The Effectiveness of tDCS And TMS for Treatment of Depression

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Abstract. Depression is a prevalent mental disorder that can lead to negative emotional states and physical reactions, including pain, insomnia, cognitive disorder and even suicidal tendencies, which largely effect one's daily life. With the increasing pressures of modern life, the incidence of depression has risen, highlighting the importance of effective treatment. While antidepressants are commonly used, they often come with side effects and may lose effectiveness over time, especially in cases of Treatment-Resistant Depression (TRD) and major depressive disorder (MDD). In order to find a more efficient and safer way to cure depression, neuromodulation techniques has been involved in the treatment. Neuromodulation techniques such as transcranial direct current stimulation (tDCS) and transcranial magnetic stimulation (TMS) have emerged as promising alternatives for depression treatment. These techniques modulate brain activity by applying electric currents or magnetic fields to specific areas of the brain. This study aims to compare tDCS and TMS in the treatment of depression by reviewing their advantages and disadvantages. Results indicate that both tDCS and TMS show promise in treating depression, with tDCS demonstrating moderate effectiveness for acute depression and TMS proving effective, especially for TRD. While both techniques have shown improvements in depressive symptoms, they differ in terms of mechanism, efficacy, safety, and convenience.

Keywords: Depression, tDCS, TMS, rTMS.

1. Introduction

Depression is a common mental disorder. People with depression tend to fall into negative emotional states, which may cause a range of physical reactions, such as pain, and even suicidal tendencies. What's more, with the continuous development of modern society, the pressure faced by people in work and life has gradually increased thus increasing the incidence of depression. In this context, the treatment of depression has gotten important.

The main form of treatment towards depression is antidepressants. However, antidepressants generally have side effects due to the change of the release of neurotransmitters or phytohormone. For example, people who continue have antidepressants may suffer from drowsiness, memory declines or unresponsiveness which will bring inconvenience to one's daily life [1].

What's more, The clinical features of major depressive disorder (MMD) are susceptibility to recurrence and chronicity, and each relapse will reduce the effect of antidepressants. In this case, MMD will develop into Treatment-Resistance-Resistance Depression (TRD), where antidepressants can hardly work.

Owing to the development of neuromodulation techniques, new treatment such as transcranial direct current stimulation (tDCS) and transcranial magnetic stimulation (TMS)错误!未找到引用源。 have been developed [2, 3]. TMS and tDCS affect brain activity respectively by applying a magnetic field and electric current to the scalp. tDCS modulates cortical excitatory activity by using two electrode (anode and cathode), which also depends on the stimulation polarity. Stimulus parameter such as stimulus intensity, frequency and lasting time could be modulated which is consistent with individualized treatment, thus archiving therapeutic results. TMS has been approved by the FDA as an effective intervention for depression. It's usually applied to the dorsolateral prefrontal cortex (DLPFC), divided into right DLPFC and left DLPFC.

Although there has been a great deal of research over the past few years confirming that neuromodulation techniques can be used to treat depression, especially major depressive depression

(MMD), the response mechanism has not been very clear yet. Hypothesis based on experiments that neuromodulation techniques do improve the symptom of depression [4, 5]. These suggest that neuromodulation techniques may have impact on synaptic plasticity, functional connectivity structure of the brain, and neural pathway.

This study is based on previous research on the effects and treatments of neuromodulation techniques for depression to compare two kinds of neuromodulation techniques, which is tDCS and TMS. This study will focus on reviewing the advantages and disadvantages of each of tDCS and TMS in the treatment of depression, as well as parameter adjustments during treatment. Subsequently, this study will focus on research gaps and a look at future applications of tDCS and TMS. Through this study, it aspires to offer a comprehensive review of tDCS and TMS in treatment of depression.

2. Method

2.1. Search strategs

This research conduct a comprehensive literature searching by literature database such as PubMed, Web of science. The search query includes the following terms: ‘tDCS’ , ‘TMS’, depression and neuromodulation techniques. Additionally, This study refer to in the references in the related article to get further information.

2.2. Screening Process

Firstly, this work screened the literature based on its title and abstract to determine whether being relevant to the topic. Secondly, full-text articles were retrieved for further assessment. According the demand of this study, literatures were included if they met the following criteria: relevance of the mechanism of tDCS or TMS; relevance of the effect of tDCS or TMS; comparison between tDCS and TMS; parameters of tDCS or TMS. Also, to compare with the effect of antidepressants, ‘antidepressants and tDCS’ and ‘antidepressants and TMS’ are also included. In this way, it’s possible to compare tDCS and TMS’s effect respectively toward the treatment of depression, and make comparison between antidepressants and neuromodulation techniques. What’s more, paper without symptom results are excluded. Figure 1 showed the paper processing in this work.

