

NERVOUS SYSTEM

ANATOMY, PHYSIOLOGY & PATHOLOGY



TAILORED FOR MEDICAL STUDENTS, USMLE, PLAB, PA & NURSING

4th EDITION



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296 PAGES

NEUROBIOLOGY OF EMOTIONS

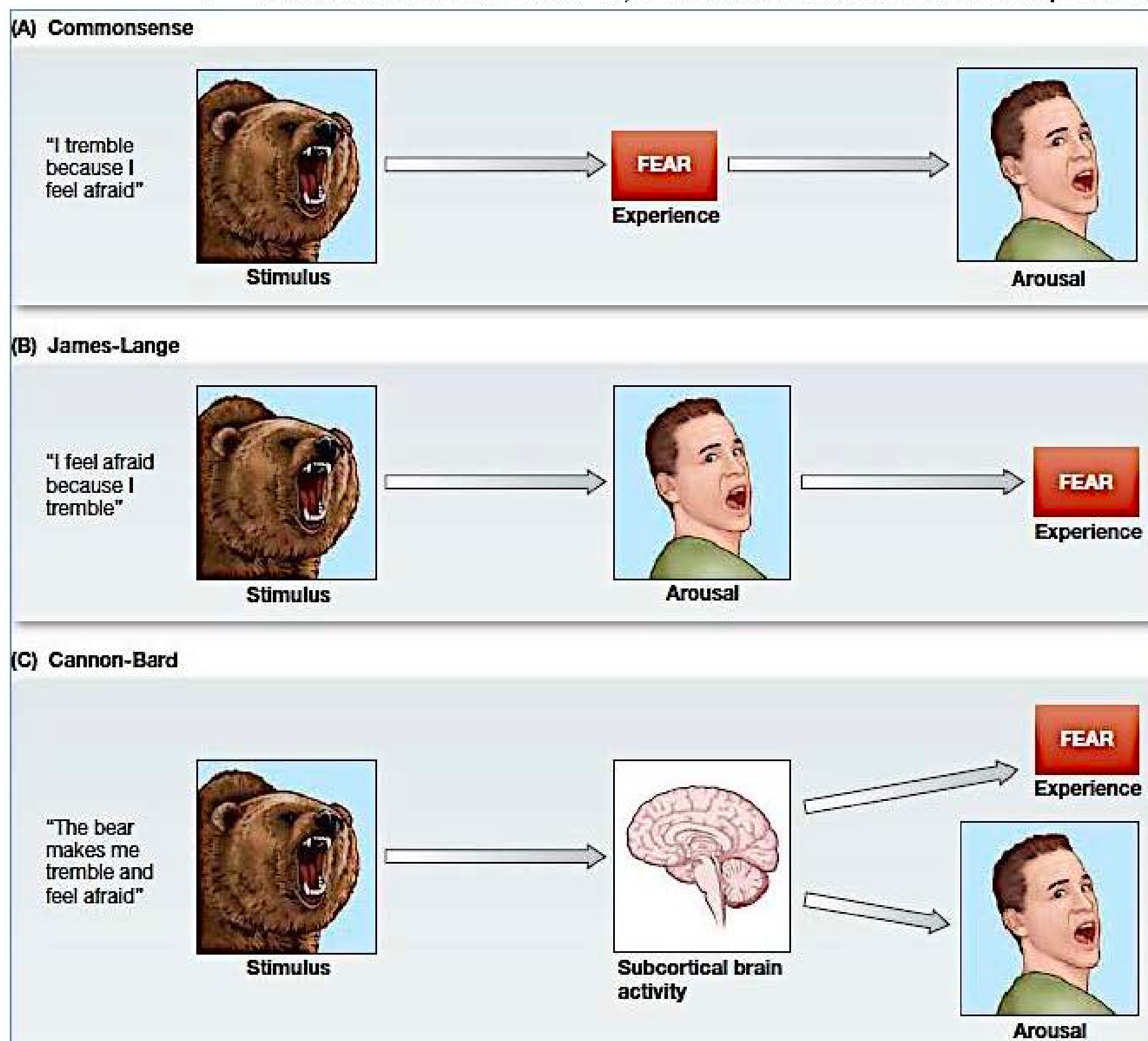
NEUROBIOLOGY OF EMOTIONS

Definitions:

