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www.reachmd.com info@reachmd.com (866) 423-7849

Differentiating Neuromodulation Therapies: VNS, DBS, ECT, TMS

## Announcer:

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### Dr. Aaronson:

This is CME on ReachMD, and I'm Dr. Scott Aaronson. Joining me today is Dr. Raman Sankar.

Dr. Sankar, let's start with a question for today. Can you briefly compare different neuromodulation mechanisms used in drug-resistant epilepsy, or DRE, as well as in treatment-resistant depression, or TRD.

#### Dr. Sankar:

Gladly, Dr. Aaronson. Of these various technologies, VNS refers to vagus nerve stimulation, and it involves modulating brain monoaminergic and thalamocortical circuits by stimulating the vagal afferents. Essentially, stimulating the vagal afferents involves activating the locus coeruleus and the raphe nuclei such that there is an intermittent pulse secretion of norepinephrine and serotonin, and it has been approved for both epilepsy and treatment-resistant depression. The important thing to recognize is it involves only peripheral electrodes and does not require any brain surgery.

DBS, on the other hand, can disrupt pathological circuitry with intracranial stimulation. And it's been used in epilepsy, depression, as well as movement disorders, where it's quite popular, but it always involves strategic placement of electrodes inside the brain. RNS also requires intracranial placement of electrode. It's important to note that, unlike VNS or DBS, RNS does not stimulate continually. It actually involves continuous monitoring of the EEG for seizure activity at a seizure focus, and then it delivers a desynchronizing stimulus when seizure activity is detected. Thus, it is a very different feedback-based technology, and it requires not only brain surgery for placement, it requires diagnostic intracranial electrode placements to know where to place the electrodes.

And Dr. Aaronson, I would like to now yield for the discussion of ECT and TMS to you.

#### Dr. Aaronson:

Thank you, Dr. Sankar. So let's discuss a little bit about nerve stimulation used in treatment-resistant depression. So we've had ECT for many, many decades. It is still the gold standard of treatment for difficult-to-treat depression. And by difficult-to-treat depression, I mean folks who do not respond to the first 2 to 10 treatments for their depression. It is by far the most powerful acute treatment we have. It involves giving people general anesthesia and effectively inducing a seizure. One of the good parts of it is we certainly have a high response rate, easily in 60% or above, folks doing better. The problem has been durability, that it does tend to demonstrate relapse about 50% of the time in people who do respond to ECT.

VNS is also used psychiatrically. We'll be discussing this in some of the data later, but it's a chronic treatment rather than an acute treatment. So we're making people better over months and years, rather than just an acute intervention.

TMS is basically using a magnet to increase neuronal activity in areas of the brain that have decreased activity within depression.

There's lots of different protocols. Standard protocol is treating people 5 days a week for 6 weeks, you see basically about a 66% response rate in people who have failed, let's say, 2 to 4 treatments in the current episode.

One of the most important things that has happened in the development of TMS is just this past year, 2 papers came out that both said the same thing, which is when they compared folks who had failed 2 treatments, medication treatments for their depression, and they were randomized to getting a third treatment for their depression or getting a course of TMS, TMS in both studies clearly had a higher efficacy in people who had failed 2 treatments.

Well, I'm going to stop there and say that this has been a terrific, great, bite-sized discussion, and we thank you for listening.

# Dr. Sankar:

Thank you, Dr. Aaronson.

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