Neurobiology

Introduction to neurosciences for Cognitive MSs.

Homeostasis

- Concept whereby body states are regulated toward a steady state
  - Proposed by Walter Cannon in 1932
- At the same time Cannon introduced negative feedback regulation
  - an important part of this feedback regulation is mediated by the ANS through the hypothalamus

Autonomic Nervous System

- Controls visceral functions
- functions to maintain a dynamic internal environment, necessary for proper function of cells, tissues, organs, under a wide variety of conditions & demands

Autonomic Nervous System

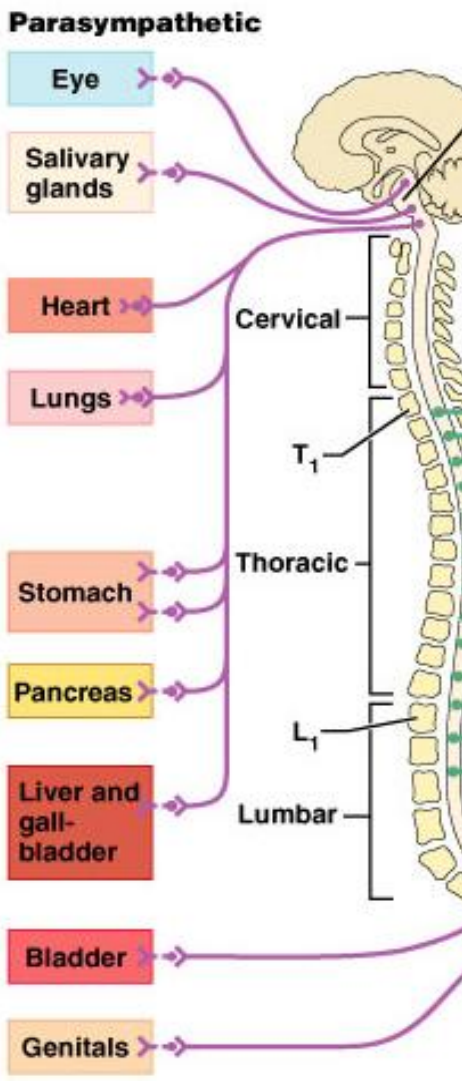
- Visceral & largely involuntary motor system
- Three major divisions
  - Sympathetic
    - Fight & flight & fright
    - emergency situations where there is a sudden Δ in internal or external environment
  - Parasympathetic
    - Rest and Digest
  - Enteric
    - neuronal network in the walls of GI tract

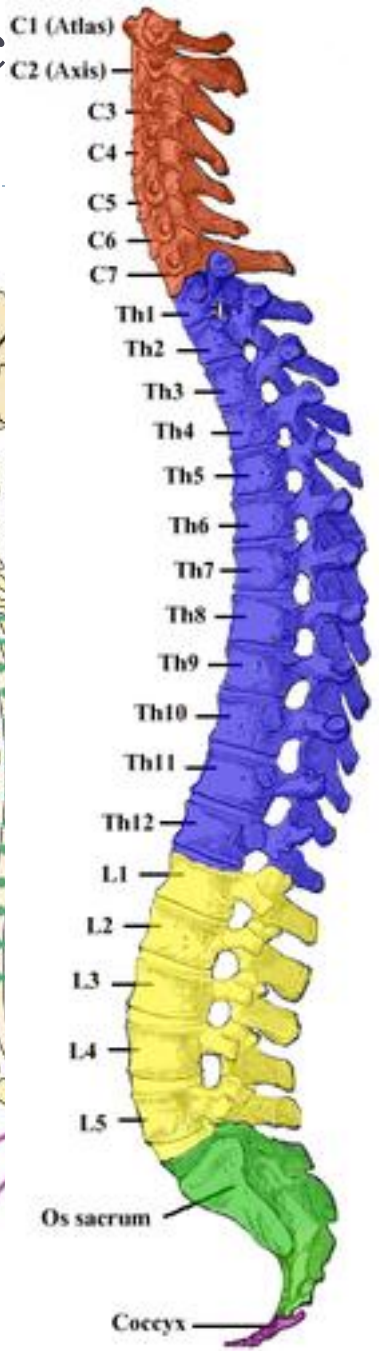
Divisions of the Autonomic Nervous System

- Sympathetic – “fight, flight, or fright”
  - Activated during exercise, excitement, and emergencies
- Parasympathetic – “rest and digest”
  - Concerned with conserving energy

Anatomical Differences in Sympathetic and Parasympathetic Divisions

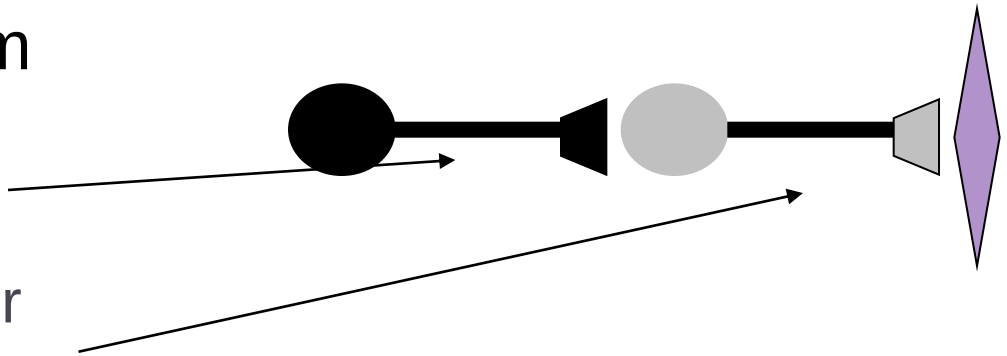
- Issue from different regions of the CNS
  - Sympathetic – also called the thoracolumbar division
  - Parasympathetic – also called the craniosacral division

