



Lecture 4

Neurophysiology &

Neuroanatomy

PSYC 304



Announcements

Reading club articles

- Readings can be found on the canvas homepage.
- Reading club 1 is on May 29th.

Midterm 1

- June 3rd
- Covers all material up to that point
- 6pm, zoom link and test in modules in Canvas, 60-90 minutes
- CFA accommodations will be made by me.



Review

Action potentials

Synaptic Transmission



Learning Objectives

By the end of this lesson, you will...

1. Be able to list the stages of chemical synaptic transmission
2. Be able to describe the mechanism by which excitatory and inhibitory neurotransmitters function
3. Distinguish between action potentials and post synaptic potentials.
4. Distinguish between temporal and spatial summation.
5. Apply basic neurophysiology principles to the knee jerk reflex neural chain.
6. Describe the strengths and weaknesses of two visualization techniques for viewings neuronal circuits.

Synaptic transmission

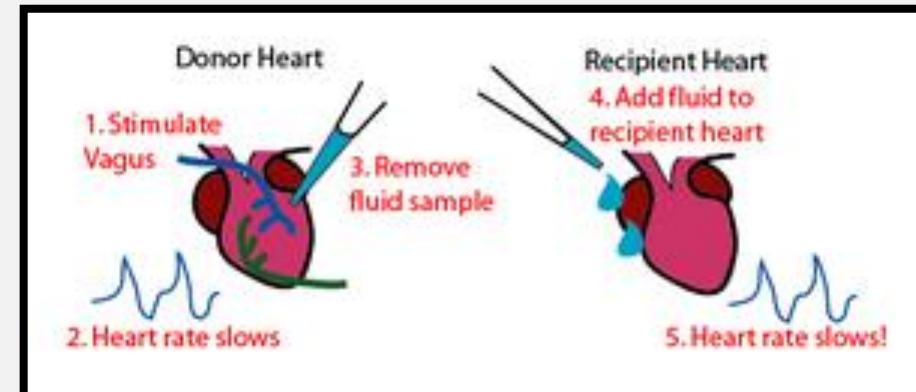
How do neurons communicate?



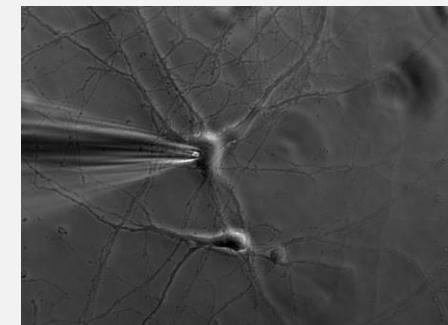
Charles Scott Sherrington
(1904)
• The Synapse

Thomas Renton Elliot (1904)
• Adrenaline (EPI)

“Adrenalin might then be the chemical stimulant liberated on each occasion when the impulse arrives at the periphery”



John Eccles (1951)
• Eccles, coombs and brock



Henry Dale (1914/1933)
• Acetylcholine (Ach)

Otto Loewi (1921)
• Vagusstoff
• Accelerans-stoff

Visualizing vesicles and receptors with EM

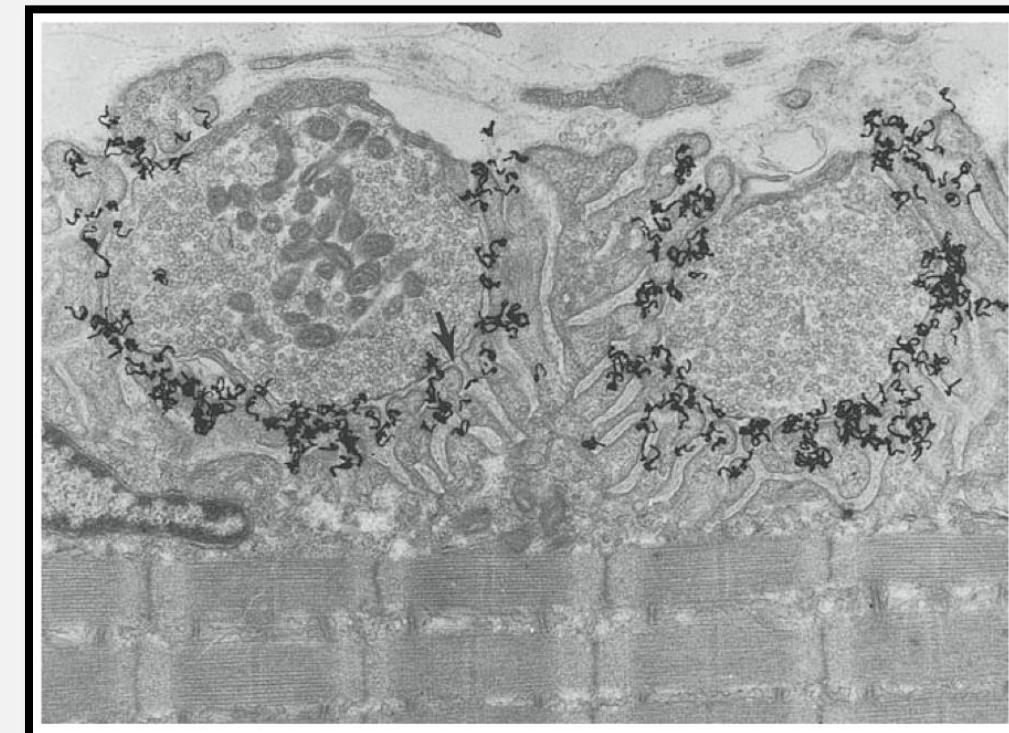
Typical CNS synapse

- vesicles, mitochondria, 2 active zones (dark fuzzy bands indicated by arrows = regions of dense synaptic machinery)



The neuromuscular junction

- Acetylcholine receptors darkly labelled, seen at postsynaptic membrane immediately across from synaptic vesicles.
- Note the insane number of vesicles.

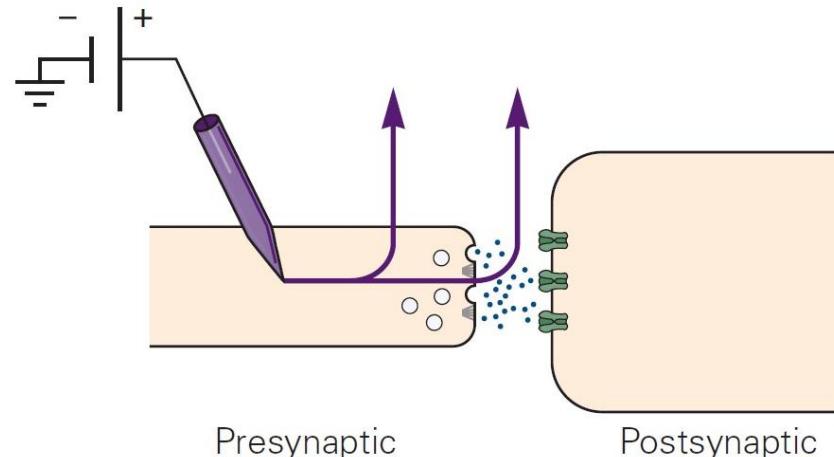


The Synapse

Chemical synapses

- Injected current causes an action potential in the presynaptic cell, release of neurotransmitters and a change in potential of the postsynaptic cell

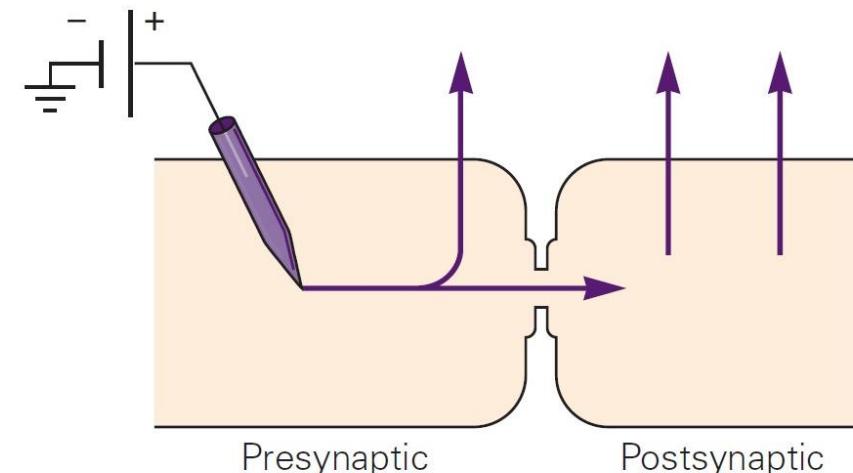
B Current pathways at chemical synapses



Electrical Synapses

- Transmit signals between neurons
- Current enters the post synaptic cell through a gap junction channel

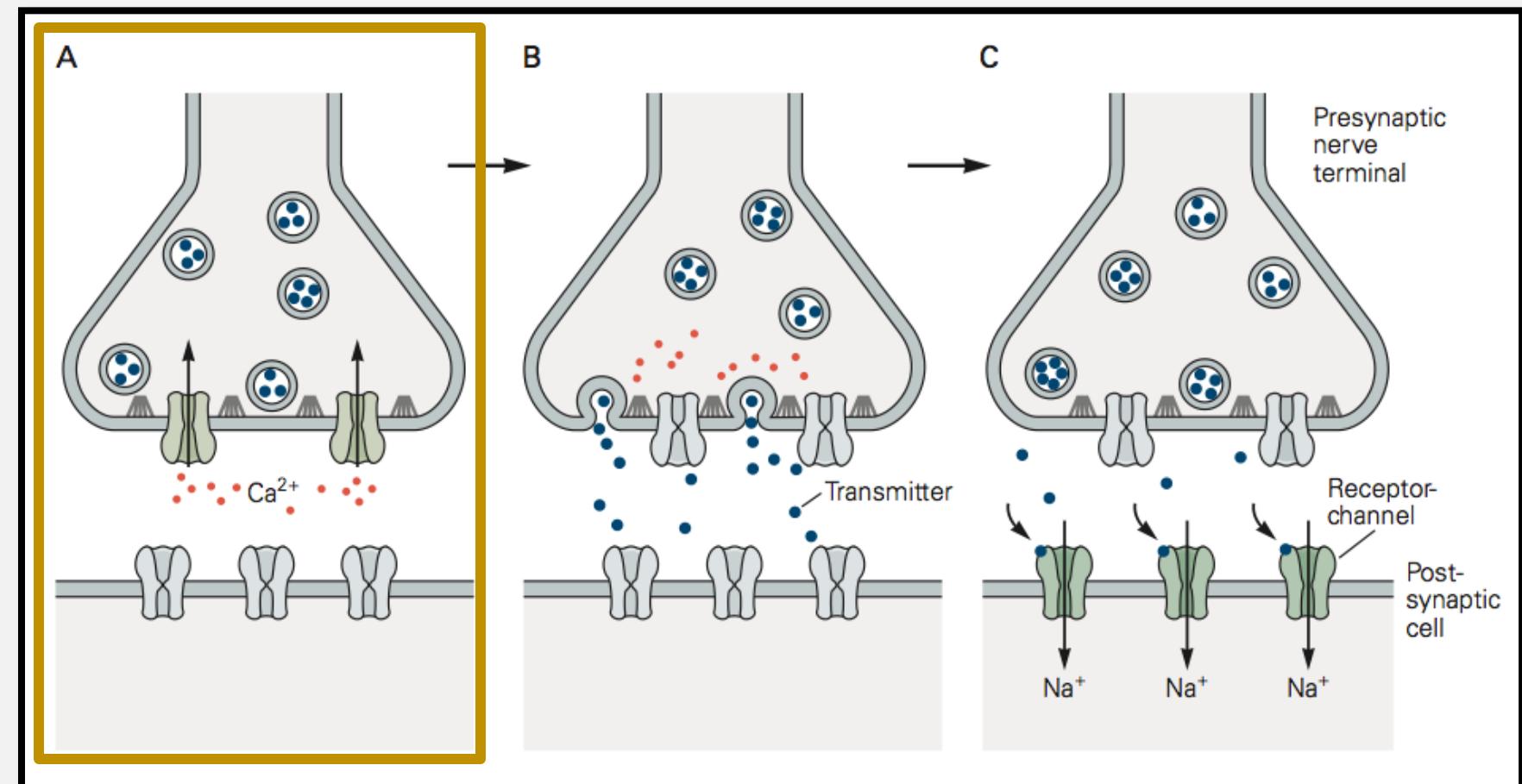
A Current pathways at electrical synapses



Synaptic Transmission

A

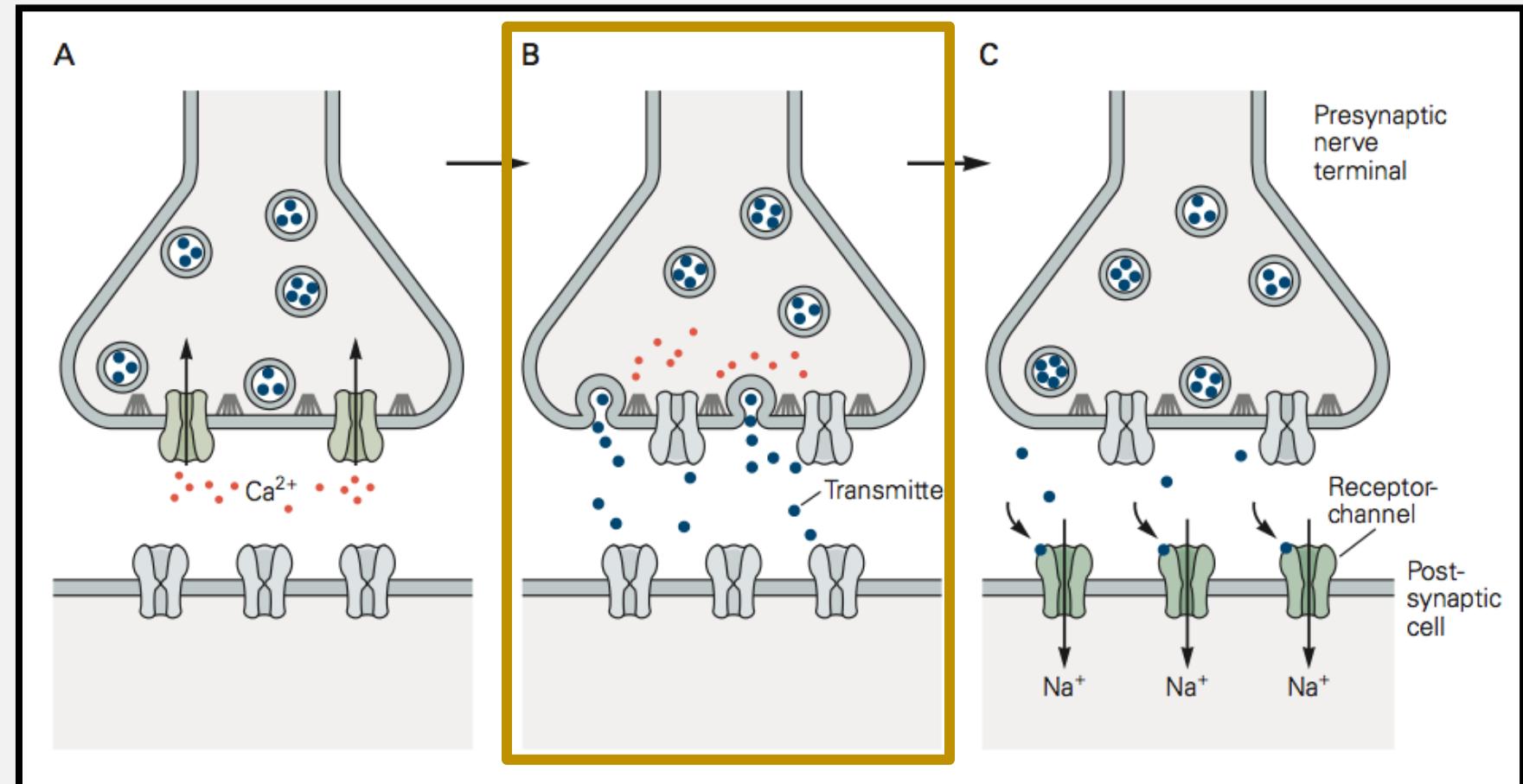
- Vesicles dock near the plasma membrane
- Presynaptic terminal depolarization
- Arriving AP causes opening of VG Ca^{2+} channels



Synaptic Transmission

B

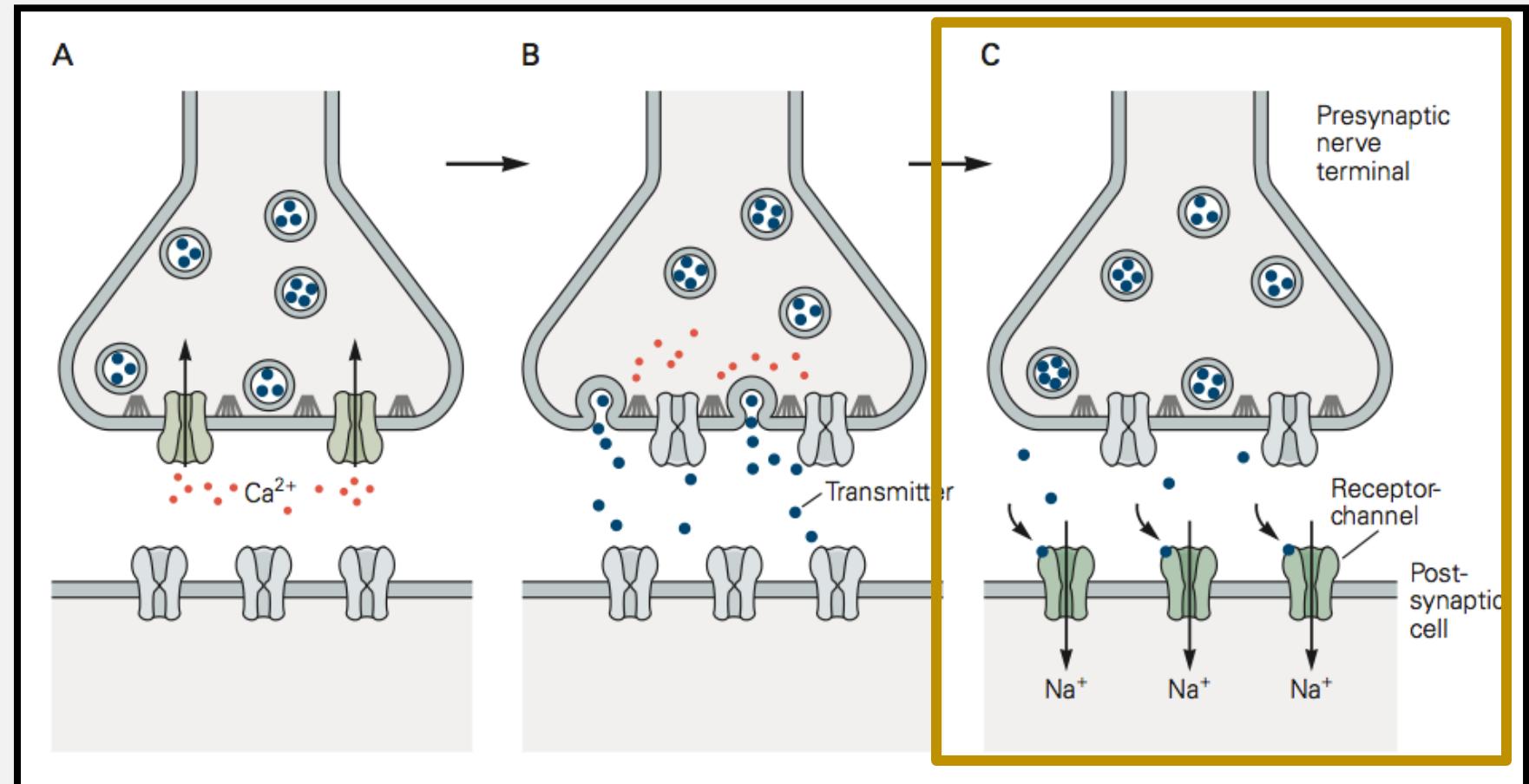
- Ca^{2+} entry triggers vesicle fusion with presynaptic membrane
- Neurotransmitter (NT) ligands spills into synaptic cleft
- **Ligands – Bind specific receptors**



Synaptic Transmission

C

- NT's bind to post synaptic membrane receptors
- **Ionotropic receptors** have associated ion channels that open when bound
- Depending on receptor – EPSP or IPSP



Terminology

Post synaptic potential

- A brief change from resting potential in the post synaptic cell

Excitatory Post synaptic potential (EPSP)

- When the post synaptic cell becomes depolarized (excited) and therefore more likely to fire an action potential

Inhibitory Post synaptic potential (IPSP)

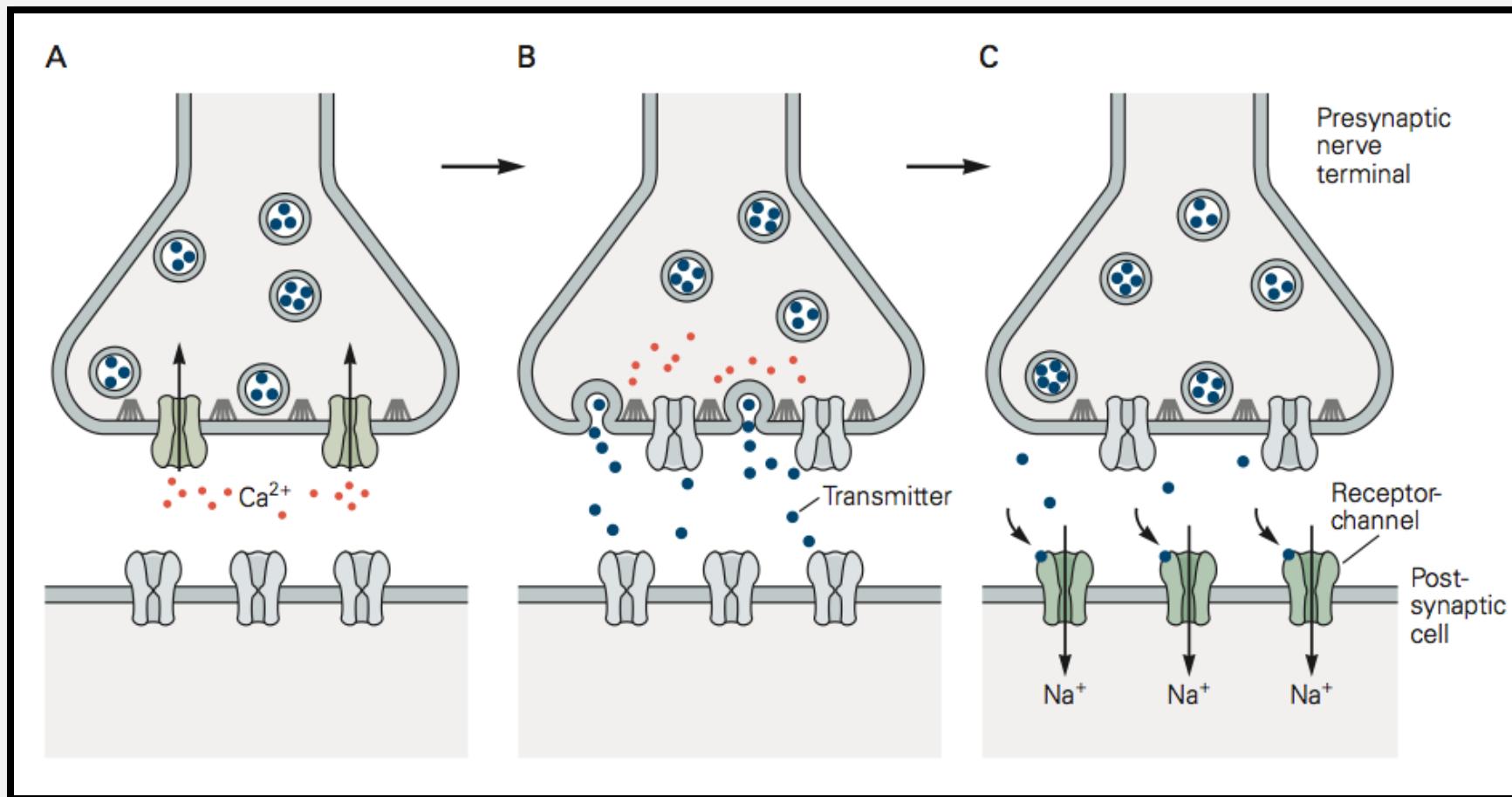
- When the post synaptic cell becomes hyperpolarized and therefore less likely to fire action potential (i.e., the AP is inhibited)

Synaptic delay

- Delay between the presynaptic AP reaching the axon terminal and creating a post synaptic potential

Test your knowledge

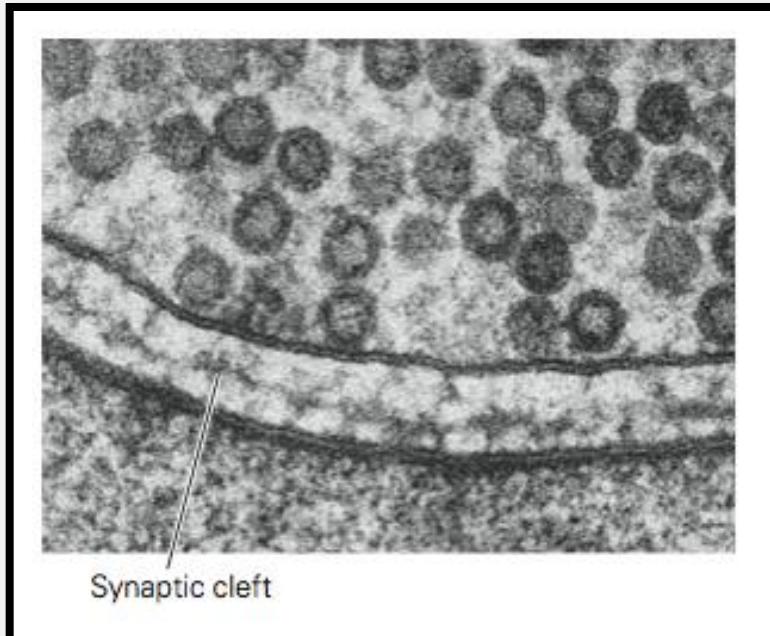
In our example... would an EPSP or IPSP occur here?



