VAGUS NERVE STIMULATION

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La richiesta di competenza neurologica nel prossimo futuro
Sesta edizione
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OUTLINE

1. Anatomy and physiology of vagus nerve: some basic concepts.

2. Vagus nerve stimulation: technical considerations.

3. Vagus nerve stimulation: medical applications.

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Some basic concepts…

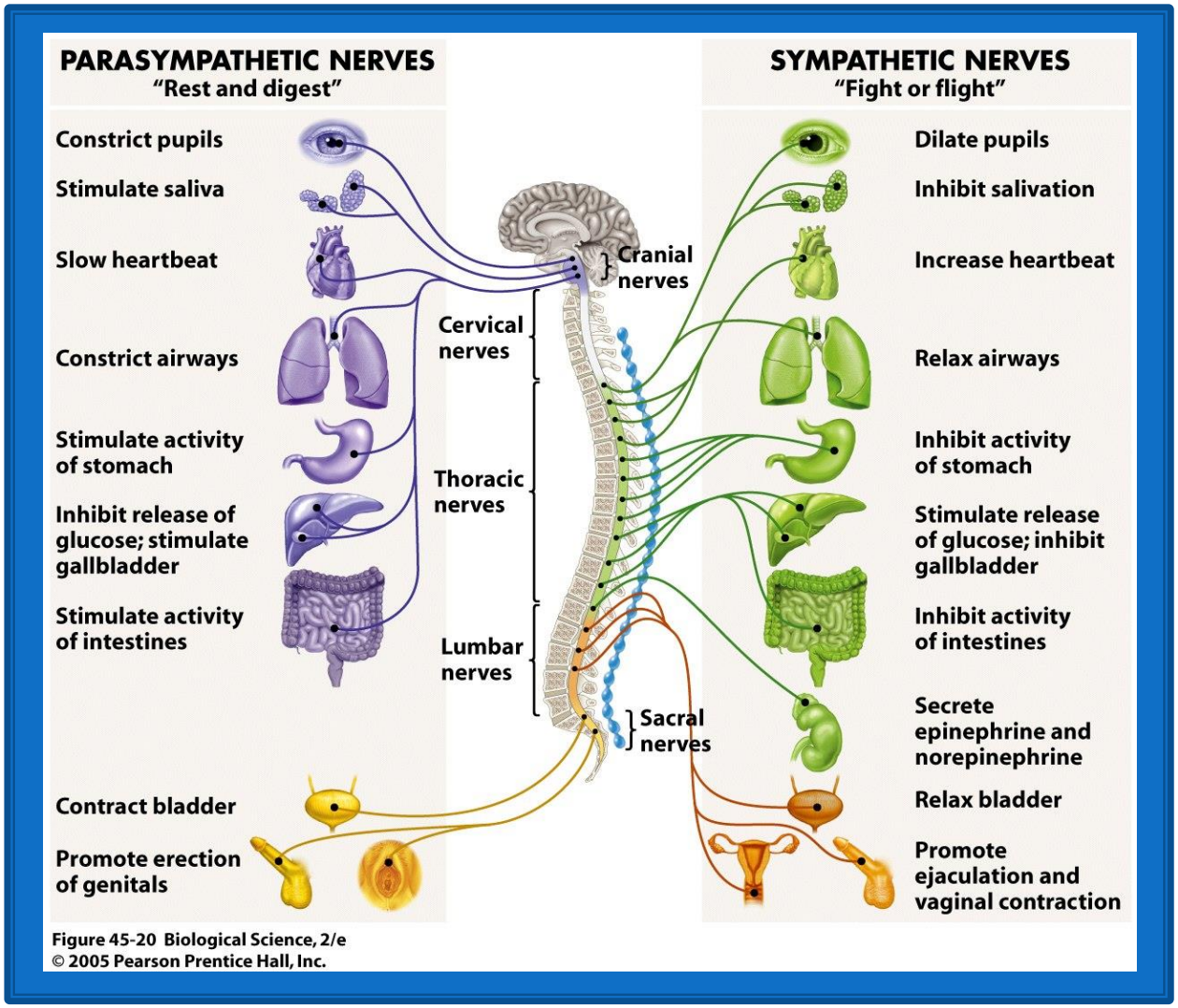
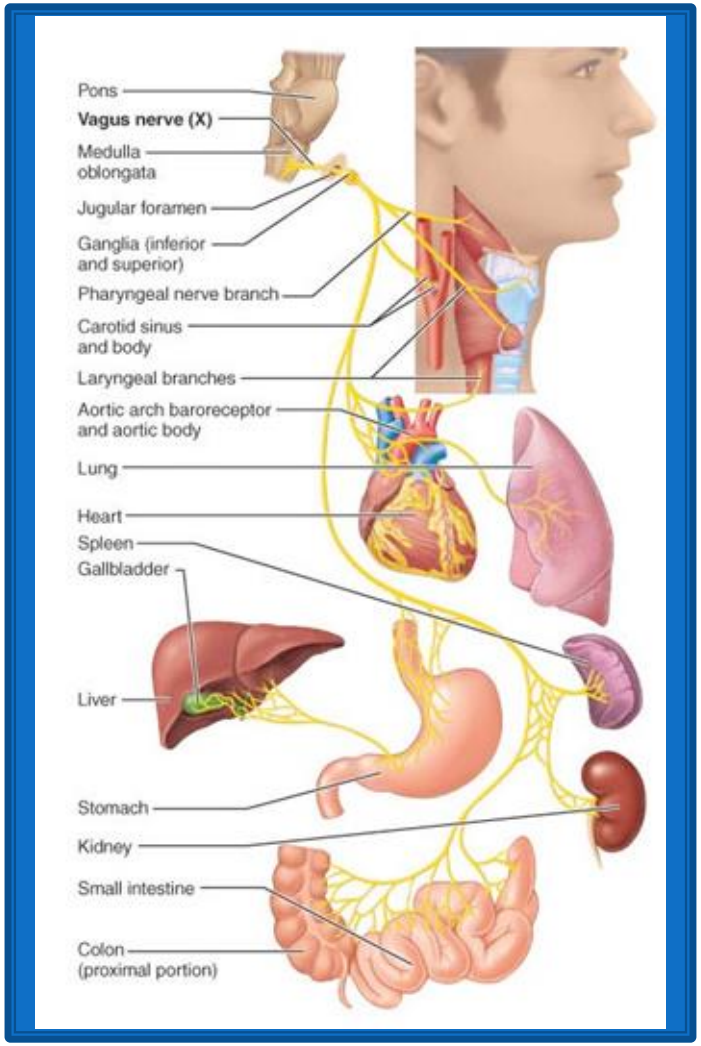


Figure 45-20 Biological Science, 2/e

Vagus Nerve



- It is the most important part of the parasympathetic system.

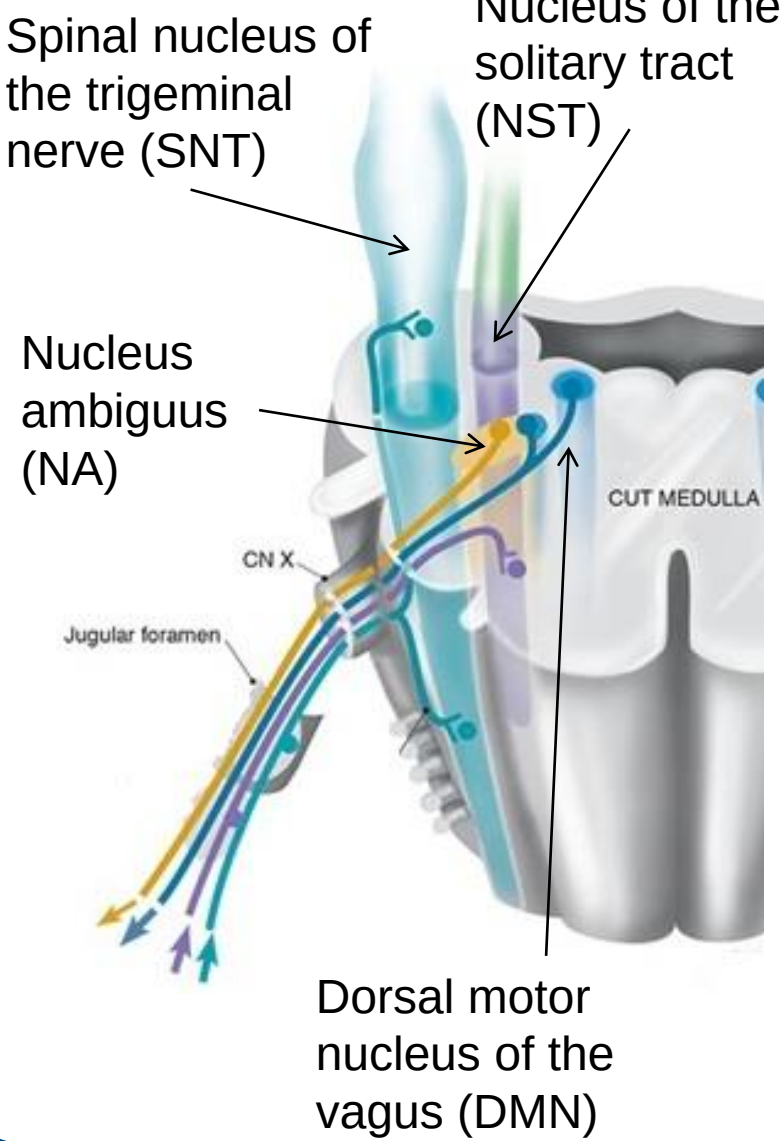
- It is the longest cranial nerve, travels from brainstem to the colon, innervating the thoracic and abdominal organs.

