EMERGING APPORACH OF TRANSCRANIAL MAGNETIC STIMULATION IN TREATING VARIOUS SPECTRUM OF DISORDERS

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ABSTRACT: -

Transcranial magnetic stimulation (TMS) is a non-invasive procedure which stimulates the activity of the brain at different areas of the brain using an electromagnetic field to improve the symptoms of wide range of neurological disorders. TMS is approved by United States Food and Drug Administration for Major depression, Obsessive-compulsive disorder, smoking cessation and anxious depression. Other wide range of diseases which are in trails for resolving symptoms are Anxiety, PTSD, Schizophrenia, Panic disorder, Chronic pain, Alzheimer s disease, parkinson's disease and epilepsy.TMS acts mainly by the principle of electromagnetic stimulation ,where an electric current passes through a coil(primary coil),magnetic field gets generated thereby magnetic flux flows to the secondary coil (neural tissue)and electric field gets generated .This stimulation caused by electromagnetic field at neurons in the various regions of the brain depending on the condition to be cured or healed . A motor response is elicited at a certain threshold when TMS is applied on the motor area/motor threshold. There are different number of parameters that are determined to reach different treatment goals which includes number of stimulations, stimulation intensity and frequency, length of interval between stimulation and different target areas of brain to be stimulated. TMS will not change a person's personality either permanently or temporarily even though there are mild side effects coming with TMS application. TMS have a very effective outcome but it also shows mild side effects like headache, discomfort, facial twitching, neck pain, sleepiness and seizures rarely. TMS has been demonstrated to achieve clinical trials and has even higher efficiency rates in naturalistic clinical practice settings. This review provides knowledge regarding the therapeutic application, safety and efficacy of TMS on various neurological and psychiatric diseases.

KEY WORDS: - *Transcranial Magnetic Stimulation, rTMS, Neuromodulation technique, Major Depressive Disorder, Temporal resolution, Spatial resolution.*

INTRODUCTION: -

Over more than couple of decades, the research on magnetic therapy, electric therapy and electrophysiological understanding of the brains activity and its pathological conditions have been studied. These studies have made contributions to the better and successful therapeutic plan (Hallett, 2007). Magnetic therapy is a Pseudo scientific therapy which involves the weak static magnetic field produced by a permanent magnet. Whereas electric therapy is the stimulation of nerves and muscles by electric field and excitable membranes gets depolarized using current injected into the body via surface or implanted electrodes (Iglesias, 2020). The electromagnetic stimulation principle is accepted beneficial than using magnetic and electric stimulation alone (Burke et al., 2019; Iglesias, 2020; Lefaucheur et al., 2020).

The field of technology in neurosciences especially in the disciplines of psychiatry, psychological, neuro-degenerative disorders moves at a rapid pace (Leon Ruiz et al., 2018; Begemann et al., 2020). TMS is a big step in this direction and offers a newer therapeutic intervention. TMS is an effective tool for the treatment of various clinical applications of the brain.One such emerging approach includes Transcranial Magnetic Stimulation (TMS) that helps in resolving symptoms of Neurological disturbances which is a gaining popularity now a days . Though there are many trials undergoing for TMS, FDA has approved application of TMS in Major Depressive Disorder, Smoking Cessation, Obsessive Compulsive Disorder and anxious depression during the years 2008, 2013, 2020 and 2021 respectively (Ferrarelli et al., 2021).

Modern technology of TMS has shown remarkable actions on the brain, growing number of studies are done for its application of therapeutic use, safety and efficacy of the treatment. Although there have been considerable beneficial results, side effects are also of little concern. Researchers strive to explore and develop newer ways with the development of TMS for more efficacies and lowering of the risks. Working principle of TMS involves Faraday's law of electro- magnetic induction in which electric current flows through a copper coil/electric coil will induce magnetic field perpendicular to current until it reaches another electric current material (Latorre et al., 2019). This induces magnetic rays that act on brain. Various studies have concluded different types of brain stimulation that can be performed by TMS which include Transcranial alternating current stimulation, transcranial electrical stimulation, vagus nerve stimulation, transcranial direct current stimulation, low field magnetic stimulation, Transcranial random noise stimulation, cranial electric stimulation, and deep brain stimulation (Parikh et al., 2022).