Visualizing vesicles during synaptic transmission

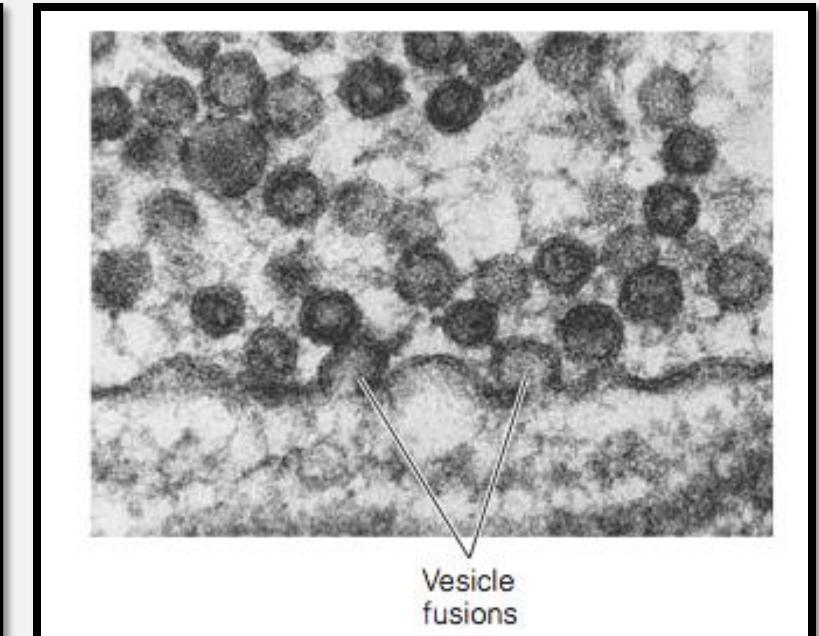
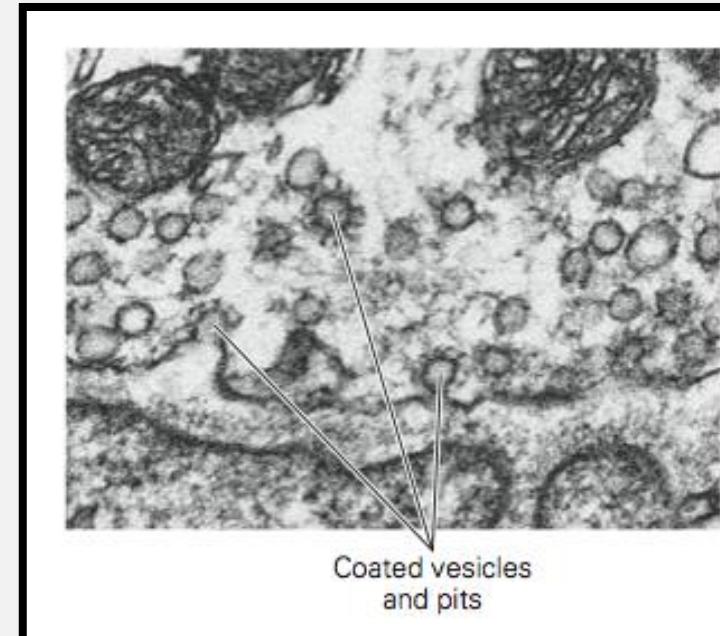
At Rest

- Vesicles docked and ready to be released
- Stimulate a depolarization and freeze the tissue



Exo and endocytosis

- 5 ms later – can see fusion with the presynaptic membrane
- 10 sec later – endocytosis of vesicles is visible.



Recording post synaptic potentials

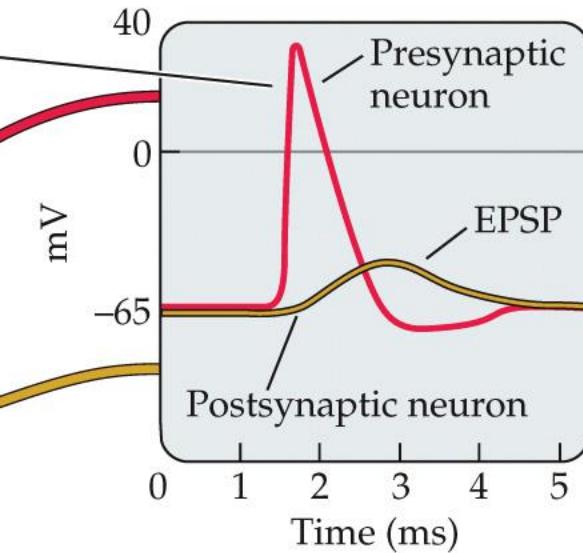
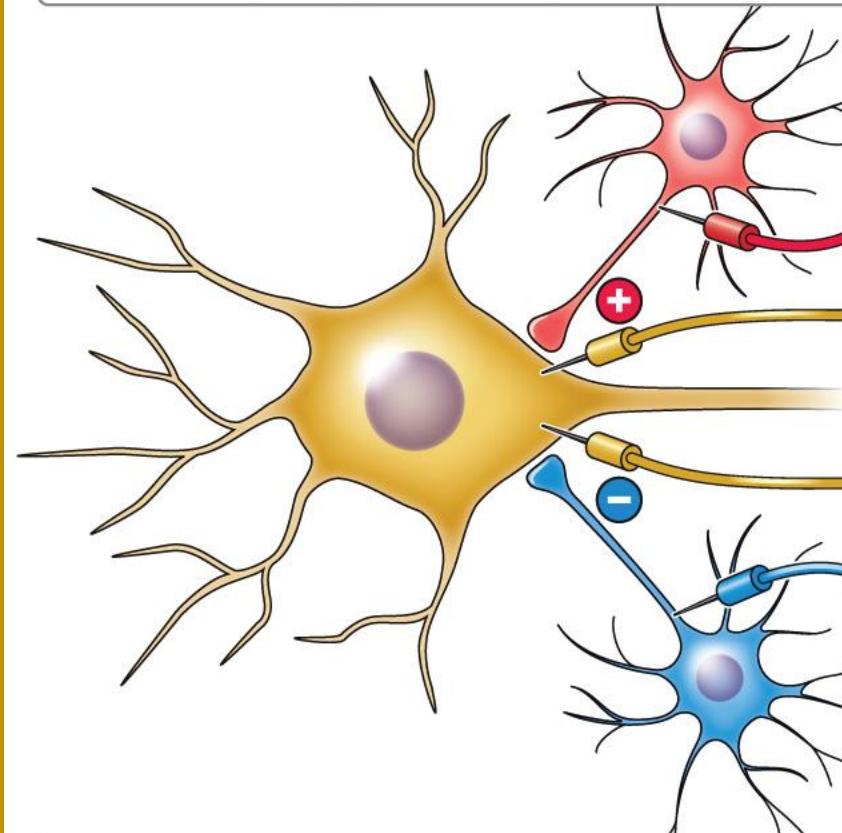
In red

- Excitatory connection

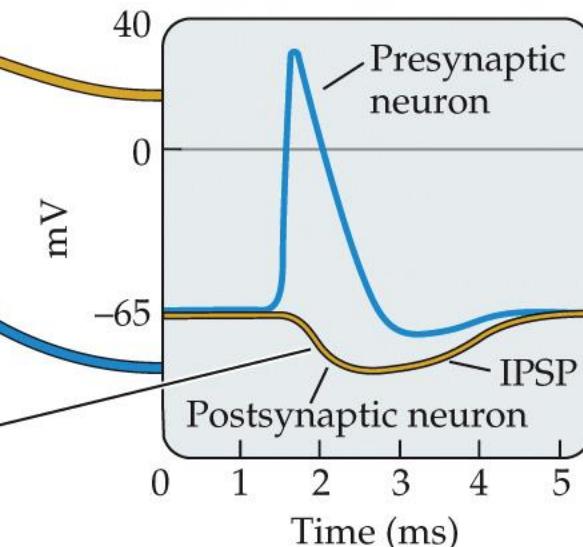
In Blue

- inhibitory connection

In this schematic model, when an excitatory presynaptic neuron (red) fires, it shows a normal action potential and causes depolarization (EPSP) in the postsynaptic neuron (yellow).



When an inhibitory presynaptic neuron (blue) fires, it also shows a normal action potential, but it causes hyperpolarization (IPSP) in the post-synaptic neuron (yellow).



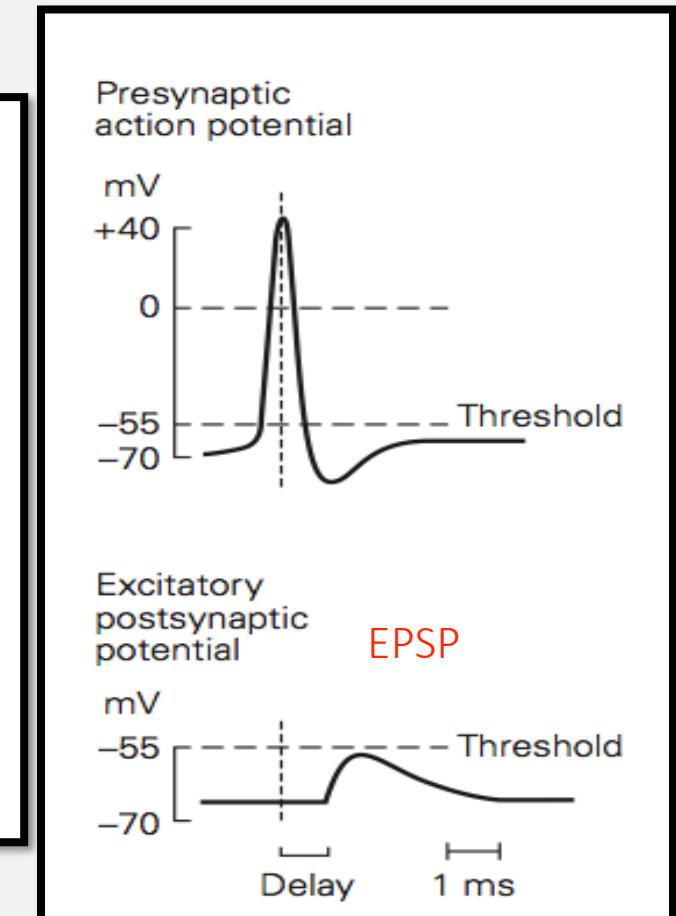
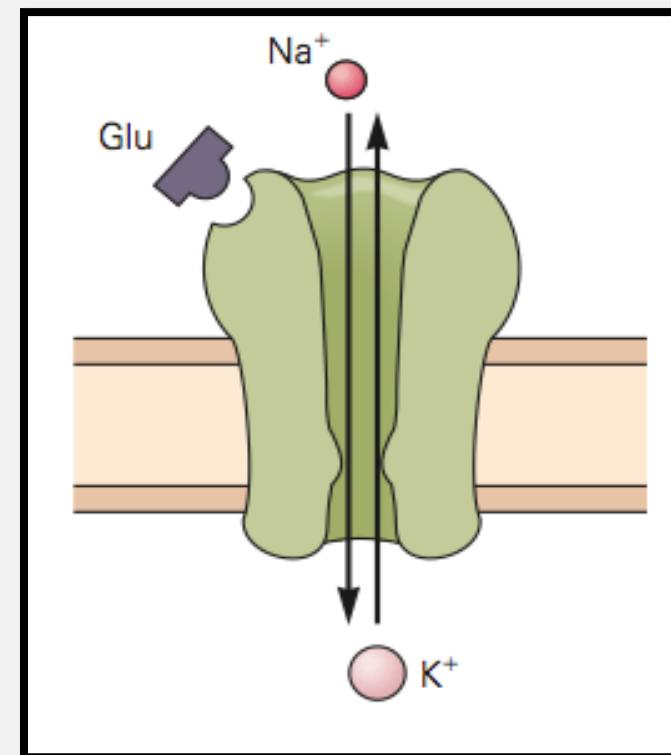
Excitatory Neurotransmitters

Glutamate

- Primary excitatory NT in the brain

AMPA Receptors

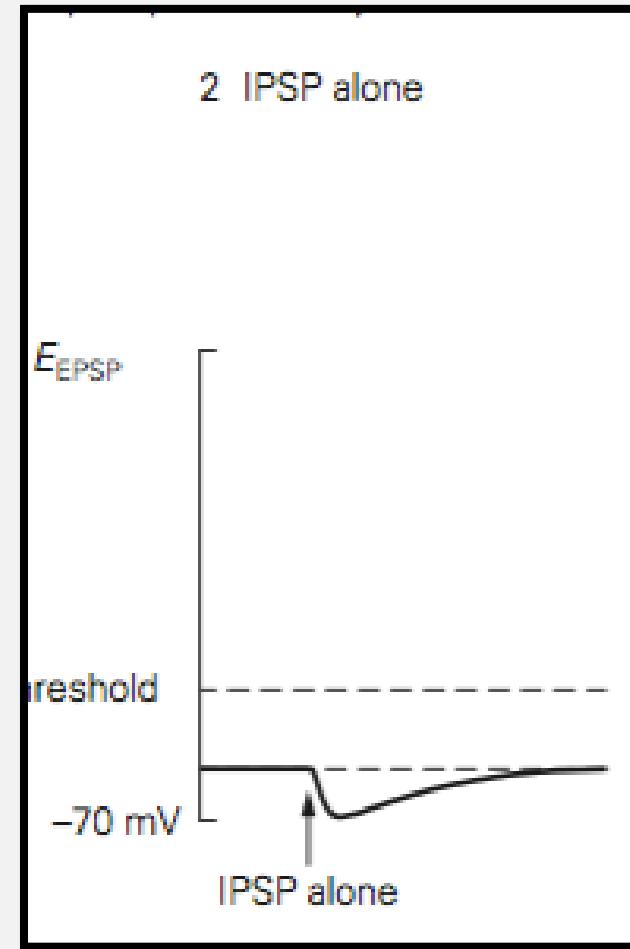
- Glutamate ionotropic receptors
- Ligand-gated
- Depolarizing
- Non-selective cation channel
- Na^+ enters, K^+ exits



Ionotropic inhibitory NT receptors

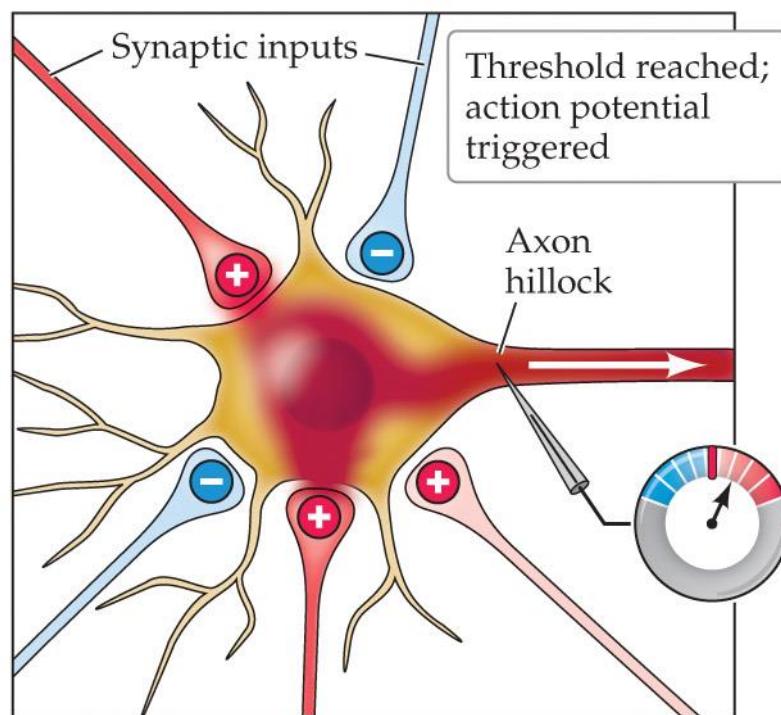
GABA

- Primary fast inhibitory NT
- Activates Cl⁻ receptor channels (GABA_A)
- Post synaptic hyperpolarization
- “Clamps” membrane at -70mV
- Prevent depolarization + APs
- Alter firing rate of neurons (provides information!)

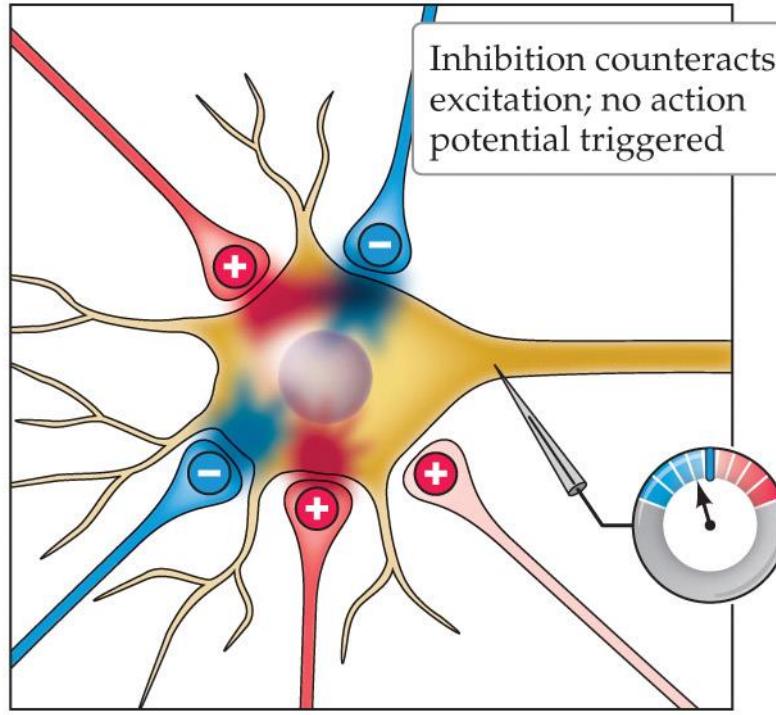


Integration of inputs

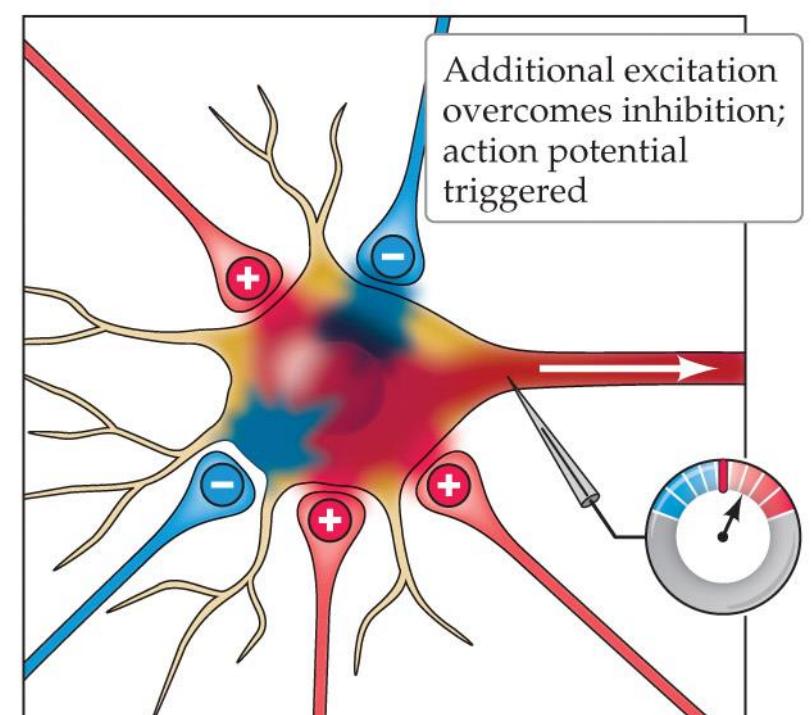
(A) Excitatory inputs cause the cell to fire



(B) Inhibition also plays a role



(C) The cell integrates excitation and inhibition

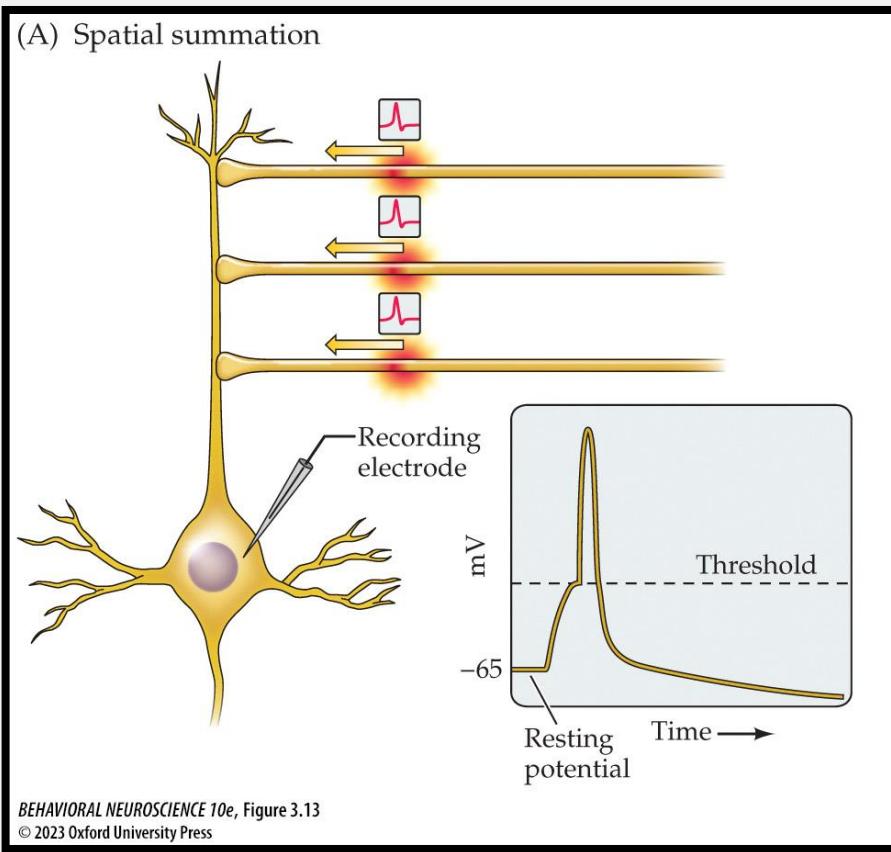


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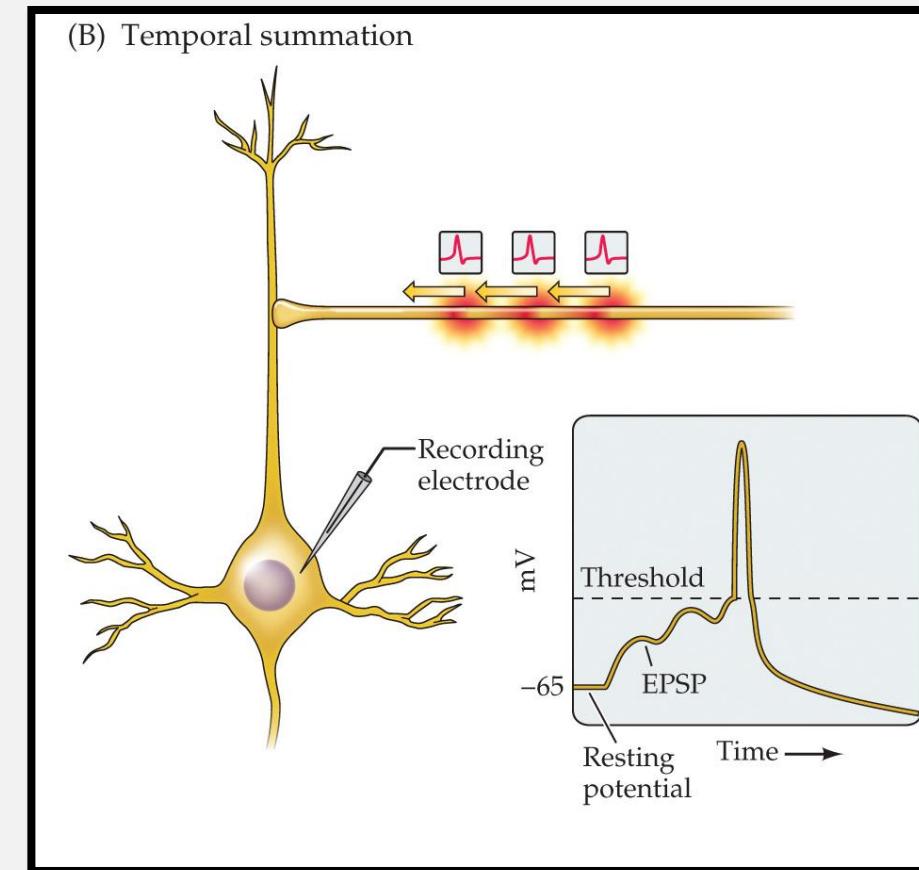
Spatial versus Temporal Summation

Spatial Summation (A)

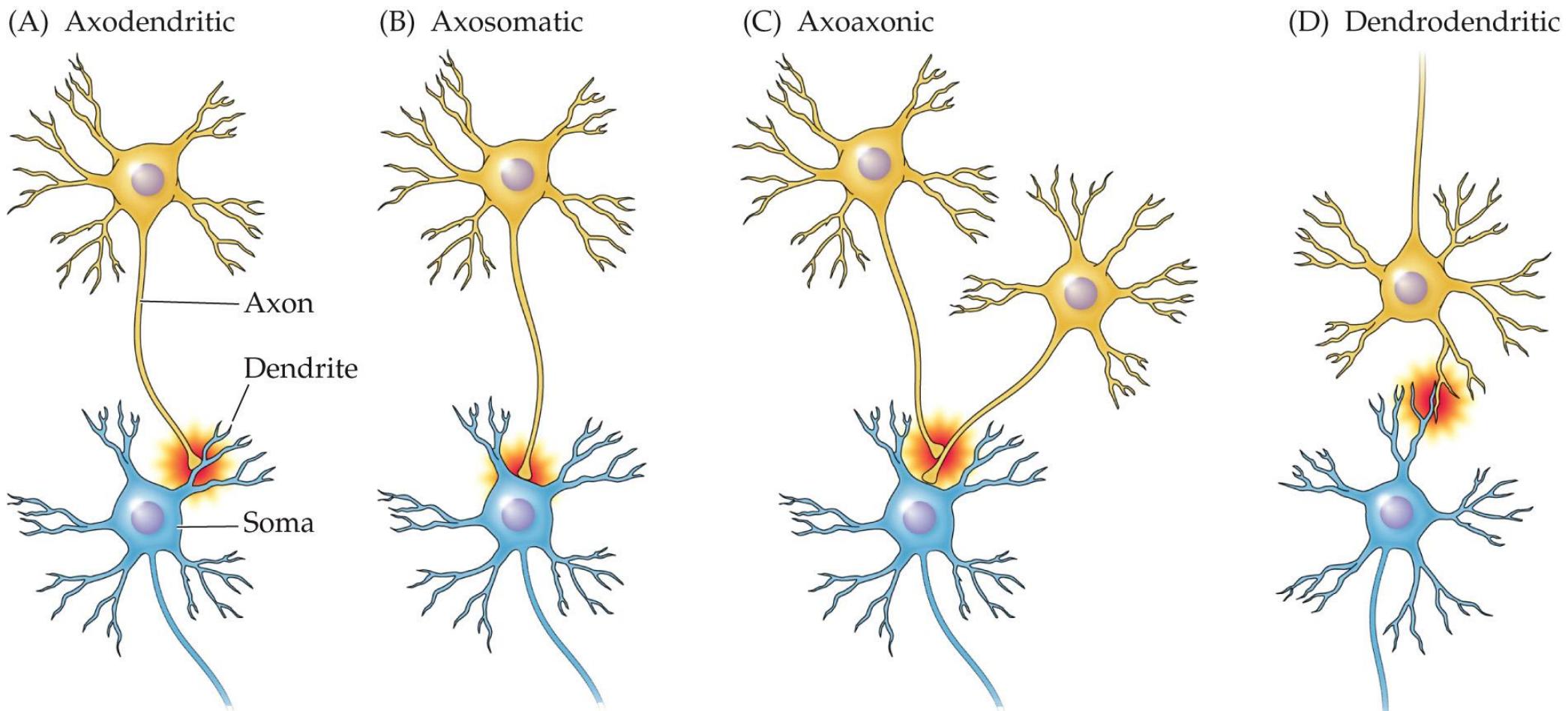


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Temporal summation (B)