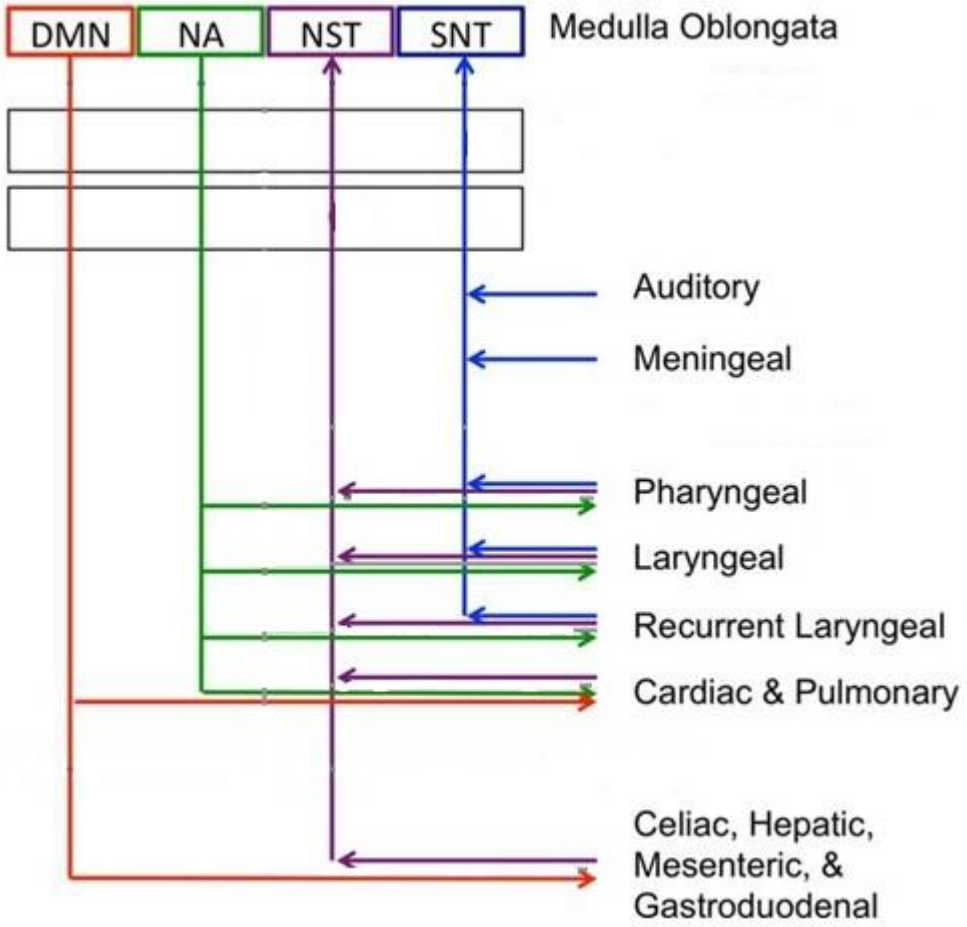
- *Vagus* from Latin (to *wander*) because it "wanders" into thorax and abdomen.

- It is a mixed sensory and motor nerve. Vagal afferents sense interoceptive stimuli while vagal efferents convey regulatory information to internal organs.

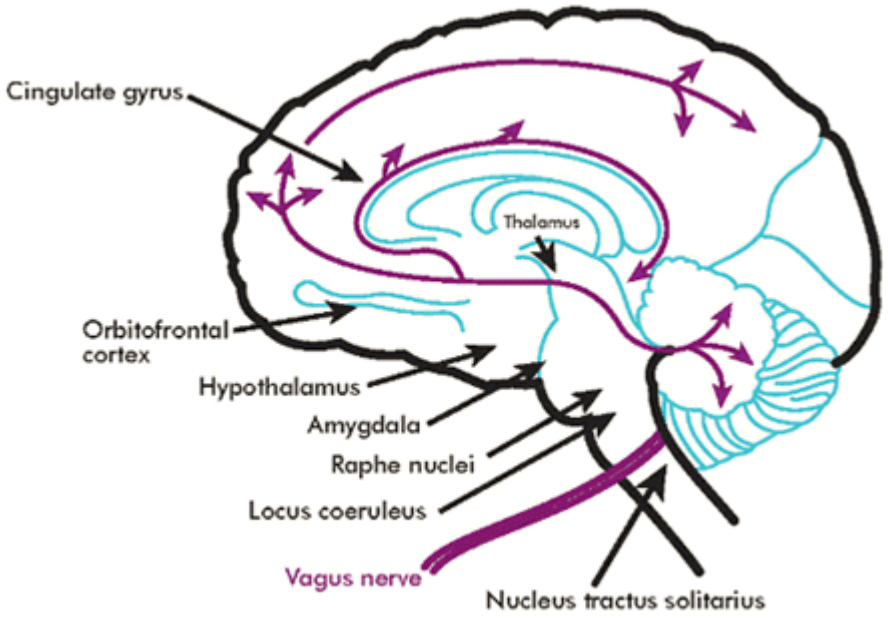
- Vagus nuclei and connections in CNS act as an "unconscious inner brain" that integrates "feelings" from the body and provides metabolic homeostatic regulation to various organs.