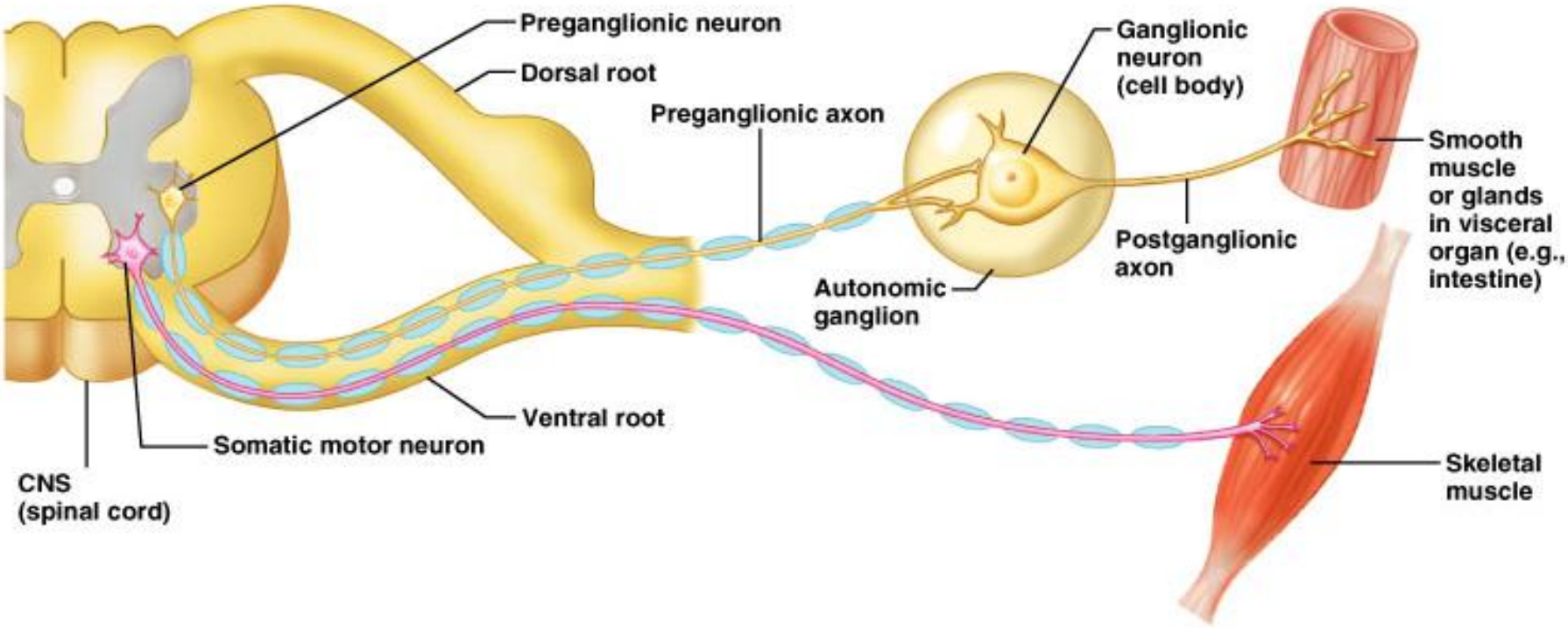




ANS

- Primarily an effector system
  - Controls
    - smooth muscle
    - heart muscle
    - exocrine glands
- Two neuron system
  - Preganglionic fiber
    - cell body in CNS
  - Postganglionic fiber
    - cell body outside CNS

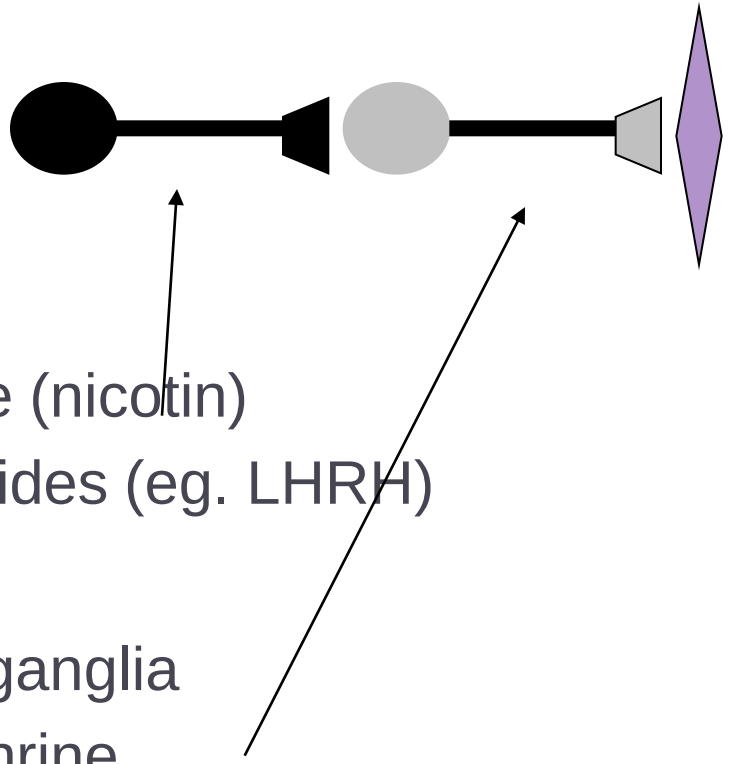



Preganglionic neuron
Dorsal root
Preganglionic axon
Ganglionic neuron (cell body)
Smooth muscle or glands in visceral organ (e.g., intestine)
Postganglionic axon
Autonomic ganglion
Ventral root
Somatic motor neuron
CNS (spinal cord)
Skeletal muscle