Types of synapses



Neuronal Circuitry

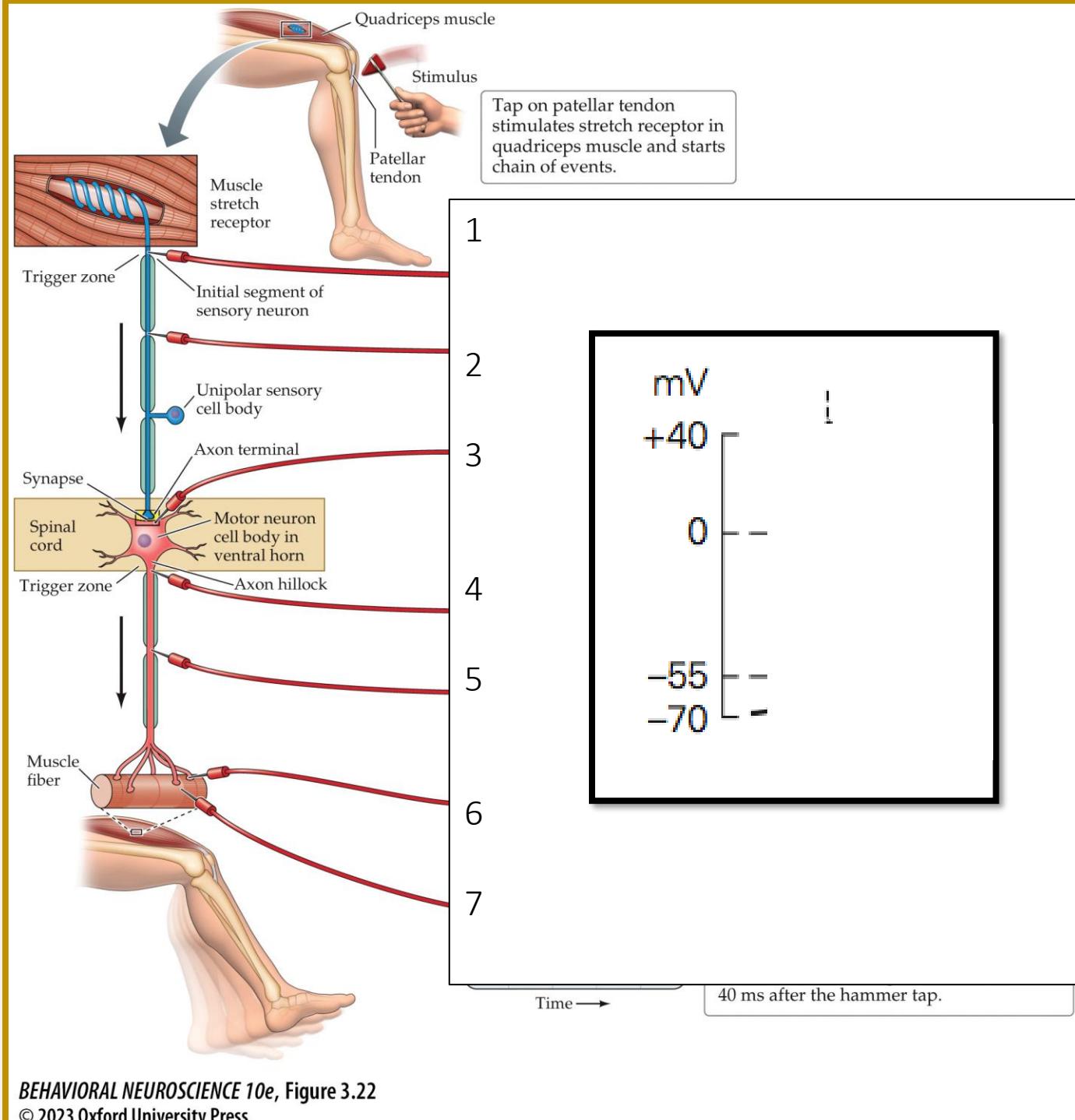
Neurons and synapses combine to make circuits.

Neural chain:

- simple series of neurons (e.g., the **knee-jerk reflex** consists of a sensory neuron, a synapse, and a motor neuron).
- Extremely fast: large myelinated axons, sensory cells synapse directly onto motor neurons, ionotropic synapses.

Knee Jerk Activity

At each recording point, draw out the potential changes. You can assume that an AP is initiated at each trigger zone





Visualizing circuits

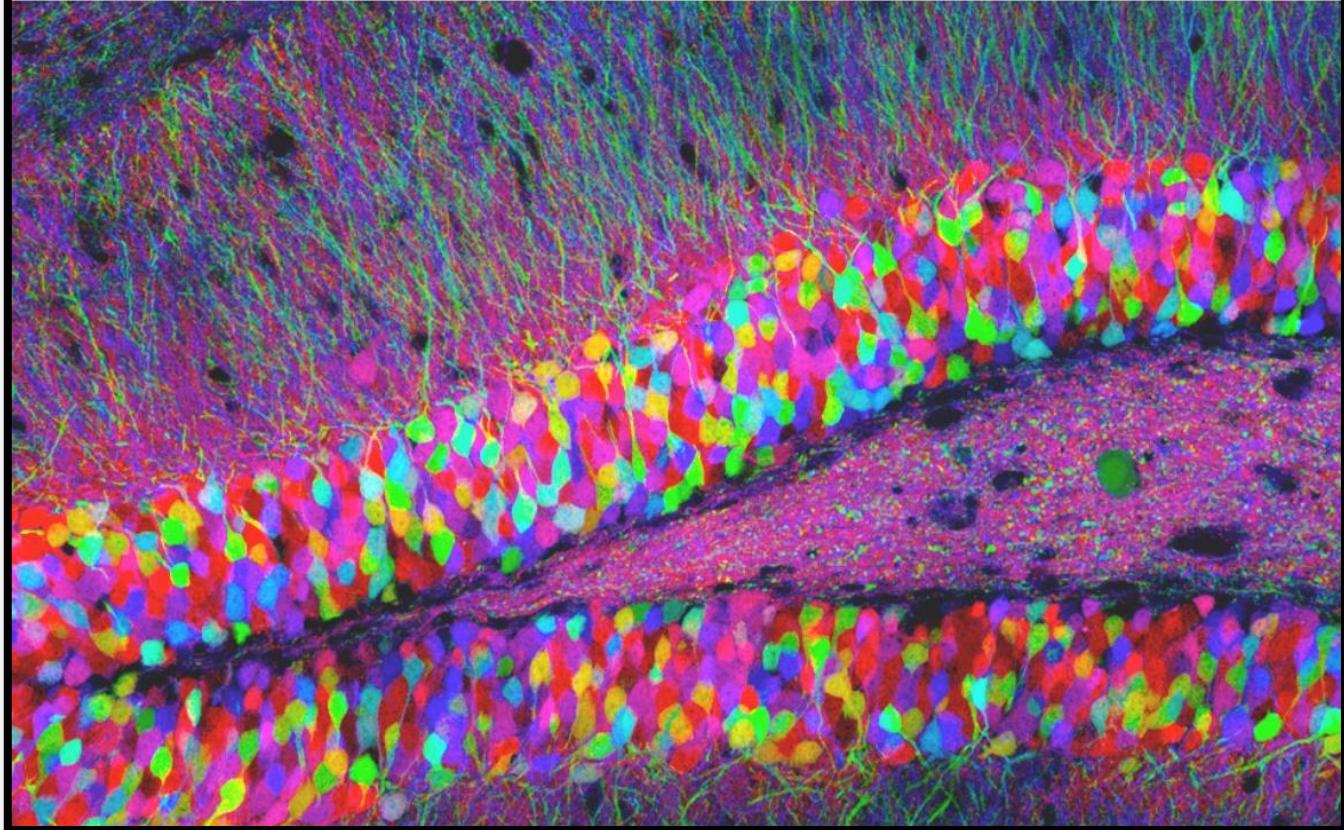
Mapping circuit connectivity with Brainbow

Expression of multiple different coloured FPs

- Randomly expressed FPs (red, blue, green) combine to create unique colours in different neurons
- Goal: trace dendrites and axons of many or all neurons – see how they connect and form circuits

Brainbow in the dentate gyrus region of the hippocampus

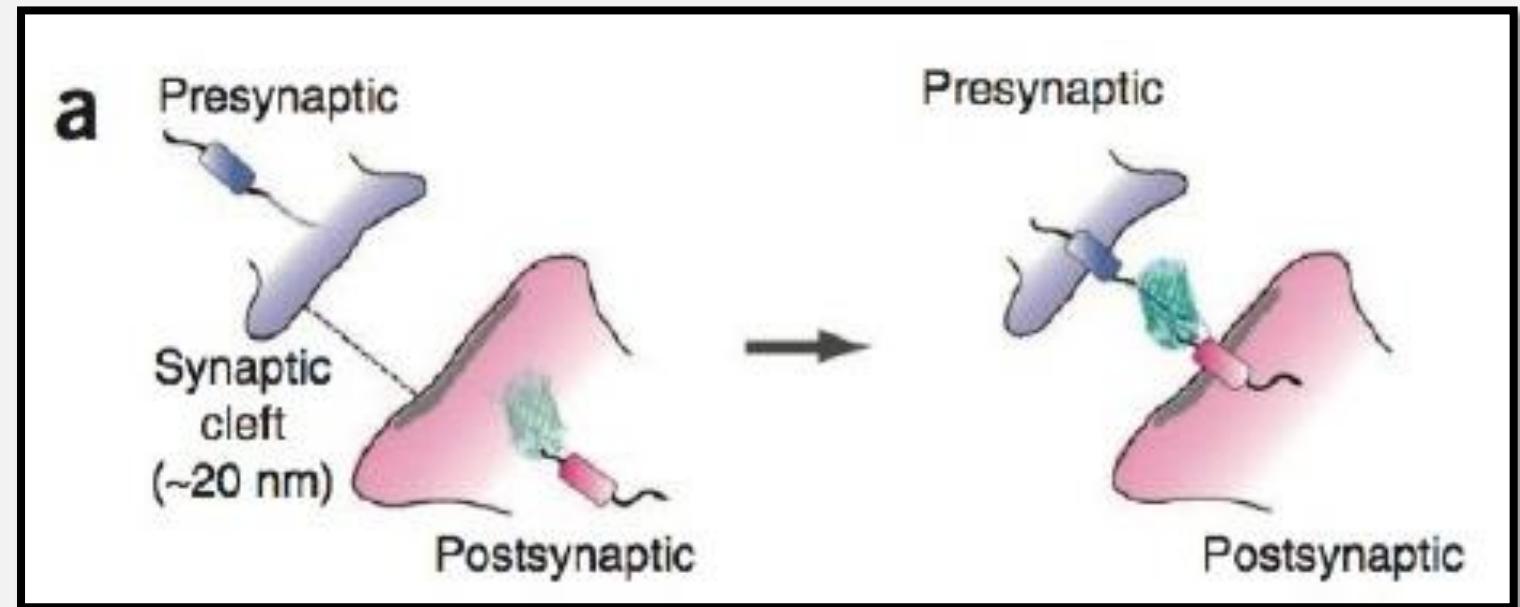
Easy to map this connectome?



Mapping connectivity with GRASP

GFP reconstitution across synaptic partners

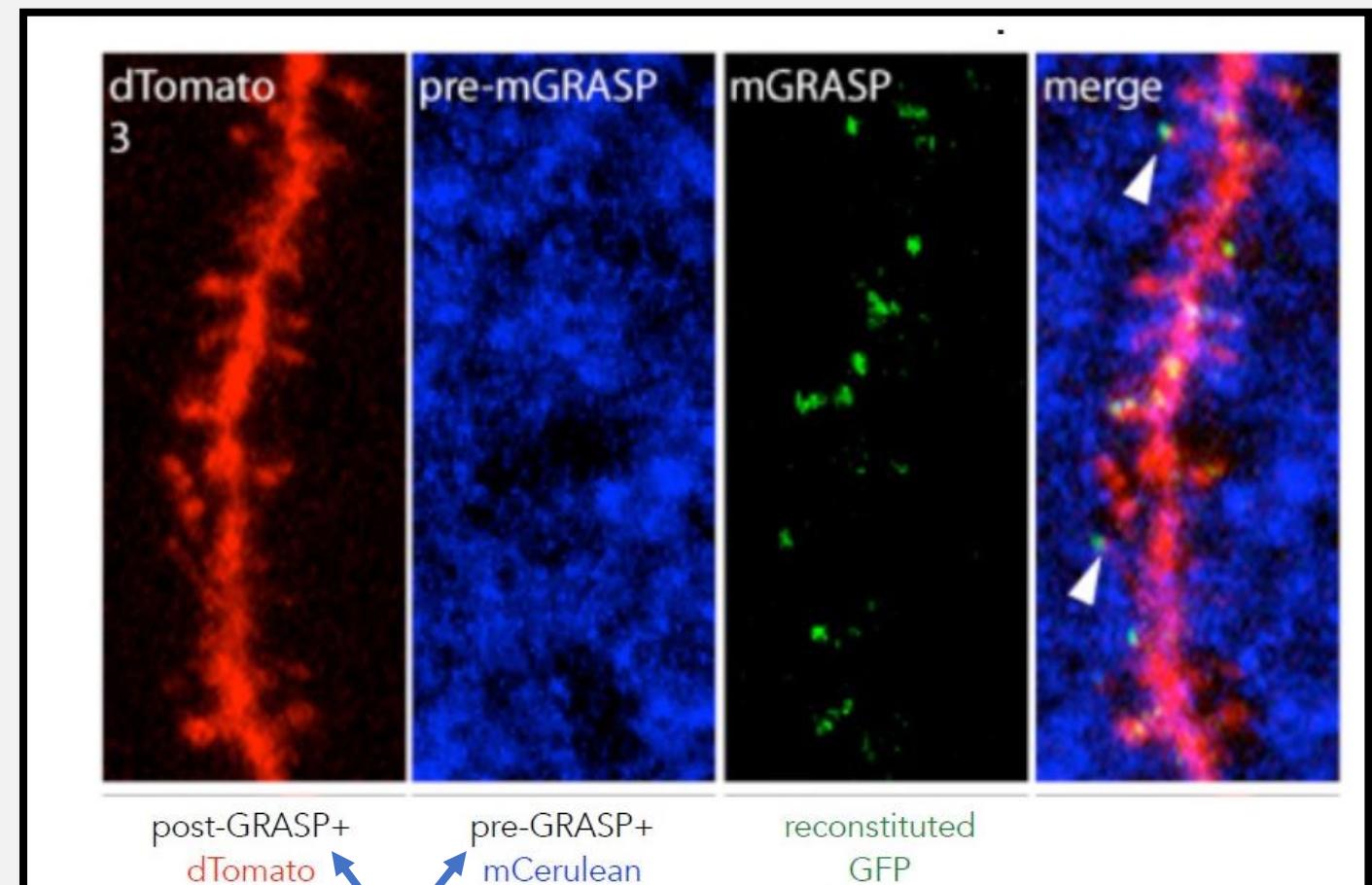
- Fluorescent labelling of “synaptically-connected” neurons
- Based on spatial proximity
- Promotors are key!
 - Label pre - machinery/post synaptic machinery with complimenting “halves” of GFP



Mapping connectivity with GRASP

GFP reconstitution across synaptic partners

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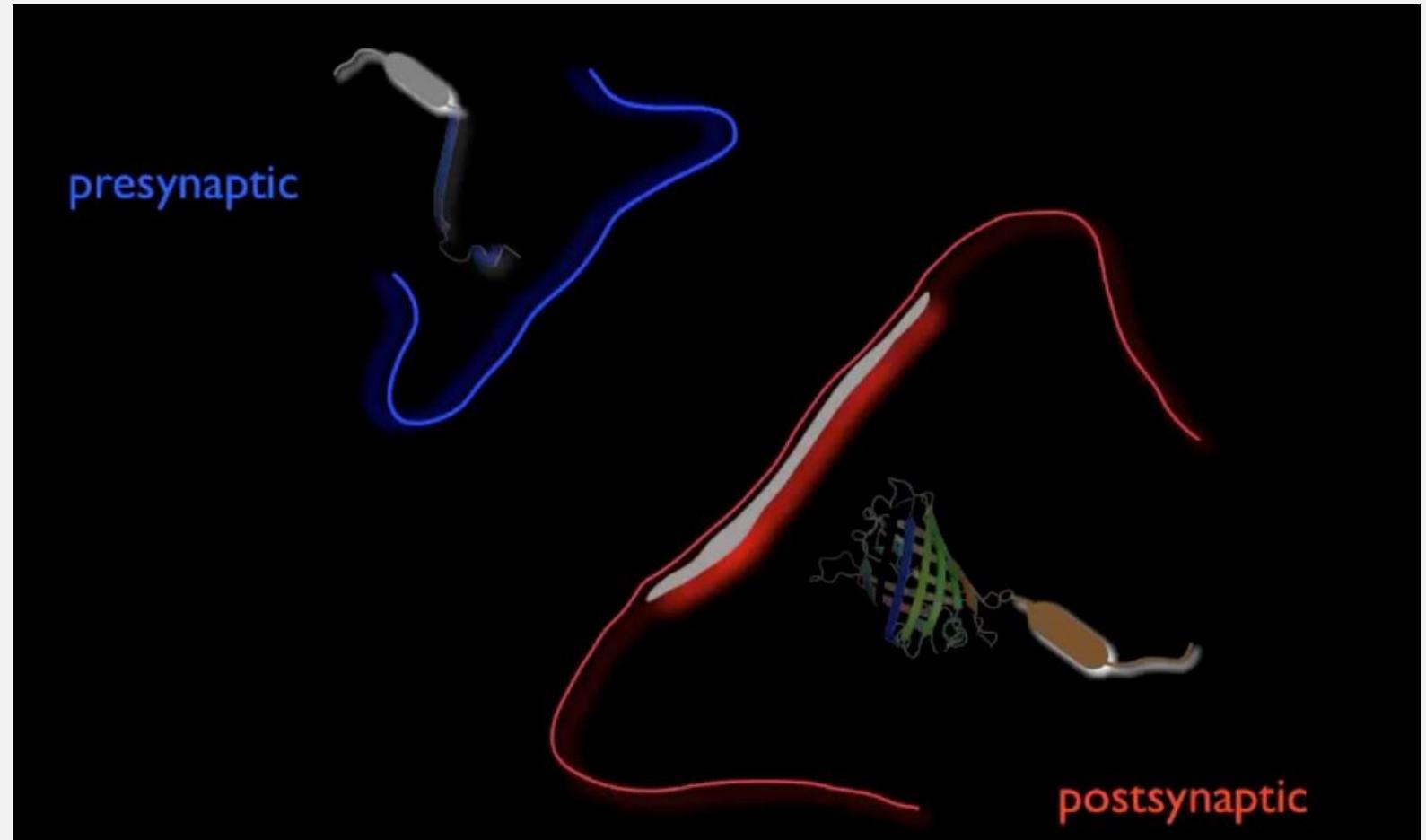


Reporters to see where pre and post molecules are

mGRASP

Mammalian GFP Reconstitution Across Synaptic Partners

- Video showing an application of mGRASP combined with 3D modeling imaging in the hippocampus



<https://www.youtube.com/watch?v=5ftqp6CLTgU>

Mapping Circuit Connectivity with Rabies Virus

In Nature

- Rabies virus has the ability to infect cells and travel retrogradely (to the presynaptic neuron).



Engineering the virus

- Be less virulent (not cause disease)
- Express a fluorescent protein
- Infect specific cells



Method

- Infect starter cells
- Virus will travel backwards across the 1 synapse
- View connection via fluorescent microscope



Human Nervous System

Learning objectives

- 1. Define and differentiate each aspect of the human nervous system**
- 2. Recognize the various functions and neurophysiological impacts of each aspect of the human nervous system**
- 3. Describe the basic developmental stages of the human brain.**
- 4. Describe major historical contributions to our understanding of the brain's structure and function.**
- 5. Differentiate between “old” and “new” phrenology.**
- 6. Use anatomical terminology to locate various structures of the human brain.**
- 7. Compare and contract gray and white matter.**
- 8. Compare and contrast various neuroimaging techniques. Recognize the utility of each imaging technique**

The Nervous System

Gross neuroanatomy

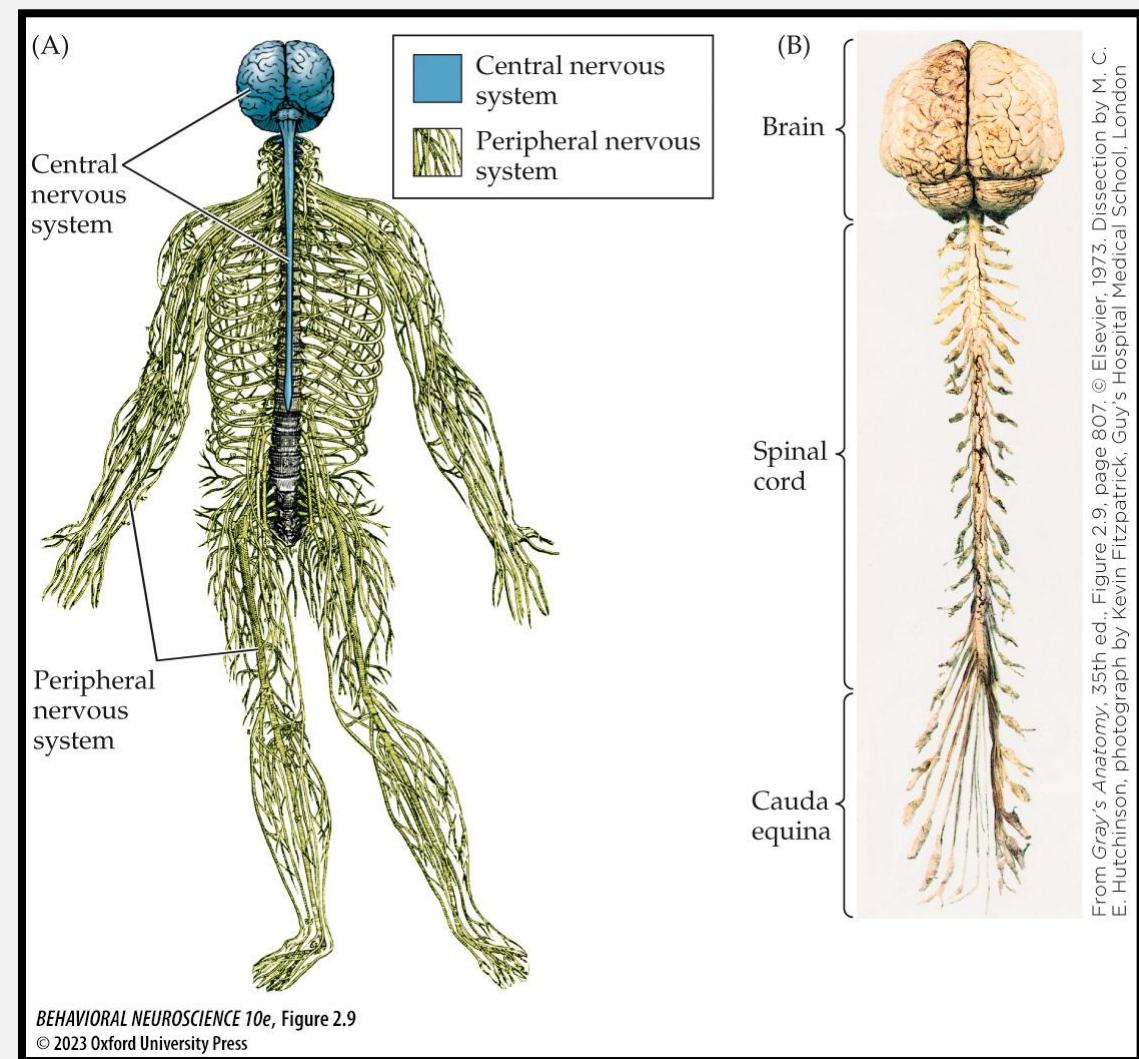
- Features of the nervous system visible to the naked eye.

Central nervous system (CNS)

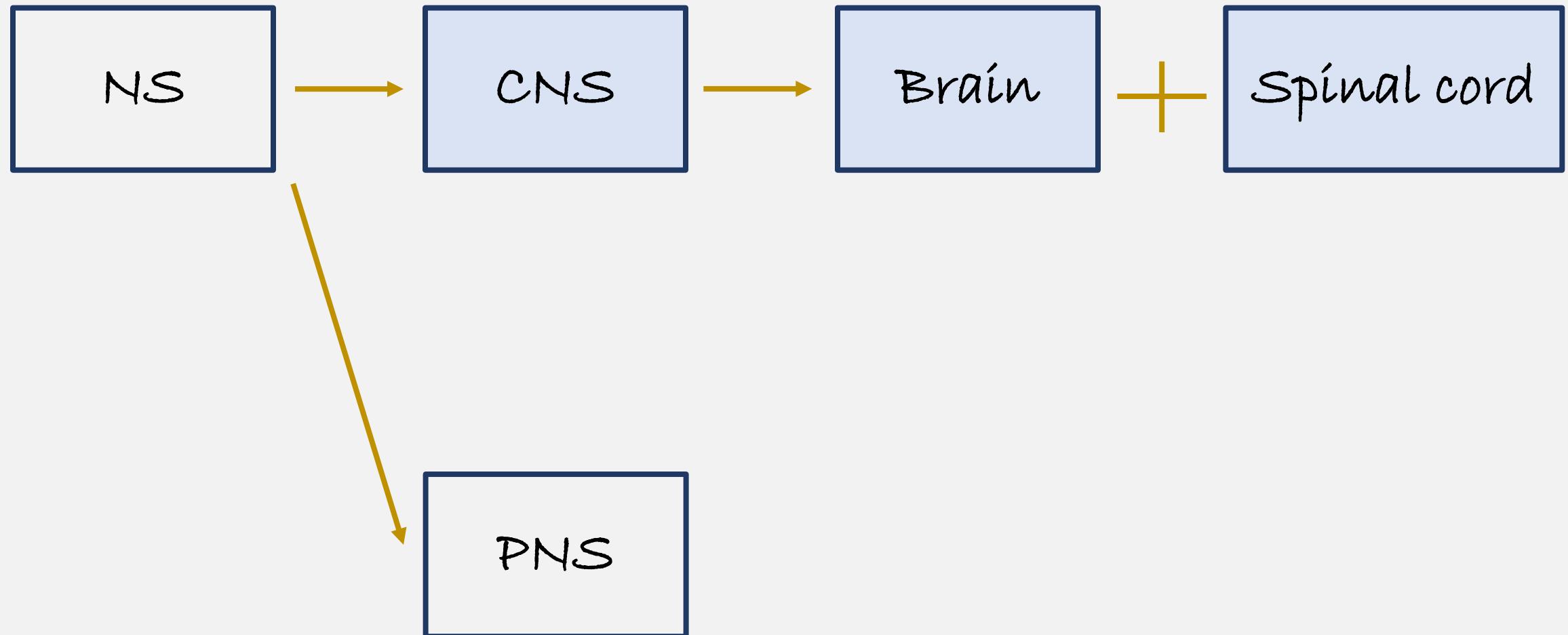
- the brain and spinal cord.

