WEEK 1 & 2

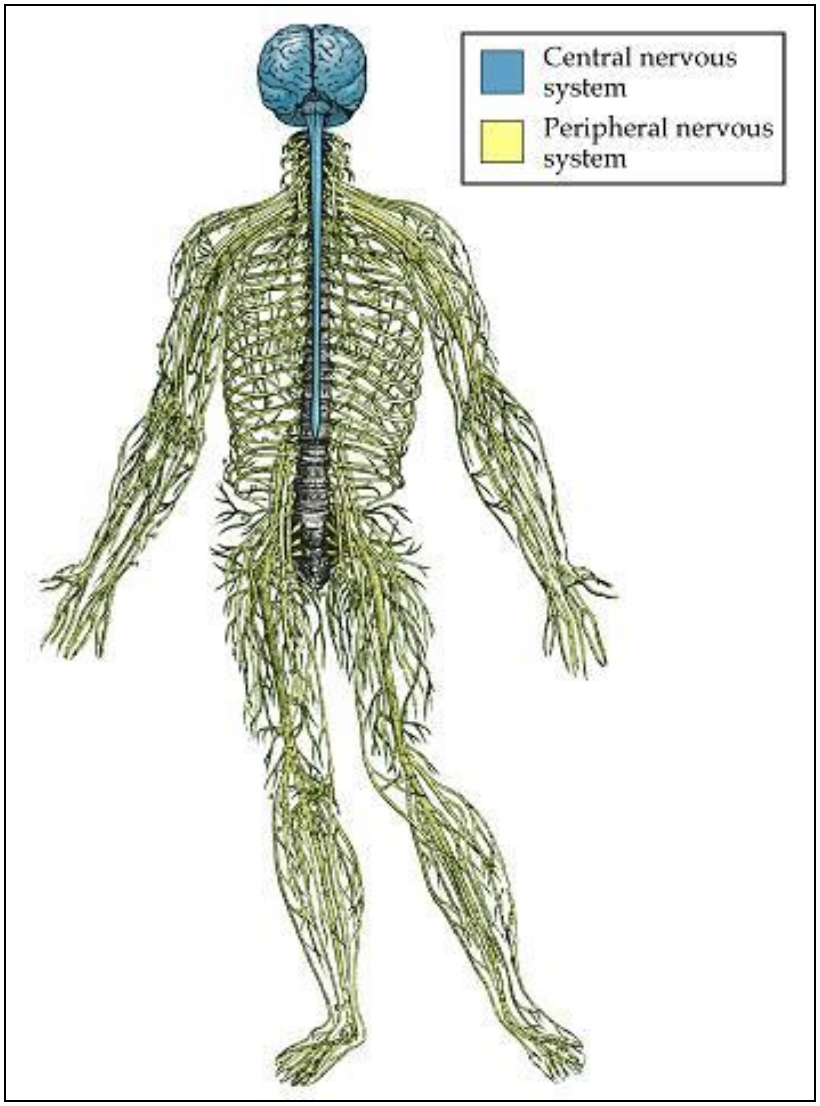
BRAIN ANATOMY

Learning objectives

- Know the major subdivision of the brain
- Know about brain areas implicated in learning
- Know about brain areas implicated in movement control
- Know about the brain’s protection mechanisms

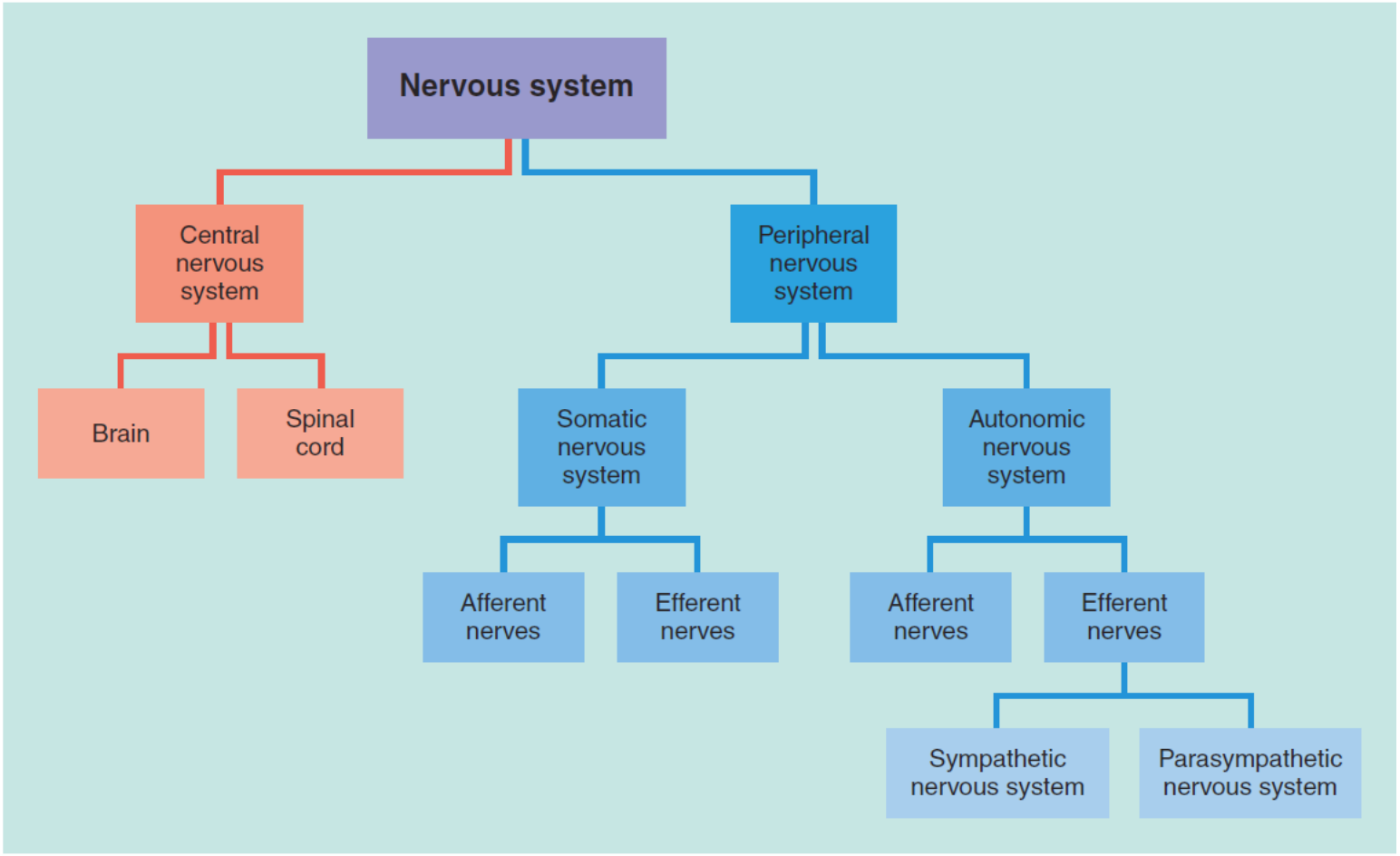
Learning objectives

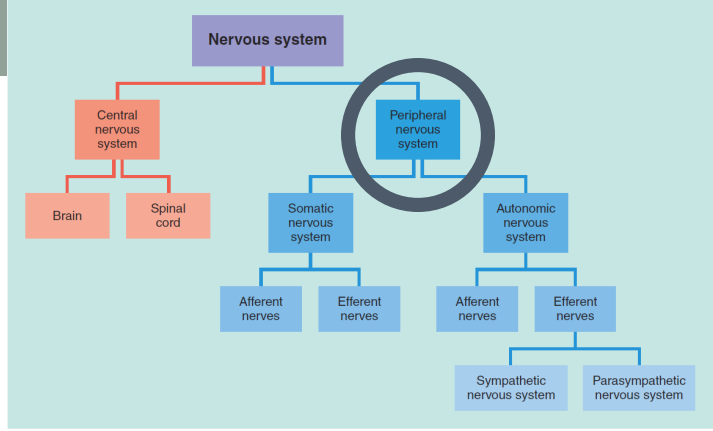
Divisions of the Nervous System



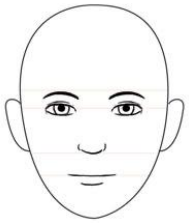
- CNS (central nervous system)
  - Brain, Spinal Cord
  - 12 pairs of cranial nerves (originate from cranium)
- PNS (peripheral nervous system)
  - 31 pairs of spinal nerves
  - Somatic and autonomic nervous system
  - Serves to bring information into the CNS and to carry signals out of the CNS

Divisions of the Nervous System



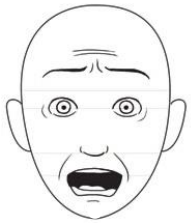


- **Peripheral Nervous System**
  - **Somatic nervous system**
    - Afferent nerves (sensory)
    - Efferent nerves (motor)
      - **“voluntary control” (e.g., muscle contraction)**
  - **Autonomic nervous system**
    - Sympathetic and parasympathetic nerves
    - Both are efferent.
    - Sympathetic and parasympathetic nerves generally have opposite effects.
      - **”involuntary control” (e.g., blood vessel diameter)**



Parasympathetic

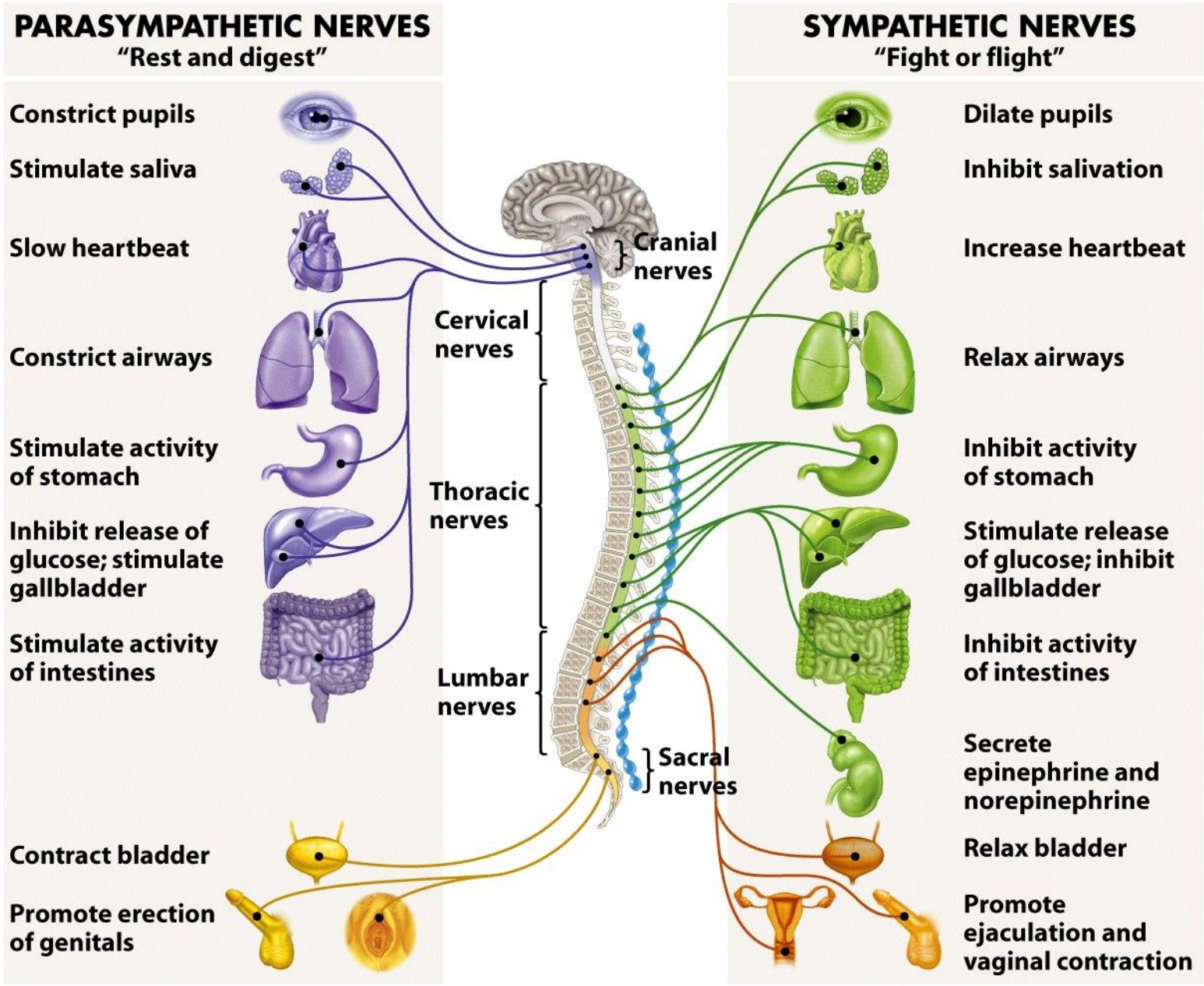
- Energy Conservation
  - Decreased heart rate and blood pressure
  - Pupil constriction
  - Decreased sweat gland activity
  - Salivation
  - Gastric Secretion
- Exits Cranial and Sacral regions of the spinal cord
- Main neurotransmitter= Acetylcholine

