

Vagus nerve stimulation

Vagus nerve stimulation (VNS) is an adjunctive treatment for certain types of intractable epilepsy and major depression. VNS uses an implanted stimulator that sends electric impulses to the left vagus nerve in the neck via a lead wire implanted under the skin.

Cyberonics VNS device

VNS implantation devices consist of a titanium-encased generator about the size of a pocket watch with a lithium battery to fuel the generator, a lead wire system with electrodes, and an anchor tether to secure leads to the vagus nerve. The battery life for the pulse generator is "between 1 [and] 16 years, depending on the settings [ie how strong the signal being sent is, the length of time the device stimulates the nerve each time, and how frequently the device stimulates the nerve]."^[1]

The device is currently only made by Cyberonics, Inc. However, other "wearable" devices are being tested and developed by other companies that involve transcutaneous stimulation and do not require surgery. These devices are similar to TENS (Transcutaneous Electrical Nerve Stimulation) devices that are often used for pain management. The electrical impulses are targeted at the left auricular (ear), at points where branches of the vagus nerve have cutaneous representation, specifically the inner left tragus, but the meatus and concha have also been targets. To date, there have been no studies conducted on the effectiveness of such devices, though several patents have already been filed. US Patent #20070067004, #20080249594, #20090287035, #20100057154.

Implantation of the Cyberonics VNS device is usually done as an out-patient procedure. The procedure goes as follows: an incision is made in the upper left chest and the generator is implanted into a little "pouch" on the left chest under the clavicle. A second incision is made in the neck, so that the surgeon can access the vagus nerve. The surgeon then wraps the leads around the left branch of the vagus nerve, and connects the electrodes to the generator. Once successfully implanted, the generator sends electric impulses to the vagus nerve at regular intervals.^[2] The left vagus nerve is stimulated rather than the right because the right plays a role in cardiac function such that stimulating it could have negative cardiac effects.^[3]

Mechanism of action

Vagus, the tenth cranial nerve, arises from the medulla and carries both afferent and efferent fibers. The afferent vagal fibers connect to the nucleus of the solitary tract which in turn projects connections to other locations in the central nervous system. Little is understood about exactly how vagal nerve stimulation modulates mood and seizure control but proposed mechanisms include alteration of norepinephrine release by projections of solitary tract to the locus coeruleus, elevated levels of inhibitory GABA related to vagal stimulation and inhibition of aberrant cortical activity by reticular system activation.^[4]

Approval and endorsement

In 1997, the United States Food and Drug Administration (FDA) approved the use of VNS as an adjunctive therapy for partial-onset epilepsy. In 2005, the FDA approved the use of VNS for treatment-resistant depression.^[5]

Although the use of VNS for refractory depression has been endorsed by the American Psychiatric Association, the FDA's approval of VNS for refractory depression remains controversial. According to Dr. A. John Rush, vice chairman for research in the Department of Psychiatry at the University of Texas Southwestern Medical Center at Dallas, results of the VNS pilot study showed that 40 percent of the treated patients displayed at least a 50 percent or greater improvement in their condition, according to the Hamilton Depression Rating Scale.^{[6] [7]} Many other studies concur that VNS is indeed efficacious in treating depression. However, these findings do not take into account

improvements over time in patients without the device. In the only randomized controlled trial VNS failed to perform any better when turned on than in otherwise similar implanted patients whose device was not turned on.^[8] To better understand the opinions of the medical professionals relating to this treatment option a compilation has been prepared from the responses to CMS (Medicare) during the write-in period from 08/07/2006 - 09/06/2006 entitled "Letters from the Medical Professionals ^[9]".

Patients

Charles E. Donovan, a study subject in the investigational trial of vagus nerve stimulation therapy for treatment-resistant depression, wrote *Out of the Black Hole: The Patient's Guide to Vagus Nerve Stimulation and Depression*.^[10]

Other uses

Because the vagus nerve is associated with many different functions and brain regions, research is being done to determine its usefulness in treating other illnesses, including various anxiety disorders, Alzheimer's disease, migraines^[5], and fibromyalgia.^[11]

Other brain stimulation techniques used to treat depression include Electroconvulsive therapy (ECT) and Cranial electrotherapy stimulation (CES). Deep brain stimulation is currently under study as a treatment for depression. Transcranial magnetic stimulation (TMS) is under study as a therapy for both depression and epilepsy.^[3] Trigeminal Nerve Stimulation (TNS) is being researched at UCLA as a treatment for epilepsy.^[12]

Adverse effects

Sleep apnea

Intermittent decrease in respiratory flow during sleep has consistently been demonstrated in patients with VNS implants^[13]. Clinically significant sleep disordered breathing associated with VNS has been described in pediatric^[14] and adult^[15] patient populations. Most patients undergoing VNS treatment experience an increase of apnoea hypopnoea index (AHI) post treatment^[15], up to approximately one third develop mild obstructive sleep apnoea post treatment,^[15] and a minority of patients develop severe obstructive sleep apnoea related to VNS therapy^[14]. These obstructive events can be alleviated by decreasing the frequency or intensity of VNS stimulation^[13], by having the patient sleep in non-supine position or by applying positive airway pressure^[15].

