# International Journal of Science and Research (IJSR) ISSN: 2319-7064

ISSN: 2319-7064 SJIF (2022): 7.942

# Transcranial Magnetic Stimulation: The New Ray of Hope for Stubborn Depression

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Abstract: Depression is a difficult concept and not everyone understands it. The condition of one who live with depression may be fatal if remain untreated. Because most of the studies worldwide shows that depression is one among the leading cause of life disabilities and even death. We were in search for many of the treatment modalities to compete depression but a 100% success rate was not met with any of these methods. Nowadays the medical field has introduced a new approach to treat depression: a non-invasive method namely transcranial magnetic stimulation. Materials and Methods: Several electronic databases, including PubMed, Wiley, Springer, Google Scholar, Web of Science, WHO, Wikipedia, Research Gate, Forbes, Medline, Healthline were searched for this article.

**Keywords:** Transcranial Magnetic Stimulation, ray of hope, stubborn depression

#### 1. Introduction

"Depression is being colour blind and constantly told how colourful the world is"-Atticus Poetry-

Author, storyteller and observer, Vancouver, Canada.

Depression is a common mental health condition that causes a persistent feeling of sadness and changes in how you think, sleep, eat and act. There are several different types. Depression is treatable — usually with talk therapy, medication or both. Seeking medical help as soon as you have symptoms is essential. Depression is a mood disorder that causes a persistent feeling of sadness and loss of interest in things and activities you once enjoyed. It can also cause difficulty with thinking, memory, eating and sleeping. It's normal to feel sad about or grieve over difficult life situations, such as losing your job or a divorce. But depression is different in that it persists practically every day for at least two weeks and involves other symptoms than sadness alone. There are several types of depressive disorders. Clinical depression, or major depressive disorder, is often just called "depression." It's the most severe type of depression. Without treatment, depression can get worse and last longer. In severe cases, it can lead to self-harm or death by suicide. The good news is that treatments can be very effective in improving symptoms<sup>1</sup>.

#### 2. Methodology

The following article is based on data searched/collected from a wide source of books, National & International journals, Internet sources (Including WHO, Wikipedia, Biomed Central, Healthline) and various databases including PubMed, Google Scholar, Wiley, Research Gate, Springer etc.

#### What is depression?

Depression (major depressive disorder) is a common and serious medical illness that negatively affects how you feel, the way you think and how you act. Fortunately, it is also treatable. Depression causes feelings of sadness and/or a loss of interest in activities you once enjoyed. It can lead to a

variety of emotional and physical problems and can decrease your ability to function at work and at home<sup>2</sup>.

Depression is caused by an imbalance of brain chemicals. Other factors also play a role. It also tends to run in families. Depression can be triggered by life events or certain illnesses. It can also develop without a clear trigger<sup>3</sup>.

#### Types of depression

Symptoms caused by major depression can vary from person to person. To clarify the type of depression you have, your doctor may add one or more specifiers. A specifier means that you have depression with specific features, such as:

- Anxious distress: depression with unusual restlessness or worry about possible events or loss of control
- Mixed features: simultaneous depression and mania, which includes elevated self-esteem, talking too much and increased energy
- Melancholic features: severe depression with lack of response to something that used to bring pleasure and associated with early morning awakening, worsened mood in the morning, major changes in appetite, and feelings of guilt, agitation or sluggishness
- Atypical features: depression that includes the ability
  to temporarily be cheered by happy events, increased
  appetite, excessive need for sleep, sensitivity to
  rejection, and a heavy feeling in the arms or legs
- Psychotic features: depression accompanied by delusions or hallucinations, which may involve personal inadequacy or other negative themes
- Catatonia: depression that includes motor activity that involves either uncontrollable and purposeless movement or fixed and inflexible posture
- Peripartum onset: depression that occurs during pregnancy or in the weeks or months after delivery (postpartum)
- Seasonal pattern: depression related to changes in seasons and reduced exposure to sunlight<sup>4</sup>

The American Psychiatric Association's Diagnostic Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) classifies depressive disorders as the following:

Volume 13 Issue 2, February 2024
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Paper ID: SR24130193036 DOI: https://dx.doi.org/10.21275/SR24130193036

