NIHDDK Workshop on
Stimulating Peripheral Activity to Relieve Conditions

Overview on the Autonomic Nervous System

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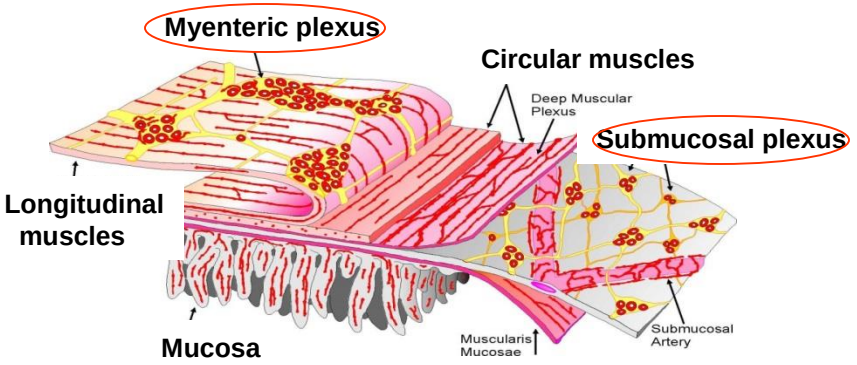
THE ANS

- The term “autonomic nervous system” was proposed by Langley in 1898 to describe:

  “The sympathetic system and the allied nervous system of the cranial and sacral nerves and the local nervous system of the gut”.
- The ANS encompasses
  - Sympathetic division
  - Parasympathetic division
  - Associated visceral afferent neurons
  - Enteric division (the largest 200-600 million neurons)



The integrative action of the ANS

- Almost all bodily functions are under the control of the ANS which adjusts the activities of organs or tissues **not under overt voluntary control.**

- For instance tension receptors in the carotid sinus and mechanoreceptors in all hollow organs conveyed information by the autonomic visceral afferent neurons which direct the activity of autonomic efferent pathways, either in the same organ or other organs.

- However, there has been much debate about whether to classify some neurons that carry afferent information to the CNS as autonomic, because many visceral afferent neurons communicate other information, for example pain from the viscera, satiety from the digestive tract or temperature.

Wilfrid Jänig: The integrative action of the autonomic nervous system: neurobiology of homeostasis. Cambridge press pp1-610 (2006)

Major functions under autonomic control

- **Heart rate, force and conduction**
- **Arterial diameter (all vascular beds)**
- **Mesenteric venous capacity**
- **Pupillary diameter, accommodation of lens.**
- **Exocrine gland secretion, including lacrimal, salivary, gastric, exocrine pancreatic, sweat glands, glands of genital organs**
- **Endocrine glands, including endocrine pancreas, adrenal gland and liver**
- **Secretion into organs: intestinal water and electrolyte secretion, pulmonary and nasal secretion.**
- **Gastrointestinal wall movement**
- **Gall bladder contraction and biliary tract motility**
- **Regulation of the urinary bladder and control of micturition**
- **Tracheal and bronchial diameter**
- **Contraction of vas deferens, vagina and other internal genitalia**
- **Mobilization of energy stores, for example from fat deposits and liver.**
- **Piloerection**
- **Modulation of immune function**

Anatomical Differences in Sympathetic and Parasympathetic Divisions

Come from different regions of the CNS

- **Sympathetic**—from the **thoracolumbar** region
- **Parasympathetic**—from the **craniosacral** region

Differing locations of ganglia

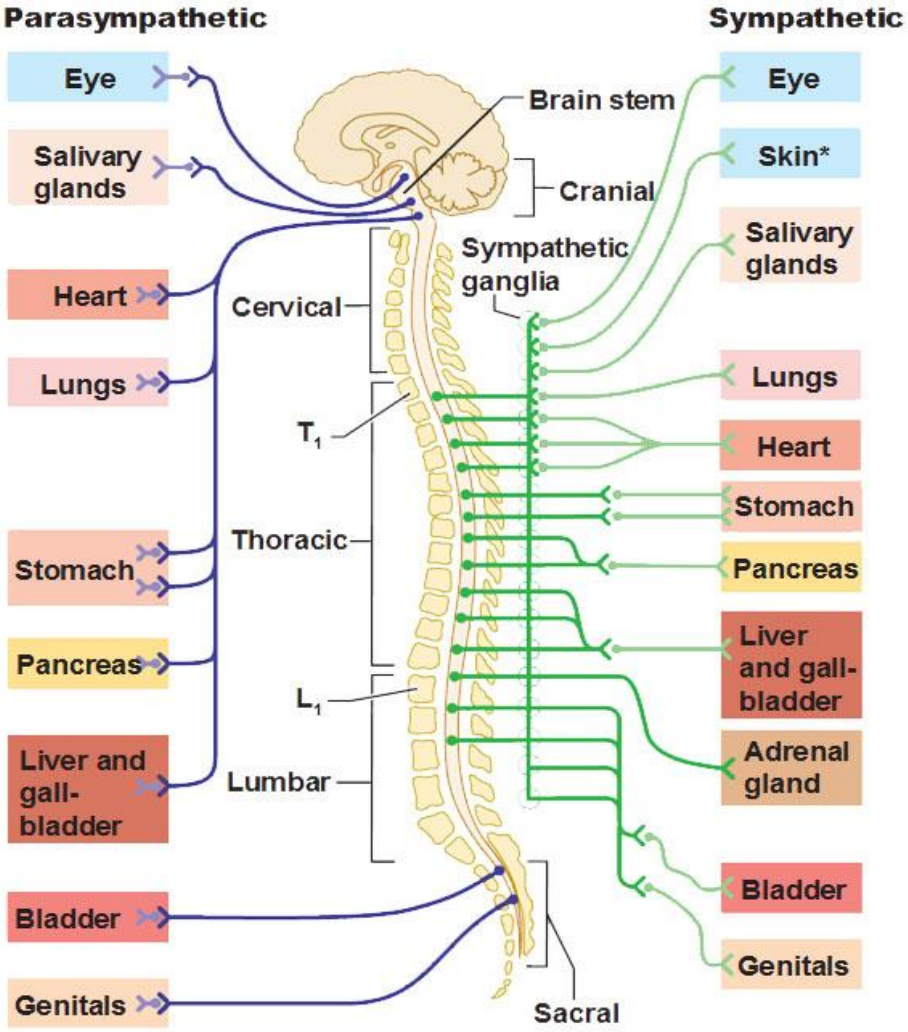
- Sympathetic – close to spinal cord in a chain
- Parasympathetic – close to target organs

