The Physics, Mechanism, and Application of Transcranial Magnetic Stimulation (TMS)

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Abstract: ***Transcranial Magnetic Stimulation (TMS) is a form of Neuromodulation, a non-invasive method to modulate neural activity in the human brain. The basis of TMS originates from Michael Faraday's work on the principle of Electromagnetic Induction. The electric pulses flow through a coil, ultimately inducing current in targeted brain areas and modulating the brain as required for various clinical conditions. Furthermore, the availability of different types of coils enables multiple forms of TMS, each having its unique use as exemplified by Single-pulsed for Migraine treatment, Paired-Pulse for studying Brain Activity, Repetitive TMS to address symptoms associated with Depression, PTSD, OCD, Chronic pain and other neuro-psychiatric conditions. All these types of TMS continue to make scientific progress and help the community, particularly by targeting specific parts of the brain that could mitigate suffering, alleviate symptoms, and address large-scale disability amongst populations.***

Keywords: Neuromodulation, Magnetic Pulse, Transcranial Magnetic Stimulation, Current, TMS, Coils, EEG, qEEG, Waveform

1. Introduction to Neuromodulation

The International Neuromodulation Society defines Neuromodulation as the alteration of nerve activity through targeted delivery of a stimulus such as electrical stimulation or chemical agents to specific neurological sites in the body. It is non-detrimental, reversible, and alters the quality of human life by treating various psychiatric and physiological disorders. Neuromodulation is a constantly evolving field that includes genetic manipulations and non-invasive modulation of neural systems. Transcranial Magnetic Stimulation (TMS) is a form of Neuromodulation. [1-2]

2. Transcranial Magnetic Stimulation (TMS)

2.1 History of Transcranial Magnetic Stimulation

Transcranial Magnetic Stimulation (TMS) is a non-invasive method of brain stimulation in humans using electric stimuli. The foundation of TMS is believed to be the work of Michael Faraday, whose principle of Electromagnetic induction theorized that a magnetic field can generate an electric current in a conducting material. [3]

The first experiments of Transcranial stimulation began by electrically stimulating the motor cortex using Transcranial Electric Stimulation (TES). A TES test was conducted in 1980 using two electrodes on the scalp to provide an electric impulse to humans; however, this test proved to be ineffective and unethical to humans as only a small fraction of current passed through to the cortex, while the rest of the current created scalp muscle contractions, therefore inducing discomfort and pain. In 1985, an alternative to TES was proposed to use a magnetic field to stimulate the cortical area, resulting in the birth of the field of Transcranial Magnetic Stimulation (TMS). [1]

The Physics behind Transcranial Magnetic Stimulation
TMS employs Faraday's principle of Electromagnetic induction to induce electric current. Due to a rapidly changing magnetic field, an electric pulse (grows to peak strength and returns to zero in less than 1 ms) is transmitted through the TMS coil. This induces a magnetic field perpendicular to the direction of the current. Similar to the electric current, the magnetic field also fluctuates rapidly, resulting in an induction of electric current in the cerebral cortex. This current flows parallel to the coil but directionally reverses the original electric impulse. [1-2]

Furthermore, the Inverse cube law of electromagnetic induction applies here. The Law states that the power of the magnetic field decreases exponentially as the distance from the coil of the current increases. The magnetic field strength decreases speedily with distance, as R-3, where R is the distance between the coil and the brain. Consequently, the electric current decreases swiftly with distance, so TMS is effective for only certain distances in the cerebral cortex. [4]

Within the brain's deeper structures, the current that flows is parallel to the brain's cortical surface, and the effect of TMS is due to the interaction between the induced current and the affected areas of the brain's tissues. [4]

2.2 Transcranial Magnetic Stimulation Hardware

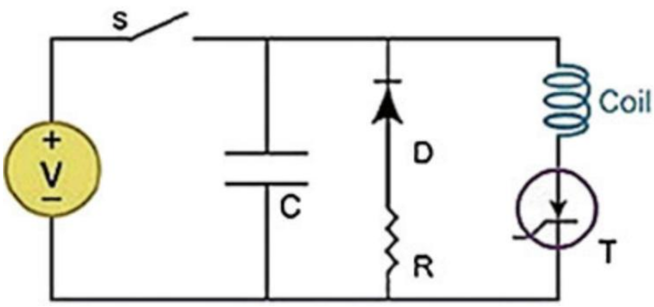

Figure 1: Hardware of a Single-Pulsed Magnetic Stimulator in a simplified circuit diagram [4]

The hardware of universal TMS devices is simplified in the circuit representation in Figure 1. The hardware is divided into two parts: Main Unit & Stimulating Coils.

