Vagal Nerve Stimulators and Anesthetic implications

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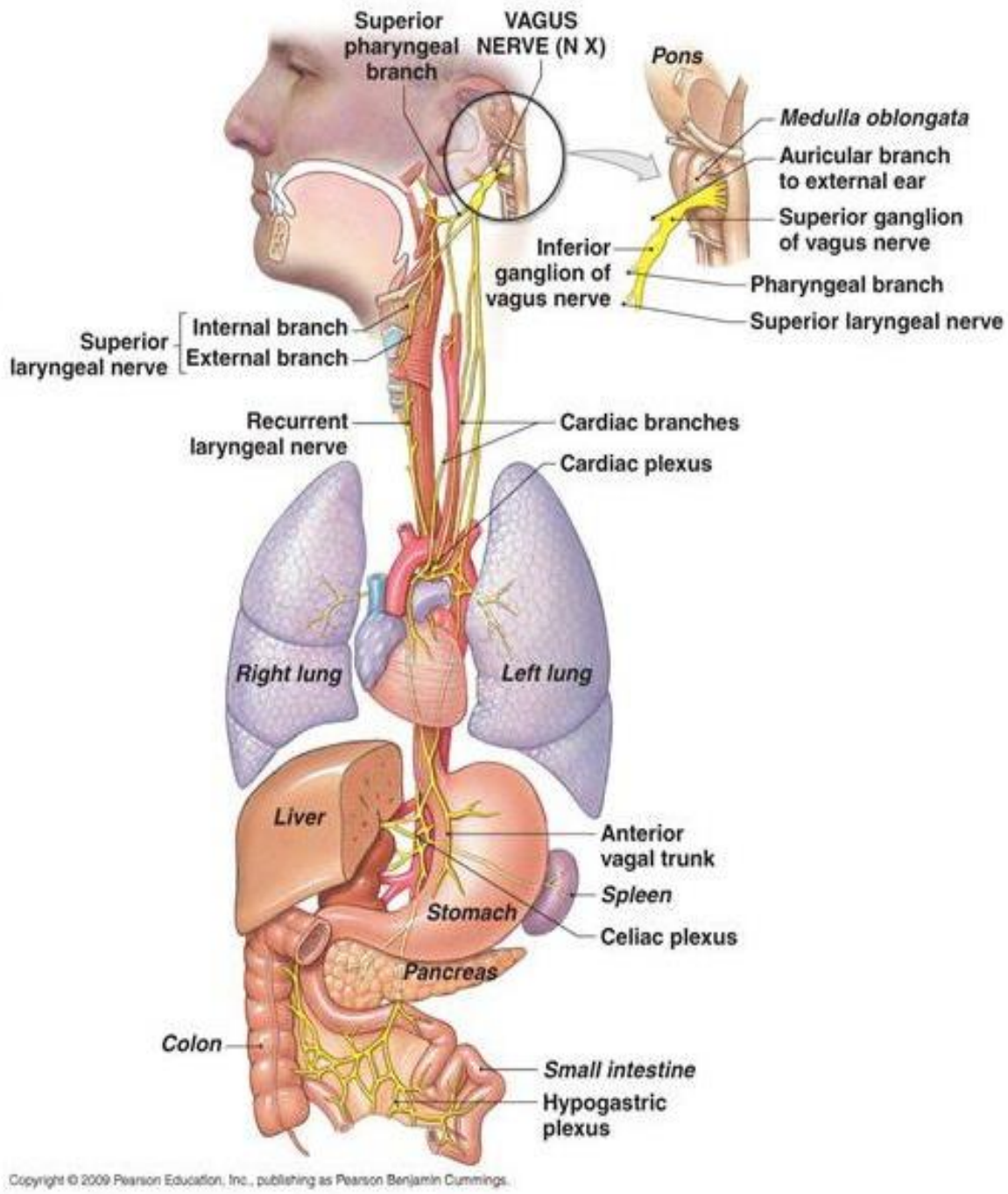
Objectives

- To discuss the indications and procedure of vagal nerve stimulator placement.
- To discuss potential complications of vagal nerve stimulator placement
- To review long-term implications of a patient with a vagal nerve stimulator presenting for an unrelated surgery

Vagus Nerve

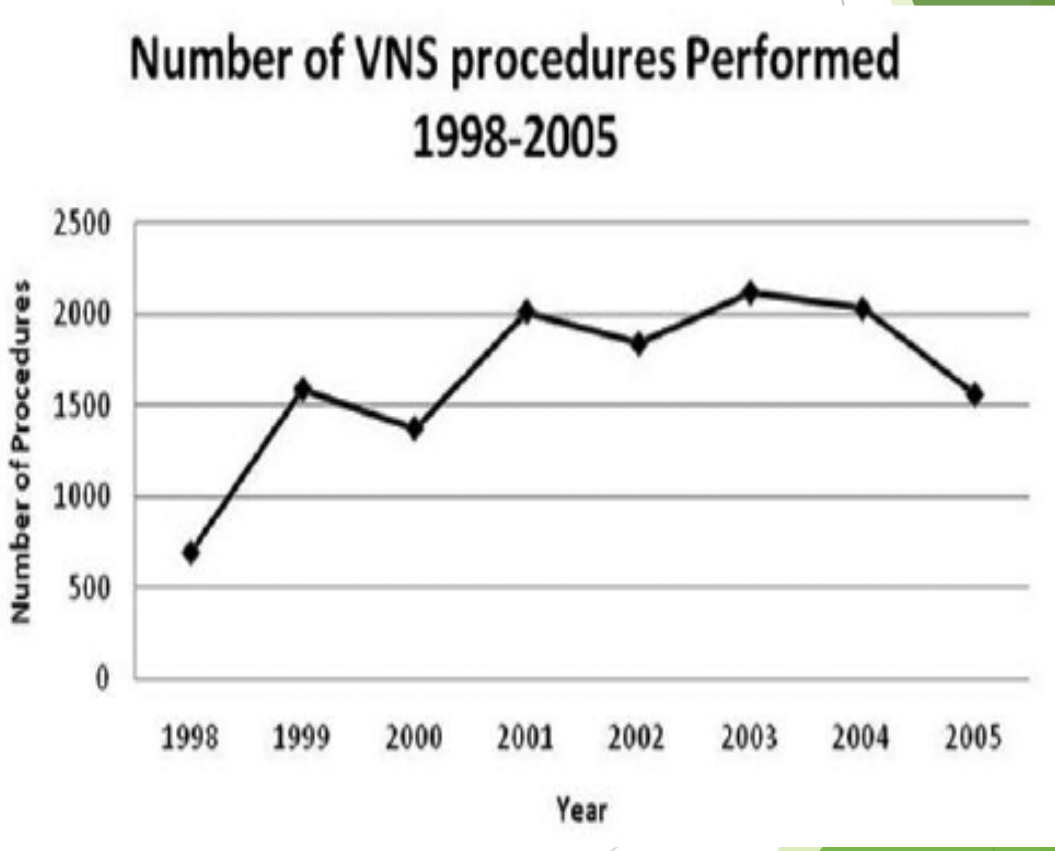
- Originates from 4 nuclei in medulla oblongata
  - Dorsal nucleus – gives rise to the preganglionic parasympathetic visceromotor fibers
  - Nucleus ambiguus – parasympathetic output to the heart
  - **Nucleus tractus solitarius – receives viserosensory info from the GI, respiratory, and taste; projects to the locus ceruleus (NE), the dorsal raphe nuclei (5-HT) and the amygdala/hippocampus.**
  - Spinal nucleus of the trigeminal nerve – receives sensory info from external auditory meatus and the back of the ear