Neurotransmitters of Autonomic Nervous System

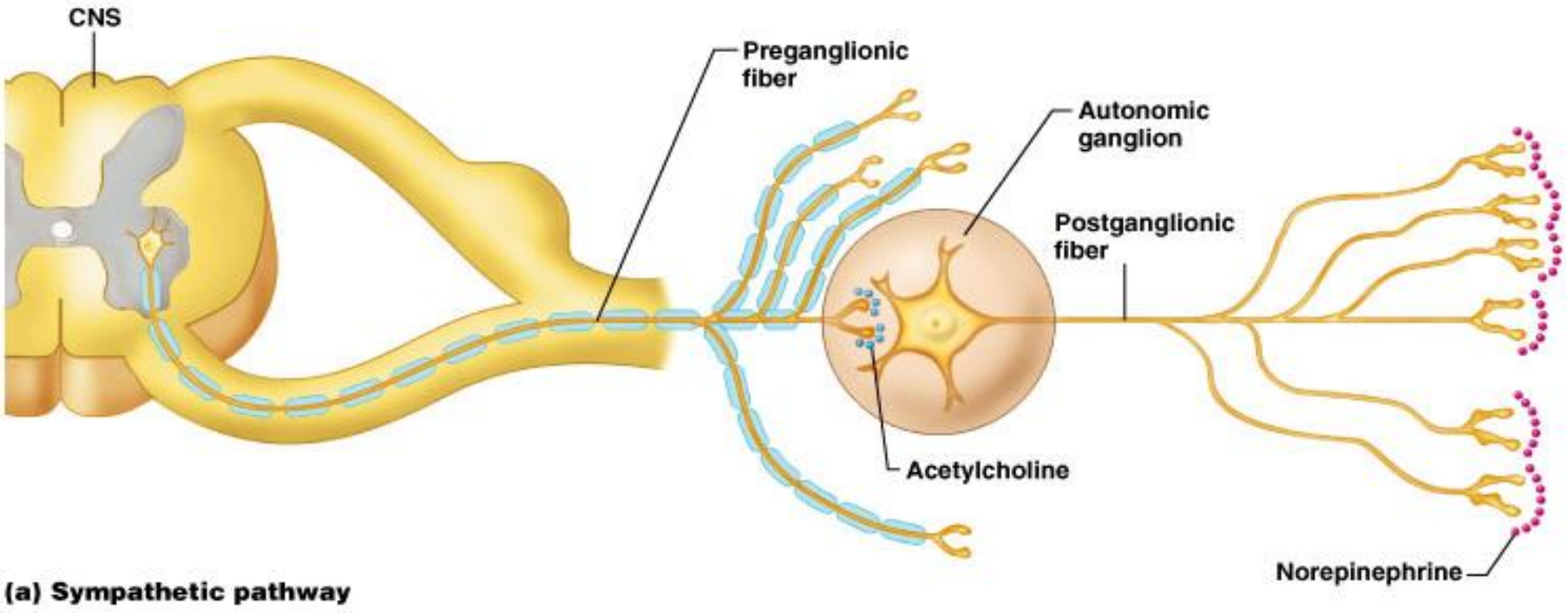
- Neurotransmitter released by preganglionic axons
  - Acetylcholine for both branches (cholinergic)

Sympathetic Nervous System



- Pre-ganglionic cells
  - intermediolateral horn cells
  - C8 to L2 or L3
  - release primarily acetylcholine (nicotin)
  - also releases some neuropeptides (eg. LHRH)
- Post-ganglionic cells
  - Paravertebral or Prevertebral ganglia
  - most fibers release norepinephrine
  - also can release neuropeptides (eg. NPY)

Anatomical Differences in Sympathetic and Parasympathetic Divisions



Sympathetic – long postganglionic fibers
Sympathetic axons – highly branched
Influences many organs
Sympathetic postganglionic axons
– most release norepinephrine (adrenergic)

Mass SNS discharge

- Increase in arterial pressure
- decreased blood flow to inactive organs/tissues
- increase rate of cellular metabolism
- increased blood glucose metabolism
- increased glycolysis in liver & muscle
- increased muscle strength
- increased mental activity
- increased rate of blood coagulation