Table 1: Various Hardware components in the Main Unit with reference to Figure 1

Hardware Component	Description
The Main Unit comprises the following components:	
Charging system	Generates the current, which induces a magnetic field. Generates 8000 A in 100 ms
Capacitors (one or more)	Allow electric pulses to be generated, stored, and discharged 1+ capacitors needed in repetitive TMS
Energy Recovery Circuits	Recharges the central unit
Thyristor	Devices capable of switching large currents in short periods The bridge between the capacitor and coil
Pulse-Shaped Circuitry	Generates monophasic/biphasic pulses

There are different types of TMS coils, with different magnetic field patterns and designs (geometries and sizes), that influence the targeting of specific brain regions:

The different types (and shapes) of TMS coils:

Figure 2a: Round Coil [4]

Figure 2b: Figure-of-eight Coil [4]

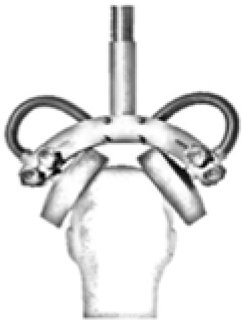

Figure 2c: Double Coil [4]

Figure 2d: H-coil [4]

1) **Circular or Round Coil (Figure 2a):**
   a) The first and simplest TMS design
   b) Generates a spherical magnetic field perpendicular to the coil.
   c) Used in Single-Pulse Stimulation
2) **Figure-of-eight Coil/Butterfly Coil (Figure 2b.):**
   a) Made by joining two circular coils together.
   b) Combined magnetic field strength is greater at the joining point than in other regions.
   c) They are preferred for repetitive TMS.
3) **Double Coil (Figure 2c):** consists of two coils (round or Butterfly coil) and is used in Paired-Pulse stimulation.
4) **H-Coil (Figure 2d)** stimulates deeper cortical levels and has a broader magnetic field distribution.

3. Types of Transcranial Magnetic Stimulation (TMS)

3.1 Single-Pulsed TMS

Single-pulsed TMS is the slowest of all types of TMS. Every 2-3 seconds, the system channels electric pulses into the cortex. This form of stimulation is used more commonly for physiological research or diagnostic purposes rather than modulating psychiatric symptoms. Single-pulsed TMS is also widely regarded as safe for human use and has a relatively high efficacy in treating migraines. [5]

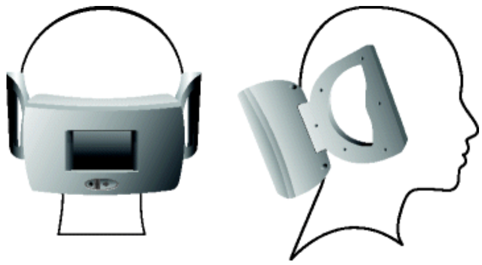

Figure 3: Single-Pulsed TMS system. [7]

The TMS coil is placed tangential to the user's scalp to achieve Single-Pulsed TMS, as shown in Fig 3. The angle at which the system is placed depends on various factors, such as coil shape and size or brain target.

Electrical energy is stored in the capacitors. When a pulse has to be delivered, the stored electrical energy is transmitted to the coils in the form of a 'time-varying' electrical current, which is several kiloamperes. The current induces a magnetic field perpendicular to the coil in nearby conductors, which includes the brain. This magnetic field further creates a current in the tissues, thus initiating modulation in the subject brain. [4-6]

3.2 Paired-Pulsed / Dual-Site TMS

Paired-pulsed TMS (ppTMS), as the name suggests, delivers magnetic pulses in bursts of two/ pairs. Paired magnetic pulses can excite or slow down neurons in the brain. ppTMS delivers two magnetic pulses at two different sites. This provides scientists with more information regarding brain activity. ppTMS is used for researching Brain Activity. Similar to single-pulsed TMS, ppTMS is not common to treat psychiatric symptoms. [5]