Differing lengths of *postganglionic* fibers

- Sympathetic – Long
- Parasympathetic – Short

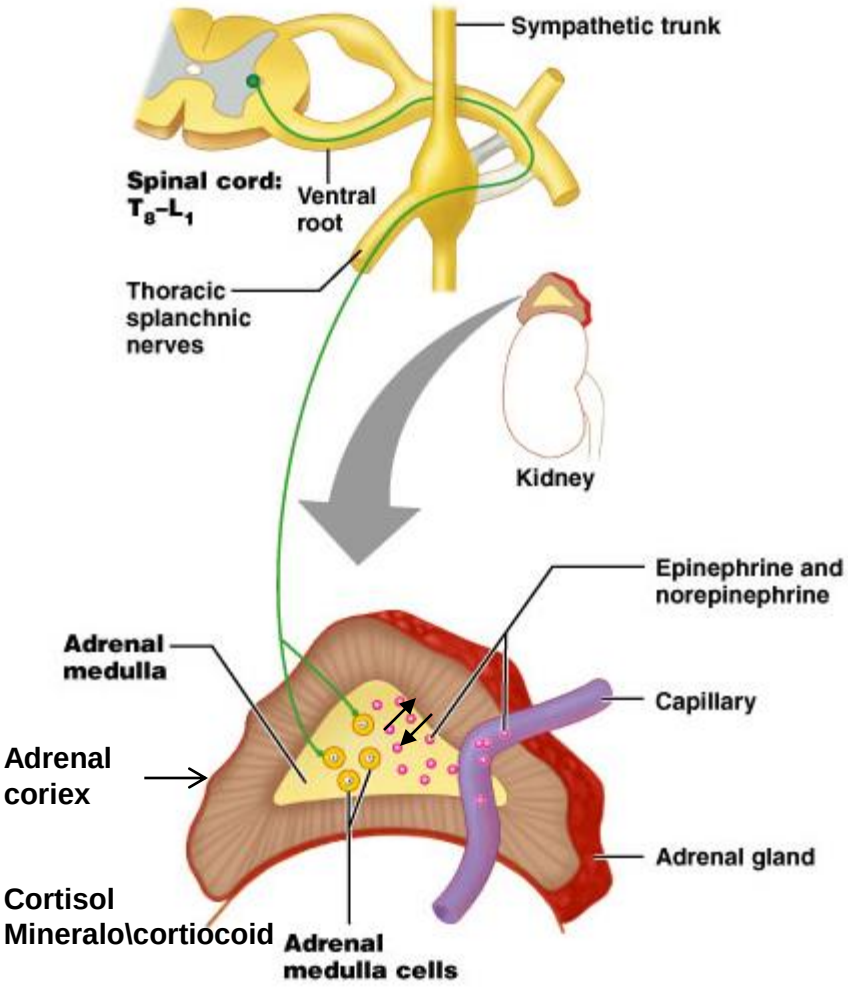
Postganglionic branching

- Sympathetic – lots, so that multiple organs can be mobilized at once
- Parasympathetic – very little branching