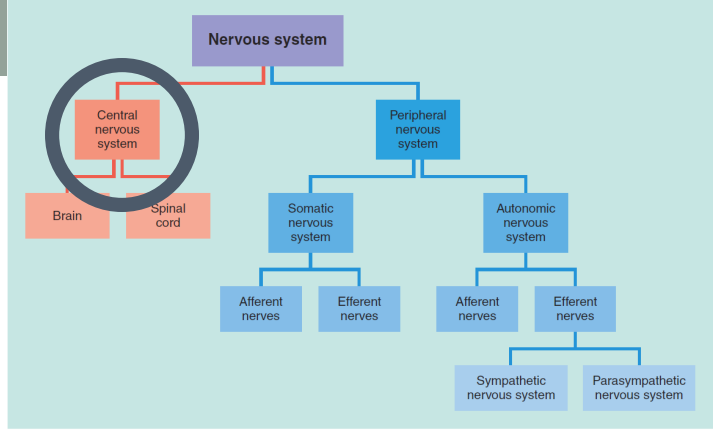


Sympathetic

- Fight-or-Flight Response
  - Elevated heart rate and blood pressure
  - Pupil dilation
  - Increased sweat gland activity
  - Dry mouth
  - Increased blood flow to muscles
- Exits Thoracic-Lumbar region of the spinal cord
- Main neurotransmitter= Norepinephrine

Divisions of the Nervous System





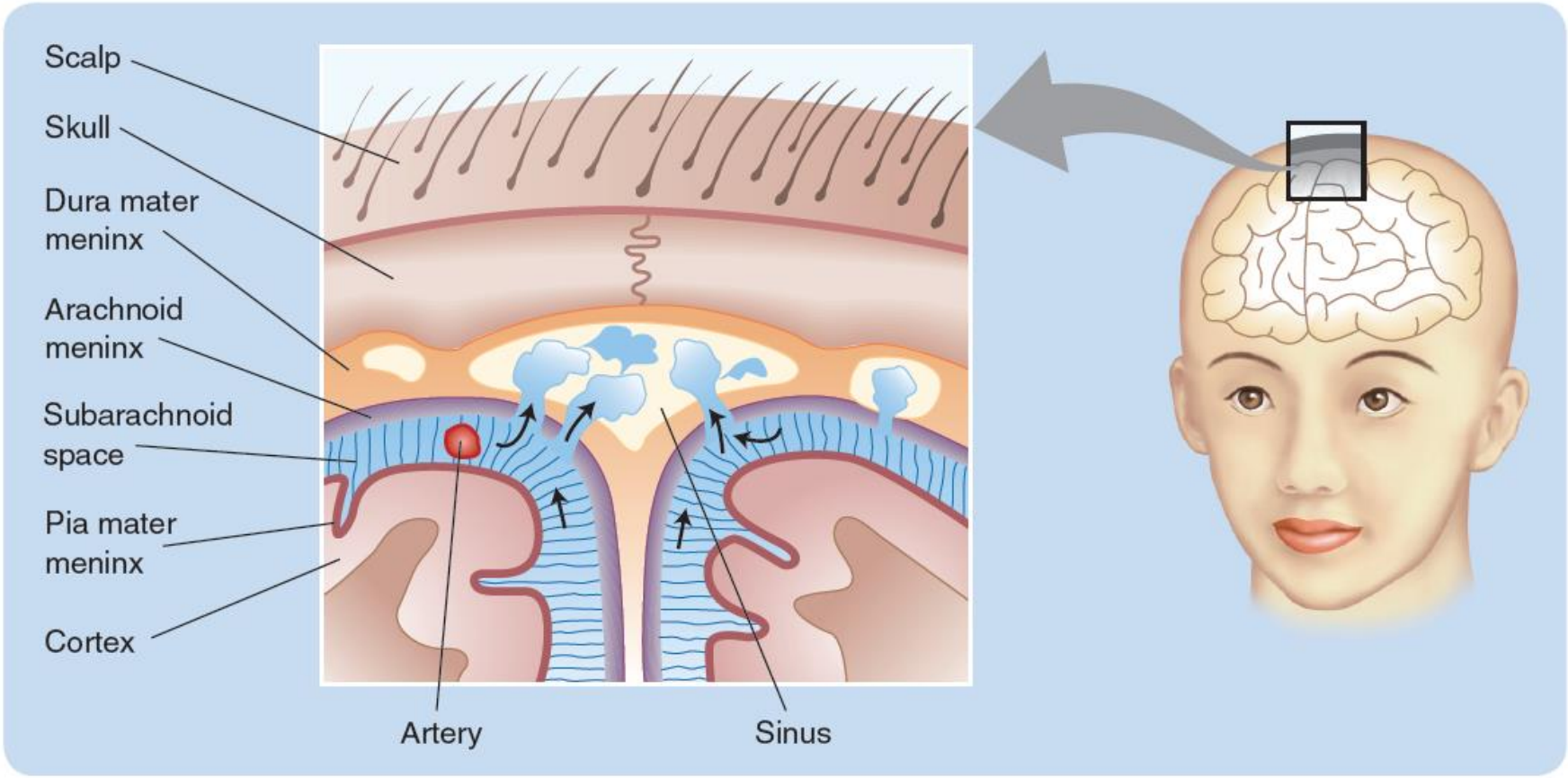
- **Central Nervous System**
  - **The brain is protected by**
    - Skull
    - 3 meninges
      - Dura mater
      - Arachnoid membrane
      - Pia mater

    → Physical protection

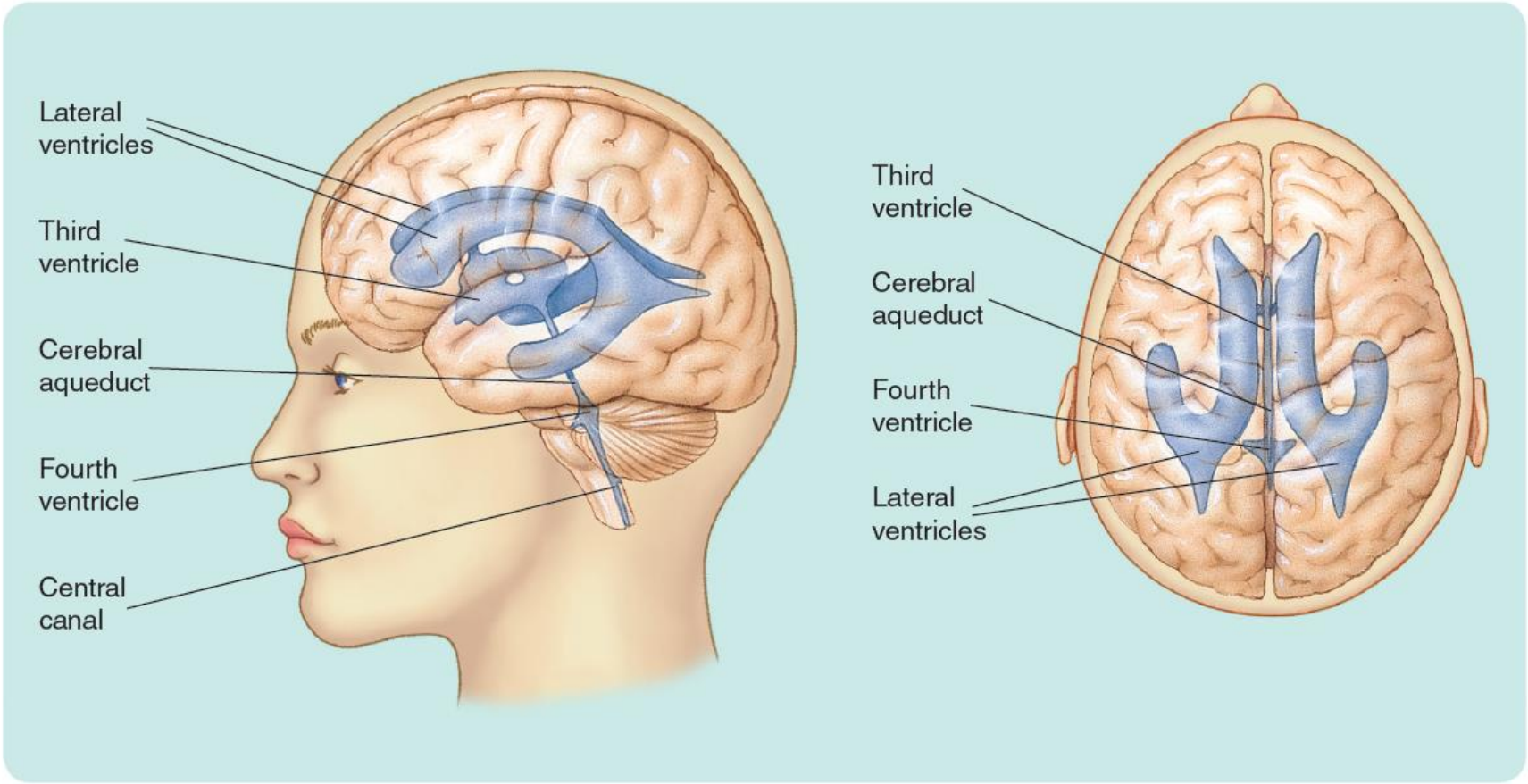
    - Cerebrospinal fluid (CSF)
      - Ventricles
      - Subarachnoid space