Peripheral nervous system (PNS)

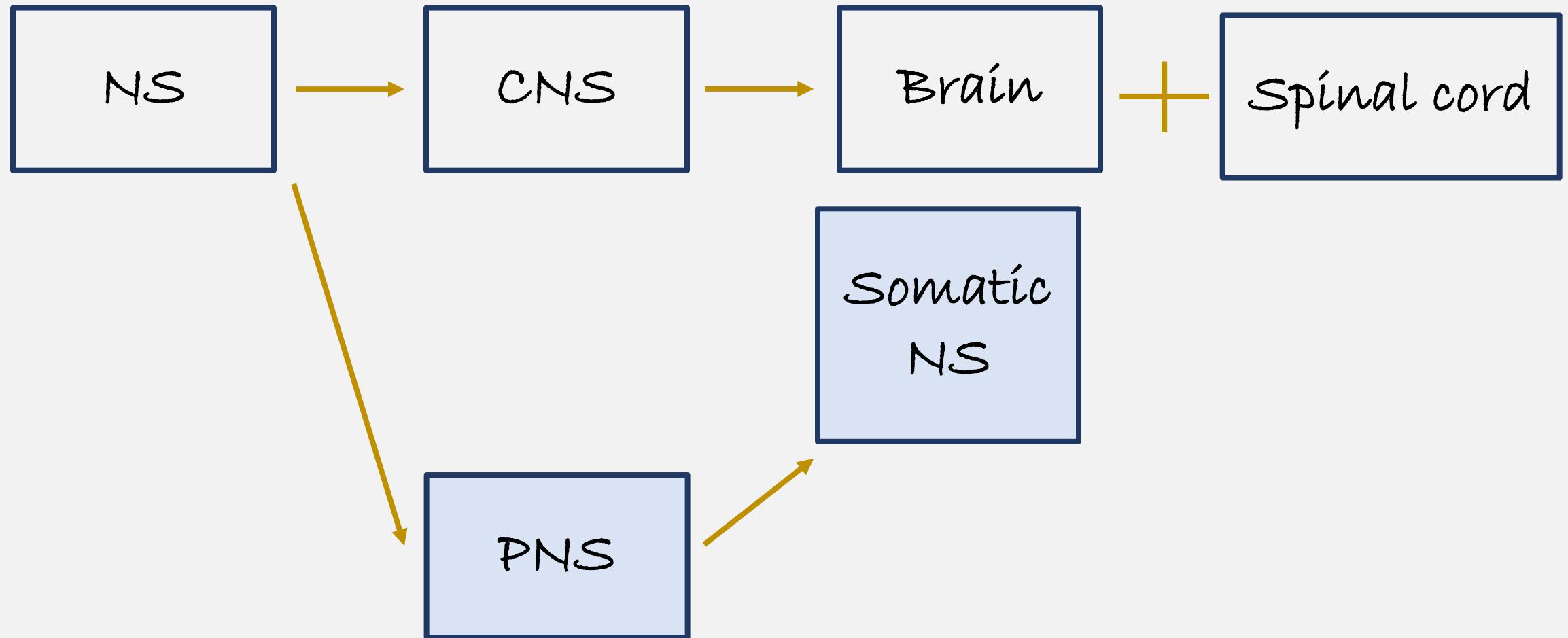
- all parts of the nervous system found outside the skull and spinal column.



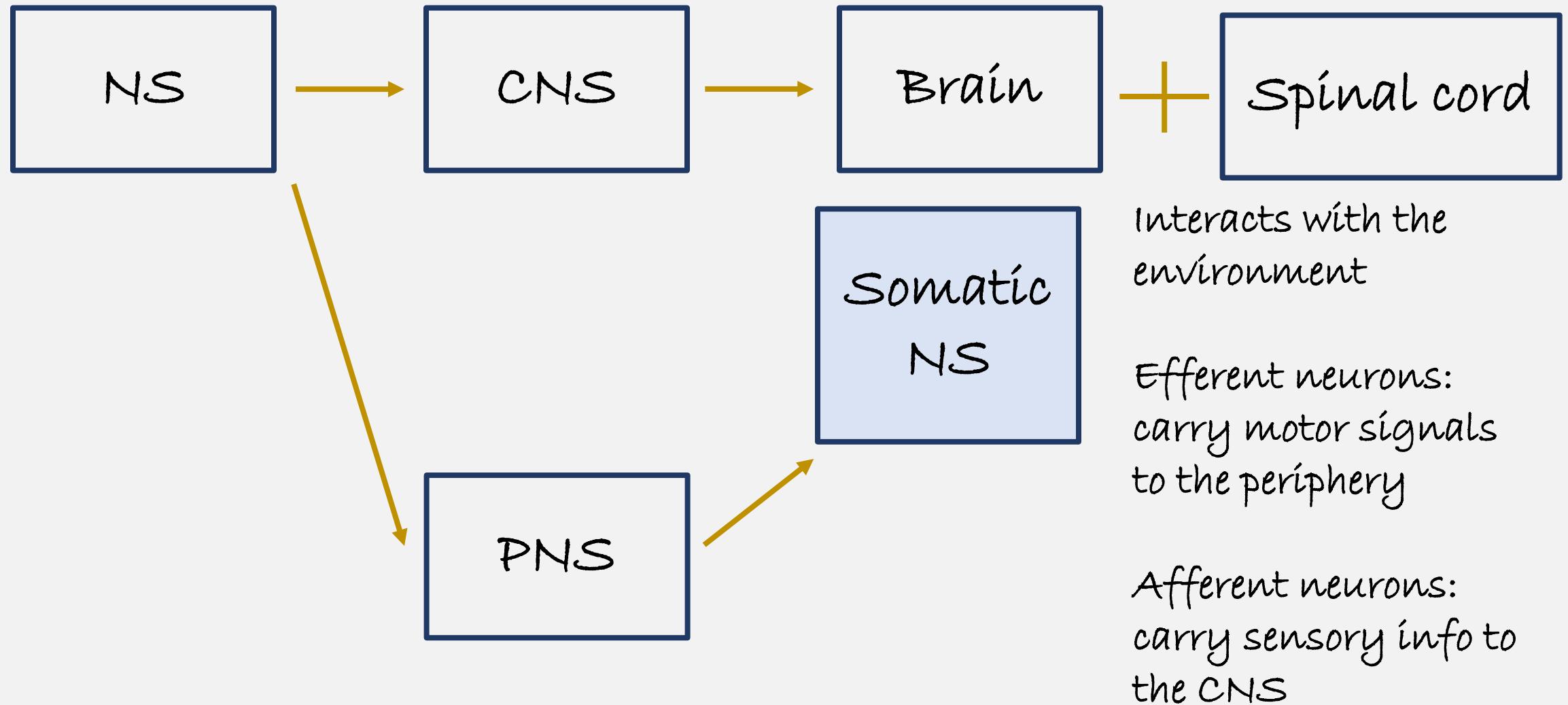
The Nervous System



The Nervous System



The Nervous System



The Somatic Nervous System

The somatic nervous system

- consists of cranial nerves and spinal nerves.

Cranial nerves

- 12 pairs; some are sensory, some are motor, some have both functions—separate axons in the nerve carry the sensory and motor signals.
- Cranial nerve is defined as a cranial nerve if it enters the periphery through a hole in the skull

The Cranial Nerves

CN I - Olfactory

CN II - Optic

CN III - Oculomotor

CN IV - Trochlear

CN V - Trigeminal

CN VI – Abducens

CN VII - Facial

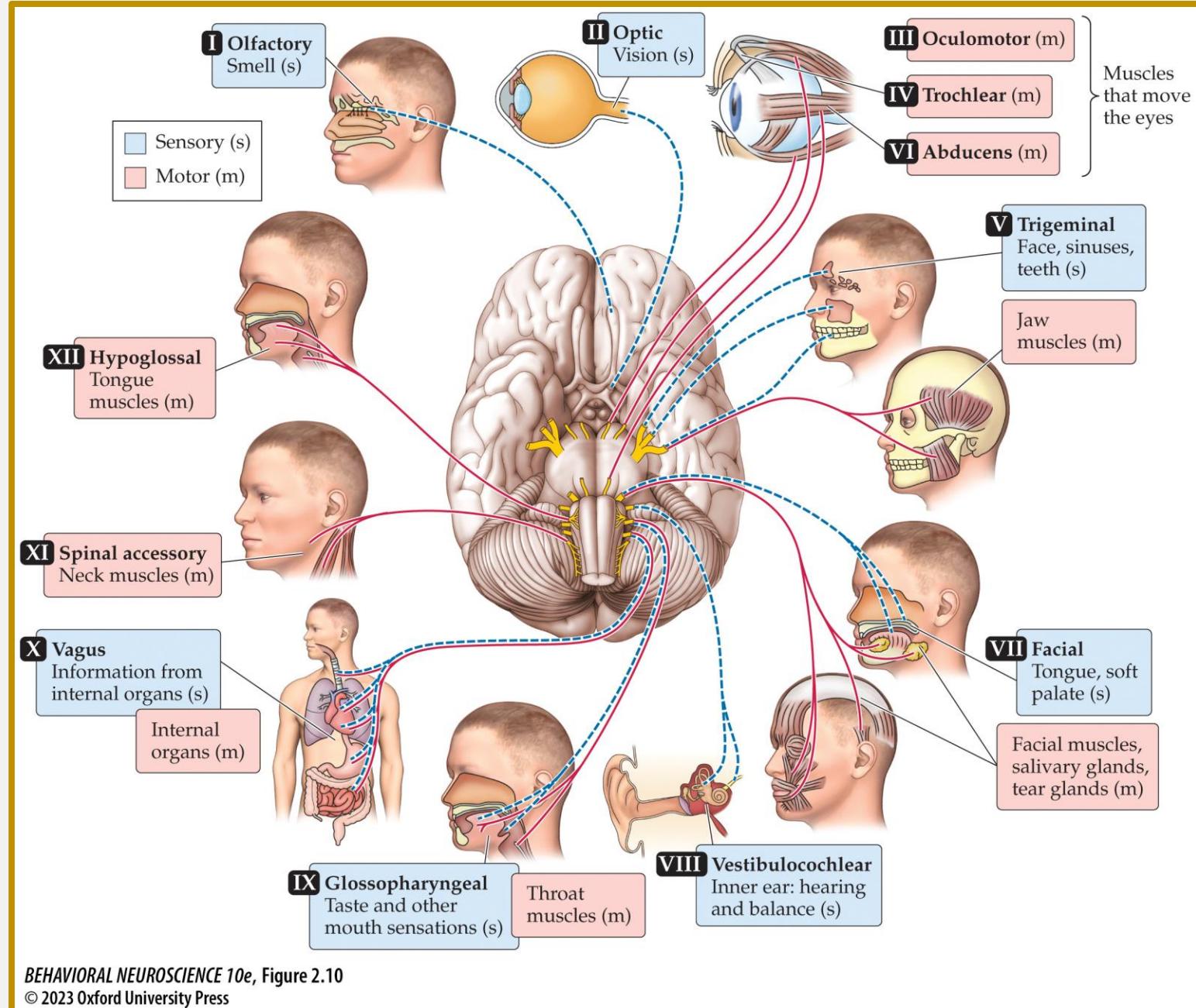
CN VIII - Vestibulocochlear

CN IX - Glossopharyngeal

CN X - Vagus

CN XI - Accessory

CN XII – Hypoglossal

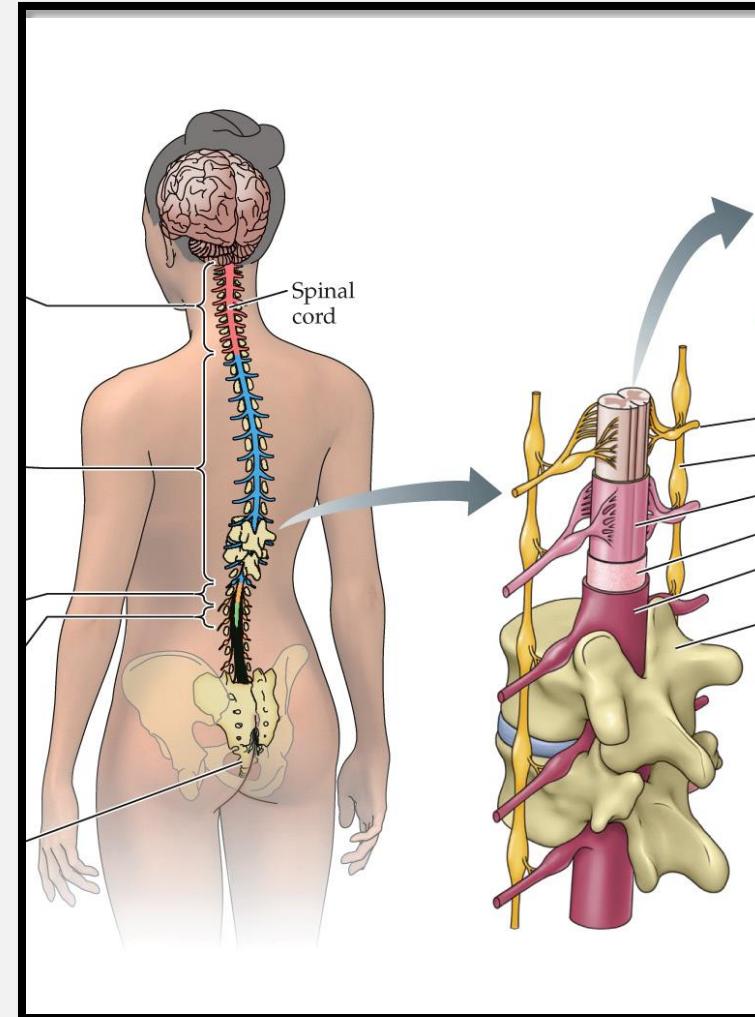


The Spine

Spinal nerves—31 pairs

Each spinal nerve is the fusion of two distinct branches, or roots:

- **Dorsal root**—carries sensory information from the body to the spinal cord
- **Ventral root**—carries motor information from the spinal cord to the muscles

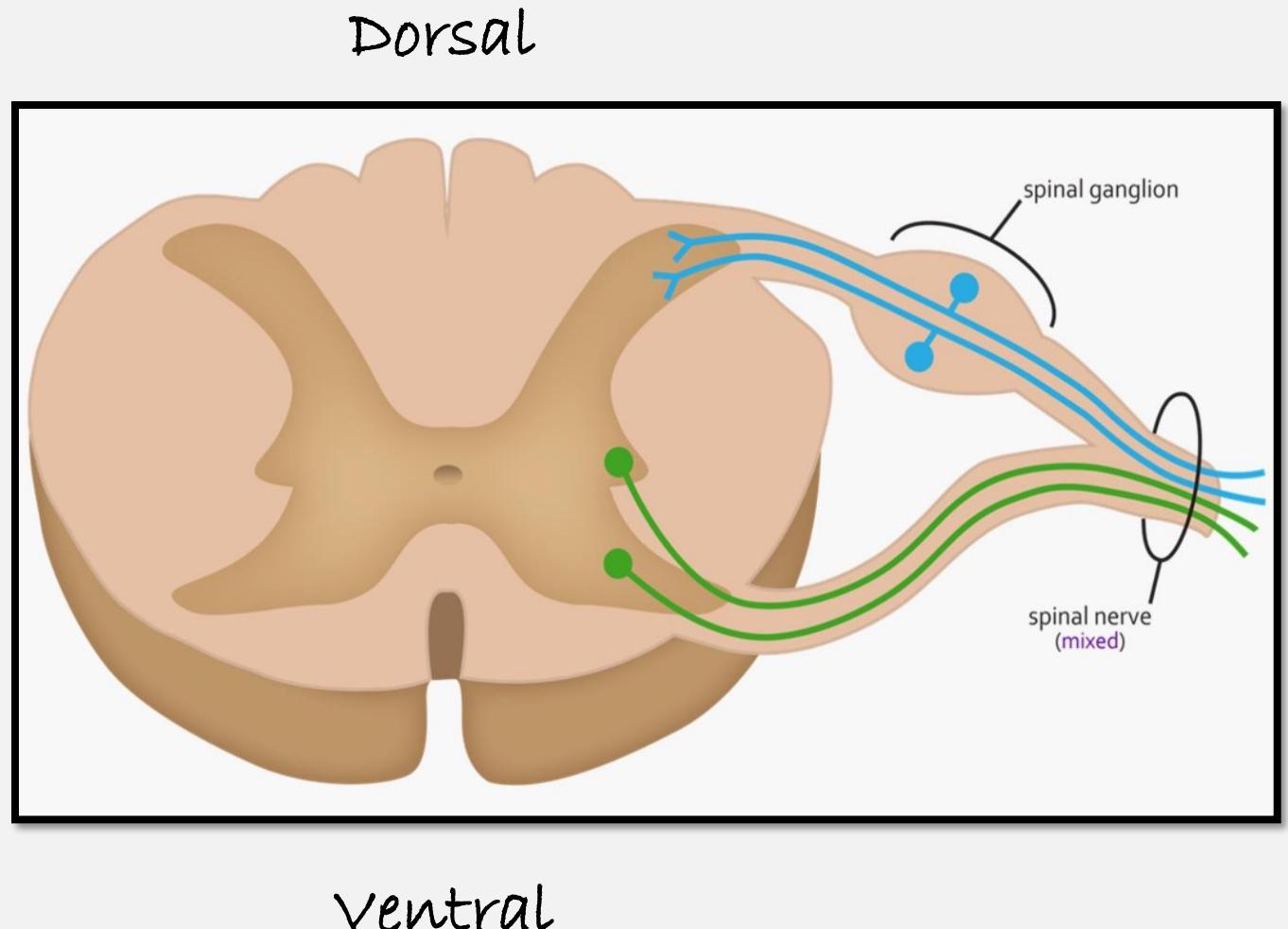


The Spine

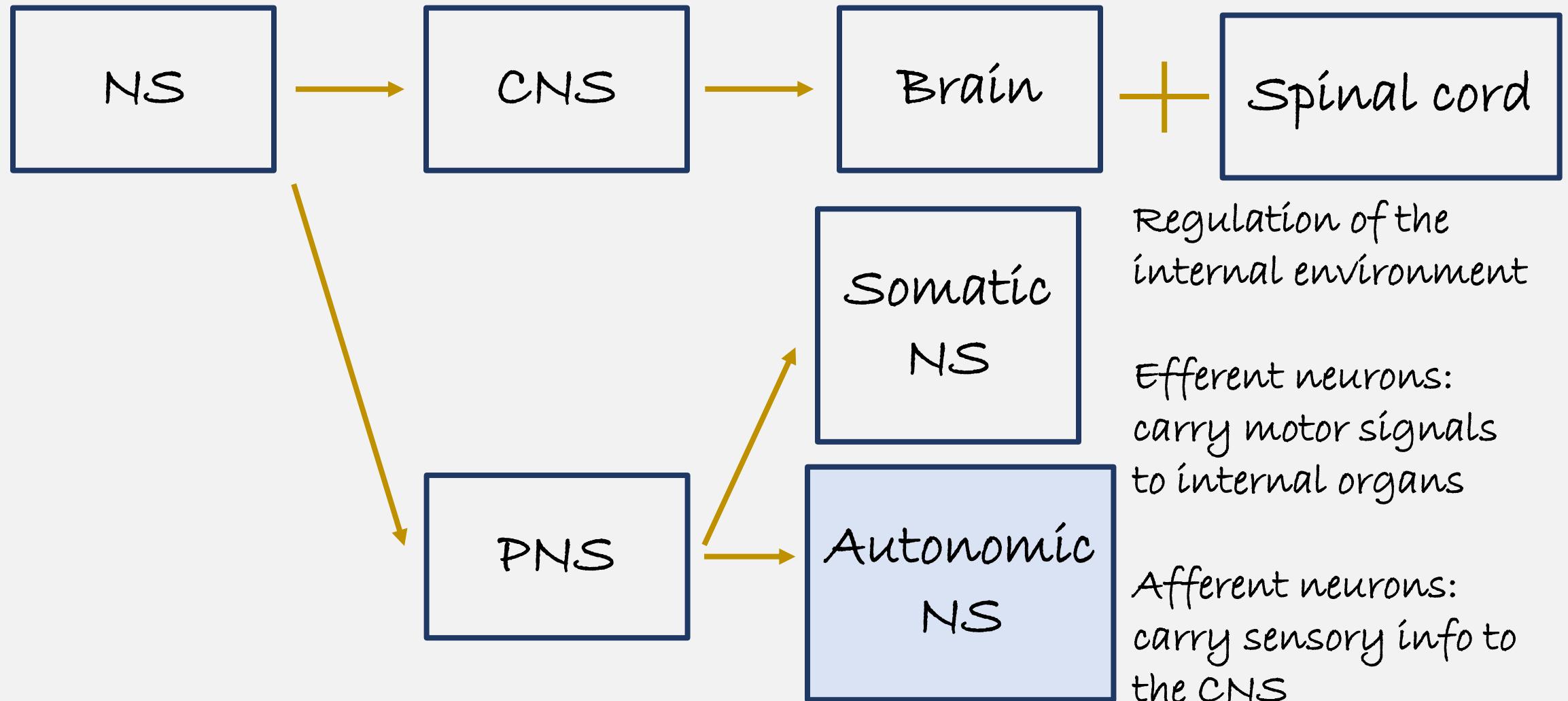
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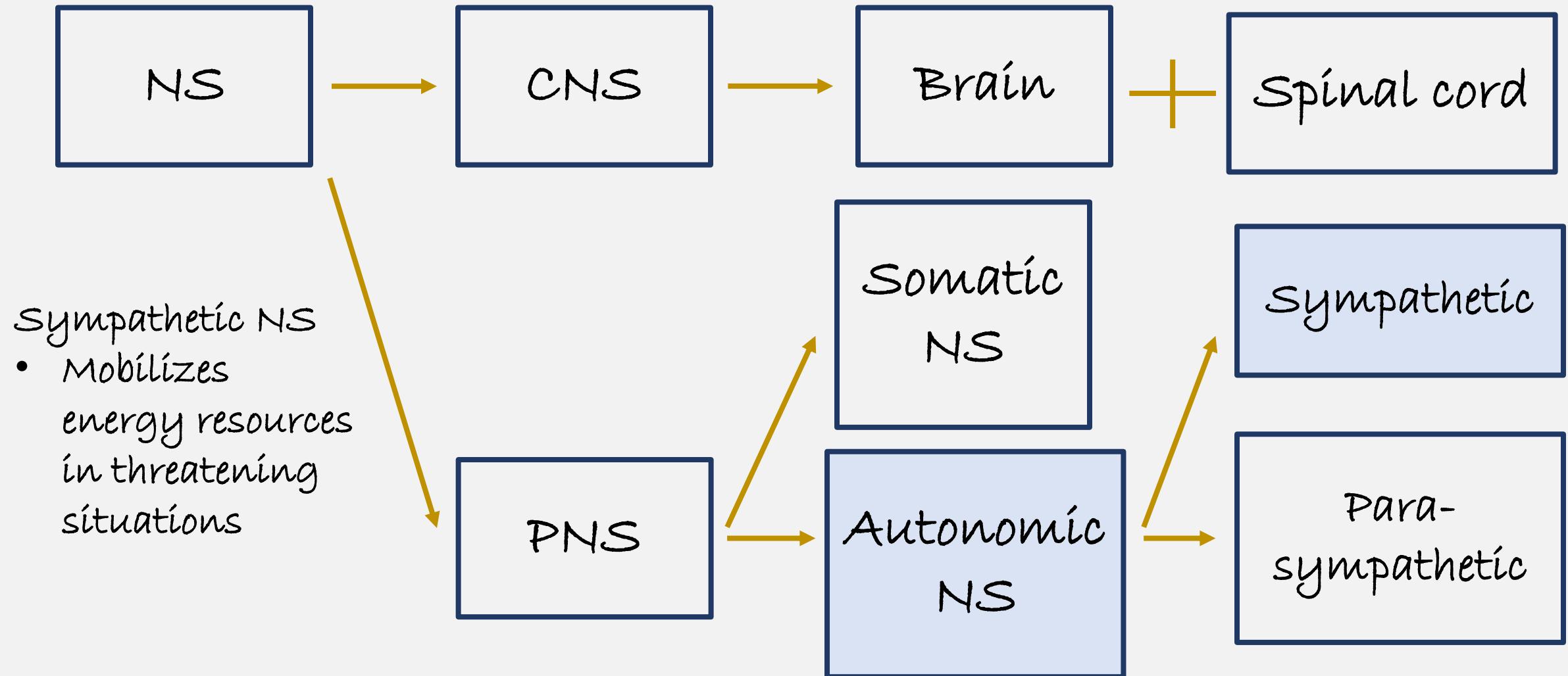
- **Dorsal root**—carries sensory information from the body to the spinal cord
- **Ventral root**—carries motor information from the spinal cord to the muscles



The Nervous System



The Nervous System



The Nervous System

Sympathetic nervous system:

- activation prepares the body for action (fight or flight response).

Main Neurotransmitter

- is **norepinephrine**. Do you know another word for epinephrine?

The Nervous System

Parasympathetic nervous system:

- activation is often in opposition to sympathetic activity (rest and digest).

Neurotransmitter

- is **acetylcholine**.

Activity

Organize the following ANS actions into sympathetic and parasympathetic columns

- Increase heartbeat
- Decrease heartbeat
- Dilate pupils (open)
- Constrict pupils (close)
- Stimulate secretion by sweat glands
- Contract bladder
- Inhibit saliva production
- Dilate blood vessels in the digestive system

The Nervous System

The autonomic nervous system

- spans the central and peripheral nervous systems.