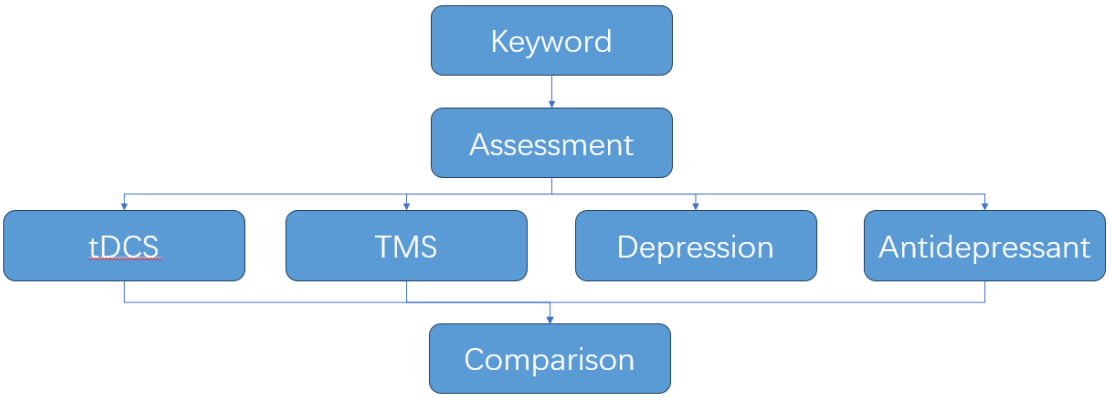

Fig 1. Search paper process in this study (Photo credited: Original)

3. Results

In recent years, rTMS which is TMS that applies multiple pulses in a short period of time has replaced the TMS. rTMS uses one or more coils to generate a pulsed magnetic field, which penetrates the skull and acts on neurons under the cerebral cortex, thereby altering the neuron's state of activity. The main reasons why rTMS is more advantageous in treating depression compared to a single session of TMS include the following. Firstly, it performs better sustained results. The continuous stimulation provided by rTMS promotes changes in the brain's neuroplasticity, resulting in longer-

lasting treatment effects. In contrast, the effects of single or low-frequency TMS may be more transient and require more frequent treatments to achieve similar results [6].

rTMS works by the coil put above patient's head. The size and shape of the coil can affect the degree and depth of focus of the magnetic field. The position and localization of the coil is critical to the accuracy and effectiveness of the stimulation, which is also critical to affecting activity in specific brain regions.

rTMS has been applied as a clinical treatment for over 20 years. Also approved by the FDA as a choice for the patients, especially when coping with the condition of the acute state and ineffectiveness after multiple pharmacological intervention. Its mechanism is to induce magnetic fields applied to the prefrontal cortex, then leading to the depolarization of underlying neurons.The most commonly used target of rTMS was the Left Dorsolateral Prefrontal Cortex (DLPFC), because it is strongly connected with other crucial areas. The decrease of cerebral blood flow was found in patient who suffer from depression. After being treating by rTMS, most of the study reported that the CBF of certain areas has increase [7], fMRI functional connectivity's silence work has decreased [8], which means that rTMS do make contribution to curing depression.

The neuroimaging mechanism reported the neuroimaging mechanism of rTMS by observing the changes through fMRI. Functional Magnetic Resonance Imaging (fMRI) is a neuroimaging technique used to measure brain activity indirectly by detecting changes in blood flow and oxygen levels in the brain. In this research [9], rTMS was proved to be a effective method to treat depression. It focus on three important networks, finding that rTMS not only causes changes in regional brain areas but also the whole neural network.

