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Learning Objectives
Upon successful completion of this educational program,

APA: Lasting Benefit Seen for TMS in Depression

By John Gever, Senior Editor, MedPage Today
Published: May 31, 2010
Reviewed by Dori F. Zaleznik, MD; Associate Clinical Professor of Medicine, Harvard Medical School, Boston and
Dorothy Caputo, MA, RN, BC-ADM, CDE, Nurse Planner

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NEW ORLEANS -- Relapse rates for patients with treatment-resistant major depression were much lower following transcranial magnetic stimulation (TMS) than is normally seen with drugs or electroconvulsive therapy, researchers said here.

Six-month results from two separate studies presented at the American Psychiatric Association meeting showed that only about 10% to 12% of patients achieving an initial remission suffered relapses after TMS therapy.

That compares with a relapse rate of about 40% over 12 months in the STAR*D study of antidepressant treatment among participants who achieved remission on a second-line drug regimen after failing citalopram (Celexa). Relapse rates following ECT have been in the same ballpark.

These were the first long-term results to be reported for patients participating in randomized trials of TMS.

The findings "suggest that the durability of effect for TMS is good," according to Philip G. Janicak, MD, of Rush University Medical Center in Chicago, who presented one of the studies during a poster session.

Janicak reported results in patients with treatment-resistant depression who had achieved remission in a sham-controlled trial of TMS.

That trial, which enrolled 301 patients initially, ran for six weeks with the sham control. Nonresponders in both groups could then receive six weeks of open-label TMS.

Janicak and colleagues analyzed six-month results for 21 patients who achieved remission with sham treatment and in 99 who remitted with TMS -- 61 in the blinded phase and 38 with open-label treatment.

Patients showing remission during the study were switched to maintenance therapy with an unspecified antidepressant drug.

Some 12% of patients who received TMS had another episode of depression during follow-up, compared with 22% of those showing remission with the sham treatment (*P* not reported).

The study protocol also allowed patients, including those remitting with sham treatment, to receive booster TMS treatments during the follow-up if they experienced a one-point change in the Clinical Global Impression-Severity scale for two consecutive weeks.

Action Points

- Explain to interested patients that transcranial magnetic stimulation delivers small electric currents to selected areas of the brain, but in a different way from electroconvulsive therapy.
- Explain that TMS is FDA-approved but the technology is relatively new and clinical experience with it in routine practice is limited. Also explain that it may not be covered by insurance.
- Note that this study was published as an abstract and presented at a conference. These data and conclusions should be considered to be preliminary until published in a peer-reviewed journal.

the reader should be able to:
1. Discuss the results of this study
2. Review the relevance and significance of the study in the broader context of clinical care

Disclosures
Dori F. Zaleznik, M.D., and John Gever, and Dorothy Caputo, MA, RN, BC-ADM, CDE, Nurse Planner, have disclosed that they have no relevant financial relationships or conflicts of interest with commercial interests related directly or indirectly to this educational activity.

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By the end of the follow-up period, about 38% of patients remitting with TMS treatment had received a booster, compared with some 66% of those initially benefiting from the sham treatment (*P* not reported).

The vast majority of patients receiving the booster treatments -- 84% -- showed at least some improvement in depressive symptoms, according to Janicak and colleagues.

Second Trial, Ditto

Similar findings were reported by Antonio Mantovani, MD, PhD, of Columbia University in New York City, in a platform presentation on long-term follow-up in the so-called OPT-TMS trial.

The 190-patient trial was also sham-controlled initially, with results reported earlier this month in *Archives of General Psychiatry*.

The findings from that trial were somewhat disappointing, in that only 14% of patients receiving TMS had complete responses during the blinded treatment, although 30% of nonresponders from both groups achieved remission during subsequent open-label treatment with TMS.

Among 61 patients who achieved remission in the study with TMS, either blinded or open-label, seven relapsed during a six-month follow-up period, for an overall relapse rate of 11.5%.

Mantovani said the relapses mainly occurred early in follow-up, although a substantial number of patients were lost to follow-up between two and four months.

Patients with relatively severe depression at study entry tended to be at greater risk for relapse, he said. But the number of previous drug-treatment failures did not predict relapse following TMS.

Participants in both studies had failed at least one previous antidepressant therapy and most had failed two or more.

What About Use with Drugs?

Another unanswered question about TMS -- whether adding it to existing antidepressant drug therapy is effective -- was addressed in a third study presented here.

Scott Aaronson, MD, of Sheppard Pratt Health System in Baltimore, reported on 21 patients who had persistent major depression despite at least two courses of antidepressant drug therapy, and who then received TMS while remaining on the most recent drug regimen.

About 57% of patients showed at least 50% improvement in Montgomery Asberg Depression Rating Scale scores relative to pre-TMS baseline, and 24% had remission, he said.

"I was very, very heartened by the results," Aaronson said. "In a very sick population, those results are quite good."

His experience with boosters has been similar to that in the study by Janicak and colleagues, he said.

"There's a number of folks for whom we have to do sort of a refresher course," Aaronson said. "We bring them in for a couple of treatments. The good news is that, once you've responded, if we can catch it before the depression gets severe, we can usually shorten the number of treatments" necessary to restore the response.

Still Work to Do on Dosing, Cost

Aaronson added that TMS is a relatively young technology and has probably not been fully optimized.

Numerous parameters can be adjusted in TMS, including pulse duration, pulse frequency, total pulses per session, and the number and frequency of sessions.

Mark Demitrack, MD, chief medical officer of Neuronetics, which sells the only FDA-approved TMS device, said the technology had been in development for about 10 years prior to its 2008 approval. He said the parameters used in most recent studies -- 10 pulses per second for four seconds, twice a minute, for a total of 3,000 pulses in each daily session -- appeared to maximize the benefit.

Aaronson said those settings were the obvious starting point since they were used in the registration trials. But, he added, "I hope we will learn a lot, in the coming years, that we may have a better idea as to, perhaps, what to do when [patients] don't respond to the parameters they used in the clinical trials."

At the moment, he said, one of the major barriers to TMS is that, despite the FDA approval, most insurers won't pay for it.

Karl Lanocha, MD, a psychiatrist who runs a stand-alone TMS clinic in Portsmouth, N.H., told *MedPage Today* that a course of treatment costs about $10,000.

He and Aaronson agreed TMS may appear high-priced, but it may save money in the long run when compared with the long-term cost of ECT or repeated attempts at drug therapy in patients with poor past responses to antidepressant medications.

The study by Janicak and colleagues was funded by Neuronetics.

The OPT-TMS study was funded by the National Institutes of Health.

Aaronson's study had no external funding.

All presenters and some of their co-investigators reported relationships with Neuronetics and/or other manufacturers of TMS equipment.

Primary source: American Psychiatric Association
Source reference:
Mantovani A, et al "How long do the TMS clinical effects last?" *APA* 2010; P. 154.

Additional source: American Psychiatric Association
Source reference:
Janicak P, et al "Long-term durability of acute response to transcranial magnetic stimulation (TMS) In the treatment of pharmacoresistant major depression" *APA* 2010; Abstract NR7-46.

Additional source: American Psychiatric Association
Source reference:
Aaronson S, "An open label study of transcranial magnetic stimulation combined with antidepressant medication for the treatment of major depressive disorder" *APA* 2010; Abstract NR4-76.

Related Article(s):

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