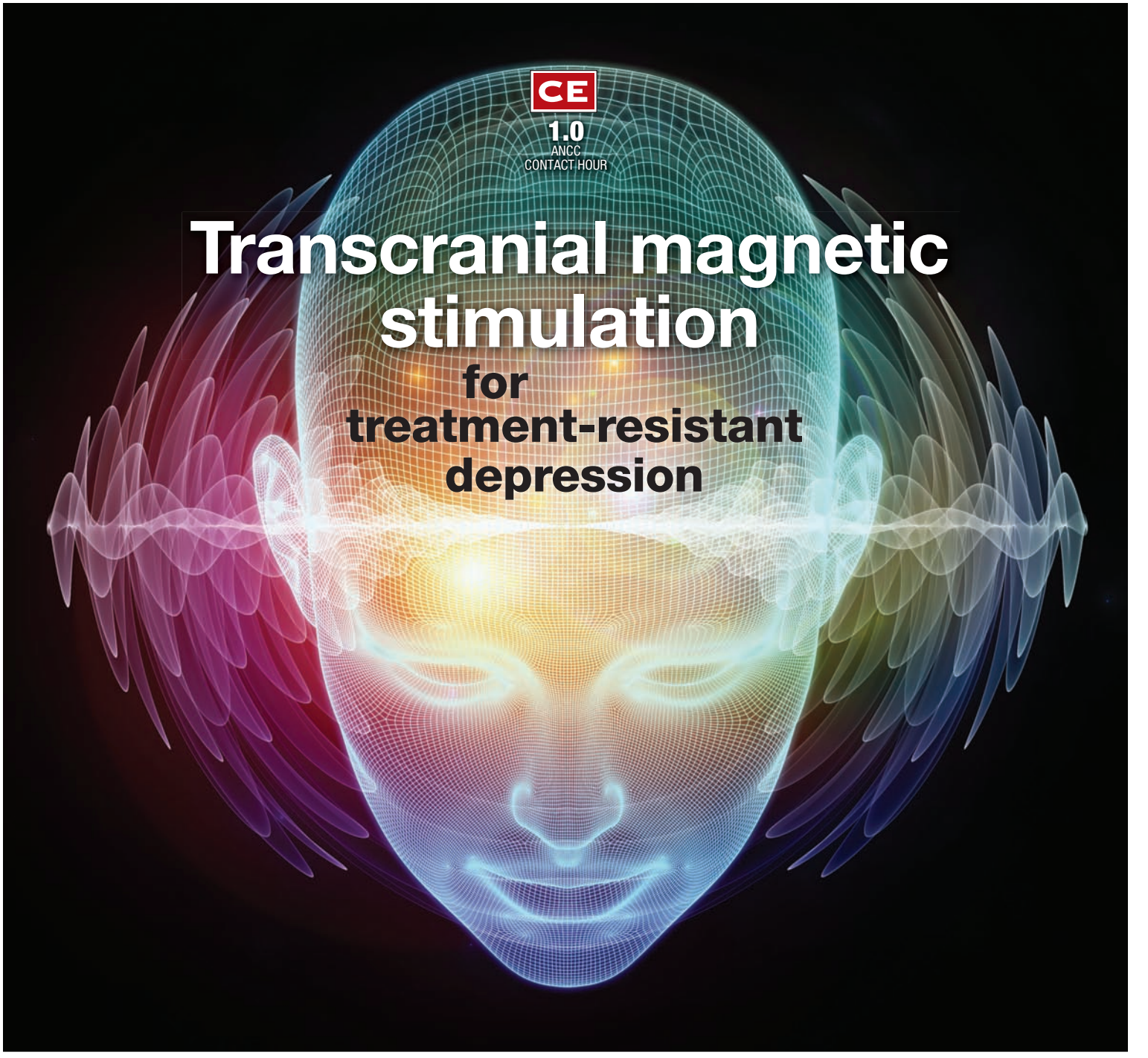

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Transcranial magnetic stimulation for treatment-resistant depression

Major depressive disorder is the leading cause of disability in the US among people ages 14 to 44, with one-third of patients diagnosed with treatment-resistant depression. These patients may benefit from transcranial magnetic stimulation.

By Sarah Nazar, MN, RN

Major depressive disorder (MDD) is ranked first among global causes of disease burden with significant morbidity and mortality. Patients diagnosed with MDD who don't respond after an adequate course of antidepressant therapy are referred to as treatment-resistant. Treatment-resistant depression (TRD) is complex and influenced by psychiatric comorbidity and coexisting medical illness. Traditionally, electroconvulsive therapy (ECT) has been used to treat patients with TRD and although effective, there are several adverse reactions that can make the patient intolerant or even unwilling to try it. A safe alternative for patients with TRD, transcranial magnetic stimulation (TMS) is a noninvasive neurostimulation technique with fewer adverse reactions. TMS has been approved for clinical practice in Australia,

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New Zealand, the European Union, Israel, the US, and Canada (see *TMS in the US and Canada*).

