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Transcranial Magnetic Stimulation

Restoring Quality of Life Through Innovative Product Solutions!

Altered Brain Function and Causal Connectivity Induced by Repetitive Transcranial Magnetic Stimulation Treatment for Major Depressive Disorder

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Objective: Repetitive transcranial magnetic stimulation (rTMS) can effectively improve depression symptoms in patients with major depressive disorder (MDD); however, its mechanism of action remains obscure. This study explored the neuralimaging mechanisms of rTMS in improving depression symptoms in patients with MDD.

Methods: In this study, MDD patients with first-episode, drug-naive (n = 29) and healthy controls (n = 33) were enrolled. Depression symptoms before and after rTMS treatment were assessed using the Hamilton Depression Rating Scale (HAMD-17). Resting-state functional magnetic resonance imaging (rs-fMRI) data were collected both before and after the treatment. Changes in the brain function after the treatment were compared using the following two indices: the amplitude of the low-frequency fluctuation (ALFF) and regional homogeneity (ReHo), which are sensitive for evaluating spontaneous neuronal activity. The brain region with synchronous changes was selected as the seed point, and the differences in the causal connectivity between the seed point and whole brain before and after rTMS treatment were investigated via Granger causality analysis (GCA).

Results: Before treatment, patients with MDD had significantly lower ALFF in the left superior frontal gyrus ($p < 0.01$), higher ALFF in the left middle frontal gyrus and left precuneus ($p < 0.01$), and lower ReHo in the left middle frontal and left middle occipital gyri ($p < 0.01$) than the values observed in healthy controls. After the rTMS treatment, the ALFF was significantly increased in the left superior frontal gyrus ($p < 0.01$) and decreased in the left middle frontal gyrus and left precuneus ($p < 0.01$). Furthermore, ReHo was significantly increased in the left middle frontal and left middle occipital gyri ($p < 0.01$) in patients with MDD. Before treatment, GCA using the left middle frontal gyrus (the brain region with synchronous changes) as the seed point revealed a weak bidirectional causal connectivity between the middle and superior frontal gyri as well as a weak causal connectivity from the inferior temporal to the middle frontal gyri. After treatment, these causal connectivities were strengthened. Moreover, the causal connectivity from the inferior temporal gyrus to the middle frontal gyri negatively correlated with the total HAMD-17 score ($r = -0.443$, $p = 0.021$).

Conclusion: rTMS treatment not only improves the local neural activity in the middle frontal gyrus, superior frontal gyrus, and precuneus but also strengthens the bidirectional causal connectivity between the middle and superior frontal gyri and the causal connectivity from the inferior temporal to the middle frontal gyri. Changes in these neuroimaging indices may represent the neural mechanisms underlying rTMS treatment in MDD.

Clinical Trial Registration: This study was registered in the Chinese Clinical Trial Registry (Registration number: ChiCTR1800019761).

Keywords: major depressive disorder, amplitude of the low-frequency fluctuation, regional homogeneity, Granger causality analysis (GCA), repetitive transcranial magnetic stimulation

DO YOU HAVE PATIENTS NOT RESPONDING TO ANTIDEPRESSANTS?

MagVenture TMS Therapy could be the solution.

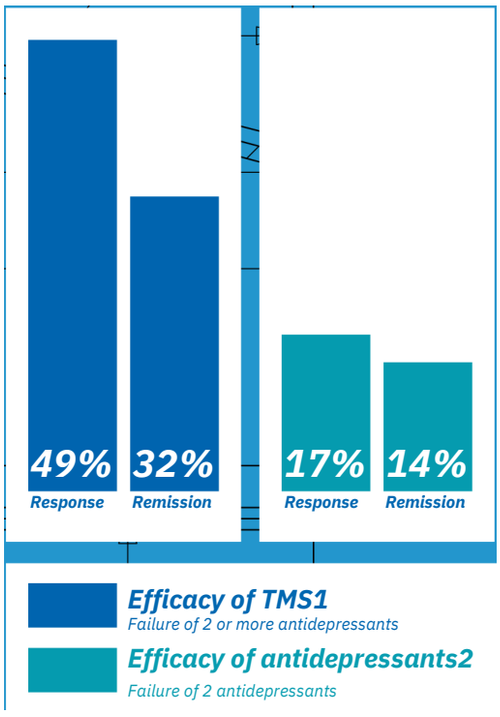
MagVenture TMS Therapy
Stimulating mental health.