Autonomic ganglia

- are groups of neurons (cell bodies) located outside the CNS.
- Side note: In the CNS, these groupings are called nuclei
- **Preganglionic neurons** run from the CNS to the autonomic ganglia.
- **Postganglionic neurons** run from the autonomic ganglia to targets in the body.

The Autonomic Nervous System

Answer key and visualization of ganglions

The Nervous System

The autonomic nervous system has a third major division:

- Sympathetic nervous system
- Parasympathetic nervous system
- **Enteric nervous system**

Enteric nervous system

- local network of neurons that governs function of the gut
- Controlled by CNS
- Maintains fluid and nutrient balance (homeostasis) in the gut.



The brain



A brief history...

The History of Research on the Brain

Early Egyptians and Greeks (Aristotle)

- 1300 – 300 BCE
- Mental capacities came from the heart
- Egyptians preserved liver, lungs, stomach, intestines and heart in Pharaoh's tombs (important to ensure continued existence in the afterlife)



Photograph by Neil Watson

The History of Research on the Brain

Herophilus (300 BCE)

- “father of anatomy”
- Performed dissections on humans and animals

Galen (~100)

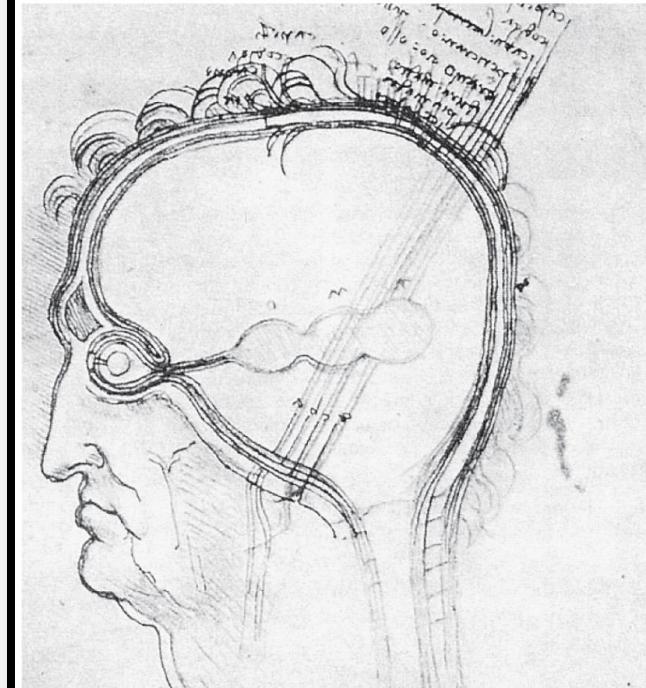
- Greco-Roman physician
- Reported behavioural changes to gladiators with injuries to the head
- Animal spirits passed along nerves to all regions of the body

The History of Research on the Brain

Leonardo da Vinci

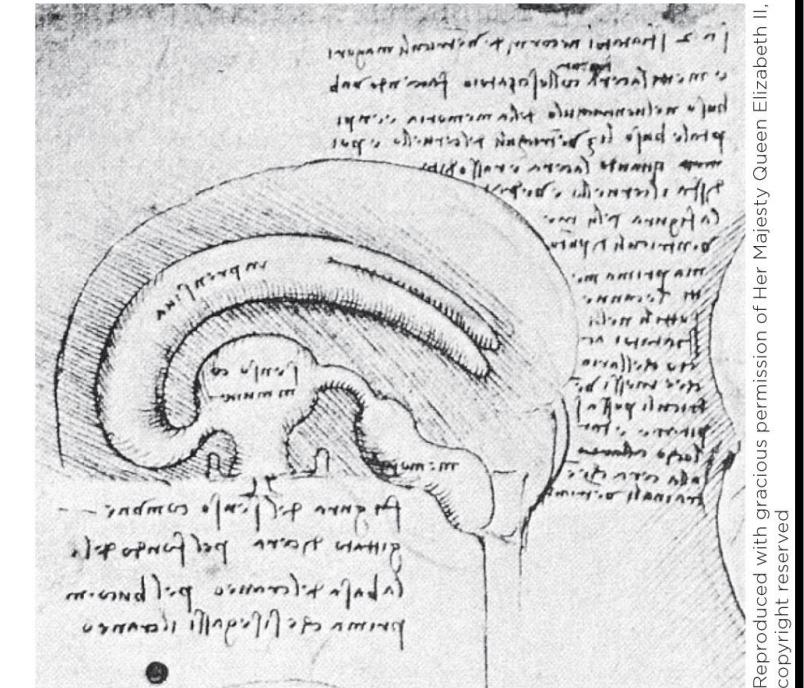


(A) Early drawing



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(B) Later drawing based on observation

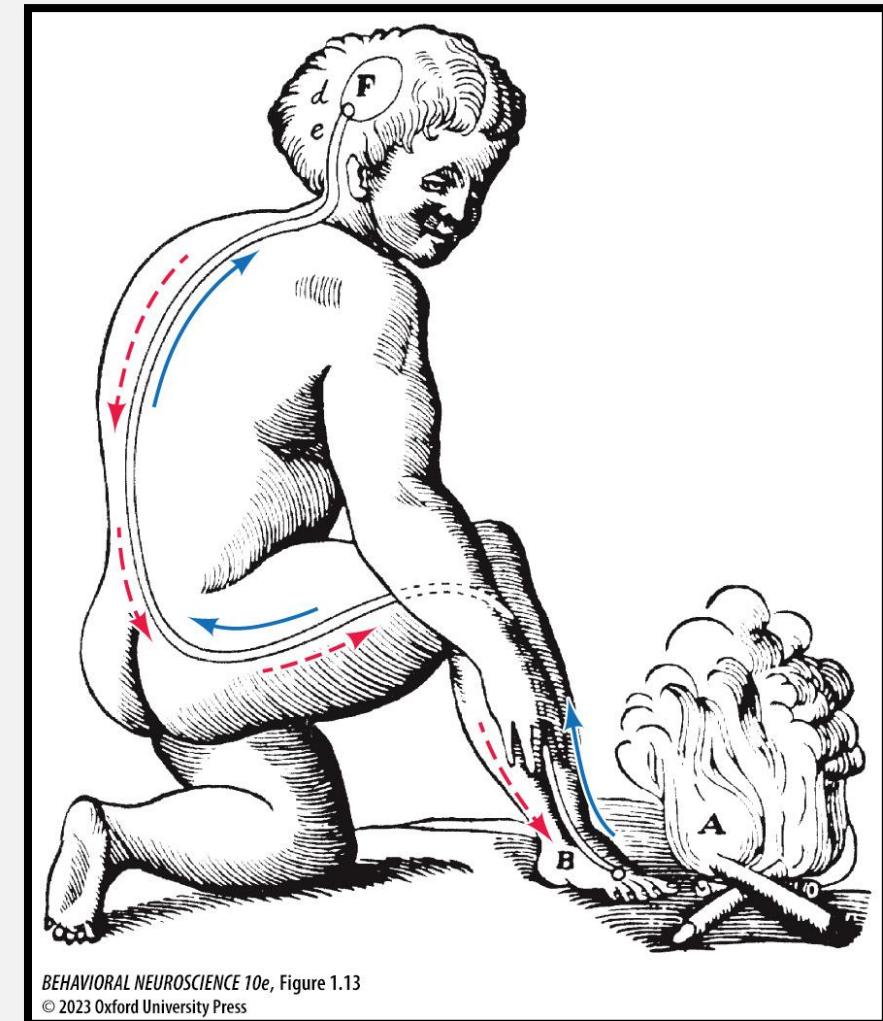


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The History of Research on the Brain

Rene Descartes (1596-1650)

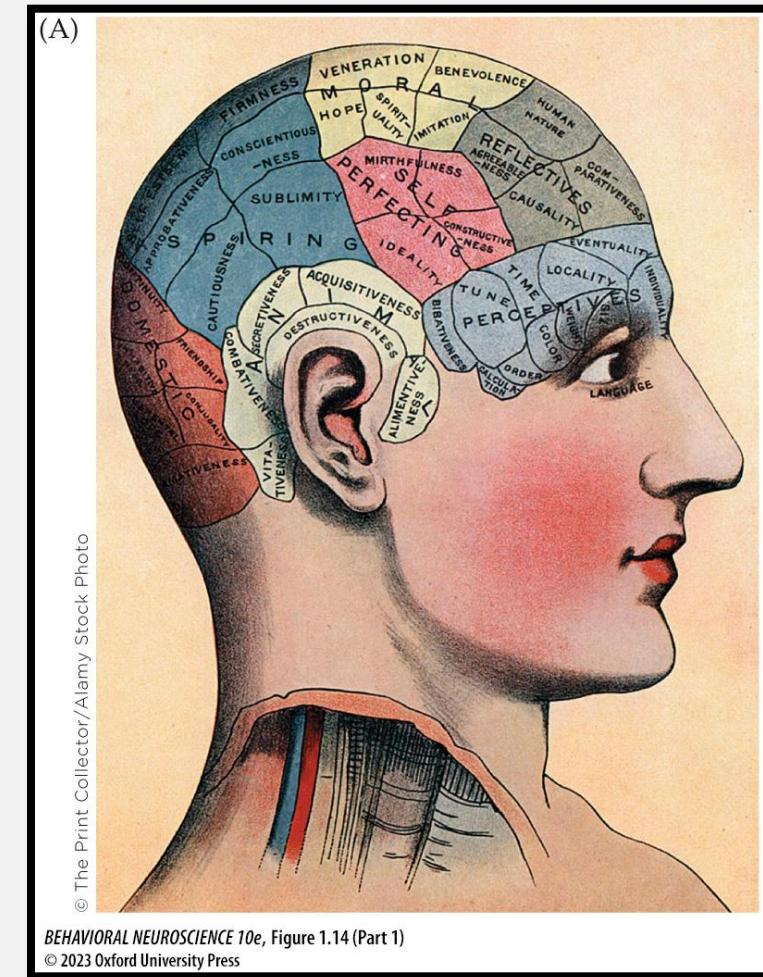
- Animal and human behaviour is like the workings of a machine
- Proposed the concept of a spinal reflex and neural pathways
- Proposed the pineal gland as the junction between the body and the mind
- **Dualism** – Humans have a non-material soul as well as a material body



The History of Research on the Brain

Phrenology (19th century)

- Assigned separate functions to different cortical areas
- Bumps on skull – causes by enlarged brain regions – matched to certain behaviours
- Opponents – stated the brain works as a whole



The History of Research on the Brain

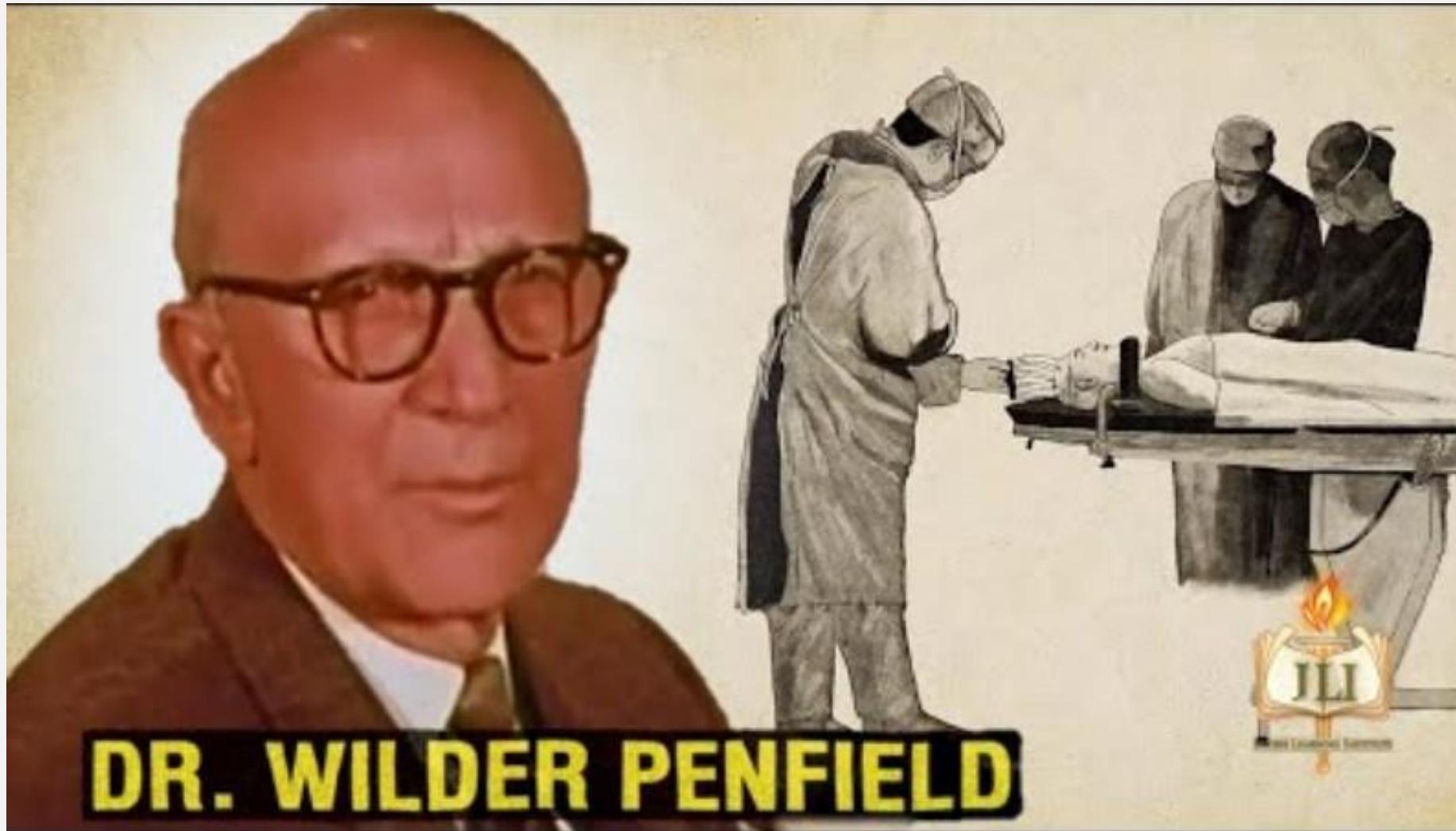
Paul Broca (1824-1880)

- Language ability restricted to a small area of the brain
- Assessed the brain of a man who was unable to produce speech for several years before death
- Lesions only in a small area of the frontal left lobe.
- Region is now called Brocas area

William James (1890)- *Principles of psychology*

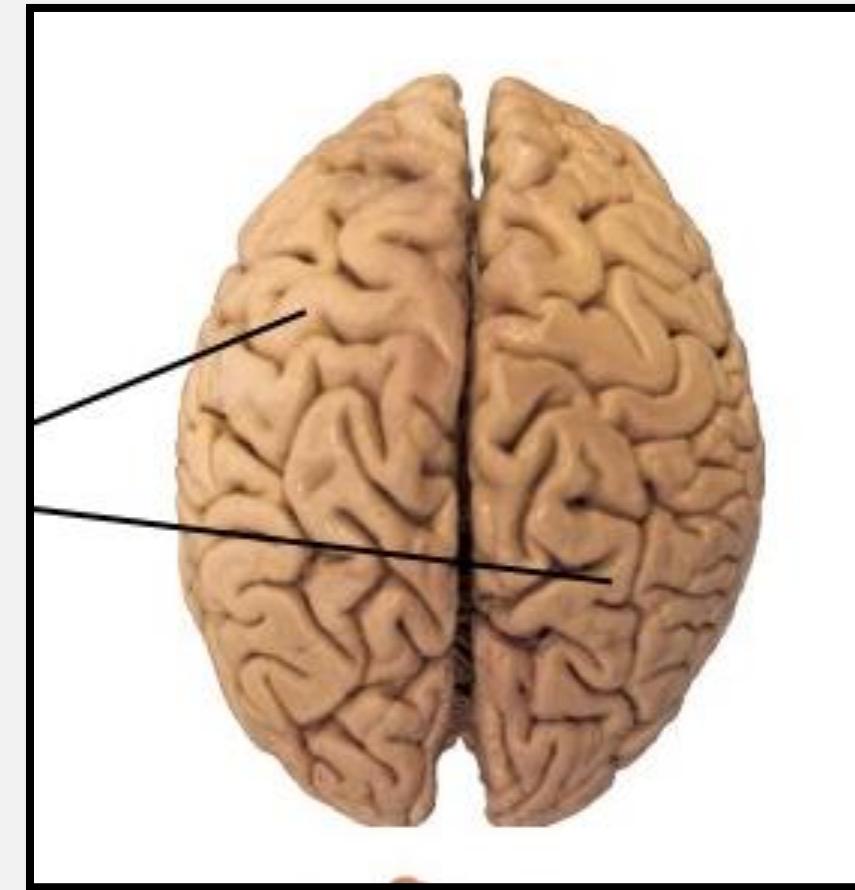
- Consciousness an aspect of the human nervous system

The history of research on the brain



The brain – basics

- The brain has two **cerebral hemispheres**.
- **Cerebral cortex:** folded outermost layer of the cerebral hemispheres, comprised mostly of neuron cell bodies, dendrites, and axons.
- Folds (**gyri** and **sulci**) increase amount of cortex that can fit into the skull, and are grouped together into lobes.