- **Affect:** "The Experience of a Feeling/Emotion that's **NOT Related to Bodily Changes.**"
- **Emotion:** "A Mental And Physiological reaction to stimuli, experienced as **Affect plus Physiological Changes** in the Body."
- **Feelings:** "A partly mental, partly physical response to a person, thing or situation, marked by pleasure, pain, attraction or repulsion."
- **Arousal:** "The Visceral (Body's) Response to stimuli; Including Autonomic Nervous System & Neuro-Endocrine Activity."
- **Cognition:** "The process of knowing, including both awareness & judgement."
- **Behaviour:** "The Active Response to Stimuli (Posture, Facial Expression, Speed, Eye Movement, Vocalisation, etc)"

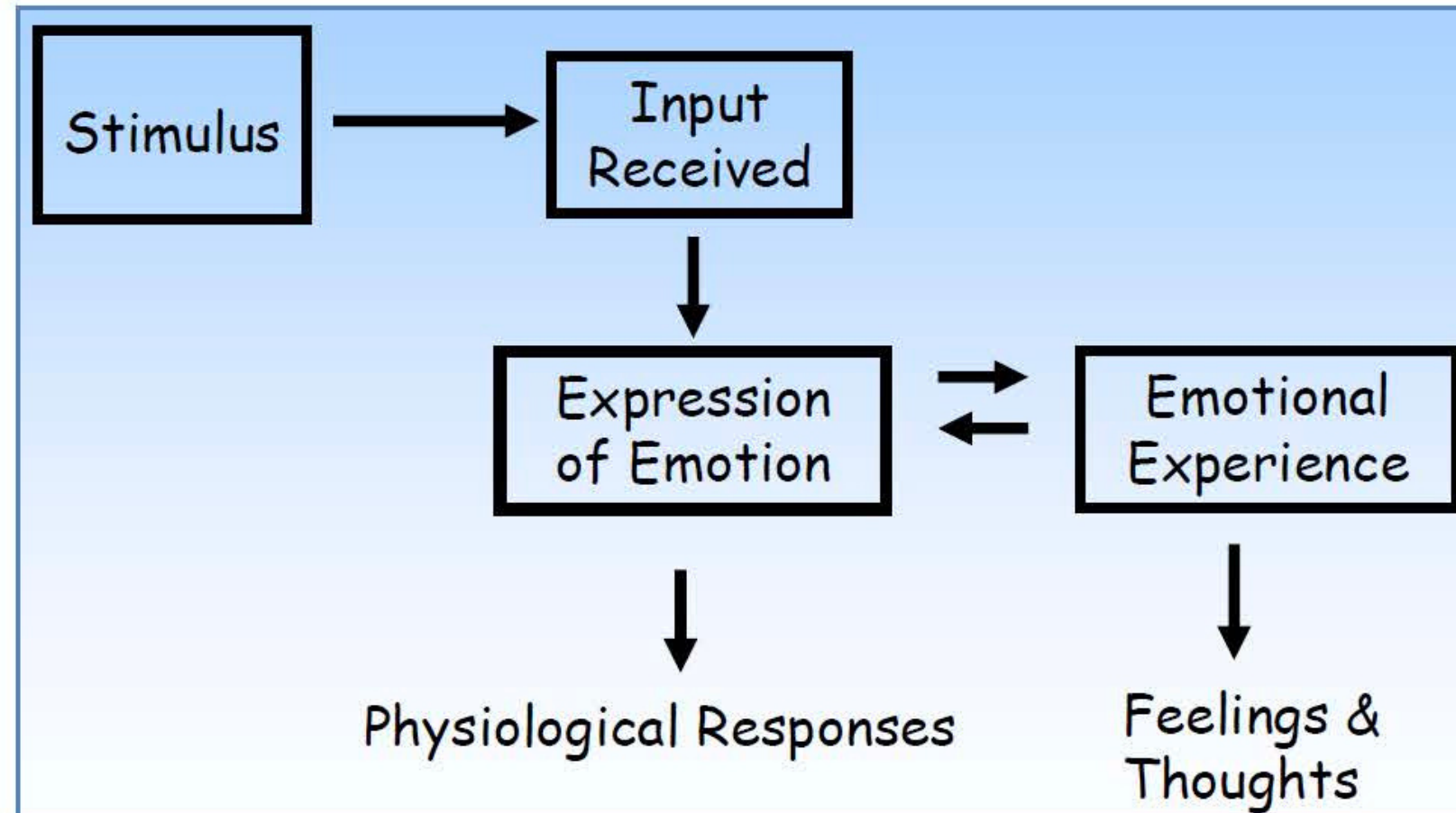
Emotion:

- **Why does it Exist?**
 - o **Critical To Survival:**
 - Both the ability to Experience Emotion and to Recognise Other's Emotions
 - Gut Reactions
 - Recognising Danger, Friend/Foe
 - Vital to Decision Making
 - Important role in learning.
- **Theories of Emotion:**
 - o A link exists between Physiological Responses to Stimuli & Effect of Emotion, but which comes first?
 - **Cannon-Bard Theory:**
 - Conscious Awareness of Emotion comes first, then the Visceral Reactions.
 - **James-Lange Theory:**
 - Visceral Reactions comes first, then the Conscious Emotional Experience follows.



- **Currently, the most Plausible Theory:**

- Visceral Reaction (Physiological Responses) comes first, causing the Emotional Experience (Feelings & Thoughts)
- However, the Emotional Experience can Influence and/or Perpetuate the Visceral Response.



- **3 Phases/Components/Types of Emotion:**

1. **Primary Emotions:**

- "What is Felt 1st" – The 1st Instantaneous Emotion - (Usually the Simplest/Primitive Emotions)
- Generally independent of culture (Universal)
 - Joy
 - Sadness
 - Fear
 - Anger
 - Surprise

2. **Secondary Emotions:**

- "What is Felt 2nd" – What the Primary Emotion Leads to – (Slightly more Complex Emotion)
- Generally a Combination of Primary Emotions + Context.
 - Affection/Love
 - Lust
 - Contentment
 - Disgust
 - Envy
 - Guilt

3. **Tertiary Emotions:**

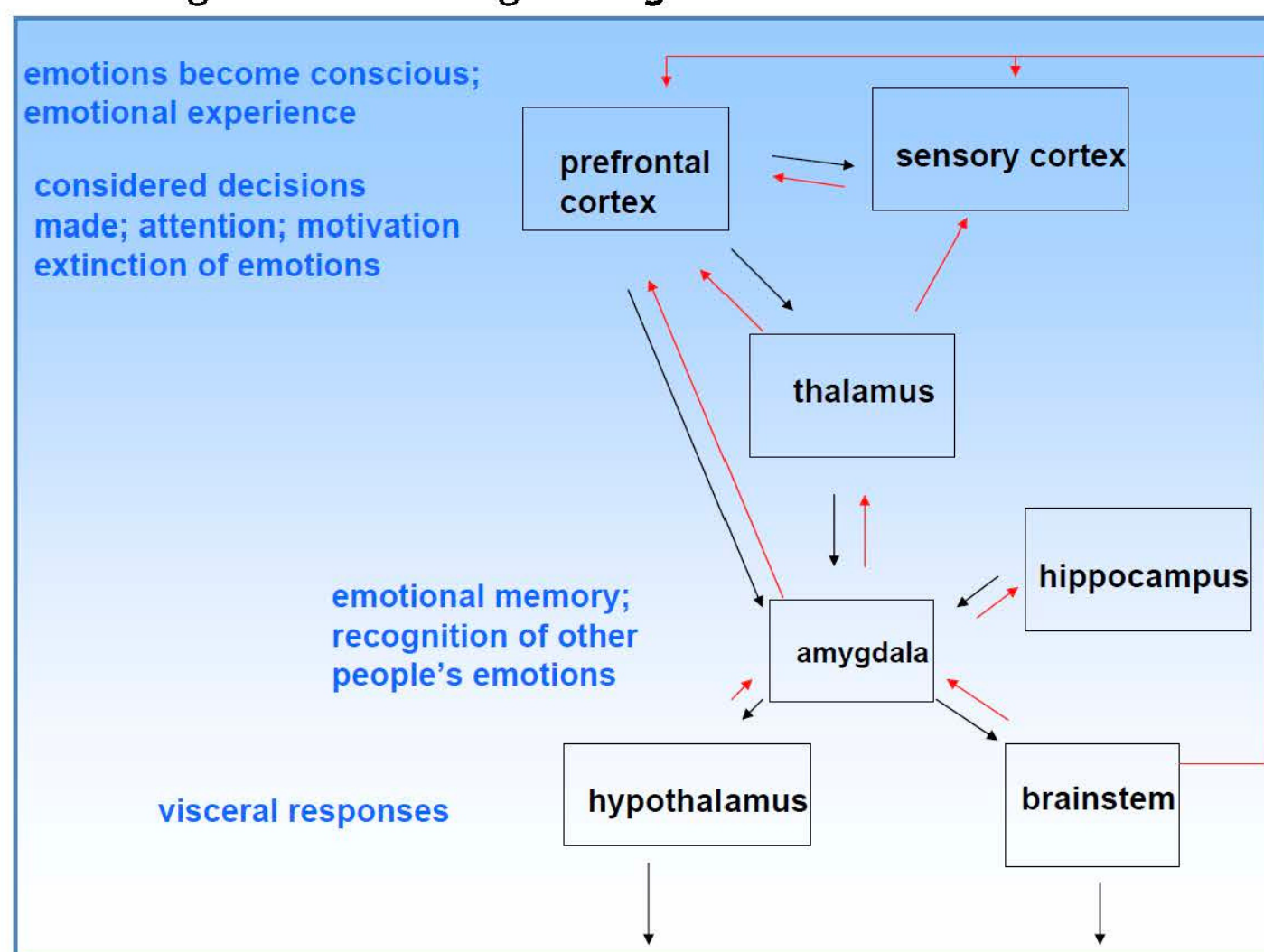
- An Aggregate of Primary and/or Secondary Emotions – (The most Complex Emotions)
- Generally the result of a Decision, taking into account Many Factors.
 - Satisfaction
 - Hope
 - Frustration
 - Gloom
 - Contempt