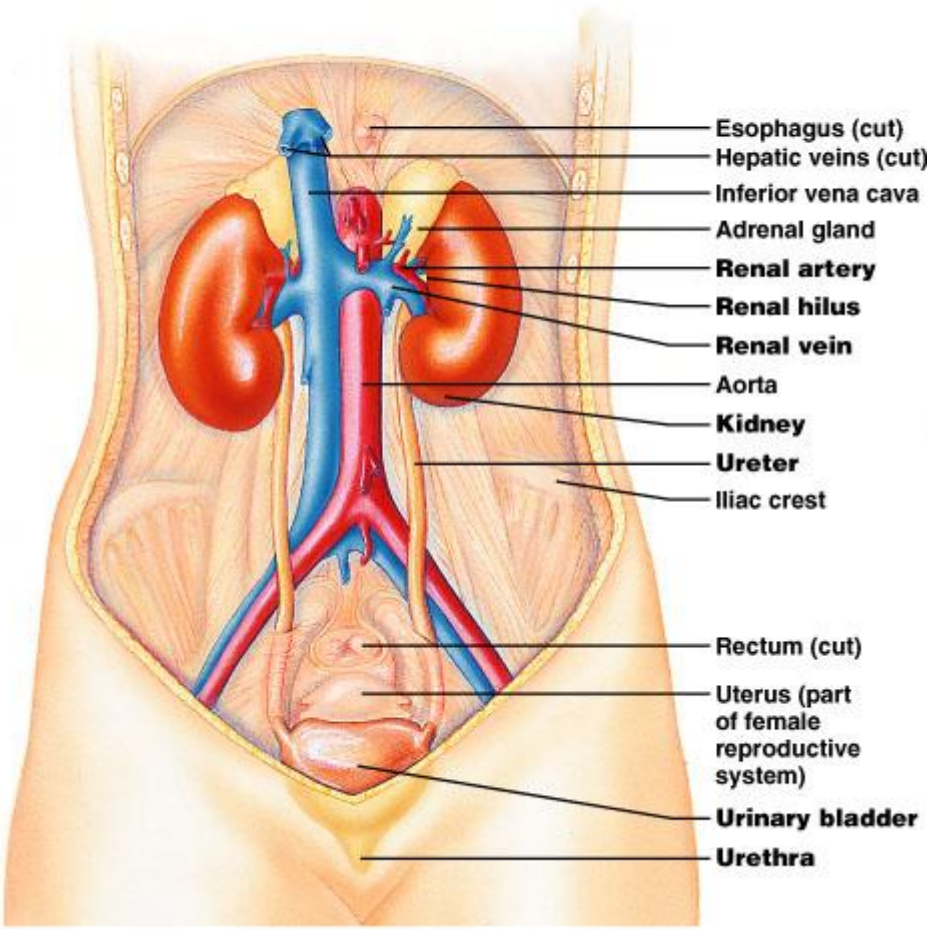
Normal Sympathetic Tone

- 1/2 to 2 Impulses/Sec
- Creates enough constriction in blood vessels to limit flow
- Most SNS terminals release norepinephrine
  - release of norepinephrine depends on functional terminals which depend on nerve growth factor

Adrenal gland is exception

On top of kidneys

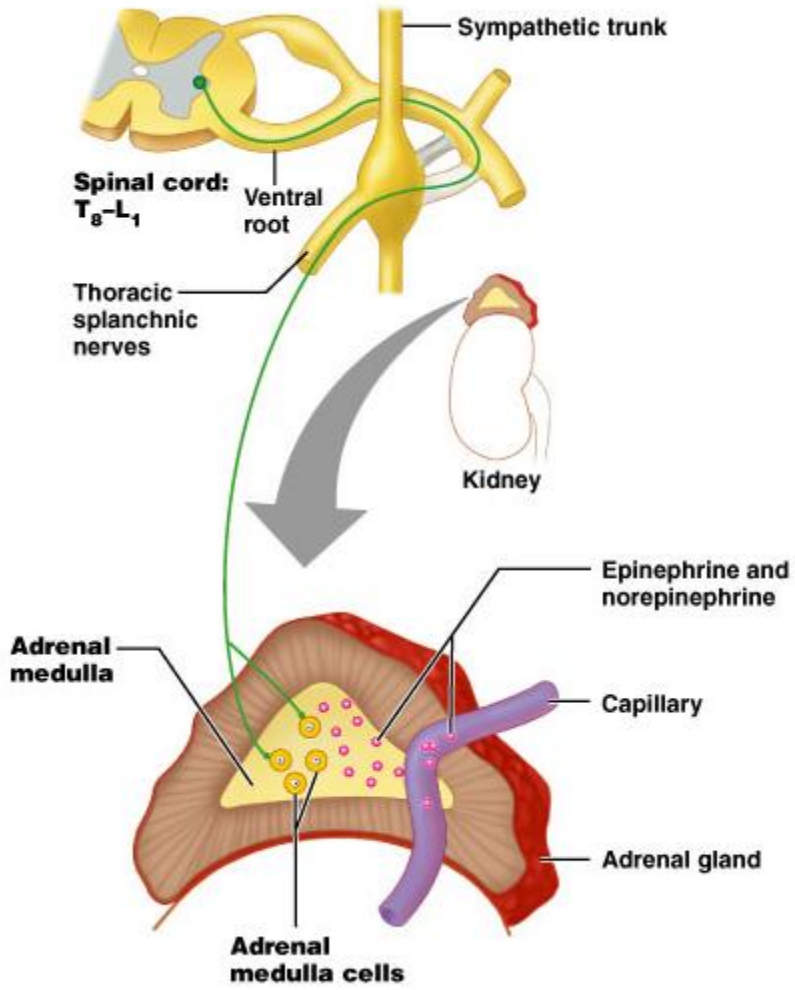
Adrenal medulla (inside part) is a major organ of the sympathetic nervous system



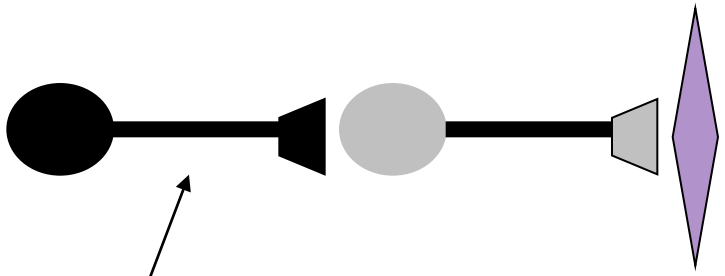
Adrenal gland is exception

- Synapse in gland
- Can cause body-wide release of epinephrine aka adrenaline and norepinephrine in an extreme emergency