There are four types of TMS .they are single-pulse, paired pulse, repetitive and deep TMS. Single-pulse transcranial magnetic stimulation (TMS) is a safe and useful tool for investigating various aspects of human neurophysiology, particularly corticospinal function, in health and disease. Paired-pulse sequence (ppTMS) is a noninvasive method to evaluate the excitability of corticocortical connections (inhibitory and excitatory connections). Repetitive TMS (rTMS), however, is a more powerful and potentially dangerous modality, capable of regionally blocking or facilitating cortical processes. Especially used in treatment of Major Depression Disorder (MDD) (O'Reardon et al., 2007; Gold et al., 2019). The electromagnetic induction generated by rTMS is painless and safely passes than other type of

TMS. Deep TMS is the least invasive method for brain stimulation which is mainly used for MDD (McClintock et al., 2018; Garnaat et al., 2018).

Repetitive TMS is a variation of TMS where stimulation is provided in sessions of same condition to create long term excitation in the brain Cortex. In rTMS, the electric activities in the brain are influenced by the magnetic fields. The electromagnetic induction generated by rTMS is painless and safely passes through the skin and skull and reaches brain.

PROCEDURE (WORKING OF TMS):-

When a patient is advised to undergo for TMS procedure, it is mandatory that the protocol is definitely followed by the therapist for the particular treatment of disease. The patient should be eligible for the TMS criteria and should be perfectly fit and fine for the treatment. The patient should be well explained about the indications and contraindications along with side effects to avoid further complications of TMS. Basically the TMS procedure involves the application of electromagnetic field against the forehead that acts on the cortex region of brain or other desired regions of brain.

Therapist will determine the ideal stimulation at the initial TMS appointment (referred to as motor threshold) along with anatomical target position for placement of magneti8c coil. The electromagnetic coil placed in the recommended position creates a magnetic field that specifically targets the left dorsolateral prefrontal cortex (DLPFC), the area of brain which is responsible for mood regulation. The applied magnetic field helps in resolving the symptoms of the disease for which TMS is applied. The TMS therapy system generates highly concentrated magnetic field, through a treatment coil which turn on and off very rapidly. The magnetic fields produced by TMS machine are similar to those of Magnetic Resonance Imaging (MRI). The magnetic field produced, do not directly affect the whole of brain but they only reach about 2-3 centimeters into the brain directly beneath the treatment coil. When the magnetic fields move into move into brain, they produce very small electric currents which activate cells within the brain that are thought to release neurotransmittors like seratonin, nor-epinephrine and dopamine. For example, In Depression, it is thought to be the result of imbalance of these chemicals in brain and as a treatment procedure, TMS can restore that balance and thus relieve the symptoms of Depression eventually the Depression itself. It is proved that symptomatic relief isn't usually noticeable until at least the third week of treatment session though one session may be enough to change the brain's level of excitability and balance.

Usually after performing one cycle of TMS, patients may experience some kind of discomfort in the forehead region which is not much significant and can be treated with some proper sleep. It is also proven that the very first cycle of TMS has showed betterment in mental condition of the patients in case of neuro disorders. For the complete cure of disorders in the patients who are treatment resistant, it is important to perform the procedure for particular sessions as per FDA approved guidelines. The procedure involves the maintenance of frequency as per guidelines that vary from disease to disease. The intensity of frequency is the most important parameter in TMS since brain is an electro conductive organ. Since the process of TMS is non-invasive and effortless, the patient can undergo for the process

whenever the individual wants it and it is an outpatient procedure. Time required by the patient is very little and prompt.

