Vagus Nerve Stimulation

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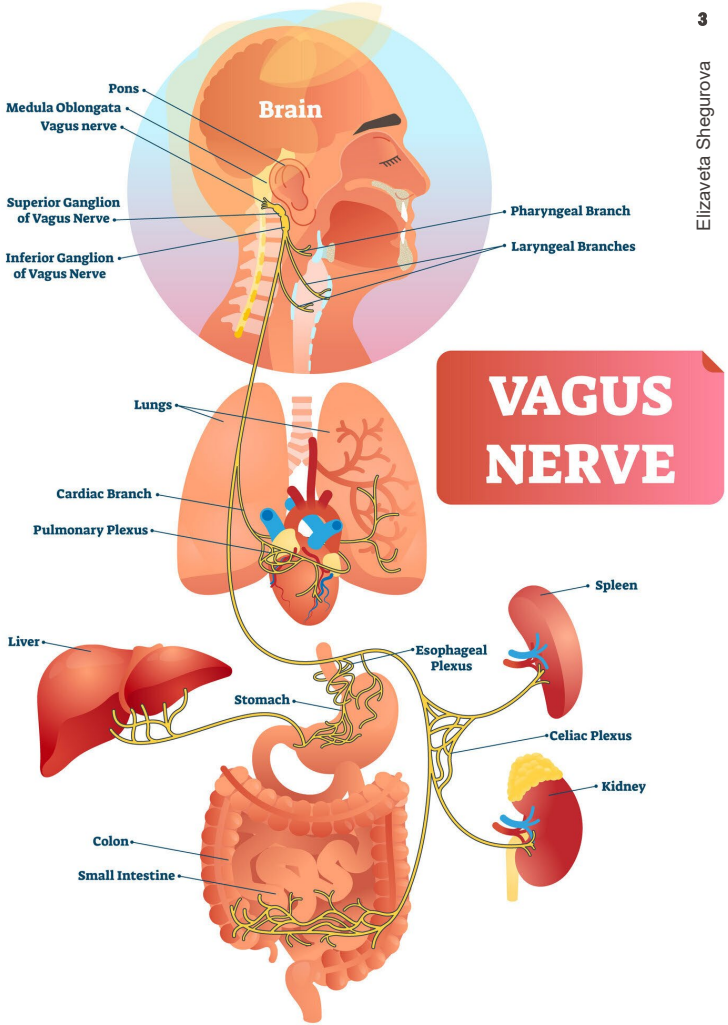
The Vagus Nerve

- **10th** paired cranial nerve
- Longest cranial nerve
- Originates from **medulla oblongata**
- Extends through **neck**, **thorax**, and **abdomen**
- Branches: Auricular, cardiac, pulmonary, and abdominal
- **Afferent Fibers (80%):** Sensory input to the brain
- **Efferent Fibers (20%):** Motor output to organs
- **Functions:**
  - Modulates heart rate
  - Controls gastrointestinal peristalsis
  - Regulates bronchoconstriction
  - Influences mood and immune responses