  (adrenaline “rush” or surge)



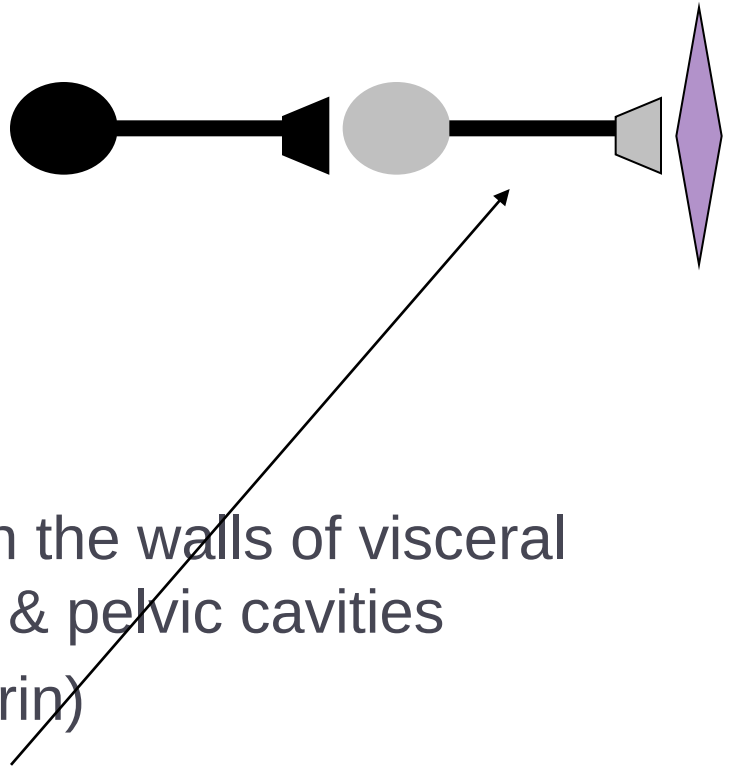
Parasympathetic Nervous System



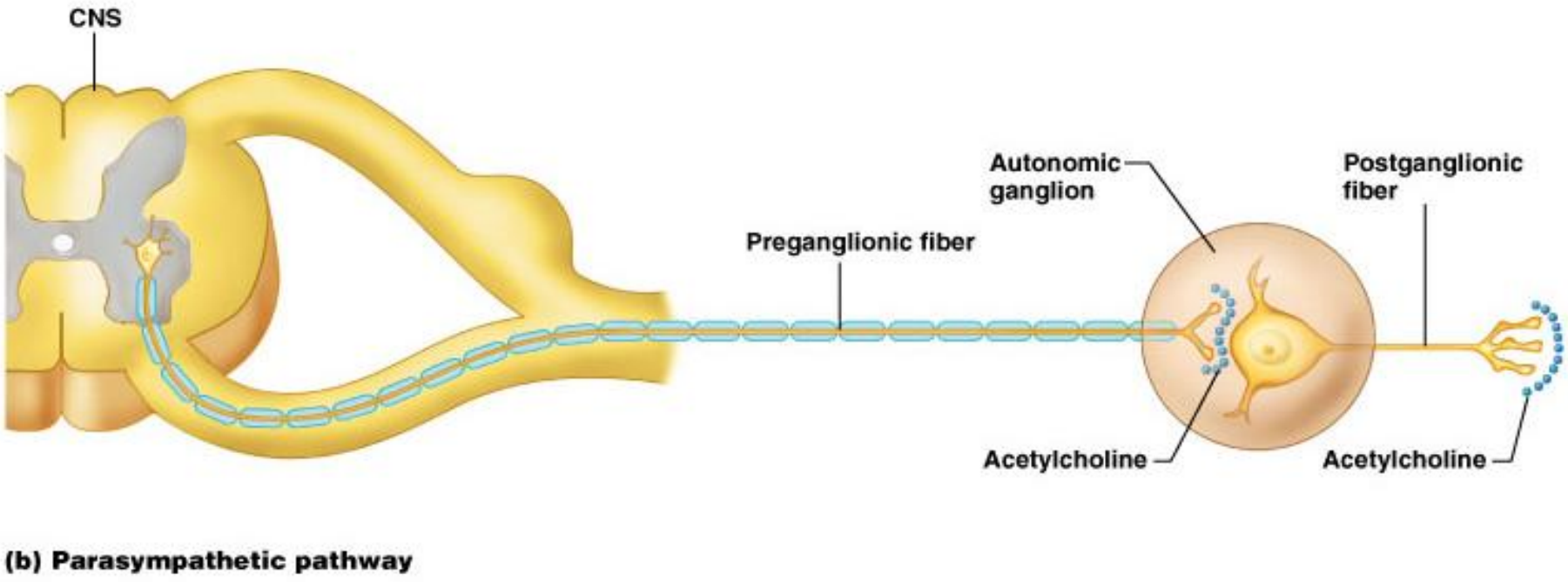
- Preganglionic neurons
  - located in several cranial nerve nuclei in brainstem
    - Edinger-Westphal nucleus (III)
    - superior salivatory nucleus (VII)
    - inferior salivatory nucleus (IX)
    - dorsal motor (X) (secretomotor)
    - nucleus ambiguus (X) (visceromotor)
  - intermediolateral regions of S2,3,4
  - release acetylcholine (nicotin)