After working as an RN in mental health and ECT, my manager asked me to expand my role and join the TMS pilot program team, which offers TMS in our hospital's outpatient mental health unit. This article aims to educate nurses about TMS as an alternative treatment for TRD, including nursing responsibilities and the nurse's role in administering TMS.

What's TMS?

TMS is a neurophysiologic procedure that noninvasively stimulates neural tissue. TMS uses electromagnetic induction, which means an electric current is passed through a coil generating a magnetic field that penetrates the skull (see *Picturing TMS*). The mechanism of action isn't clear, but evidence suggests that TMS causes long-term inhibition and excitation of neurons in certain brain areas. The stimulation impacts how the brain is working, which seems to ease depression symptoms and improve mood. Applying pulses repetitively results in depolarization of nerve cells, causing the release of neurotransmitters that corrects impaired cell functioning and aids in healing. Hypofunctioning of the dorsolateral prefrontal cortex (DLPFC) has been implicated in the pathology of depression and remains the preferred area for stimulation.

During the procedure, a magnetic coil is placed against the patient's skull with the coil at a 45-degree angle to the floor while the patient is awake and reclined in a special chair. The patient and administrator wear earplugs to reduce and protect against the sound of the magnet, which makes a woodpecker-like tapping noise. Electromagnetic pulses generate an electric current through the coil, inducing a magnetic field that penetrates the DLPFC.

TMS can be delivered as a single pulse or repeated pulses (referred to as repetitive TMS or rTMS). After one train of pulses is administered, there's a rest period; depending on the parameters, this lasts anywhere from 11 to 26.5 seconds before the next train of pulses is delivered. One device on the market offers the rTMS protocol, delivering 75 pulses, with a 26.5 second interval between pulses, that are administered in 37.5 minutes daily, 5 days a week for 20 to 30 sessions.

Another available device offers an intermittent theta burst stimulation (iTBS) protocol. In this protocol, magnetic pulses are administered at a higher frequency (50 Hz) compared with the standard protocol, which only uses 10 Hz. iTBS delivers 600 pulses in only 3 minutes, less than one-tenth of the time the standard protocol takes to administer. The advantage of iTBS is that more patients can be treated each

TMS in the US and Canada

In 2002, Health Canada approved rTMS for TRD and in 2008, the FDA cleared several TMS devices for the treatment of TRD in the US. In 2018, iTBS was approved in the US and Canada to treat patients diagnosed with TRD.

In the US, the estimated cost per TMS course (20 to 30 sessions) ranges from $1,108 for iTBS and $1,844 for rTMS (US currency). In Canada, a TMS course of 20 to 30 sessions costs approximately $1,500 for iTBS and $3,000 for rTMS (Canadian currency). In both the US and Canada, one full course of TMS is less expensive than one course of ECT.

In several US states, federal and commercial healthcare insurers cover TMS therapy for the treatment of patients who haven't achieved remission after one course of antidepressant therapy. It's important that patients who are considering TMS treatment check their insurance coverage because some insurers require patients to try several antidepressants before the treatment is covered. In Canada, TMS treatment is publicly funded in Quebec, Saskatchewan, Yukon, and certain Alberta health service centers; however, some private clinics offer TMS paid through private insurance or out of pocket by patients.

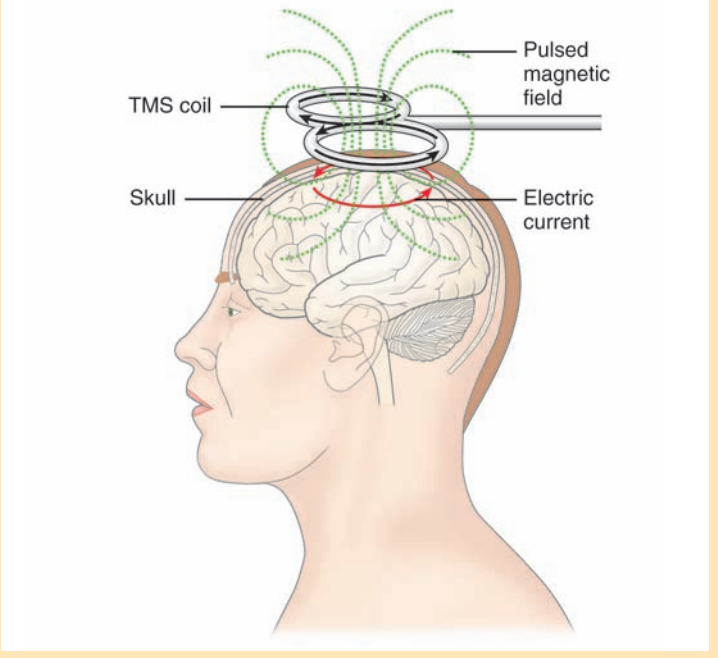
day. In one case, a patient was dealing with chronic neck pain, so this protocol allowed her to have only 3 minutes in the chair versus 37.5 minutes with the standard protocol. Another patient preferred iTBS to the standard protocol because he could leave work and be treated during his lunch hour.