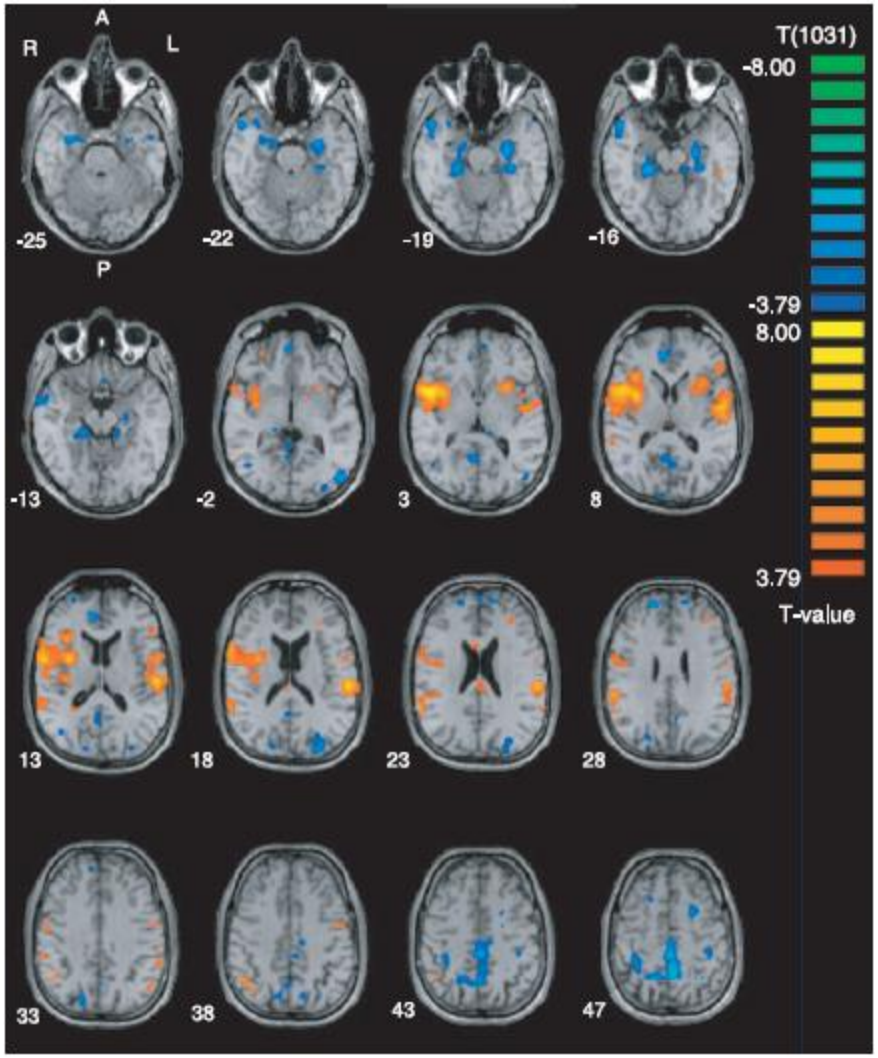
Vagus Nerve:
Nuclei





Vagus nerve: central pathway





Kraus et al. 2007

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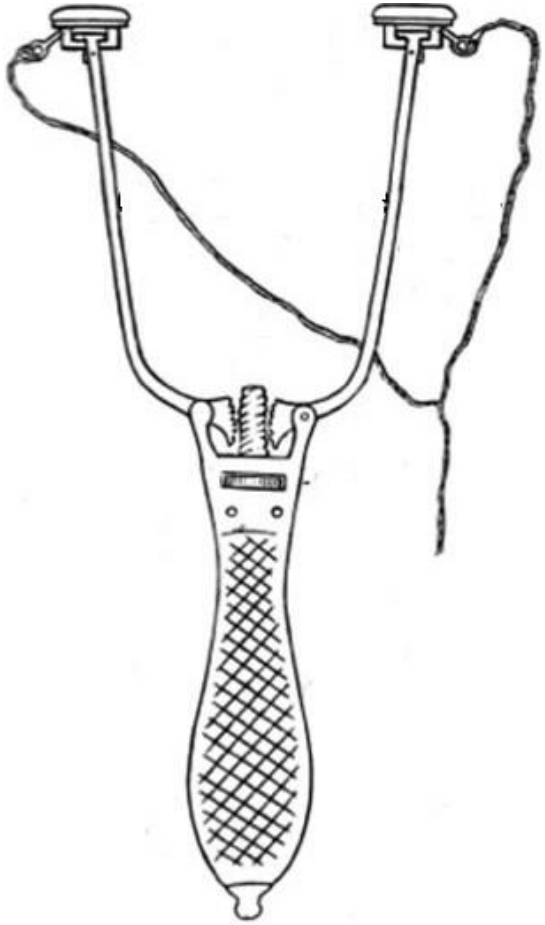
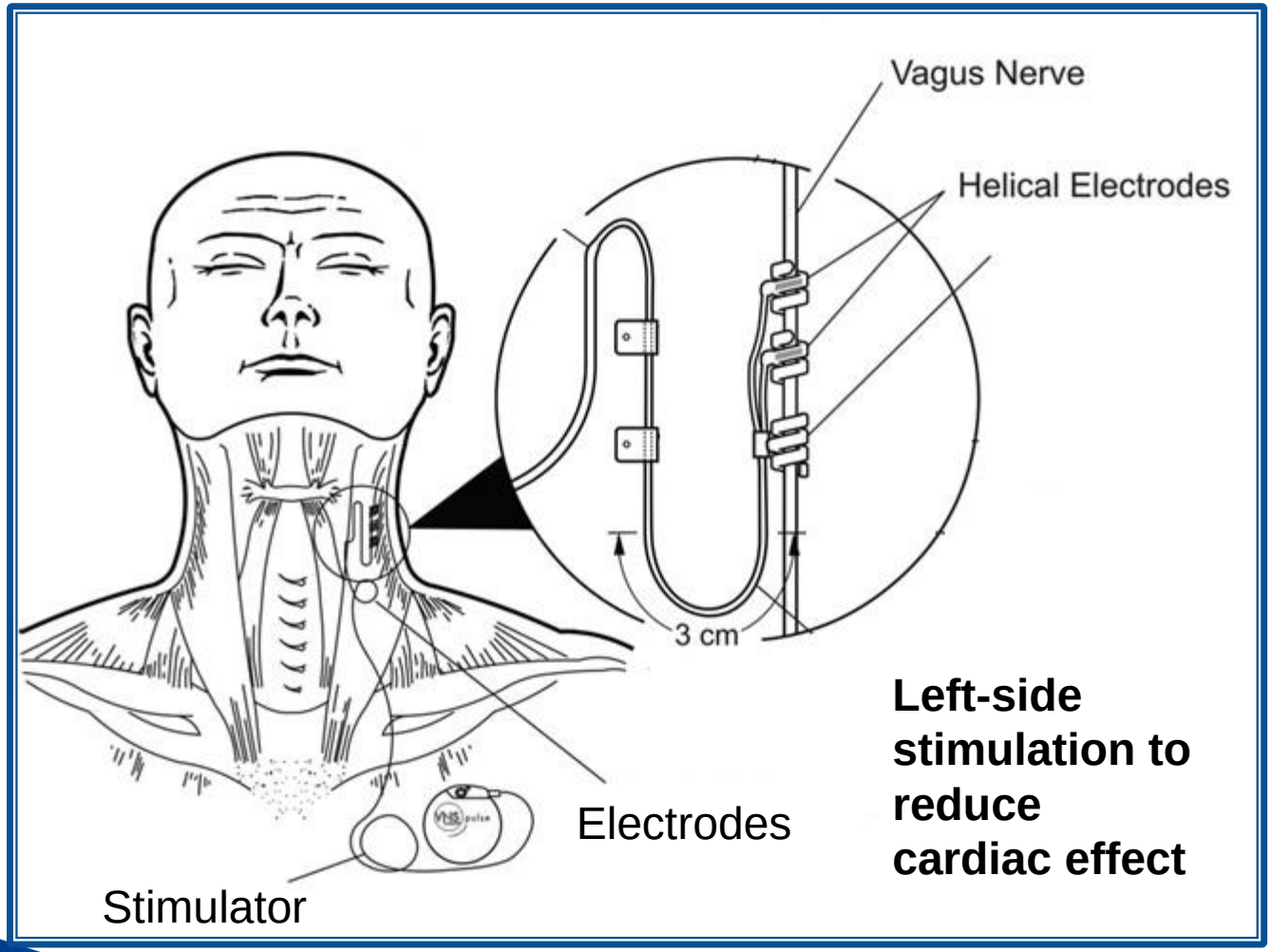
The origins of VNS



Corning JL. New York Med J 1884;39:212-215

Traditional VNS



Adverse effects

Surgery-related

- Incision pain
- Infection at the device

Stimulation-related

- Headache
- Sore throat
- Hoarseness
- Cough
- Shortness of breath
- Neck pain
- Difficulties in swallowing
- Sleep Apnea

These adverse events were generally mild and well tolerated, and most typically occurred when the generator was on.

Traditional VNS: innovations

Closed-loop technology

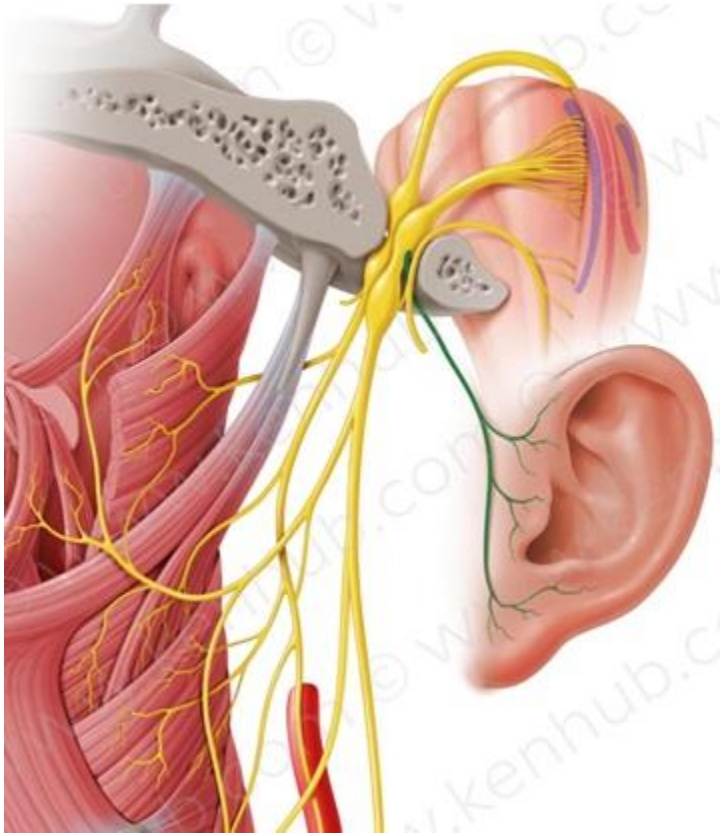
Unidirectional stimulation

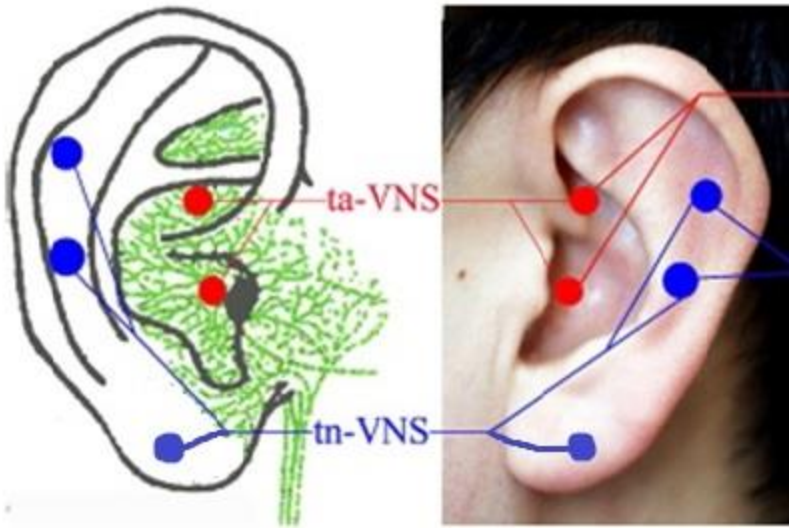
Non-invasive VNS

Transauricular VNS

Transcervical VNS

Transcutaneous VNS





Rong et al. 2012

- The ear is the only place on the surface of the human body where there is afferent vagus nerve distribution.

- Sham stimulation is possible if the electrodes are attached outside the area of vagal innervation (eg. ear lobe).

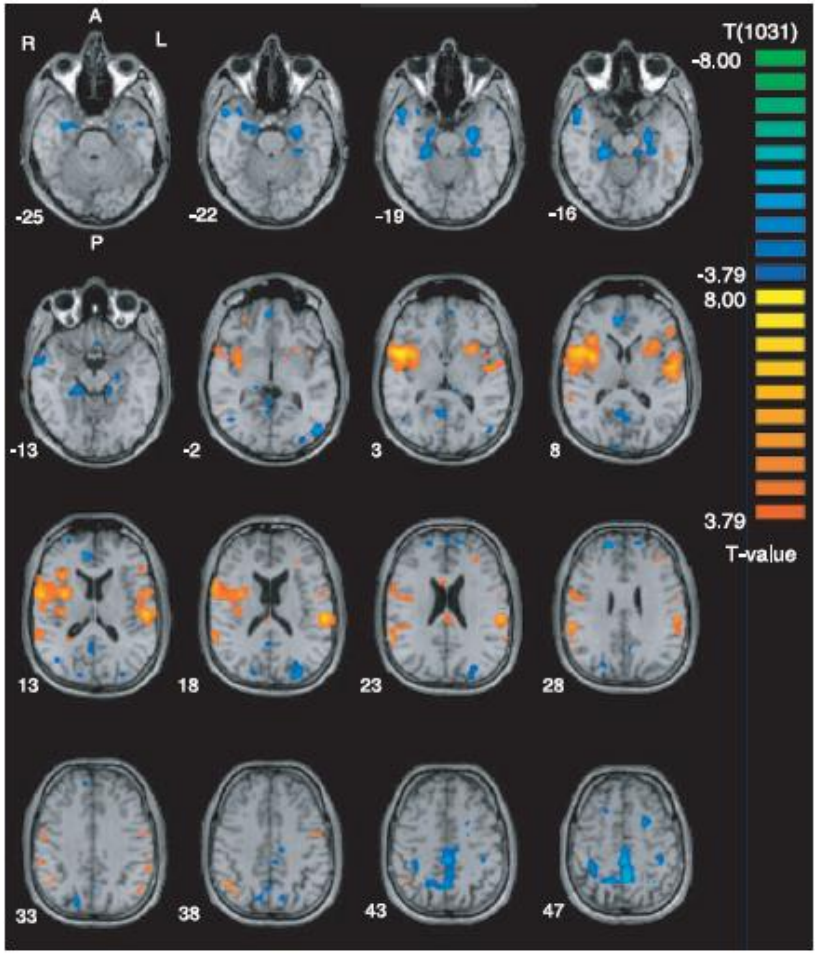
Transcutaneous VNS

The effects of transcutaneous VNS are similar to traditional, invasive VNS.