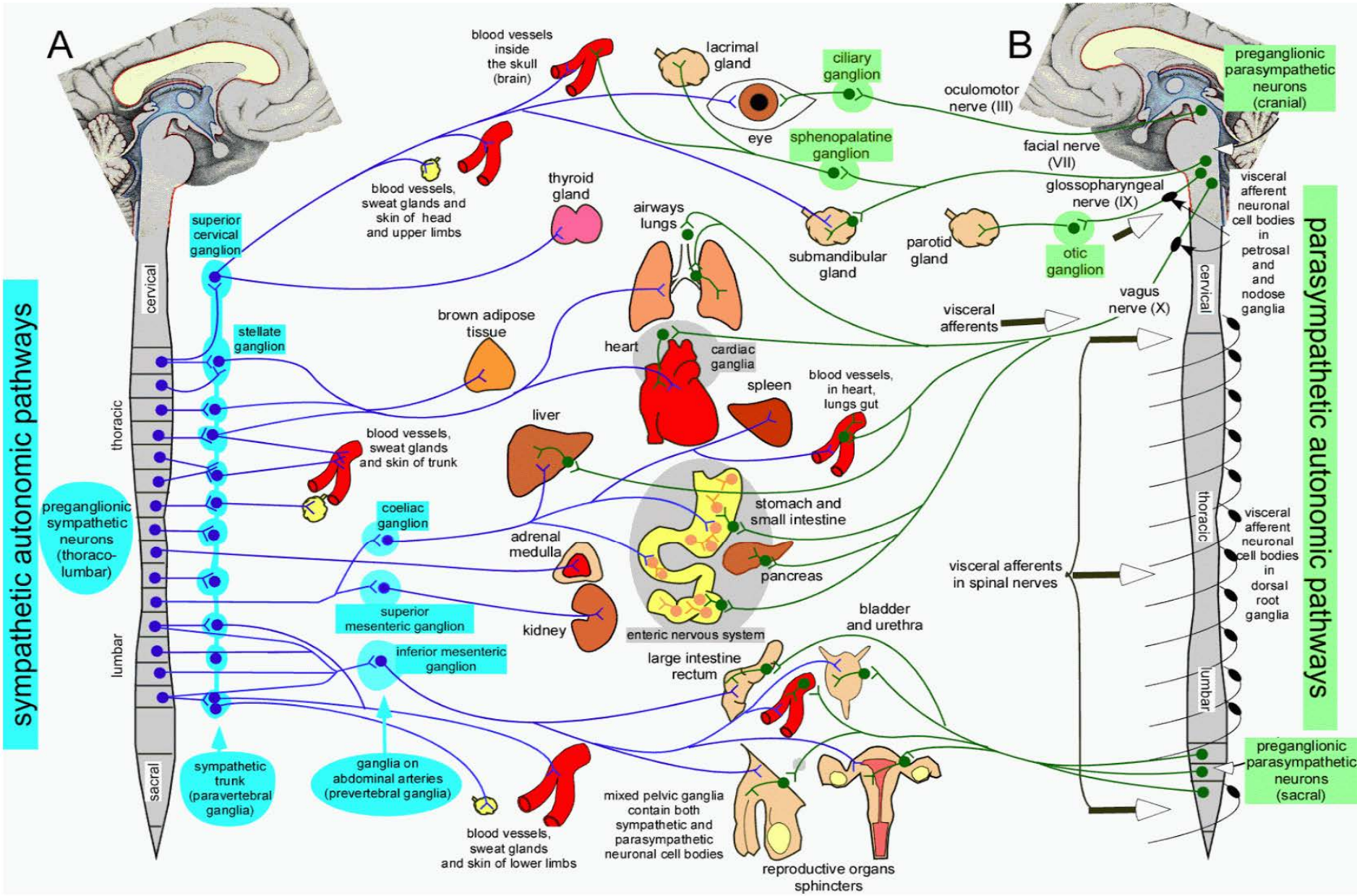
Sympathetic innervation of the adrenal medulla

- Direct projections from sympathetic neurons into the gland, can therefore partly reflects preganglionic outflow.
- Chromaffin-cortical cells crosstalk ensures normal function of the gland (products of enterochromaffin cells or sympathoadrenal nerve endings stimulate the steroidogenic activity of adrenocortical cells and conversely).



Bornstein SR. Endocr Dev. 2011;20:28-37

Organs and function are regulated through ANS circuits



Lung, heart, liver, pancreas, gastrointestinal tract, kidney, bladder, immune system, reproductive organs

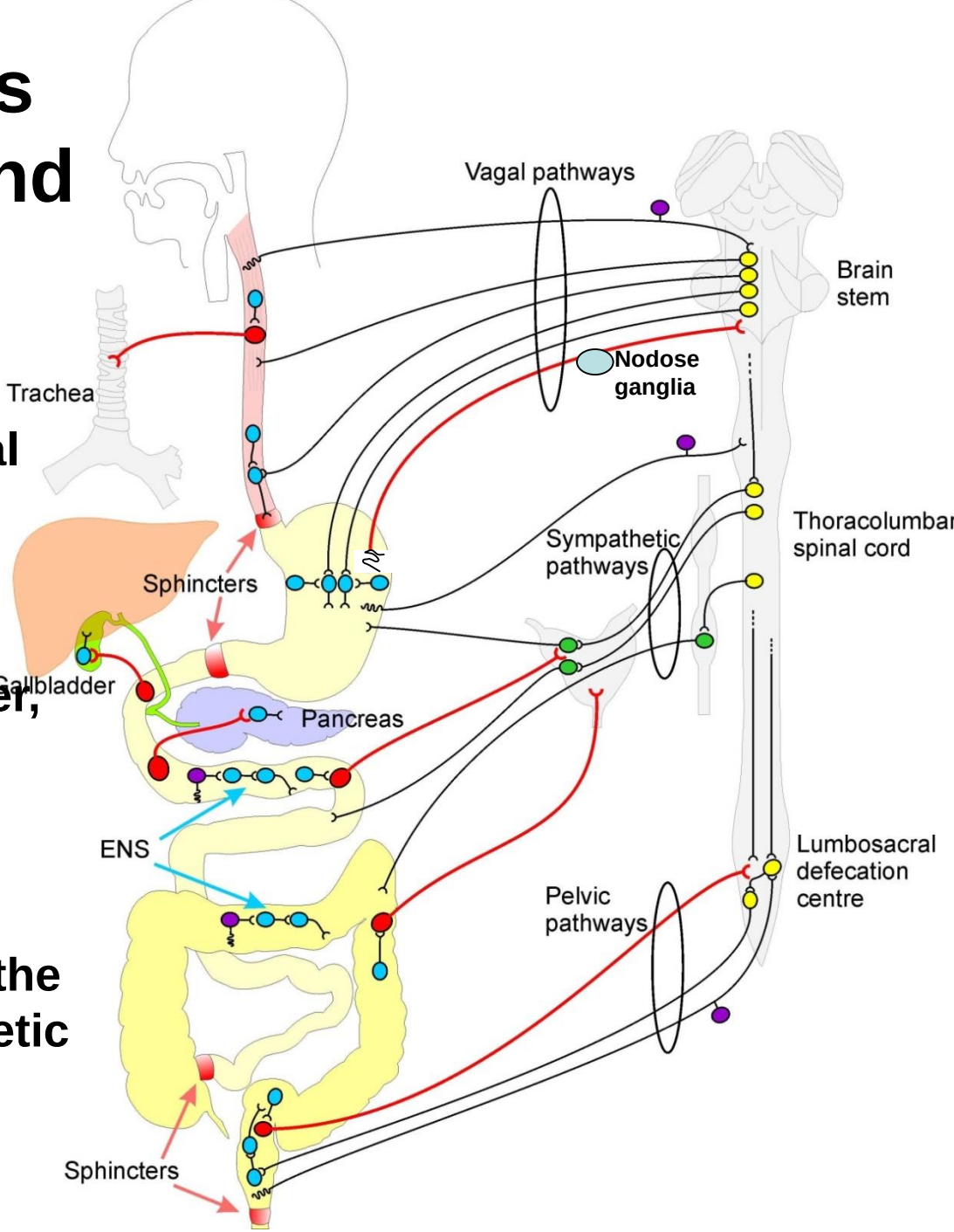
Neural projections between the ENS and CNS