Parasympathetic Nervous System

- Postganglionic cells
  - cranial ganglia
    - ciliary ganglion
    - pterygopalatine
    - submandibular ganglia
    - otic ganglia
  - other ganglia located near or in the walls of visceral organs in thoracic, abdominal, & pelvic cavities
  - release acetylcholine (muszkarin)



Anatomical Differences in Sympathetic and Parasympathetic Divisions



(b) Parasympathetic pathway

Parasympathetic – short postganglionic fibers
Parasympathetic axons – few branches
Localized effect
Parasympathetic postganglionic axons
– release acetylcholine

Parasympathetic nervous system

- The vagus nerves innervate the heart, lungs, bronchi, liver, pancreas, & all the GI tract from the esophagus to the splenic flexure of the colon
- The remainder of the colon & rectum, urinary bladder, reproductive organs are innervated by sacral preganglionic nerves via pelvic nerves to postganglionic neurons in pelvic ganglia

Effects of Stimulation

- Eye: S dilates pupils
  P- constricts pupil, contracts ciliary muscle & increases lens strength
- Glands :in general stimulated by P but S + will concentrate secretion by decreasing blood flow. Sweat glands are exclusively innervated by cholinergic S
- GI tract: S -, P + (mediated by enteric)
- Heart: S +, P -
- Blood vessels: S constriction, P largely absent

Effects of Stimulation

- Airway smooth muscle: S dilation P constriction
- Ducts: S dilation P constriction
- Immune System: S inhibits, P ??

Vegetativ neurotranszmitterek

Transzmitter	Receptor	Agonista	Antagonista	Előfordulás
ACh	nAChR	ACh nikotin	hexamethonium dekamethonium	vegetativ ganglionok
	mAChR	ACh muszkarin	atropin	pasy effektorok egyes sy effektorok (pl. verejték-mirigyek)
Katekol-aminok (adrenalin, noradrenalin, izoproterenol)	α_1	NA≥A>>I fenilefrin clonidin	fenoxibenzamin prazosin	sy effektorok (rezisztenciaerek)
	α_2	NA≥A>>I fenilefrin	fenoxibenzamin	preszinaptikus feedback sy effektorok (vénák - ?)
	β_1	I>A≥NA	propranolol	sy effektorok (szív)
	β_2	I>A>>NA isoprenalin	propranolol	sy effektorok (bronchusok, vázizomzat artériái)

Table 16.3 Effects of the Sympathetic and Parasympathetic Divisions on Various Tissues

Organ	Sympathetic Effects and Receptor Type*	Parasympathetic Effects and Receptor Type*
Adipose tissue	Fat breakdown and release of fatty acids (α_2, β_1)	None
Arrector pili muscle	Contraction (α_1)	None
Blood (platelets)	Increases coagulation (α_2)	None
Blood vessels		
Arterioles (carry blood to tissues)		
Digestive organs	Constriction (α_1)	None
Heart	Dilation (β_2), constriction (α_1)†	None
Kidneys	Constriction (α_1, α_2); dilation (β_1, β_2)	None
Lungs	Dilation (β_2), constriction (α_1)	None
Skeletal muscle	Dilation (β_2), constriction (α_1)	None
Skin	Constriction (α_1, α_2)	None
Veins (carry blood away from tissues)	Constriction (α_1, α_2), dilation (β_2)	
Eye		
Ciliary muscle	Relaxation for far vision (β_2)	Contraction for near vision (m)
Pupil	Dilated (α_1)‡	Constricted (m)‡
Gallbladder	Relaxation (β_2)	Contraction (m)
Glands		
Adrenal	Release of epinephrine and norepinephrine (n)	None
Gastric	Decreases gastric secretion (α_2)	Increases gastric secretion (m)
Lacrimal	Slight tear production (α)	Increases tear secretion (m)
Pancreas	Decreases insulin secretion (α_2)	Increases insulin secretion (m)
	Decreases exocrine secretion (α)	Increases exocrine secretion (m)

Table 16.3 Effects of the Sympathetic and Parasympathetic Divisions on Various Tissues

Organ	Sympathetic Effects and Receptor Type*	Parasympathetic Effects and Receptor Type*
Salivary	Constriction of blood vessels and slight production of a thick, viscous saliva (α_1)	Dilation of blood vessels and thin, copious saliva (m)
Sweat		
Apocrine	Thick, organic secretion (m)	None
Merocrine	Watery sweat from most of the skin (m); sweat from the palms and soles (α_1)	None
Heart	Increases rate and force of contraction (β_1, β_2)	Decreases rate of contraction (m)
Liver	Glucose released into blood (α_1, β_2)	None
Lungs	Dilates air passageways (β_2)	Constricts air passageways (m)
Metabolism	Increases up to 100% (α, β)	None
Sex organs	Ejaculation (α_1), erection§	Erection (m)
Skeletal muscles	Breakdown of glycogen to glucose (β_2)	None
Stomach and intestines		
Wall	Decreases tone (α_1, α_2, β_2)	Increases motility (m)
Sphincter	Increases tone (α_1)	Decreases tone (m)
Urinary bladder		
Wall (detrusor)	None	Contraction (m)
Neck of bladder	Contraction (α_1)	Relaxation (m)
Internal urinary sphincter	Contraction (α_1)	Relaxation (m)

*When known, receptor subtypes are indicated. The receptors are α_1- and α_2-adrenergic, β_1- and β_2-adrenergic, nicotinic cholinergic (n), and muscarinic cholinergic (m).
†Normally blood flow increases through coronary arteries because of increased demand by cardiac tissue for oxygen (local control of blood flow is discussed in chapter 21). In experiments that isolate the coronary arteries, sympathetic nerve stimulation, acting through α-adrenergic receptors, causes vasoconstriction. The β-adrenergic receptors are relatively insensitive to sympathetic nerve stimulation but can be activated by epinephrine released from the adrenal gland and by drugs. As a result, coronary arteries vasodilate.
‡Contraction of the radial muscles of the iris causes the pupil to dilate. Contraction of the circular muscles causes the pupil to constrict (see chapter 15).
§Decreased stimulation of alpha receptors by the sympathetic division can cause vasodilation of penile blood vessels, resulting in an erection.