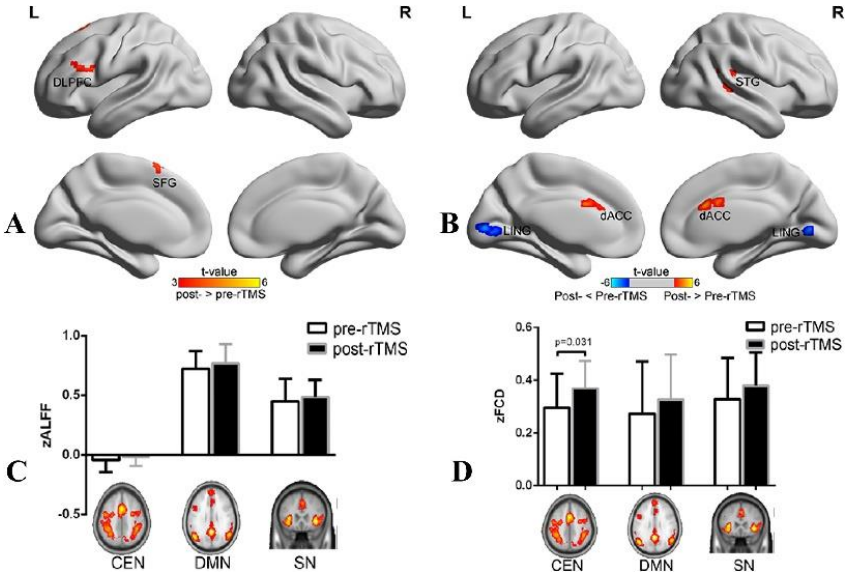

Fig 2. fMRI evidence [8]

Figure 2 showed that after rTMS treatment, there was nearly no difference between three networks. However, FCD in CEN demonstrate a noticeable increase while two other areas.

DMN and SN showed no distinguishment. The study has proved that rTMS could induce a regional functional increase in average functional connectivity density in left DLPFC and CEN, showing the mechanism of brain imaging. When facing the TRD, the combination with antidepressants of TMS is more effective.

Comparing to the antidepressant, three treatments of rTMS per week share the same effect with 5 traditional treatment per week. What's more, this research showed that more intensive treatment introduce a good perspective [10].

According to [11], TMS therapy is indicated for the treatment of major depressive disorder in adult patients who have failed to achieve satisfactory improvement from prior antidepressant medications during the current episode.

The already known main risk of rTMS is the possibility that it may triggering seizures as side effect. But in general, it doesn't create a bad impact on cognitive level. However, the risk of triggering seizures is relative low.

tDCS treats disease by applying weak direct current to specific areas of the brain through electrodes attached to the scalp. In contrast to other non-invasive brain stimulation techniques, it does not directly report evoked brain activity, but rather alters the excitability of spontaneous brain activity through subthreshold modulation of neuronal membrane potential. In general, the anode of tDCS increases neuronal excitability and the cathode decreases neuronal excitability. tDCS can also produce a long term potentiation (LTP) or a long term depression (LTD) of neuronal excitability by modulating synaptic plasticity. The sustained neuroplasticity modulation induced by DCS may be the basis of its therapeutic effect on psychiatric disorders. tDCS is able to increase or decrease local neuronal activity depending on the polarity of the applied stimulus. Continuous tDCS stimulus could lead to neuroarchitectural changes in predetermined brain targets in depression, suggesting a plasticity effect that may propagate across brain networks [12]. In tDCS, the anode is located above the left dorsolateral prefrontal cortex (DLPFC) and the cathode is located in the right supraorbital region. What's more, with a current of 20mA in the left DLPFC, tDCS's effectiveness reaches the best. This work suggest a 30-minute session works best for tDCS [13].

Plenty of researches proved that clinical response rates, remission rates, and improvement rates of depressive symptoms were higher after the active tDCS program compared to the placebo sham-controlled tDCS program [14, 15].

This work suggest that after tDCS treatment, the sleep disorder show no apparent response, while symptoms including somatization of anxiety, cognitive disorder marked a significant improvement [16]. For the lasting time, suggest that results reach the peak after 6 weeks of treatment, leading to the conclusion that the shortest time for the tDCS treatment is 6 weeks [17]. the work has shown that compared to Fluoxetine [18], a selective 5-hydroxytryptamine reuptake inhibitors (SSRI) antidepressants, the effect of tDCS is more significant. It's possible to suggest that tDCS may work better than antidepressants. Also, tDCS show moderate effectiveness on acute depression, but for treatment-resistant depression, it shows little effectiveness.

What's the difference between rTMS and tDCS? Unlike TMS, where single magnetic pulses induce action potentials by surpassing the depolarization threshold of neurons, tDCS does not exceed the threshold due to its weak and constant polarization. However, as a treatment for major disorder depression, the application of tDCS is developed based on the use of TMS.

In terms of mechanism, both rTMS and tDCS are two non-pharmacologic treatments that are non-invasive techniques. rTMS stimulates the cerebral cortex by generating changing magnetic fields that stimulate activity in specific brain areas. Stimulation is usually done in the frontal lobe or forehead area. tDCS, on the other hand, uses direct current to generate tiny electrical currents in the cerebral cortex to modulate the excitability of neurons. Stimulation is usually performed in the temporal or frontal lobes. They work with different principles and therefore have some differences in terms of therapeutic efficacy, safety and other aspects.