TMS IN TREATING DEPRESSION:-

Depression is a common mental disorder, characterized by sadness, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, feelings of tiredness and poor concentration.It gradually impairs a person'sability to function at school or work, or cope with day to day life. At severe depressive stage it can lead to suicide. Globally, depression have been always a great cause of health concern and an estimated 3.8 %of the population suffering from it according to World Health Organization (WHO). In India 45.7 million people are suffering from it. Higher prevalence rate was seen in females (3.9%) than males (2.7%) (Croarkin et al., 2019; Cirillo et al., 2019).

There are many conventional therapies for depression including Anti-depressant therapy, psychotherapy and Electroconvulsive therapy. Adequately two-thirds of the depression patients gradually develop resistance towards anti -depression drugs ,they may go for Electroconvulsive or shock therapy.Though ECT is considered as golden standard for treatment resistant depression ,it is hard to many patients to tolerate its side effects on memory on cognition .There have been arose the need of newer technique -Transcranial magnetic stimulation to treat depression. The United States Food and Drug Administration (FDA) have approved TMS for the treatment of major depression in 2008.

It has been over a decade after FDA approval, TMS have shown its efficacious and therapeutic role .It has proven its satisfactory response in adults with treatment resistant depression. The rTMS was well tolerated and only few adverse effects have been reported. rTMS acts on different regions of the brain following three protocols. Firstly, Low frequency (LF-rTMS) stimulation of the left dorsolateral prefrontal cortex (DLPFC) inturn increases the levels of glutamate at 20 Hz and increases the levels of dopamine at 10 Hz in MDD and increases the 5-HT2A receptor binding indices increases in Unipolar depression. High frequency (HF-rTMS) stimulation of the right DLPFC shows it increases the dopamine and glutamte at different frequencies. And the last one is the combination of the both Low frequency (LF-rTMS) and High frequency (HF-rTMS). Mostly it have been proven that low frequency on left dorsolateral prefrontal cortex (DLPFC) has more effect than high frequency (HF-rTMS). Definitely, TMS is a boon for treatment- resistant depression patients.
Frequency:- As per FDA approved protocol the frequency used to treat MDD is 1-3HZ depending on severity of the condition and that lasts for 4 seconds stimulation&26 seconds pause with the duration of 37 minutes. It is performed for 5 days per week in 20- 30 sittings each cycle (Gold et al., 2019).

TMS IN TREATING OCD:-

Obsessive-compulsive disorder (OCD) is a mental illness that is characterized by obsessions and compulsions ,where as obsessions are repeated unwanted thoughts or sensations and compulsions is a condition of the urge to do something over and over again .Usually patients come with up with compulsive behaviour, meaningless repetition of words or actions, anxiety, depression and other psychological and behavioral symptoms .Obsessive

- compulsive disorder (OCD) is one of the psychological illness that affects 1-3 % of the world's population. Despite of all pharmacological and psychotherapies, 40% patients experience limited improvement and slow or negligible reduction in symptoms. There the need to introduce a newer approach for treating OCD patients and transcranial magnetic stimulation was studied, trailed and tested over more than two decades. Finally, the FDA (Food and Drug Administration) had approved the use of TMS in treating OCD patients in 2018. TMS is placed using a wire coil, during stimulation a brief amount of high current is produced in the coil which in turn generates strong magnetic field for about 100 microseconds in few areas of the brain. Especially in these areas like Dorsolateral Prefontal Cortex (DLPFC), Orbito-frontal cortex (OFC) and Pre-Supplementary Motor Area (pre - SMA).Where as orbito-frontal cortex and pre-supplementary motor area(pre-SMA) may be targeted because of its over activity in OCD patients (Carmi et al., 2019; Fitzsimmons et al., 2022).

Frequency:- TMS in treating OCD is widely used with the application of magnetic filed with the frequency of 3Hz for about 30-40 minutes with 12 seconds pause in each sitting. It is performed for 5days per week and that lasts for about 4-6 weeks.

