

Research roundup 2005

News about treatment-resistant depression (TRD) and VNS Therapy

Last year provided a wealth of new research about TRD and about VNS Therapy. Many psychiatrists define TRD as depression that has not responded to 4 or more adequate trials of antidepressant treatments. After prescribing antidepressants for many years, psychiatrists have found that most antidepressant medications are effective in 65% to 80% of patients.¹ Many people who do not get well on their first antidepressant will improve with the second or third. But for reasons that are not well understood, some people do not get better even after 4 or more treatments for depression. They may require a different type of ongoing treatment for their depression—a reason for the ongoing research.

New research provided new estimates of how many people have depression. A 2005 survey of over 43,000 adults, published in the medical journal *Archives of General Psychiatry*, estimated that about 5% had depression over the previous 12 months. The lifetime risk was 13%.² At least 20% of Americans with depression, or approximately 4 million people, experience TRD, according to estimates of treatment resistance published in the journal *Psychiatric Clinics of North America* in 2003.¹ So if you have TRD, you are not alone.

Another important study, published in the *Journal of Clinical Psychiatry*, provided hope for the 4 million with TRD. It discussed the long-term benefits of VNS Therapy (vagus nerve stimulation), a device-based treatment for TRD approved by the U.S. Food and Drug Administration (FDA) in 2005. The study described long-term results for 59 patients with treatment-resistant depression at 4 different medical centers around the country. Patients had taken at least 2 antidepressant treatments during their current depression without success.³

Percentage of patients who showed improvement at 24 months



After 2 years of VNS Therapy in addition to other treatments, 42% of patients experienced a significant improvement in mood and 22% had almost no symptoms of depression. The side effects were tolerable—4 out of 5 people continued to receive VNS Therapy at the end of the 2-year study. This was an open-label study—psychiatrists and patients knew what treatment was being tested—and the results could not be directly compared to results for other treatments. Dr. Ziad Nahas of the Brain Stimulation Laboratory, Department of Psychiatry, Medical University of South Carolina, was the primary author of the paper.³

References: 1. Fava M, Rush AJ, Trivedi MH, et al. Background and rationale for the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study. *Psychiatr Clin North Am.* 2003;26:457-494. 2. Hasin DS, Goodwin RD, Stinson FS, Grant BF. Epidemiology of major depressive disorder: Results from the National Epidemiologic Survey on Alcoholism and Related Conditions. *Arch Gen Psychiatry.* 2005;62:1097-1106. 3. Nahas Z, Marangell LB, Husain MM, et al. Two-year outcome of vagus nerve stimulation (VNS) for treatment of major depressive episodes. *J Clin Psychiatry.* 2005;66:1097-1104.

INSIDE!

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Meet Ann, a VNS Therapy patient

Ann, a veterinarian, began feeling extremely stressed in the late 1980s. Her life as she knew it started to slip away. By 1995, she felt exhausted and was diagnosed with depression. Talk therapy with a clinical psychologist helped to keep her alive but did not decrease her depressive symptoms.

She also began taking medication. Some helped briefly but others just caused weight gain and extreme fatigue. After a weekend trip, she would sleep for 3 days straight.

Ann sold her beloved veterinary clinic because she could not handle the stress. She spent many days staring at the ceiling, plagued with boredom and hopelessness. "My depression was like sensory deprivation, where you can't smell coffee brewing, hear birds singing, or feel the sun shining. All the good feelings in my life were gone. I felt only sadness and pain."

Since talk therapy, medications, and even transcranial magnetic stimulation—an experimental treatment—had not helped at all, she asked a nearby medical center to keep her abreast of clinical trials for depression. In May 2001, Ann was contacted about a trial for VNS Therapy. She jumped at the chance to enroll.

Ann felt her mood stabilize immediately after the device was implanted. During the next 6 months, she saw gradual improvement until her depression was almost gone.

For the last 4 years, Ann has been almost depression-free without antidepressants. A mild seasonal affective disorder makes her feel a bit blue during the winter—but not depressed. "Last year, I treated this with a sun lamp, which helped tremendously." The only side effects of VNS Therapy Ann experiences are hoarseness and a sensation in her neck when she positions herself a certain way. "These are of no consequence compared to the depression I endured for years," she says.

Today, at the age of 61, Ann is productive and happy again. Living on a farm, she gets up in the morning and goes all day—taking care of the house, the vegetable garden, and the

animals. In addition, she works 35 hours a week as a book indexer. She spends her free time with her devoted husband, who spent so many years worrying about her. "I've come back from the dead. I'm so grateful to VNS Therapy," she says.

Ask the doctor

David L. Dunner, MD

Director, Center for Anxiety and Depression
Seattle, Washington



What can I do if I want to stop the voice changes briefly?

After the VNS Therapy implant procedure, each patient receives a VNS Therapy Patient Essentials Kit containing a magnet. You can use the magnet to stop stimulation during certain situations or activities when even mild side effects might be inconvenient. For example, if you experience changes in voice tone during stimulation, you may want to temporarily stop stimulation if you plan to sing or speak in public. You can hold or place the magnet over the pulse generator during this activity. Or you may stop stimulation if it becomes uncomfortable.