    → Buoyancy and shock absorption

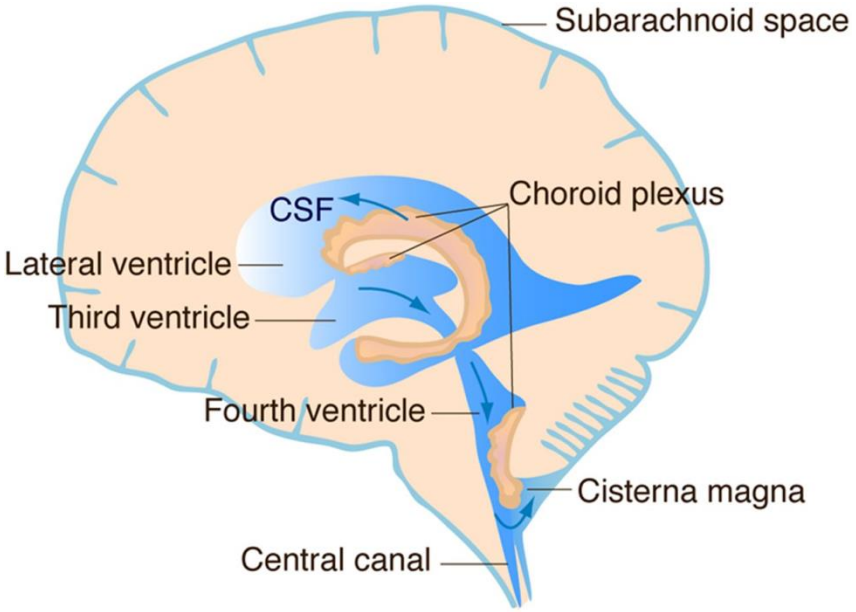
Meninges and CSF

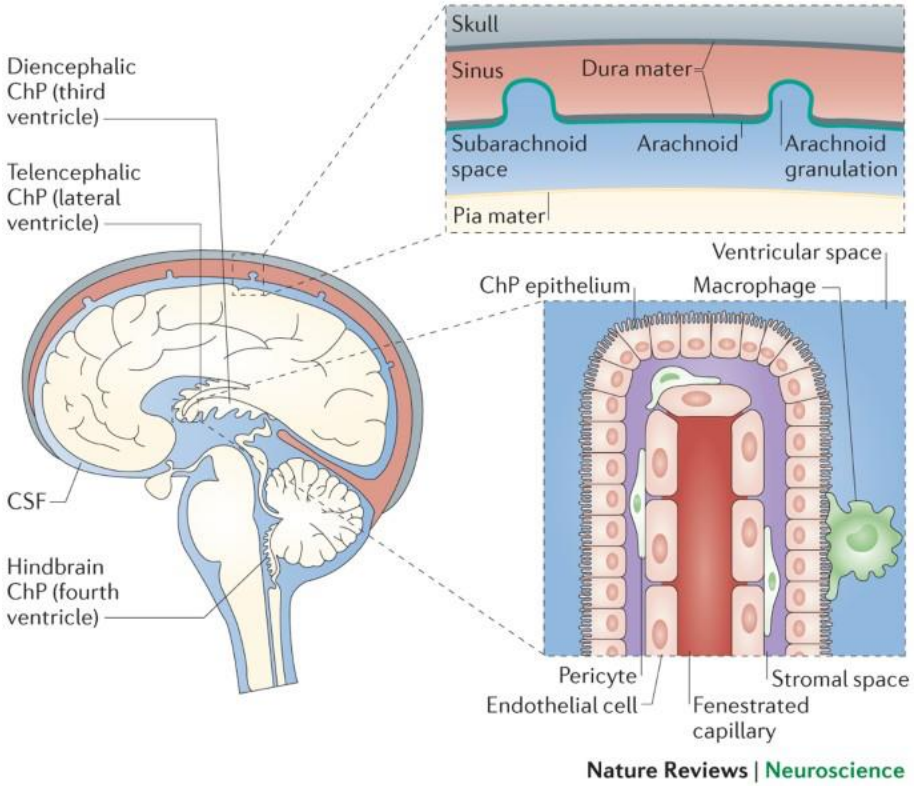


CSF: Ventricles



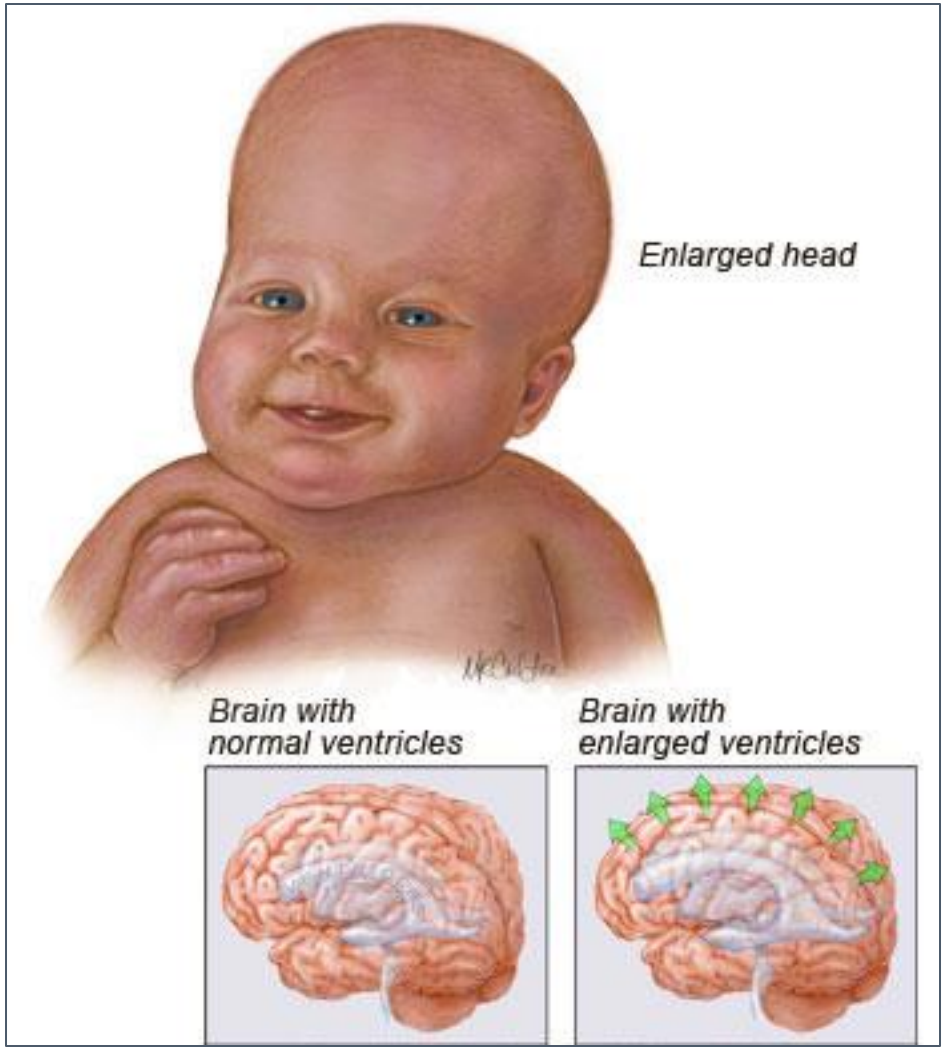
CSF is produced by the Choroid Plexus





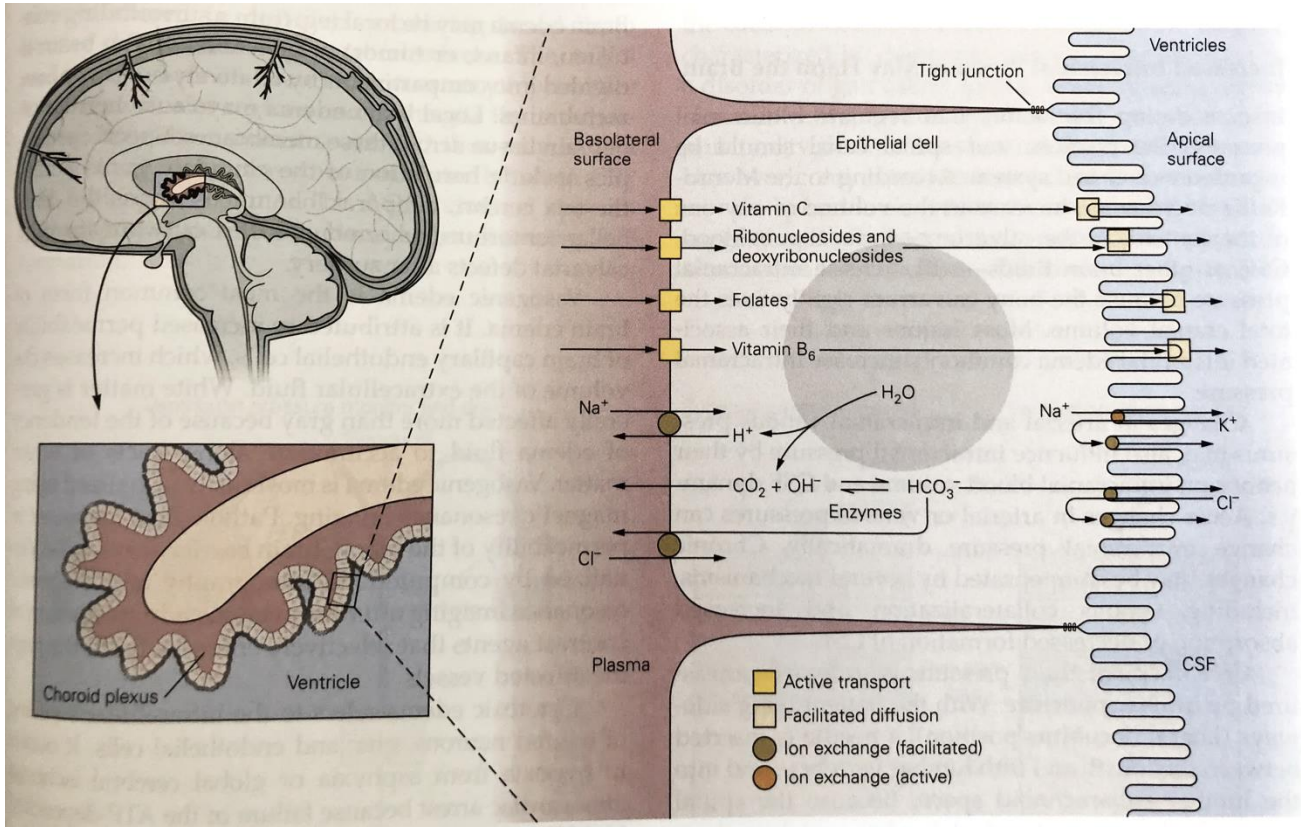
- Functions:
  - Mechanical cushion
  - Removal of brain metabolites
  - Provide a constant extracellular environment for neurons and glia

Hydrocephalus – no draining of CSF



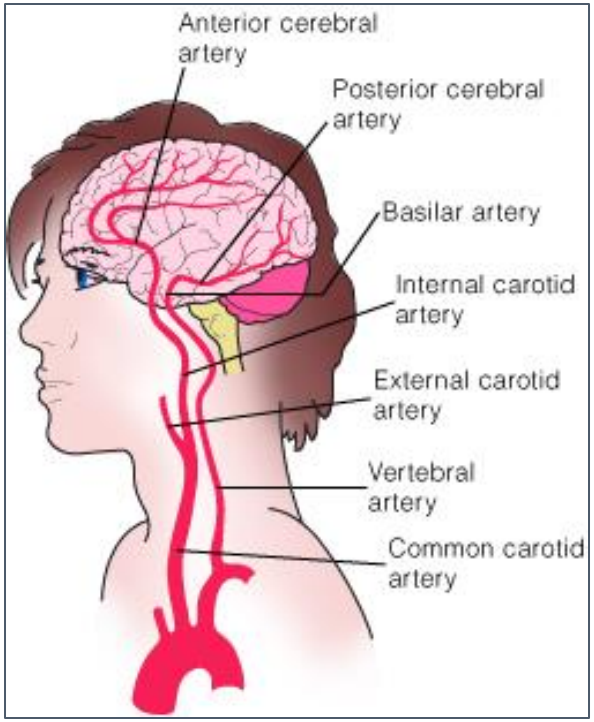
CSF functions

- Mechanical cushion
- Removal of brain metabolites
- Provide a constant extracellular environment for neurons and glia



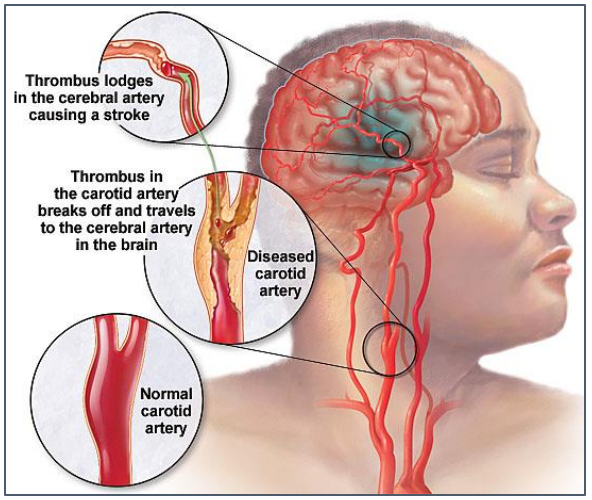
Blood supply of the brain

- Two branches from the dorsal aorta
  - Internal carotid arteries
    - Anterior circulation of the brain
  - Vertebral arteries
    - Posterior circulation of the brain