TMS IN SMOKING CESSATION:-

Smoking cessation, usually called quitting smoking or stopping smoking is the process of discontinuing tobacco smoking .This greatly reduces the risk of developing smoking - related health damage issues. Cigarette smoking remains a significant public health concern.About 15%of global deaths are attributed to pre mature deaths due to smoking.

FDA approved TMS for its indication for smoking cessation in 2020.So many researches were performed in order to conclude its safety and efficacy for smoking cessation .TMS modulates neural processing in the brain ,there by inducing a short capacitor discharge of electric current into a stimulated coil, and inturn subsequently generate magnetic field, which then induces neural cell membrane potentials depolarizing in cortical tissue under the coil and affect the related nerve loop activity.(ref -). A 20 Hz rTMS sequentially applied to the left DLPFC and the SMFC for 10 days produced a high smoking cessation rate, which was confirmed by both the behavioral measures and the fMRI data. rTMS caused smoking cessation for the entire 25-day follow-up time, reduced craving for smoking,Sudden smoking abstinence caused increased CBF ,after 10 days there have been considerable reduction in CBF. Mostly, TMS induces at the nucleus accumbens, prefrontal cortex and the ventral tegmental area (VTA) are focused while treating a smoker for better clinical effect on reducing craving for a cigarette. Most of the studies have concluded that TMS at definite frequency have shown remarkable role in smoking cessation (Zangen et al., 2021; Young et al., 2021).

Frequency:- To resolve the symptoms and habits of smoking, the frequency used is 10Hz (Repetitive) for about 15 minutes. The whole rTMS procedure for smoking cessation lasts for about 2 weeks with 10 sessions.

TMS FOR DISEASES UNDER CLINICAL TRIALS:-

TMS in treating few other diseases is yet to be approved which include Alzheimer's disease, Schizophrenia, Chronic pain, Parkinson's disease, Stroke rehabilitation, Post traumatic stress disorder, Anxiety, Multiple sclerosis and Nicotine addiction. The clinical trails for the mentioned diseases are underway and are likely to get approval in further years in the upcoming decades.

TMS FOR ANXIETY:

TMS is an innovative approach in treating generalized anxiety disorder. Since magnetic pulses are acting on the brain, it calms and controls our responses to threats or fears. Though research is limited, doctors have seen success using TMS to treat anxiety. Studies have significantly shown that it benefits for individuals who have been diagnosed with 'anxious depression' or depression and co-morbid anxiety. In such cases both depression and anxiety have been reduced through TMS (Cirillo et al., 2019; Burke et al., 2019).

ANXIOUS DEPRESSION

After conducting so many studies FDA had approved TMS for anxious depression in 2021, yet protocol for use has been least considerate. Mostly TMS is efficacious in anxious depression as both anxiety and depression are correlated because of its similar action on the brain activity .And TMS focuses on DLPFC and relative differences of intensity of action at the left and right hemispheres. Here, it improves functionality of the brain and stimulates the ability of the prefrontal cortex's ability to regulate emotions .Mainly, magnetic fields raises the activity in the left DLPFC and reduce the activity in the right DLPFC. There by lowering the activity levels in the right brain helps to relieve from anxiety. Hence, TMS have upgraded time to time and its efficacy over mental illness spectrum is getting increased gradually (Croarkin et al., 2019; McClintock et al., 2018).