How is VNS Therapy different from ECT?

VNS Therapy is different from ECT in several ways.

Mode of action. VNS Therapy works differently from ECT. ECT affects large parts of the brain. Through the vagus nerve, VNS Therapy affects specific sites in the brain—sites associated with the symptoms of depression. And unlike ECT, VNS Therapy does not cause a seizure.

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Ask the doctor (continued)

Time frame. ECT works quickly, but often the effects wear off after a while. The benefits of VNS Therapy improve over time and are sustained long term.

Side effects. VNS Therapy has a completely different safety profile from ECT, with few memory problems.

Ask a VNS Therapy patient

Do you use the magnet often? When?

Karmen: I used it once, after my dose was increased. For some reason, my teeth hurt during stimulation, so I used the magnet until I could get back to the medical center and have my dose lowered. Probably if I were an opera singer, I would use a magnet whenever I sang, in rehearsals or performances.



Lana: I use my magnet several times a week. Although other people say they do not notice the voice changes from VNS Therapy, I find it distracting. So I turn it off during important conversations.

NOTE: The testimonials in this document are only examples of VNS Therapy results. Individual treatment results will vary.

Please see the full indication and safety information enclosed.



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Connections: a VNS Therapy resource program for you

- Brochures
- Live phone conferences—VNS Therapy Phone Facts Sessions
 - Hear from a patient about his or her experience with VNS Therapy
 - Listen to a psychiatrist experienced with VNS Therapy
 - Tuesdays, February 7 and 21, March 7 and 21
 - 7:00 PM Central Time
 - Call TOLL-FREE 1-866-598-9336
- Nurse case managers who can answer your questions about VNS Therapy and help with insurance benefits verification
- For more information, call **1-877-NOW-4VNS** (1-877-669-4867) or visit www.VNSTherapy.com

February tip of the month

As a young man, Abraham Lincoln experienced severe depression. "I am now the most miserable man living," he wrote to a friend. "If what I feel were equally distributed to the whole human family, there would be not one cheerful face on earth." With medical treatment and emotional support from his friends, he eventually recovered and went on to become one of America's greatest leaders. Celebrate his birthday February 12.



VAGUS NERVE STIMULATION

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SAFETY INFORMATION FOR THE VNS THERAPY™ SYSTEM*

INTENDED USE/INDICATIONS – UNITED STATES

The VNS Therapy System is indicated for the adjunctive long-term treatment of chronic or recurrent depression for patients 18 years of age or older who are experiencing a major depressive episode and have not had an adequate response to four or more adequate antidepressant treatments.

CONTRAINDICATIONS

The VNS Therapy System cannot be used in patients after a bilateral or left cervical vagotomy. Do not use short-wave diathermy, microwave diathermy, or therapeutic ultrasound diathermy on patients implanted with the VNS Therapy System. Diagnostic ultrasound is not included in this contraindication.

WARNINGS

This device is a permanent implant. It is only to be used in patients with severe depression who are unresponsive to standard psychiatric management. It should only be prescribed and monitored by physicians who have specific training and expertise in the management of treatment-resistant depression and the use of this device. It should only be implanted by physicians who are trained in surgery of the carotid sheath and have received specific training in the implantation of this device.

Physicians should inform patients about all potential risks and adverse events discussed in the VNS Therapy System *Physician's Manual*, including information that VNS Therapy has not been determined to be a cure for depression. Patients being treated with adjunctive VNS Therapy should be observed closely for clinical worsening and suicidality, especially at the time of VNS Therapy stimulation parameter changes or drug or drug dose changes.

Patients who have pre-existing swallowing, cardiac, or respiratory difficulties (including, but not limited to, obstructive sleep apnea and chronic pulmonary disease) should discuss with their physicians whether VNS Therapy is appropriate for them since there is the possibility that stimulation might worsen their condition. Patients with the VNS Therapy System or any part of the VNS Therapy System implanted should not have full body MRI.

ADVERSE EVENTS

The most commonly reported ($\geq 10\%$) side effects from stimulation included hoarseness, increased cough, neck pain, dyspnea (shortness of breath), dysphagia (difficulty swallowing), paresthesia (prickling feeling in the skin), and laryngismus (sore throat). The most commonly reported ($\geq 10\%$) side effects from the implant procedure included incision pain, hoarseness, incision site reaction, device site pain, device site reaction, pharyngitis (sore throat), dysphagia, and hypesthesia (numbness).

*THE INFORMATION CONTAINED IN THIS SUMMARY REPRESENTS PARTIAL EXCERPTS OF IMPORTANT PRESCRIBING INFORMATION TAKEN FROM THE PRODUCT LABELING. THE INFORMATION IS NOT INTENDED TO SERVE AS A SUBSTITUTE FOR A COMPLETE AND THOROUGH UNDERSTANDING OF THE VNS THERAPY SYSTEM, NOR DOES THIS INFORMATION REPRESENT FULL DISCLOSURE OF ALL PERTINENT INFORMATION CONCERNING THE USE OF THIS PRODUCT. (CAUTION: U.S. FEDERAL LAW RESTRICTS THIS DEVICE TO SALE BY OR ON THE ORDER OF A PHYSICIAN.)