Neurophysiologic findings

Capone et al. 2014

Neuroimaging findings



Kraus et al. 2007

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Approved indications

- Epilepsy (drug-resistant)
- Depression (drug-resistant)
- Pain (migraine, cluster headache)

Potential applications for other disorders

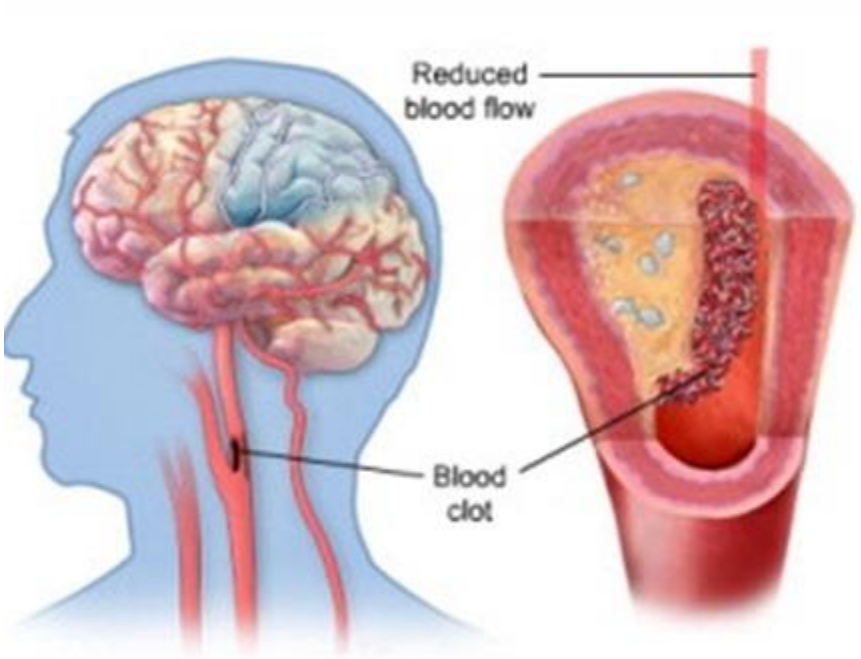
An incomplete list:

- Stroke (Baig et al. 2022)
- Cardiac failure (Carandina et al. 2021)
- Rheumatic diseases (Levine et al. 2014)
- Chronic pain (Chakravarthy et al. 2015)
- Obesity (de Lartigue 2016)
- Asthma(Steyn et al. 2013)
- Schizofrenia (Smucny et al. 2016)
- Posttraumatic stress disorder (Peña et al., 2012)
- Traumatic brain injury (Neren et al. 2016)
- Tinnitus (Engineer et al. 2011)

Ischemic Stroke

ACUTE: from minutes to hours

CHRONIC: from months to years



NEUROPROTECTION

NEUROPLASTICITY

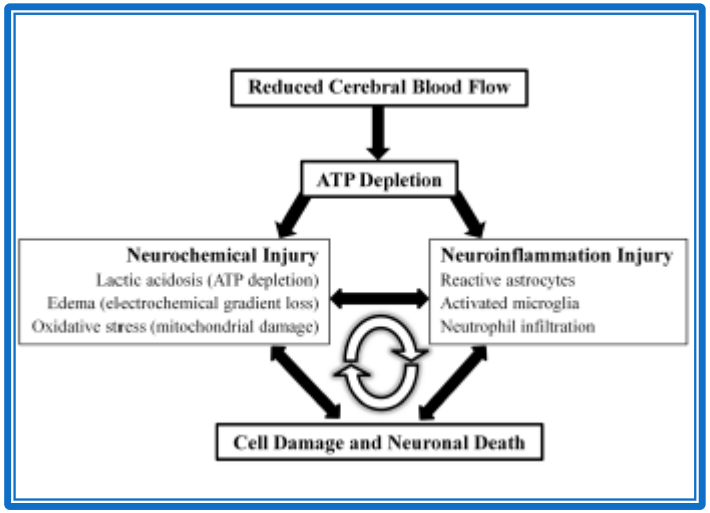
VNS

ACUTE ischemic stroke

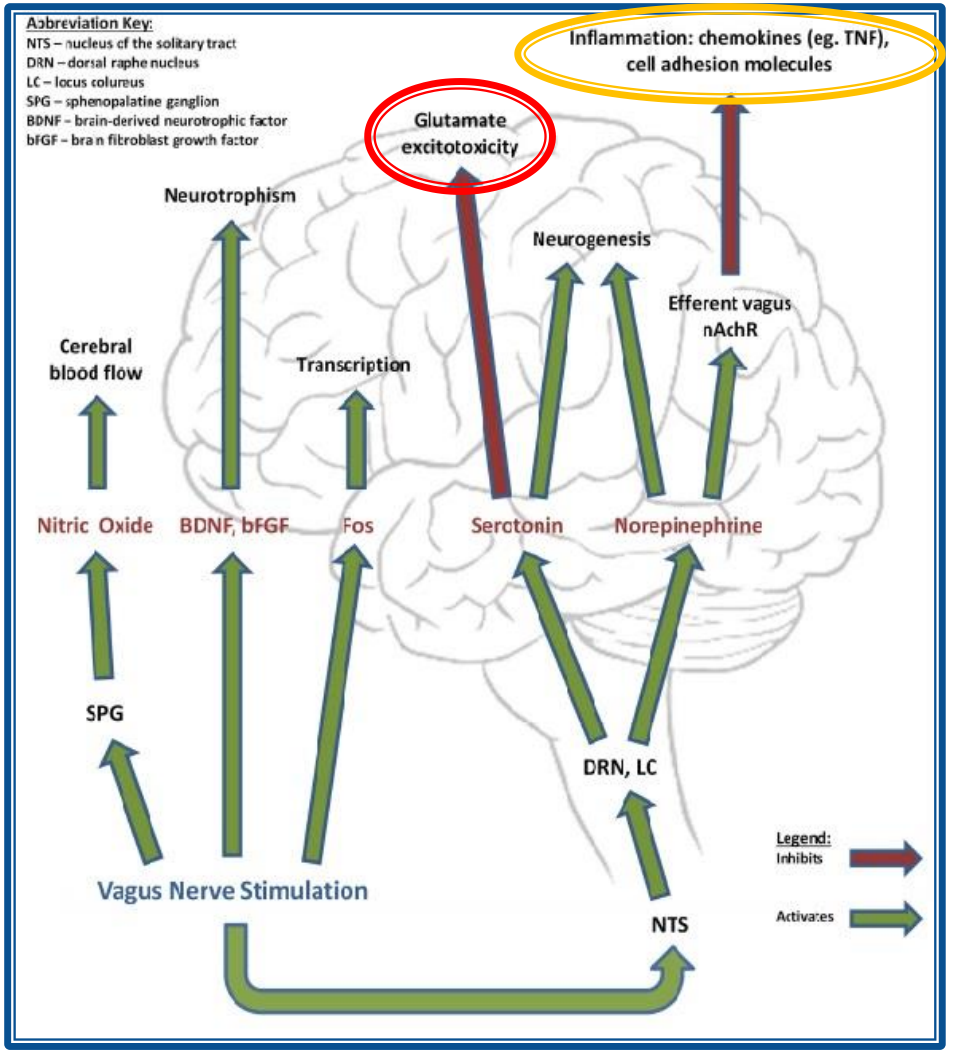
Experimental studies in animal models demonstrated that VNS:

- attenuated infarct size
- reduced neurological deficit

Cai et al. 2014



PATHOPHYSIOLOGY OF STROKE

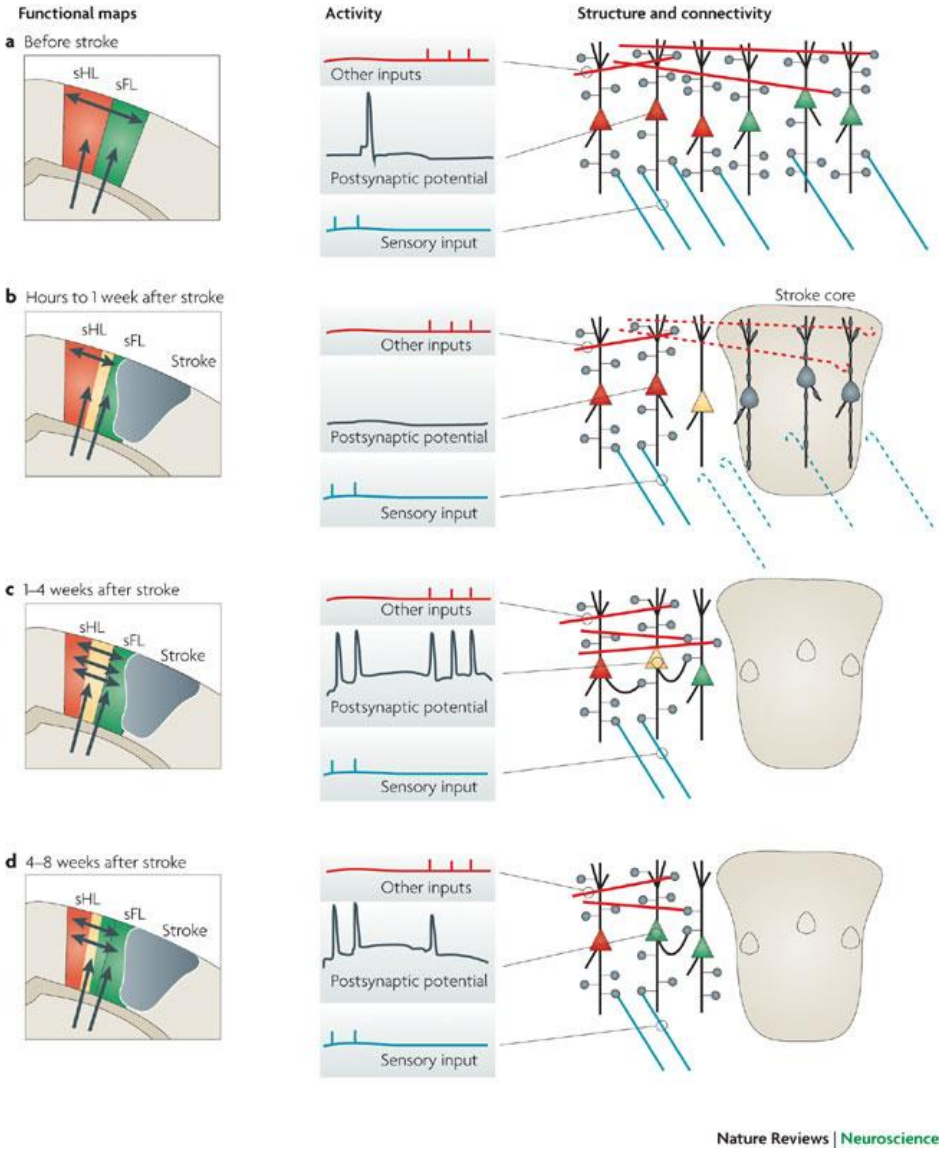


POSSIBLE MECHANISMS OF ACTION FOR VNS IN ACUTE STROKE

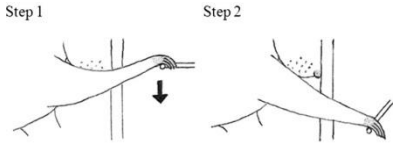
CHRONIC ischemic stroke

- After a stroke, reorganization of cortical motor representations occurs in the surrounding undamaged tissue and in the contralesional hemisphere.
- **Plasticity in these areas is believed to be the substrate for functional recovery.**
- Rehabilitative training leads to some functional gains, but in the majority of cases, the improvement is incomplete.