- In the neck, lies in the carotid sheath between the common carotid artery and the IJ vein



Vagal nerve stimulation - History

- Bailey & Bremer (1938) – VNS produced EEG changes.
- Dell & Olson (1951) – VNS evoked responses in the thalamus.
- Zabara (1985) – Electrical stimulation of the vagus nerve produced inhibition of neural processes and terminated SZ in dogs
- Penry et al (1988) – First implant of VNS in a human
- In 1997, FDA approved VNS as an adjunctive Rx for medically intractable SZ

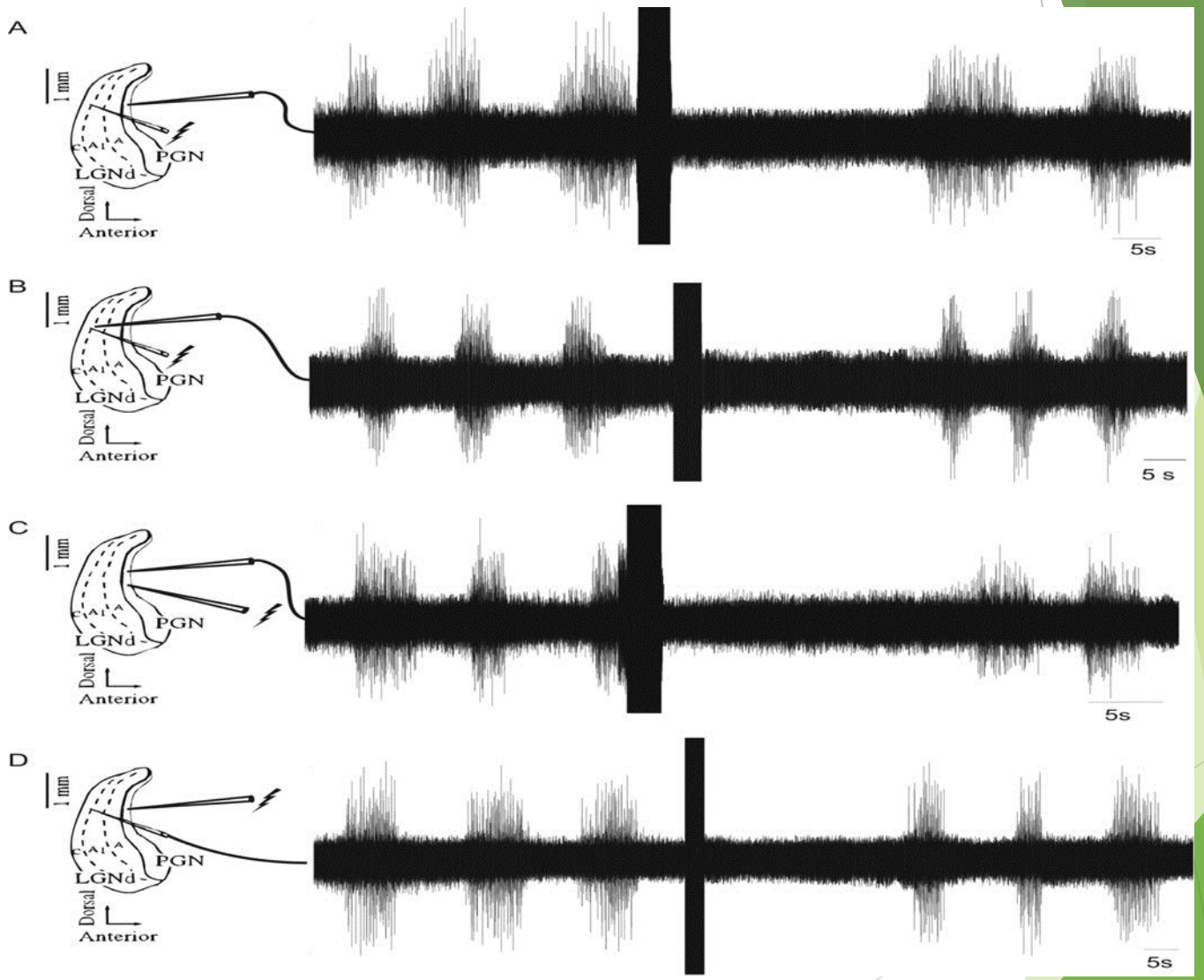


Lee KH et al. (2011)

-- High-frequency stimulation (HFS) of the thalamic brain slices from ferrets.

