Q&A With the Expert

When Depression Meds Fail, Transcranial Magnetic Stimulation Might Be Plan B

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Dr. Becker has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

Your patient has now failed four antidepressant medications, both alone and as cocktails. What else can you pull out of your bag of tricks? Dr. Becker suggests considering transcranial magnetic stimulation (TMS), which he maintains is underutilized. "Many of my colleagues right down the hall from me still don't think of TMS for treatment or don't know who to refer for it," he says. "I think it should be more readily considered for a lot of patients out there."

For a look at how TMS works, how effective it is, how it compares with electroconvulsive therapy (ECT), whether some brands of TMS machines are better than others, and what you have to do to make sure your patient's health insurance plan picks up the tab, we spoke with Dr. Becker, who prescribes this treatment for some of his patients.

TCPR: How treatment-resistant does a patient have to be with antidepressants before you should consider trying TMS?
Dr. Becker: When TMS initially came out in 2008, it was approved for people who had failed one medication trial. But I'll tell you, from doing a number of insurance reviews, that health insurers are going to require on average about four treatments—so four medicines, and usually from at least two different classes. But in terms of who actually responds to TMS, it's all over the map. There are people who have tried two medicines and just couldn't tolerate them or deal with the side effects, and there are those who have failed 10-plus medicines who went on to do well with TMS.
TCPR: What's the efficacy rate in general?
Dr. Becker: It's really pretty good. In initial studies conducted to get FDA approval for the machine, which had very strict inclusion/exclusion criteria, the response rates were around 30%–40%, with a remission rate of 20%. But more recent studies, which have been more "naturalistic," have reported response rates of 60% with remission rates of about 30% (Carpenter LL et al, *Depress Anxiety* 2012;29(7):587–596).
TCPR: In your opinion, are those studies convincing in terms of having good placebo-sham comparisons—meaning we can believe that the blind wasn't broken and that there was not some kind of expectancy effect?
Dr. Becker: One of the things everybody comes back with is, "How do you do blind TMS?" because you can feel it when they are doing the procedure. But in looking at those studies, I think they did a reasonable job, with reasonable shams. Of course, there's just something about coming and interacting with somebody five days a week for six weeks in a row, having a schedule, that can have a positive effect on an acute major depressive episode, independent of any specific effect from TMS. But it's also possible that TMS itself can enhance psychotherapy.
TCPR: How would TMS affect or improve psychotherapy?
Dr. Becker: Studies have shown that TMS may improve the ability to learn new tasks, and it appears to increase neuroplasticity, helping to grow neural connections so different regions of the brain talk to each other, which in turn might facilitate therapy. If you think about it, what you're trying to do with therapy is break old patterns of thinking and create new ones, so you can think of TMS as perhaps a tool to further that effect.
TCPR: Beyond the possible neuroplasticity effect, is there some sort of consensus about what the basic mechanism is likely to be?
Dr. Becker: We know from imaging studies that the left dorsolateral prefrontal cortex is underactive in depression. And when you stimulate somebody with high-frequency TMS, you increase excitability in the neurons of that brain region. That has downstream effects because all the different brain regions are interconnected, so even though you are only stimulating the more superficial aspects of brain tissue, the idea is that there are connections that reach to some of the deeper brain structures as well.
TCPR: It sounds pretty different from the way ECT seems to work, which is by providing an electrical stimulus that causes a seizure and stimulates the entire brain.
Dr. Becker: Yes, ECT (which requires general anesthesia) is a more generalized approach. If you're having a seizure, you're getting a massive firing of all your neurons.
TCPR: Can you tell us a little bit about the differences between the NeuroStar and the Brainsway TMS machine, and whether there are any newer devices with differences in how they provide the stimulus?
Dr. Becker: There are four current manufacturers of TMS machines: the two you just mentioned and also Magstim and MagVenture. NeuroStar, Magstim, and MagVenture all use the figure-8 coil. Brainsway uses the H coil, which causes a stimulation that penetrates

Continued on page 8

Expert Interview
Continued from page 7

a bit deeper in the brain. The Brainsway device also has a shorter stimulation time, around 20 minutes versus 37.5 minutes for the other devices.