Szerv, szervrendszer	Paraszimpatikus ingerlés	Szimpatikus ingerlés	Adrenerg receptor
Szívizom	csökkent szívfrekvencia	fokozott szívfrekvencia	β_1
	csökkent (pitv.) izomerô	fokozott izomerő	β_1

Szerv, szervrendszer	Paraszimpatikus ingerlés	Szimpatikus ingerlés	Adrenerg receptor
Érrendszer			
Bőratériák	-	vazokonstrikció	α_1
Hasi artériák	-	vazokonstrikció	α_1
Vázizomartériák	-	vazokonstrikció	α_1
		vazodilatáció (keringő adr.)	β_2
		vazodilatáció (kolinerg)	
Koronáriák	vazodilatáció (?)	vazokonstrikció	α_1
		vazodilatáció (csak adr.)	β_2
Erektilis szervek	vazodilatáció	?	
Vénák	-	vazokonstrikció	α_1
Agyi artériák	vazodilatáció (?)	vazokonstrikció	α_1

Szerv, szervrendszer	Paraszimpatikus ingerlés	Szimpatikus ingerlés	Adrenerg receptor
Gasztroint. traktus			
Fali simaizomzat	fokozott motilitás	csökkent motilitás	α_1 és β_2
Záróizmok	elernyedés	kontrakció	α_1
Bronchusok	kontrakció	elernyedés (fôleg adrenalin)	β_2
Piloerect. izom	-	kontrakció	α_1
Húgyhólyag			
Detrusor izom	kontrakció	elernyedés	β_2
Belső záróizom	-	kontrakció	α_1

Szerv, szervrendszer	Paraszimpatikus ingerlés	Szimpatikus ingerlés	Adrenerg receptor
Szem			
Dilatator pupil.	-	mydriasis	α_1
Sphinchter pup.	miosis	-	
Ciliáris izom	akkomodációi	jelentéktelen elernyedés	β_2
Exokrin mirigyek			
Nyálmirigyek	erôs serosus szekréció	kisfokú (mucin) szekréció	α_1
Könnymirigyek	szekréció	-	
Emésztômirigy	szekréció	- vagy csökkent szekréció	α_1
Orr-garat mirigy	szekréció	-	
Bronchialis mir.	szekréció	?	
Verejtékmirigy	-	szekréció (kolinerg)	

Anyagcsere

Máj	-	glikogenolízis glukoneogenezis	β_2
Zsírszövet	-	lipolízis	β_2
Inzulinszekréció	-	csökkenés	α_1

Enteric Nervous System

- Located in wall of GI tract (100 million neurons)
- Activity modulated by ANS

Enteric Nervous system

- Preganglionic Parasympathetic project to enteric ganglia of stomach, colon, rectum via vagus & pelvic splanchnic nerves
  - increase motility and tone
  - relax sphincters
  - stimulate secretion

Enteric Nervous System

- Myenteric Plexus (Auerbach's)
  - between longitudenal & circular muscle layer
  - controls gut motility
    - can coordinate peristalsis in intestinal tract that has been removed from the body
  - excitatory motor neurons release Ach & sub P
  - inhibitory motor neurons release Dynorphin & vasoactive intestinal peptide

Enteric Nervous System

- Submucosal Plexus
  - Regulates:
    - ion & water transport across the intestinal epithelium
    - glandular secretion
  - communicates with myenteric plexus
  - releases neuropeptides
  - well organized neural networks

Visceral afferent fibers

- Accompany visceral motor fibers in autonomic nerves
- supply information that originates in sensory receptors in viscera
- never reach level of consciousness
- responsible for afferent limb of viscerovisceral and viscerosomatic reflexes
  - important for homeostatic control and adjustment to external stimuli

Visceral afferents

- Many of these neurons may release an excitatory neurotransmitter such as glutamate
- Contain many neuropeptides
- can include nociceptors “visceral pain”
  - distension of hollow viscus

Neuropeptides (visceral afferent)

- Angiotension II
- Arginine-vasopressin
- bombesin
- calcitonin gene-related peptide
- cholecystokinin
- galamin
- substance P
- enkephalin
- somatostatin
- vasoactive intestinal peptide

Autonomic Reflexes

- Cardiovascular
  - Baroreceptor –HeartRate increases if RR decreases.
  - Bainbridge reflex- HR increases if venous pressure increases
- GI autonomic reflexes
  - smell of food elicits parasympathetic release of digestive juices from secretory cells of GI tract
  - fecal matter in rectum elicits strong peristaltic contractions to empty the bowel

Higher control of ANS

- Many neuronal areas in the brain stem reticular substance and along the course of the tractus solitarius of the medulla, pons, & mesencephalon as well as in many special nuclei (hypothalamus) control different autonomic functions.
- ANS activated, regulated by centers in:
  - spinal cord, brain stem, hypothalamus, higher centers (e.g. limbic system & cerebral cortex)

Central Autonomic Regulation

- Major relay cell groups in brain regulate afferent & efferent information
- convergence of autonomic information onto discrete brain nuclei
- autonomic function is modulated by Δ's in preganglionic SNS or Para tone and/or Δ's in neuroendocrine (NE) effectors