-- HFS was associated with a significant rise in extracellular glutamate and abolished spindle wave oscillations in thalamocortical relay neurons.

-- This may be a mechanism by which either VNS or Deep Brain Stimulation (DBS) of the thalamus may be effective in treatment of seizure.

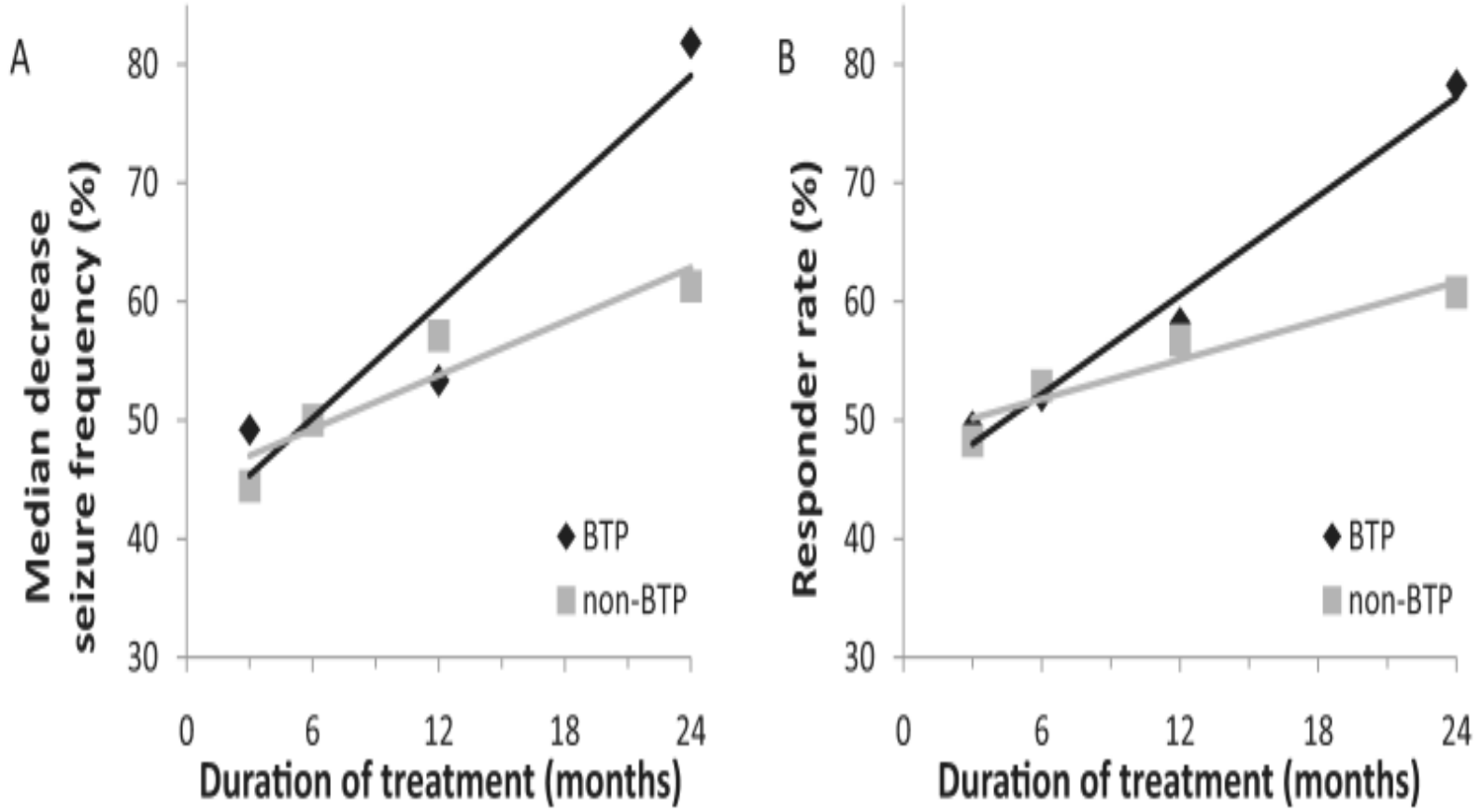


Mechanism of the anti-SZ effect of VNS?

- Desynchronization of neuronal activity?
  - The nucleus tractus solitarius (NTS) projects to the amygdala and then to the limbic system, which most often generates complex partial SZ.
  - These thalamo-cortical neurons are hyper-synchronized during SZ in animal models.
  - VNS may reverse this hyper-synchronization and abort SZ.
- Changes in neurotransmitters?
  - The NTS also projects to the locus ceruleus, rich in norepi-containing neurons.
  - If you lesion the LC or deplete its NE, then the anti-SZ effect of VNS is abolished.
  - VNS also increases CSF concentrations of GABA and 5-hydroxy-indole acetic acid and decreases CSF glutamate and aspartate.

VNS therapy Patient Outcome Registry by Cyberonics, Inc.

- 1285 physicians at 978 centers who prescribe VNS report to the Registry.
- Patel KS et al (2013)
  - Found 244 f/u visits in 114 patients with brain tumor-related SZ and 3846 visits in 1780 patients with SZ without brain tumor.
  - Compared efficacy of VNS



Efficacy of VNS in Rx of intractable SZ in children

- Gurbani S et al. (2016)
- 35 patients under 12 years of age
- Post VNS implant, followed patients for 2 years.
- Measured frequency of SZ episodes