ISSN: 2319-7064 SJIF (2022): 7.942

- Clinical depression (major depressive disorder): A
  diagnosis of major depressive disorder means you've
  felt sad, low or worthless most days for at least two
  weeks while also having other symptoms such as sleep
  problems, loss of interest in activities or change in
  appetite. This is the most severe form of depression and
  one of the most common forms.
- Persistent depressive disorder (PDD): Persistent depressive disorder is mild or moderate depression that lasts for at least two years. The symptoms are less severe than major depressive disorder. Healthcare providers used to call PDD dysthymia.
- **Disruptive mood dysregulation disorder (DMDD)**: DMDD causes chronic, intense irritability and frequent anger outbursts in children. Symptoms usually begin by the age of 10.
- Premenstrual dysphoric disorder (PMDD): With PMDD, you have premenstrual syndrome (PMS) symptoms along with mood symptoms, such as extreme irritability, anxiety or depression. These symptoms improve within a few days after your period starts, but they can be severe enough to interfere with your life.
- Depressive disorder due to another medical condition: Many medical conditions can create changes in your body that cause depression. Examples include hypothyroidism, heart disease, Parkinson's disease and cancer. If you're able to treat the underlying condition, the depression usually improves as well<sup>5</sup>.

**Table 1:** How much have depression rates increased?

According to a 2022 study Trusted Source looking at 2015 through 2020, the rates of depression in the United States increased as follows:

Ages	2015	2020
12-17	12.7%	16.9%
18-25	10.3%	17.2%
26-34	7.5%	9.9%

There was no increase in older age groups. In general, the researchers found that in 2020, having depression for longer than a year occurred in 1 in 10 Americans and almost 1 in 5 adolescents and young adults<sup>6</sup>.

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

Transcranial magnetic stimulation (TMS) is a procedure that uses magnetic fields to stimulate nerve cells in the brain to improve symptoms of major depression. It's called a "non-invasive" procedure because it's done without using surgery or cutting the skin. Approved by the U.S. Food and Drug Administration (FDA), TMS usually is used only when other depression treatments haven't been effective. The FDA also approved TMS for obsessive-compulsive disorder (OCD), migraines and to help people stop smoking when standard treatments haven't worked well. Research continues into other potential uses for TMS, including epilepsy. When used for depression, OCD and to stop smoking, this treatment involves delivering repeated magnetic pulses, so it's called repetitive TMS or rTMS<sup>7</sup>.

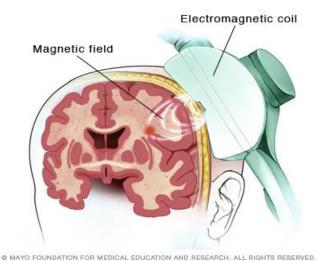


Figure 1: Figure of Magnetic field and Electromagnetic Coil

### 3. Mechanism of Action

TMS uses principles of EM induction. According to the principle of EM induction when an electric current is passed through a coil (primary coil), a magnetic field is generated. When the magnetic flux flows to the secondary coil (neural tissue), a secondary electrical field is induced, and this causes stimulation of the same. Neurons have bent or curved axonal processes, passing at right angles to the lines of force of the magnetic field. They act like secondary coils and thus experience electrical effects. Therefore, by changing the direction of current flow at HFs, rapidly alternating magnetic fields can be generated which in turn stimulate the underlying neurons and their fibers. The phenomenon of applying such stimulation in pulses is known as pulsed EMF stimulation which causes persistent depolarization. These pulsed stimulations are known to correct impaired functioning of cells and aid healing. Repetitive TMS works on similar principles and thus leads to observable clinical effects8

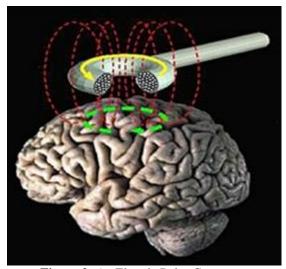


Figure 2: An Electric Pulse Generator

An electric pulse generator, or stimulator, is connected to a magnetic coil connected to the scalp. The stimulator generates a changing electric current within the coil which

Volume 13 Issue 2, February 2024
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# International Journal of Science and Research (IJSR) ISSN: 2319-7064

ISSN: 2319-7064 SJIF (2022): 7.942

creates a varying magnetic field, inducing a current within a region in the brain itself.

#### How TMS therapy works

The therapy is done by a TMS technician or TMS physician. It's an outpatient procedure, so it may be done in a medical clinic. If it's done in a hospital, you won't need to stay overnight.

