT and has fewer cognitive side effects. However, treatment is slow. Dual frontal ECT has similar efficacy to bilateral ECT, but bilateral ECT is more rapid, and bilateral ECT is more appropriate than dual frontal ECT in emergency situations [3].

Despite its historical efficacy, ECT's clinical adoption remains limited due to persistent societal stigma and uneven access to trained practitioners. Future efforts could focus on public education campaigns and standardized training protocols to bridge this gap, as evidenced by the European Forum for ECT's initiatives. According to previous meta-analyses of the efficacy of ECT used in curing MDD patients, in 19 relevant studies from the United States, Italy and other countries, 2422 MDD patients with an average age of 51. 2 years had a response rate up to 74. 2% and a remission rate of 52. 3% to ECT. ECT has a higher response rate and remission rate than drug therapy [4]. ECT also has a better stabilizing effect on patients at risk of suicide. Avery D et al. found that suicide attempts occurred in 0. 8% of patients treated with ECT, but in 4. 2% of patients with MDD treated with medication [5]. It can be seen that the efficacy of ECT is quite significant. However, it has side effect, such as nausea, vomiting, anterograde and retrograde amnesia. Most patients will have mild cognitive problems, but they will recover within a few days to a few weeks after the completion of treatment, and anterograde amnesia will recover in about 2~4 weeks. In contrast, retrograde amnesia can last for weeks to months, or even more than a year. As a result, ECT is constantly being improved.

Overall, ECT is a treatment that can alleviate major and treatment-resistant depression disorder, especially when other medications and psychotherapies have not been effective. Although the Modified Electroconvulsive Therapy (MECT) improved the safety and comfort of the patient, it did not completely eliminate the more serious side effects. At present, the discover of principle of ECT has still not been completed, and research on it continues. Most adults in society have a negative attitude towards ECT, and many older adults say that they will never consider ECT as a therapy for mental disorders in their lifetime. A 2018 U. S. report on ECT acceptance showed that only 1% of American refractory MDD patients received ECT, compared with 0. 25% of patients with general MDD [6]. At the same time, social discrimination, prejudice and lack of medical resources in hospitals in different regions, and the popularity of ECT in hospitals in different regions and the huge differences in the training of relevant medical personnel have all led to the underutilization of ECT. So far, maximizing the therapeutic potential of ECT requires coordinated efforts across multiple sectors of society and provide help to people with depression. With the establishment of institutions such as the European Forum for ECT and the efforts of medical workers, it is believed that in the near future, ECT will be understood by people, no longer misinterpreted as a terrible thing, and can be used more widely and rationally to treat patients with MDD and reduce their distress. The second is the study of the principle of ECT, hoping to explore the effects of epilepsy and electric current generated during the use of ECT and the specific principle of ECT treatment in the future, so as to facilitate the better improvement of ECT and the development of other related technologies.

## **2.2. Transcranial Magnetic Stimulation (TMS)**

In 1985, transcranial magnetic stimulation (TMS) was first used by Barker for the stimulation of the motor cortex, creating an unprecedented precedent for non-invasive brain stimulation treatment [7]. It involves placing an insulated wire on the patient's scalp to generate a magnetic field using a large, short current. This magnetic field goes across the scalp and skull, resulting in an induced current in the brain's surface area to affect neural transmission. However, the exact and complete mechanism of action remains unclear.

TMS is mainly divided into three modes according to its different stimulation pulses, which are single-pulse TMS (sTMS), double-pulse TMS (pTMS) and repetitive TMS (rTMS). The rhythm of sTMS can be manually controlled and is mainly used for routine electrophysiological testing. Secondly, double-pulse TMS can be used in the study of nerve conduction because it can stimulate the same place at different intensities or use two pulses separately. Finally, repetitive TMS is mainly used as a therapy for MDD patients due to its continuous stimulation and relative freedom of intensity regulation. rTMS has been shown to treat MDD by increasing or decreasing the cortical excitability of directly targeted and indirectly connected remote brain regions by continuously stimulating the sum of excitatory postsynaptic potentials with high or low intensity, modulating their balance of excitability and inhibition [8]. rTMS is a treatment that has been around for about 40 years and is recognized for treating diseases without anesthesia, non-invasiveness, application and seizure induction, and simply by changing the magnetic field to regulate excitation and inhibition within the brain. There is no doubt that rTMS has its own unique features and indispensable location. In a meta-analysis of 24 studies obtained after screening by Elham Hassanzadeh et al. [9]. Compared with the relatively rough electrical stimulation of ECT, rTMS does not damage the cognitive ability and memory of patients due to its special working principle, and even has certain benefits. However, it cannot be ignored its adverse reaction that it will induce seizures in patients. Although the risk is very small, the magnetic field generated by high-intensity rTMS is strong enough to directly induce thumb twitching. Without preparation or injection of anesthetics and muscle relaxants, seizures can cause considerable damage to the patient. Although rTMS has a series of advantages such as relative safety, non-invasiveness, and adjustability, it cannot produce the same rapid effect as ECT. Therefore, it is still not possible to replace ECT as an efficient and urgent therapy for drug-resistant MDD.