Frequency:- The frequency used to relieve symptoms of anxiety is 1Hz -10Hz over 10-30 sessions. The Pulses provided per stimulation are 750-3600 with 110% of rest motor threshold

TMS IN TREATING POST TRAUMATIC STRESS DISORDER:-

Post traumatic stress disorder, a condition that is characterised by failure to recover after witnessing or experiencing a terrifying event. TMS plays a major role to overcome the stress by brain signalling that relieves it which is caused by such events. The primary treatment suggested for post traumatic stress disorder is anti-depressant medication and psychotherapy. Dorsolateral prefrontal cortex yields promising results for relieving post traumatic stress when applied with Repetitive transcranial magnetic stimulation. TMS in treating PTSD have shown maximum efficacy when functional neuroimaging techniques were involved in which TMS increase blood flow or metabolism in right limbic, paralimbic, and frontal cortical structures when recalling the traumatic event associated with their symptoms. Preferential right hemispheric involvement in the experience of unpleasant emotion was observed in may studies. It was found that right limbic and paralimbic structures

are intimately involved with emotional symptoms associated with trauma and could be the target of neuro biological treatment strategies (Leon Ruiz et al., 2018).

Frequency:- The suggested frequency for treating PTSD is 20 Hz rTMS per sitting daily in 10 sessions over two weeks .Total number of sittings included are 15-20 sittings.

TMS IN TREATING SCHIZOPHRENIA:

Schizophrenia is characterised by thoughts or experiences that seem out of touch with reality, disorganised speech or behaviour and decreased participation in daily activities. Difficulty with concentration and memory may also be present. The primary treatment for schizophrenia is pharmacotherapy and alternative therapy as TMS .TMS is applied to individuals suffering from schizophrenia to induce chemical activity in brain that resolves symptoms of Schizophrenia. Studies were first performed on patients with schizophrenia and magnetic field is administered with a large round coil to the vertex, thereby stimulating broad regions of bilateral prefrontal and parietal cortices. The study concluded that 60% of medicated patients with chronic schizophrenia got benefitted with TMS in a single session. The patients were subjected with magnetic field with a smaller round coil positioned on the right pre-frontal cortex. 70% of patients showed positive signs towards resolving symptoms of schizophrenia in the further sessions of TMS. It was proved to be effective when the coil was positioned over the left temporo-parietal cortex at the frequency with 1Hz rTMS (Mehta et al., 2019).

When the study was performed in a different set of patients, it was found that hight frequency rTMS applied to the Prefrontal cortex on the basis of high-frequency rTMS might be useful in reversing the hypofrontality observed in schizophrenia. The patients administers with 20Hz rTMS to the midline prefrontal cortex for at least two weeks , reduction in negative symptoms was observed .More studies is needed to be performed to know the effectiveness of TMS in treating the negative symptoms using high frequency of magnetic field (Nucifora et al., 2019).

Frequency:- The initial frequency used in treating schizophrenia is 1Hz in 10 rTMS sessions with 110% of motor threshold, 30 trains of 60-second duration in performing right Dorsolateral prefrontal cortex.

TMS IN TREATING PANIC DISORDER:-

Panic disorder is a type of anxiety disorder which causes panic attacks that are sudden feeling of terror when there is no real danger. It is characterised by loss in control and physical symptoms like fast heartbeat, sweating, trembling or shaking, shortness of breathe. Panic attacks are stabilised using medications and also by providing emotional and mental support at the times they are experiencing attacks. The patients who are not benefitted with medications are subjected to TMS in treating the symptoms of panic attacks. The majority of neuroimaging studies have shown elevated right sided activity in the frontal and hippocampal-Para hippocampal regions in fear paradigms and anxiety disorders. According to studies it is stated that low frequency rTMS may be helpful in dampening the lateralised hyperexcitability that uses 1Hz rTMS for the positive symptoms of anxiety disorders. The

hypothesis stated that high frequency rTMS on the dorsolateral prefrontal cortex will decrease anxiety centres in patients facing the anxiety symptoms (Li et al., 2014).

Frequency:- The initial frequency used in treating schizophrenia is 1Hz in 10 rTMS sessions with 110% of motor threshold, 30 trains of 60-second duration in performing right Dorsolateral prefrontal cortex.