TCPR: Didn't NeuroStar recently announce that it now has an ultra-brief treatment?

Dr. Becker: Yes, that just came out, and it is likely what we'll see in the future for all TMS machines. One of the things I hear from patients all the time is, "Boy, I don't have an hour a day for six weeks. I have to drive here. Traffic's terrible. I'd have to miss too much work." So one of the big imperatives right now is getting this down to 20 minutes. Or, what if we could get it down to even 5 minutes, so that you get the same amount of treatment but in a condensed period of time? Of course, then you're trying to balance that with any seizure risk—because if you crank up the intensity high enough with a magnet, you can cause a seizure.

TCPR: What about giving treatments every other day, or once a week, rather than every day?

Dr. Becker: Going back to the original studies that got the FDA approval, it was about 20 treatments before people separated from placebo. So that's four weeks. If you go to every other day, you could be talking about 8 weeks. People are suffering and they want to get better yesterday.

TCPR: How do people feel about the treatments themselves? Do they tolerate them well?

Dr. Becker: It depends on the treatment protocol. The magnetic pulses are described in terms of hertz, a measure of the frequency of pulses. The standard protocol is high frequency, which is 10 hertz, or 10 pulses per second. High frequency can be uncomfortable.

TCPR: How so?

Dr. Becker: I once volunteered to have TMS myself to help train some staff on the machine. It was not pleasant. It feels like a woodpecker tapping on your head. However, virtually all the patients who have done it have told me that after four or five sessions they don't feel it anymore, so I think there's a habituation response there. But during those first several sessions, I think people can be a little taken aback.

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TCPR: Then there's the time commitment to consider. If I were a patient with depression, I might find it really hard to commit to coming to the office five days a week for a number of weeks. On the other hand, if after a month or so of TMS I didn't have to take any medication for a while, it might seem like an attractive option. How do you talk to patients about trade-offs?

Dr. Becker: I think it depends on the patient. Someone who has been plagued by multiple recurrences of depression is more likely to consider the time spent getting the treatment worthwhile. And the durability of TMS is pretty good. One study found that of patients who had an initial response to TMS, 60%–65% maintained that response at 12 months (Dunner DL et al, *J Clin Psychiatry* 2014;75(12):1394–1401). Even the majority of people who relapsed responded to a repeat course. Usually you can get a response to relapse with less than the full 6 weeks.

TCPR: Do most patients stay on medication during the treatments?

Dr. Becker: For the typical TMS candidate who has had multiple episodes of depression, I will generally say, "Hey, we are going to do this and hope we get you better, but medications are going to remain part of your treatment plan. You might not be on the five medications you're on right now, or on the doses you're on right now, but there'll need to be some medication maintenance."

TCPR: Have you had any patients who responded to TMS so well that you were able to reduce their medication?

Dr. Becker: I saw a woman in her 60s fairly recently who came to my office for the consultation and looked like she had just rolled out of bed. She sobbed through the entire interview and was really anxious, with that kind of almost hand-wringing depression. She had done great with ECT in the past, but she didn't want to go through it again because she didn't want the anesthesia or the cognitive side effects she had experienced, so she was hoping to try TMS instead. She was so sick I thought we were going to end up doing ECT in the end. But we did the TMS, and she was a complete remitter and was able to avoid any medications.

TCPR: When combining medications with TMS, is there anything in particular to know? Do you have to think about what meds a patient should be on when getting TMS, or is there no relationship?

Dr. Becker: The main thing is that we don't want patients on anticonvulsants or benzodiazepines because they will decrease cortical excitability, which is exactly what we're trying to increase with TMS. For example, we've had people come to us on Lamictal and they didn't want to titrate off. So we tried letting them stay on it with TMS, and we weren't even able to get any sort of motor response to even begin to initiate a TMS protocol. We had to say, "Look, you've got to taper off, and then we can try it again."