Coming to the efficiency, rTMS has been shown to have significant healing effect in the treatment of depression, especially in patients for whom antidepressant medications are ineffective or intolerable. The efficacy may last for several months, and it remains effective in patients who relapse. In patients with relapses, rTMS is still working, but the effect will be slightly reduced accordingly. tDCS is also demonstrated to be effective in reducing some symptoms of depression, for example, the cognitive disorder. However, it may not be as effective as rTMS.

As mentioned before that it's possible for TMS to trigger the seizures as side effect, while tDCS nearly show no risk of it. Since the tonic change in resting membrane potential induced by tDCS doesn't trigger an action potential. Possible side effects for TMS may include headaches, scalp pain, or muscle tension, but are usually mild and transient. tDCS is generally considered safer when compared to rTMS because of its less intense stimulation and fewer side effects. The possible side effects are mild headaches, skin irritation, or burns, but these are rare.

When considering the accuracy, due to the coils used in the rTMS, the positioning function of rTMS is better the tDCS, as tDCS stimulate brain activity by placing two electrodes, a cathode and an anode. In this way, according to the right-hand rule, the direction of the current and the direction of the coil can determine the direction of the magnetic field, bringing rTMS a more accurate positioning function.

Concerning the portability, rTMS usually requires treatment in a specialized facility or hospital, takes about 30 minutes per session, and usually requires multiple sessions. While tDCS can be performed either in a hospital or home environment, patients can even operate the equipment themselves. Treatment time is shorter, usually 20-30 minutes.

Meta-analysis showed that tDCS was effective but moderately effective in the treatment of acute depression and less effective in TRD. What's more, rTMS applied to TRD has little effect. So it can be concluded that the rTMS and tDCS show limitation on treating TRD. Better parameter for treating TRD remain to be developed in the future.

In summary, although both rTMS and tDCS are effective non-pharmacologic treatments, they differ in terms of effectiveness, safety and convenience. The choice of treatment usually depends on the patient's specific circumstances, preferences, and the advice of the healthcare professional.

4. Discussion

Though tDCS and rTMS have made some progress in treating depression, the truly mechanism of them have not been discovered yet. Their specific mechanisms involve multiple ways, including modulation of neuronal membrane potentials, neurotransmitter release, and alterations in synaptic plasticity. For patients who relapse, the reintroduction of rTMS and tDCS still has a role to play.

Their effect also depends on the stimulus site, lasting time and parameter such as frequency. And these parameter remain to be determined as the optimal parameter has not been found yet. Clear mechanisms of these two NIBS have not been discovered yet. The current research focused on the efficacy assessment, the neurochemical mechanisms remain undetermined. So in the future, the best optimal parameter remains to be determined, including stimulus site, frequency and lasting time.

Though heterogeneity is not evident in existing studies, it remains a issue. Heterogeneity in terms of population, outcomes, tDCS parameters and concomitant treatments needs to be further investigated so that its clinical benefit can be fully demonstrated. In the future, individualized treatment may become a priority. In this way, by defining symptoms, brain structure, and neuroadaptive factors, the treatment outcomes of tDCS and rTMS could improve.

Combination with other kind of treatment may also be a future research directions. Treatments combined with antidepressants have turned out to be more effective than single treatment option. Other like combinations such as psychotherapy and exercise have not been heavily covered yet. For example psychotropic drugs may amplify or minimize the effects of tDCS, it's essential to find out in which way the effects of tDCS can be maximized. In the future, electromagnetic coupling may becoming a new direction for research. In rTMS and tDCS, a magnetic field or electric current propagates through the scalp and skull into the brain tissue. When applied simultaneously, their electromagnetic fields may interact with each other, which is called electromagnetic coupling, thereby altering each other's effects. It can be inferred that this interaction may enhance or diminish the effects of both techniques, bringing new fields to be explored.

5. Conclusion

In conclusion, tDCS and rTMS have become a possible way to cure depression, especially for the MDD and TRD. Evidence has shown that these two noninvasive brain stimulation could improve one's cognitive disorder, anxiety, which also works better than antidepressants. What's more, combination therapy with antidepressants shown great improvement in patients who suffer from depression. We can see promising future of tDCS and rTMS as treatments of depression since they

perform well in most of cases. However, limitation do exist since the true mechanism of these two NIBS have not been developed yet. And the best parameter of tDCS and rTMS, for example, the stimulus site, frequency, currency, currently 2mA, continue to be developed. Through this research, its efficiency and perspective can be seen clearly. Overall, tDCS and rTMS have already made great progress for being new treatments for depression, especially the TRD and MDD, their future is still filled with many opportunities and challenges. There is no doubt that with continued research and innovation, people can hope to further improve these treatments and provide more effective treatment options for people with depression.

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