

## VNS Therapy has long-lasting antidepressant effects

### News from the American Psychiatric Association (APA) annual meeting

If you are experiencing treatment-resistant depression (TRD), you know how difficult it is to find an antidepressant that not only works, but also continues to work over time. That's why long-term research on VNS Therapy for people with TRD presented at the APA meeting in Toronto this past May was particularly important.

#### Depression relief that lasts

A research team headed by Harold A. Sackeim, PhD, of the College of Physicians and Surgeons of Columbia University, New York, found that the benefits of VNS Therapy were long lasting.

The patients participating in this study had experienced unipolar and bipolar depression for an average of 25 years. Everyone in the study had TRD: Their depressions had not responded to many treatments, including talk therapy, medications, and, in some cases, ECT. Their depression was chronic (continuous depression lasting 2 years or more) or recurrent (2 or more periods of depression over time).<sup>1-4</sup>

People with TRD who showed substantial clinical benefit within 3 months or 12 months after starting VNS Therapy maintained the improvement at remarkably high rates at 2 years. Up to 70% of patients experienced a durable response with VNS Therapy.<sup>1,2</sup>

"These data...are rather remarkable..., particularly for the patient population [with chronic and recurrent treatment-resistant depression] studied here," said Dr. Sackeim. "These findings regarding long-term sustained effectiveness are very encouraging for psychiatrists, patients with treatment-resistant depression, and payers—all of whom are looking for more effective and cost-effective treatment options."<sup>1</sup>

#### Imaging research demonstrates how VNS Therapy affects the brain

Understanding how VNS Therapy affects the brain is another important area of research. A team of researchers headed by Charles R. Conway, MD, of St. Louis University School of Medicine, St. Louis, Missouri, presented new

information in this area at the APA meeting in Toronto. The researchers used positron emission tomography (PET) to find out how VNS Therapy affects the flow of blood in the brain. They found changes in blood flow in the brains of people receiving VNS Therapy, both immediately after the start of VNS Therapy and 3, 6, 12, and 24 months later.<sup>5</sup>

Dr. Conway's research on the short-term effects of VNS Therapy was also recently published in the journal *Psychiatry Research: Neuroimaging*.<sup>6</sup>

VNS Therapy caused immediate increases and decreases in blood flow in different regions of the brain. These results demonstrated that short-term activation of VNS Therapy in patients with TRD was associated with significant changes in blood flow to regions of the brain involved in mood disorders.<sup>5,6</sup>

A second report from the St. Louis team used PET scans to demonstrate longer-term differences in blood flow to regions of the brain after 24 months of VNS Therapy. This research, being prepared for publication, may provide insight to how VNS Therapy provides antidepressant improvement that increases over time.<sup>5</sup>

"This research advances our understanding of the short- and long-term mechanisms of action of VNS Therapy as an effective antidepressant treatment," commented Dr. Conway. "Our [short-term] findings are consistent with prior brain imaging studies demonstrating that...VNS Therapy modulates activities in the areas of the brain implicated in mood disorders. Our long-term findings importantly identify a new rationale for the unique, sustained, and improving response observed...with VNS Therapy."<sup>9</sup>



### INSIDE!

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### Meet Jerry, a VNS Therapy patient

Now 55 years old, Jerry has had depression for as long as he can remember, but 5 years ago it became unbearable. He attempted suicide and was hospitalized—the first of several hospitalizations.

Jerry tried over 17 different medications and over 100 sessions of ECT. Although some of the drugs helped briefly, their benefits didn't last. "ECT helped as suicide prevention, but it never really relieved my debilitating depression. And it caused memory loss." Before his long-term depression, Jerry had been a minister, but his ECT treatments erased portions of his memory.

Meanwhile, Jerry's depression worsened, leaving him helpless. He couldn't do things that most people take for granted—answering the phone or the doorbell, leaving his home, driving a car, or even getting out of bed. He also lost his job, reducing him to life on disability assistance. "I felt I was in a black pit with no way out—hopeless."

In the summer of 2005, Jerry's psychiatrist told him about VNS Therapy. Intrigued by what he heard, Jerry researched it. He and his psychiatrist decided VNS Therapy should be the next step in his treatment.

After so many treatment failures, Jerry had little hope that VNS Therapy would help. "But a little hope is better than none at all," he explains. He began receiving VNS Therapy in December 2005.

To Jerry's surprise, within the first few months, he felt markedly better. He began to venture outside and interact with other people. Now, 6 months after the procedure, Jerry continues to improve. "I go out now. I answer the door. I do everything," he exclaims. He acclimated quickly to his new lifestyle by taking computer courses and studying religion. He is now relearning things that were once second nature to him. Fortunately, his concentration has improved greatly, and he can study up to 8 hours a day.

Jerry has not had ECT during this period. He and his psychiatrist have carefully begun to reduce his medication. He is currently working on his doctoral degree. He hopes to return to work as a guidance counselor. "I'm thankful for VNS Therapy and look forward to continued improvement."

