

TRANSCRANIAL

MAGNETIC

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STIMULATION:

The Future of Depression Treatment

Growing up, nothing was more comforting to Liam than his mother's smile. His mother was a beautiful woman without a doubt, but it was the genuineness of her smile that made him look for it in the mirror. She had that contagious smile, and when she was happy, he was happy. Once, when he was young enough for her to tie his shoes, he asked his mother what her favorite color was. She told him it was yellow. This surprised him. She did not own anything yellow. When he asked why, she said that yellow was a happy color. He said that yellow was his favorite color too. She smiled, and it was the last time he did not doubt the sincerity of it.

In November of 2021, Liam's mother began transcranial magnetic stimulation (TMS) for her treatment-resistant depression (TRD). In the years leading up to her TMS treatment, his mother had tried three medications in the span of two years, spent countless hours in therapy, and had been a part of an outpatient mental health facility program that spanned weeks. Despite all the effort and commitment she had put into feeling better, nothing was working. It was then that TMS would be recommended to Liam's mother as an alternate form of treatment.

MAJOR DEPRESSIVE DISORDER (MDD)

Major depressive disorder (MDD), used interchangeably with depression henceforth, is a serious mood disorder characterized by persistent depressed mood, lack of interest in once pleasurable activities, low energy, changes in appetite, poor sleep, and, in severe cases, suicidal thoughts and tendencies. To be diagnosed with MDD, a patient must demonstrate at least five of the named symptoms. Prevalence of depression has increased by 25% since 2017 [1], and is expected to become the leading cause of the burden of disease worldwide by 2030 [2]. Current methods of treatment include SSRIs – typically the first line of defense against depression, SNRIs – often used in cases with comorbid pain disorders, and less common medications such as serotonin modulators, tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), or antipsychotics. Treatment-resistant depression (TRD) is considered a form of major depressive disorder (MDD) in which an individual fails to respond to two or more antidepressant trials [3]. For those not interested in medication or have difficulty dealing with side effects from them, cognitive behavioral therapy (CBT) is an alternative that can be used on its own or complementary to medication/other forms of treatment [2]. More recently, receiving FDA approval in 2008, transcranial

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magnetic stimulation (TMS) is being put forth as a non-invasive procedure claiming to alleviate symptoms of depression.

WHAT IS TRANSCRANIAL MAGNETIC STIMULATION (TMS)?

Transcranial magnetic stimulation (TMS) is a method of brain stimulation designed to be non-invasive and generally painless. A copper coil is placed over the scalp to deliver localized pulses of electromagnetic current that excites the neurons below [3]. TMS aims to stimulate areas of the brain where low levels of activity are associated with symptoms of depression [4]. Treatment typically takes place over the course of 4-6 weeks, with stimulation occurring almost daily for no more than an hour [5]. Variations on intensity of the current and time span of treatment depend on individual circumstances. Currently, TMS is most notably used in the treatment of major depressive disorder (MDD) – one of the most common psychiatric disorders worldwide. Of those struggling with MDD, up to 30% fail to respond to standard treatment and are deemed “treatment resistant” [3]. The goal of TMS treatment is to provide those with TRD another option of treatment besides medication or therapy. Though still in its infancy,

accumulating evidence has supported that TMS is a viable contender in the treatment of MDD, with a seemingly limitless potential in the realm of neurological disorders.