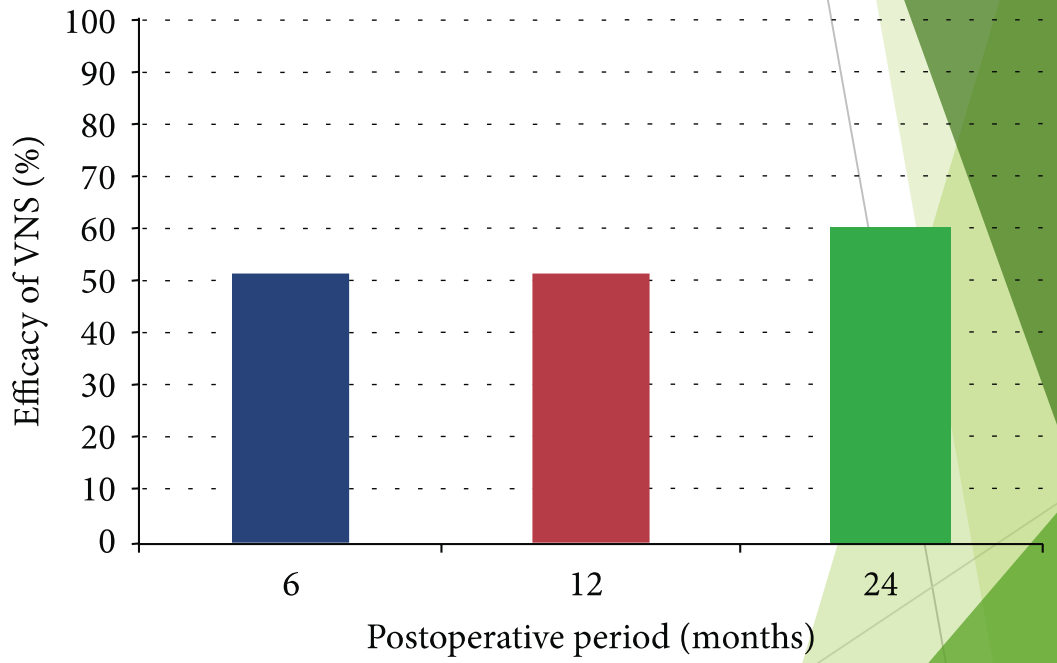
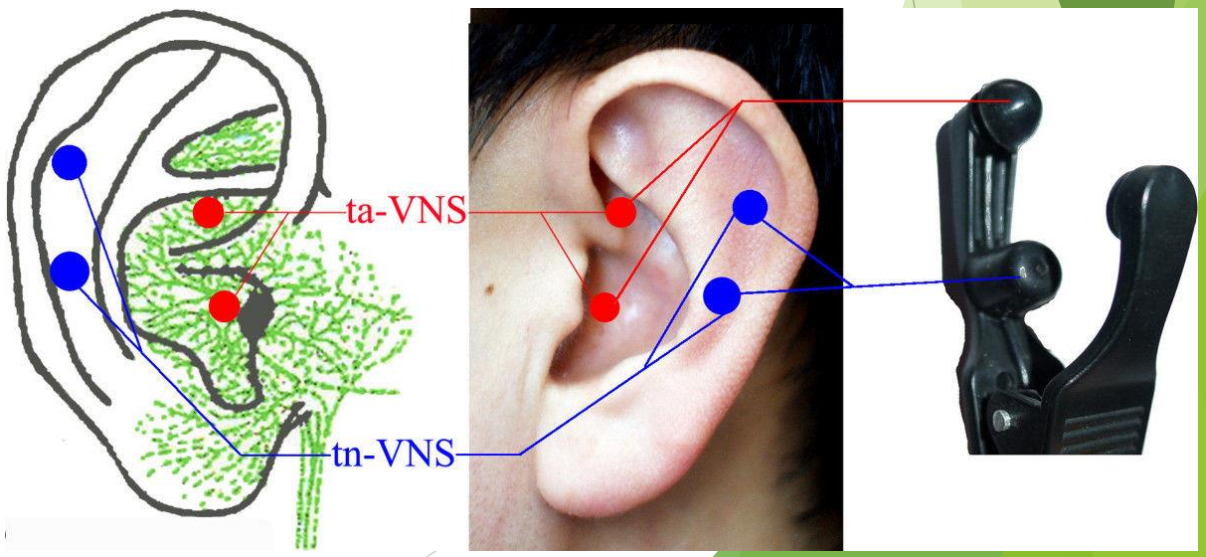


FIGURE 1: Efficacy of VNS (≥50% reduction in seizure frequency) at 3 study periods.

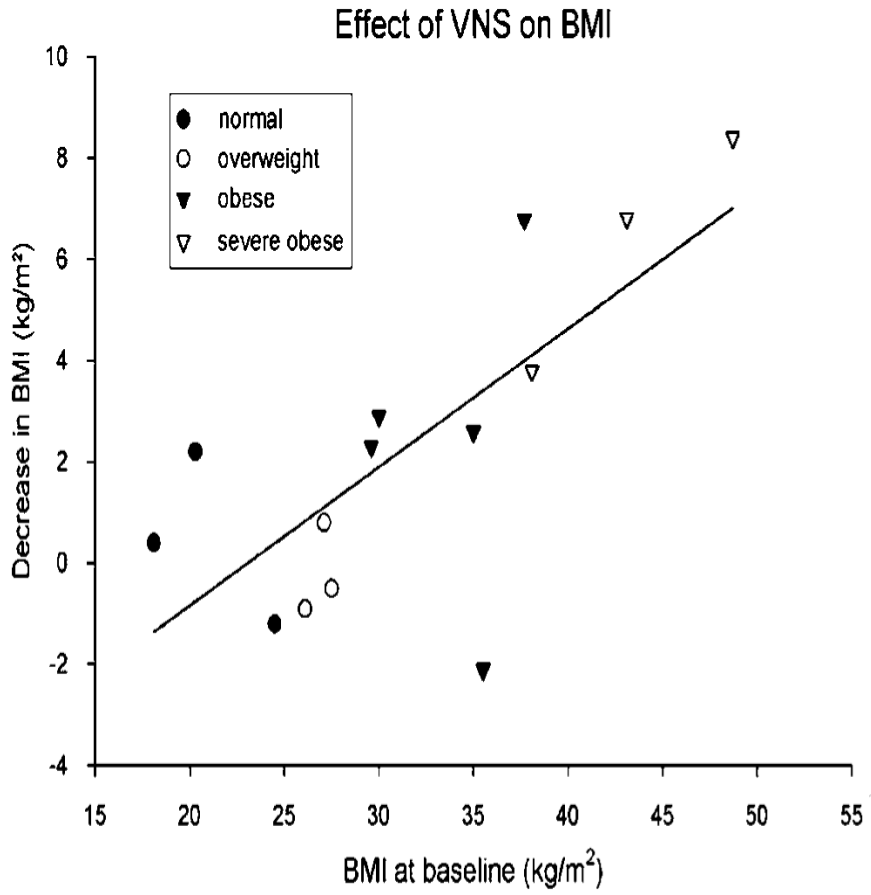
VNS for Rx of Depression?