TMS IN TREATING CHRONIC PAIN:-

Chronic pain is defined as an unpleasant sense of discomfort that persists or progresses over a long period of time which lasts for month to years. It is found that 27% of population is prevalent to chronic pain which is similar to other chronic conditions. After referring all the articles and newsletters, it is concluded that rTMS is beneficial for treating neuropathic pain of various origins such as pain from peripheral nerve disorders, central pain, fibromyalgia, and migraine. TMS stimulates brain cortex by producing brief magnetic pulses that passes inoffensively through the skull and into the brain. This magnetic pulse which induce change in cortical excitability at stimulation site and transynaptically at distant areas. rTMS is hypothesised to induce alterations in the activity of cortical and subcortical brain structures which are related to pain modulation and processing, including medial thalamus, anterior cingulate, orbitofrontal cortices and periaqueductal grey matter. Additionally, rTMS reduces chronic pain by acting at the dorsal horn level by triggering descending inhibitory neuronal pathways. In other perspective, rTMS is also known to alter neuronal activities in the periaqueductal grey matter, which is related to pain processing (Moisset et al., 2020; Fernandes et al., 2022).

Frequency:- As per study conducted on low frequency rTMS(1Hz,1600 pulses/session) over the right dorsolateral prefrontal cortex(DLPFC) showed effective rapid onset pain relief. As per the other study on high frequency rTMS(20Hz,2000pulses/session) shows better efficacy on pain relief over sham sessions and the effect shown lasts for 15 days to 1 mon

TMS IN TREATING ALZHEIMER'S DISEASE:-

Alzheimer's disease is defined as a progressive neurological disorder that slowly destroys memory and thinking skills. It is found to be the most common cause of dementia depending upon the brain changes. With regard to Alzheimer's disease, rTMS protocols are classified as two types, they are High frequency protocol and Low frequency protocol with frequency of <1Hz and >3Hz respectively. In treating Alzheimer's disease the recommended frequency was ranging from 10Hz to 20Hz. Low frequency is also called as Conventionl frequency where as Patterned frequency is called as High frequency which is periodically applied to treat the symptoms of Alzheimer's disease. TMS is targeted to first apply on Right dorsolateral pre frontal cortex and then immediately followed by rTMS over the left Dorsolateral prefrontal cortex. In the occurrence of AD, over expression of Beta-amyloid causes epileptiform activity within the entorhinal-hippocampal circuitry that, together with homeostatic responses to aberrant firing, may contribute to memory dysfunction in humans with AD. On application of TMS beta-amyloid is inhibited through the magnetic pulses and improves the neurological impulses in the brain (Koch et al., 2018; Mimura et al., 2021).

Frequency:- The frequency used in treating AD is 10Hz per 40 seconds each session with the threshold of 110%. The duration lasts for about 6-8 weeks.

TMS IN TREATING PARKINSON'S DISEASE:-

Parkinson's disease is a neurodegenerative disorder characterised by tremors, muscular rigidity, postural instability and slow movement of muscles that majorly affect middle aged and elderly individuals. Generally dopamine receptor agonists are used in treating Parkinson's diseases but in the patients who are not responding to the medication alone are exposed to TMS in resolving symptoms for same. Initially the patients suffering from PD are assessed whether high frequency or multifocal rTMS of motor and prefrontal cortex benefits motor and mood symptoms in patients with Parkinson's disease. The FDA approved protocol states that rTMS is effective in treating motor symptoms in PD. The patients are administered with anti-PD drugs 1 hour before performing TMS .The patient is made to sit on the chair in proper position with installed EMG electrodes over abductor pollicis brevis muscle to record motor evoked potentials. A super rapid stimulator was connected to 70mm diameter figure of 8 coil .The left and right M1 sites was determined as the scalp location from which TMS evoked motor evoked potentials of maximal amplitude in the contralateral abductor pollicis brevis . In left M1 site, the resting motor threshold potential was determined which is located 5cm anterior to the optimal left M1 location from Abductor pollicis brevis. It mainly targets motor cortex and the left Dorsolateral prefrontal cortex. In each session, real or sham rTMS was delivered over the left Dorsolateral prefrontal cortex, left and right M1 sites sequentially (Kamble et al., 2014).