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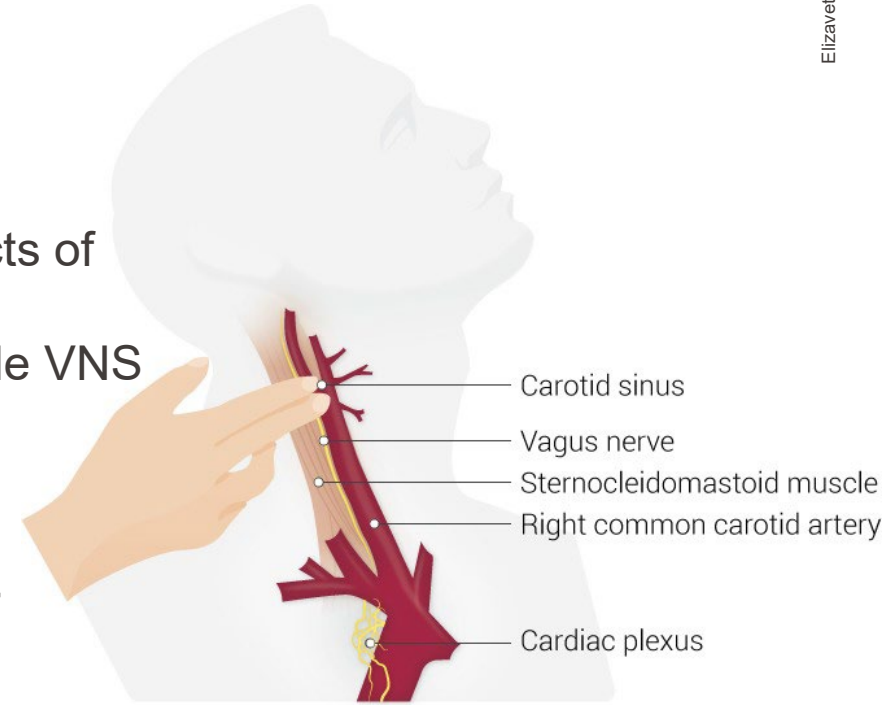
History of Vagus Nerve Stimulation (VNS)

- **1880s:** Carotid massage noted to suppress seizures
- **1930s-1940s:** Animal studies demonstrated anticonvulsant effects of vagal stimulation
- **1980s:** Development of implantable VNS devices
- **1997:** FDA approval for refractory epilepsy
- **2005:** FDA approval for treatment-resistant depression
- **Current Research:**
  - Investigating applications in Alzheimer's disease, obesity, and chronic pain



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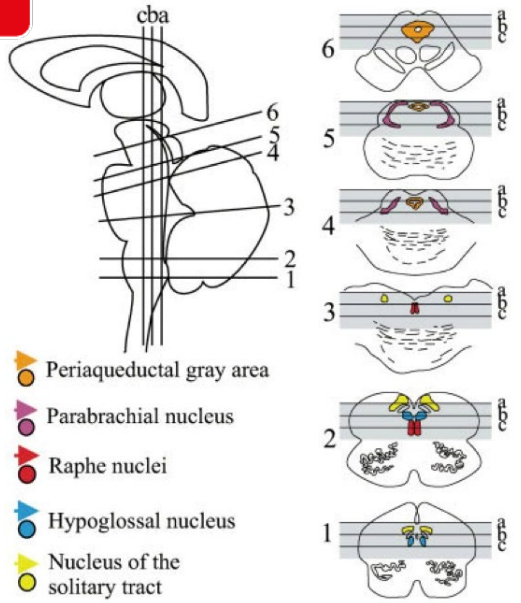
Mechanisms of Vagus Nerve Stimulation

- **Neural Pathways:**

Electrical impulses delivered to the vagus nerve → Activation of afferent fibres transmitting signals to the nucleus tractus solitarius → Modulation of brain regions: amygdala, hypothalamus, and cortex

- **Neurochemical Effects:**
  - Increased release of neurotransmitters: serotonin, norepinephrine, and GABA
- **Anti-inflammatory Actions:**
  - Activation of the cholinergic anti-inflammatory pathway
  - Reduction of pro-inflammatory cytokines