- **Physiological Context of Emotion:**

- The physiological state of a person & body can influence resulting emotions & emotional reactivity.
 - Well-being
 - Depression
 - Calm
 - Tense
 - Fatigue

Brain Regions Involved in Recognition, Induction & Regulation of Emotions:

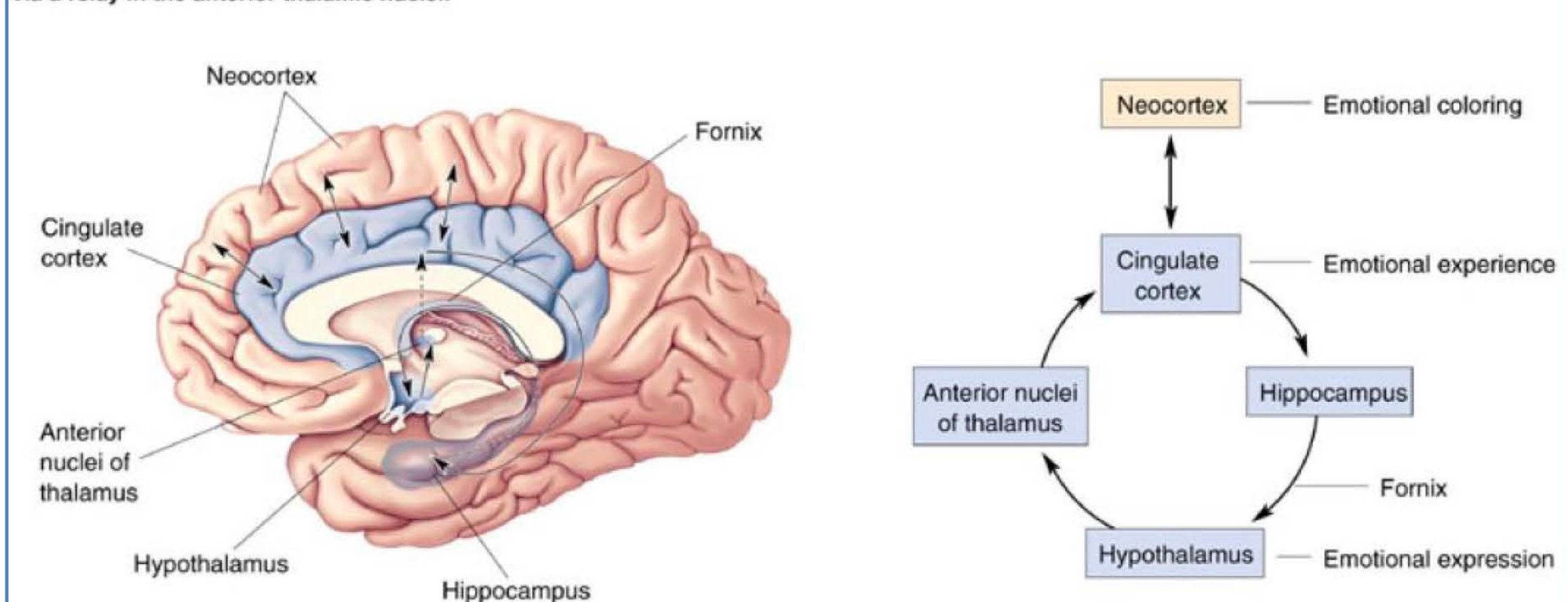
- **Thalamus:**
 - **Funnels Sensory info** to **Amygdala**, and the **Cerebral & Cingulate Cortices**.
 - Important in Fact-Based (*Explicit*) **Memory**.
- **Cingulate Gyrus:**
 - Regulates **Attention**
 - Emotional '**Colouring**'
- **Ventromedial Prefrontal Cortex:**
 - Conscious **Recognition of Emotions**
- **Cerebral Hemispheres:**
 - R-Brain → More Associated with Negative Emotions
 - L-Brain → More Associated with Positive Emotions
- **Sensory Cortices & Association Areas:**
 - Recognition of Stimuli.
 - Sensory Cortices: (Visual, Auditory, Olfactory, Gustatory, Tactile)
 - Sensory Association Areas: (Novel Vs. Familiar)
- **Insula:**
 - Involved with Recognition & Feeling of **Disgust**



