Cells of the CNS

1) Neurons
-100 billion in total, but only 10% of all brain cells - vary in size (GABAergic interneurons 5-100 µm motor cortex)
-Most neuronal proliferation in first 5 months (starts to drop off)
-Most neuronal migration and differentiation ~ 4-9 months (can happen prior)
-Neuronal connections (synapses) continue to form postnatally = synaptic plasticity

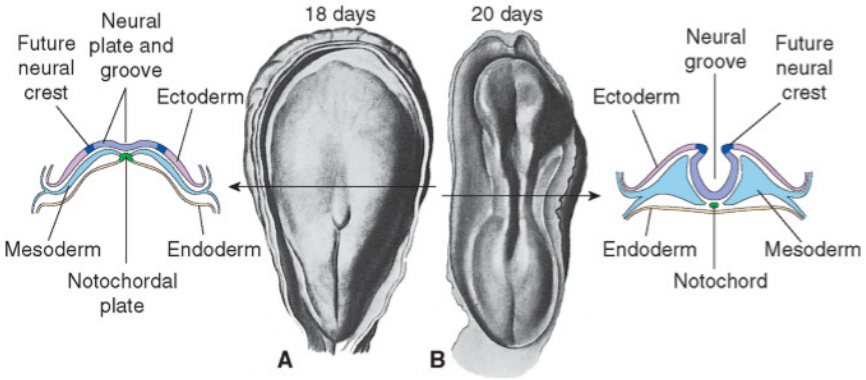
-Soma/Cell body: contains nucleus
-Dendrites: processes which receive synaptic input from other neurons; carry information TO soma
-Axon: single process which transmits information to dendrites of other neurons; carry information AWAY from soma

2) Glial cells
-Glial differentiation later than neuronal differentiation

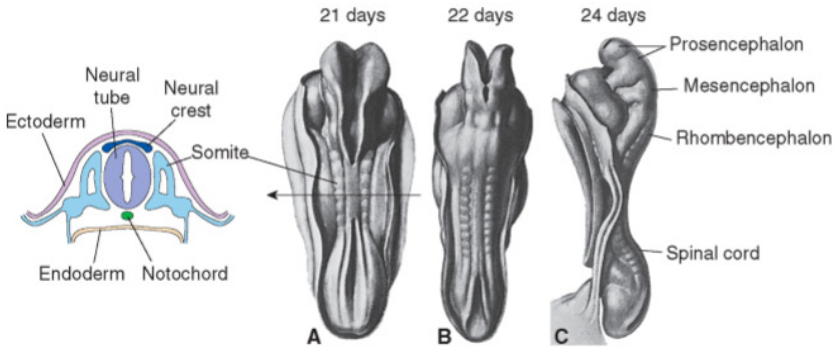
-Astrocytes: homeostasis of brain environment, structural support, removing neurotransmitters (e.g. glutamate), form the blood brain barrier, response to cell injury by releasing inflammatory mediators
    -Not electrically active
-Oligodendrocytes: myelination of axons to increase transmission speed
    -Occurs postnatally
-Microglia: resident immune cells of CNS (reside in brain parenchyma until foreign matter enters/ neuron dies), phagocytosis of foreign matter/ dead or injured neurons, and response to injury
    -Change morphology depending on the state of activity (active/resting state)
-Ependymal cells: line ventricles and choroid plexus to form a barrier between brain and CSF, produce CSF

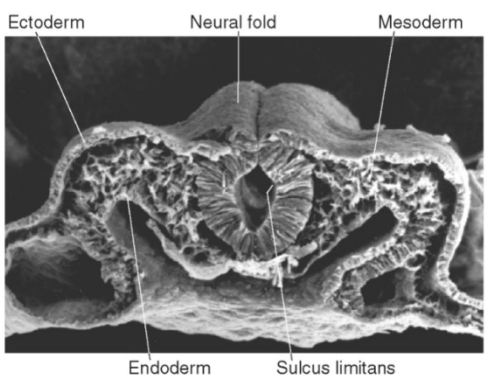
Brain Development

•Formation of the neural groove (Week 3)
-Midline mesoderm releases signalling molecules to the overlying ectoderm
-Ectoderm thickens to form the neural plate
-Neural plate folds inwards and deepens to form the neural groove (CNS) – attached to ectoderm by FNC

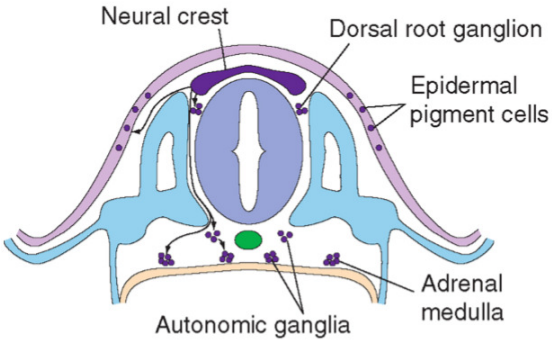


•Primary neurulation (Week 4)
-Neural groove closes to form the neural tube (early week 4)
-Neural tube closes (days 21-26): middle (future spinal cord) → rostral (future brain) → caudal
-Neural tube detaches from the ectoderm (skin) and the neural crest cells (PNS) detach from the neural tube





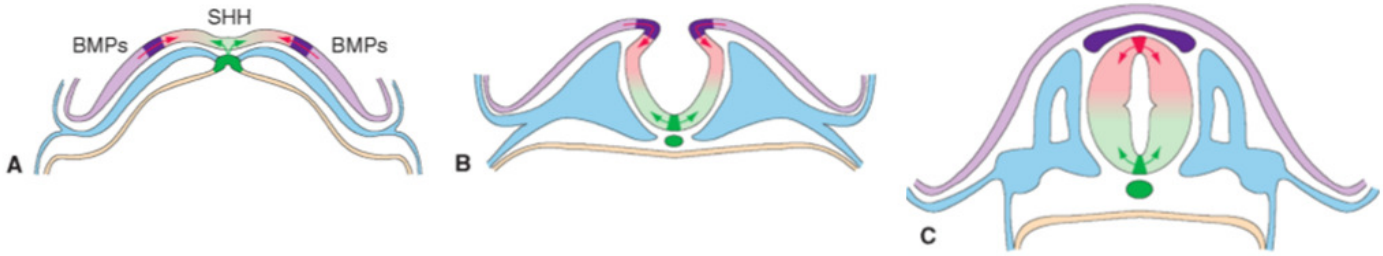
▪Neural Crest cells



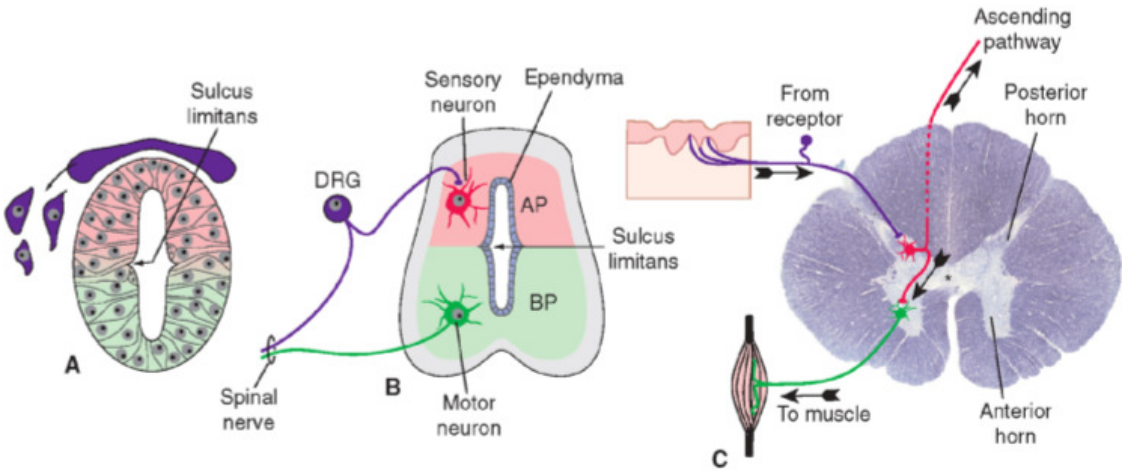
-Dorsal root ganglion: soma of the sensory nerves (dendrites project to skin and axon projects to spinal cord)
-Autonomic ganglion: sympathetic and parasympathetic nervous system
-Adrenal medulla

▪Dorsal-ventral patterns of differentiation
-Dorsal and ventral parts of the neural tube have different set of cell types (different morphology/ function)

Dorsal	Ventral
Ectoderm next to the neural plate produces an opposing signalling molecule	Midline mesoderm (later the notochord) produces an opposing signalling molecule
Bone morphogenetic proteins (BMPs)	Sonic hedgehog (SHH)
Sensory neurons projecting into spinal cord from the dorsal root ganglion (from neural crest cell) with dendrites projecting to the periphery	Motor neurons projecting out of spinal cord to muscles they innervate



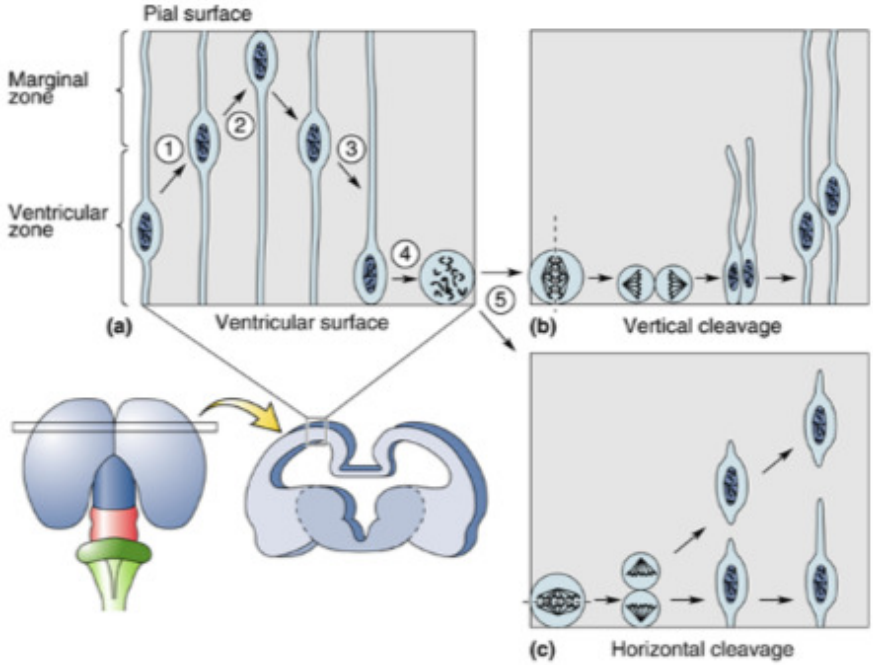
▪Alar versus basal plate derivatives
-Different gradients of signalling molecules establish a functional organisation, which persists in the adult spinal cord
-Alar plate derivatives become sensory neurons → dorsal spinal cord
-Basal plate derivatives become motor neurons → ventral spinal cord



-**Sulcus limitans** = groove inside the neural tube (half-way along) which cuts dorsal and ventral half of the spinal cord which persists in adult brain = differentiates between sensory and motor orientations

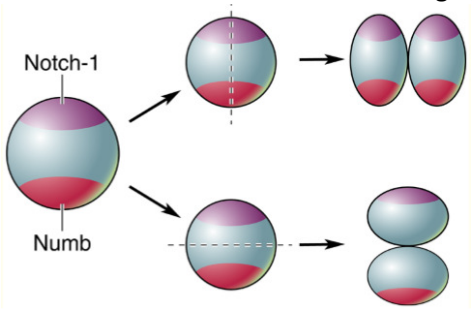
Cellular Brain Development

•The genesis of neurons - 3 stages of the development of neuronal structure:
1) Cell proliferation
-Peaks between week 5 – month 5



-Pial surface = outside of the neural tube
-Ventricular surface = inside of the neural tube