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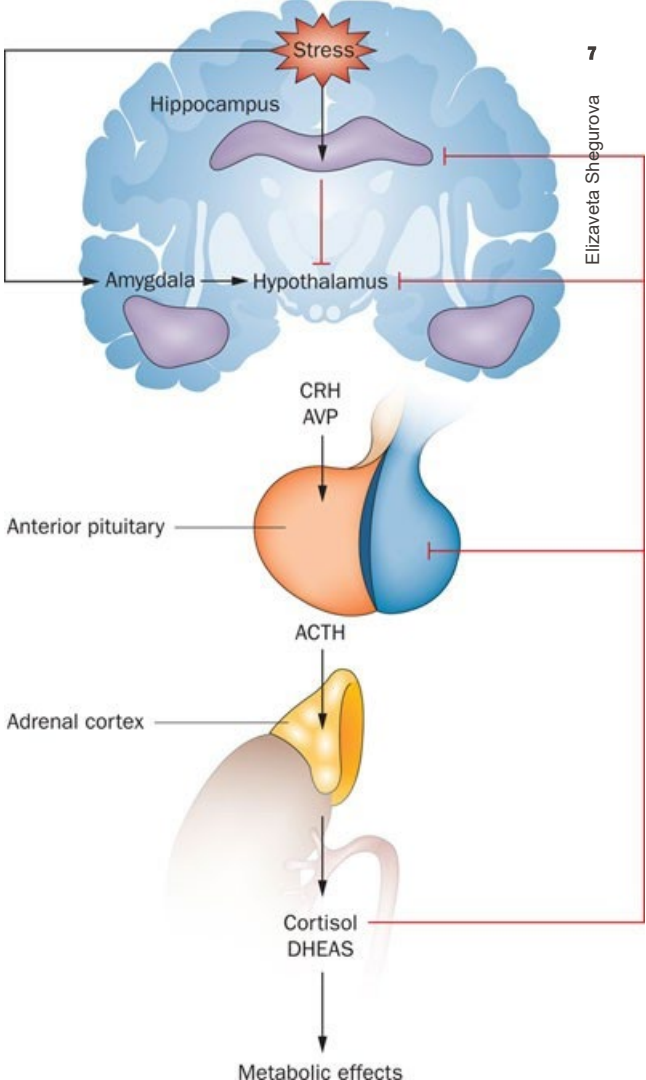
Refractory Epilepsy

- Seizures persisting despite treatment
- Affects ~30% of epilepsy patients.
- **Causes:**
  - Structural brain abnormalities
  - Genetic predispositions
  - Infections
- **Consequences:**
  - Increased risk of injury, cognitive decline, and sudden unexpected death
  - Social and psychological challenges due to uncontrolled seizures
- **VNS:**
  - Modulates brain regions involved in seizure generation (thalamus and cortex)
  - Reduces seizure frequency by ≥50% in half of treated patients
  - Enhances quality of life

Treatment-Resistant Depression

- Major depressive disorder that does not respond to treatment
- Affects ~10-20% of individuals with depression
- **Symptoms:**
  - Persistent sadness, anhedonia (loss of pleasure), fatigue, concentration difficulties, and suicidal ideation
- **Pathophysiology:**
  - Dysregulated neurotransmitter systems (e.g., serotonin, norepinephrine)
  - Impaired neuroplasticity and hypothalamic-pituitary-adrenal (HPA) axis dysfunction
- **VNS :**
  - Improves neurotransmitter activity and neuroplasticity.
  - Sustains remission in ~27-30% of patients over long-term follow-up
  - Often combined with standard treatments like antidepressants or psychotherapy