- **Intrinsic primary afferent neurons (IPAN) involved in local reflex circuit.**

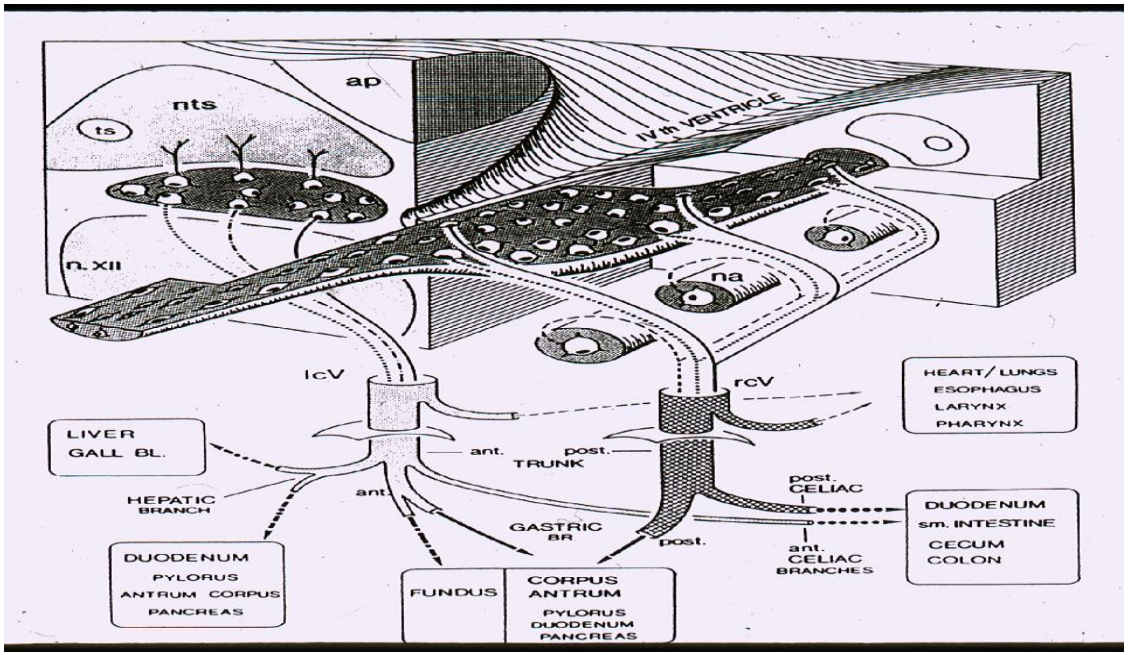
- **Intestinofugal neurons to: sympathetic ganglia, gallbladder, pancreas, airways allowing organs to organs interactions.**

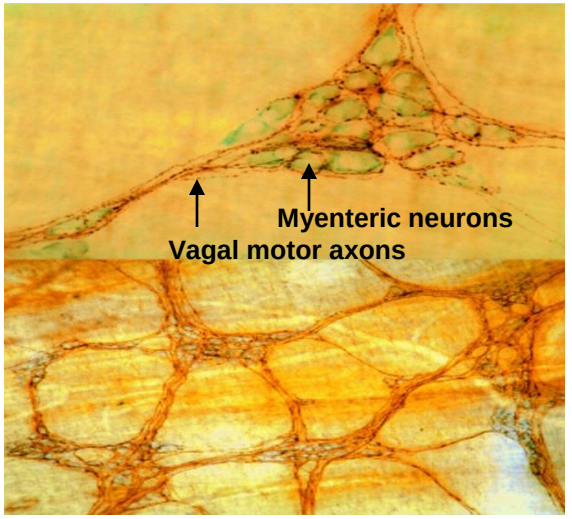
- **Extrinsic afferents that reach the CNS and efferent parasympathetic (vagal/lumbosacral) and sympathetic pathways**

Furness, 2014



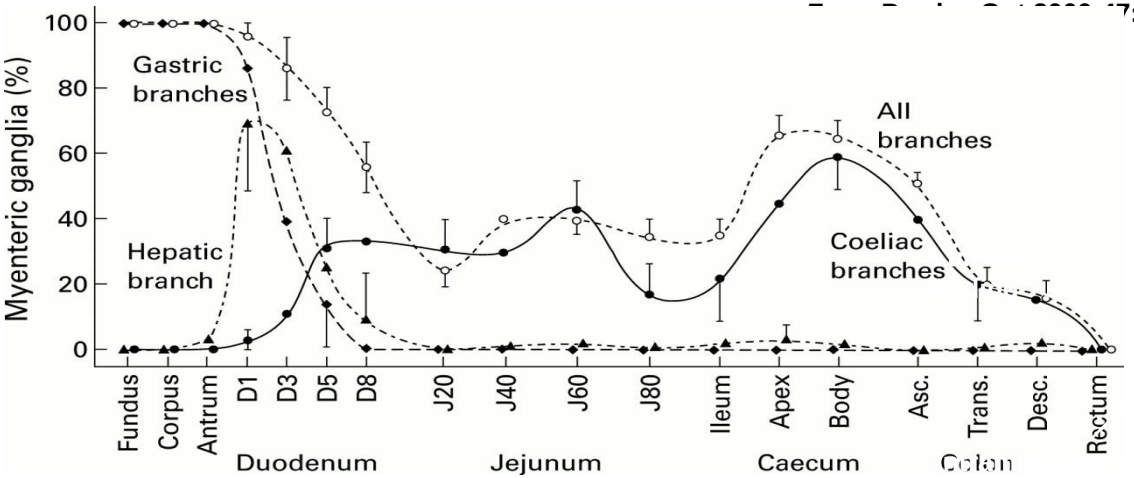
A rich network of vagal connections extends from the brain to enteric plexus neurons