WHAT IS TRANSCRANIAL MAGNETIC STIMULATION (TMS)

TMS is indicated for use in people with major depressive disorder who have not responded to antidepressant medication. TMS has been recommended by the American Psychiatric Association since 2010. In 2015, the Institute of Health and Care Excellence (NICE) in the UK assessed the safety and efficacy of TMS for depression and published guidance on the procedure.

MagVenture TMS Therapy consists of repeated cycles of TMS followed by rest periods. Diagnosis and initial session is performed by a licensed physician. The remaining treatment sessions will typically be conducted by trained staff under the supervision of the physician. TMS is non-invasive, does not require any anaesthesia and is not to be confused with Electroconvulsive Therapy (ECT). People can immediately get back to their usual activities.

- **CE approved**
- **Outpatient procedure**
- **Non-invasive, no anaesthesia**
- **Excellent response and remission rates**



1 Blumberger et al. 2018, The Lancet
2 Rush et al. 2006, Am J Psychiatry

TMS in short:

- An alternative to antidepressants
- Series of pulsed magnetic stimuli to the brain
- CE approved for the treatment of major depressive disorder
- Non-invasive treatment – no anesthesia
- Free from common antidepressant drug side effects such as weight gain, dry mouth, and sexual dysfunction

Cautions:
TMS treatment may not be effective or appropriate for all your patients.

Even though TMS has very few side effects compared to antidepressants, additional side effects may occur. Treatment should only be carried out by licensed physicians or educated technicians supervised by physicians.

The Benefits

Depending on your situation and how many patients you expect to treat per day, we have the right solution for you. We provide treatment solutions from entry-level – with smaller systems ideal for start-up or small clinics – as well as more advanced high-performance solutions suited for a very high patient throughput

Providing safe treatment solutions which are highly effective and comfortable for the patient, as well as reliable and easy to use for you as a healthcare practitioner, is a key priority for MagVenture.

The MagVenture TMS Therapy system comes with a range of features to provide optimal patient comfort, including a fully adjustable chair and neck support as well as the lowest noise level3.

Our system is upgradable for possible future treatment protocols and with our add-on patient management system, developed in accordance with major data safety regulations, you can spend more time on your patients and less time on administration.

5 reasons to choose MagVenture TMS Therapy

1. **Proven treatment efficacy, usability, and quality**
2. **High patient throughput**
3. **Simple setup, including pre-defined treatment protocols**
4. **System setups for any practice size**
5. **Represented in 60+ countries, providing onsite installation, training of staff, and ongoing technical support.**

3 Dhamne et al, 2014, Brain Stim.: A Measure of Acoustic Noise.

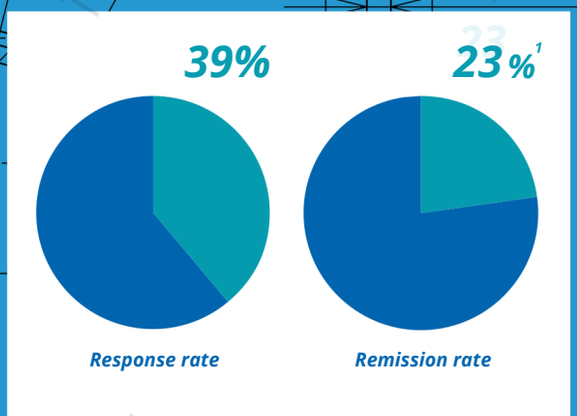
Comorbid Anxiety

Clinical benefit of TMS for patients with Major Depressive Disorder.

MagVenture TMS Therapy® is the first CE approved TMS solution to include a clinical benefit for comorbid anxiety in patients with Major Depressive Disorder. Although depression and anxiety are traditionally regarded as separate disorders, they are highly comorbid: 40%–50% of people diagnosed with major depressive disorder will also have symptoms of anxiety, or vice versa.

- ***3- to 37minute TMS treatment procedure***
- ***Non-invasive, no anaesthesia***
- ***Proven effective in reducing symptoms of anxiety in patients with depression.***
- ***Well-established, outpatient session***

The efficacy of TMS for comorbid anxiety



1 Graphics by MagVenture, based on:
Clarke et al., 2019, Journal of Affective Disorders:
Efficacy of repetitive transcranial magnetic stimulation in the treatment of depression with comorbid anxiety disorders

TMS for depression with anxiety symptoms

MagVenture TMS Therapy® is an advanced neuromodulation technology that uses magnetic pulses to stimulate the affected areas in the brain.