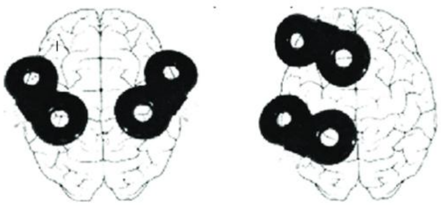

Figure 4: Paired-Pulsed TMS – coils delivering magnetic pulses at two different sites. [8]

3.3 Repetitive TMS

Repetitive TMS (rTMS) is most commonly used in TMS therapy, using a figure-8 coil. rTMS was FDA-approved in 2008 to address treatment-resistant depression. rTMS has also been studied to treat post-traumatic stress disorder, obsessive-compulsive disorder, Tourette's Syndrome, Chronic pain, anxiety, bipolar and movement disorders. [4-5]

rTMS stimulates specific regions deep inside the brain by producing low-intensity and high-intensity magnetic fields, further modulating cortical excitement. A high-intensity Magnetic field (>5Hz) increases cortical excitement, and contrarily, a low-intensity field (<1Hz) dampens cortical excitement. rTMS refers to the delivery of 'trains' of TMS pulses over a cortical region. Low-frequency pulses are delivered continually, while High-frequency pulses are delivered in short bursts with 100 ms to several seconds intervals between trains, as shown in Fig 4. [4-5, 9]

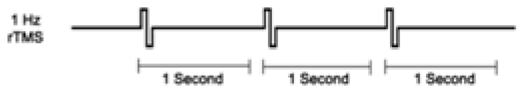

Figure 5a: Continuous delivery of low frequency rTMS for several seconds. [5]

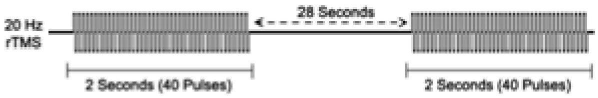

Figure 5b: Delivery of high frequency rTMS for short bursts, in form of trains, followed by seconds of inter-train interval. [5]

3.4 Deep TMS

Deep TMS is an upcoming, innovative, and exciting method of Transcranial Magnetic Stimulation that has been studiedfor concussions, PTSD, depression, OCD, anxiety and addiction. It uses an H-coil to generate magnetic impulses in deeper areas of the brain. [5]

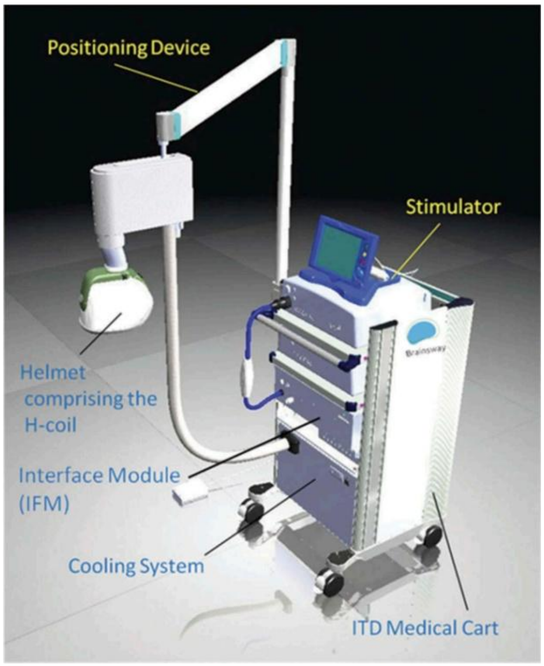

Figure 6: A Deep TMS system and an H-coil Helmet [10]

The helmet shown in Fig 6 consists of a H-coil. An electric pulse is passed through the H-coil, creating a varying magnetic field, thus inducing a current in a targeted brain region.

3.5 qEEG-Guided TMS

Electroencephalography (EEG) is the measurement of electrical patterns at the surface of the scalp which reflect cortical activity and are commonly referred to as "brainwaves". Quantitative EEG (qEEG) is the analysis of the digitized EEG, and in lay terms, this is sometimes called "Brain Mapping".