Screening for obstructive sleep apnoea (OSA) in patients with a seizure disorder who are undergoing a VNS implant is also important because adequate treatment of previously undiagnosed and untreated OSA is likely to result in better seizure control in these patients^[16].

Patients undergoing vagal nerve stimulator placement are at risk for developing OSA related to the VNS and should therefore be screened clinically for the presence of OSA after the procedure. Continuous Positive Airway Pressure (CPAP) is a viable therapeutic option for patients who develop OSA related to the VNS. Other options include increasing the cycle length or stimulation frequency of the device. With increasing number of indications and the number of patients undergoing the procedure, awareness of this causation is important for appropriate diagnosis and treatment of OSA related to vagal nerve stimulators.

Symptoms such as loud snoring or intermittent cessation of breathing during the night or daytime symptoms as behavioral changes, fatigue and sleepiness may alert the patient or parent to the presence of obstructive sleep apnoea, but these symptoms are generally insensitive and a sleep study (diagnostic polysomnography) is generally required to diagnose the presence of obstructive sleep apnoea. The fact that many of these patients are children and may have associated cognitive deficits makes diagnosing the problem even more difficult without a sleep study.

Other

VNS causes stimulation of the superior and recurrent laryngeal nerves and is associated with problems ranging from alteration of voice(66%), coughing(45%), pharyngitis(35%) and throat pain(28%)^[14] and hoarseness (very common) to frank laryngeal muscle spasm and upper airway obstruction (rare)^[17]. The left vagus has proportionally lesser number of cardiac efferent fibers and placing the stimulator on this side potentially limits the arrhythmogenic effects of vagal stimulation but reversible bradyarrhythmias associated with vagal nerve stimulators have been well described^[18]. Other nonspecific symptoms such as headache, nausea, vomiting, dyspepsia^[18], dyspnea and paresthesia.^[3]

See also

- Electrotherapy
- Electrical brain stimulation
- Deep brain stimulation
- Transcranial Magnetic Stimulation
- Cranial Electrotherapy Stimulation

Further reading

- Donovan, Charles E. (III) (2004). *Out of the Black Hole: The Patient's Guide to Vagus Nerve Stimulation and Depression*. St. Louis: Wellness Publishers, L.L.C. ISBN 0-9748484-1-7.
- FDA-MAUDE Database ^[19]

External links

- VNS: A New Tool for Brain Research and Therapy (PDF file) ^[20].
 - VNSTherapy.com ^[21].
 - VagusNerveStimulation.com ^[22] Publisher's website for *Out of the Black Hole*.
 - VNSdepression.com ^[23] Proactive website and message forum sharing an accumulation of information and patient experiences relating to the VNS Therapy.
 - VNS Message Board ^[24] - Independent forum where VNS patients share their experiences
 - FDA OKs Brain Stimulator for Depression ^[25] - Comments on vagus nerve stimulation for depression
 - Public Citizen petition to the FDA not to approve VNS ^[26]
 - The VNS From A Patient's Point Of View ^[27]
 - Battle Lines in Treating Depression ^[28]
 - [29] Australian VNS Information
 - FDA Warning Letter to Cyberonics, Inc. ^[30]
 - Cyberonics Receives Third Determination Letter ^[31]
 - International Neuromodulation Society ^[32]
 - North American Neuromodulation Society ^[33]
 - Therapeutic Neuromodulation Weblog ^[34]
-