- Anecdotally, it was found that patients with intractable SZ and major depression who were treated with VNS demonstrated improvement in both SZ and depression.
- Nahas Z et al. (2005)
  - 59 adult patients with major depression or bipolar disorder
  - Treated with VNS for 2 years
  - Remission was achieved in 15% at 3 months, 27% at 1 year, and 22% at 2 years.
- FDA approved VNS as adjunctive Rx for treatment-resistant MDD in 2005.
- Mechanism?
  - TCA's and MAO inhibitors work by increasing NE and 5-HT.
  - VNS projects and increases activity of the locus ceruleus (NE) and the dorsal raphe nuclei (5-HT)
- Rong P-J et al. (2012)



VNS for Rx of Obesity?

- Satiety
  - Gastric distention is transmitted via the vagal afferents.
  - CCK (cholecystokinin) may be involved in this process.
  - This transmission is blocked by capsaicin (*Hot foods 🔥🔥🔥🔥🔥
- Pardo JV et al (2007)
  - 12 patients with MDD, being treated with VNS
  - After 1 year of VNS, ↓ in BMI was proportional to the BMI at baseline.



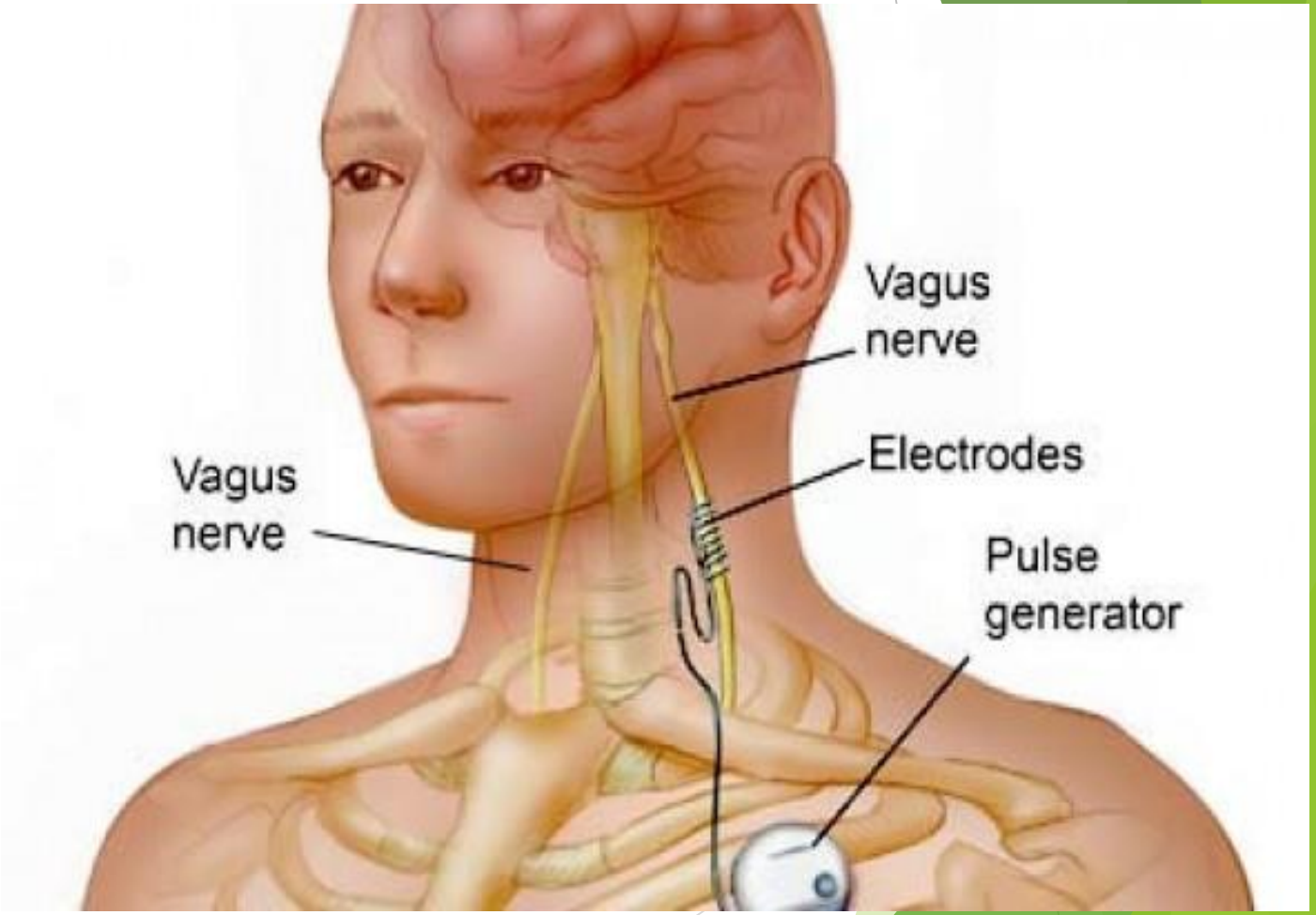
The sky is the limit for VNS …

- VNS for intractable hiccups?
- VNS for neurogenesis
- VNS for memory and cognition improvement, for dementia
- VNS for immune modulation of autoimmune or inflammatory diseases like rheumatoid arthritis via efferent vagal inputs to the spleen
- Waking up a man from a “vegetative” coma? (Corazzol M et al.)
- ….