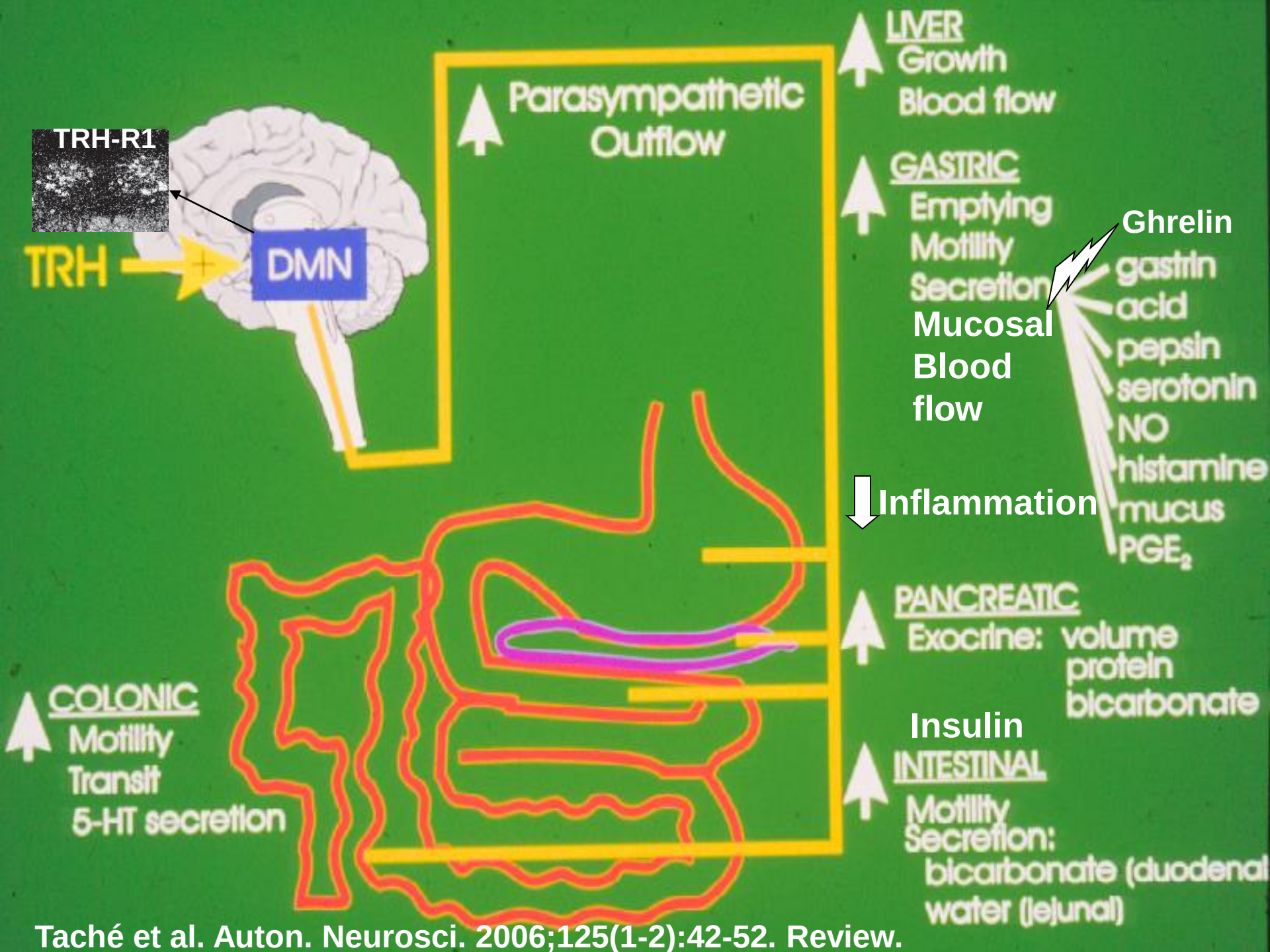


Vagal axons ramify extensively contacting large numbers of gastric myenteric neurons with network of varicose endings investing almost all neurons