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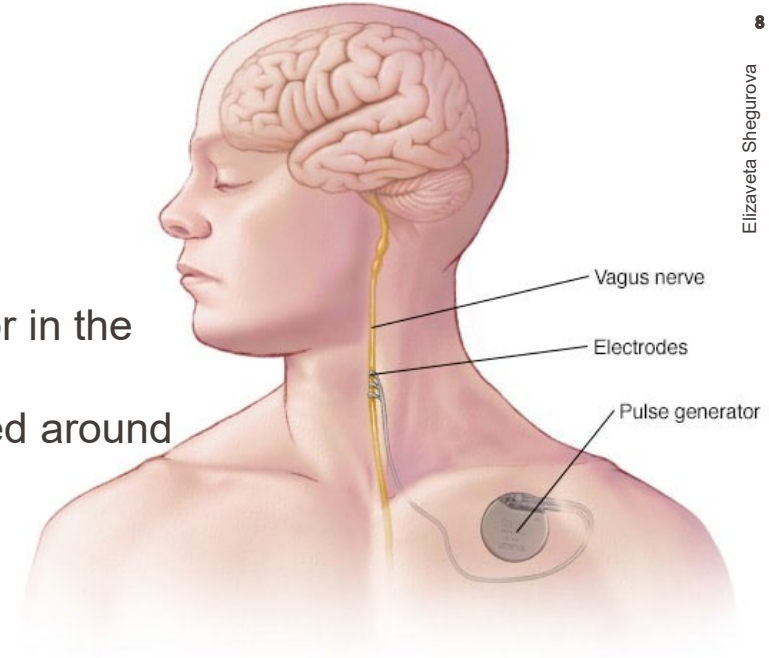
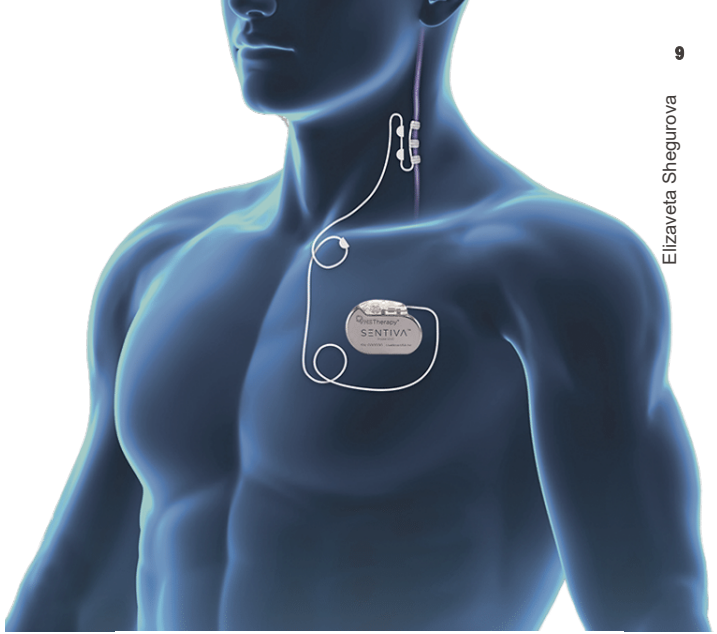
Left Cervical Vagus Nerve Stimulation

- **Procedure:**
  - Surgical implantation of a pulse generator in the left chest
  - Lead wires connect to electrodes wrapped around the left cervical vagus nerve.
- **Advantages:**
  - Minimised cardiac side effects
- **Clinical Applications:**
  - Approved for refractory epilepsy and treatment-resistant depression
  - Emerging evidence for use in chronic heart failure and inflammatory diseases.



LivaNova

- **Device:**
  - **Pulse Generator:** Surgically implanted battery-operated device placed subcutaneously in the left chest wall
  - **Lead Wires:** Connect the generator to electrodes wrapped around the left cervical vagus nerve.
  - **Programmer:** A handheld device used by clinicians to adjust stimulation parameters.
- **Stimulation Parameters:**
  - Frequency: 20-30 Hz.
  - Pulse Width: 250-500 microseconds.
  - Current Intensity: Adjustable from 0.25 to 3.5 mA.
  - Duty Cycle: Customizable on/off periods.
- **FDA-Approved Indications:**
  - Refractory epilepsy (1997).
  - Treatment-resistant depression (2005).
- **Efficacy:**
  - Long-term seizure reduction in 40-50% of patients with epilepsy.
  - Sustained symptom improvement in depression over 5 years.