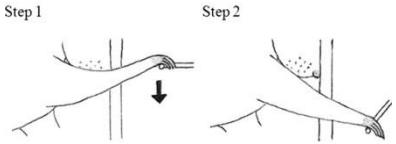
Hays, 2015



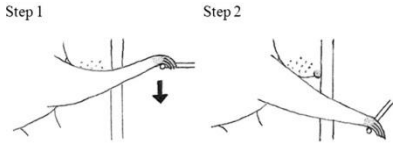
CHRONIC ischemic stroke



Motor Training

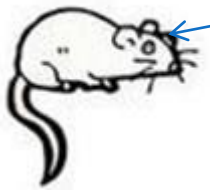


Motor Training
+ VNS

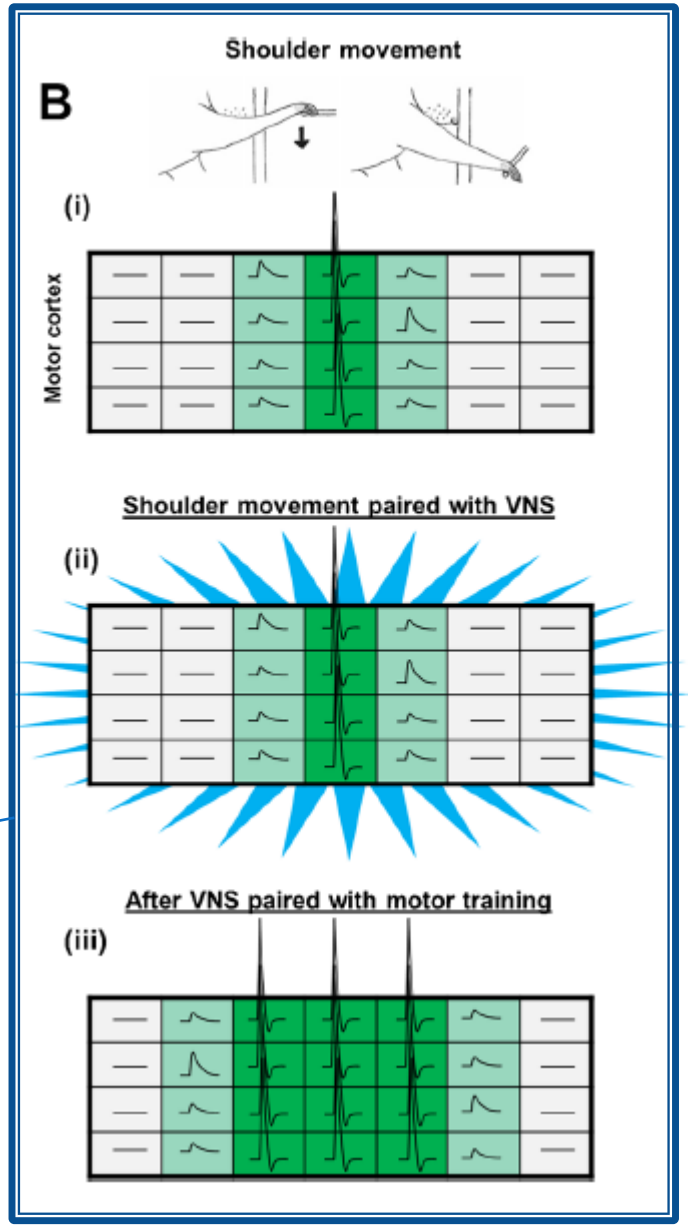


Motor Training
Alone

5 days

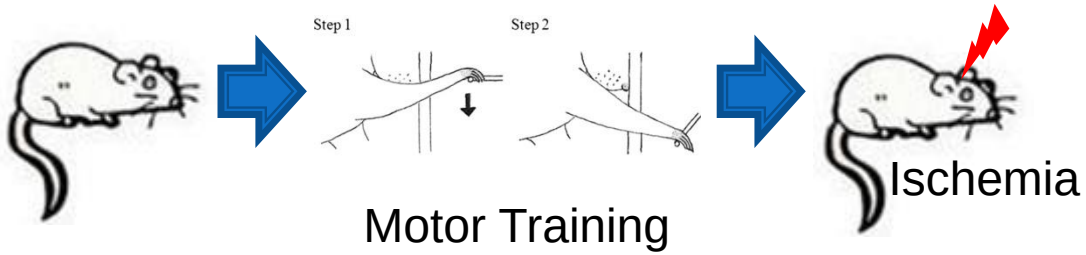


Cortical mapping



Porter et al. 2012

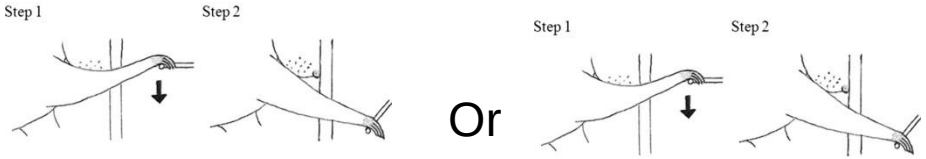
CHRONIC ischemic stroke



Motor Training

Ischemia

5 weeks



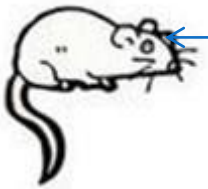
Or

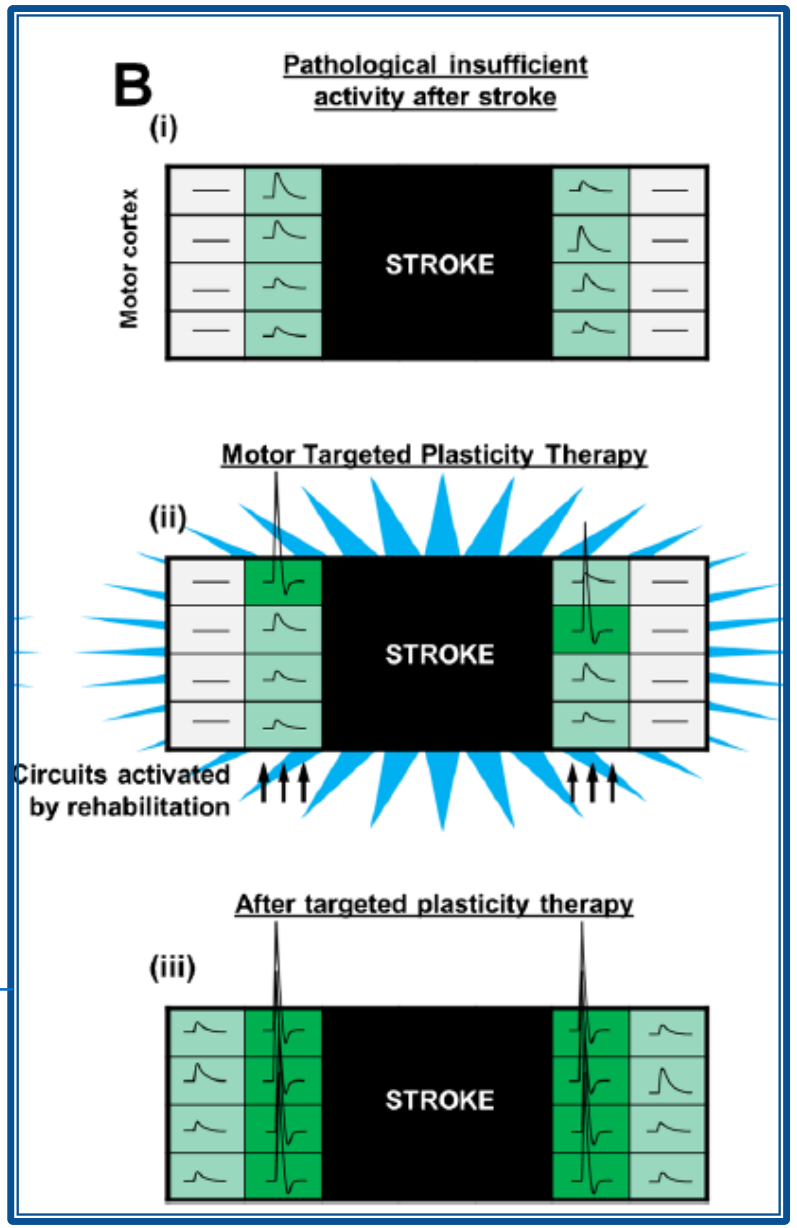
Rehabilitation + VNS

Rehabilitation Alone

Cortical mapping

Functional evaluation



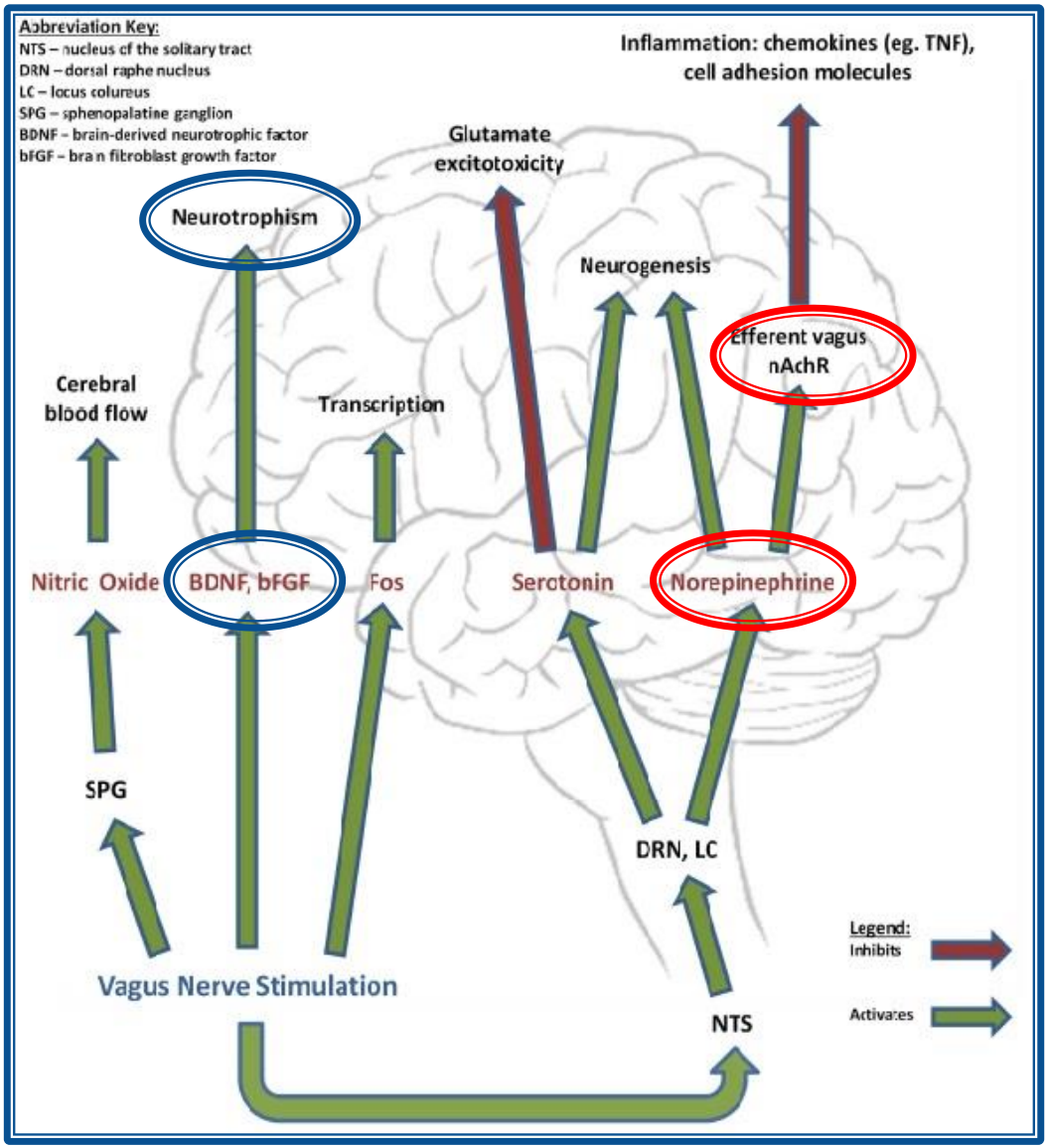


Khodaparast et al. 2014

CHRONIC ischemic stroke

POSSIBLE MECHANISMS OF ACTION FOR VNS IN CHRONIC STROKE:

…Targeting neuroplasticity!