Quantitative Electroencephalography (qEEG) is a procedure that processes the recorded EEG activity from a multi-electrode recording using a computer. This multi-channel EEG data is processed with various algorithms, such as the "Fourier" classically or, in more modern applications, "Wavelet" analysis. The digital data is statistically analyzed, sometimes comparing values with "normative" database reference values. The processed EEG is commonly converted into color maps of brain functioning called "Brain maps."

This aids in designing treatment plans and diagnosing neurological and psychological problems. The comprehensive outline reports any abnormality in the brain, such as mental or neurological disorders. It can also be used to monitor the treatment and progress of changes in brain function over time. [5, 11-13]

qEEG Transcranial Magnetic Stimulation is a form of Guided TMS. qEEG TMS utilizes the brain mapping method of EEG to provide a personalized treatment plan and monitor neurological and psychiatric outcomes in real time. [11-13]

For example, Fig. 7a and 7b depict a person with OCD being treated with the benefit of qEEG TMS. The pre-TMS brain map is shown in Fig 7a, and the post-TMS brain map is shown in Fig 7b.

The color-coded display represents:

- **Red:** Overactivity (3)
- **White:** Normal (0)
- **Blue:** Underactivity (-3)

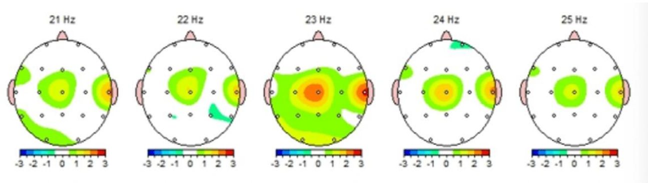

Figure 7a: Pre-TMS EEG brain map of a person with OCD [11]

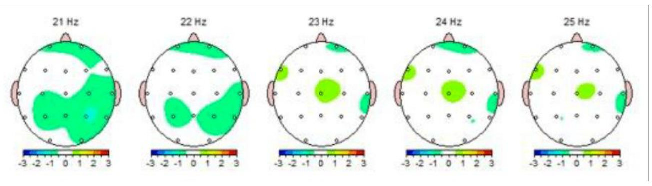

Figure 7b: Post-TMS EEG brain map of an individual with OCD [11]

3.6 PrTMS

Personalized TMS (PrTMS) is an evolution of standard rTMS over time. It utilizes Spectral EEG to map and diagnose brain arrhythmia and guide the brain toward wellness. It involves tailoring the parameters of TMS, such as the intensity, frequency, duration, and target location, to optimize treatment outcomes for each specific patient.

The adjustment of the frequency and location of treatment weekly enhances the effectiveness of TMS and improves clinical outcomes. These small, personalized adjustments in stimulation dose parameters, based on the patient's response to stimulation, have resulted in notable improvements in memory, sleep, focus, and success in difficult-to-treat conditions such as Autism, traumatic brain injury (TBI), concussions, post-traumatic stress disorder (PTSD), insomnia, depression, anxiety, and other related conditions.

PrTMS is used to treat brain arrhythmia directly in order to optimize each individual's brain function to the degree and specifications they require.

Fig 8 showcases a person with brain arrhythmia with a disruptive wave form and incoherence of alpha wave activity in the front of the brain. Following PrTMS, the coherence of alpha wave activity is restored, as indicated by sharp alpha waves highlighted in the front of the brain Fig 8.[16]

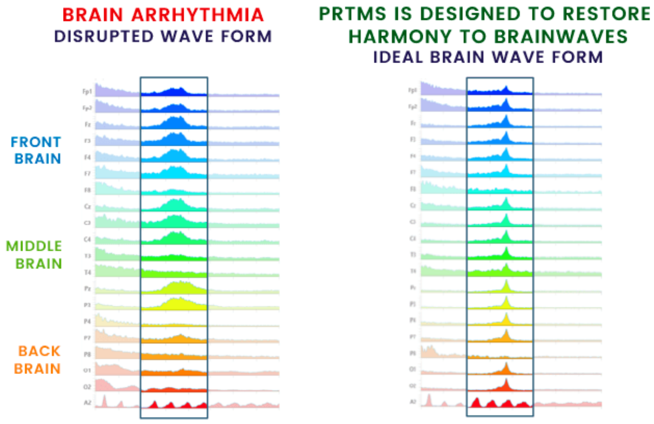

Figure 8:
Left: Disrupted Brain wave form.
Right: Ideal Brain wave form (post-PrTMS) [16]