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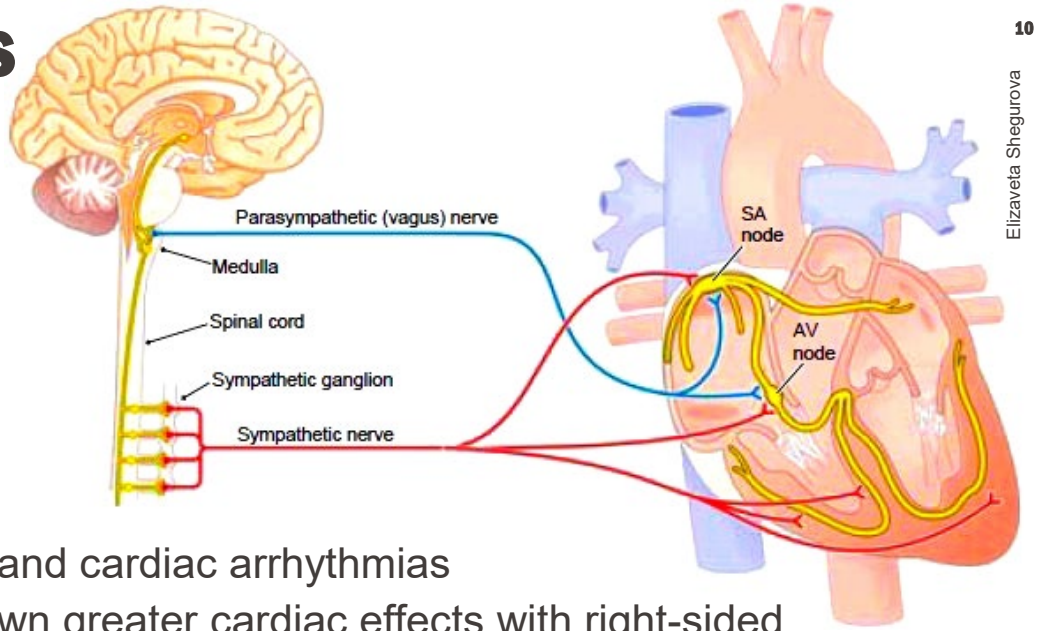
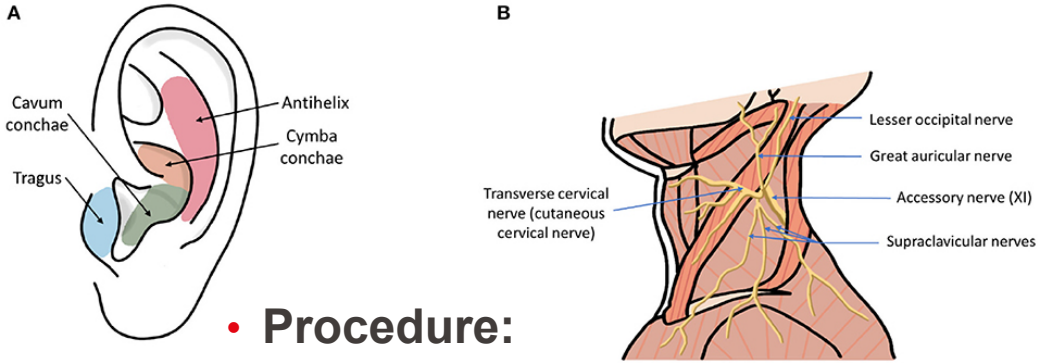
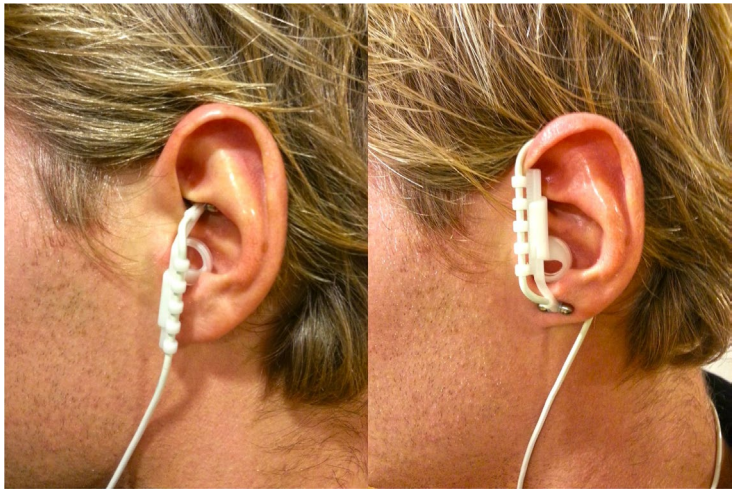
Right Cervical Vagus Nerve Stimulation



- **Considerations:**
  - Can induce bradycardia and cardiac arrhythmias
  - Animal studies have shown greater cardiac effects with right-sided stimulation
- **Clinical Applications:**
  - Generally avoided due to potential cardiac risks
  - Some investigational uses in controlled settings

Transcutaneous Vagus Nerve Stimulation





- **Procedure:**
  - Non-invasive stimulation through skin
  - Targets auricular branch (ear) or cervical branch (neck) of the vagus nerve
- **Advantages:**
  - Non-invasive, avoiding surgical risks
  - Accessible for a broader range of patients
- **Limitations:**
  - Lower efficacy compared to implantable VNS for severe cases.
  - Inconsistent stimulation parameters and protocols across studies.