TMS therapy is an effective treatment option for patients with Major Depressive Disorder.

In addition, MagVenture TMS Therapy® can reduce the symptoms of comorbid anxiety in patients suffering from depression. Most common side effects are headache and nausea.

The total treatment time is 20-30 sessions in total, once per day, five times per week:

- 3 or 37 minutes over the left side of the head (left-DLPFC) or
- 8 minutes applied on the right side (right-DLPFC).

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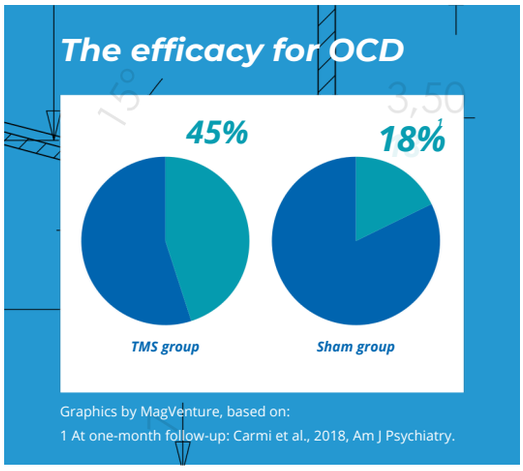
MagVenture TMS Therapy
Stimulating mental health.

ADJUNCT TREATMENT OF ***OBSESSIVE-COMPULSIVE DISORDER***

MagVenture has developed a magnetic coil which is particularly suited to reach the deeper cortical areas needed for the TMS therapy of OCD.

- ***18-Minute treatment sessions***
- ***Designated treatment solution to reach deeper lying structures***



TMS for OCD

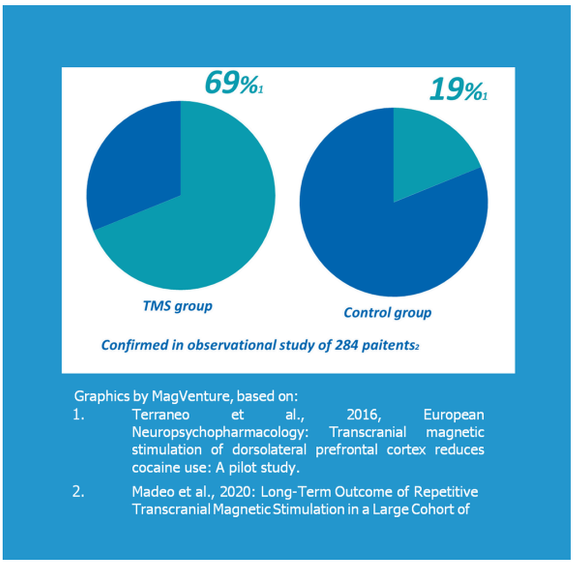
Transcranial Magnetic Stimulation (TMS) uses repeated, magnetic pulses to stimulate a specific area in the brain in order to reduce OCD symptoms. Treatment spot is the dorsomedial prefrontal cortex. Most common side effects are headache and nausea.

Treatment time is 6 weeks for a total of 29 sessions:

- 1 treatment session per day for 5 days (week 1-5)
- 1 treatment session per day for 4 days.

TREATMENT OF ADDICTION
Psychoactive Substance Use Disorder (PSUD)

> ***The experimental group treated with TMS showed a significant reduction in cravings, relapses, and dropouts compared to a control group.***
>
> *Luigi Gallimberti*
> *Psychiatrist, toxicologist and professor,*



TMS for Addiction

MagVenture TMS Therapy® is an advanced neuromodulation technology that uses magnetic pulses to stimulate the affected areas in the brain.

MagVenture TMS Therapy® is intended to be used as a treatment of psychoactive stimulant use disorder (PSUD) in adult patients. Most common side effects are headache and nausea.

The total treatment time is 13 weeks for a total of 34 treatment sessions:

- Two treatments per day for five days, followed by:
- 2 treatments per day one day weekly for 12 weeks.
- Additional TMS sessions may be applied, for instance, in case of a relapse or the risk of relapse.

MagVenture's CE approval is based on a pilot study1 as well as the largest naturalistic study with the longest followup period available so far2. These studies have contributed to the world's first CE approval for TMS therapy for addiction (PSUD)2.

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MagVenture TMS Therapy
Fighting depression. Together.

