

# VNS Therapy™ connections™

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## VNS Therapy efficacy studies published in *Biological Psychiatry*

### Research Report

The September 1, 2005, issue of the medical journal *Biological Psychiatry* contained 3 articles describing important research on vagus nerve stimulation as a treatment for treatment-resistant depression (TRD). In them, a team headed by Dr. A. John Rush of the department of psychiatry of the University of Texas Southwestern Medical Center in Dallas gave details of the studies used to gain approval of VNS Therapy from the U.S. Food and Drug Administration.

Each of the 3 articles features a different aspect of the research, which involved 235 outpatients with long-term depression (210 patients) or bipolar disorder (25 patients). On average, their current depression had lasted over 4 years, despite 2 to 6 medications (an average of 4) taken at the recommended doses for at least 4–6 weeks.

In the first of the 3 studies, "Vagus Nerve Stimulation for Treatment-Resistant Depression: A Randomized, Controlled Acute Phase Trial," 112 patients received VNS Therapy. Another 110 patients had the implant procedure, but the device was not turned on. All patients continued taking their previous medications. After 10 weeks, the patients receiving VNS Therapy had slightly better scores on standardized questionnaires used to measure depression. Although the study did not show rapid improvement, it did show that VNS Therapy was safe and well tolerated.<sup>1</sup>

The second study, "Effects of 12 Months of Vagus Nerve Stimulation in Treatment-Resistant Depression: A Naturalistic Study," showed that longer-term VNS Therapy was effective. After the initial 10-week study discussed above, the VNS Therapy devices were turned on for the patients who had not had VNS Therapy previously. After 12 months of therapy, the patients had significantly better average scores



on standardized measures of depression. The most commonly reported side effects were changes in voice, shortness of breath, and neck pain.<sup>2</sup>

The third study, "A One-Year Comparison of Vagus Nerve Stimulation With Treatment as Usual for Treatment-Resistant Depression," compared the results shown in the second article with those from 124 similar patients who did not receive VNS Therapy. Instead, these patients had a year of standard treatment (medications, talk therapy, and others). The people receiving VNS Therapy in addition to other antidepressant treatments were much more likely to experience meaningful mood improvement. The authors concluded that adding VNS Therapy to previous treatments was associated with "a great antidepressant benefit over 12 months." Dr. Mark S. George of the department of psychiatry, Medical University of South Carolina in Charleston, was the chief author of this article.<sup>3</sup>

**References:** 1. Rush AJ, Marangell LB, Sackeim HA, et al. Vagus nerve stimulation for treatment-resistant depression: a randomized, controlled acute phase trial. *Biol Psychiatry*. 2005;58:347-354. 2. 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. 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.

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## Meet Marna, a VNS Therapy patient

"I first became depressed in my late teens." After a divorce at 25, "I was so disconnected that I didn't want to look at myself because I felt sorry for the girl in the mirror. I finally saw a psychiatrist and went on an antidepressant medication. Typically, drugs worked well at first, but after a while the response diminished. Sometimes in 6 months, sometimes in 2 years, the drugs lost their effectiveness. My psychiatrist would increase the dose until it was as high as it could go. Then I'd have to stop that drug to give my body a rest and start on a different drug with a new set of side effects. Eventually that one would stop working too.

"I must be a great actress. I could always force myself to go to work and make everybody believe that everything was OK. When I could no longer make it to work, I called in and said I had the flu. I'd miss 5 days of work and never get out of bed."

In 2000, "I heard about VNS Therapy when my father saw someone who had VNS Therapy for chronic depression on *Good Morning America*. She was doing so well that my parents immediately wrote down the name and called me."

At first, Marna recalled, "I was nervous" at the thought of the implant procedure. "But then I thought, well, life cannot be lived the way I'm living it." If she had the procedure, "at least nobody could say I finally gave in. I always wanted people to know I was a fighter. Then I thought about it for maybe 5 minutes and said I'm going to do it, no matter what."



"I didn't notice a lot of antidepressant effect at first, but my friends and family did. After 6 to 8 weeks, my mom and dad heard a difference in my voice. They saw a difference in little things that I didn't notice.

"It really wasn't until a year after the surgery that I noticed a big difference. After 18 months, I felt

much, much better, and I began to tell people this is working. It's 3 years later, and I'm feeling better and better all the time.

"For me it is a personal transformation. I'm living in color now, where before I was losing my life in black and white. Then I felt as if I was living in slow motion—now I'm living at normal speed."

## Ask a VNS Therapy patient

### How did you decide to have VNS Therapy?

**Holly:** I was deeply depressed and my doctors were considering ECT. My psychiatrist heard about a clinical study for VNS Therapy and suggested that I might qualify. I was enrolled in the study and implanted in June 2001. ECT seemed like a desperate measure, and I was happy to have another option.

**Ann:** Since a variety of conventional treatments hadn't worked, I'd reached the point where I thought my only hope for recovery was a treatment under study. I learned about the VNS Therapy studies after the first study was closed. When the second study began, I wanted to participate. Because VNS Therapy had been already used for epilepsy, I was not concerned about unknown side effects.

### Can you feel the VNS Therapy pulses?

**Holly:** Only infrequently, not even once a month. It feels like a little tightening in my neck and lasts no more than a second.

**Ann:** Yes, I feel a slight burning sensation in my neck. At first this was somewhat bothersome, although I never considered it a significant side effect. As time has gone on, I notice the sensation less. I think this is partially from simply getting used to the feeling and partially because such things are less bothersome when I am not depressed.



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## Ask the doctor

### Thomas L. Schwartz, MD

Assistant Professor, Psychiatry and Behavioral Sciences,  
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### What is VNS Therapy?

VNS stands for vagus nerve stimulation. The vagus nerves are a pair of large nerves carrying much information from the body, up through the neck, to appropriate areas of the brain. In VNS Therapy, a device similar to a pacemaker is placed in the chest wall. It sends small electrical pulses via a wire up to the vagus nerve in the left side of the neck. Then the vagus nerve delivers these pulses directly to areas of the brain felt to be responsible in some ways for depression. The pacemaker turns itself on every few minutes to deliver a tiny electrical pulse that is not painful, nor harmful to the patient. Repeatedly affecting these brain areas may slowly reverse depression symptoms over time.

### What are the side effects of VNS Therapy?

In my experience, the number 1 side effect of VNS Therapy is voice change, usually mild hoarseness every several minutes when the device turns on. During these 30-second on-periods, the left half of the voice box may not work well due to the small electrical pulses going up the vagus nerve. This side effect usually diminishes over the first year of treatment, though it continues in a minority of patients. The patient can turn the pacemaker off temporarily, for example if he or she has a job interview or an important phone call.

Other side effects may include cough, shortness of breath, difficulty swallowing, prickling in the skin, and neck pain. This device is unique in that there are no major side effects affecting the whole body like dizziness or sexual problems. Because the device is always working, you cannot forget to take it, unlike missed doses of antidepressant pills. VNS Therapy also does not interact with other antidepressants or other medications.

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, December 6 and 20, January 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**

### Antidepressant tip of the month

Pharmacies may have shorter hours over the holidays.



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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.)