Before the procedure, you'll need to remove items that are sensitive to magnets, like jewellery.

Here's what you can expect during TMS:

- a) Your technician will have you wear earplugs to minimize the clicking sound of magnetic impulses. They'll have you sit in a comfortable chair. You won't need general anesthesia, and you'll be awake throughout the treatment.
- b) If it's your first session, your technician will measure your head to determine where to place the magnetic coil. They'll also take other measurements to personalize the settings on the TMS machine. Your technician will place the coil above the front area of your brain. Next, they'll start the treatment.
- c) You'll hear a clicking sound as the magnetic impulses are released. You'll also feel a tapping or knocking sensation beneath the magnetic coil.
- d) The treatment can last 30 to 60 minutes. You can drive yourself home after the procedure and resume normal activities.

You'll need to repeat the procedure 5 days a week, for about 4 to 6 weeks. The exact length of your treatment depends on your response and specific condition<sup>10</sup>.

#### **Scalp Position of Coil**

While administering TMS, it is important to determine the position of the scalp and coil orientation for optimal therapeutic effects. In experimental models, the growing cells respond differently to moving electric fields. They tend to align preferentially either parallel or antiparallel to the field vector, a process known as galvanotaxis. Forces in the direction perpendicular and parallel to the electric field are in competition with one another in a voltage-dependent manner, which ultimately govern the trajectories of the cells in the presence of an electric field. Since hypo functioning of the left dorsolateral prefrontal cortex (DLPFC) has been implicated in the pathophysiology of several psychiatric illnesses including depressive disorder; it remains the preferred area for stimulation in most of the studies. There are two ways of determining surface landmark of DLPFC:5 cm technique – About 05 cm toward the left of the vertex a point is marked and about 02 cm ahead of that lies the motor cortex. The motor cortex is functionally localized as a scalp position where TMS evokes a motor movement and a measurable motor-evoked potential (MEP) in the contralateral hand. The prefrontal cortex stimulation site is determined as 5 cm anterior further ahead of the motor strip in the parasagittal line. It corresponds to an area between F3 and F5 position of 10-20 system of EEG recording. Neuronavigational method - This method is theoretically more precise and employs MRI scan to pinpoint DLFPC with live video navigation. Fitzgerald et al. studied 51 patients with treatment-resistant depression using this method and compared matched controlled subjects with standard 5 cm technique and found the superior response at the end of 3 weeks. However, the method is yet to gain popularity probably owing to the high costs of equipment involved. According to existing literature, 5 cm method remains fairly reliable and popular method as far as daily rTMS sessions are concerned.

Coil orientation in repetitive transcranial magnetic stimulation

In routine clinical and experimental models with rTMS, the amplitude of muscle evoked potential (MEP) is an indicator of the maximum effect of a particular orientation with reference to head position. Optimal stimulation has been reported if coil current was at an angle of 45° with respect to the sagittal plain<sup>11</sup>.

#### **Indications**

The therapeutic potentials for rTMS have been demonstrated for the following:

- Treatment-resistant depression
- Obsessive-compulsive disorder
- Posttraumatic stress disorder
- Tourette disorder
- Chronic pain syndrome
- Generalized anxiety disorder (GAD)
- Bipolar disorder
- Movement disorders such as Parkinson disease, functional tremors, focal epilepsy, cortical myoclonus, spasticity<sup>12</sup>.

#### **Contraindications to TMS:**

- Pacemaker
- Spinal or bladder stimulator
- Previous skull opening or trauma
- History of epilepsy (relative)
- Presence of metallic foreign body <sup>13</sup>

#### **Different types of TMS**

There are different ways to perform TMS. They have to do with the magnet's strength or various ways to apply the magnetic field.

- 1) Magnet strength: The unit for measuring the strength of a magnet is the tesla (T). Most TMS magnets generate a magnetic field with a strength of 1.5T to 2T, similar to a magnetic resonance imaging (MRI) scanner. However, the area of the magnetic field is much smaller than it is for an MRI because the TMS magnet is so much smaller.
- 2) Pulse frequency: Each time the magnetic field turns on and off is a pulse. The number of pulses per second is the frequency (which is measured in hertz, abbreviated Hz). TMS can involve low-frequency pulses at 1 Hz (1 pulse per second) or high-frequency pulses at 5 Hz to 10 Hz (5 pulses per second to 10 pulses per second). TMS that uses repetitive pulses is known as repetitive TMS (rTMS).
- 3) <u>Pulse patterns</u>: TMS can also use different patterns of pulses for treatment. An example of this is theta-burst stimulation (TBS). During TBS, a triplet of 5 Hz bursts happens, for a total of 15 pulses in a second. Using these

Volume 13 Issue 2, February 2024
Fully Refereed | Open Access | Double Blind Peer Reviewed Journal
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## International Journal of Science and Research (IJSR)

ISSN: 2319-7064 SJIF (2022): 7.942

burst patterns speeds up treatment, making it about five or six times faster than other methods.