Introducing: Express TMS®

3 min TMS sessions!

The road to remission has never been shorter.

CE approved

FDA cleared

- **Express TMS®: Shortest, CE approved and FDA cleared TMS treatment of major depressive disorder**
- **Excellent response and remission rates, based on largest RCT to date**
- **Non-invasive and no anesthesia**

5 reasons to get Express TMS® in your practice

1. With just 3 minutes per TMS session, you can shave off more than 5 hours of active treatment time for each of your patients.
2. NO roll-off, ensuring accurate dosage for your patient every time.
3. The standard CE approved or FDA cleared TMS protocol (37 minutes per session), can still be used.
4. Available with a MagVenture TMS Therapy® system or as upgrade from your current MagVenture TMS Therapy system (MagPro X30 or X100 configuration).
5. Extremely efficient liquid coil cooling, allowing for continuous treatments.

What is Theta Burst?

A standard TMS protocol is applied with 3,000 unpatterned stimulation pulses. TBS, however, delivers the pulses in a patterned protocol, so-called

Express TMS® by MagVenture
3 minutes and 9 seconds in total per session (20-30 in total).

600 pulses of TBS of the Left DLPFC at 120% of resting motor threshold. Bursts of 3 pulses at 50 Hz. Bursts repeated at 5 Hz for 600 pulses total, with a cycle of 2 seconds on, 8 seconds off.

Left DLPFC: treatment spot

The effectiveness of TMS from the world's largest RCT shows

49%
respond to the treatment

32%
achieve remission of their symptoms

**Blumberger et al, 2018, The Lancet

MagVenture Pain Therapy
Riding the waves of relief.

MAGVENTURE PAIN THERAPY

The magnetic approach to pain relief

mPNS offers up to 87% pain relief

**magnetic Peripheral Nerve Stimulation **For respondent patients only. Bedder M, Parker L.: Magnetic Peripheral Nerve Stimulation (mPNS) for Chronic Pain, 2023*

THE MAGNETIC APPROACH TO PAIN REDUCTION

MagVenture Pain Therapy is for healthcare professionals specializing in pain management who want, non-invasive solutions for patients dealing with chronic, intractable, post-traumatic, and post-surgical pain.

MagVenture Pain Therapy is an FDA cleared, non-invasive treatment method called Magnetic Peripheral Nerve Stimulation (mPNS) that employs targeted magnetic pulses, offering comprehensive and sustained pain relief.

It gives new hope to patients and healthcare providers by addressing chronic pain effectively and with no side effects.

- ***FDA cleared***
- ***Non-invasive and pain free treatment***
- ***87% average pain relief with mPNS***
- ***13 minutes average time per treatment***
- ***Non-drug treatment***

Electrical and Magnetic

A basic comparison between managing peripheral pain with electrical stimulation (TENS) and the approach using magnetic peripheral nerve stimulation (mPNS).

Electrical stimulation	Magnetic stimulation
Associated pain	Painless
Main effect on superficial nerves	Activates deeper nerves
Restricted range of nerve activation	Reaches a broader nerve segment
Skin contact necessary	Skin contact not necessary
Home use	Professional use

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MagVenture TMS Therapy
Fighting depression. Together.

TMS and ECT	ECT	rTMS
Indication	**FDA:** "For the treatment of catatonia or a severe major depressive episode (MDE) associated with major depressive disorder (MDD) or bipolar disorder (BPD) in patients age 13 years and older who are treatment-resistant or who require a rapid response due to the severity of their psychiatric or medical condition."	**FDA:** "Treatment of Major Depressive Disorder in adult patients who have failed to receive satisfactory improvement from prior antidepressant medication in the current episode."
Technology	Electrical stimulation and induced seizure	Magnetic stimulation, no induced seizure
Anesthesia required?	Yes	No
Antidepressants?	As determined by physician	As determined by physician
Number of patients per hour	Approximately 10	Approximately 10
Total number of treatment sessions per patient	Approximately 10 treatments	20-30 treatments
Recovery period post-treatment?	Yes. Following ECT, the patient needs to recover from the treatment including the anesthesia and muscle relaxant.	No. TMS is a non-invasive procedure and patients may resume to their normal daily activities immediately after treatment.
Most common somatic side effects	Headache and tiredness	Headache and nausea
Most common cognitive side effects	Anterograde memory impairment and confusion	None
Response to treatment	79% response 75% remission	49-51% response 30% remission

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