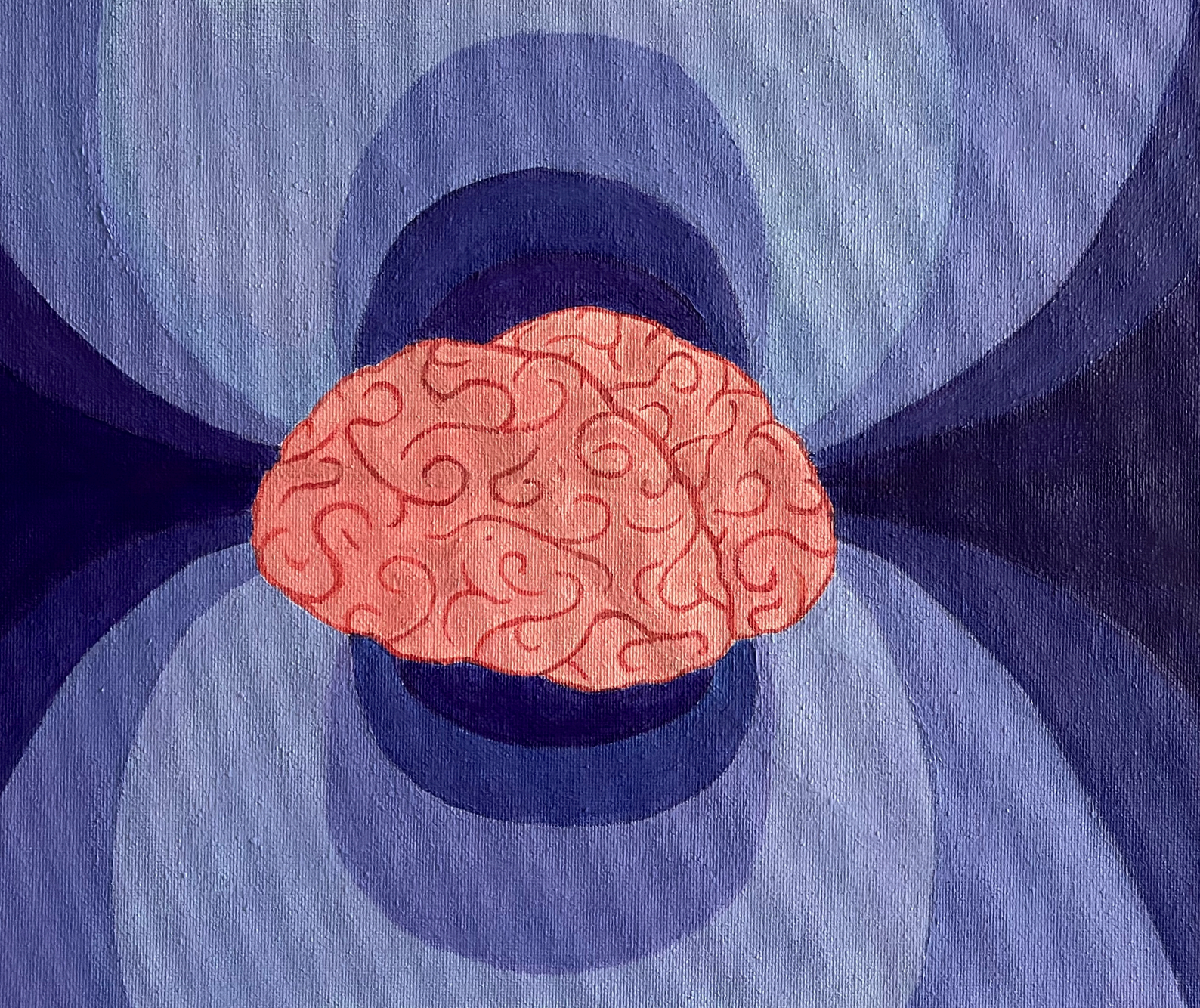
THE PHYSICS MAKING TMS POSSIBLE

While transcranial magnetic stimulation is an achievement of neuroscientific technique, it is important to acknowledge the physics that made it possible. The properties of electromagnetism were carried over into TMS treatment for the first time in 1985, when Anthony Barker and his colleagues introduced a non-invasive technique for brain stimulation. Barker was able to implement what Michael Faraday demonstrated in 1831, that a changing magnetic field could induce an electric current through a loop of wire acting as a conductor [7]. Originally, Barker’s research involved the use of magnetic fields to stimulate the nerves connecting the central nervous system (CNS) to the rest of the body. The first demonstrations of TMS involved scientists stimulating the motor cortex [8]. Since the motor cortex is responsible for planning and producing movement,