Stroke – Interruption of the blood supply to the brain

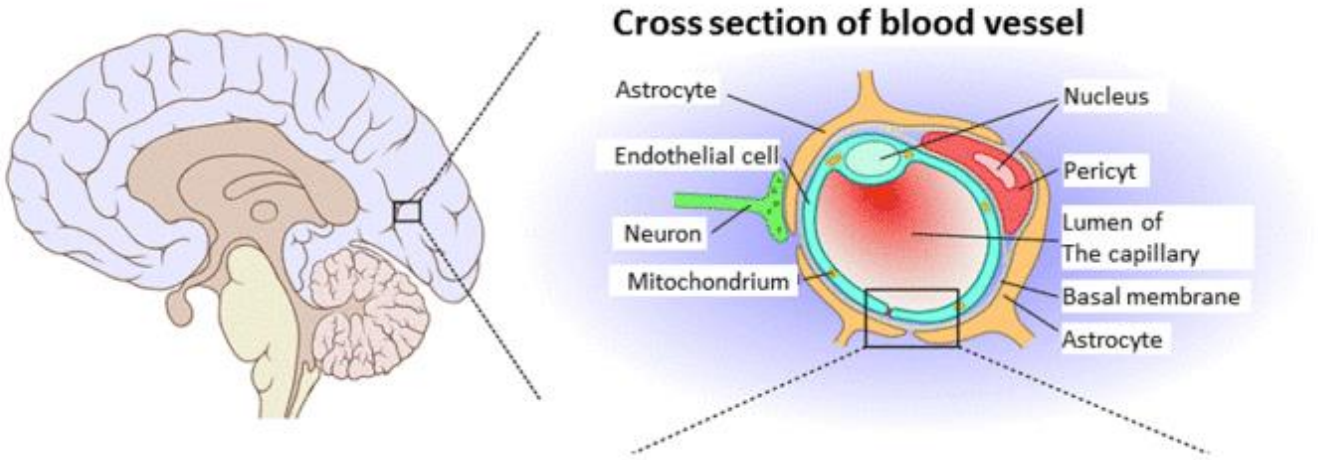
- 3rd most common death in the US (1st: Heart disease; 2nd: cancer)
- 3 types:
  - Thrombotic stroke
    - caused by artherosclerotic buildup of leukocytes in blood vessel walls
    - 50% frequency
  - Embolic stroke
    - caused by a plug in blood vessels (“embolus”)
    - 30% frequency
  - Hemorrhagic stroke
    - caused by rupture in blood vessels
    - 20% frequency



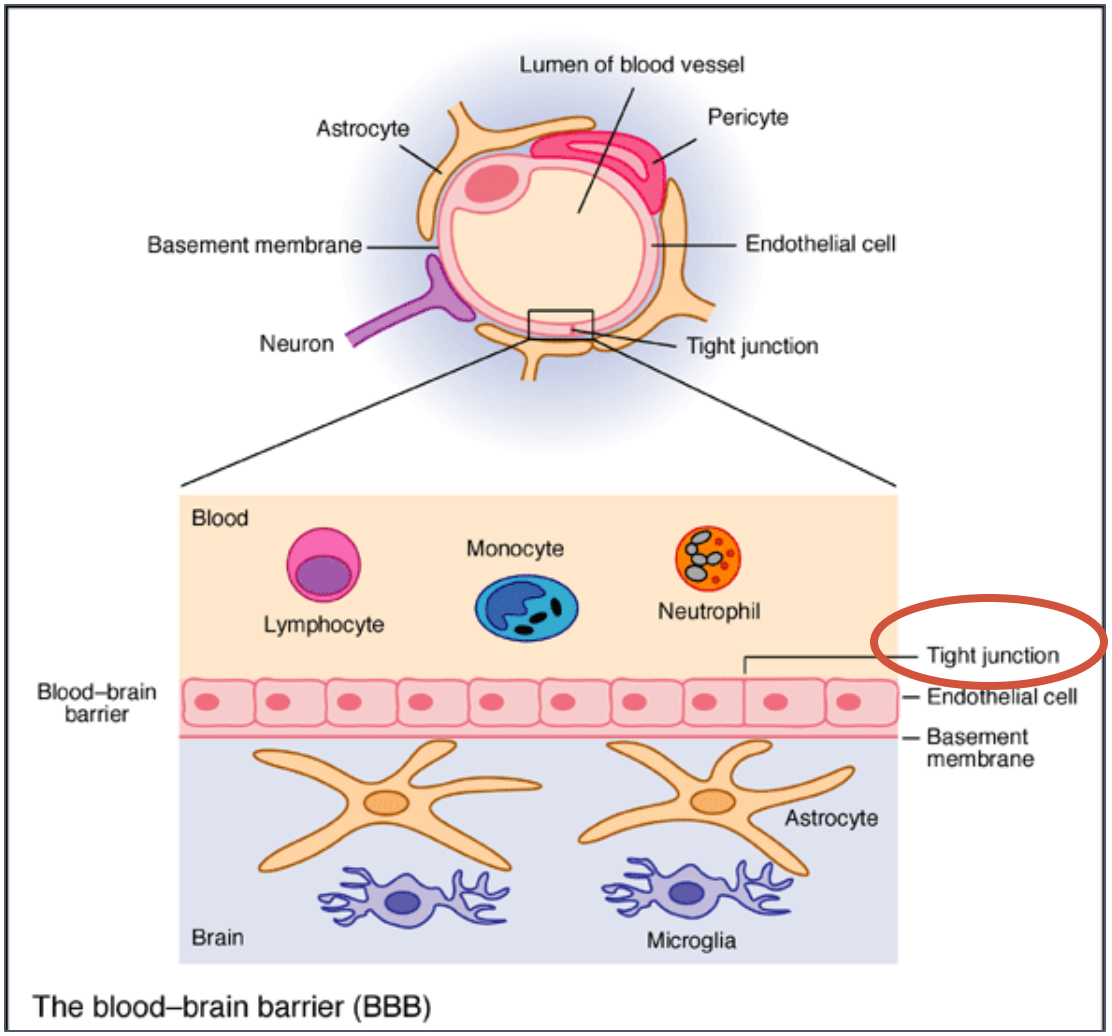
The Blood-Brain Barrier (BBB)

- Specialized structure preventing the entry of toxins (and drugs…) from the blood into the brain

- Composed of
  - Endothelial cells / astrocytes / pericytes / basal membrane



The Blood-Brain Barrier (BBB)



The blood–brain barrier (BBB)

BBB dysfunction and consequences

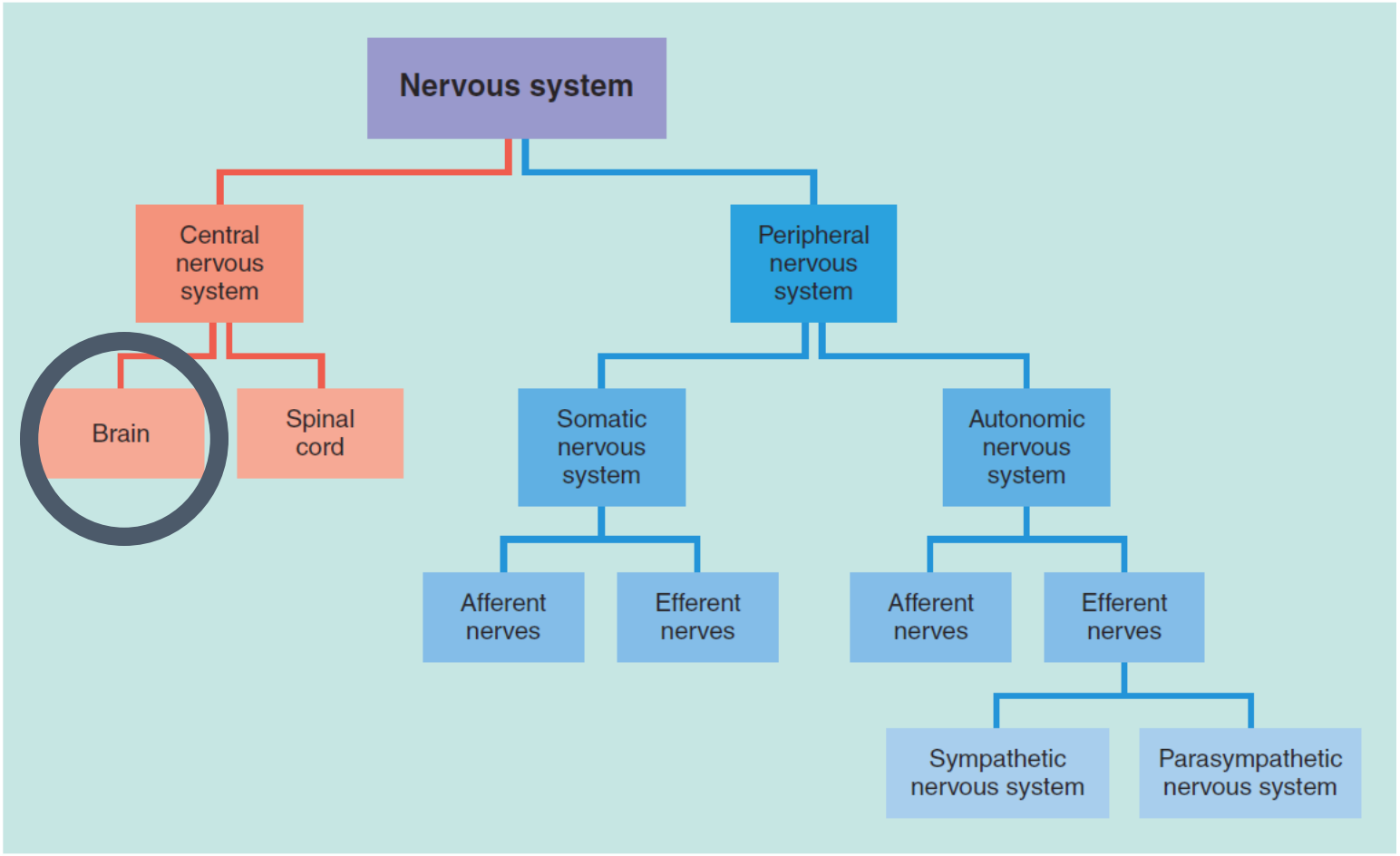
Diseases	BBB proteins and affected mechanisms
Alzheimer's disease	BBB disruption and permit peripheral IgG to brain. Decrease P-gp and accumulate amyloid-β in brain [67].
Parkinson's disease	BBB disruption increases therapeutic agent concentration and reduces efficacy of Pgp [6].
Stroke	Astrocytes secrete TGFβ that downregulates tissue plasminogen activator (tPA) and anticoagulant thrombomodulin (TM) [68].
Epilepsy	Transient BBB opening and upregulation of multiple drug resistance (MRD1) Pgp [69].
Trauma	Opening of BBB, release of IL-6 from astrocytes, and neuroinflammation [70].
HIV	BBB TJ disruption. Loss of glycoproteins and apoptosis of endothelial cell lead to increase diameter of cortical vessels [71].
Infectious processes	Increase CSF/serum albumin ratio. Bacterial lipopolysaccharides affect BBB TJ [72].
Brain tumours	Breakdown of BBB TJ, overexpress folate, insulin, and transferrin receptor, and downregulation of claudin 1/3 [73].
Ischaemic brain oedema	BBB breakdown due to MMP9 release by neutrophils and degradation of occludin, claudins, and JAM [74].

What have we learnt so far?

How is the brain protected?