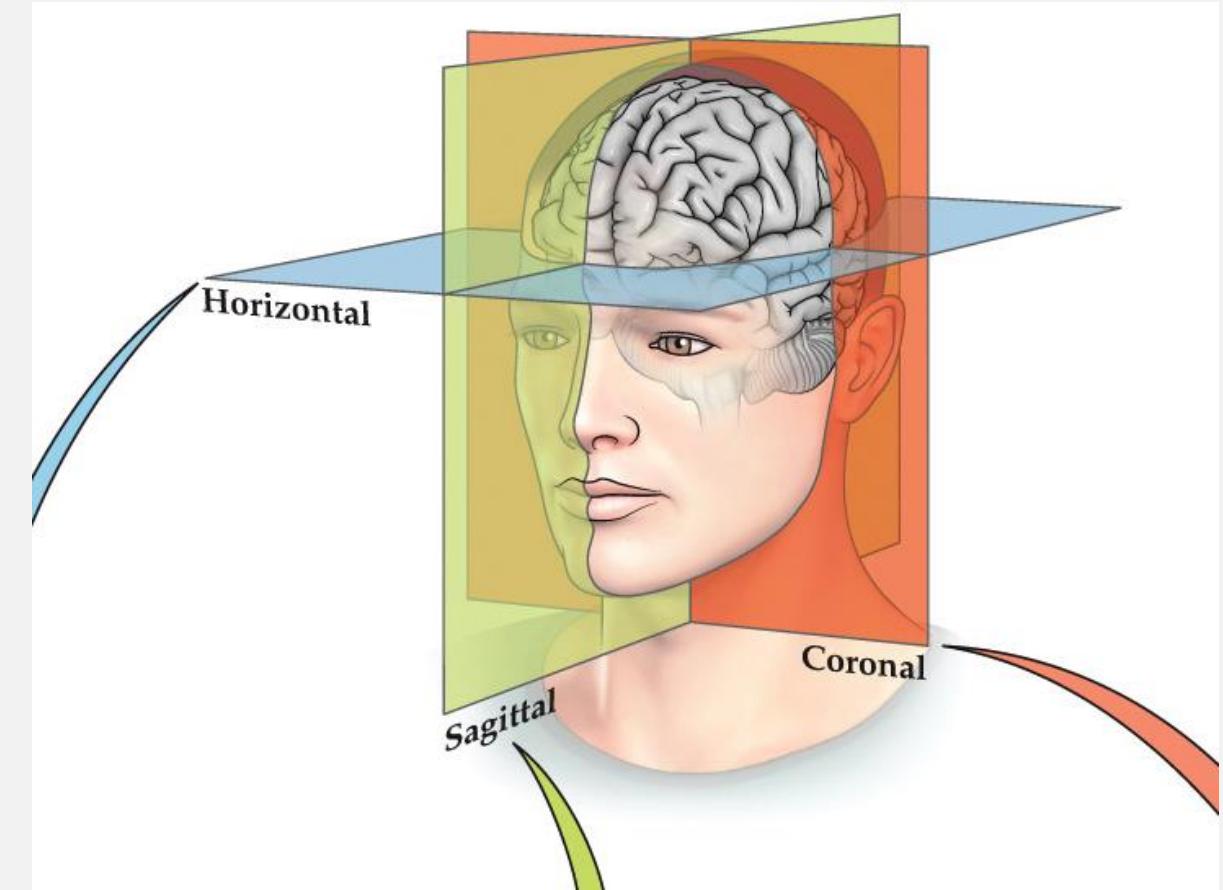


Anatomical Conventions

Horizontal

Sagittal

Coronal



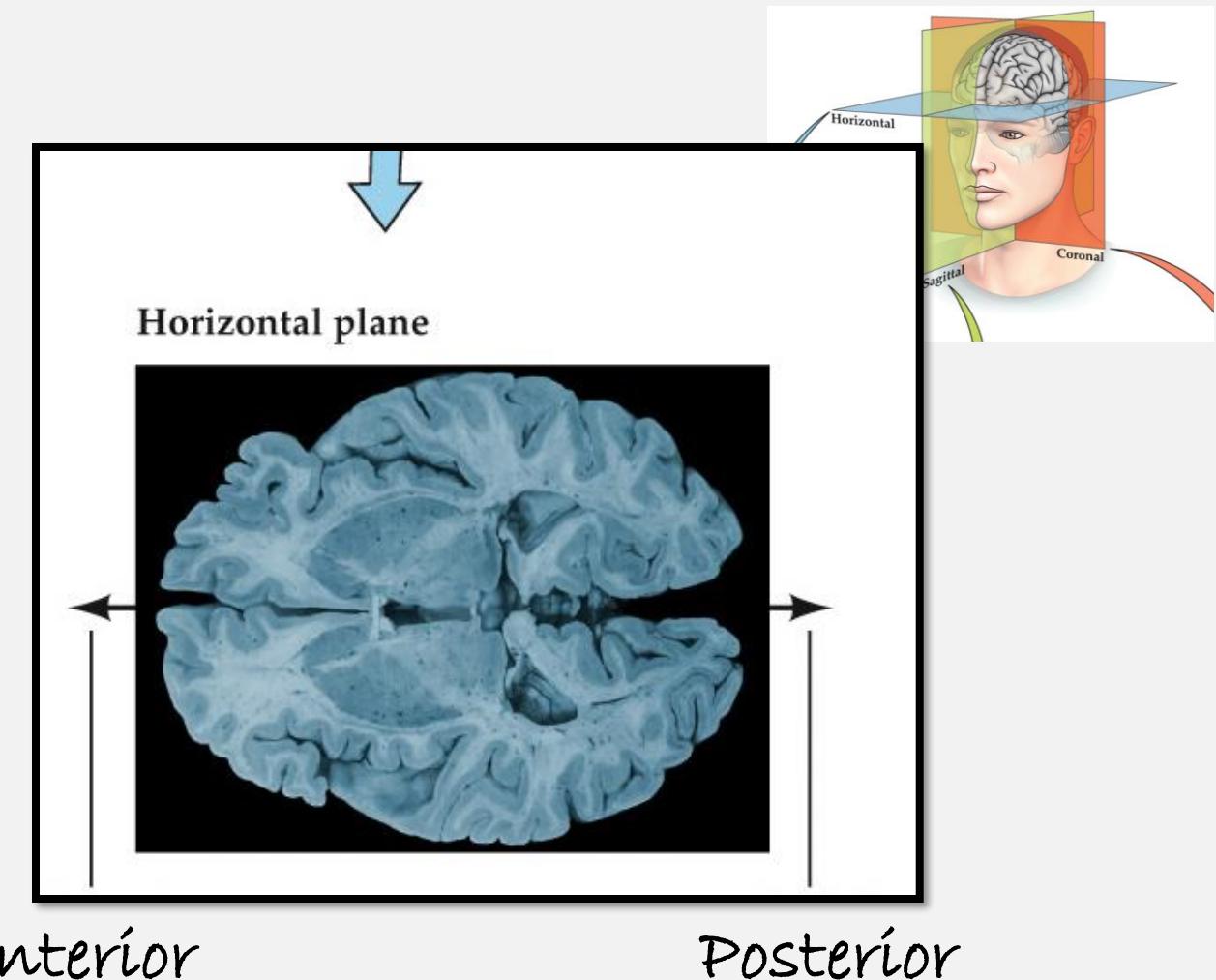
Anatomical Conventions

Horizontal

- divides the brain into an upper and lower part

Sagittal

Coronal



Anatomical Conventions

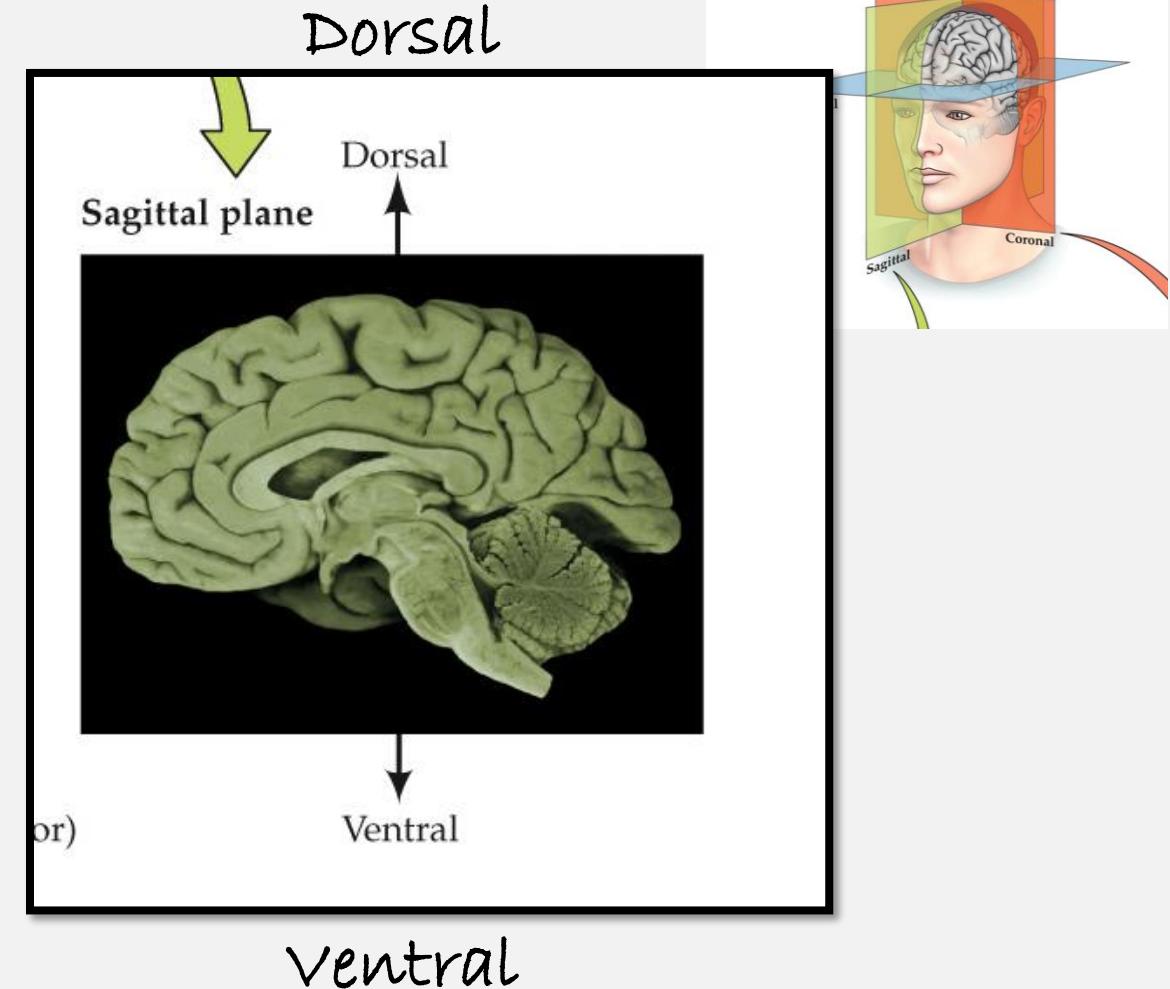
Horizontal

- divides the brain into an upper and lower part

Sagittal

- Divides the body into left and right halves

Coronal



Anatomical Conventions

Horizontal

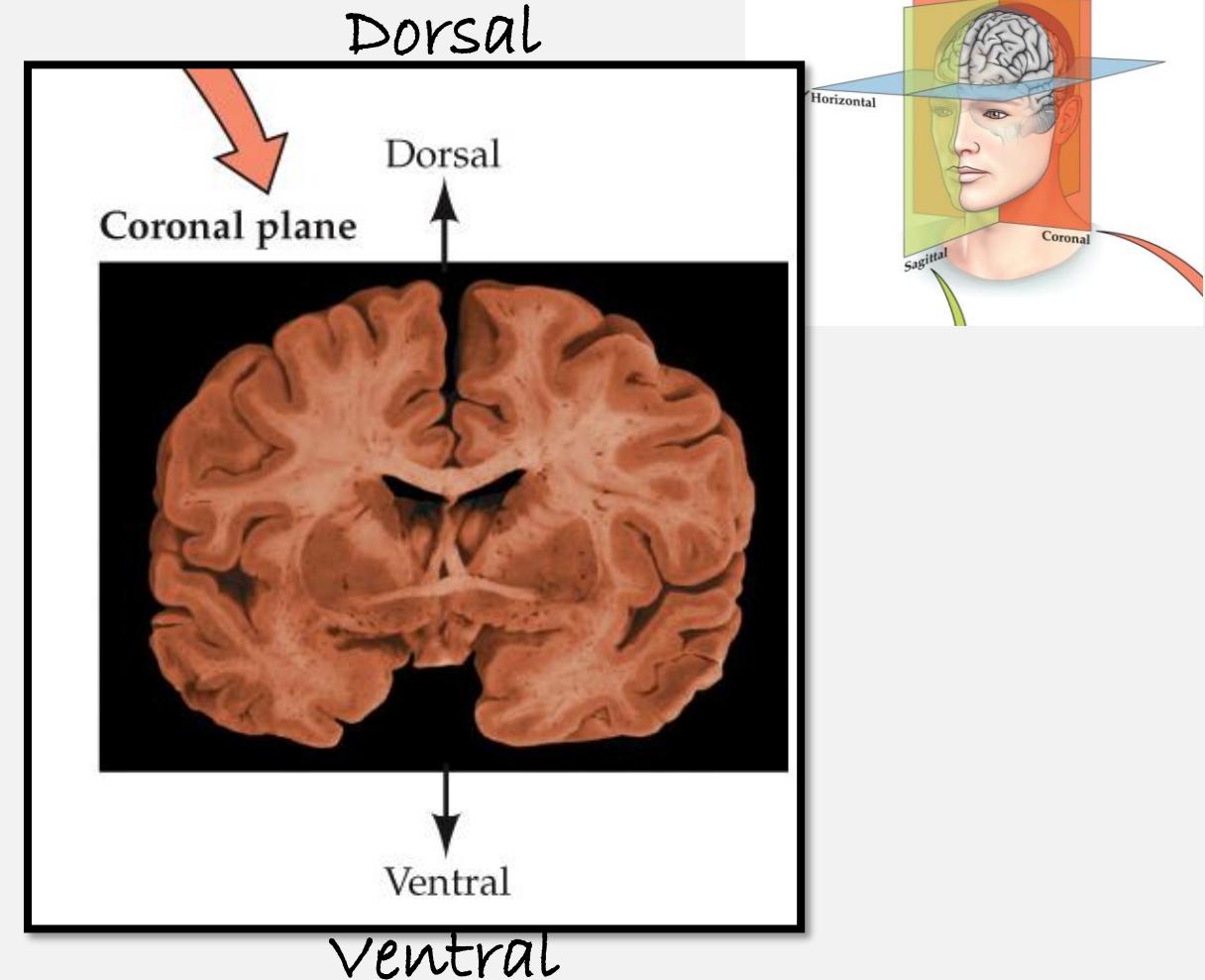
- divides the brain into an upper and lower part

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Coronal

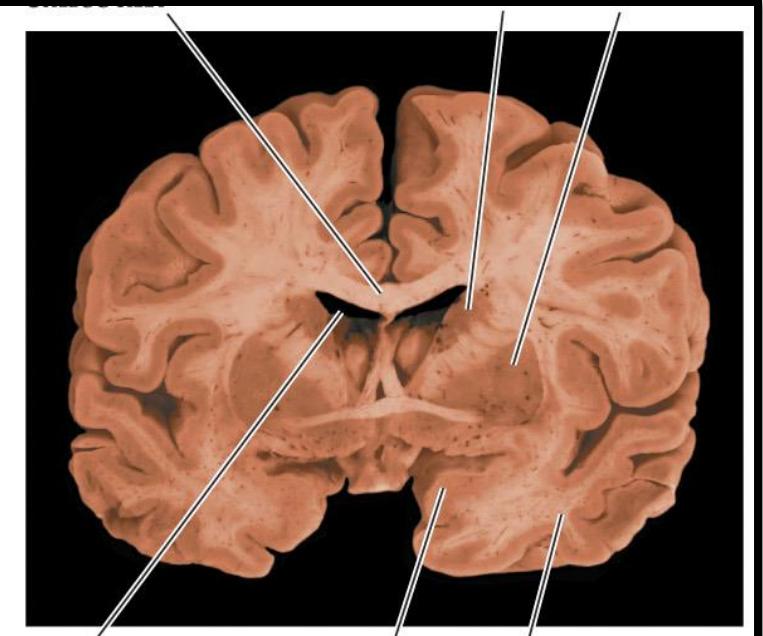
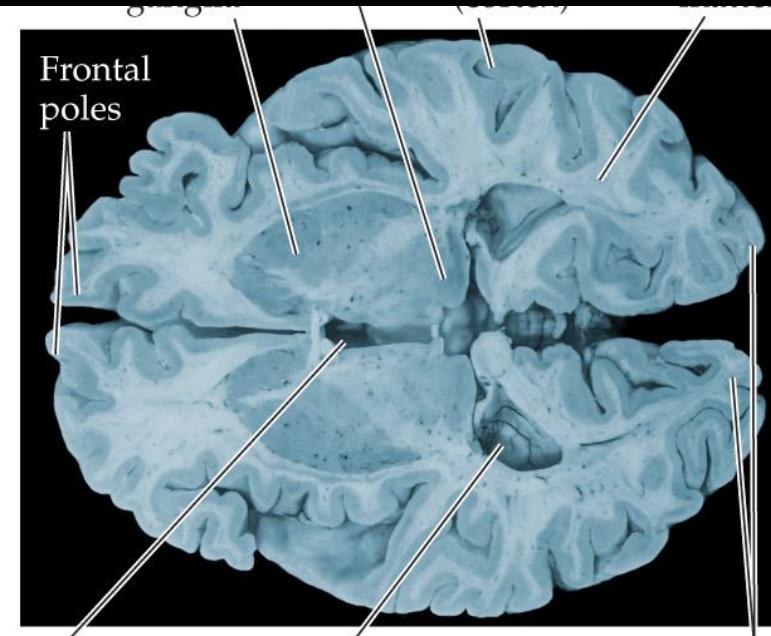
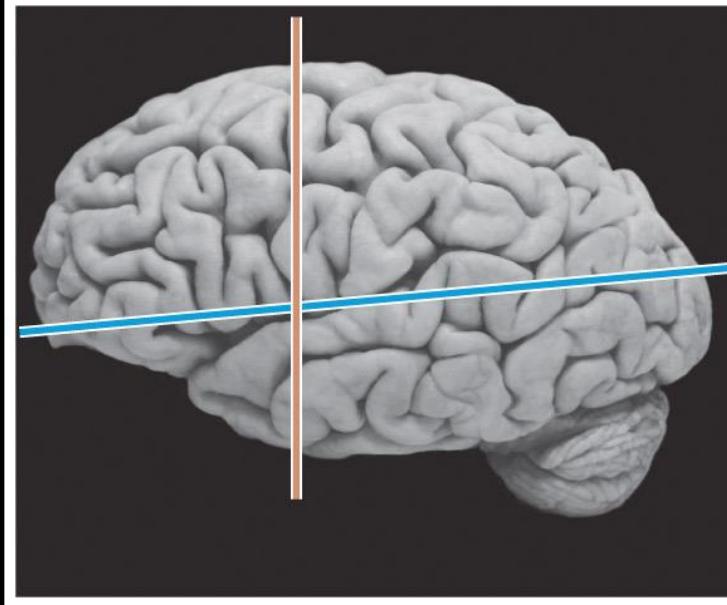
- divides the body into front (anterior) and back (posterior) regions



The brain –What do you observe?

Two colors of brain tissue:

- **Gray matter**
- **White matter**



The brain

The cortex has four lobes:

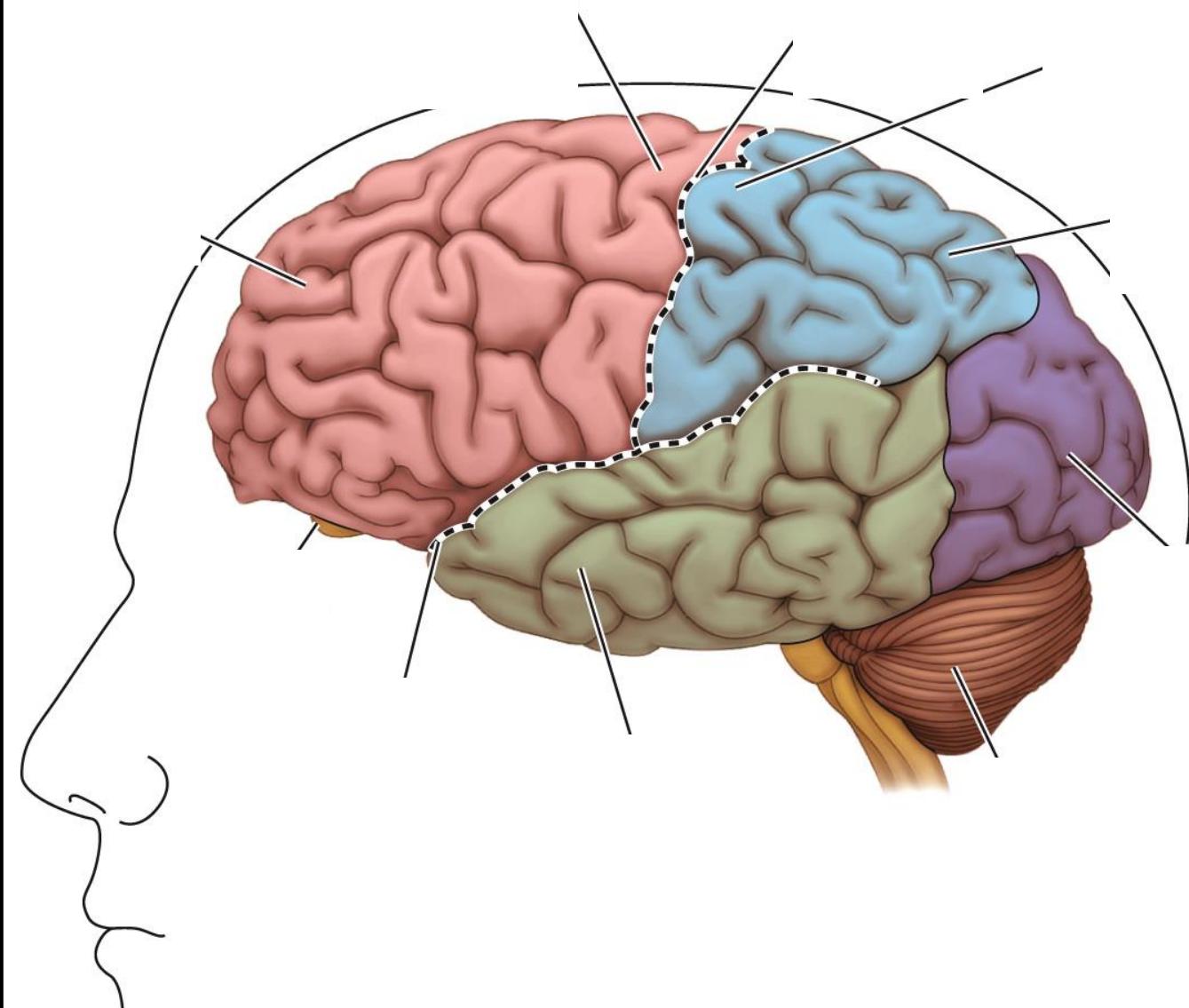
- **Frontal**—movement and high-level cognition
- **Parietal**—spatial cognition, sensory processing
- **Occipital**—visual processing
- **Temporal**—auditory processing, sense of smell, aspects of learning

Activity

On the next 2 slides there are images from different angels of the human brain. From your memory please label the following aspects of the brain:

- Frontal lobe
- Temporal lobe
- Parietal lobe
- Occipital lobe
- Cerebellum
- Spinal cord
- Brain stem
- Central Sulcus
- Lateral fissure

(A) Lateral view



Activity

From your memory please label the following aspects of the brain:

Frontal lobe

Temporal lobe

Parietal lobe

Occipital lobe

Cingulate cortex (limbic lobe)

Cerebellum

Spinal cord

Brain stem - midbrain, pons,
medulla

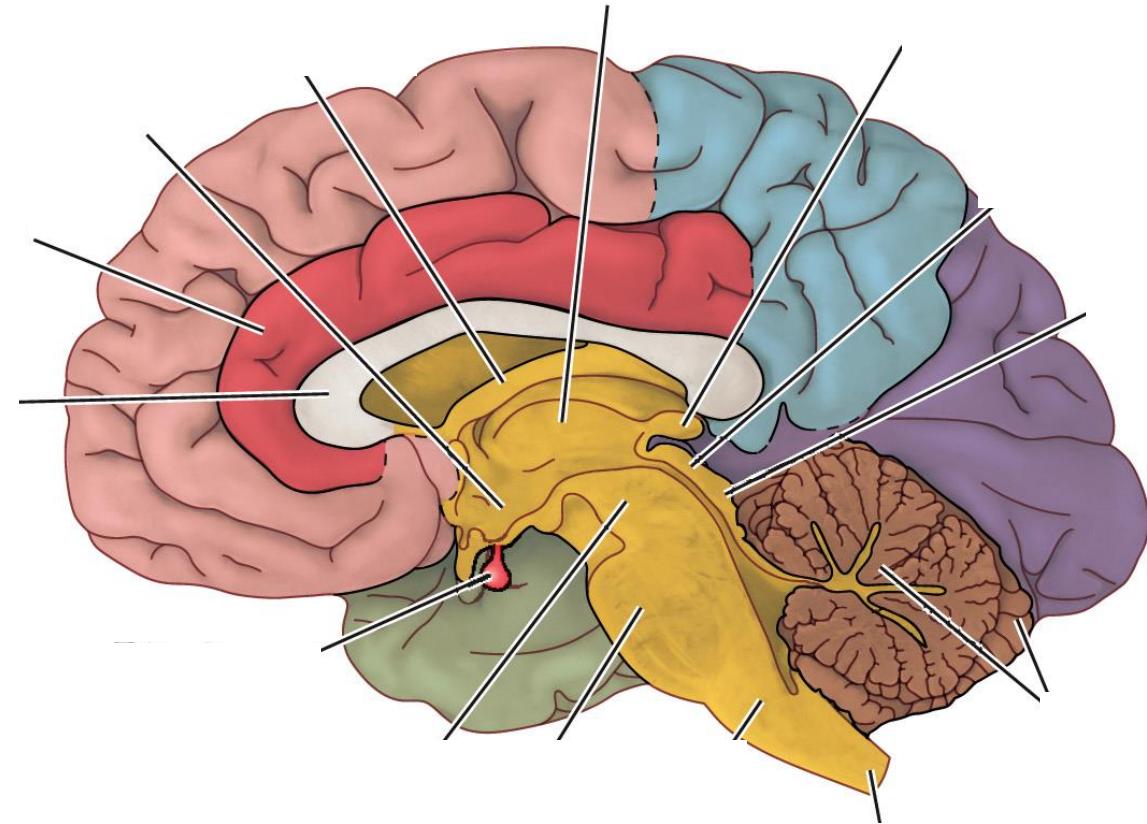
Central Sulcus

Thalamus

Hypothalamus

Corpus callosum

(B) Midsagittal (midline) view





Answer key

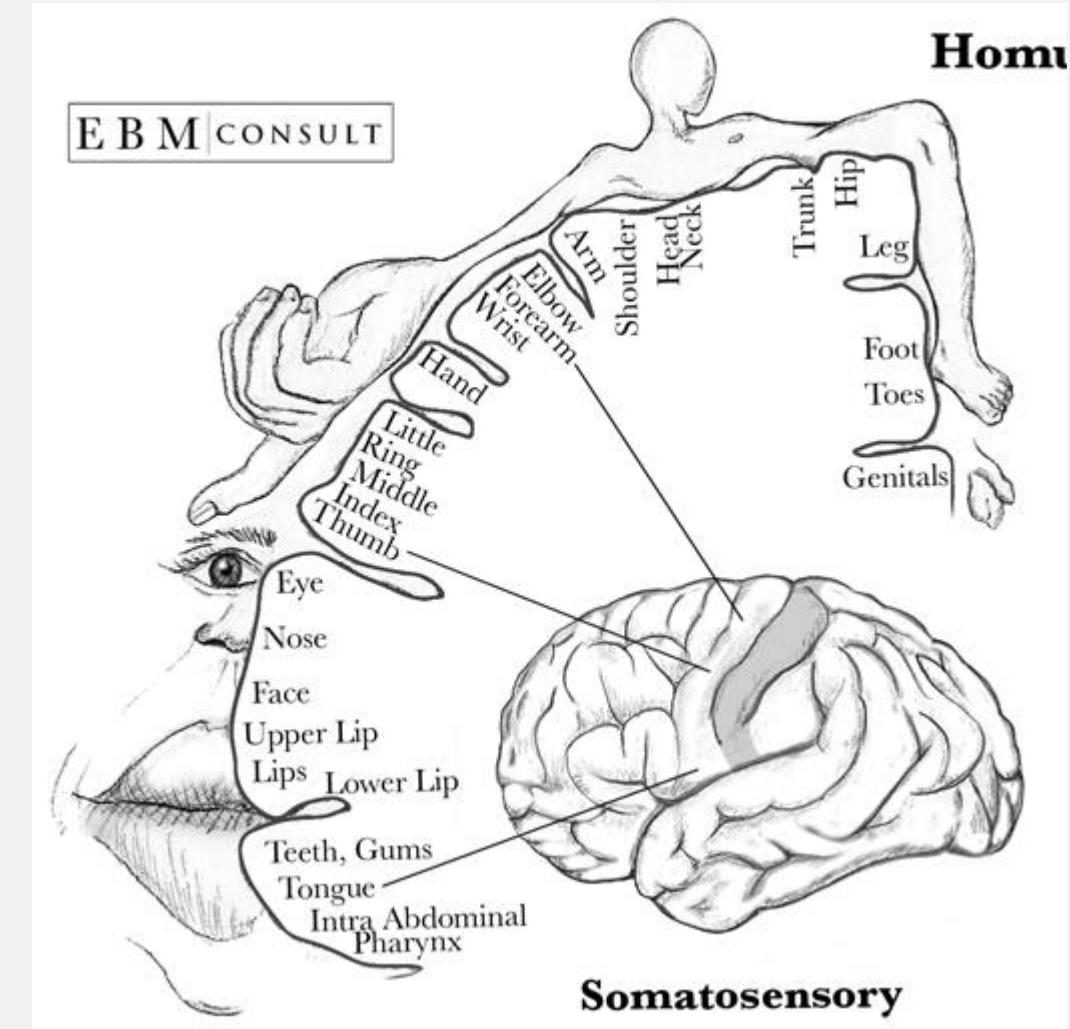
Follow the language

The postcentral gyrus

- is a strip of cortex behind the central cortex that is important for touch.

Sensory Homunculus

- The human body maps onto the somatosensory cortex (part of the parietal lobe)



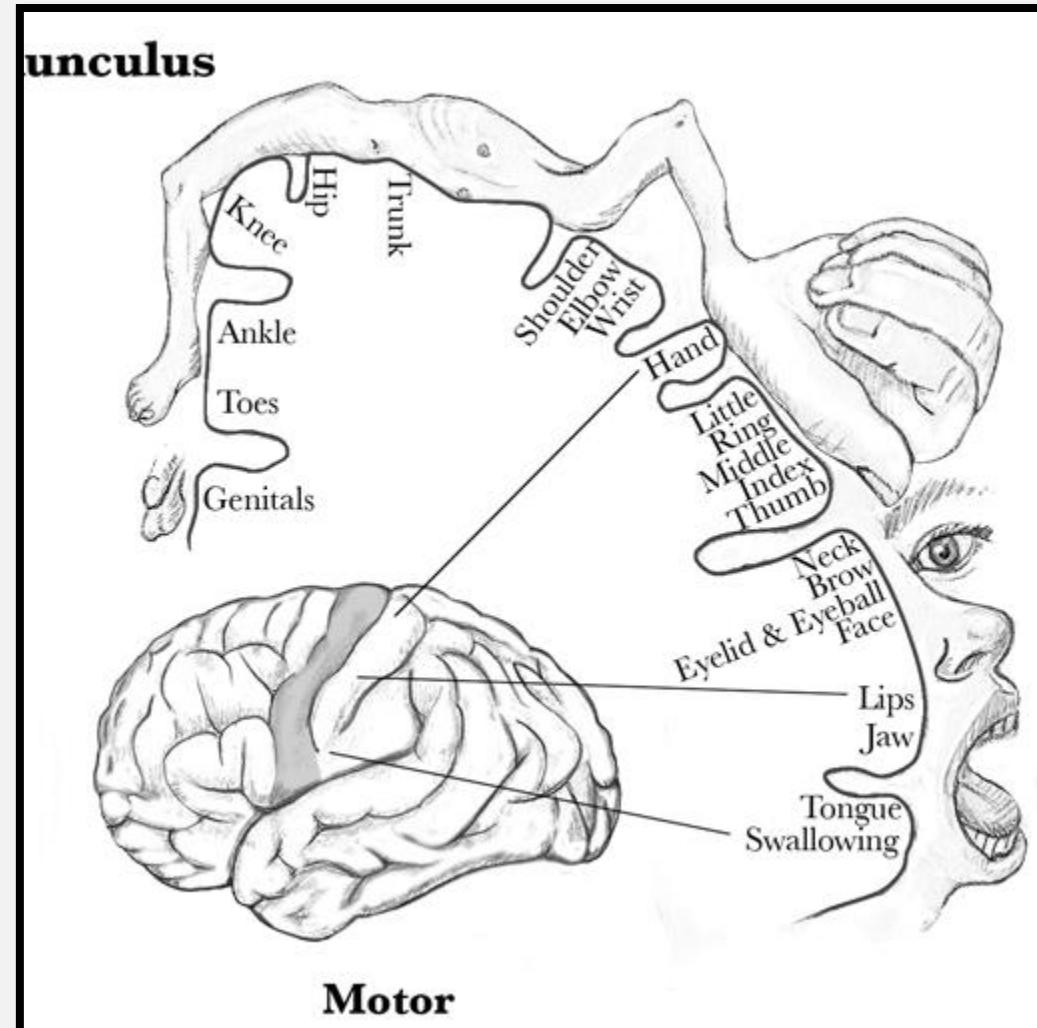
Follow the language

The precentral gyrus

- In the frontal lobe, important for motor control .