The Papez Circuit:

- **1. Thalamus** relays Sensory Input to Cingulate Cortex.
- **2. Cingulate Cortex** - gives you the Emotional Experience
 - also relays to the **Neocortex**, which gives Context/Colouring to the Emotion.
 - also relays to the **Hippocampus** →
- **3. Hippocampus** Relays to the Hypothalamus – Causes the Emotional Expression (Visceral Response)

The Papez circuit. Papez believed that the experience of emotion was determined by activity in the cingulate cortex and, less directly, other cortical areas. Emotional expression was thought to be governed by the hypothalamus. The cingulate cortex projects to the hippocampus, and the hippocampus projects to the hypothalamus by way of the bundle of axons called the fornix. Hypothalamic effects reach the cortex via a relay in the anterior thalamic nuclei.



Source: Unattributable

The Limbic System:

- *****Amygdala***:**

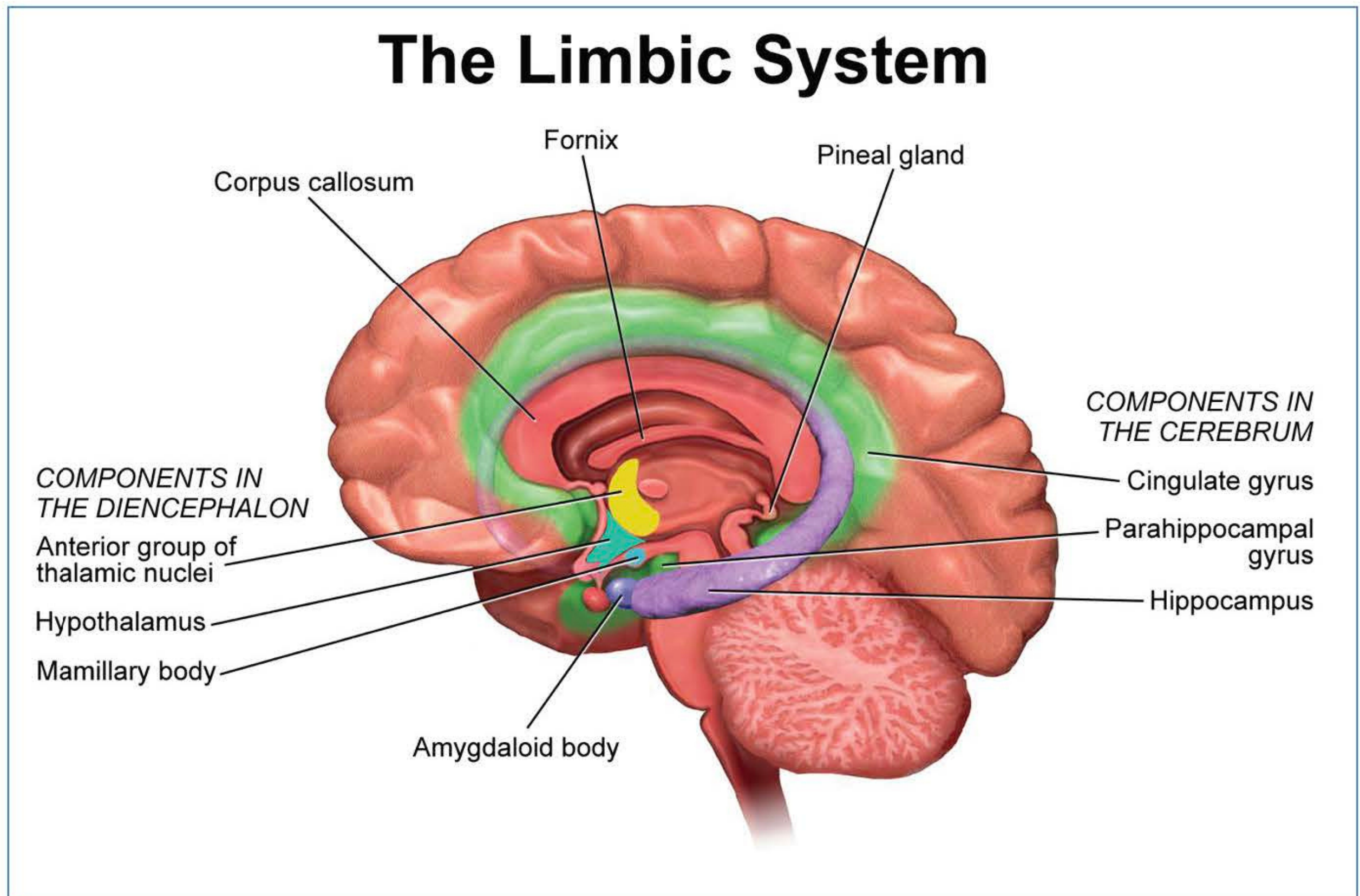
- #1 Structure involved in Emotion → The “Heart” of the Limbic System.
- “The Fight/Flight Centre”
- Linked to all but 8 areas of the Cortex → ∴ Thought to be #1 integrator of Cognitive & Emotional Info.
- **Afferents (Receives Input From...):**
 - **Brainstem** – inputs associated with Physical States (BP/HR/etc)
 - **Hypothalamus** – inputs associated with Physical States (BP/HR/etc)
 - **Thalamus** – Sensory Info
 - **Hippocampus** – inputs associated with Explicit Memory
 - **Cortex** – Sensory Inputs & Decisions related to Perceived Threats
- **Efferents (Sends Output to...):**