References

- [1] Cyberonics, Inc. (2007.) VNS Therapy Patient Essentials: Depression.
- [2] Panescu, Dorin (2005). Emerging Technologies: Vagus Nerve Stimulation for the Treatment of Depression. *IEEE Engineering in Medicine and Biology Magazine*.
- [3] George, Mark S. et al. (2000). Vagus Nerve Stimulation: A New Tool for Brain Research and Therapy. *Biological Psychiatry*, 47, 287-295.
- [4] Ghanem T, Early SV. Vagal nerve stimulator implantation: an otolaryngologist's perspective. *Otolaryngol Head Neck Surg* 2006; 135(1):46-51.PMID 16815181
- [5] Groves, Duncan A., Brown, Verity J. (2005). Vagus Nerve Stimulation: A Review of its Applications and Potential Mechanisms That Mediate its Clinical Effects. *Neuroscience and Biobehavioral Reviews*, 29, 493-500.PMID 15820552
- [6] Doctor's Guide: *Vagus Nerve Stimulation Successful For Depression* (<http://www.pslgroup.com/dg/15131a.htm>)
- [7] Neurology Channel: Vagus Nerve Stimulation (<http://www.neurologychannel.com/vagus/>)
- [8] FDA Summary of VNS Data (http://www.fda.gov/ohrms/dockets/ac/04/briefing/4047b1_02_Summary of Safety and Effectiveness.pdf)
- [9] http://www.vnsdepression.com/p7-00_lettersfromthemedicalprofessional.htm
- [10] Donovan, C. (2005.) *Out of the Black Hole: The Patient's Guide to Vagus Nerve Stimulation and Depression* Wellness Publishers, LLC. Also: <http://www.vagusnervestimulation.com/>
- [11] <http://clinicaltrials.gov/ct/show/NCT00294281?order=3>
- [12] "UCLA Develops Unique Nerve-stimulation Epilepsy Treatment; "Brain Pacemaker" Designed as External or Implant Device" (<http://newsroom.ucla.edu/page.asp?RelNum=7163>). Press release. 2006-07-25. . Retrieved 2006-07-26.
- [13] Malow BA, Edwards J, Marzec M, Sagher O, Fromes G. Effects of vagus nerve stimulation on respiration during sleep: a pilot study. *Neurology* 2000; 55(10):1450-1454.PMID 11094096
- [14] Hsieh T, Chen M, McAfee A, Kifle Y. Sleep-related breathing disorder in children with vagal nerve stimulators. *Pediatr Neurol* 2008; 38(2):99-103.PMID 18206790
- [15] Marzec M, Edwards J, Sagher O, Fromes G, Malow BA. Effects of vagus nerve stimulation on sleep-related breathing in epilepsy patients. *Epilepsia* 2003; 44(7):930-935.PMID 12823576
- [16] Vaughn BV, D'Cruz OF, Beach R, Messenheimer JA. Improvement of epileptic seizure control with treatment of obstructive sleep apnoea. *Seizure* 1996; 5(1):73-78.PMID 8777557
- [17] Bernards CM. An unusual cause of airway obstruction during general anesthesia with a laryngeal mask airway. *Anesthesiology* 2004; 100(4):1017-1018.PMID 15087642
- [18] Hatton KW, McLarny JT, Pittman T, Fahy BG. Vagal nerve stimulation: overview and implications for anesthesiologists. *Anesth Analg* 2006; 103(5):1241-1249.PMID 17056962
- [19] http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/Results.cfm?start_search=1&SearchString=cyberonics&SearchYear=A&ProductCode=&ProductProblem=&DeviceName=&KNumber=&PMANumber=&Manufacturer=&BrandName=&EventTypes=&ReportDateFrom=&ReportDateTo=&PAGENUM=10&Key_Count=1500
- [20] <http://www.bcm.edu/psych/mdoc/research/vnsintro.pdf>
- [21] <http://www.vnstherapy.com/>
- [22] <http://www.vagusnervestimulation.com/>
- [23] <http://www.vnsdepression.com/>
- [24] <http://www.vnsmessagelboard.org/>
- [25] <http://counsellingresource.com/features/archives/2005/in-practice/depression-brain-stimulator/>
- [26] <http://www.citizen.org/publications/release.cfm?ID=7385>
- [27] <http://www.howdydave.com/vns.html>
- [28] <http://www.nytimes.com/2006/09/10/business/yourmoney/10cyber.html?ex=1315540800&en=7877734ab451d64f&ei=5090&partner=rssuserland&emc=rss>
- [29] <http://www.aurorabioscience.com.au>
- [30] http://www.fda.gov/foi/warning_letters/archive/g5129d.pdf
- [31] <http://www.prnewswire.com/cgi-bin/stories.pl?ACCT=109&STORY=/www/story/12-18-2006/0004493422&EDATE=>
- [32] <http://www.neuromodulation.com>
- [33] <http://www.neuromodulation.org>
- [34] <http://www.brainstimulation.info>

Article Sources and Contributors

Vagus nerve stimulation *Source:* <http://en.wikipedia.org/w/index.php?oldid=377898482> *Contributors:* Aftermath, AlioTheFool, Brucewestfall, Casliber, Cdonovan, Chowbok, Chris the speller, Colin, DanMS, DanielCD, Deodar, Deville, Dionysia, Dmoskal, Dyuku, El3ctr0nika, Epolk, Gsp, Jeff G., Jfdwolff, Jyaroeh, Katsesama, Kellydcarter, Lifetime56, Megaman en m, Moez, Nspenn, OlEnglish, Owlvee, Pbui44, Phil Boswell, Pt, RJHall, Redleife, Rich Farmbrough, Richardcavell, Rishirajmd, Rjwilmsi, Rmky87, SDC, Sir Coolio, Sjowarner, Skarner, That Guy, From That Show!, Thatperson, Tktktk, UsedToBeYoung, WhatamIdoing, 50 anonymous edits

License

Creative Commons Attribution-Share Alike 3.0 Unported
<http://creativecommons.org/licenses/by-sa/3.0/>