4) Magnetic coil type and stimulation target: Different kinds of magnetic coils can target different brain structures. Deep TMS (dTMS), which involves an H-shaped helmed coil, targets deeper brain structures than rTMS and TBS. Research shows dTMS is effective in treating conditions such as obsessive-compulsive disorder (OCD)<sup>14</sup>.

#### What are the advantages of TMS?

TMS has several advantages that make it a useful treatment.

- It's non-invasive. You don't need surgery for this procedure, and you can go about your day once a session ends. It also doesn't involve anaesthesia of any kind.
- It's safe. Seizures are the most common serious side effect of TMS, but these are very rare. Your risk of having a seizure from TMS is less than 0.01% for each session. Other side effects are usually mild and only last a few minutes.
- It's effective. The success rates of TMS vary by condition, but the available research clearly shows that it works.
- It can save lives. One of the key conditions that TMS treats, major depressive disorder, can be so severe that it leads to death by suicide. TMS can save lives when it brings improvements to depression symptoms or causes depression to go into remission entirely.
- It can work cooperatively with other treatments. TMS often happens along with other treatment techniques, such as medications, mental health therapy and more <sup>15</sup>.

#### Who should avoid this treatment?

TMS is considered safe, but it's not for everyone.

You should avoid this treatment if you have metal in your head, such as:

- · deep brain stimulators
- electrodes
- neck or brain stents
- aneurysm clips or coils
- shrapnel or bullet pieces
- facial tattoos with metallic ink
- metal plates
- cochlear implants
- permanent piercings
- The magnetic fields in TMS can make these implants heat up or move, which can cause serious injuries.

It's OK to get the treatment if you have braces or dental fillings.

#### You may also need to avoid TMS if you:

- have a history of epilepsy or seizures
- are taking stimulants
- have a medical condition that increases the risk of seizures
- Side effects of transcranial magnetic stimulation
- TMS side effects are uncommon. If complications do occur, they may include:
- mild headaches (most common)
- light-headedness

- scalp pain
- neck pain
- tingling
- facial twitching
- sleepiness
- altered cognition during treatment
- Symptoms like headaches and light headedness usually go away after several treatments<sup>16</sup>.

#### 4. Discussion

Repetitive transcranial magnetic stimulation (rTMS) is a recently developed noninvasive brain stimulation method for the treatment of psychiatric and neurological disorders. Although, its exact mechanism of action is still not clear, current evidence points toward its role in causing long-term inhibition and excitation of neurons in certain brain areas. As evidence steadily grows in favour of rTMS as a therapeutic tool; there is a need to develop standardized protocols for its administration. There have been no reports of any serious side effects with rTMS, though its use is restricted in those having magnetic implants or recent adverse neurological or cardiac event. Of all the psychiatric indications of rTMS, the evidence is most robust for treatment of refractory unipolar depression. This paper reviews contemporary literature highlighting the evolution of rTMS as a diagnostic and therapeutic tool, especially in the management of treatment-resistant depression<sup>17</sup>

#### 5. Conclusion

This review article points out the intensity of depression and the new method to treat depression, Transcranial magnetic stimulation. Approximately 280 million people in the world have depression. Depression is about 50% more common among women than among men. Yes, depression is real, but almost treatable. Approximately 50% to 60% of people with depression who have tried and failed to receive benefit from medications experience a clinically meaningful response with TMS.

#### **Acknowledgement:**

Sincere thanks to my father **Mr. Mohan ram Lora** and my husband **Mr. Ram Niwas** for their uninterrupted support. We deeply acknowledge the original work of the respective authors from whom we made our references.

#### **Budget:**

Self-funding

#### **Conflicts of Interest:**

None

#### **Ethical Clearance:**

Not required

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Volume 13 Issue 2, February 2024
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