- The VNS market is expected to grow at 10 % (CAGR) per year during 2016~2022 (https://www.marketresearchengine.com/vagus-nerve-stimulation-market).

How is the VNS implanted?

- GA, prepped like Lt CEA
- A stimulating electrode is implanted next to the Lt VN in the carotid sheath.
- A pulse generator is inserted in the SQ pocket over the pec major fascia.
- The generator may be turned on 14 days post op.



Why the left VN?

- Right VNS has been used in cases of Lt VNS failure and has been partially effective in SZ control.
- However,
  - Rt VN innervates the SA node → more potential for bradyarrhythmias.
  - Rt VN stimulation may lead to bronchospasm and reactive airway disease.

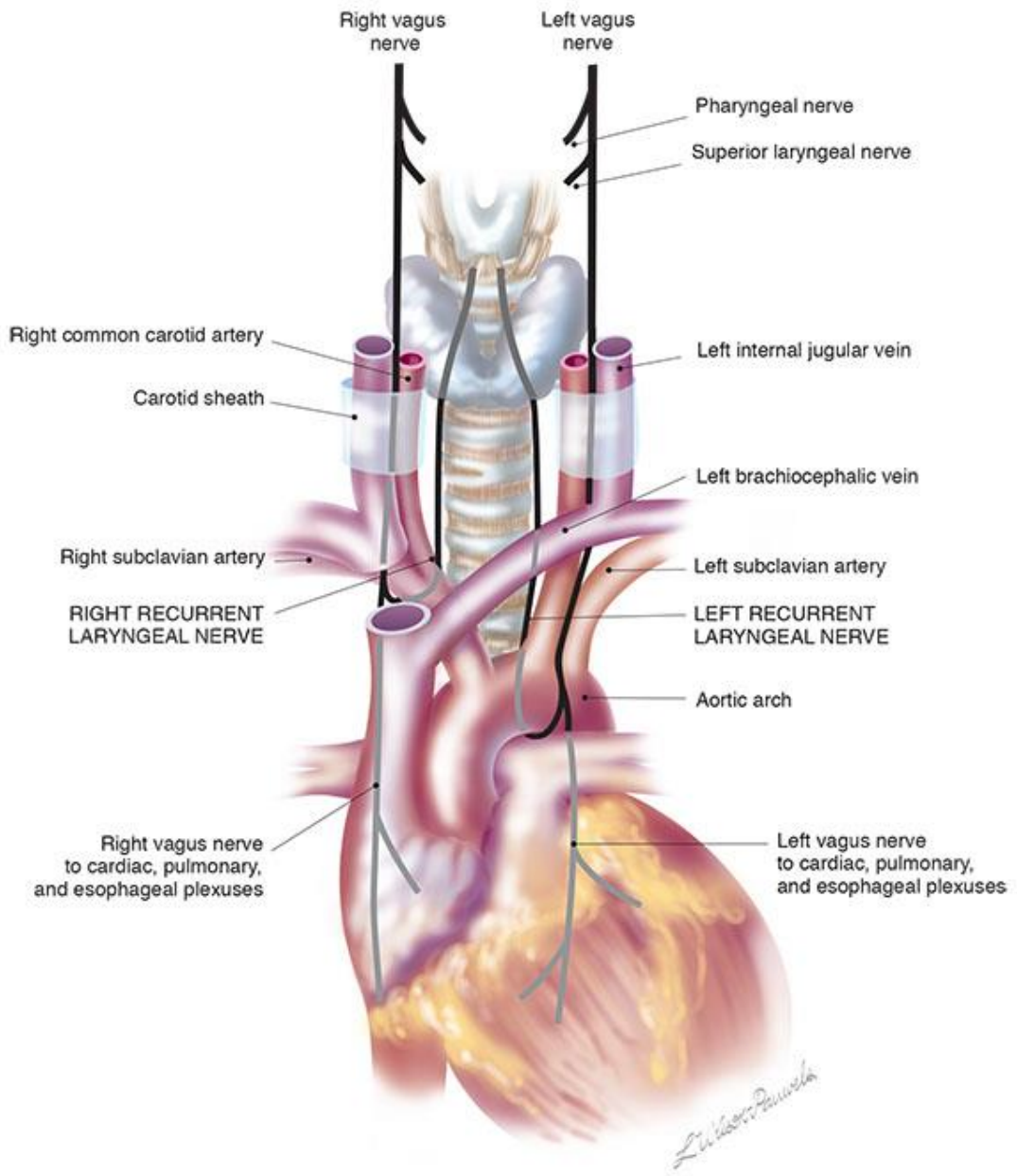


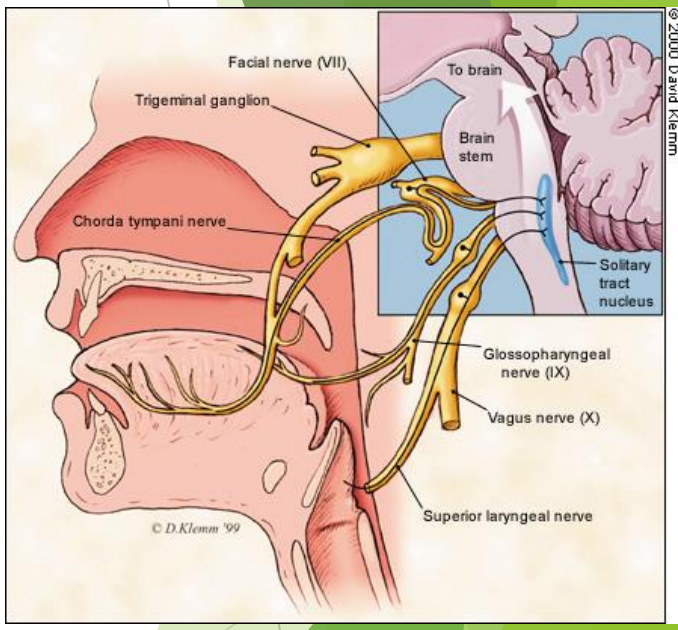
Figure X–4 Route of the right and left recurrent laryngeal nerves (nerve is shown in black for clarity).