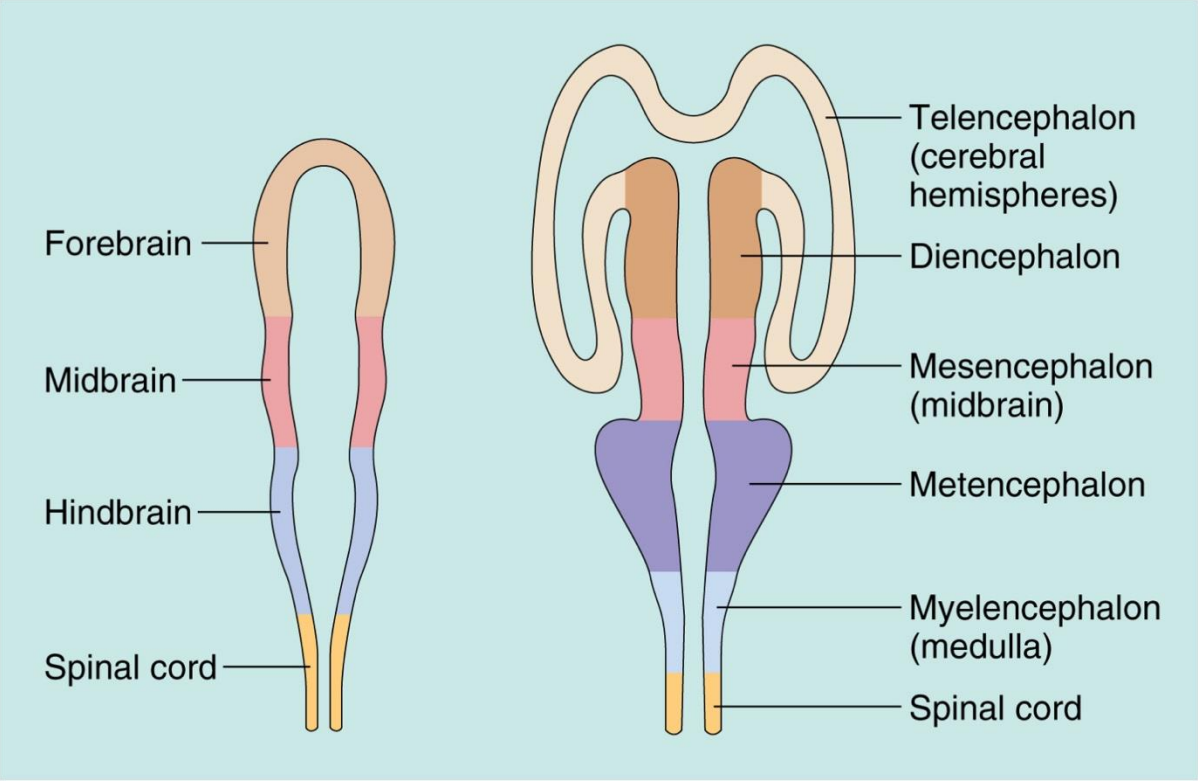
What is the role of the sympathetic nervous system?