All in all, rTMS, as a relatively new interventional psychiatric therapy, definitely has a role comparable to ECT and a bright development prospect. Nowadays society, rTMS also faces the same problems as ECT, for example, rTMS-related machines are not widely promoted, and more relevant operators need to be trained. Not only that, the specific principle of TMS has not yet been identified completely, and similar to ECT. TMS is also an extremely crude treatment method in use, so the exploration of the specific mechanism of action of TMS is also an extremely important task in the future. The gradual understanding of its mechanism of action is more conducive to the use and improvement of TMS, the development of emerging technologies, and more importantly, the protection of patients' health. At present, there is no good way to directly compare the efficacy of rTMS and ECT. However, for the past few years, the research on the use of the two therapies separately before and after, and the latter as the first user, is also a very promising research direction [9].

## **2.3. Transcranial Direct Current Stimulation (tDCS)**

Transcranial direct current stimulation (tDCS) is a Non-invasive therapy for Cerebral stimulation that in contrast to transcranial magnetic stimulation (TMS) does not require magnetic field sensing and achieves neuromodulation through direct current stimulation. In contrast to TMS, tDCS does not require magnetic field sensing and achieves neuromodulation through direct current stimulation. TMS relies on a Pulsed Electromagnetic Field to induce an induced current in the brain, and the depth and focus of the stimulation are significantly affected by the type of coil, while tDCS applies a constant current through the electrode patch, which is easier and less costly to operate, but has relatively low spatial resolution. Compared with ECT, it mainly reduces the intensity of the current and can change

the position of the electrode, which means it can change the part of the current flow relatively freely. By delivering a low-intensity direct current (1-2mA) via scalp electrodes, tDCS modulates neuronal excitability through alterations in resting membrane potentials, targeting regions like the dorsolateral prefrontal cortex to enhance emotional regulation [10]. In the treatment of depression, the anode typically targets the left dorsolateral prefrontal cortex (DLPFC), an area closely associated with emotion regulation and cognitive control, and often presents with reduced metabolic activity in patients with depression. Studies have shown that anodic stimulation of DLPFC increases the activity of local times new roman-GABA inhibitory interneurons, while improving emotional processing by modulating the functional connectivity of the prefrontal-limbic circuit [11].

It has been effective in a wide range of psychiatric disorders, mainly in studies of the effects on people with MDD. Due to the weak current, the treatment effect is not as good as ECT and rTMS. Therefore, it cannot be used as the main treatment, but it can be used as an adjunct to the treatment of patients by virtue of its portability. Safety and tolerability aspects, tDCS is safe for both adults and adolescents, with minimal and transient side effects that are rarely controversial, with common adverse effects including scalp tingling, mild headache, and transient skin redness and swelling without reports of seizures or cognitive decline. It is safer than repetitive transcranial magnetic stimulation (rTMS), and almost all of these side effects disappear with the end of the course [12]. Early clinical trials have shown that a single dose of tDCS treatment may temporarily improve depressive symptoms. In the SELECT-TDCS multicenter trial, Brunoni et al. included 120 patients with moderate to severe disease and found that the response rate (40.6%) of 6-week tDCS treatment (30 minutes per day) was significantly higher than that of the pseudo stimulation group (19.1%), and the efficacy was comparable to that of selective serotonin reuptake inhibitors (SSRIs) [13]. In the early drug treatment of MDD patients, the adjuvant effect of tDCS is significant in the first two weeks, and the difference in tDCS effects gradually diminishes after two weeks as the drug begins to play a more significant role. [8]. Therefore, it is recommended that tDCS can be added as an augmentation method to the early drug therapy of MDD patients.

Transcranial direct current stimulation (tDCS), as a non-invasive neuromodulation technique, has shown great prospects in clinical treatment and scientific research in recent years. Combined with the current research progress and market trends, its future development is very wide. Here are three examples, The first is the individualized treatment model, combined with machine learning algorithms to integrate multimodal data (such as Electroencephalography (EEG), Functional Magnetic Resonance Imaging (fMRI), Genetic markers) to develop efficacy prediction models; After a detailed analysis of the regulatory effects of tDCS on neuroplasticity (LTP/LTD), glial cells (glutamate regulation in astrocytes) and inflammatory pathways (such as neurotransmitter-mediated immune responses), it is proposed that the molecular mechanism of glial-neuronal interaction should be further verified through animal models in the future [11]. Finally, AI-assisted decision-making, which uses machine learning to analyze large-scale clinical data, predict the probability of a patient's response to tDCS, and dynamically adjust treatment parameters. Such techniques have been preliminarily validated in some multicenter trials.

The rest of the interventional psychiatric treatments, such as VNS, are themselves mainly used for the treatment of patients with epilepsy, while DBS is extremely repetitive compared to ECT and TMS. The rest of the treatments are relatively rare; an in-depth analysis is omitted for brevity.

### **3. Conclusion**

Among various psychiatric interventional treatments, electroconvulsive therapy (ECT) remains the preferred option for treating severe and refractory depression (especially cases with suicide risk or drug resistance) due to its characteristic of rapid onset. Repetitive transcranial magnetic stimulation (rTMS) is more suitable for the long-term management of mild to moderate refractory depression due to its non-invasive advantage; Transcranial direct current stimulation (tDCS), due to its portability and safety, is often used as an add-on to medication or psychotherapy. These interventional therapies

have shown complementary value in the treatment of treatment-resistant depression and are expected to improve efficacy and expand clinical application in the future with the optimization of nutriregulation techniques (such as precise targeted stimulation, the popularity of wearable devices) and the advancement of interdisciplinary research (such as artificial intelligence parameter regulation).

### Authors Contribution

All the authors contributed equally and their names were listed in alphabetical order.

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