Frequency:- The course of rTMS consists of 2000 stimuli per session for the left Dorsolateral prefrontal cortex 1000 stimuli for each M1. The patients receive 25 mins of real TMS or sham TMS for 25 mins in the left dorsolateral prefrontal cortex and 12.5 minutes for each M1 with no pauses included in between sessions. Each participant will receive 10 rTMS sessions over 2 weeks.

TMS IN TREATING EPILEPSY:-

Epilepsy is a brain disorder that is characterized by an enduring predisposition to generate epileptic seizures by the neurobiological, cognitive, psychological and social consequences of this condition. Generally, anti-convulsant drugs are used in controlling seizures yet nearly a third of epileptic patients suffer either from uncontrolled seizures or unable to tolerate side effects of medications. Despite surgery, there are newer technological approaches arising these days in treating epilepsy and one such technique is exposing epileptic patients to TMS. According to few studies from clinical trials, it is stated that patients who are resistant to anti-epileptic drugs are administered with TMS to manage uncontrollable seizures. Pre-clinical experiments of TMS show both modulation and measurement of changes with respect to increase in cortical inhibition. Few studies have also described rTMS action in both ictal and interictal states of epilepsy (Manganotti and Del Felice, 2013; Hamed, 2020; Walton et al., 2021).

TMS in the therapy of various diseases as approved by FDA:-

Treatment For Specific Disease	Frequency	Duration of Stimulation	Sessions Required
Depression	1-3 Hz	37 minutes (4 sec stimulation and 26 sec pause)	20-30 sittings
OCD	3 Hz	30-40 minutes (5 sec stimulation and 20 sec pause)	5 Days/week
Smoking Cessation	10Hz	15 minutes	10 sittings for 2 weeks

TMS in the therapy of various diseases which are under Clinical trials:-

Treatment For Specific Disease	Frequency	Duration of Stimulation	Sessions Required
Anxiety	1-10 Hz	Pulse stimulation-750-3600 110% rest motor threshold	10-30 sessions 3 cycles
Schizophrenia	1Hz	10rTMS 110 % Rest motor threshold. 60 Seconds simulation	10 sittings
PTSD	1Hz	110 % Rest motor threshold. 30 Stimulations – 60 Seconds	10 rTMS sessions/ 12 – 15 weeks
Panic Disorder	1Hz	110 % Rest motor threshold. 60 Seconds	10 rTMS sessions
Chronic Pain	1Hz 20Hz/2000 P per session	1600 pulses per session	Sham Sessions 15 Days to 1 month stimulation
Alzheimer's Disease	10Hz	40 Seconds per simulation 110 Rest motor Threshold	6 – 8 Weeks
Epilepsy	1Hz/ 0.5Hz	15 Min with 500 stimulations	Twice a week – for 4 weeks
Parkinson's Disease	2000 stimulation per session/ 1000 stimulation per session when required	10 rTMS	25 Min Real TMS/ Sham TMS(12.5 each M1 – 2 Weeks)

CONCLUSION:

Transcranial magnetic stimulation has shown promising results as a therapeutic tool for various neurological and psychiatric diseases. It has shown its contribution to the maintenance and enhancement of treatment effects. This review spotlights mainly about the exploration of TMS from clinical trial to the FDA approved treatment guideline for Major depressive disorder (MDD), Obsessive-compulsive disorder (OCD), smoking cessation and anxious depression. Also addresses the scope of TMS among other indications and the need of development of certain protocol for the indication. Though the evidence for the use of FDA approved indications are very strong, but they are limited to PTSD and even more limited for schizophrenia, Parkinson's disease, Alzheimer's disease, epilepsy, chronic pain and other neurological diseases. However due to methodological limitations in many clinical studies, there have been discrete conclusions and policy decisions for its rational use. Hence, this review helps as a minute corner stone for future clinical researches.

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