Continued on page 9

Expert Interview
Continued from page 8

TCPR: So no anticonvulsants and no benzodiazepines. I imagine it can be tough for patients to come off benzos for the treatment.
Dr. Becker: Well, I have had a number of people that do fine with TMS taking benzos. What we tell them is, "Just don't take your Ativan the morning you're coming in," and that tends to be okay. But we have had issues with people who have popped a Xanax before they walked in and, well, that wasn't a good idea.
TCPR: Drugs or not, do you do any kind of maintenance TMS after the initial 6-week course?
Dr. Becker: We do a taper at the end. The standard practice is that after the 30 sessions over the course of 6 weeks, there is a taper-down phase where you administer 3 treatments one week, 2 treatments the following week, then 1 treatment the last week. At that point, we release the patient with instructions to call us if the depression returns. If it does, we will usually restart a course of daily TMS until the patient remits again. This generally occurs with less than 30 treatments as in the initial protocol.
TCPR: What's your time commitment during the actual TMS sessions?
Dr. Becker: We have a TMS coordinator and operator who's in the room with the patient for the duration of the treatments. She's not a trained, licensed therapist, but she has led some groups on the inpatient units and can talk to people about their lives and what's bothering them, similar to supportive therapy.
TCPR: Are physicians required to see TMS patients every day?
Dr. Becker: No, and different practices may see patients on different schedules. In some, you might see the doctor once a week. I see my patients every day, but typically it's for just a few minutes. Although I'm not in the room with the patient during the session, I'm in the building in case something were to happen.
TCPR: Switching gears a bit, is it pretty standard for insurance companies to reimburse for TMS as long as the patient has had treatment resistance to at least four drugs, as you said earlier?
Dr. Becker: Yes, especially over the last year and a half or so, it has been much easier to get TMS paid for. You have to get a prior authorization, and insurance companies tend to want a detailed medication history—and they are pretty specific about dosage and duration and response or side effects. But once you flush out the medication history, they'll approve it. And they'll consider side effects as a failure, too, so just because somebody didn't get up to 200 mg of Zoloft doesn't mean that person didn't have an adequate trial. If the patient was having GI distress and couldn't tolerate higher doses, the insurance company will count that as a failure.
TCPR: What are your thoughts about off-label uses of TMS?
Dr. Becker: In my practice, I keep it all on-label: major depressive disorder. I'm excited to see some of the research coming out on things like OCD, post-stroke depression, and Parkinson's disease—and I think TMS will be shown to be effective for some of those other conditions. But I don't believe we're there yet.
TCPR: Now that you've been working with TMS, do you tend to refer fewer patients for ECT?
Dr. Becker: I still think ECT is the most effective; I've not seen anything to show me otherwise. My referral pattern is to talk to people about both options. The way I phrase it is, "TMS is less invasive. There really are no side effects that you have to worry about, and I feel it's got a good chance of getting you better." Then, if a patient responds by telling me, "Doc, I don't have four weeks or six weeks to wait on a treatment with a 60% chance of getting me better; I've got to get better right now," we will have a more serious conversation about ECT. And of course, for anybody who I think is at imminent risk for suicide, or for patients who display elements of psychotic symptoms or catatonic symptoms, I refer straight to ECT, not TMS.
TCPR: What do you end up doing for those patients who fail a trial of TMS? Do most of them end up getting ECT?
Dr. Becker: ECT certainly comes into the discussion for patients who fail to respond to TMS; in my mind, ECT is the next step in the treatment algorithm. Some patients decline ECT, though, given the driving restrictions, the anesthesia, etc. From my own experience, I can tell you that the majority of patients I have treated with ECT post-TMS do respond.
TCPR: That's really elucidating. Anything else?
Dr. Becker: I've been doing TMS for a few years, and I've been impressed with the results. I've seen a number of people benefit from it, and of particular importance is that there really are no side effects other than the headache, which for most people is pretty mild. So I think having a treatment that is effective and isn't going to put weight on you or put you to sleep is a really good option for folks to have.

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