*I'm thankful  
for  
VNS Therapy*

### Ask a VNS Therapy patient

#### How was your experience with VNS Therapy different from your experience with ECT?

**Lauri:** I quickly noticed many advantages of VNS Therapy compared to the ECT I had received. I didn't have the memory loss I had with the ECT, or headaches. The most beneficial aspect is that instead of the slowly diminishing elevated mood I had after ECT, VNS Therapy allowed my mood level to increase gradually, remaining steady.

**Tamara:** VNS Therapy and ECT are as different as night and day. I had many ECT sessions until I felt better, usually 2 ECT treatments per session for several weeks. As a result, I lost more than 30 years of memory, with small flashes now and then.

After a VNS Therapy dosage adjustment, I can feel the sensation—not a pain—going from my upper chest to the lower part of my neck, which lasts about 3 days. My throat is a little sore and I'm hoarse during the pulses a few minutes apart. VNS Therapy has not caused additional memory loss.

#### How long did it take before you noticed improvement with VNS Therapy?

**Lauri:** I was pleasantly surprised—by the end of the first month, my husband felt my mood was better and more even. I began noticing changes around 2 months after starting VNS Therapy. I didn't expect this because I had set my goal to wait a year before noticing improvement. So you can imagine how excited I was at the 2-month mark, when my psychiatrist felt I was doing so well that we didn't even increase my dose.

**Tamara:** I started noticing a difference in how I felt almost immediately. After the second dosage adjustment, my family noticed a difference. At first, my psychiatrist upped my dosage 0.25 milliamp every 2 weeks until we reached 1.0 milliamp. After my initial dosage adjustment, he went by how I was feeling and coping, how my mood was, and how long it's been since the previous adjustment. We discuss it and decide together if the dosage needs adjustment.



**Ask the doctor**



**David L. Dunner, MD**

Director, Center for Anxiety and Depression  
University of Washington  
Seattle, Washington

**Can people who've had ECT receive VNS Therapy? And vice versa?**

Yes, VNS Therapy is effective in people who have had electroconvulsive therapy (ECT). And people who have VNS Therapy can receive ECT.

VNS Therapy has been shown to succeed in people who have had ECT.<sup>7</sup> Of the patients in clinical studies of VNS Therapy, about a third had had ECT during their current depression. Almost half had received it at some time in their lives.<sup>2-4</sup> People who had received ECT were just as likely to experience improvement over time as those who had not.<sup>7</sup>

VNS Therapy patients can receive ECT if they need it. The only special requirement is that the VNS Therapy pulse generator must be turned off during ECT.

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

**References:** **1.** Cyberonics press release. Houston, Tex: Cyberonics, Inc.; May 25, 2006. Two-year data showing decreases in suicidality in patients with treatment-resistant depression treated with VNS Therapy presented at annual American Psychiatric Association meeting. Available at: [http://www.cyberonics.com/PressRelease\\_detail.asp?ID=2E27E8C0-6C8F-403A-96D1-3066E2C22368](http://www.cyberonics.com/PressRelease_detail.asp?ID=2E27E8C0-6C8F-403A-96D1-3066E2C22368). Accessed June 26, 2006. **2.** Depression Physician's Manual. VNS Therapy™ Pulse Model 102 Generator and VNS Therapy™ Pulse Duo Model 102R Generator. Houston, Tex: Cyberonics, Inc.; 2005. **3.** George MS, Rush AJ, Marangell LB, et al. A one-year comparison of vagus nerve stimulation with treatment as usual for treatment-resistant depression. *Biol Psychiatry*. 2005;58:364-373. **4.** Rush AJ, Sackeim HA, Marangell LB, et al. Effects of 12 months of vagus nerve stimulation in treatment-resistant depression: a naturalistic study. *Biol Psychiatry*. 2005;58:355-363. **5.** Cyberonics press release. Houston, Tex: Cyberonics, Inc.; May 25, 2006. Neuroimaging research presented at annual American Psychiatric Association meeting provides new mechanism of action insight for VNS Therapy in treatment-resistant depression. Available at: [http://www.cyberonics.com/PressRelease\\_detail.asp?ID=52190098-00BC-4249-B17E-36281775C5E6](http://www.cyberonics.com/PressRelease_detail.asp?ID=52190098-00BC-4249-B17E-36281775C5E6). Accessed June 26, 2006. **6.** Conway CR, Sheline YI, Chibnall, George MS, Fletcher JW, Mintun MA. Cerebral blood flow changes during vagus nerve stimulation for depression. *Psychiatry Res Neuroimaging*. 2006;31:179-184. **7.** Data on file. Cyberonics, Inc.; Houston, Tex.

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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, August 1 and 15, September 5 and 19, October 3 and 17
  - 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](http://www.VNSTherapy.com)



**A cool tip for summer**

It's August, the month of "hazy, hot, and humid," when it's easy to get dehydrated. Make sure you drink enough water, especially if you take medications.

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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.)