:iv30-iv32

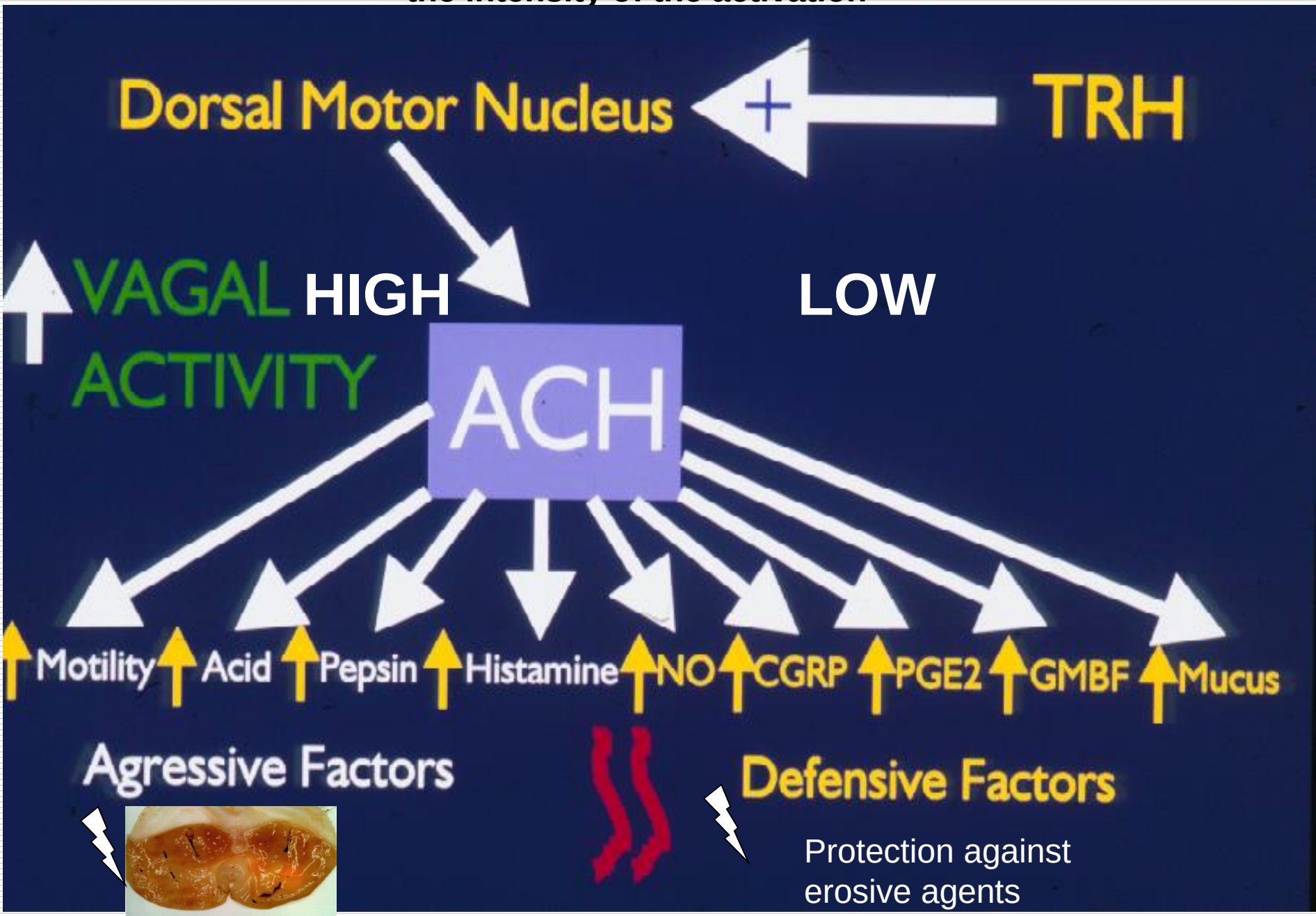


Percentage of all myenteric ganglia receiving vagal efferent innervation in the GI tract Berthoud & Powley Am J Physiol 260:R200–R207 (1991).



Taché et al. Auton. Neurosci. 2006;125(1-2):42-52. Review.

Dual actions of vagal activation on the integrity of the gastric mucosa linked with the intensity of the activation



Distal and proximal ventral gastric vagal (VGV) branches have distinct efferent responses to iv CCK-8 in rats: *Importance to record both afferent and efferent signals and functional response at specific targets*