Hays, 2015
Cai et al. 2014

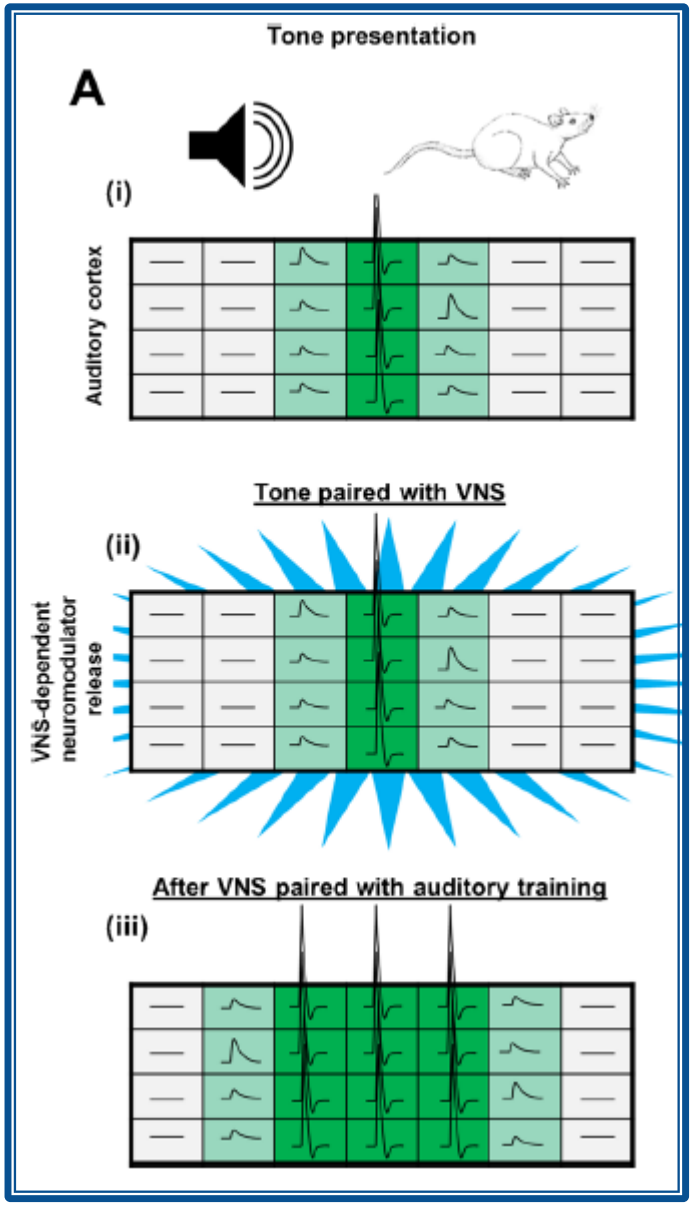
Tinnitus and auditory cortex

Tinnitus: *the perception of sound when no sound is present.*

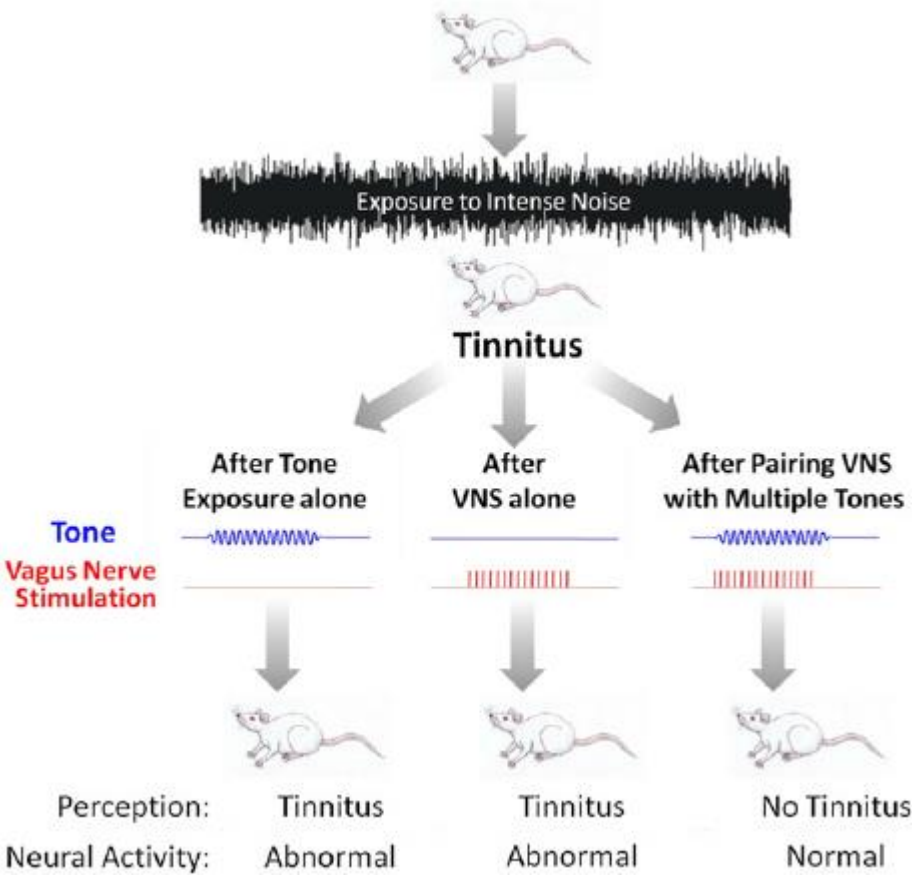
- It is a common disorder that can significantly reduce quality of life.
- Current treatments are largely ineffective.
- Maladaptive plasticity within auditory circuitry of the brain is at least, in part, responsible for chronic tinnitus

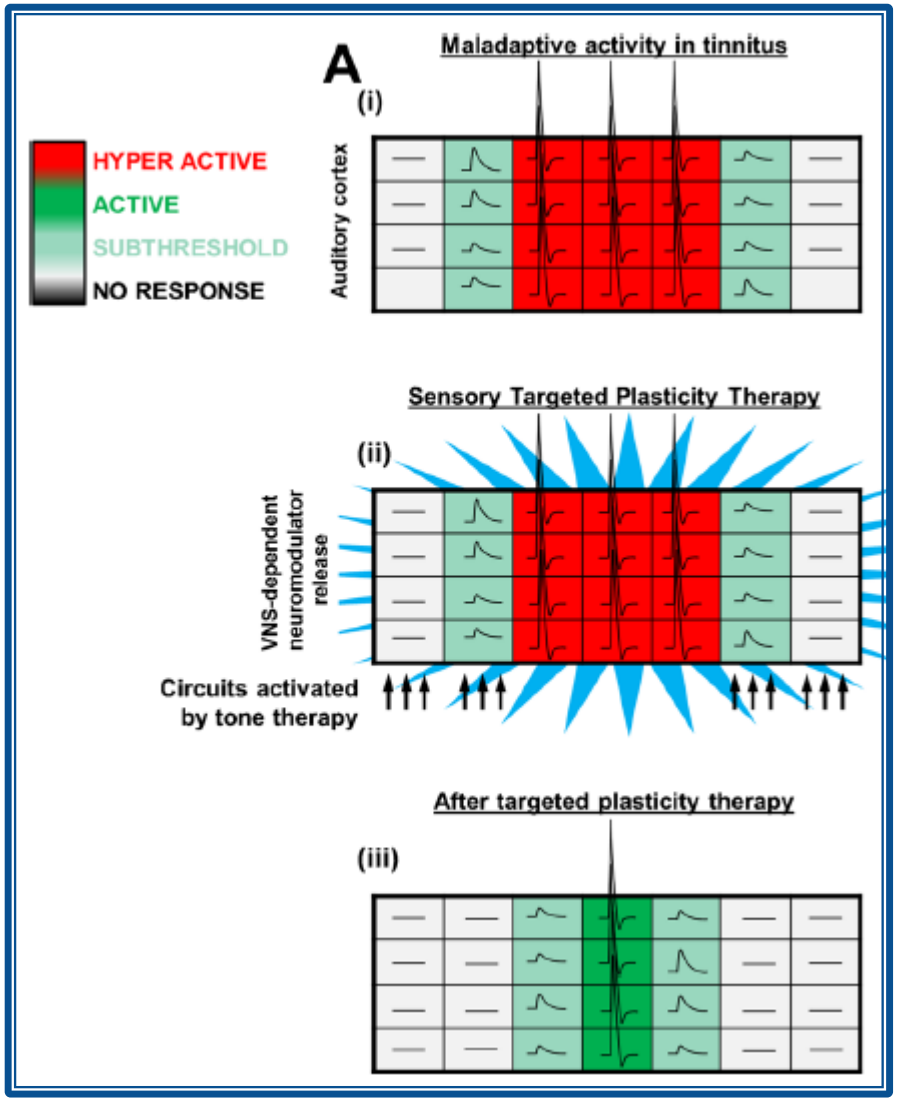
VNS paired with tones can drive specific **plasticity** to alter spectral and temporal response characteristics of central auditory neurons.

Engineer et al. 2011



Tinnitus and auditory cortex

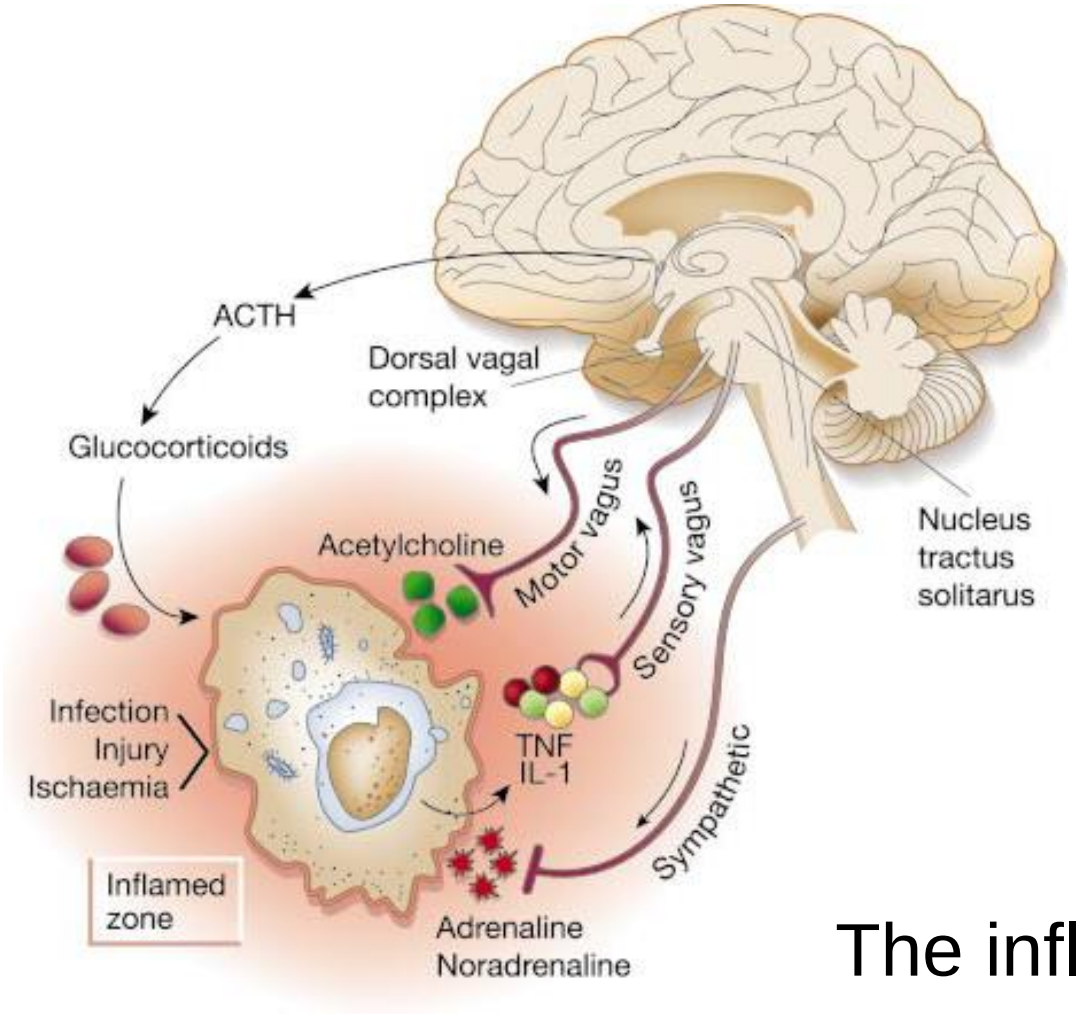




VNS paired with tones can reverse pathological plasticity and ameliorate chronic tinnitus