Motor Homunculus

- Motor control is somatotopically mapped along the precentral gyrus

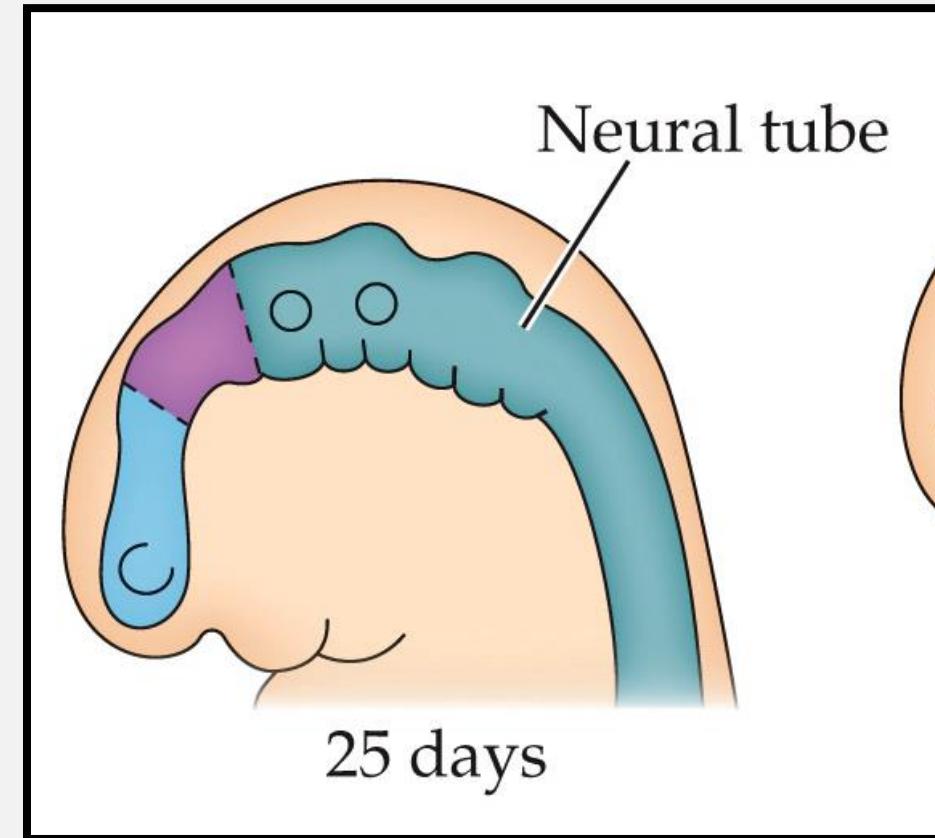


Brain development – 25 Days

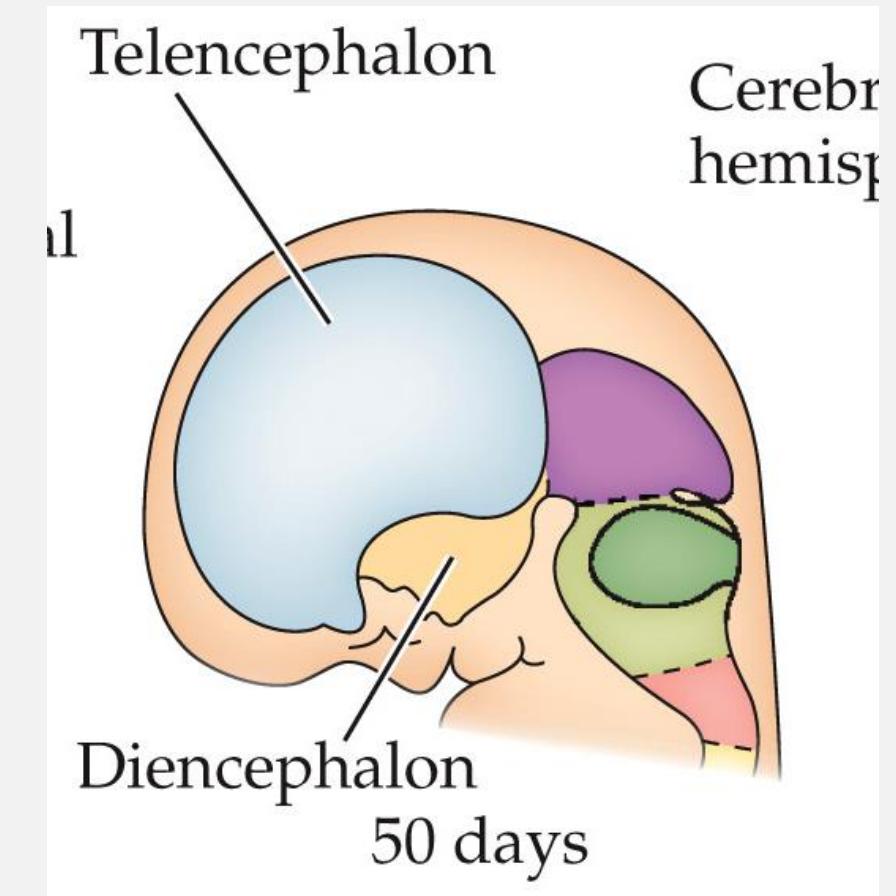
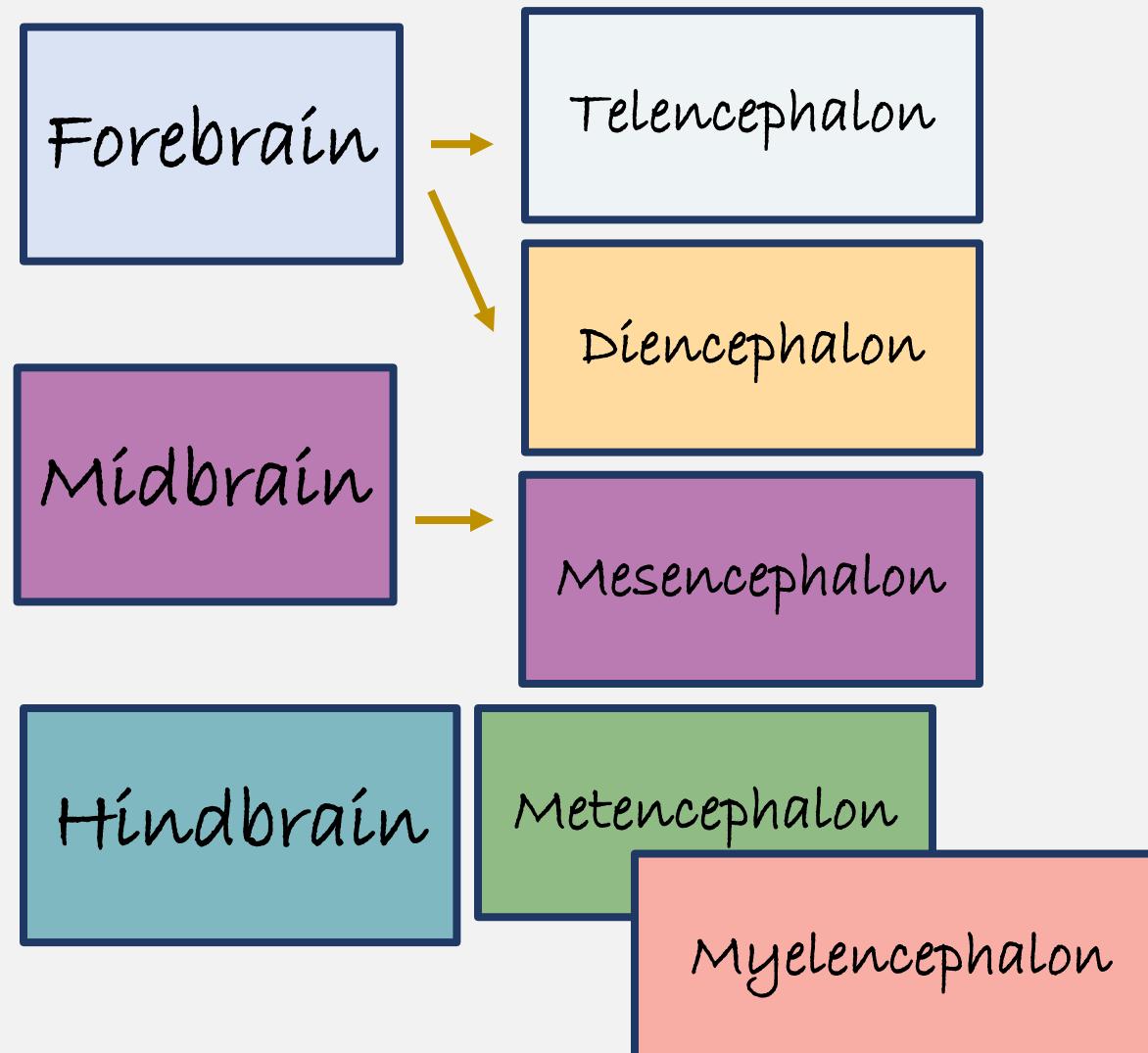
Forebrain

Midbrain

Hindbrain



Brain development – 50 Days



Myel - marrow,
spinal cord

The Hindbrain

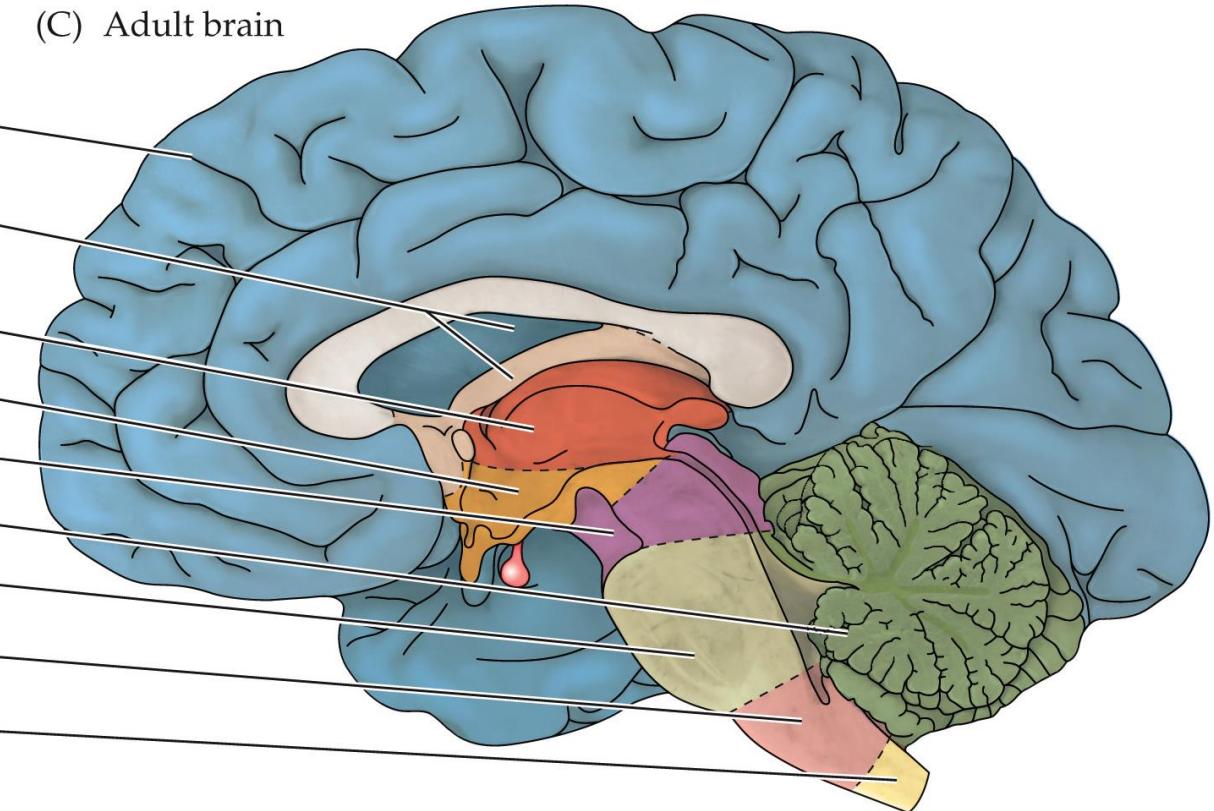
Myelencephalon

Medulla - regulates
breathing and
heartrate

All neurons
passing from the
brain to the spinal
cord pass through
the medulla

Medulla
(Brainstem)

(C) Adult brain



Met -
beside/after



The Hindbrain

Metencephalon

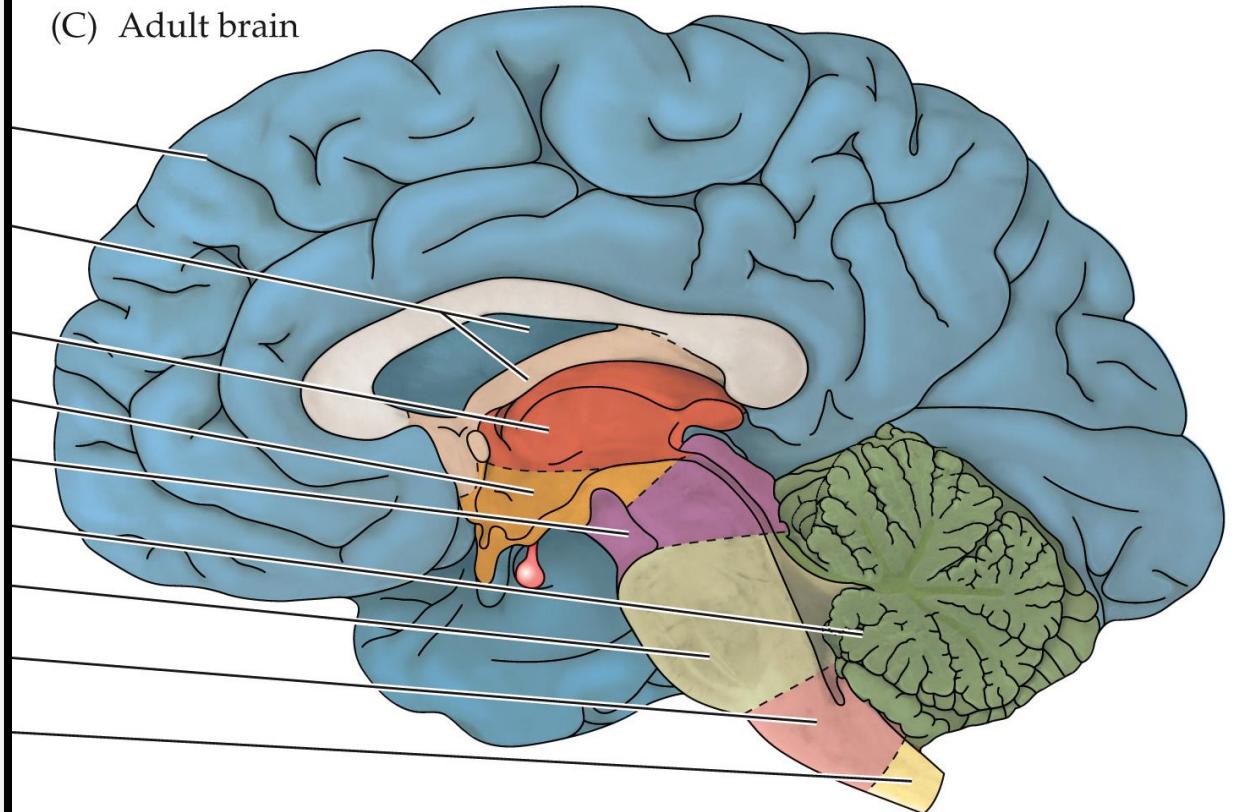
Pons - "bridge"
connects medulla to
midbrain

cerebellum -
Balance,
coordination

Pons
(brainstem)

Cerebellum

(C) Adult brain



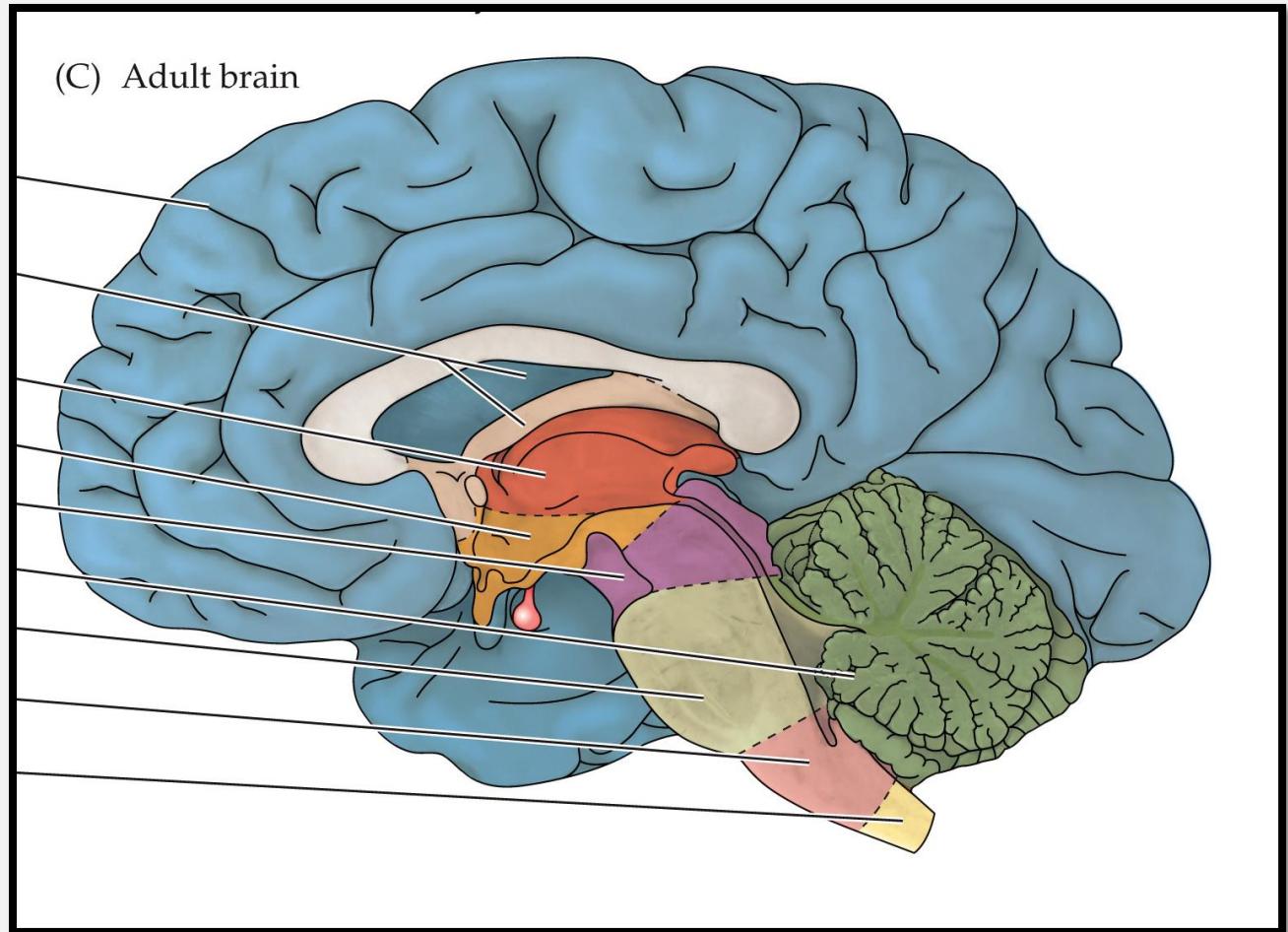
The Midbrain

Mesencephalon

Midbrain
(Brainstem)

Midbrain - Tectum:
sensory and motor
functions

Reticular formation
Sleep, arousal,
temperature control,
motor control



Forebrain structures

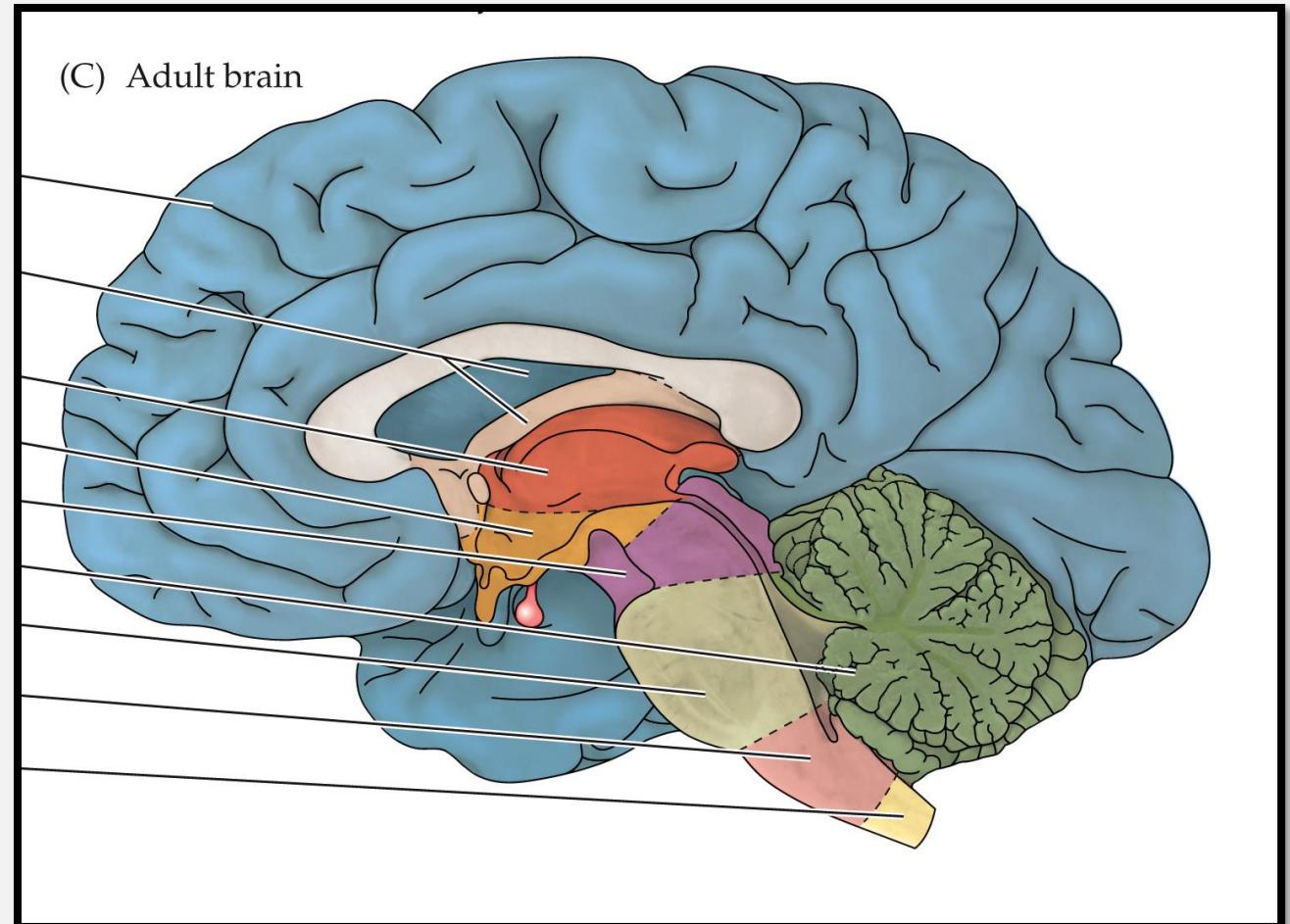
Diencephalon

Thalamus - relay station for all incoming sensory information

Thalamus

Hypothalamus

Hypothalamus - "below" the thalamus, contains nuclei with many vital functions (hunger, thirst, temperature regulation, sex, and more); also controls the pituitary

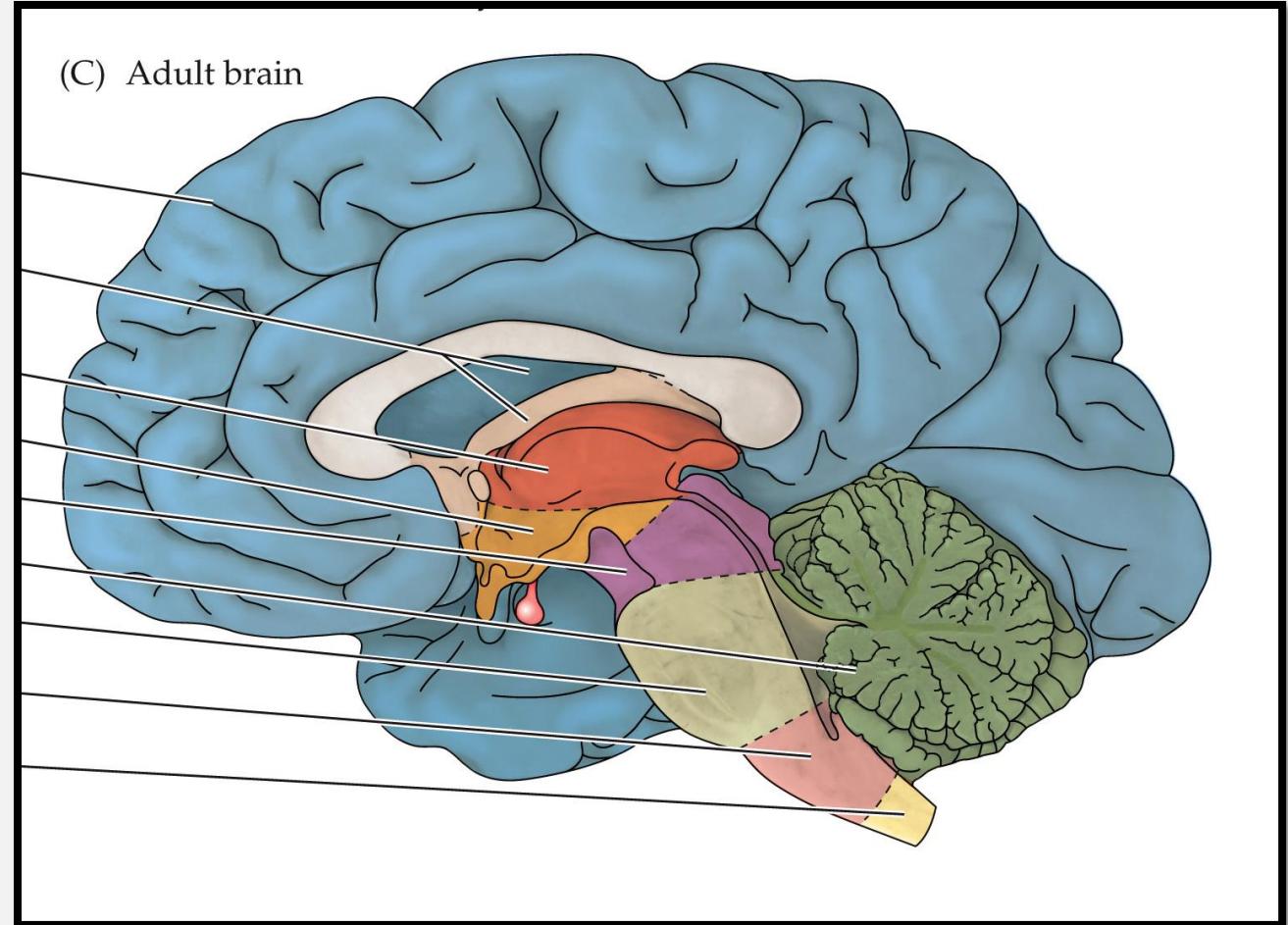


Forebrain structures



Higher cortical functioning

Tel - far off
distant





Brain imaging techniques

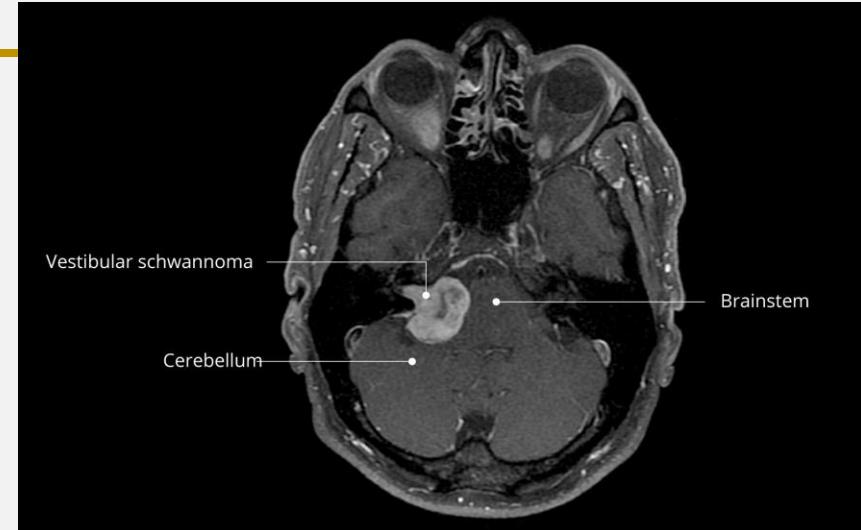
Brain-Imaging Techniques

Computerized axial tomography

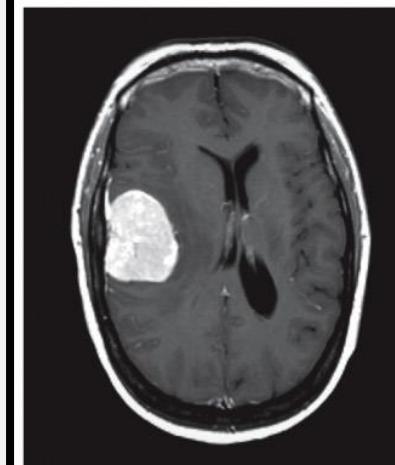
- **(CAT or CT)**—a measure of X-ray absorption with ionizing radiation at several positions around the head; maps tissue density
- Great for imaging bones, detecting tumours, bleeds (best for solid structures)