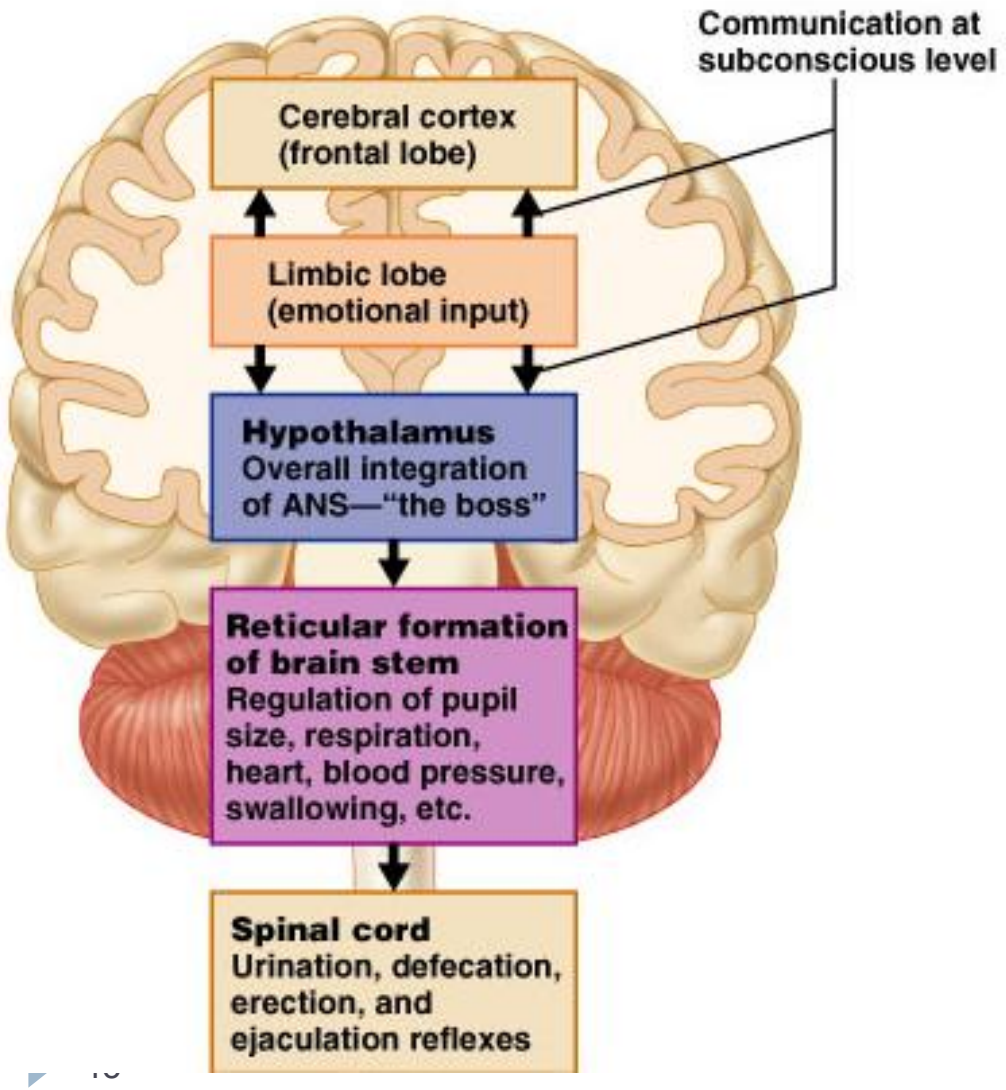
Central Autonomic Regulation

- different components of central autonomic regulation are reciprocally innervated
- parallel pathways carry autonomic info to other structures
- multiple chemical substances mediate transduction of neuronal infomation

Important Central Autonomic Areas

- Nucleus Tractus Solitarius
- Parabrachial Nucleus
- Locus Coeruleus
- Amygdala
- Cerebral Cortex
- Hypothalamus
- Circumventricular Organs (fenestrated caps)

Central control of the Autonomic NS



Amygdala: **main limbic region for emotions**

-Stimulates sympathetic activity, especially previously learned fear-related behavior

-Can be voluntary when decide to recall frightful experience - cerebral cortex acts through amygdala

-Some people can regulate some autonomic activities by gaining extraordinary control over their emotions

Hypothalamus: **main integration center**

Reticular formation: **most direct influence over autonomic function**

- Hipothalamus
  - Integrates the info from the homeostasis
  - Organises those responses that are necessary to maintain homeostasis (autonom, endocrin, somatic components)

HT

	Elülső rész, regio preoptica	Középső rész	Hátsó rész
Akut sérülés	insomnia hyperthermia diabetes insipidus	hyperthermia diabetes insipidus endokrin zavarok	hypersomnia emócionális zavarok vegetatív zavarok poikilothermia
Krónikus károsodás	insomnia komplex endokrin zavar (pubertas praecox) hypothermia szomjúságérzet hiánya	**Medialis rész** memóriazavar emócionális zavarok hyperphagia, obesitas endokrin zavarok **Lateralis rész** emócionális zavarok étvágytalanság szomjúságérzet hiánya	amnesia emócionális zavarok poikilothermia vegetatív zavarok kompex endokrin zavar (pubertas praecox)
Működés	alvás/ébrenlét, hőszabályozás, endokrin szabályozás	érzékelés, hő- és folyadékháztartás, endokrin szabályozás	érzékelés, öntudat, hőszabályozás, komplex endokrin szabályozás