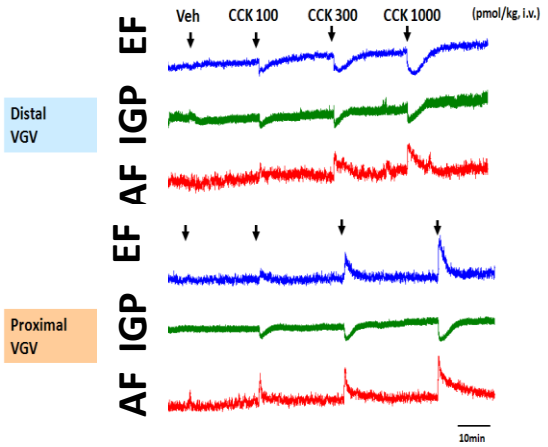
Gastric reservoir vago-vagal reflex

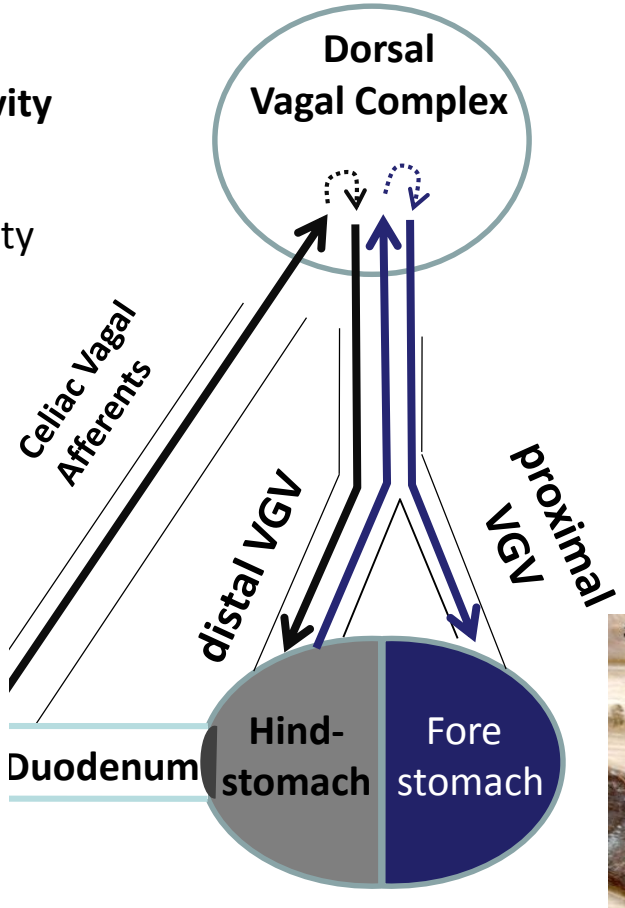
iv CCK

↑ Celiac vagal afferent activity

↓ distal VGV efferent activity

↓ antral pump activity



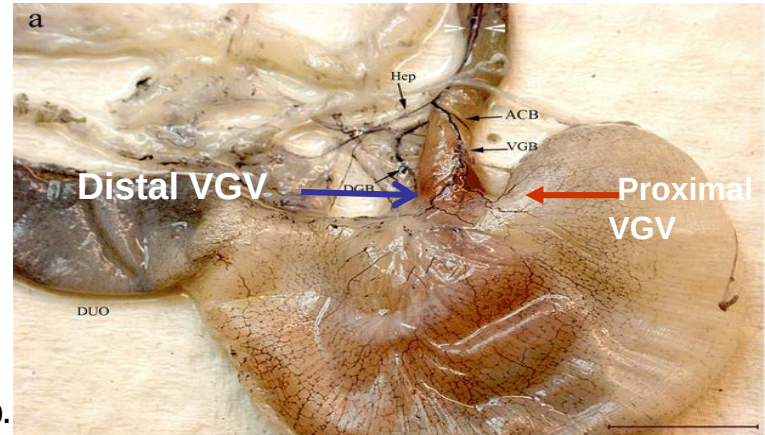


iv CCK

↑ distal VGV afferent activity

↑ proximal VGV efferent activity

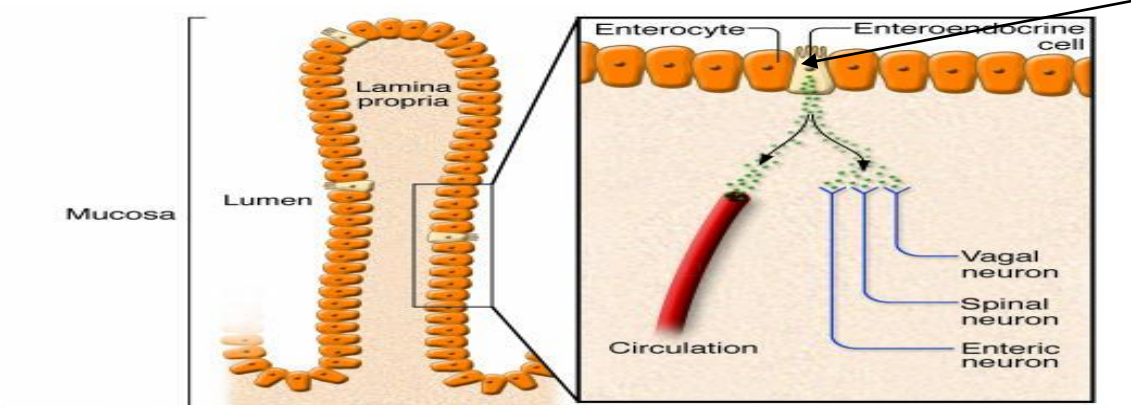
↑ gastric accommodation



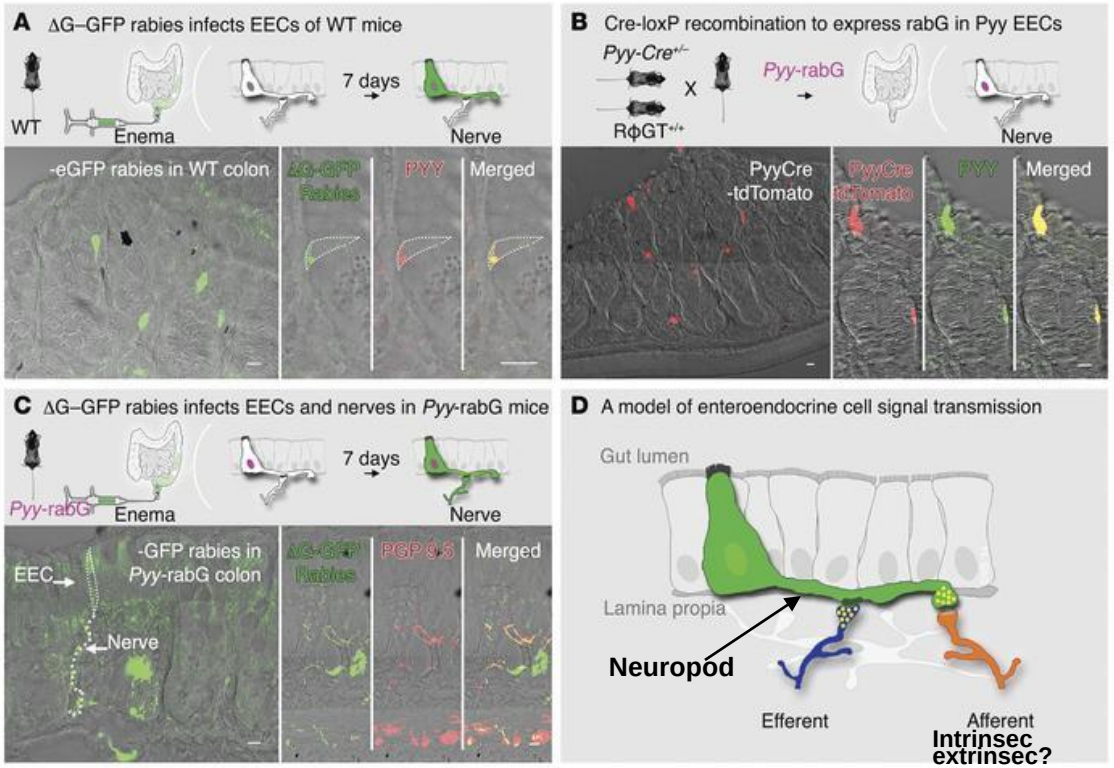
Adelson DA et al. J. Phsiol 589:371-393, 2011

Wang, F.B. and Powley, T.L. Vagal innervation of intestines: afferent pathways mapped with new en bloc horseradish peroxidase adaptation. Cell Tissue Res. (2007) 329(2):221-30.