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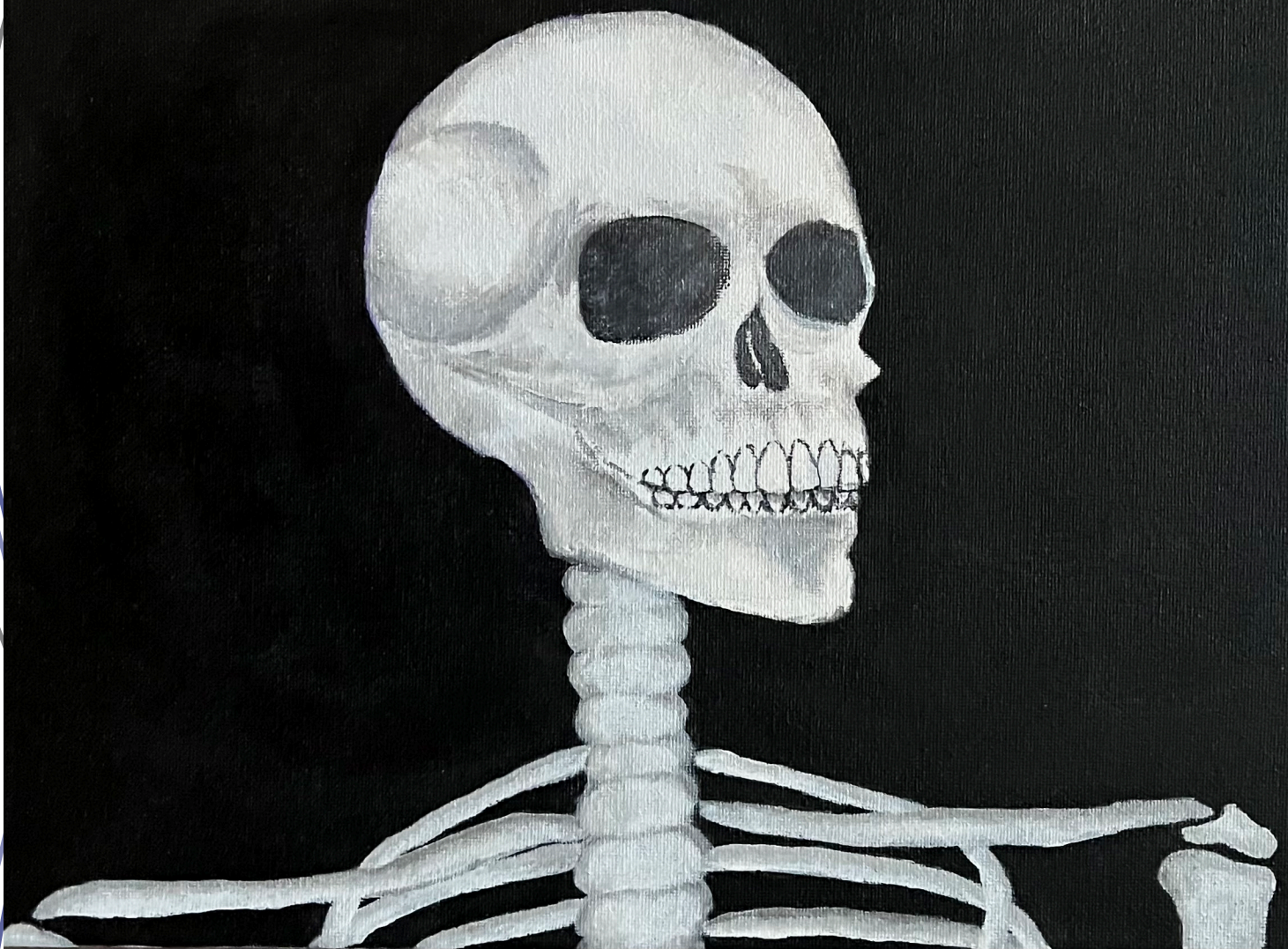


stimulation is used to provoke small but noticeable movement in the hands. The therapy was initially used to treat motor disorders, but interest and research focusing on TMS's potential to treat treatment-resistant depression grew exponentially throughout the 1990s. Almost one hundred clinical trials and meta-analyses would be conducted proposing the effects of TMS on depression before its FDA approval in 2008 [9]. Yet, approval for the treatment of MDD is still only the beginning for TMS, as research continues to illustrate the broad applications of magnetic stimulation to treat a variety of health issues.

APPLICATION OF TMS TO MDD

During the initial appointment for a patient undergoing TMS treatment, a clinician will stimulate the motor cortex to produce small movements in the hand. Movement of the hand proves that the stimulation applied to the motor cortex is intense enough to manipulate brain activity within that region

[5]. The proper identification of the motor cortex will also allow the clinician to better identify the region of the brain targeted for depression treatment, the dorsolateral prefrontal cortex (DLPFC). The term "dorsolateral" refers to the area of the prefrontal cortex that is positioned in the back and to the outer side. While it is well supported that mood regulation is the product of a network of brain regions working together, the DLPFC has been selected as the target of TMS due to its easy accessibility [10]. A coil generating an electromagnetic field is positioned over the DLPFC to deliver repeated pulses of current into the targeted region. The repetition of TMS therapy for depression has led to the interchangeable term "repetitive-transcranial magnetic stimulation" (rTMS) to be used when describing the same procedure. Other methods of TMS, like deep TMS (dTMS), are still being researched, and are not discussed in relation to the treatment of MDD [10].