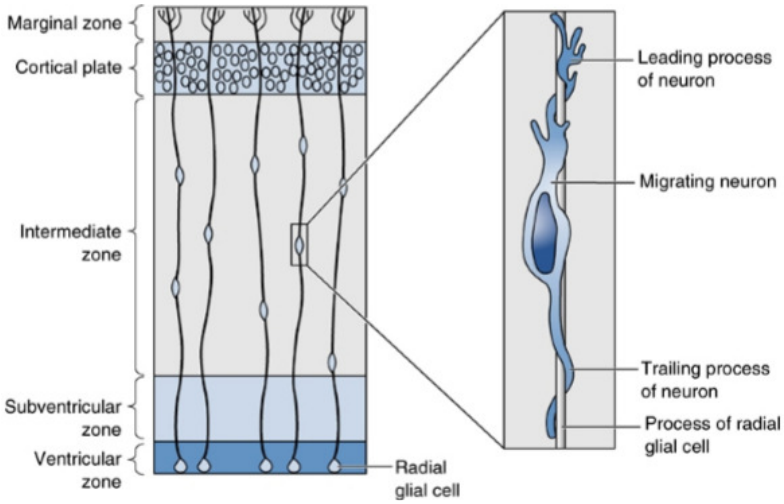
-For cell division, precursor neuronal cell moves from the ventricular surface to the pial surface where the DNA is copied and falls back down to the ventricular surface
-The cell divides in 2 different cleavage planes (due to different signalling molecules)

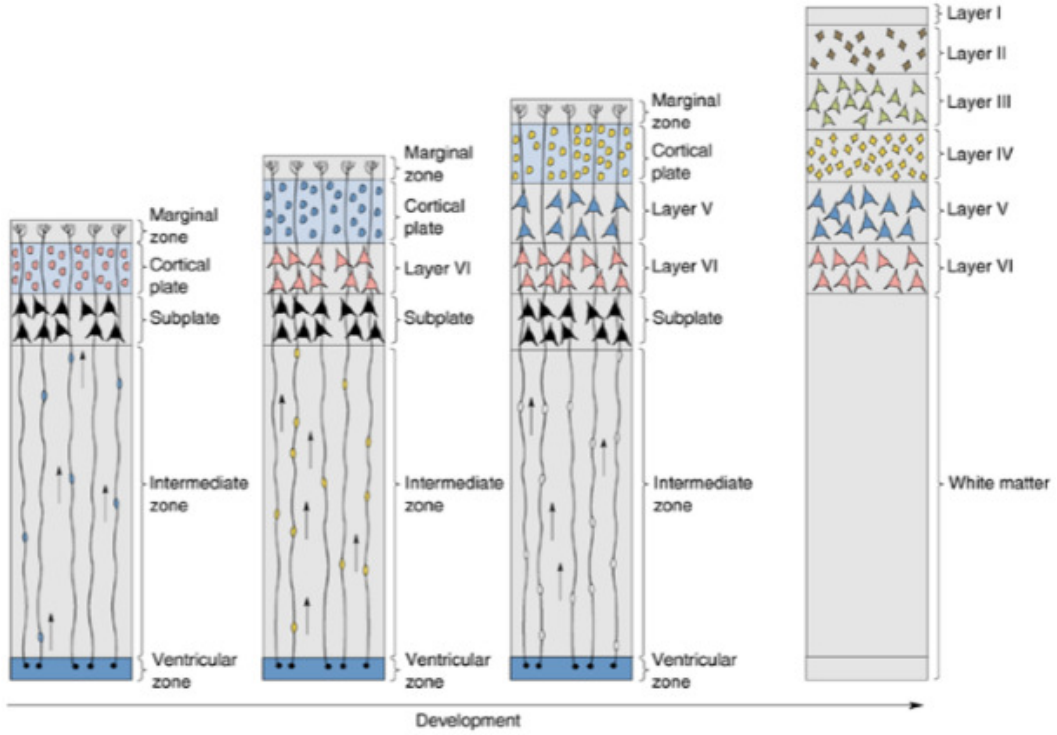


a) Vertical cleavage
-Early development (need more neurons)
-Both daughter cells contain Notch-1 and Numb
-They both stay at the ventricular surface then continue cell division

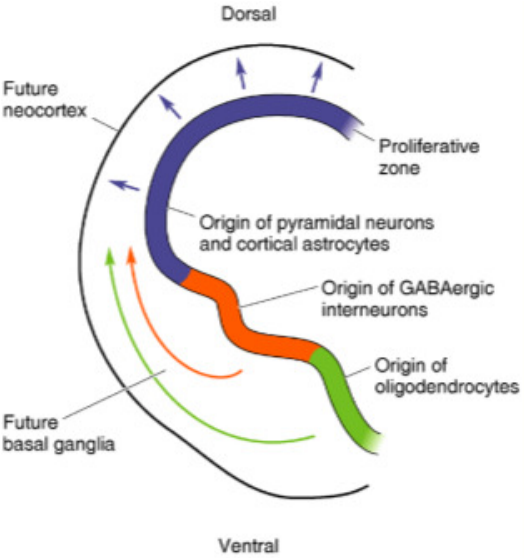
b) Horizontal cleavage
-Later development (no new cell types needed)
-One daughter cell contains Notch-1 while the other contains Numb
-Notch-1 cell migrates away and stays at the pial surface (final position) and stops dividing
-Numb cell stays at the ventricular surface then continues cell division

2) Cell migration
-'Inside-Out' development of the cortex
-**Radial glial cells**: Long process that stretches from ventricular to pial surface provides scaffold on which cortex is built and guide migration of neuroblasts (immature neurons from horizontal cleavage) along their thin fibres
-Neuroblasts cross the subplate to arrive in the cortical plate (first cells become layer VI neurons → layer I neurons)
-The subplate radial glial 'template' is then eliminated (cell death)

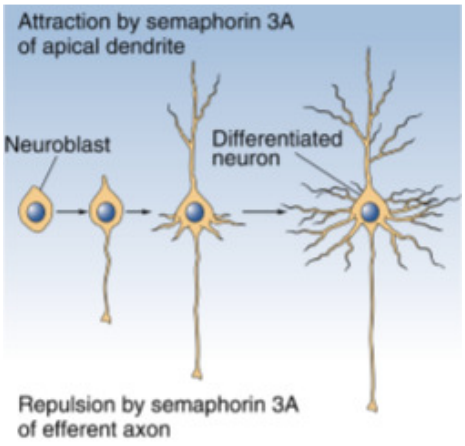




3) Cell differentiation
-Different cell types are generated in different anatomical locations of the telencephalon
-Dorsal telencephalon: excitatory neurons, astrocytes
-Ventral telencephalon: oligodendrocytes
-Middle of telencephalon: GABAergic interneurons



-Cell takes the appearance and characteristics of a neuron – signalling molecules in the local region control the differentiation



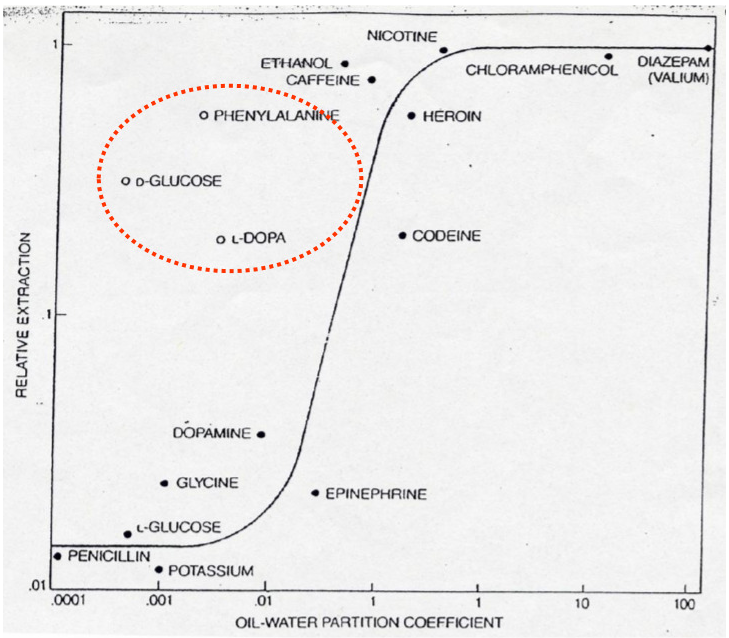
-Differentiation of astrocytes peaks at birth
-Differentiation of oligodendrocytes postnatal

<u>Blood Brain Barrier</u>

▪History
-In 19th century, chemists developed industrial dyes for use in textiles. Histologists used them to stain tissues. Some dyes turned out to be useful as therapeutic agents but when injected into animals they did not enter brain.
-Edwin Goldman showed that brain can be stained if the dyes are injected directly into the CSF.
-Ehrlich/ Shtern introduced the concept of BBB

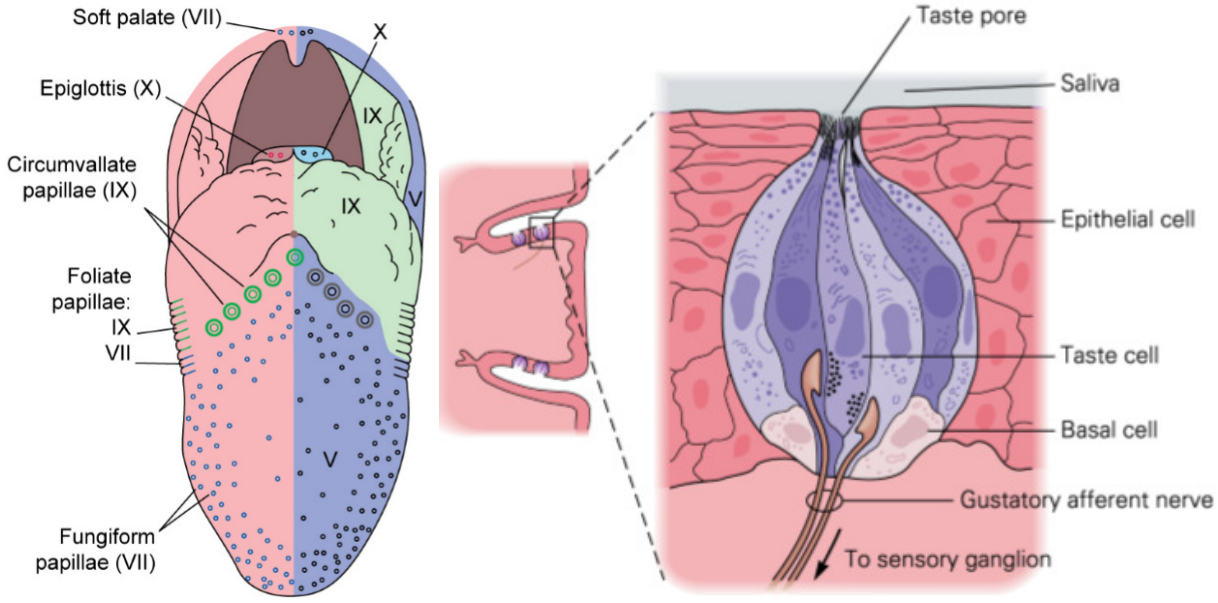
•Function = To protect brain from neuroactive/ neurotoxic substances
-Brain has many different cells, they have receptors on the outside that can change their activity
-Neuroactive and neurotoxic compounds have to be kept out
-Desirable substances (Glucose, essential amino acids, hormones, vitamins) must be allowed to enter

•Permeability
-Oil/Water partition coefficient = "lipophilic" or "hydrophilic" nature of chemical compounds
-More lipophilic compounds pass more easily across the BBB



-Low oil-water partition coefficient/ lipophilicity → low relative extraction/ permeability

Gustation



-Papillae cover the entire surface of tongue, epiglottis, oesophagus

-Papillae don't regenerate

-On the side surface of the papillae, there are invaginations comprised of taste buds

-Each taste bud contains 10-50 individual sensory taste cells which are synapsed with axons of gustatory neurons that butt the ends of these sensory receptors

