Neuromodulation Today
Vagus Nerve Stimulation
Neural Network Modulation

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VNS for Epilepsy

- VNS to interrupt seizures suggested by a seventy year history of published research
- Direct brain stimulation had a very bad stigma in the 1980’s.
- Several animal models demonstrate VNS interrupts seizures
- Clinical studies started in 1988 with 30 seconds ON/5 minutes OFF with goal of randomly interrupting seizures. Stimulation could also be triggered by an external magnet. FDA approved in 1997.
VNS for Epilepsy

- Significant mood elevation observed in patients treated for epilepsy.
- Seizure control improves over the first 3-6 months.
- Although triggered stimulation is effective for many seizures, the main effect seems to be a gradual increase in “seizure threshold”.
- Commercial experience reported in registry is that about 65% patients have at least a 50% reduction in seizures.
- VNS FDA approved for treatment resistant depression July 2005.
- Insurance coverage difficult - CMS and major private insurers have denied national coverage.
VNS Implant Diagram
Model 102 Pulse Generator with Model 302 Bipolar Lead

- Anchor Tether
- (+) Electrode
- (-) Electrode
- Caudal
- Circumneural (cn) Bipolar Electrode
- Rostral
VNS System Modulation

- No invasion of neural tissue.
- Reversible - Electrodes can be removed from the nerve.
- Patients receive therapy 24/7. Mitigates compliance and drug substitution issues.
- The vagus nerve can be thought of as a “Super highway” into brain
- Preferentially stimulate the >80,000 afferent fibers
- Enters NTS and branches bi-laterally to both sides of brain
- Projections via overlapping pathways into parts of brain associated with seizure and depression control
Vagal Afferent Pathways in CNS

- Vagal afferents
- Heart
- Blood vessels
- Airways & Lungs
- GI tract

**Endocrine System (hormonal)**

**Limbic System (behavioral)**

**Pre-motor System (autonomic)**

- NTS

**Locations**

- INS
- Cing
- BST
- Amyg
- Thal
- Hypothal
- PBN
- LC
- DRN
- NTS
- DMX
- AMB
- VLM
- IML

*Courtesy of Thomas Cunningham, PhD, University of Texas Health Science Center at San Antonio*
The Vagus Nerve Projects to Key Brain Regions

Vagal Projections to the CNS

INS = insular cortex; ILC = infralimbic cortex; PBN = parabrachial nucleus; LC = locus coeruleus; DRN = dorsal raphe; NTS = nucleus tractus solitarius; AMB = nucleus ambiguus; VLM = ventrolateral medulla; IML = intermediolateral cell column

Courtesy of Thomas Cunningham, PhD, University of Texas Health Science Center at San Antonio.
Effects of VNS on The Nucleus of the Solitary Tract

2 hr 3 wk

* is significantly different from sham, P < 0.05

 Courtesy of Thomas Cunningham, PhD, University of Texas Health Science Center at San Antonio
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Courtesy of Thomas Cunningham, PhD, University of Texas Health Science Center at San Antonio.
Spontaneous firing rates of DRN 5-HT neurons with VNS

Door and Debonnel, J Pharmacol Exp Ther. 2006 Aug;318(2):890-8
Effects of VNS on The Dorsal Raphe

Acute VNS (2 h)  
Chronic VNS (3 wk)

* is significantly different from sham, \( P < 0.05 \)

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Courtesy of Thomas Cunningham, PhD, University of Texas Health Science Center at San Antonio.
LC NE Neuron firing rates with VNS

Door and Debonnel, J Pharmacol Exp Ther. 2006 Aug;318(2):890-8
Effects of VNS on The Locus Coeruleus

Acute VNS (2 h)  Chronic VNS (3 wk)

* is significantly different from sham, P < 0.05

Courtesy of Thomas Cunningham, PhD, University of Texas Health Science Center at San Antonio
Summary and Questions

- Neuromodulation of the vagus nerve provides an FDA Approved pathway for treating refractory epilepsy and depression.
- Is VNS the most effective neuromodulation pathway for seizure or depression control?
- Can the VNS signals be optimized for increased efficacy?
- Efficacy builds slowly for epilepsy and depression. Can the rate of response be increased?
- The durability of response is quite impressive for these disorders. Can the durability be further improved?
- Does automatic seizure detection and activation really help efficacy for the treatment of epilepsy?
- Can responders be identified prior to implant?