Divisions of the Nervous System

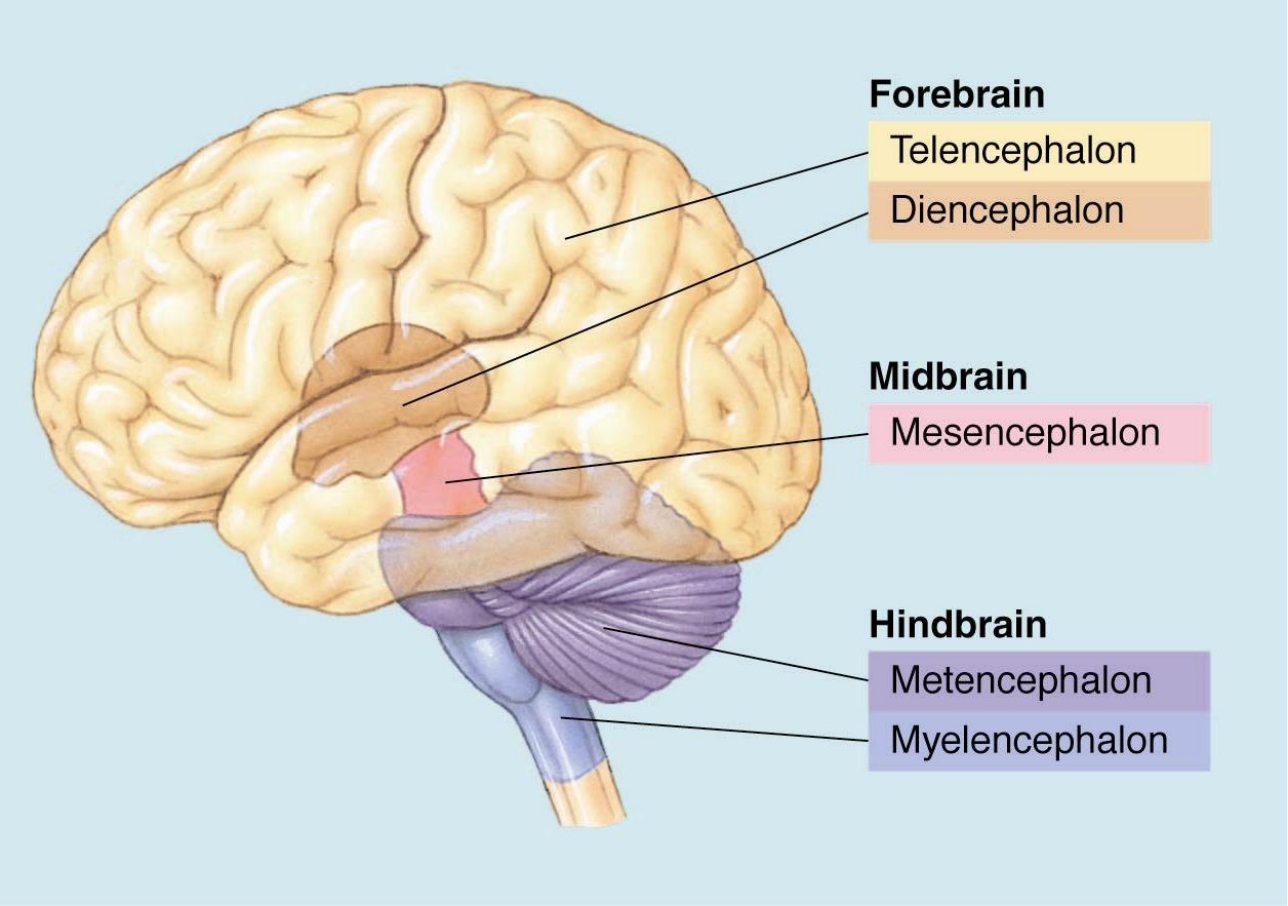


The 5 Major Division of the Brain

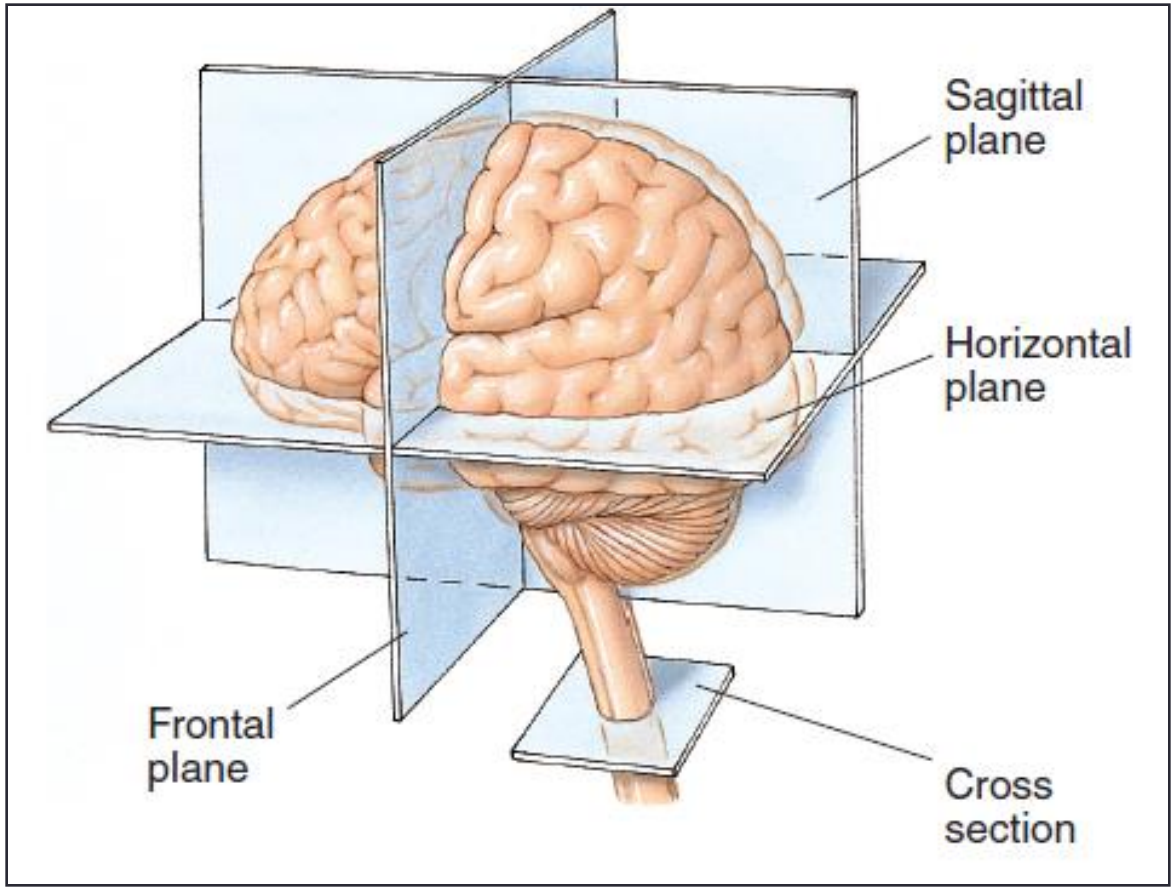
- From 3 to 5 …



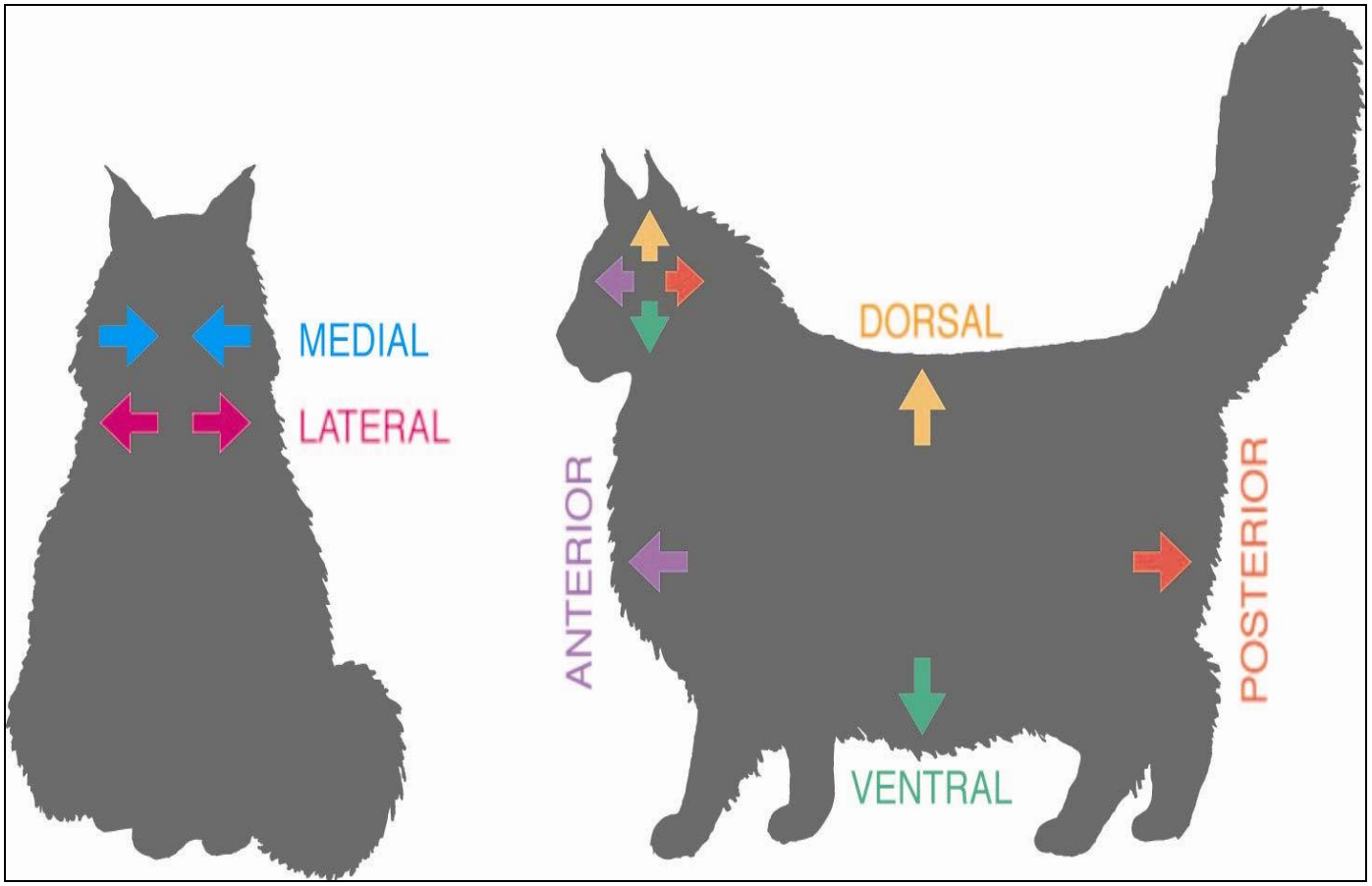
The 5 Major Division of the Brain



Planes of the CNS

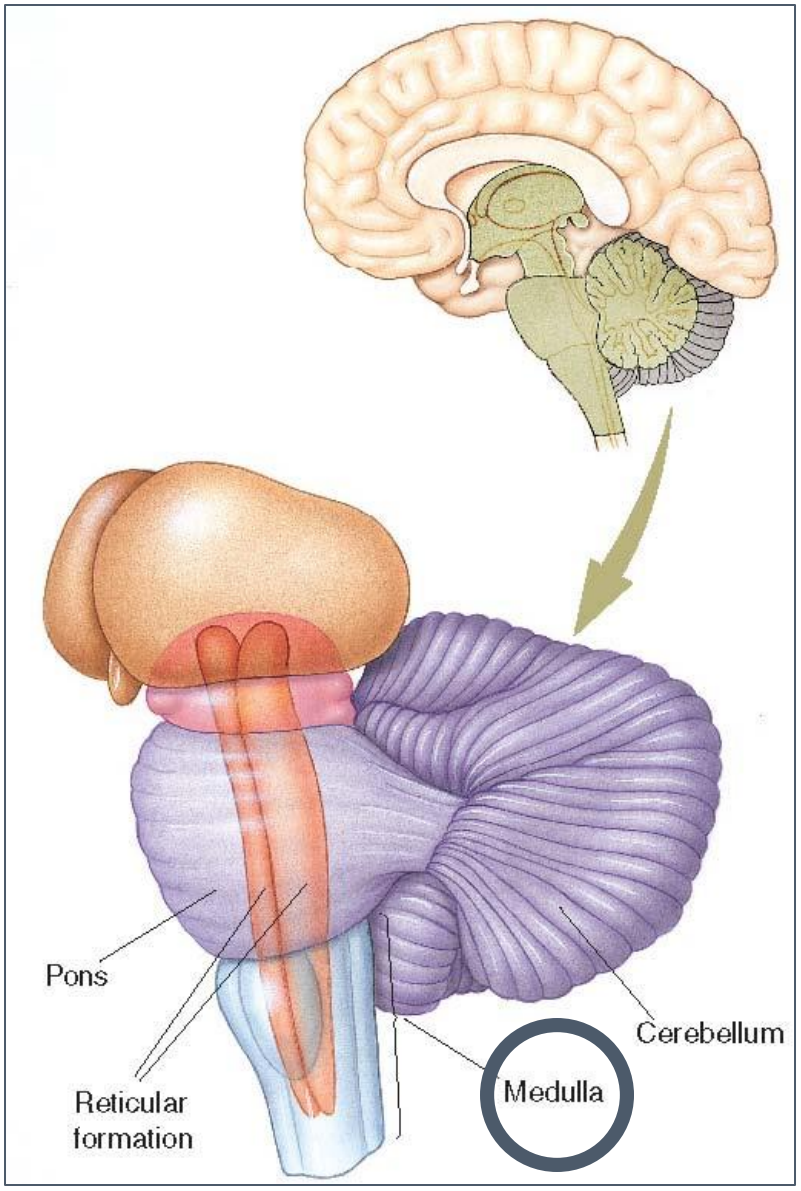


Directions in the CNS – vertebrates

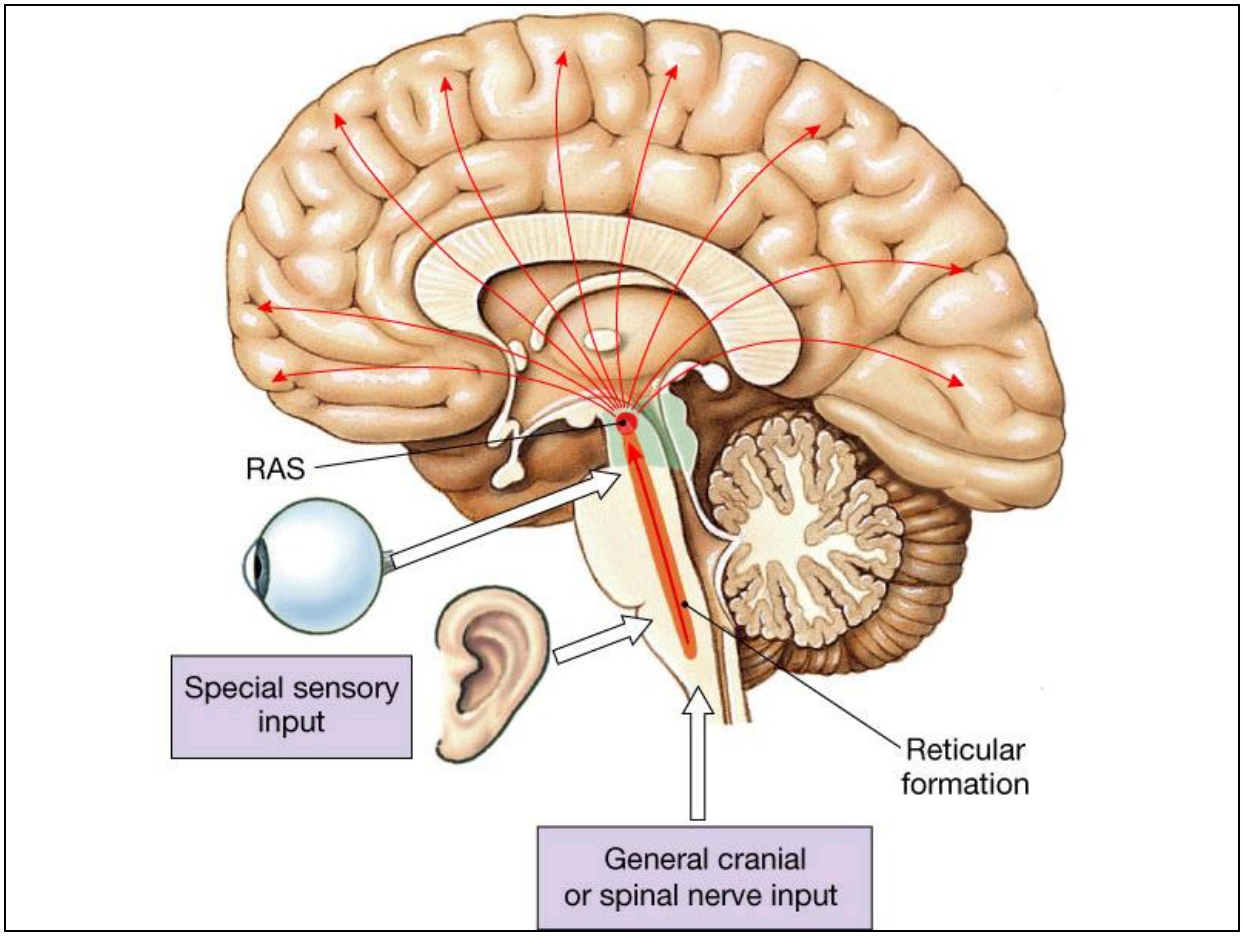


1) Myeloncephalon (Medulla)

- Site of the cranial nerve nuclei
- Site of **reticular formation**
  - Regulates basic life functions
    - respiration
    - heart rate
    - vomiting
    - salivation
  - Also implicated in vision, audition and other functions via Reticular Activating System (RAS)



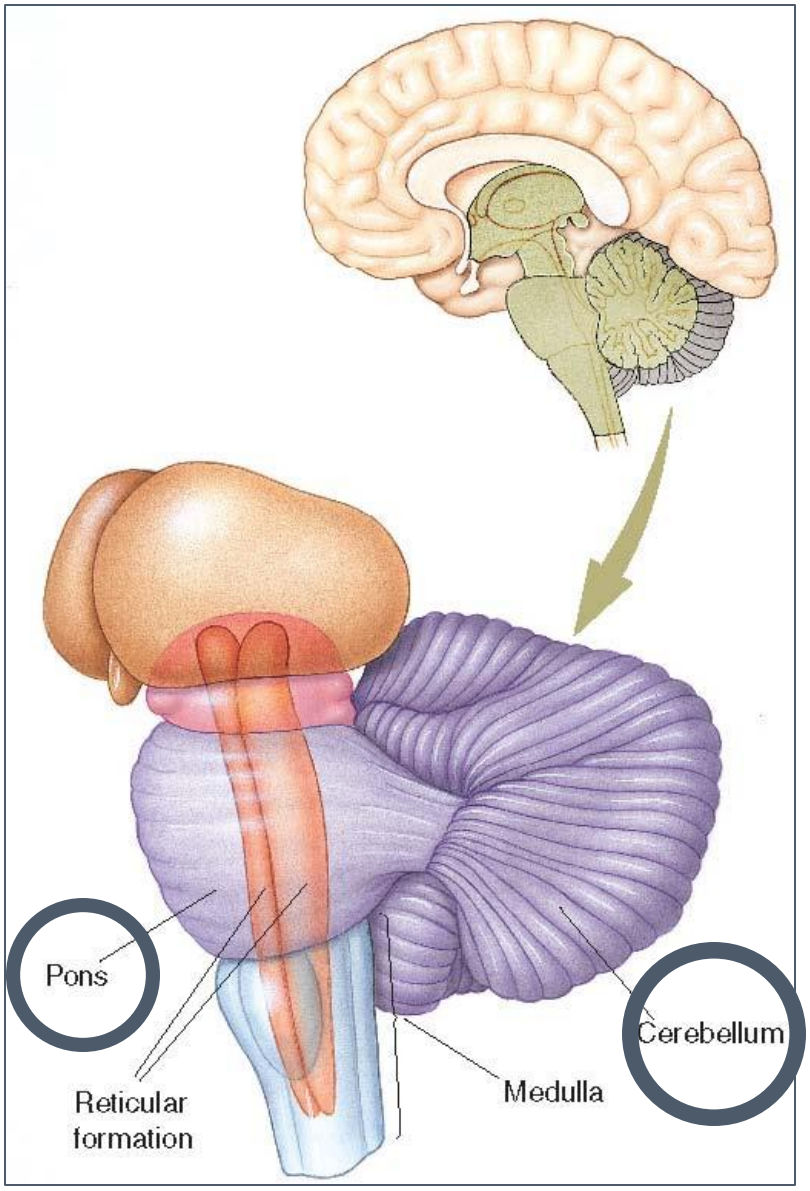
1) Myeloncephalon – Reticular Activating System