Potential acute/subacute complications of VNS placement

- Hoarseness – seen in > 50%; may last months
- Dyspnea – seen in 15~20%
- Dysphagia/dyspepsia/nausea
- Cough

- These are often related to the intensity of stimulation and resolve with reduction in current intensity. (Sackeim HA et al. 2001)

- Occasionally severe tonsillar pain, associated with odynophagia.
  - Mimics glossopharyngeal neuralgia
  - Part of the vagus nerve travels with the glossopharyngeal nerve → VNS leads to vago-glossopharyngeal neuralgia.
  - Resolution will require adjustment of stimulation settings.

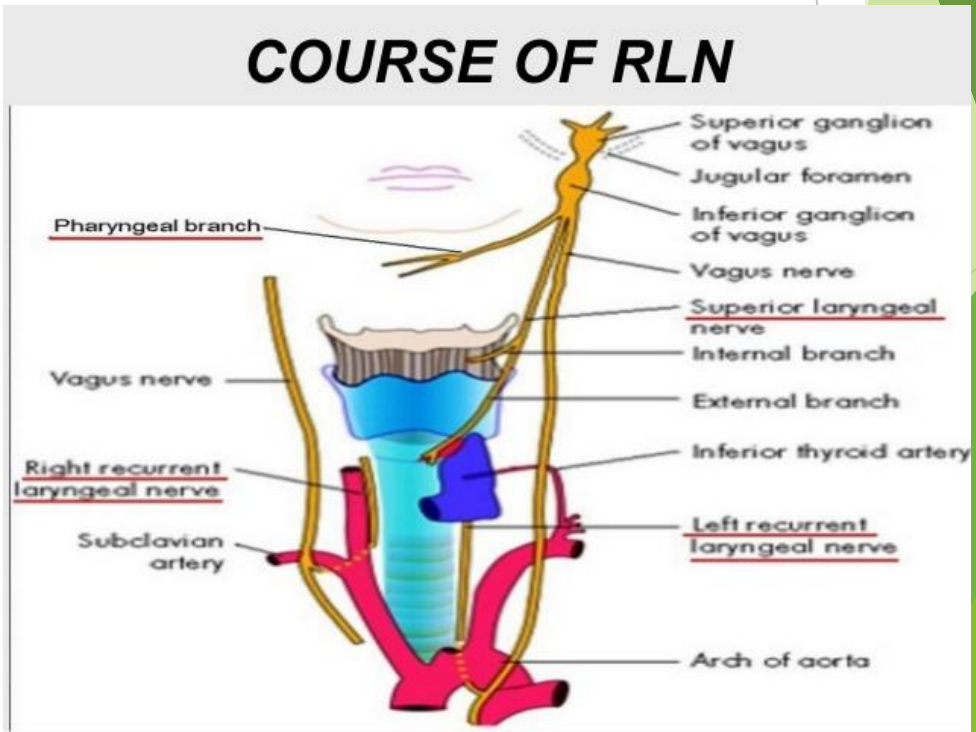


Side effects of long-term VNS (1): Laryngeal dysfunction

- Partial airway obstruction
  - From partial adduction of laryngeal muscles
  - Respiratory pattern in sleep is also altered → apneas and hypopneas become more frequent with VNS → OSA may be exacerbated.
  - Partial airway obstruction below the level of LMA is a potential concern under GA.
  - Or, repeated adduction against ETT can damage the laryngeal muscles.

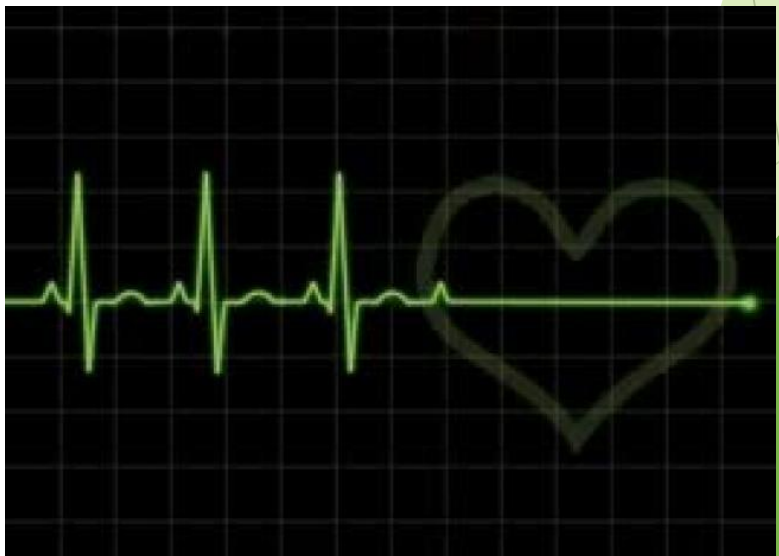
- Malow BA et al. (2000)
- Marzec M et al. (2003)
- Nagarajan L et al. (2003)
- Zumsteg D et al. (2000)

- Incomplete closure of the larynx on swallowing
  - Possible increase in the risk of aspiration