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gammaCore

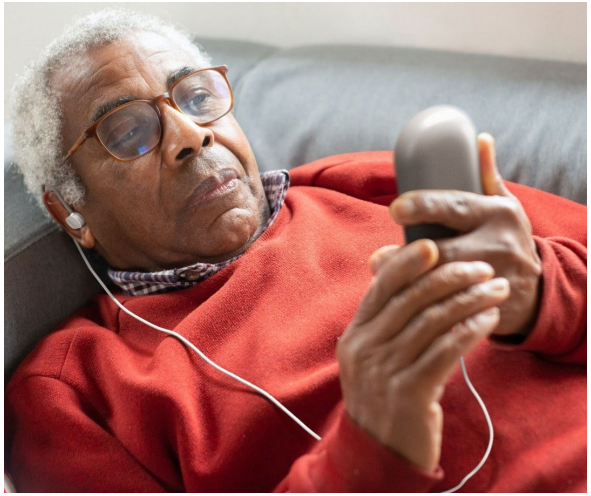
$295

- Portable, handheld device designed for non-invasive vagus nerve stimulation.
- Composed of two flat stimulation surfaces that deliver electrical pulses
- FDA-approved for acute and preventive treatment of cluster headaches and migraines.
- Targets the vagus nerve in the neck region

Nurosym

$750

- Wearable device delivering transcutaneous auricular vagus nerve stimulation
- Targets the tragus of the ear via a small electrode
- Treatment of anxiety, stress, inflammation, and mood disorders
- Adjustable intensity for patient comfort
- Sessions are typically conducted several times daily for cumulative effects



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Pulsetto

$269

- Wearable neckband device delivering bilateral transcutaneous vagus nerve stimulation
- Uses dual electrodes to stimulate both vagus nerves
- Treatment of stress, anxiety, and sleep disturbances
- App integration for personalised use

Neuvana's Xen

$449

- Earbud-based system for auricular vagus nerve stimulation
- Stimulates the cymba concha of the left ear
- Provides relaxation, stress relief, and overall wellness
- App integration
  - Synchronises stimulation with music for a calming experience

Safety and Side Effects

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- **Implantable VNS – Common Side Effects:**
  - Hoarseness, coughing, dyspnea, neck pain
- **Rare Complications:**
  - Wound infections, lead migrations, vocal cord paralysis
- **tVNS – Common Side Effects:**
  - Mild skin irritation, tingling, and discomfort
- **Rare Complications:**
  - None reported due to its non-invasive nature
- **Safety Measures:**
  - Patients with implantable devices should avoid full-body MRI and diathermy
  - Device programming can mitigate side effects by adjusting parameters.

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Clinical Efficacy

- **Epilepsy:**
  - 50% responder rate (≥50% seizure reduction) in drug-resistant cases
  - Paediatric efficacy demonstrated with good safety profiles
- **Depression:**
  - 30% remission rate in treatment-resistant depression (5-year studies)
  - Enhanced when combined with standard care or psychotropic medication
- **Emerging Conditions:**
  - **Rheumatoid Arthritis:**
    - Modulates TNF-alpha levels, reducing joint inflammation
  - **Alzheimer's Disease:**
    - Early trials show improved memory and reduced beta-amyloid plaques