Because of its myriad of basic life functions, damage to the reticular formation often leads to coma or death

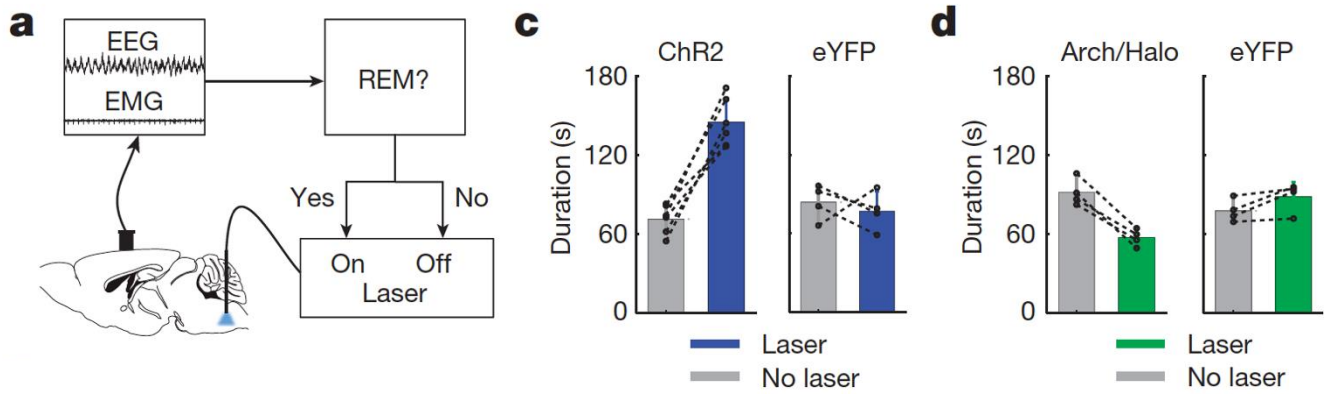
2) Metencephalon

- Site of **reticular formation**
- **Pons**
  - a “bridge” for many fibers passing from one side of the brain to the other
  - involved in
    - sleep
    - arousal
    - muscle tone

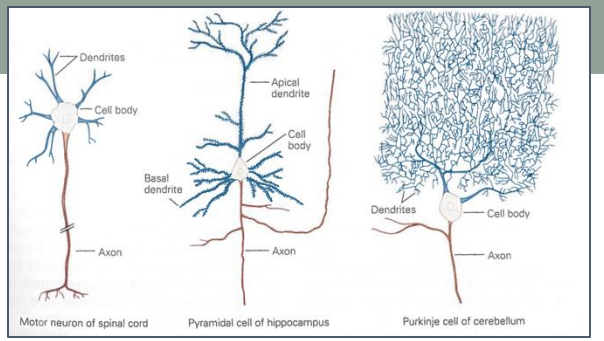


2) Metencephalon c'd

- **Pons and sleep**

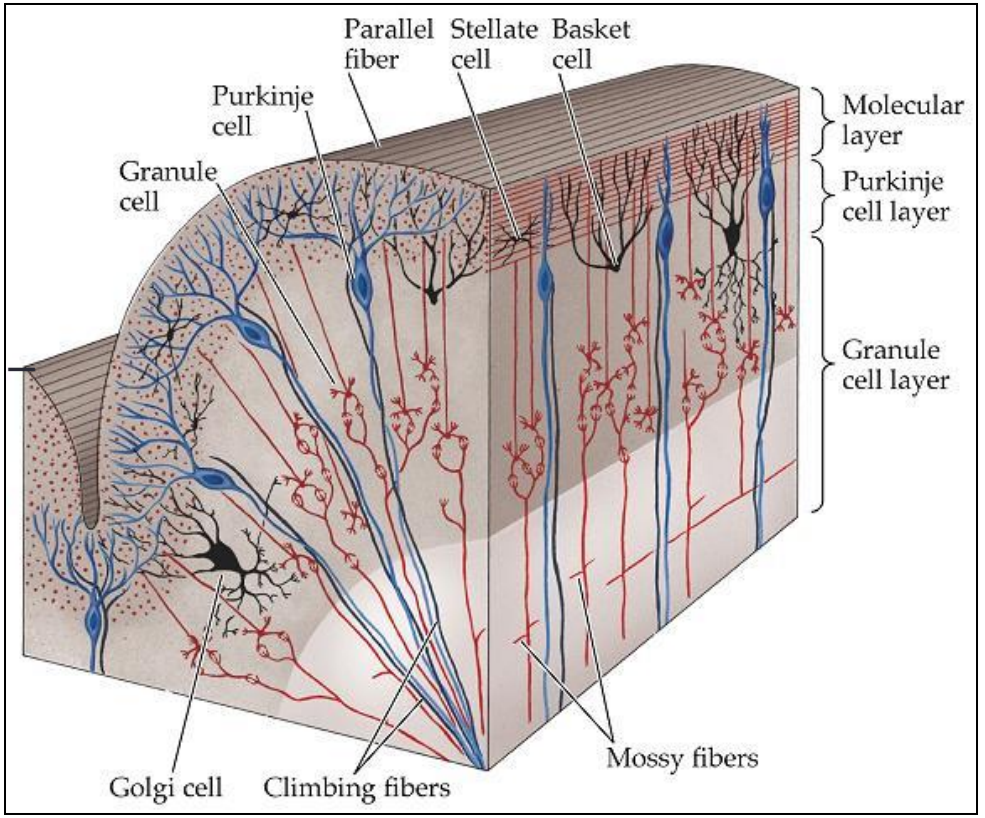


c, d, duration of REM sleep;
eYFP=control virus



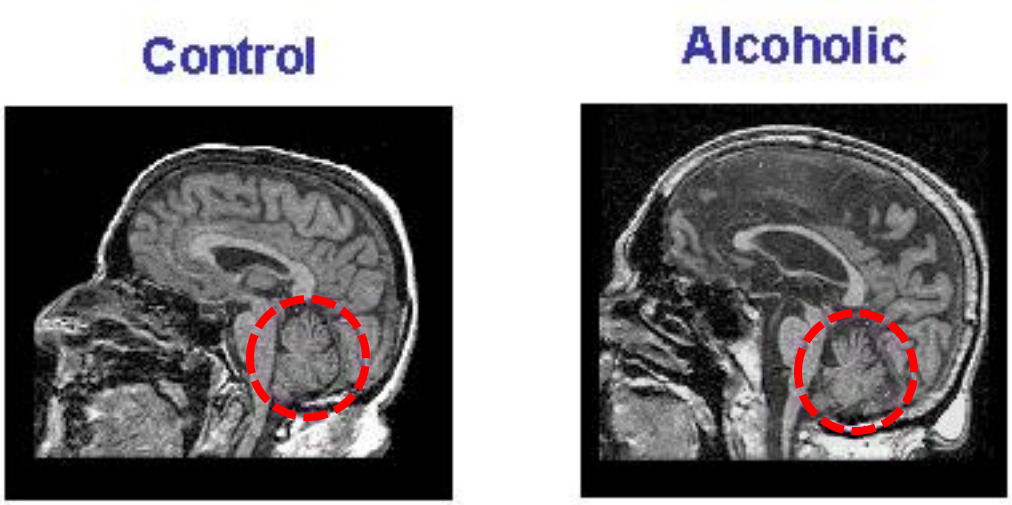
2) Metencephalon c'd

- **Cerebellum**
  - Specialized cell layers
    - Molecular Layer (output)
    - Purkinje Cell Layer (regulatory inhibitory)
    - Granule Cell Layer (input)
  - Major Functions
    - Balance
    - Motor Coordination
    - Timing and sequencing of rapid movements
    - Sensorimotor Learning



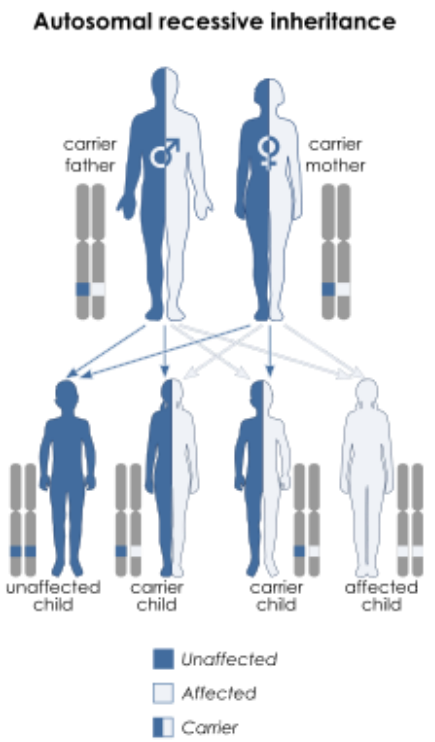
2) Metencephalon c'd

- **Damage to the cerebellum:**



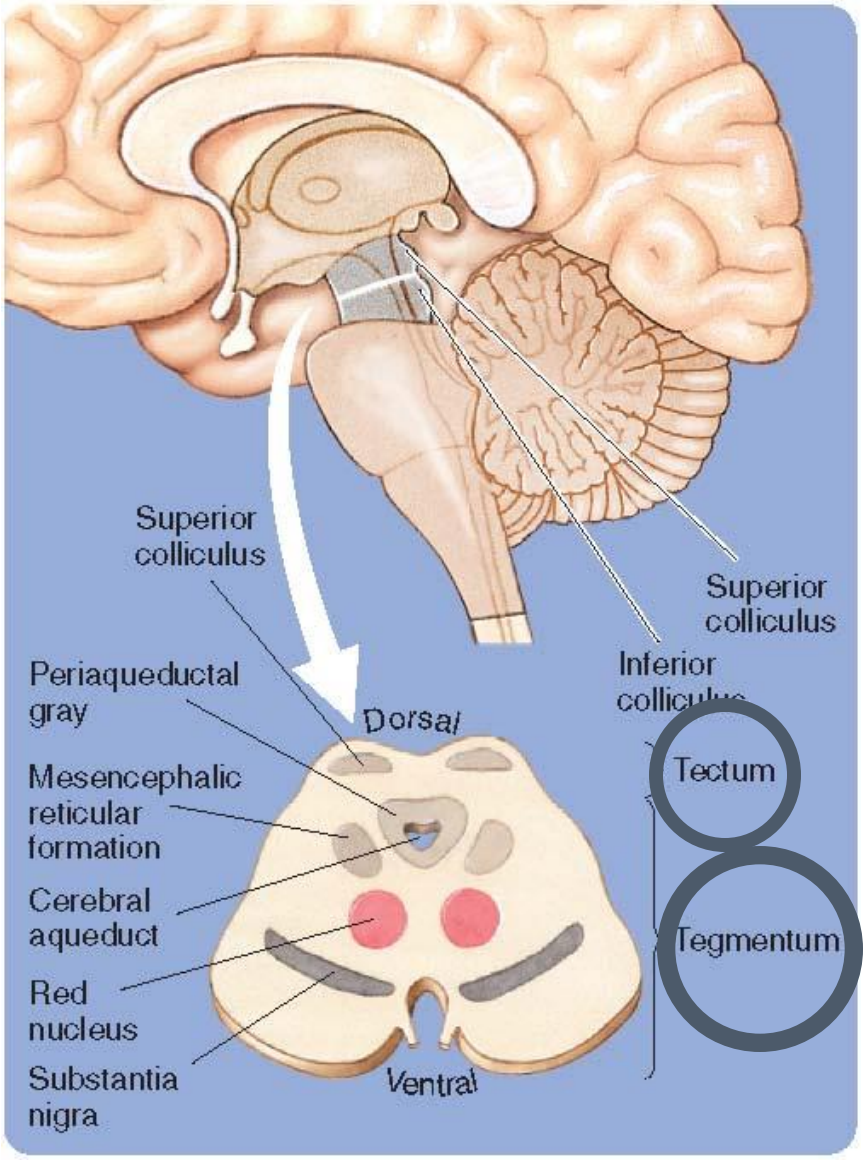
2) Metencephalon c'd

- **Developmental cerebellar ataxia: Niemann-Pick Type C**
  - Monogenetic neurodevelopmental disorder
    - Prevalence 1:150'000
  - Metabolic dysfunctions
  - Loss of myelination in the brain (cerebellum)