Indications and contraindications

Standard treatments for MDD include psychotherapy, medications, and, in severe cases, ECT. The problem is that some patients can't tolerate the adverse reactions of medications; in the case of TRD, patients don't respond to medications at all. TMS is appropriate for patients with MDD even if they're medication-resistant or have comorbid anxiety. Current research suggests that TMS may be beneficial for adolescents with mood disorders; women with perinatal depression; and adults diagnosed with posttraumatic stress disorder, obsessive-compulsive disorder, or schizophrenia. TMS hasn't been cleared by the FDA or Health Canada for these conditions, and further studies supporting the safety and efficacy in treating them are warranted.

TMS isn't appropriate for patients diagnosed with MDD who also have comorbid psychotic symptoms or acute suicidal ideation. In these cases, ECT is more appropriate. TMS is restricted for patients with magnetic implants and those who've had recent adverse neurologic or cardiac events. Tattoos containing ferromagnetic ink are another contraindication for TMS. It's also important to know the current medications patients are taking because some medications, such as bupropion, can lower the seizure threshold. Taking this medication in conjunction with TMS may potentiate the risk of a seizure, which is often considered a contraindication.

Picturing TMS



Source: Timby BK, Smith NE. *Introductory Medical-Surgical Nursing*. 12th ed. Philadelphia, PA: Wolters Kluwer; 2018.

Adverse reactions

The greatest concern is the risk of generalized seizure. Factors that influence seizure risk include epilepsy, when the motor threshold site location isn't precise, or stimulation parameters exceed recommended safety ranges. TMS delivered to patients without risk factors using a figure-8 coil causes fewer than 1 seizure per 30,000 sessions. Syncope and presyncope are adverse reactions that occur more often than seizures. The administrator monitoring the patient's treatment should be trained to respond appropriately to adverse events, such as seizures or syncopal episodes.

Common adverse reactions of TMS include scalp discomfort at the stimulation site, headache, facial pain, and facial twitching. In one case, a patient experienced scalp pain at the area where the coil was placed. The TMS prescriber suggested that she apply lidocaine/prilocaine gel a few hours before treatment to numb

Differences between ECT and TMS

	ECT	TMS
Energy	Electric	Magnetic
Relative amount of energy used	High	Low
General anesthetic required	Yes	No
Ability to drive afterward	No	Yes
Medication considerations	Mood stabilizers and benzodiazepines affect the seizure threshold; these medications may need to be held for 12 or 24 hours before ECT	Bupropion, imipramine, and clozapine lower the seizure threshold; TMS may be limited to patients not taking these medications
Adverse reactions	Memory loss (short/long), headaches, stomach upset, confusion, muscle aches	Scalp discomfort, headaches, facial pain/twitching, 0.003% risk of seizure (1 in 30,000 treatments)

the area. This alleviated the scalp discomfort and allowed her to complete the TMS sessions. In another case, a patient developed uncomfortable facial twitching, which was resolved by adjusting the coil's angle.

One of the most common patient complaints is headaches. Patients often describe these headaches as "tension headaches" or "pressure" felt in their temples that subsides after a few hours. Oral over-the-counter analgesic medications such as ibuprofen can be taken before or after treatment, and patients have reported this to be helpful. Research indicates that TMS doesn't increase migraine risk in patients with or without a history. One patient had a long history of migraines and by the end of the treatment sessions, he indicated he hadn't had a migraine since initiating treatment. Growing evidence supports treating chronic migraines with rTMS, but more research is required to determine protocols to keep migraines in remission.

What does the evidence say?

TMS has been studied in randomized controlled trials and determined to be safe and well tolerated. Unlike ECT, TMS doesn't require sedation with anesthesia and has no evidence of cognitive impairment, so patients can perform normal daily activities such as driving immediately after the procedure (see *Differences between ECT and TMS*).