-Taste cells have access to the external environment through taste pores

-Chemicals in the food are moved to the sensory surface by saliva

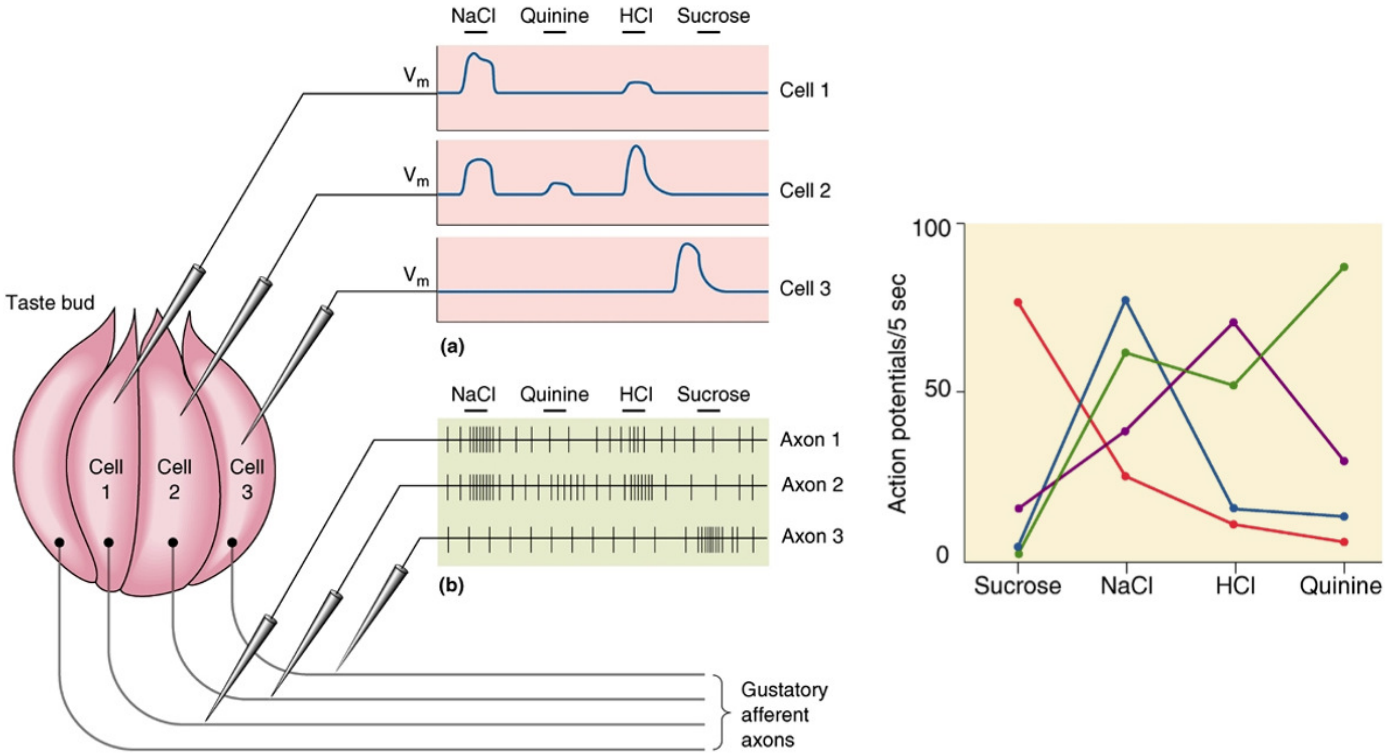
-Ability to produce saliva = ability to sense taste (less saliva is produced with age)

-Basal cells = "progenitor" cells in the basal lamina (limited lifespan)

-1 single nerve axon synapses to 1 taste cell

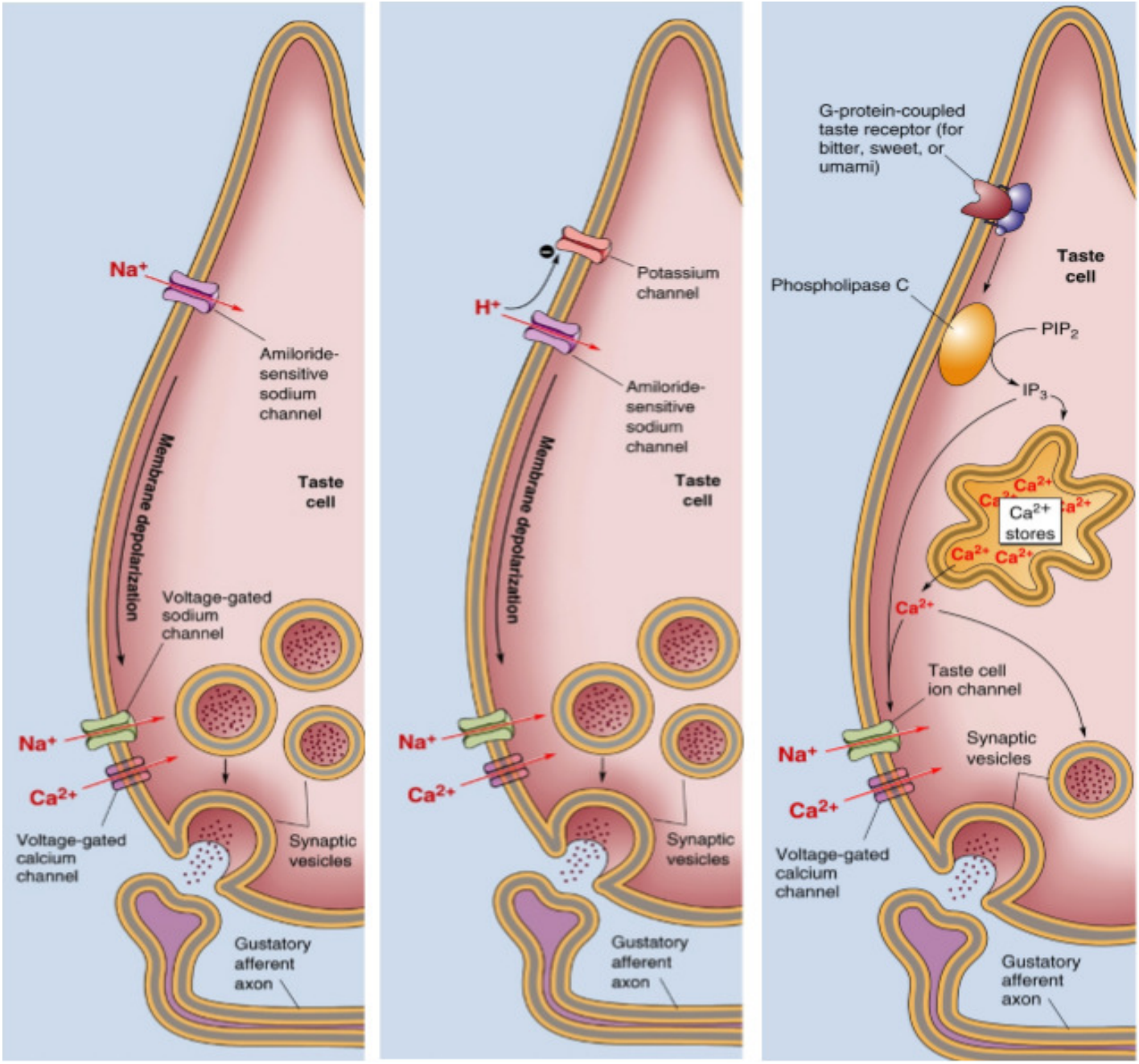
-The axon is NOT part of the sensory receptor and comes from ganglia

-The olfactory receptor is a neuron that has its axon projecting to CNS



-Certain taste cells show specificity and only transduce 1 taste while other cells are broadly tuned (more than 1 taste)

-The signals generated in the sensory receptor are maintained in gustatory axons with fidelity during the transmission process

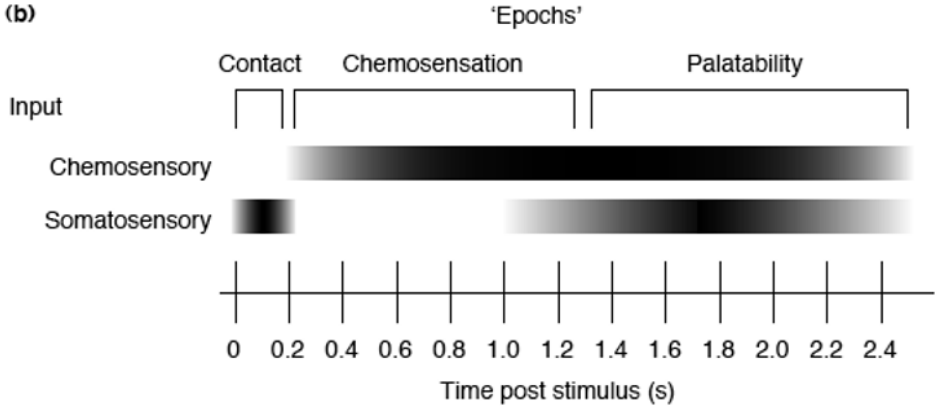


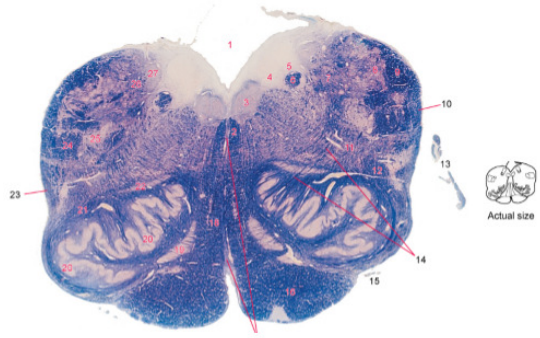
Salty	Sour	Bitter, Sweet or umami
-Saliva liberates Na^+ from food -Na^+ enters the Na^+ channel on cell membrane (epithelial Na^+ channel) -Membrane depolarised -Voltage gated Na^+ and Ca^{2+} channels open -Ca^{2+} enters cell -Neurotransmitter in vesicles released on to sensory fibres -Activates nerve fibre -Depolarisation	-Saliva liberates H^+ from food -H^+ enters through Na^+ channels -H^+ inhibits the K^+ channels and prevents K^+ efflux -Membrane depolarised -Voltage gated Na^+ and Ca^{2+} channels open -Ca^{2+} enters cell -Neurotransmitter in vesicles released on to sensory fibres -Activates nerve fibre -Depolarisation	-Specialised G-protein coupled receptors -Bitter: wide range of receptor subtypes -Sweet and umami: one receptor subtype (2 subunits) -Chemicals bind to GPCR -Phospholipase C activates IP_3 -Ca^{2+} release from intracellular stores -Neurotransmitter in vesicles released on to sensory fibres -Activates nerve fibre -Depolarisation -Small contribution from voltage gated Na^+ and Ca^{2+} channels

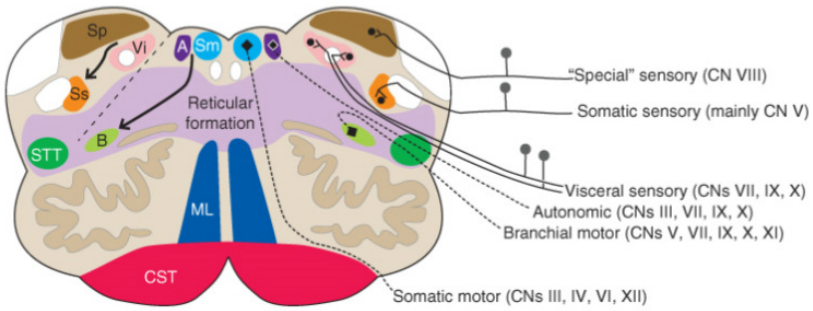
•Nerve fibres
-The taste cell (receptor) communicates with nerve fibre and sends signal
-The nerve fibre leaves the intraoral cavity and communicates with CNS where electric signals are transduced to construct a taste perception