4. Applications of TMS [4]

4.1 Psychiatric Applications:

1) **Major Depressive Disorder (MDD):** TMS has been FDA-approved for the treatment of Major Depressive Disorder in cases where traditional treatments such as medication and psychotherapy have been ineffective. It is often used when other options have failed or when patients prefer non-pharmacological interventions.
2) **Bipolar Disorder:** TMS has shown promise as a potential treatment for bipolar depression. It can be used to target depressive symptoms in individuals with bipolar disorder, either as a stand-alone treatment or in combination with other therapies.
3) **Generalized Anxiety Disorder (GAD):** Some studieshave explored the use of TMS in treating symptoms ofgeneralized anxiety disorder, although this application is less established than its use in depression.
4) **Obsessive-Compulsive Disorder (OCD):** TMS is being investigated as a potential treatment for OCD, particularly for individuals who do not respond well to standard treatments, namely cognitive-behavioral therapy (CBT) or medication.
5) **Post-Traumatic Stress Disorder (PTSD):** TMS is also being studied as a potential treatment for PTSD. Modulating brain activity in regions associated with fear processing and emotional regulation may help reduce symptoms in some individuals with PTSD.

4.2 Physiological Applications:

1) **Chronic Pain**: Although TMS cannot cure Chronic Pain, it can relieve some symptoms. For instance, migraines can largely be relieved using Single-Pulsed TMS, or Chronic Lower Back Pain can be alleviated by modulating the pain pathways of the brain using TMS.
2) **Parkinson's:** Individuals with Parkinson's often go through severe anxiety and depression - TMS can help relieve anxiety and depression. Moreover, research into the neural mechanisms affected by Parkinson's, is being actively conducted. Studies show that researchers use TMS to study specific brain regions and their potential impact on motor and non-motor systems.

5. Future of Transcranial Magnetic Stimulation

5.1 Transcranial Magnetic Stimulation is being explored for:

1) **Schizophrenia**: It is a mental health disease with many symptoms, such as lack of emotion, apathy, and societal withdrawal. TMS may be able to help with these symptoms. The research is ongoing but not conclusive. Current treatment of Schizophrenia involves pharmaceuticals with disabling systemic side-effects that can be potentially avoided, should TMS treatments become effective.
2) **Autism**: TMS is being explored as a potential treatment option for individuals with Autism Spectrum Disorder (ASD), particularly to address core symptoms, including verbal communication, agitation, impulsivity, anxiety, and poor eye contact.
3) **Substance Use Disorders:** TMS has been studied as a tool to help reduce cravings and dependence in individuals with substance use disorders, including alcohol and drug addiction.

5.2 TMS in the Future

1) **Personalized Treatments in the future:** As brain mapping and EEG technologies evolve, the future is optimistic for disabling neuro-psychiatric disorders. These techniques can provide a more accurate diagnosis and targeted personalized treatments based on EEG bio-markers.
2) **Improved Targeting and Personalization:** The future of TMS may involve more precise and individualized treatment approaches. Advanced imaging techniques, such as functional MRI (fMRI), could identify specific brain regions and neural circuits implicated in various psychiatric and neurological disorders. This would allow for more targeted TMS treatments tailored to each patient's unique neurobiology.
3) **Home-Based TMS:** Portable TMS devices are under development. In time, TMS services will be offered at homes, thus eliminating/reducing mental health-related problems, depression, and anxiety in the general public.
4) **Non-Psychiatric Applications:** TMS is not limited to only neuro-psychiatric disorders. Neuromodulation is utilized in research settings to enhance human performance in competitive sports and the military.
5) **TMS in Research:** TMS continues to be used as a research tool to study brain function, map cortical areas, and investigate the neurophysiological basis of various cognitive and motor functions.

6. Conclusion

The review paper aims to discuss neuromodulation with a specific focus on Transcranial Magnetic Stimulation. The article provides a comprehensive insight into the history of TMS, the various devices, and its multifaceted applications.

As TMS continues to evolve, ground-breaking technological research has expanded its use and applications from probing brain function to treating disabling, complex neuro-psychiatric disorders.

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