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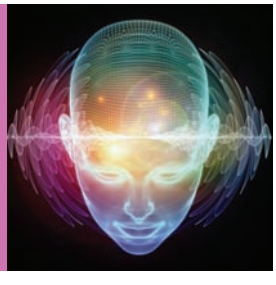

Conducted in 2018, the THREE-D brain stimulation trial compared the iTBS protocol with the standard rTMS protocol. There wasn't any reduction in response or remission rates when using the iTBS protocol, even though it takes less than

consider this

Your patient has been referred to the TMS program and is eager to start treatment. When you complete the initial telephone intake/screening, you're the patient's first contact. Typically, patients have tried several antidepressants and are unable to tolerate the adverse reactions or simply don't respond, so they may be discouraged. These circumstances often create a sense of hopelessness and, in some cases, patients have taken a leave of absence from work and are relying on TMS as a last resort to get well. You need to ensure that your patient has no contraindications for the treatment and be sure to answer any questions/concerns while developing a rapport. Contraindications can be different than nurses face in their daily work. For example, in one telephone screening, the patient had to consult his tattoo artist to ensure that the tattoo on his neck didn't contain ferromagnetic ink. In another telephone screening, the patient was required to consult her orthodontist to determine the composition of an implant in her lower jaw.

After your patient's case is reviewed by the TMS prescriber and treatment is approved, he or she is booked for a consultation. I've found that patients appreciate meeting the TMS nurse, a person they've already spoken to and are familiar with, so I try to meet them in person. After the consultation, your patient is booked for mapping and motor threshold determination; patients often have a family member attend this appointment with them. This is an opportunity to provide education and answer any questions or concerns.

At each visit before administering the treatment, you should inquire about any medication changes, how your patient slept, and if there's been any recent substance use, all factors that can lower the seizure threshold. One patient reported having several drinks the evening before one of his TMS treatments while at a family gathering. After consulting with the TMS prescriber, the decision was made to delay treatment by 1 day. During scenarios such as this, it's important to remain objective and focus on educating your patient about risk factors and the importance of self-care during treatment.

Treatment response can vary. After a course of TMS, one patient indicated that she wasnt isolating herself anymore and planned to return to work. In some cases, patients don't respond, and I've used this opportunity to educate them about other treatment options such as ECT.

one-tenth of the time to administer. Both protocols had similar adverse reactions, safety, and tolerability without compromising the effect.

In a survey conducted in 2015 by the American Society of Clinical Psychopharmacology, member respondents referred almost half of their patients for rTMS when they didn't respond to initial treatment for depression. In 28% of those cases, respondents noted a marked improvement. In open-label clinical trials after 4 to 6 weeks of treatment, half of the patients treated with TMS experienced a reduction in symptoms of 50% or more and one-third experienced remission. Treating TRD using rTMS or iTBS has received a consistent response rate of 50% to 55% and remission rates of 30% to 35%.

Currently, studies are being conducted to examine the safety and tolerability of TMS over long-term use.

Patient evaluation

The TMS prescriber is either a physician or psychiatrist. Once a referral is received, the TMS nurse performs a comprehensive review of the patient's health status and his or her medical records to ensure that the patient is suitable for the program. After this information is verified, the TMS nurse contacts the patient directly by phone or in person if they've been admitted to the inpatient mental health unit. An interview is conducted using a screening questionnaire as a guide, allowing for the collection of information regarding the patient's health status and mental

Nursing interventions

cheat sheet

- Ensure that the consent form has been signed by the appropriate parties.
- Ensure that the TMS prescriber has written an order for TMS administration, including the parameters, protocol, and motor threshold required.
- Confirm the patient's full name and date of birth.
- Review current medications with the patient.
- Determine what the patient understands about TMS and provide health education accordingly.
- Ensure that all metal has been removed above the shoulders (such as earrings).
- Administer the symptom severity instrument, such as the PHQ-9, and record the values in the treatment record.
- Place a pillow cover over the headrest of the TMS chair and invite the patient to sit in the chair.
- Ensure that the patient is positioned comfortably and make sure his or her earplugs are in correctly.
- Insert your own earplugs.
- Ask the patient to put on his or her head cap and then adjust the cap as necessary.
- Ensure that the coil is placed in line with the treatment location and then remind the patient not to move so the coil is always touching his or her head.
- Turn the device on and input the treatment parameters per the TMS prescriber's order.
- Inform the patient that you'll countdown "3, 2, 1, 0."
- After the countdown, use the foot pedal to initiate the session and start treatment.
- Assess the patient for adverse reactions.
- Notify the patient when he or she is halfway done (the device will show 50% complete).
- Remove the coil from the patient's head after the last train (the device will stop).
- Tell the patient that he or she can remove the head cap and earplugs.
- Assess the patient for adverse reactions before he or she gets out of the chair and respond accordingly.
- Document the parameters in the treatment record.
- Document any changes in mood or other pertinent patient concerns.

health history. The data collected include the patient's current medications and any contraindications for treatment. During the screening process, it's important to inform patients of the time requirement to ensure that they can make the commitment.