-Primary afferent taste fibres are found in groups of cell bodies (ganglion)
1) Facial nerve: geniculate ganglion
2) Glossopharyngeal nerve: inferior glossopharyngeal ganglion/ petrosal ganglion
3) Vagus nerve: inferior vagal ganglion/ nodose ganglion

-Trigeminal nerve detects heat (e.g. from chilli pepper) – somatosensory sensation, not gustatory
-Somatosensory sensation is the first part of the taste experience before chemosensory sensation



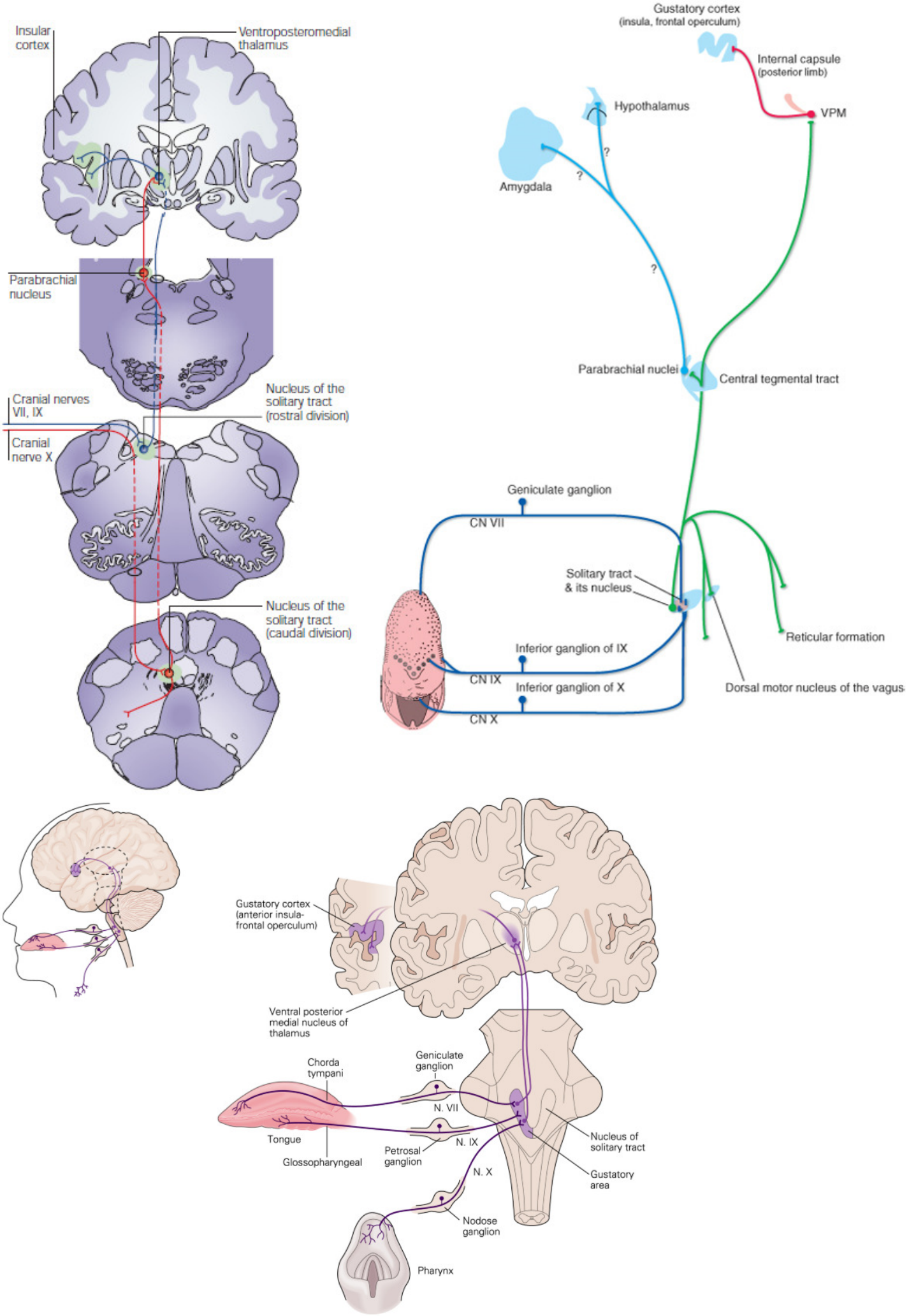




-Section 5: cross-section of tight bundle of fibres that travel through the dorsomedial medulla
-White area surrounding 5: nuclei (cell bodies) where the fibres synapse (NTS)

-All primary afferent taste fibres project to the Nucleus of the Solitary Tract (NTS) in the dorsomedial part of open medulla
-Gustatory nucleus of the NTS is in the rostral 2/3 and **all** the first order neurons (CN7,9,10) synapse
-NTS = first relay station

-NTS neurons project ipsilaterally to the parabrachial nucleus
    -Found at the junction of the pons and midbrain
    -Surrounds the superior cerebellar peduncle (brachium conjunctivum)
        -Nerves that leave the cerebellum and head to red nucleus and cortex form a brachium


Insular cortex
Ventroposteromedial thalamus
Parabrachial nucleus
Cranial nerves VII, IX
Cranial nerve X
Nucleus of the solitary tract (rostral division)
Nucleus of the solitary tract (caudal division)
Gustatory cortex (insula, frontal operculum)
Internal capsule (posterior limb)
Hypothalamus
VPM
Amygdala
?
?
?
Parabrachial nuclei
Central tegmental tract
Geniculate ganglion
CN VII
Solitary tract & its nucleus
Reticular formation
Inferior ganglion of IX
CN IX
Inferior ganglion of X
CN X
Dorsal motor nucleus of the vagus
Gustatory cortex (anterior insula-frontal operculum)
Ventral posterior medial nucleus of thalamus
Chorda tympani
Geniculate ganglion
N. VII
Tongue
N. IX
Petrosal ganglion
Glossopharyngeal
N. X
Nucleus of solitary tract
Gustatory area
Nodose ganglion
Pharynx

Visceral Motor System

•Motor system

Somatic motor system	Viscera motor system
Rapid (myelinated)	Slow (lightly or unmyelinated)
Contraction of one muscle that's innervated	Multiple and widespread
Precise and accurate	Wide coordinated and graded control -Activity in one region requires activity in other regions to shift -Intrinsic level of activity is regulated
Only peripheral targets	Peripheral and deep visceral targets
Commands only skeletal muscle	Commands all tissue and organ except skeletal (smooth muscle, cardiac muscle, glandular cells)
Within CNS	Outside CNS
Monosynaptic pathway (lower motor neuron-skeletal muscle)	Disynaptic pathway (Synapse at ganglion and at the target structure)

•Divisions of autonomic nervous system

-2 divisions work in a concerted, coordinated way, allowing another to be manifested by being inactivated

Sympathetic division		Parasympathetic division	
Increased heart rate and blood pressure	Heart and **blood vessels**	Slower heart rate, fall in pressure	Heart
Depressed digestive function	Guts	Increased digestive functions	Guts
Mobilized glucose reserves	Liver	Store glucose	Liver
Orgasm and urine storage	Gonads	Erection, lubrication and micturition	Gonads
		Decreased sweating	Skin
Short preganglionic fibre		Long preganglionic fibre	
Long postganglionic fibre		Short preganglionic fibre	
Ganglion close to brainstem and spinal cord		Ganglion on the surface of structure being regulated	

•Sympathetic division

▪Sympathetic chain/trunk

-Interconnected sympathetic ganglia running the entire length of vertebral column

-In the cervical region, sympathetic ganglia are joined to form 3 large ganglia

-Superior

-Middle

-Inferior

-In the thoracic, lumbar and sacral region, there are paravertebral ganglia associated with vertebral levels

-2 sympathetic chains fuse in the midline just below the coccyx to form the ganglion impar (common ganglion)

-Prevertebral ganglia found on aorta or organ of innervation

-On abdominal aorta, there are celiac, superior mesenteric and inferior mesenteric ganglia associated with the major arteries

▪Sympathetic supply

1) T1-L2/3 – Local structures

-Leave lateral horn of the spinal cord and travel in ventral roots to join the spinal nerve

-Enter sympathetic ganglion and synapse on sympathetic postganglionic cell

-Postganglionic fibre leaves and re-enters spinal nerve to enter dorsal and ventral primary rami

-Ventral rami: Visceral structures

-Dorsal rami: Skin and muscle of neck and back

-Supply local structures: blood vessels, intercostal and abdominal muscles, back muscles, anterior part of thumb