Magnetic resonance imaging (MRI)

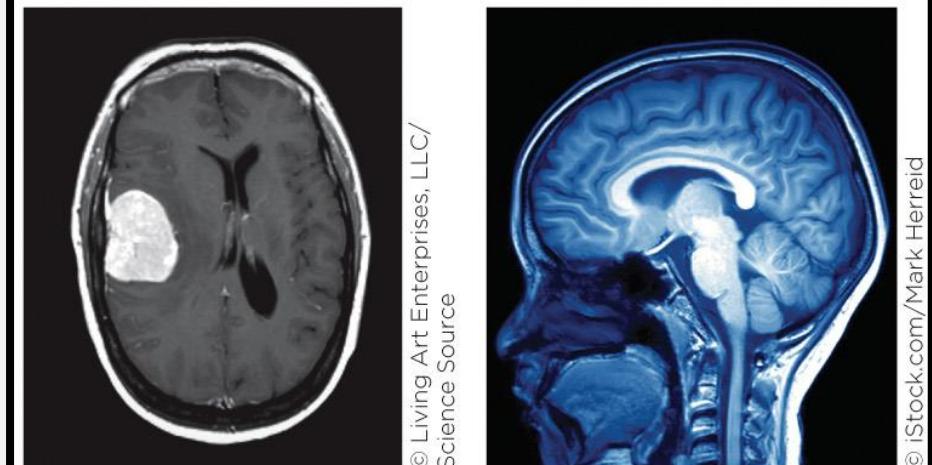
- produces high-resolution images using radio frequency energy.
- Better for detailed images of softer tissue



(A) Computerized tomography
(CT)



(B) Magnetic resonance imaging
(MRI)

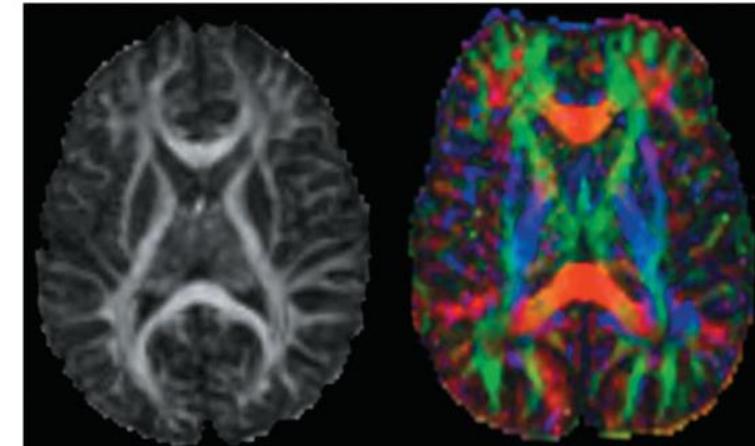


Brain imaging techniques

Diffusion tensor imaging (DTI)

- uses MRI technology to study white matter tracts; based on **fractional anisotropy (FA)** – fancy way of saying water diffusing in along the length of white matter tracts.
- Study MS, stroke, *TBI*, Alzheimer's, plan surgery & *study development*

(C) Diffusion tensor imaging (DTI)
Fractional anisotropy



DTI tractography



B. Bernall and N. Altman, 2010. *MRI* 28: 217-225 (left) and M. Vandermosten et al., 2012. *Neurosci Biobehav Rev* 36:1532-1552 (right)

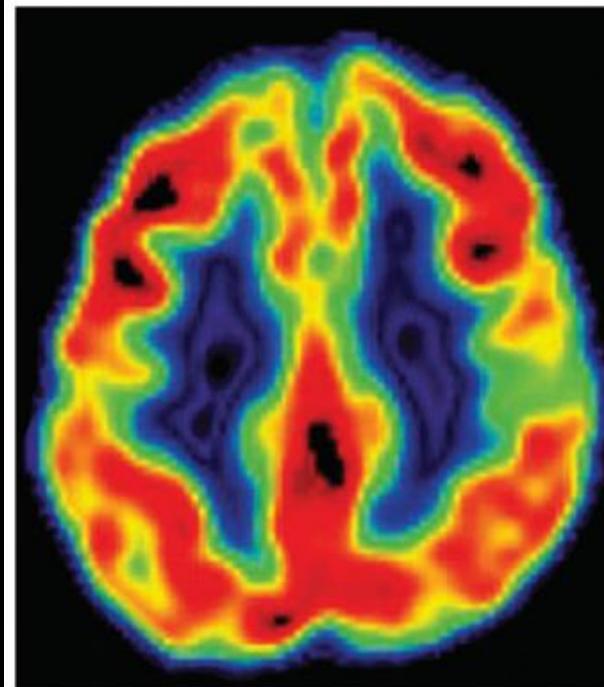
Brain Imaging Techniques

Positron emission tomography (PET)

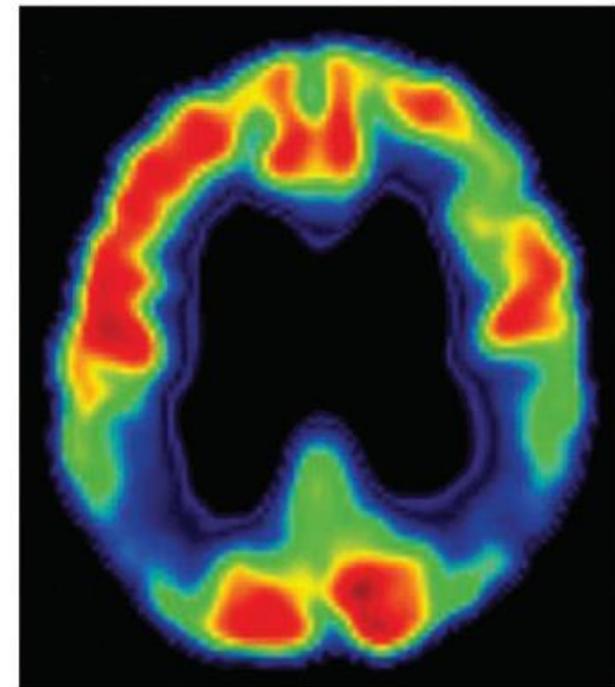
- produces images of brain activity: identifies brain regions that contribute to specific functions.
- Involves a radioactive tracer (form of glucose).
- Metabolically active tissue will use more glucose
- Tracer emits gamma waves as it breaks down
- Detects cancer, observe heart damage, study brain function

(D) Positron emission tomography (PET)

Healthy (horizontal view)



Person with Alzheimer's disease



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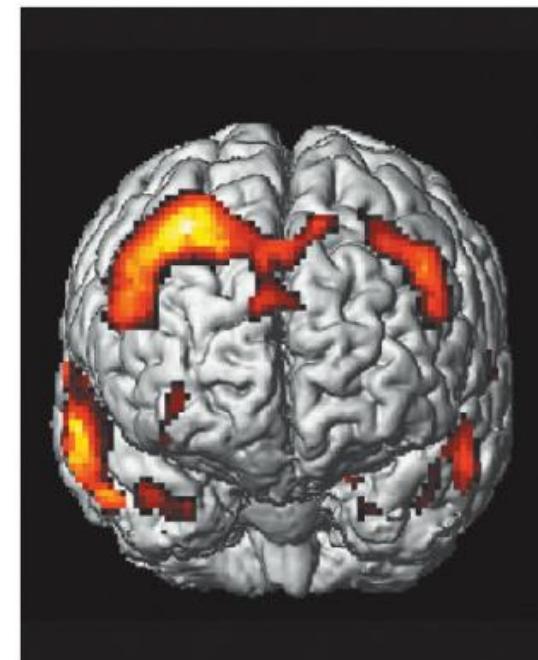
Brain Imaging Techniques

Functional MRI (fMRI)

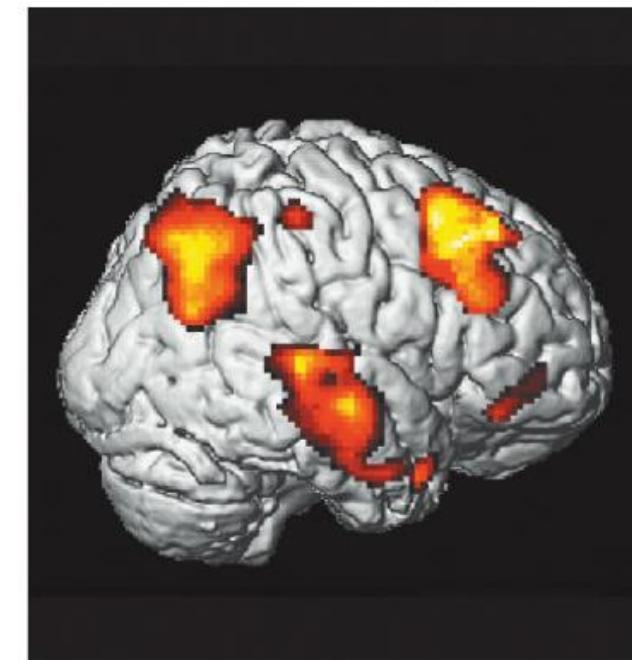
- detects small changes in brain metabolism, such as oxygen use, in active brain areas.
- fMRI can show how networks of brain structures collaborate.

(E) Functional magnetic resonance imaging (fMRI)

Anterior 3-D view

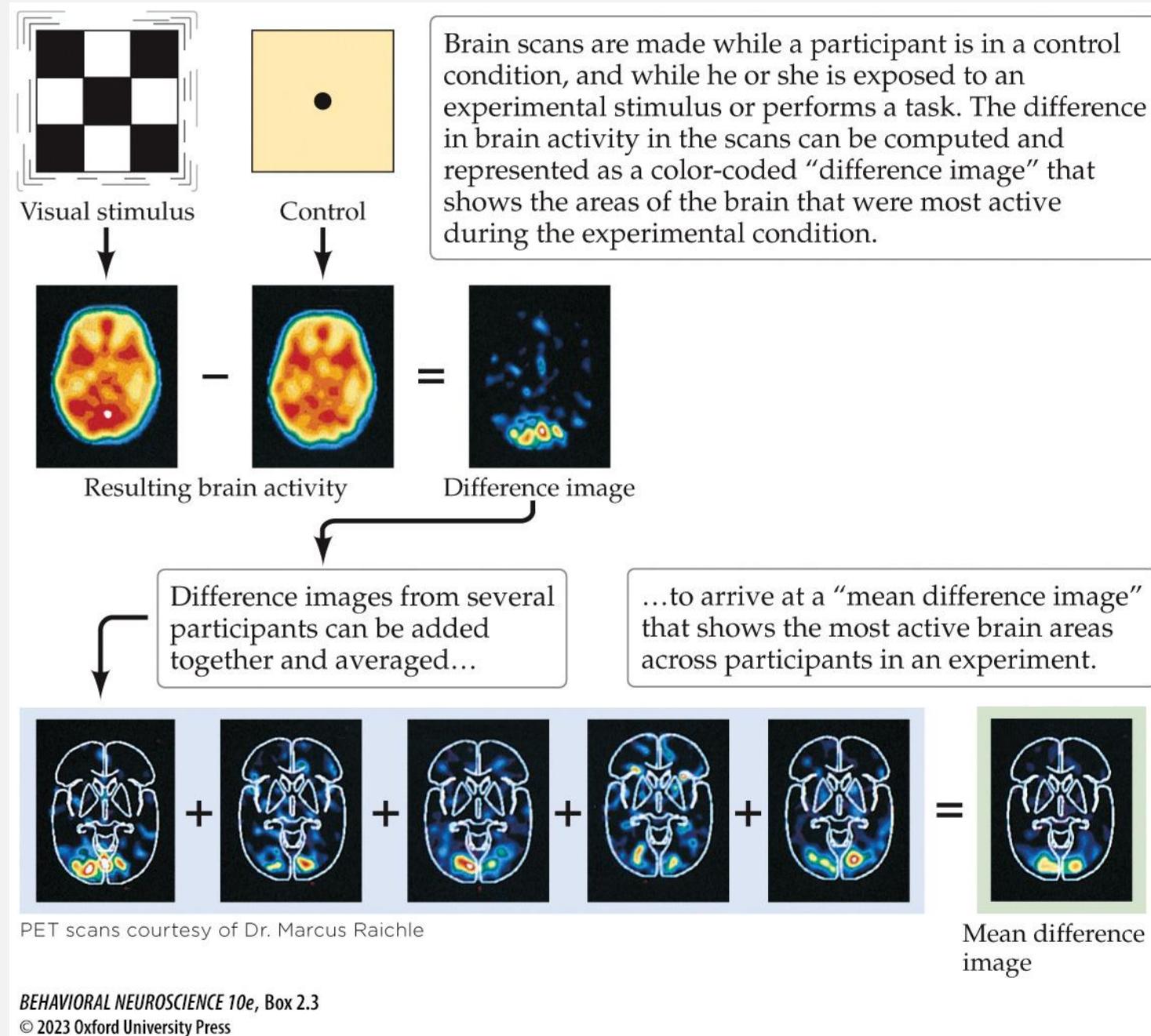


Lateral 3-D view of right hemisphere



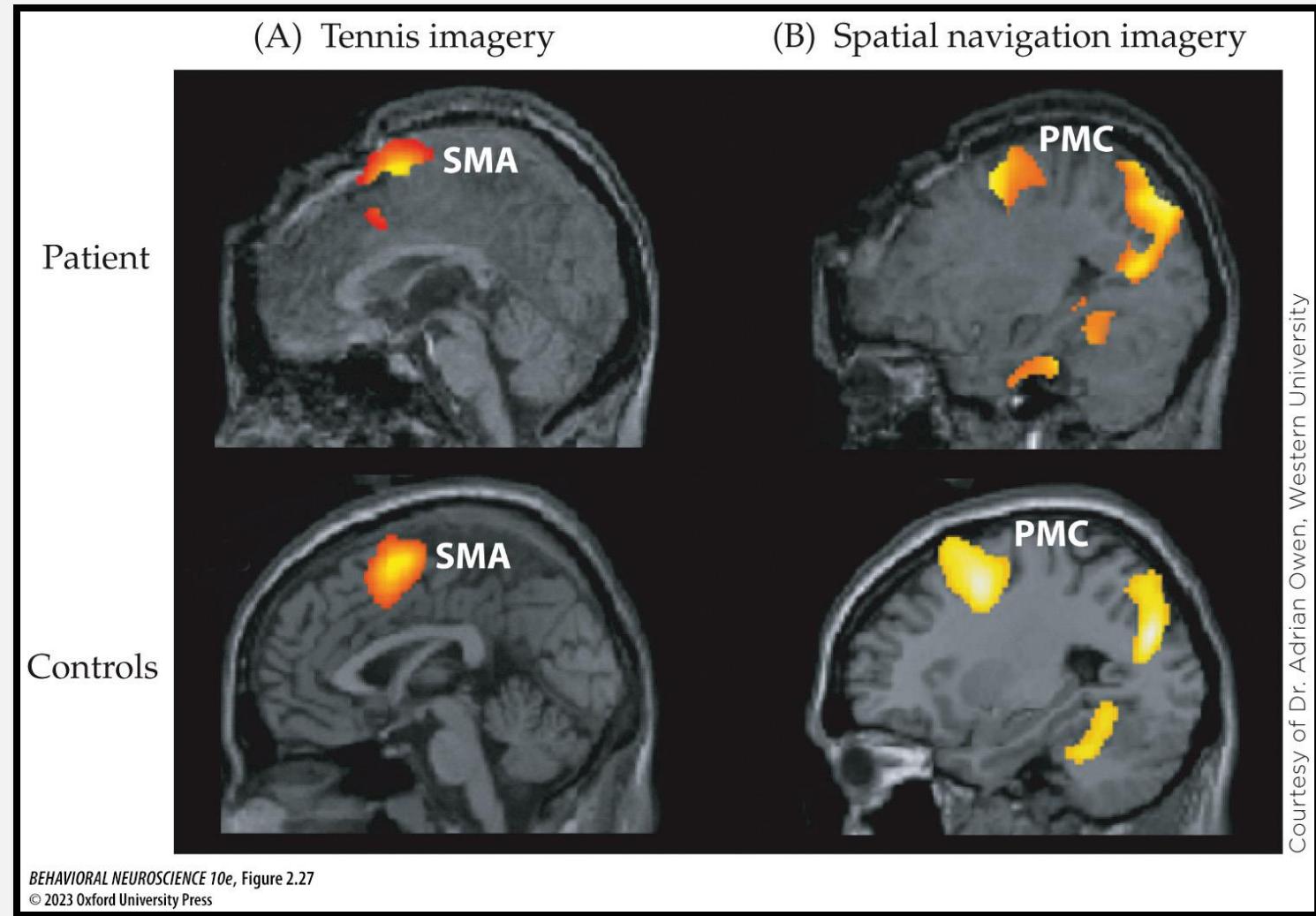
Courtesy of Dr. Semir Zeki, University College London

BOX 2.3 Isolating Specific Brain Activity (1)



Brain Imaging Techniques

- Imaging can overcome the limitations of other methods of assessment and complement traditional studies of brain **lesions** (regions of damage).
- One question that can be addressed is the state of consciousness of people in comas.
- **Study:** Prompted brain activity in an individual in a Coma



Cutting edge research

Social neuroscience

- aims to understand brain activity as it relates to our interactions with others.

Dyadic functional MRI (dfMRI)

- employs an MRI scanner that is fitted with specially designed dual head coils (encircling the head to produce brain images).

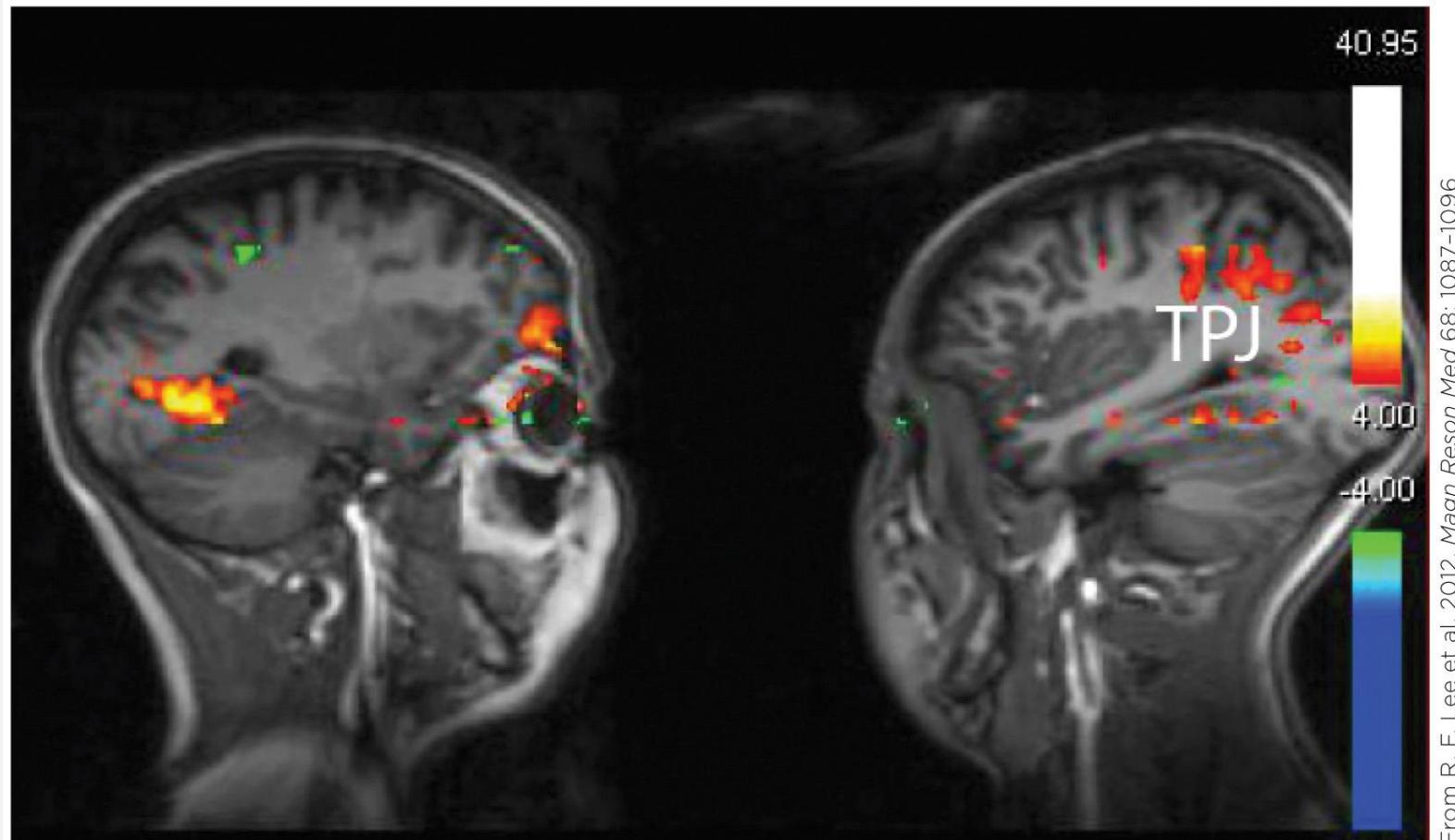


The Cutting Edge: Two Heads are Better Than One



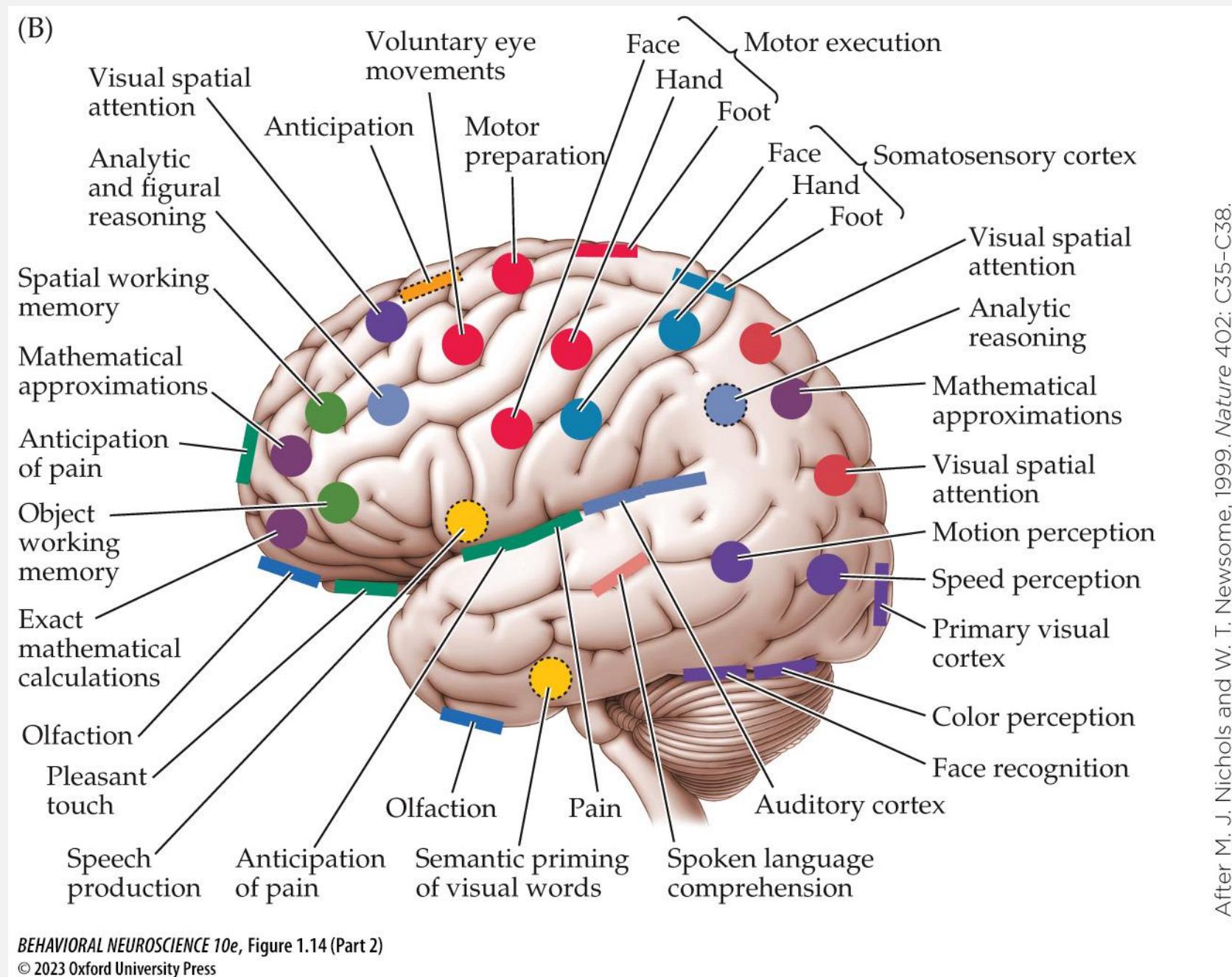
2

- As a pair of friends blinked and gazed at each other's faces, enhanced BOLD signal was observed in the region of the temporoparietal junction (TPJ, a region previously implicated in social cognition), the fusiform face area, and the frontal cortex.



BEHAVIORAL NEUROSCIENCE 10e, Figure 2.31
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FIGURE 1.14 Old and New Phrenology (Part 2)



After M. J. Nichols and W. T. Newsome, 1999. *Nature* 402: C35-C38.