Side effects of long-term VNS (2): bradyarrhythmia

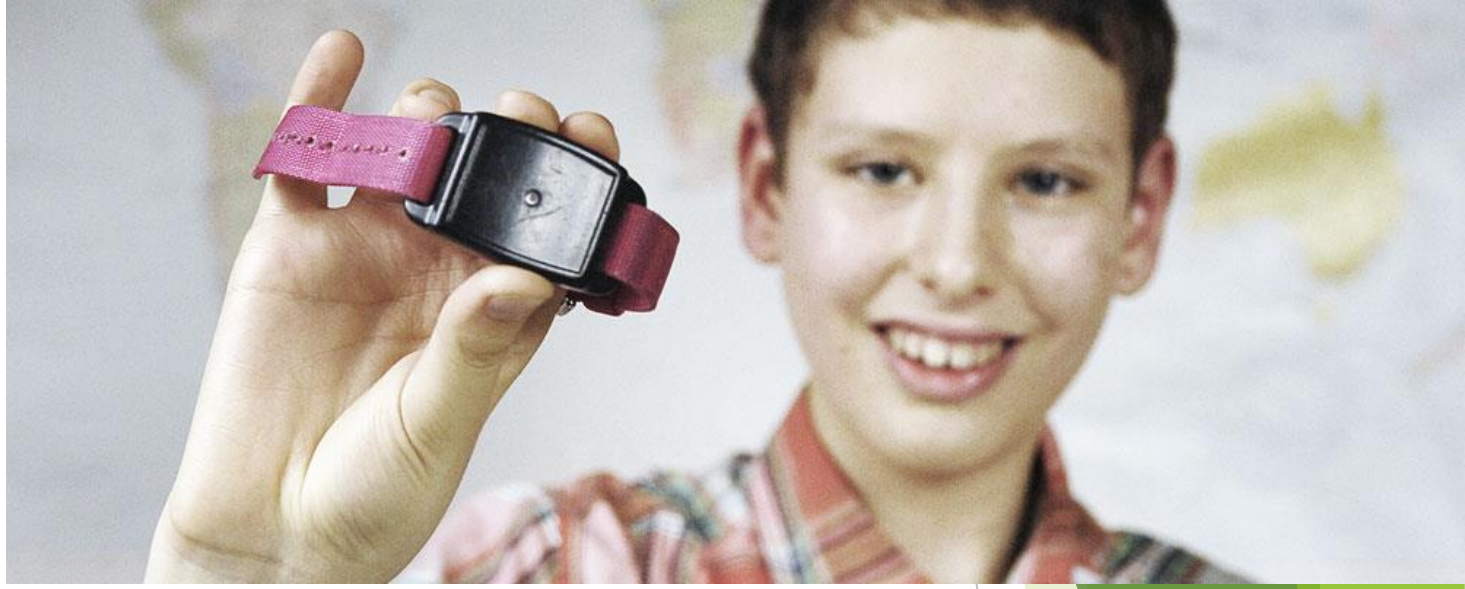
- Rt VN innervates the SA node.
- Lt VN innervates the AV node.
- VN stimulation can lead to significant bradycardia and even asystole. (Aseconape JJ et al. 1999)



When a patient with VNS presents for an unrelated surgery …

- Consider the indication for VNS placement.
  - SZ
  - Obesity
  - MDD, etc.
- This will help determine whether to turn off VNS or leave it on.

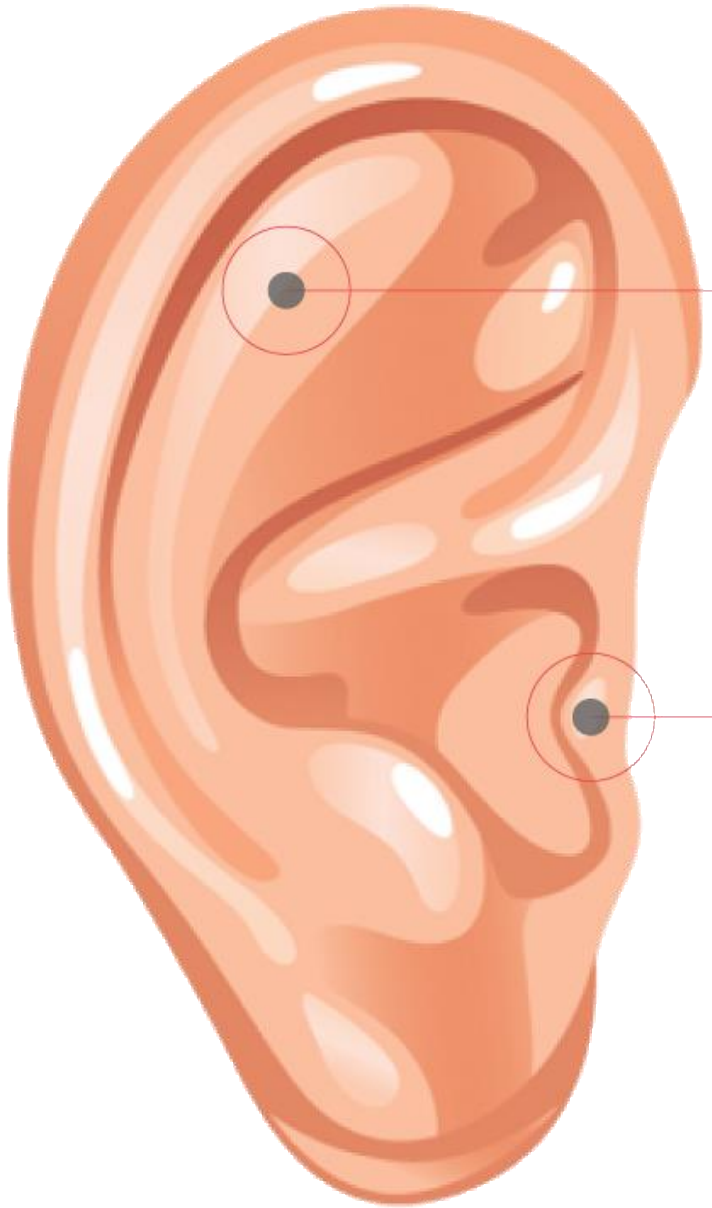
VNS magnet



- Placing the Magnet over the generator > 1 sec (“one, one thousand”) and quickly removing it
  - Generates a burst of stimulation to stop SZ
  - Then the generator will return to the original settings
- Leaving the Magnet over the generator > 65 sec
  - Preprogrammed output from the generator will be inhibited.
  - Removing the magnet will restore the original settings.

Intraop management of VNS

- If SZ is the indication for VNS and if the surgery is not near the generator, then it would be best to leave the VNS on.
- If obesity or MDD is the indication for VNS and/or if the surgery is near the generator (e.g., thyroidectomy), then it would be best to turn the VNS off intraop.



Shenmen point
a point that makes you feel less hungry

Hunger point
a point that stops from binging