2) Above T1 and below L2/3 – Distant structures

-Leave IML and travel in ventral roots to join the spinal nerve

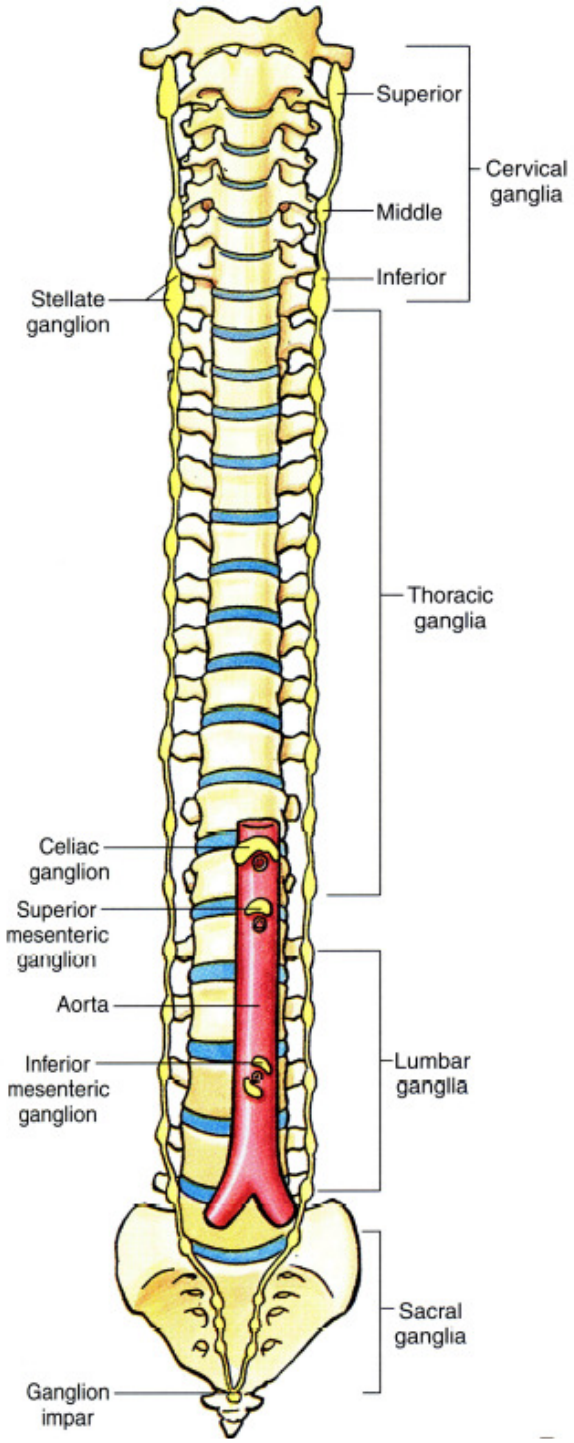
-Enter the sympathetic ganglion

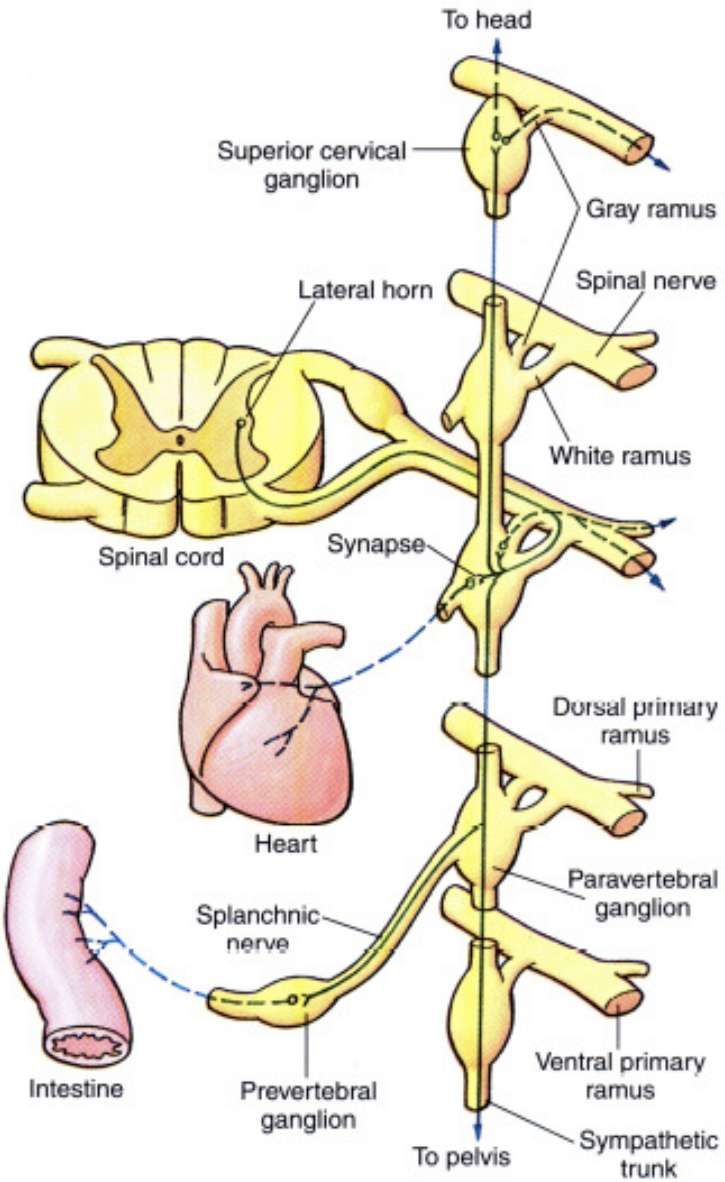
-Ascend and descend within sympathetic chain
-Synapse on postganglionic cell
-Postganglionic fibre leaves and re-enters spinal nerve to enter dorsal and ventral primary rami
-Or postganglionic fibre hitchhikes on cranial nerve
-Supply distant structures: head, lower extremities

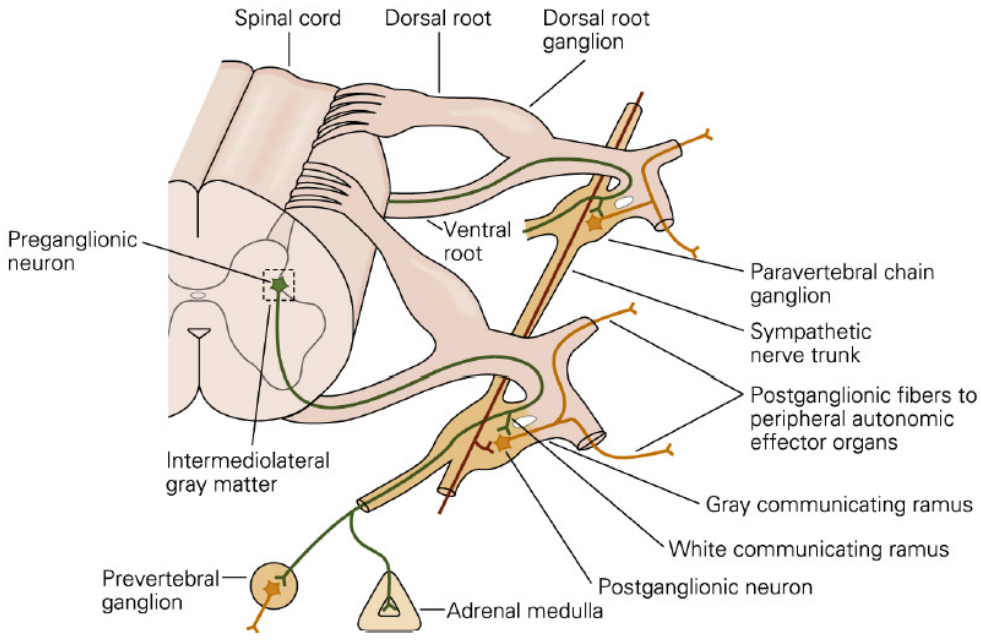
3) Viscera – Medial structures
a) Heart
-Leave IML and travel in ventral roots to join the spinal nerve
-Enter sympathetic ganglion (inferior cervical ganglion = stellate ganglion)
-Synapse on post-ganglionic cell
-**Postganglionic** fibre leaves the ganglion and forms a **cardiac nerve**
-Supply cardiac muscle

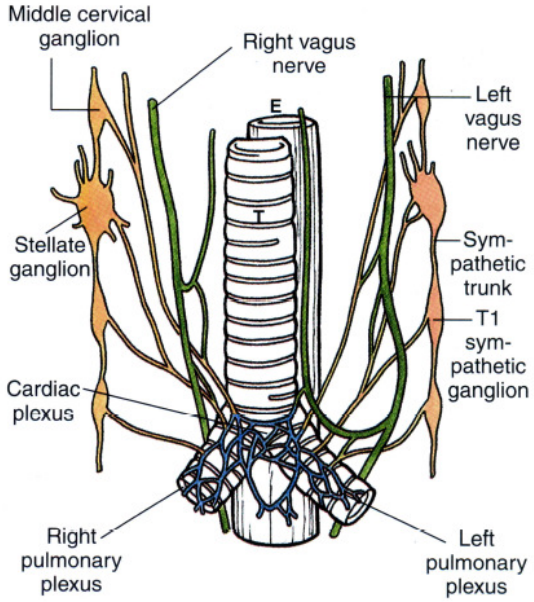
b) Guts and gonads
-Leave IML and travel in ventral roots to join the spinal nerve
-Enter sympathetic ganglion
-Ascend/descend/stay within sympathetic chain
-**Preganglionic** fibre leaves the ganglion medially and forms a **splanchnic nerve**
-Synapse on prevertebral ganglion sitting on abdominal aorta
-Postganglionic fibre hitchhikes on blood vessel (and supplies it)
-Supply gut or gonad

4) Adrenal medulla
-Innervated by preganglionic fibres NOT postganglionic fibres
-Adrenal medulla contains modified ganglionic cells (is almost a ganglion itself)

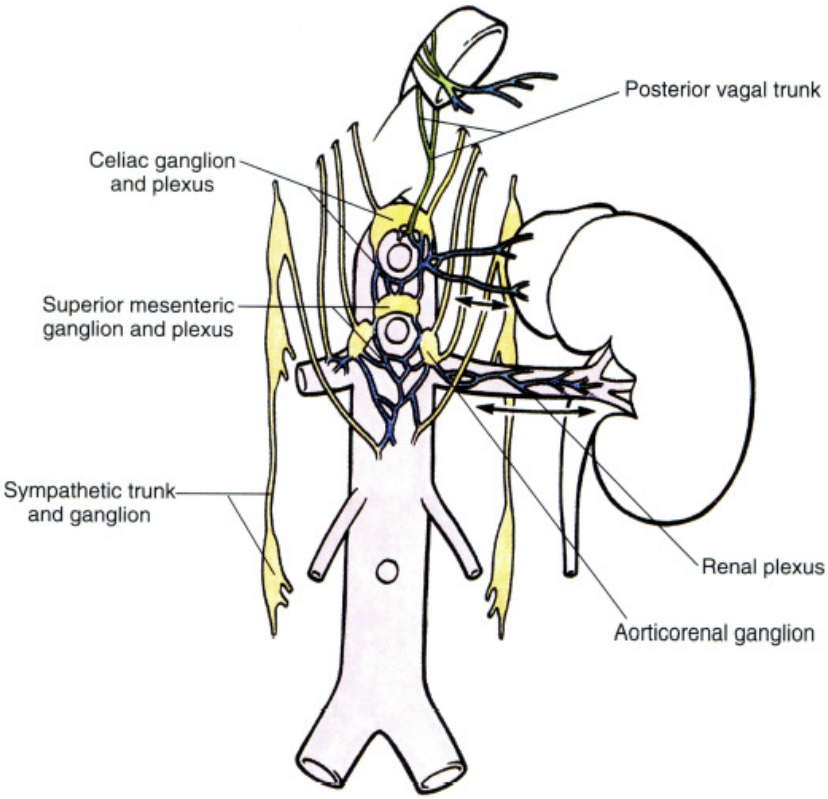

Superior
Middle
Inferior
Cervical ganglia
Stellate ganglion
Thoracic ganglia
Celiac ganglion
Superior mesenteric ganglion
Aorta
Inferior mesenteric ganglion
Lumbar ganglia
Sacral ganglia
Ganglion impar

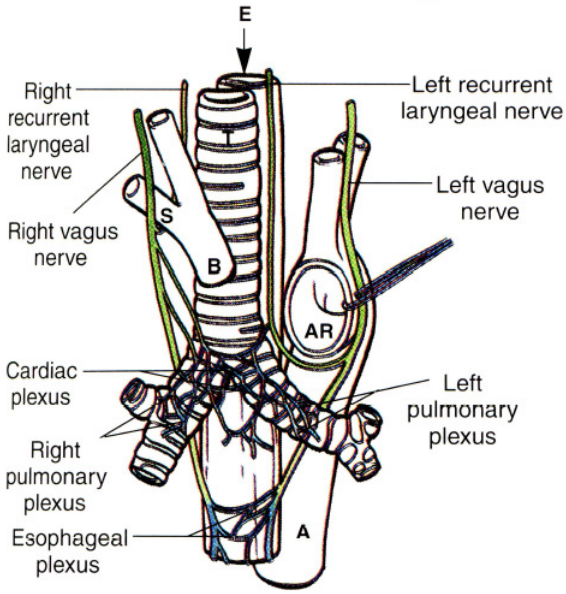

To head
Superior cervical ganglion
Gray ramus
Spinal nerve
Lateral horn
White ramus
Spinal cord
Synapse
Heart
Dorsal primary ramus
Paravertebral ganglion
Splanchnic nerve
Intestine
Prevertebral ganglion
Ventral primary ramus
To pelvis
Sympathetic trunk


Spinal cord
Dorsal root
Dorsal root ganglion
Preganglionic neuron
Ventral root
Paravertebral chain ganglion
Sympathetic nerve trunk
Postganglionic fibers to peripheral autonomic effector organs
Intermediolateral gray matter
Gray communicating ramus
White communicating ramus
Postganglionic neuron
Prevertebral ganglion
Adrenal medulla



Cardiopulmonary plexus:
-Nerve mass that supplies the heart and lungs
-Formed by postganglionic fibres from inferior cervical ganglion and T1-2 thoracic ganglion