Once the patient is screened, the case is reviewed with the TMS team. Based on the outcome of the review, a consult is booked with the TMS prescriber. During the consult, a great deal of time is spent reviewing the procedure and potential adverse reactions, and an information handout is given to the patient. When the patient returns for the motor threshold determination, this information is reviewed again. If the patient agrees with the treatment plan, a consent form is signed and witnessed by the TMS prescriber and the nurse. At this point, the TMS prescriber also discusses treatment parameters with the patient and decides on either the rTMS or iTBS protocol.

Determining motor threshold

Before the patient starts treatment, the TMS prescriber needs to determine the amount of magnetic energy needed. This is determined by assessing the resting motor threshold, which is the minimum stimulation intensity required to produce 5 reliable motor responses out of 10 stimuli in the contralateral thumb (the thumb that's on the opposite side of the coil during motor threshold determination). The resting motor threshold is used as a reference point for the DLPFC to determine stimulation parameters.

The patient sits comfortably in the treatment chair while his or her arm rests on a pillow with the palm of the hand open. The coil is placed over the motor cortex and adjusted to the lowest intensity that will reliably produce movement in the contralateral thumb. The standard practice for dosing rTMS and iTBS with the figure-8 coil is to administer a

on the web

TMS courses and workshops

Clinical TMS Society Grand Round Webinars:
www.clinicaltmssociety.org/events/grw

Duke University School of Medicine Transcranial Magnetic Stimulation Fellowship:
https://psychiatry.duke.edu/transcranial-magnetic-stimulation-course

PULSES TMS Training Course:
www.clinicaltmssociety.org/events

stimulus at a percentage of the resting motor threshold, which is normally 120%.

Treatment sessions

According to the 2018 Consensus Recommendations for the Clinical Application of Repetitive Transcranial Magnetic Stimulation, the TMS device operator should be a clinical professional trained in assessing resting motor threshold who can independently administer TMS under the supervision of the prescriber. Before the patient begins treatment, the nurse refers to the order for TMS, which outlines the parameters, including motor threshold, stimulation intensity, frequency, train duration, scalp location, and number of pulses. The nurse also ensures that the consent form has been signed by the patient and prescriber.

When the patient enters the TMS treatment room, his or her full name and date of birth are verified before treatment. During each session, the patient completes a depression and anxiety symptom severity instrument, which is used to monitor symptoms and document efficacy. Our program administers the 9-item Patient Health Questionnaire (PHQ-9), an instrument that measures symptoms of depression. The instrument is completed by the patient and rated by the nurse. These values are documented in the treatment record, along with the TMS parameters for each session.

When the patient is comfortably positioned in the TMS chair, he or she wears a personalized cap that has the DLPFC marked according to the resting motor threshold determination. Once the patient and operator have their earplugs in, the coil is positioned over the DLPFC at a 45-degree angle to the floor. The operator then programs the device settings according to the treatment protocol and parameters before counting down the first train. For the duration of the session, the operator is on standby to monitor for any potential adverse reactions.

Follow-up consultation

Approximately 6 to 8 weeks after the patient has completed the prescribed sessions, a follow-up consult occurs. The TMS prescriber typically completes the PHQ-9 with the patient so progress can be measured. The benefit of these visits is that treatment outcomes are measurable, which allows for data analysis and further research on efficacy.

Final thoughts

TMS is an evidence-based treatment for TRD that's increasingly being implemented. It's well tolerated, has minimal physical and cognitive adverse reactions and a low risk of drug interactions, and is a safe alternative to ECT. Nurses can independently administer TMS under the supervision of the TMS prescriber and are fully involved in pretreatment screening and treatment sessions. Becoming a part of the TMS program at my hospital has allowed me to be involved in data collection and analysis of patient response to treatment and develop a role in which I'm able to use assessment skills, be involved in patient treatment plans, and educate staff and patients. Working with the interdisciplinary TMS team has been both challenging and rewarding, giving me the opportunity to expand my practice as a nurse, researcher, and educator. ■

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Transcranial magnetic stimulation for treatment-resistant depression

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