Future Directions

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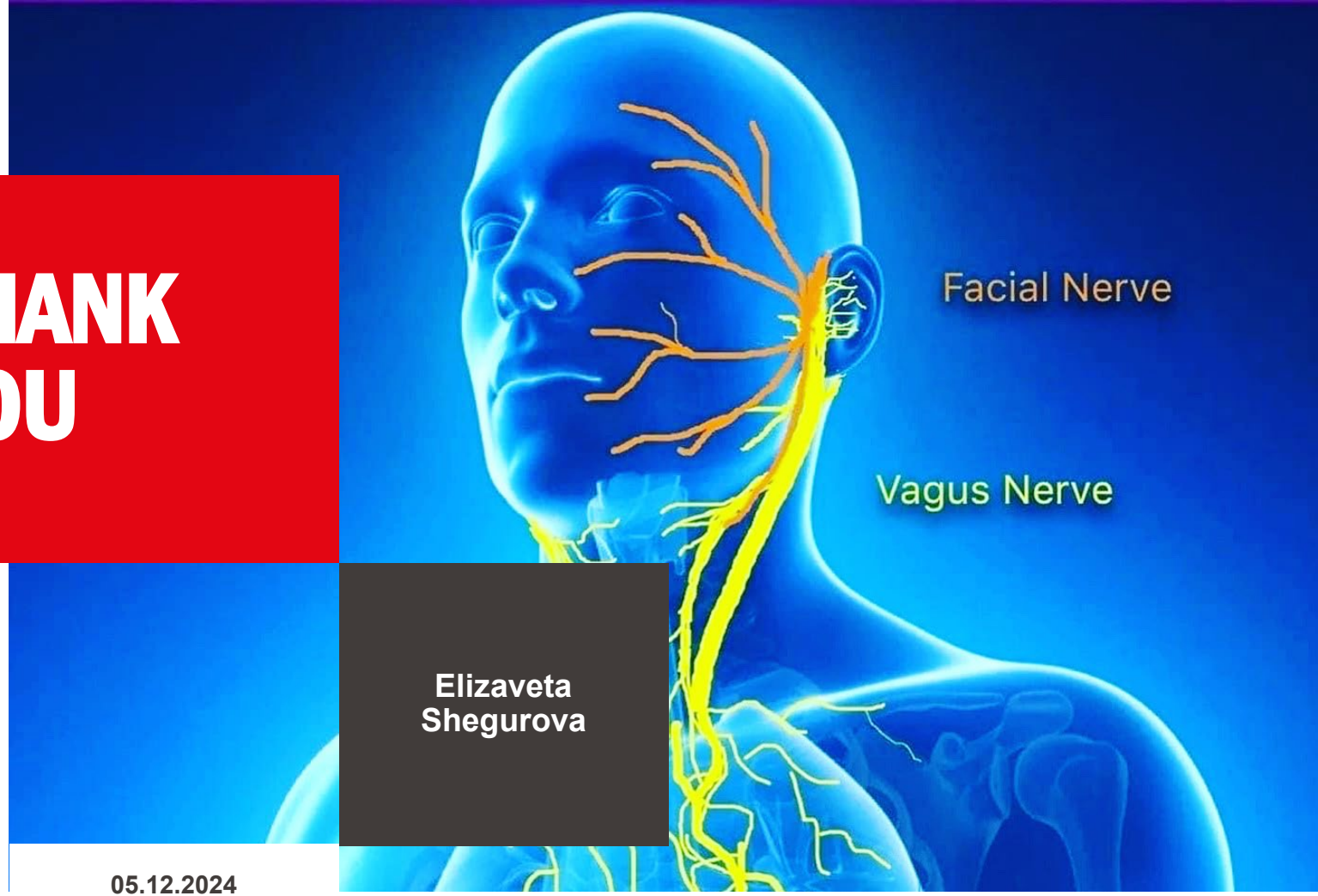
- **Closed-Loop Systems:**
  - Real-time monitoring and adjustment of stimulation parameters
- **Miniaturized Devices:**
  - Injectables for minimally invasive applications
- **Expanded Indications**
  - Stroke recovery: Promotes neuroplasticity and motor function improvement
  - Obesity management: Modulates appetite-regulating pathways
  - PTSD and anxiety disorders: Ongoing trials
- **Challenges:**
  - Addressing patient variability in response
  - Reducing costs and improving accessibility

THANK YOU



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