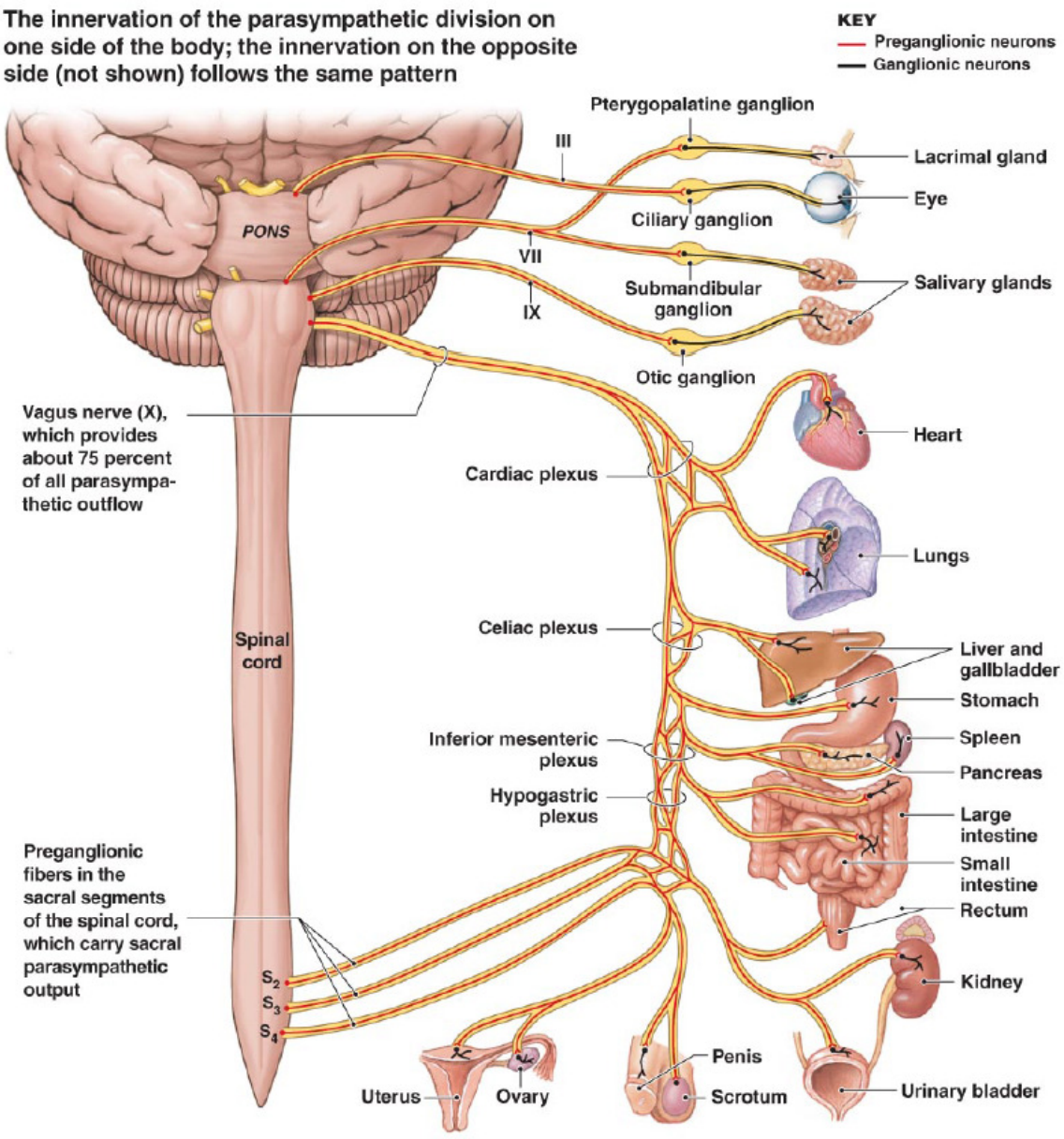


-Right and left vagus nerves join the cardiac plexus
-Cardiac plexus contains:
  -Sympathetic postganglionic fibres (cardiac nerves)
  -Parasympathetic postganglionic neurons (cell bodies and short fibres innervating the heart)
  -Vagal fibres synapsing onto the parasympathetic postganglionic neurons

•Parasympathetic division
-Parasympathetic fibres do NOT innervate blood vessels
-Changes in blood pressure is a consequence of parasympathetic activity on cardiac output
-Parasympathetic fibres innervate same regions as sympathetic fibres (except blood vessels)

▪Parasympathetic ganglia
1) Cranial nerves
-Oculomotor (CN III) – pupillary activity
-Facial (CN VII) and glossopharyngeal (CN IX) – production of saliva, tears and mucosa
-Vagus (X) – all visceral structures from **neck to splenic flexure** (in pelvic cavity)
-Emerges from lateral medulla, related to olivary eminence
-Preganglionic fibres communicate with the plexus and synapse on the postganglionic neurons within the ganglia lying on the walls of visceral organs
-Lungs, GIT, liver, sensory fibres of reproductive system

2) Sacral spinal cord (S2-4)
-Below splenic flexure (pelvic cavity not innervated by the vagus nerve)
-Sacral preganglionic neurons originate from **sacral parasympathetic nucleus** between the dorsal and ventral horns
-They leave with sacral spinal nerves and enter the plexus
-They synapse on postganglionic neurons lying on the organs and short postganglionic fibres supply the organs
-Gut, motor control of reproductive system



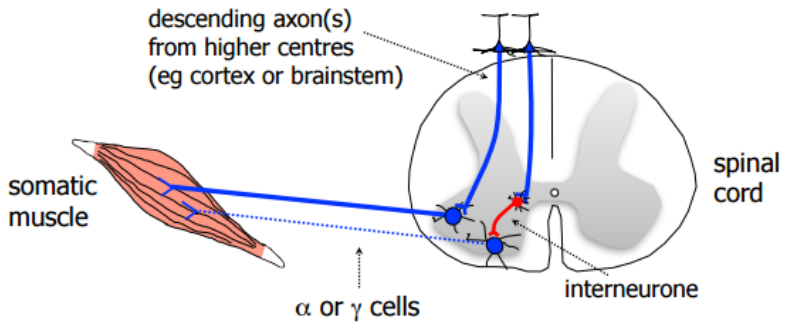
Motor Pathways

-There are two types of movement:

Goal-driven	Automated
Voluntary	Automatic, learnt and familiar
Cortex	Cortex, cerebellum and basal ganglia
Skilled and basic pathways	Skilled and basic pathways

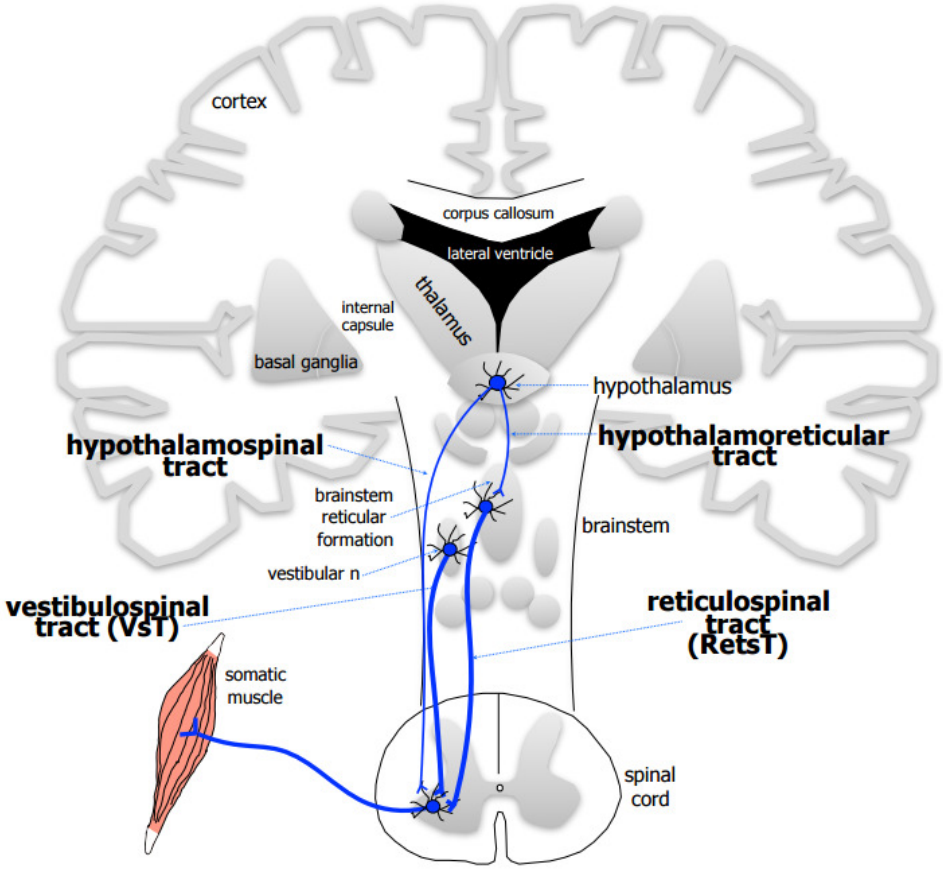
-Automated movement: cerebellum helps you learn a new movement then the learnt movement is stored in basal ganglia; cortex activates the programmed movement by sending input to basal ganglia

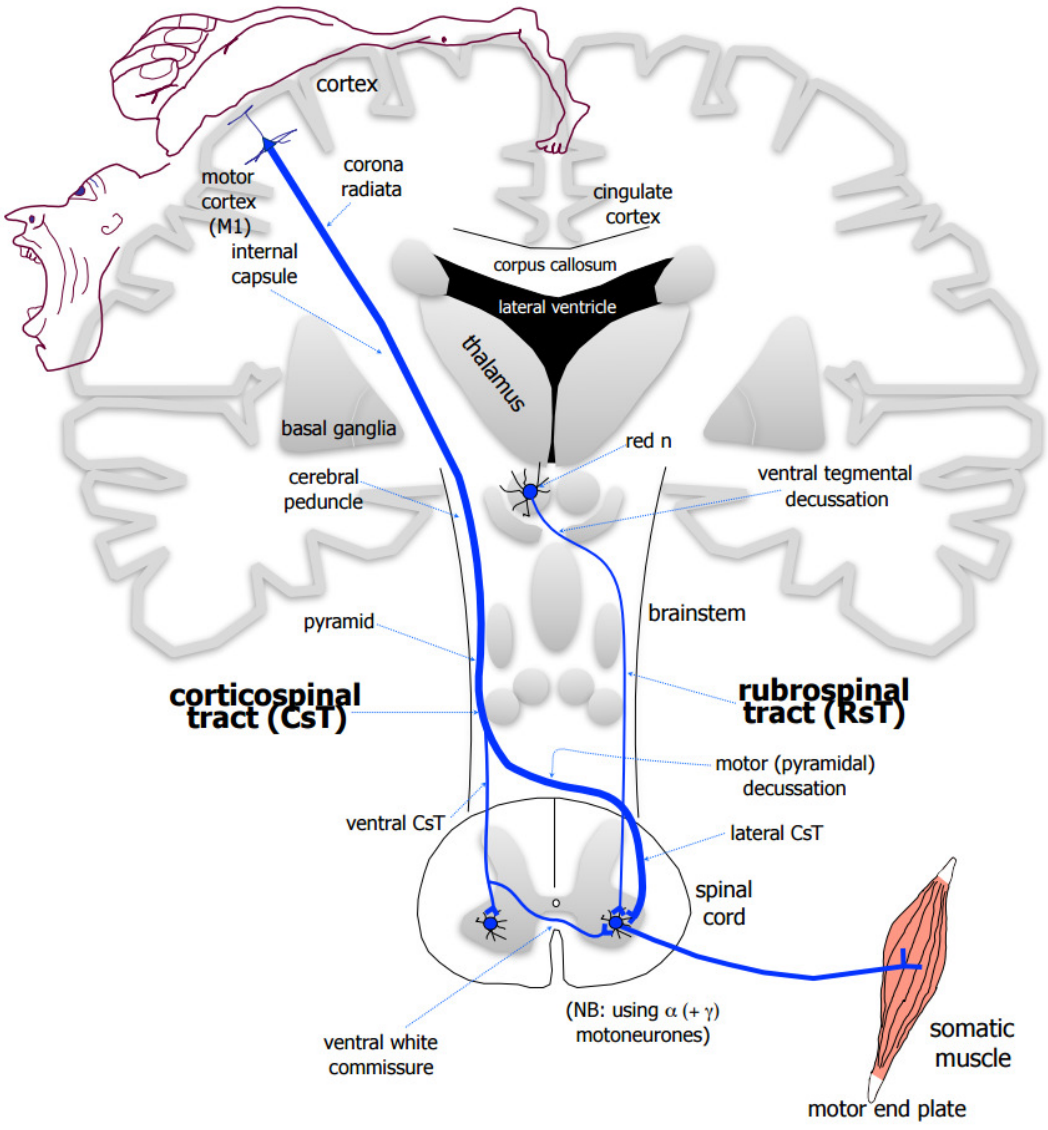
-Motor pathways are **descending, output pathways** related with muscles and movements
-Upper motor neurons are excitatory (glutamate and/or aspartate as neurotransmitter)
-The pathways can lead to:
    -Excitation - UMN direct synapse with LMN
    -Inhibition - UMN synapse with inhibitory interneuron
        -Inhibit stretch reflex – relax the muscle
        -Inhibit patellar reflex – prevent exaggerated reflex
-Lower motor neurons are α cells (skilled) and γ cells (basic)
-Lesion in the descending pathway leads to spastic paralysis and exaggerated reflexes