When these magnetic fields are repeatedly turned on and off over the dorsolateral prefrontal cortex, an electric current is generated to manipulate brain activity in that region. Depending on the frequency of the electromagnetic field, neuronal communication can be excitatory or inhibitory [11]. The specific mechanisms manipulated by TMS as a treatment for depression require further research, but its effectiveness in treating depression is undeniable when compared to placebo. Recent studies have suggested that changes in cerebral blood flow to areas of the prefrontal cortex associated with the paralimbic system may be correlated to effective treatment [12]. Furthermore, it has been postulated that “reconfiguring limbic and prefrontal interactions” is crucial to modulating symptoms of depression. More research will need to be conducted to determine the exact effects of TMS on brain activity, as it has also been theorized to strengthen synaptic

transmission, leading to lasting change. While the long-term effects of TMS are not conclusive, the procedure shows potential to induce changes in neural activity that last long after the actual treatment [10].

ACCESSIBILITY AND SAFETY OF TMS

Most insurances are willing to cover TMS, but different providers may require different prerequisites for beginning treatment. Some insurances require a patient to have failed in responding to at least two antidepressants, others require four, and some even ask for patients to have attempted medications of different classes along with psychotherapy sessions [13]. Despite the range in pre-requisites, TMS is growing in accessibility around the world as it continues to prove its capability to fight treatment-resistant depression. Those who have been diagnosed with a seizure disorder such as epilepsy, or who have ferromagnetic metals implanted around the skull can not be considered for TMS therapy [14]. Considering the

prior depression treatment required for qualifying for TMS, the procedure is typically recommended for adults. However, studies conducted on a pediatric population have concluded that TMS is "safe and well-tolerated in children" [15]. As adolescent mental health issues continue to increase, it may be time to consider new and advanced treatment options.

When beginning TMS treatment, patients will be advised of what the treatment will consist of, as well as possible side effects they may experience during and after stimulation. Patients will be asked to attend treatment sessions about 5 days a week for 4 to 6 weeks, with sessions typically lasting about 20-50 minutes. Ranges in frequency, duration, and intensity rely entirely on the unique protocol for that patient [5]. While rTMS is considered safe and well-tolerated in most patients, the most frequently reported side effect of continuous treatment is headache. In extremely rare cases, rTMS can induce seizures if limitations on stimulation are not adhered to within the parameters designed for that patient [16]. Extensive questionnaires and assessments are done prior to treatment to properly evaluate a patient's risk factors and minimize the likelihood of such an adverse reaction. When considering TMS as a treatment for treatment-resistant depression, the potential benefits typically outweigh the potential consequences.

RESPONSES

Over a decade after its FDA approval for the treatment of depression, transcranial magnetic stimulation has proven to be a worthwhile alternative treatment to antidepressant medication for many patients. A "clinically meaningful response" to TMS treatment has been documented in roughly 50-60% of individuals who have not responded well to medications. Of these individuals who have had a successful experience, approximately one-third will experience a full recovery [5]. In other words, their symptoms are alleviated entirely after completion of TMS treatment. It is recommended that patients continue to meet with their clinician after responding to TMS to monitor symptoms and continue a treatment plan. Some patients begin to reexperience symptoms about a year after rTMS treatment and require a maintenance TMS treatment or adjunct medication [10]. Communication and cooperation between a clinician and their patient should allow for a unique treatment plan that works for the individual. Questions regarding the standard for maintenance TMS and supplementary medication require further research, but the current

evidence suggests that the optimization of TMS treatment is coming sooner rather than later.

CONCLUSION

The increasing burden of major depressive disorder (MDD) calls into question the effectiveness of current treatment methods. It is necessary to introduce and continue researching novel treatments to improve quality of life, work, and play on a global scale. Transcranial magnetic stimulation (TMS) provides those suffering from treatment resistant depression another option. Through the use of a changing magnetic current, relatively focal areas of the brain are targeted for stimulation. By inducing electrical activity in the dorsolateral prefrontal cortex, symptoms of depression have seen improvement. Through open communication with their clinician, patients should be able to work out a treatment plan that works best for them to achieve the best results possible. TMS has already been approved to treat OCD and migraines, and studies are currently being conducted to test its potential in treating many other disorders like stroke, epilepsy, Alzheimer's, PTSD, and much more [16]. Transcranial magnetic stimulation has demonstrated the ability to revolutionize the treatment of neurological disorders, combining lessons in physics and neuroscience to enhance the health and happiness of those suffering from treatment resistant depression. 🧠

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