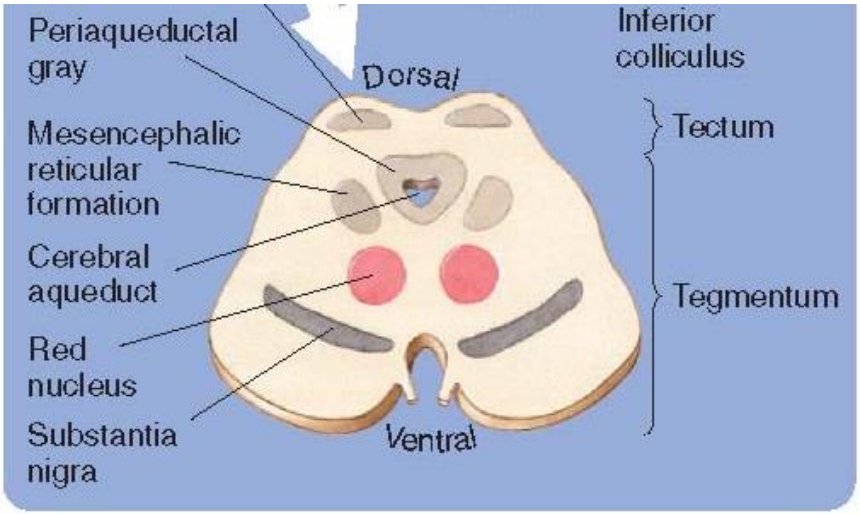
3) Mesencephalon

- **Tectum**
  - Inferior colliculi: Audition
  - Superior colliculi: Vision
- **Tegmentum**
  - Reticular formation
  - Periaqueductal grey
  - Substantia nigra
  - Red nucleus



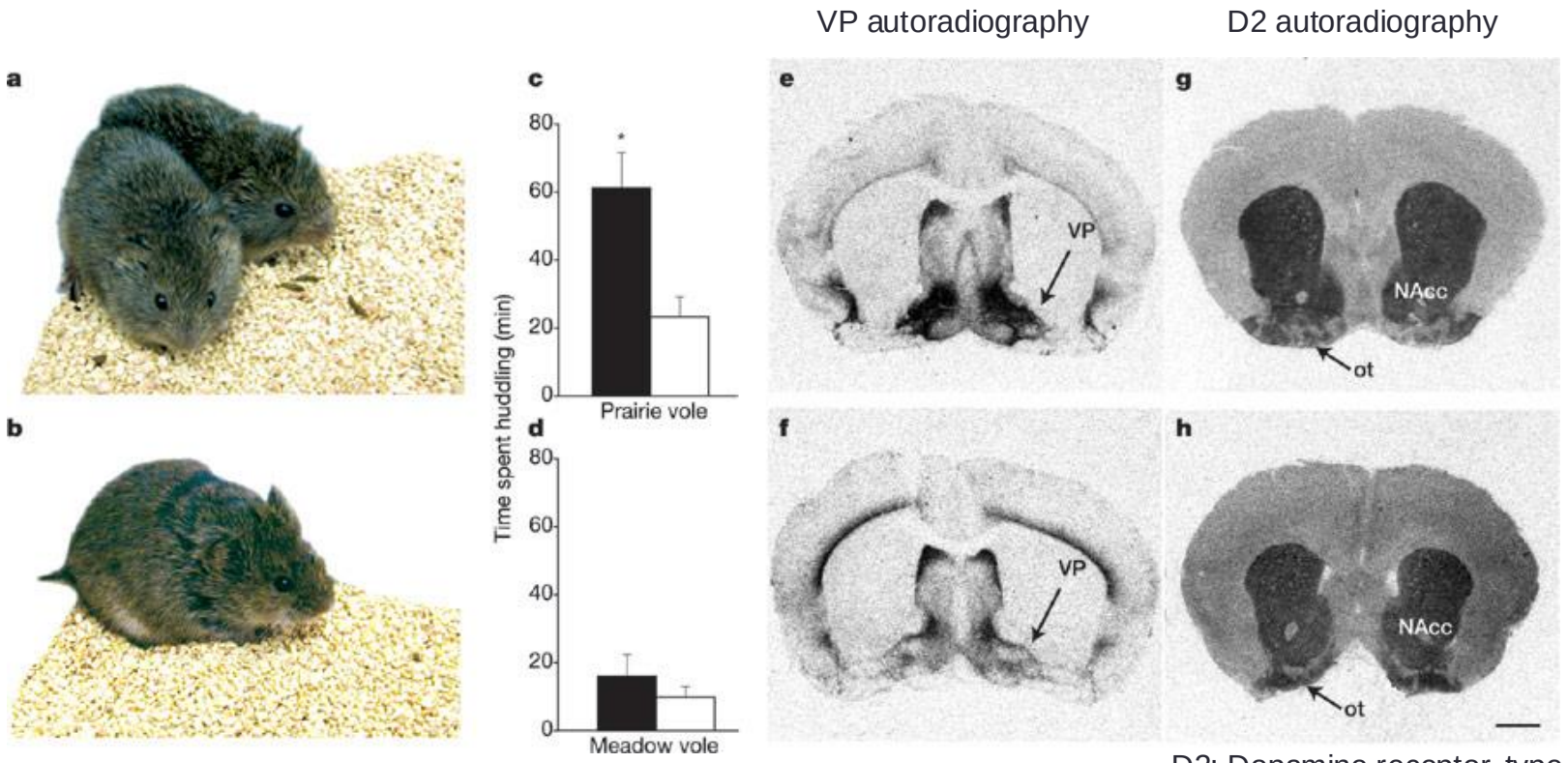
3) Mesencephalon c'd

- **Periaqueductal grey**
  - Pain sensation
  - Defensive behavior
  - Maternal behavior
    - High density of oxytocin/vasopressin receptors



3) Mesencephalon c'd

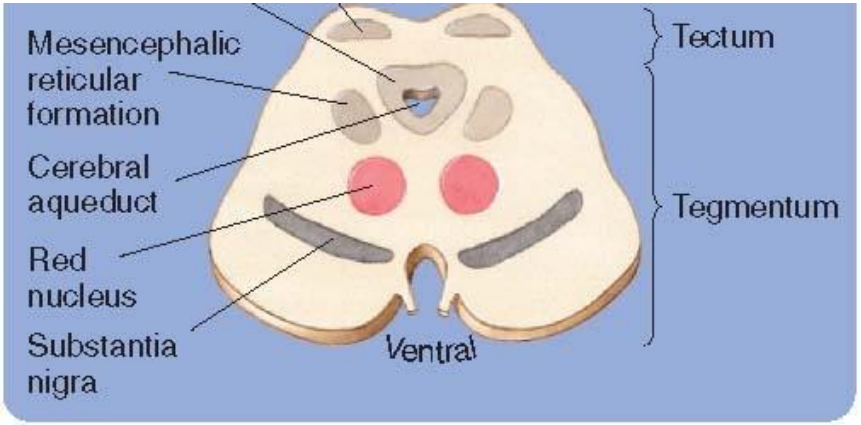
- **The case of colonial prairie voles vs. solitary meadow voles**



D2: Dopamine receptor, type II
VP, vasopressin receptor
Ot, olfactory tubercule
NAcc, nucleus accumbens

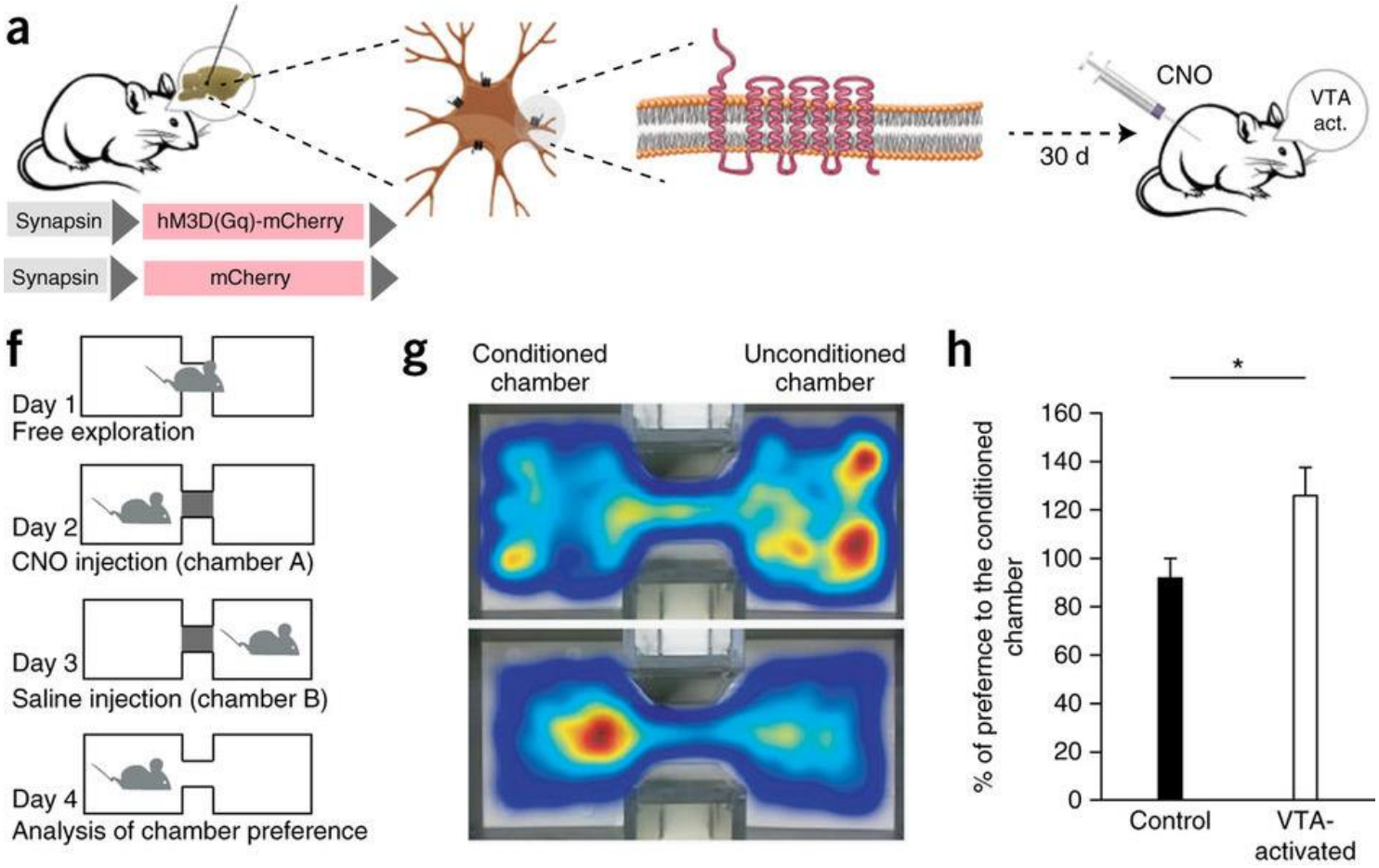
3) Mesencephalon c'd

- **Substantia nigra**
  - Sensorimotor function
  - Compromised in Parkinson's disease and Schizophrenia
- **Red nucleus**
  - Sensorimotor function - Gait



- **Ventral tegmental area**
  - Reward system (mesocorticolimbic)

- **Activating the VTA drives reward-related behaviors**



What have we learnt so far?

What are the major subdivisions of the brain along the ventro-dorsal axis?

Which brain area is important for sleep regulation?