•Motor pathways

Basic	Skilled
Medial set – medial spinal cord	Lateral set – lateral spinal cord
Phylogenetically older; crucial for life	Phylogenetically newer; improves quality of life
γ neurons (> α neurons)	α neurons (> γ neurons)
Proximal muscles	Distal muscles (fingers and hands)
Basic, gross movements -Maintain posture/ locomotion	Skilled, fine movement
Goal-driven and automated -Taking one step forward to reach for an object	Goal-driven and automated
Voluntary and involuntary (postural reflexes)	Voluntary
Brain stem -Vestibulospinal tract (vestibular nucleus) -Correct balance -Reticulospinal tract (reticular formation) -Generate locomotion, control posture, muscle tone and stretch reflex	Cortex -Corticospinal tract
Hypothalamus -Hypothalamoreticular tract -Hypothalamospinal tract -Control viscera for homeostasis -Control emotional motor behaviour to respond to the environment (especially in emergency)	Red nucleus (midbrain) -Rubrospinal tract (helps corticospinal tract)


cortex
corpus callosum
lateral ventricle
thalamus
internal capsule
basal ganglia
hypothalamus
hypothalamospinal tract
hypothalamoreticular tract
brainstem reticular formation
brainstem
vestibular n
vestibulospinal tract (VsT)
reticulospinal tract (RetsT)
somatic muscle
spinal cord


cortex
motor cortex (M1)
corona radiata
cingulate cortex
internal capsule
corpus callosum
lateral ventricle
thalamus
basal ganglia
red n
cerebral peduncle
ventral tegmental decussation
pyramid
brainstem
corticospinal tract (CsT)
rubrospinal tract (RsT)
motor (pyramidal) decussation
ventral CsT
lateral CsT
spinal cord
(NB: using α (+ γ) motoneurones)
ventral white commissure
somatic muscle
motor end plate

▪Corticospinal tract

-Origin: Layer V excitatory neurons of

-Primary motor cortex

-Premotor cortex and supplementary motor area

-Primary sensory cortex

-Cingulate cortex

-One cell innervates one muscle group according to the homunculus

-Spatial representation is related to density of innervated receptors = how skilled the muscle is

-1 million axons forming long white matter path: corona radiata and internal capsule

-Internal capsule contains other tracts e.g. thalamocortical, thalamostriatal axons

-Cerebral peduncles

-90% of fibres (forming the lateral corticospinal tract) decussate at the pyramidal decussation (caudal medulla) while 10% of fibres (forming the ventral corticospinal tract) decussate at the ventral white commissure (spinal cord)

-Termination:

-Ventral horn: low motor neurons (α, γ)

-Dorsal horn: **sensory gating** – S1 and cingulate cortex tone/dampen down all areas of afferentation except the area you want to focus your attention to – amplified sensation in area being stimulated

-No recovery after lesion in this tract (c.f. recovery for basic movement pathways)

-Assisted by rubrospinal tract

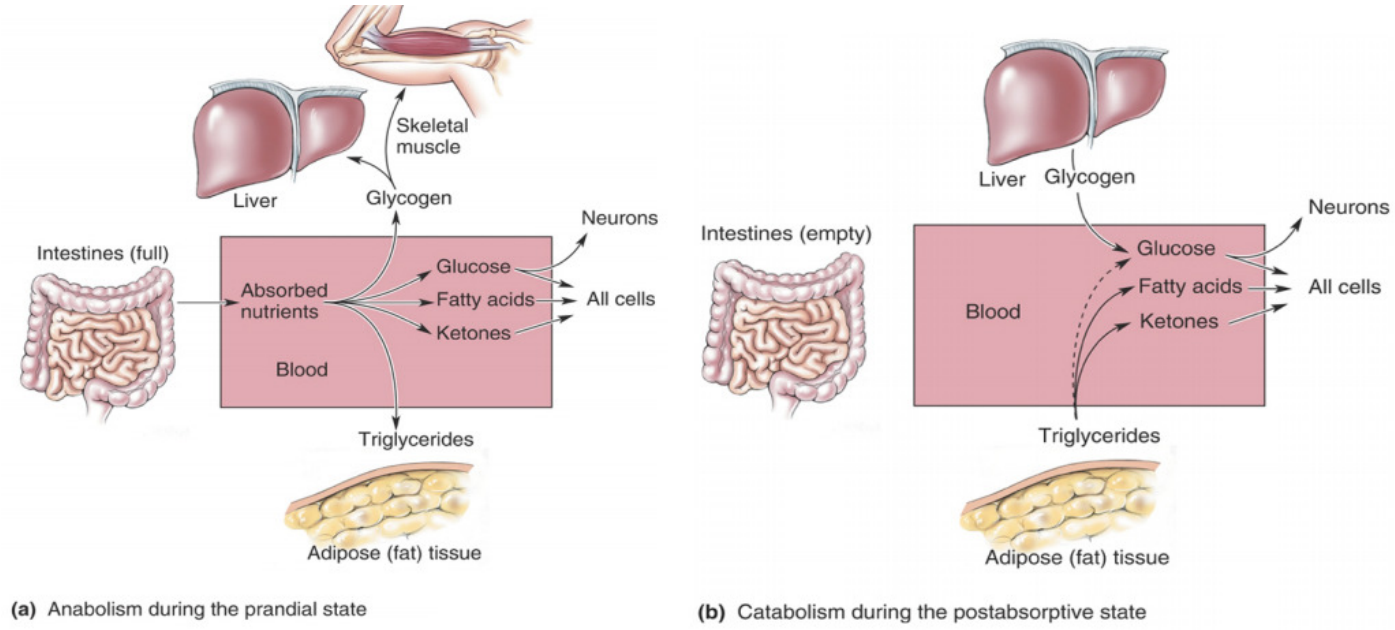
•Role of cortex

Cortex	Location	Function	Action	Subcortical help	Lesion
Parietal	Caudal parietal lobe	-Attention to the world -Sensory gating	Identify the object to attend to	Pulvinar (decide what's relevant and irrelevant)	-Attention and recognition loss -Neglect syndrome
Secondary motor (SMA + PM)	Caudal frontal lobe	-Plan, program and imagine movements -Maintain posture	Planning various sets of movements	Basal ganglia	-No complex moves -Forced grasp reflex -Posture/tone loss
Prefrontal	Rostral frontal lobe	Moral and social sense	Selection of appropriate program	Basal ganglia	-No moral and social consideration
Primary motor	Precentral gyrus and paracentral lobule	Generate simple movement (extension/ flexion)	Execution	Cerebellum	-No movement (paralysis) -No control of reflexes

Hypothalamus II: Feeding and Drinking Behaviour

▪Homeostasis
-Maintenance of the internal environment of the body within a narrow physiological range
-Role of hypothalamus: regulates energy balance, temperature, sleep
-Three components of neuronal response:
-Endocrine (humoral) response – Pituitary gland
-Autonomic (visceromotor) response – Sympathetic and parasympathetic preganglionic neurons
-Somatic motor response – Higher cortex to drive behaviour

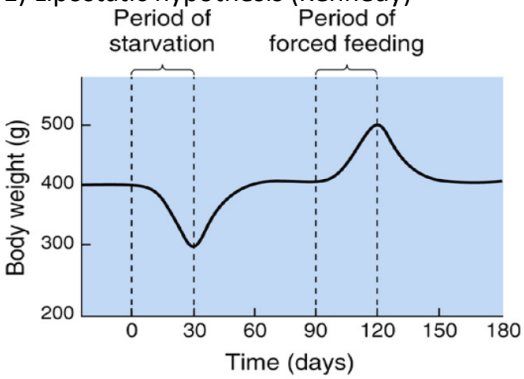
▪Energy balance
-Intake = expenditure → Normal body fat
-Intake > expenditure → Obesity
-Intake < expenditure → Starvation



(a) Anabolism during the prandial state
(b) Catabolism during the postabsorptive state

-During the prandial state, excess nutrients are converted to glycogen for storage in liver and skeletal muscle and to triglycerides for storage in adipose tissue
-During the postabsorptive state, glycogen is converted back and fat is broken down to ensure a constant supply of nutrients

•In vivo experiments
1) Lipostatic hypothesis (Kennedy)



-A rat will adjust its food intake so precisely to its energy needs that its fat stores remain almost constant
-The rat's body weight is maintained at a constant point even after periods of starvation and excessive eating
-Hypothalamic damage permits excessive intake and causes obesity

2) Parabiosis of obese and normal mice (Coleman)
-The obese mouse became normal weight after parabiosis

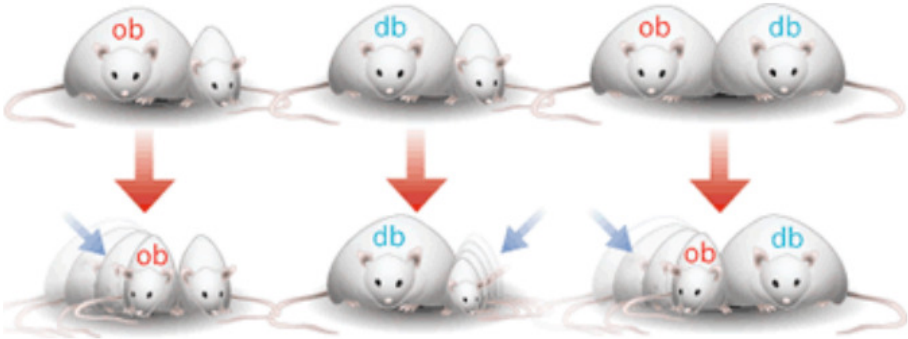
-There is a humoral (blood-borne) factor provided by the normal mouse that travels across to the obese mouse's brain to modulate its food consumption behaviour
-It communicates to the brain about the level of body fat
-Obese mouse is unable to produce sufficient "satiety factor" to regulate its food consumption

3) Discovery of leptin
-Leptin is an endocrine, plasma protein encoded by the *obese* gene
-Released from adipocytes in proportion to how much adipose there is
-Functions to regulate the body fat stores
-Leptin release decreases appetite and increases energy expenditure (metabolism)
-Leptin depletion incites adaptive responses to fight starvation and encourage feeding behaviour

-Leptin deficiency can cause obesity in some people
-Daily injection of leptin can reduce the body weight and fat by reducing food intake and increasing energy expenditure

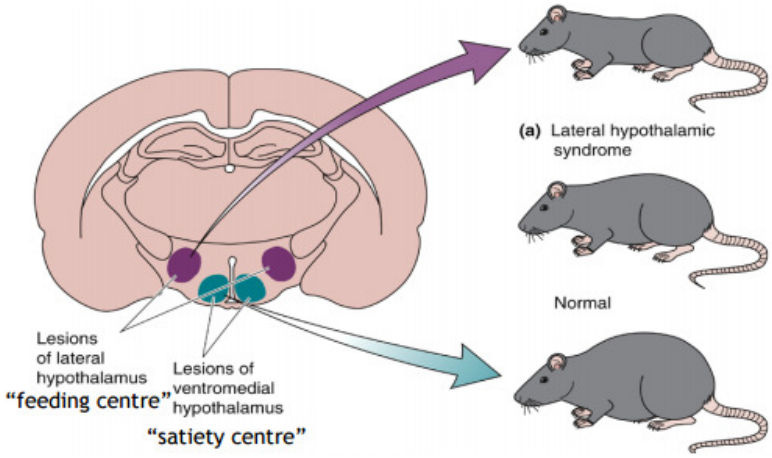
-Leptin receptor deficiency can cause obesity