Engineer et al. 2011

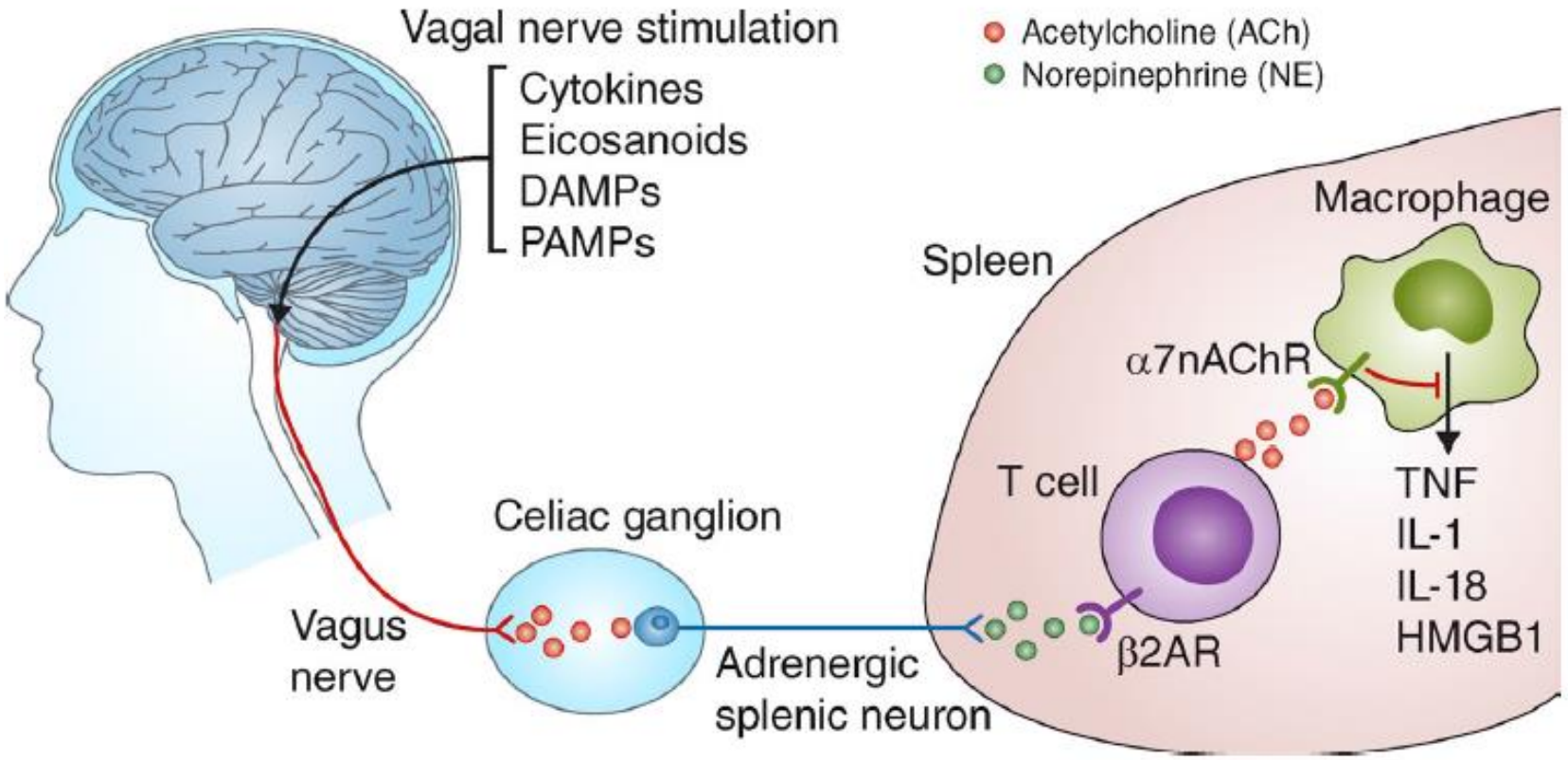
Immunity



The inflammatory reflex (Tracey 2002)

Immunity

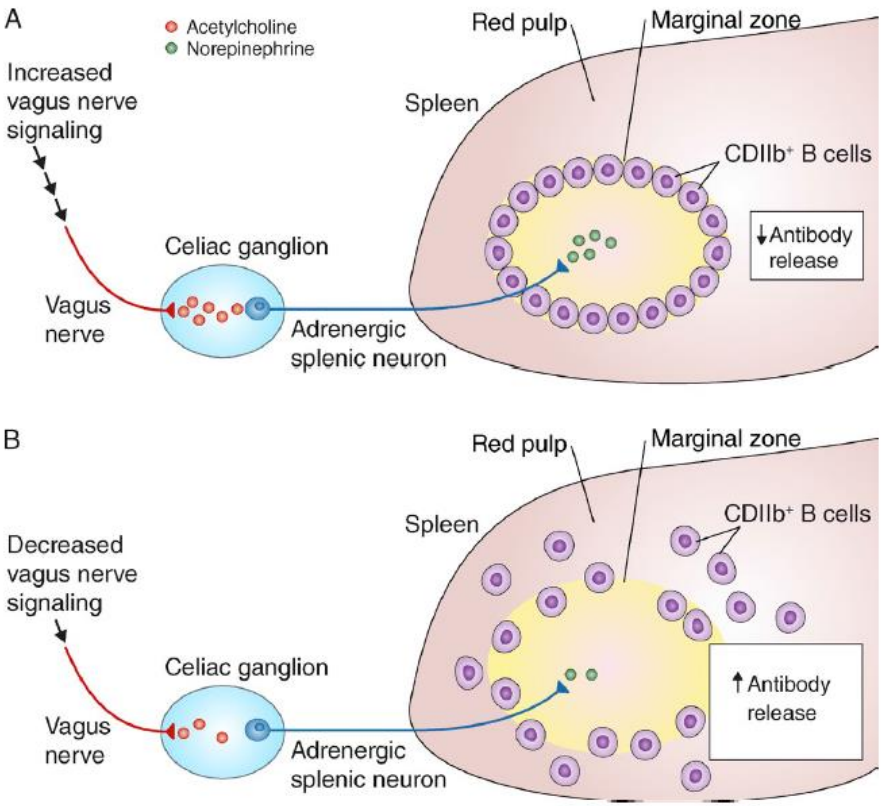
The cholinergic anti-inflammatory pathway



Andersson and Tracey 2012

Immunity

Neural influence on B cells trafficking and antibody secretion.

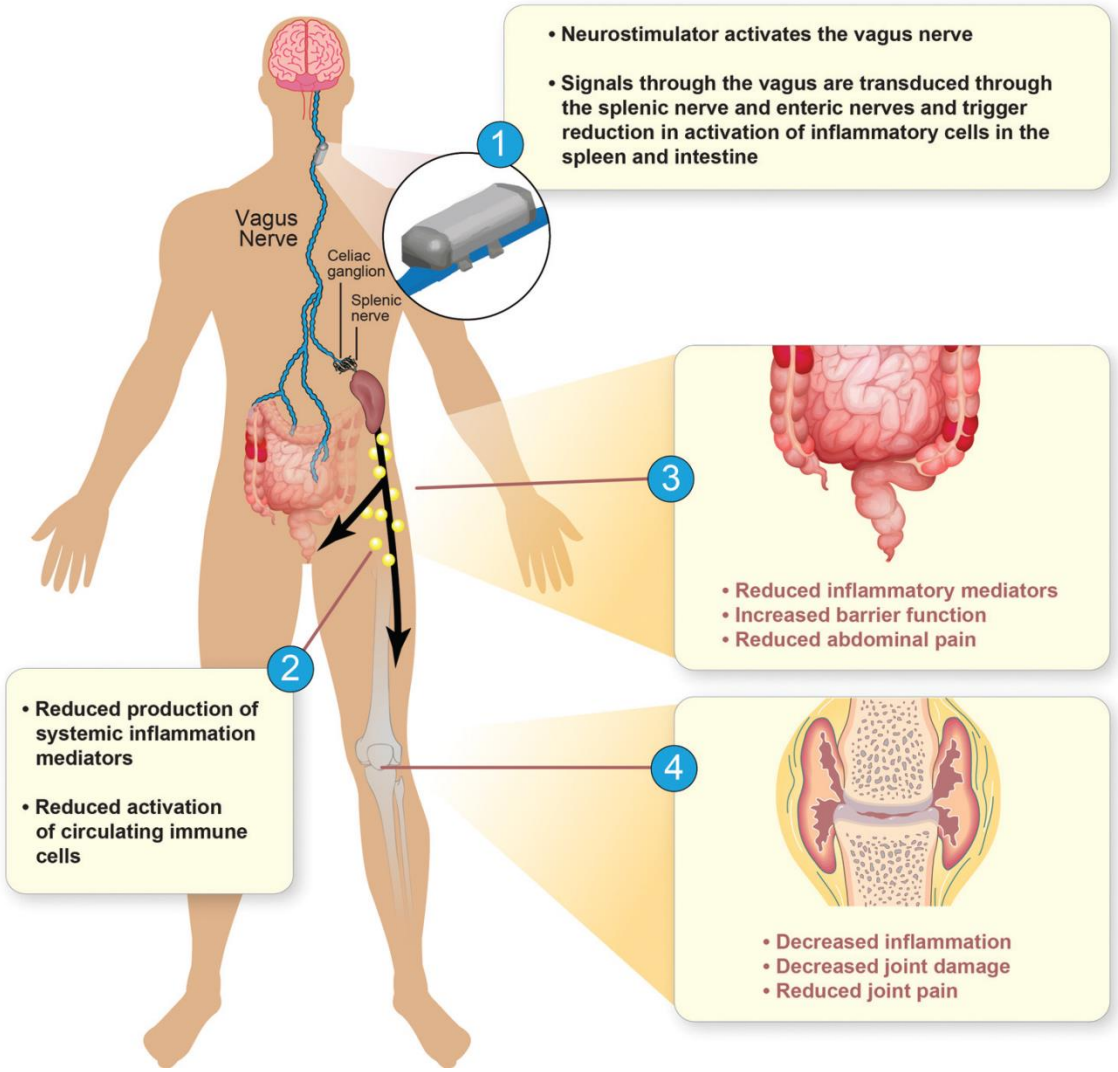


Andersson and Tracey
2012

Immunity

The anti-inflammatory properties of vagus nerve could be exploited to treat disease characterized by exagerate, pathological inflammation such as:

- Inflammatory bowel disease (IBD), comprising Crohn's disease and ulcerative colitis
- Rheumatoid arthritis (RA)



Levine et al. 2014

Challenges for Translating VNS Therapies into Clinical Practice

- Better delineation of mechanism of action.
- Defining factors that limit/influence effectiveness of VNS (Age? Sex? Genetics? Comorbidities? Drugs?).
- Optimizing VNS Parameters (intensity, frequency, duration, protocols).
- Development and validation of non-invasive tools for VNS.
- Designing large randomized trials to demonstrate efficacy of VNS in different diseases