How enteroendocrine cells relay sensory signals from the gut lumen onto nerves is poorly understood.



Sensing food and bacteria



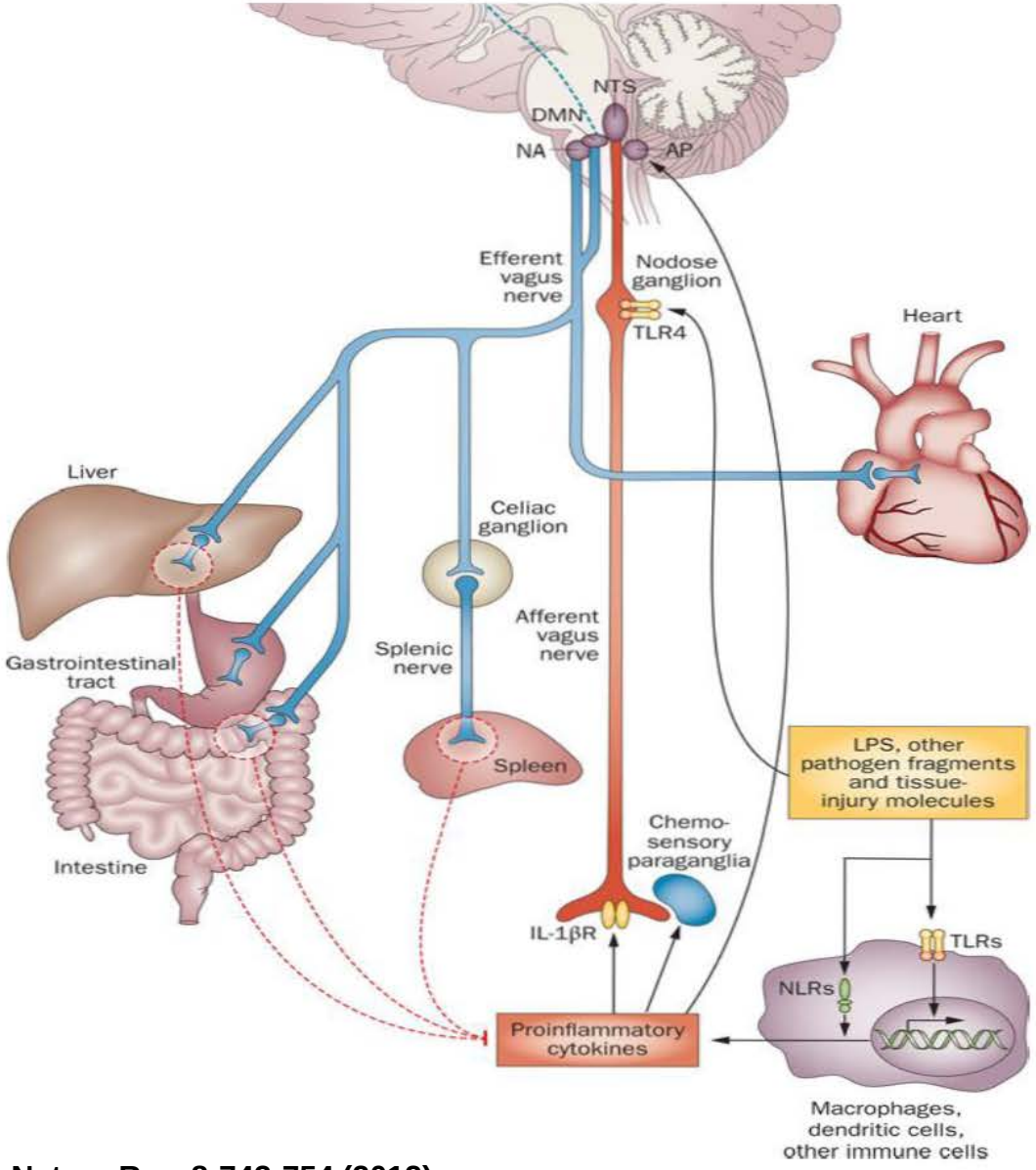
Classical view:
Paracrine transmission

Emerging view:
Direct contact between enteroendocrine cells and nerves through neuropoods.

- precise topographical representation of sensory signals from the gut;
- potential physical path for viruses in the lumen of the gut to gain access to the peripheral or central nervous system.

Liddle et al. J Clin Invest. 2015;125(2):782–786.

Autonomic signalling pathways to and from the abdominal organs: Needs more detailed analysis to unravel anti-inflammatory circuits



Pavlov and Tracey Nature Rev. 8:743-754 (2012)

Bridging the gaps in knowledge

Structural level

- Structural detailed map derived from high-resolution tracing of afferent and efferent nerve fibers at various levels of target organs and interspecies differences in organ innervation.

Functional level

- Generate simultaneous recordings of neural signals and organ function and associated end-organ biomarkers in response to physiological stimuli and disease models.

- Investigate at the molecular and cellular levels mechanisms through which ANS efferent signaling at different intensities translated into changes of organ function using established tools such as brain peptides known to be physiological relevant to influence ANS.

- How afferent signals arising from changes at target organs transfers to different autonomic reflex locally, within interconnected organs and integration at spinal and supraspinal.

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Thanks!

Dr. David Adelson, PhD