4) Leptin resistance – Parabiosis of normal with genetically diabetic mice



-Diabetic mouse caused both normal and obese mouse to lose weight and starve to death
-High concentrations of leptin from the diabetic mouse (high level of adiposity) travelled across and activated the normal/ obese mouse's brain to drive starvation
-Diabetic mouse lacks a leptin receptor in hypothalamus

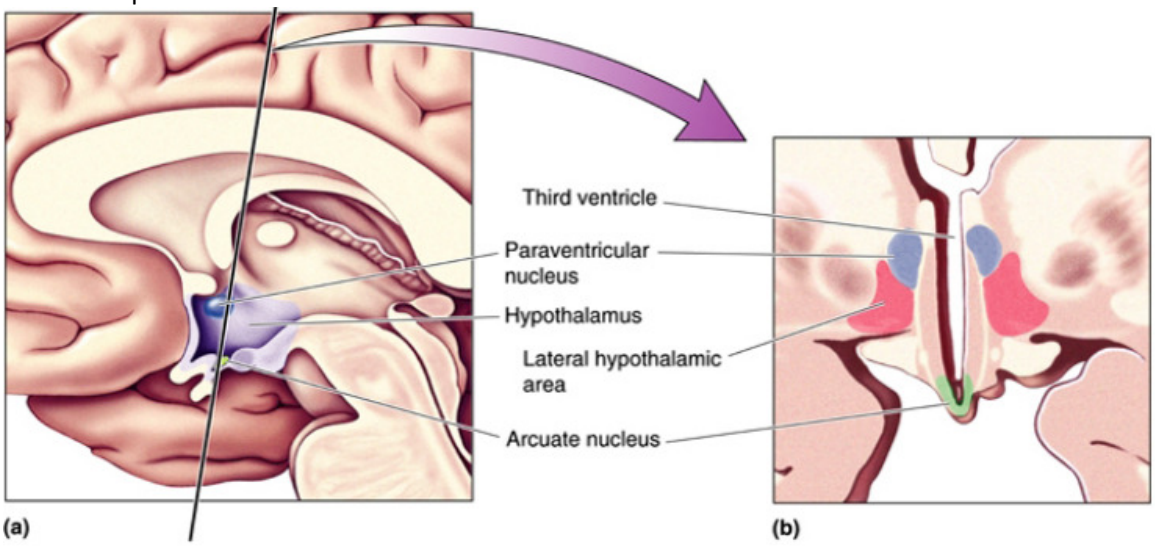
5) Hypothalamic lesions and adiposity



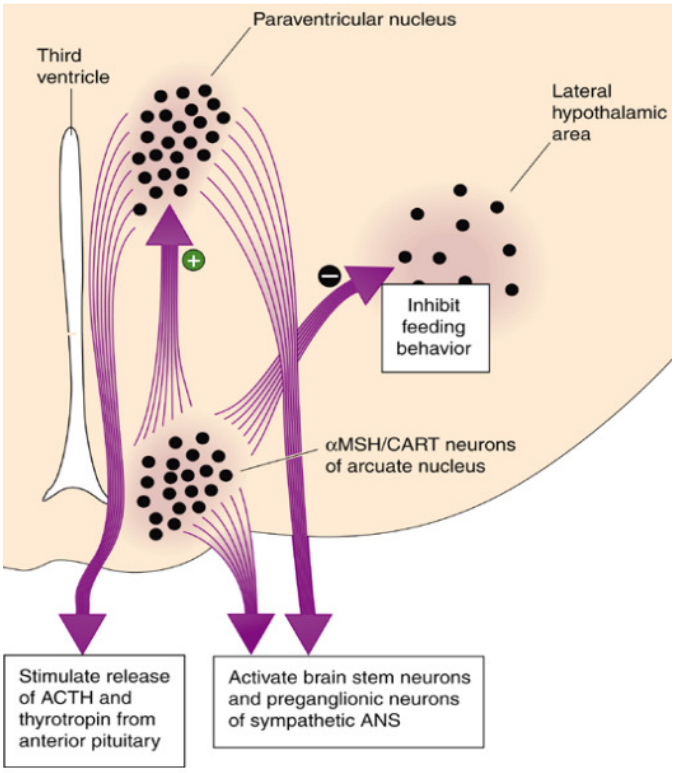
-Ventromedial hypothalamus = satiety centre
-Lesion of ventromedial hypothalamus led to insatiable hunger and abnormal obesity in rat
-Lateral hypothalamus = feeding centre
-Hyperphagia/obesity: Activation of the lateral hypothalamus in cats resulted in intense eating of edible and inedible objects
-Aphagia/starvation: Bilateral lesions of the lateral hypothalamus in rats and cats causes them to stop eating; they refuse to eat even when food is placed in their mouths

6) Dual-centre hypothesis
-Lesions restricted to the ventromedial nucleus of the hypothalamus were neither necessary nor sufficient for, and did not contribute to, the production of hypothalamic obesity
-Hypothalamic lesions and knife cuts that do produce obesity damage the nearby ventral noradrenergic bundle or its terminals
-Dual-centre hypothesis is rejected

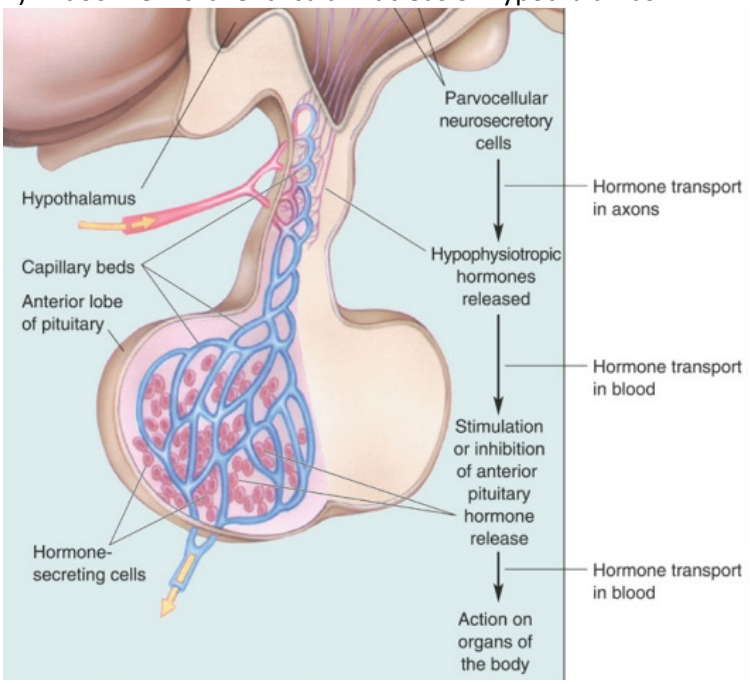
•Arcuate nucleus
-Located at the base of the third ventricle, in periventricular zone
-Contains specialised form of BBB and samples substances in the CSF
-Detects leptin level in blood



•Effects of elevated leptin levels on the hypothalamus
-Activation of arcuate neurons that release α-MSH and CART neuropeptides
-Anorectic peptides = diminish appetite
-Anorectic peptides project to regions that orchestrate coordinated response of endocrine, autonomic and somatic motor responses
-Inhibits feeding behaviour and increases metabolism to regulate energy balance



1) Endocrine: Paraventricular nucleus of hypothalamus



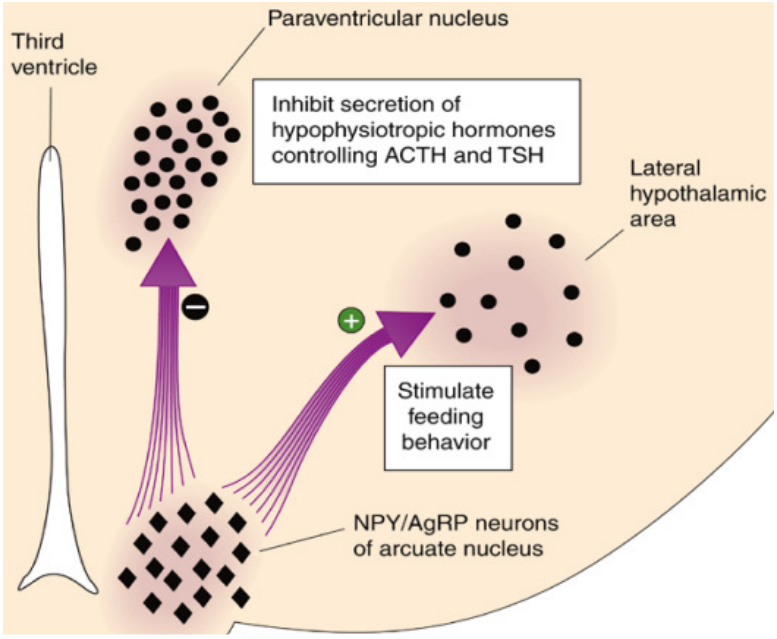
	HPA axis	HPT axis
Hypophysiotropic hormones	CRH	TRH
Anterior pituitary hormones	ACTH	TSH
Hormones released by adrenal and thyroid gland	Cortisol	Thyroxine (T4) and triiodothyronine (T3)
Effect on metabolism	Increase in gluconeogenesis in liver and carbohydrate metabolism	Increase in basal metabolic rate

-Paraventricular nucleus also connects directly to preganglionic neurons of SNS and PNS

2) Autonomic: Intermediolateral gray matter of spinal cord
-Activation of SNS by arcuate and paraventricular nuclei
-↑ Body temperature by shivering
-↑Thermogenesis in brown adipose tissue

3) Somatic motor: Lateral hypothalamus
-Inhibit feeding behaviour

•Effects of decreased leptin levels on the hypothalamus
-Activation of arcuate neurons that release NPY and AgRP
-Orexigenic peptides = increase appetite
-Opposite to the effects of α-MSH and CART
-AgRP is an antagonist of the MC4 receptor on lateral hypothalamic neuron which inhibits feeding behaviour when activated by agonist α-MSH
-Orexigenic peptides project to regions that orchestrate coordinated response of endocrine, autonomic and somatic motor responses
-Stimulates feeding behaviour and reduces metabolism (energy conserved until next feeding) to regulate energy balance



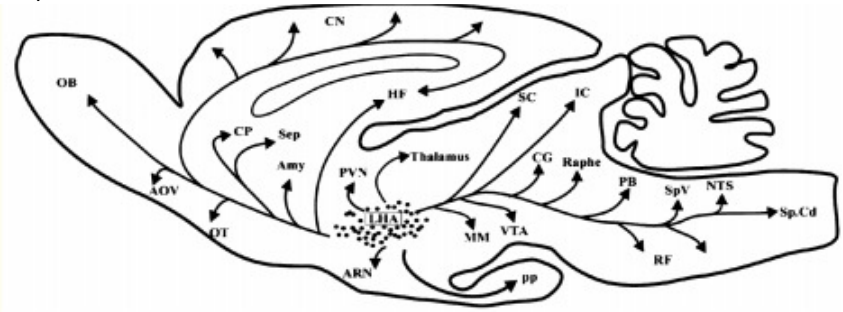
1) Endocrine: Paraventricular nucleus
-NPY and AgRP inhibit secretion of TRH and CRF (hypophysiotropic hormones controlling ACTH and TSH)
-Reduce TSH and ACTH release from anterior pituitary and subsequent activation of glands of the body

2) Autonomic: Brainstem; dorsal motor nucleus of vagus, nucleus ambiguus
-Activation of PNS by arcuate and paraventricular nuclei

3) Somatic motor: Lateral hypothalamus
-Activation of neurons intrinsic to lateral hypothalamus + axons of mfb (medial forebrain bundle) passing through the lateral hypothalamus
-Increase in Melanin Concentrating Hormone (MCH) and Orexin – peptide neurotransmitters
-These NTs inform cortex about leptin levels
-Engages somatic motor systems to search for food
-Stimulates feeding behaviour

-Lateral hypothalamic peptidergic projections are widespread over ALL areas of cortex (somatomotor system, brainstem, forebrain):

MCH



Orexin