 - **Brainstem** – influences Visceral Fear-Driven, Fight/Flight Responses.
 - **Hypothalamus** – Influence on Memory & Aggression
 - **Thalamus** – Influences processing of new sensory info
 - **Hippocampus** – Fear is an important driver for learning & memory
 - **Pre-Frontal Cortex** – Fear is important in Decision Making & Cognition
- **Regulates:**
 - Fear & Aggression
 - Vigilance & Attention
 - Recognition of Emotion (in Self & Others)
 - Emotional Contribution to Memory. (Emotional Implicit Memory)

- **Hypothalamus:**

- **Visceral Responses** to Emotion
- **Aggression**
- **Sex Drive**

- **Brain Stem:**

- **Visceral Responses** to Emotion



Neurotransmitters & Emotion:

- ***Noradrenaline: (A Target for Antidepressants):**

- **Activated By:**
 - Novel, Unexpected Stimuli
- **Released By:**
 - **Locus Coeruleus** (A Nucleus In the Pons involved with physiological responses to stress & panic.)
- **Regulates:**
 - Mood/Arousal
 - Anxiety
 - Pain
 - Sleep/Wake Cycles
 - Motor Activity

- ***Serotonin: (A Target for Antidepressants):**

- **Activated By:**
 - General activity/arousal
- **Released By:**
 - Raphe Nuclei (A group of Nuclei In the brainstem)
- **Regulates:**
 - Mood
 - Emotions
 - Sleep/Wake Cycles
 - Dominance/Aggression
 - Anxiety

- ***Dopamine:**

- **Activated By:**
 - Pleasurable Activities
- **Released By:**
 - Ventral Tegmental Area (VTA)
 - Substantia Nigra
- **Regulates:**
 - *Somehow* plays a role in Regulation of Perception of Emotion
 - Involved in Reward Centre

- **Glutamate & GABA:**

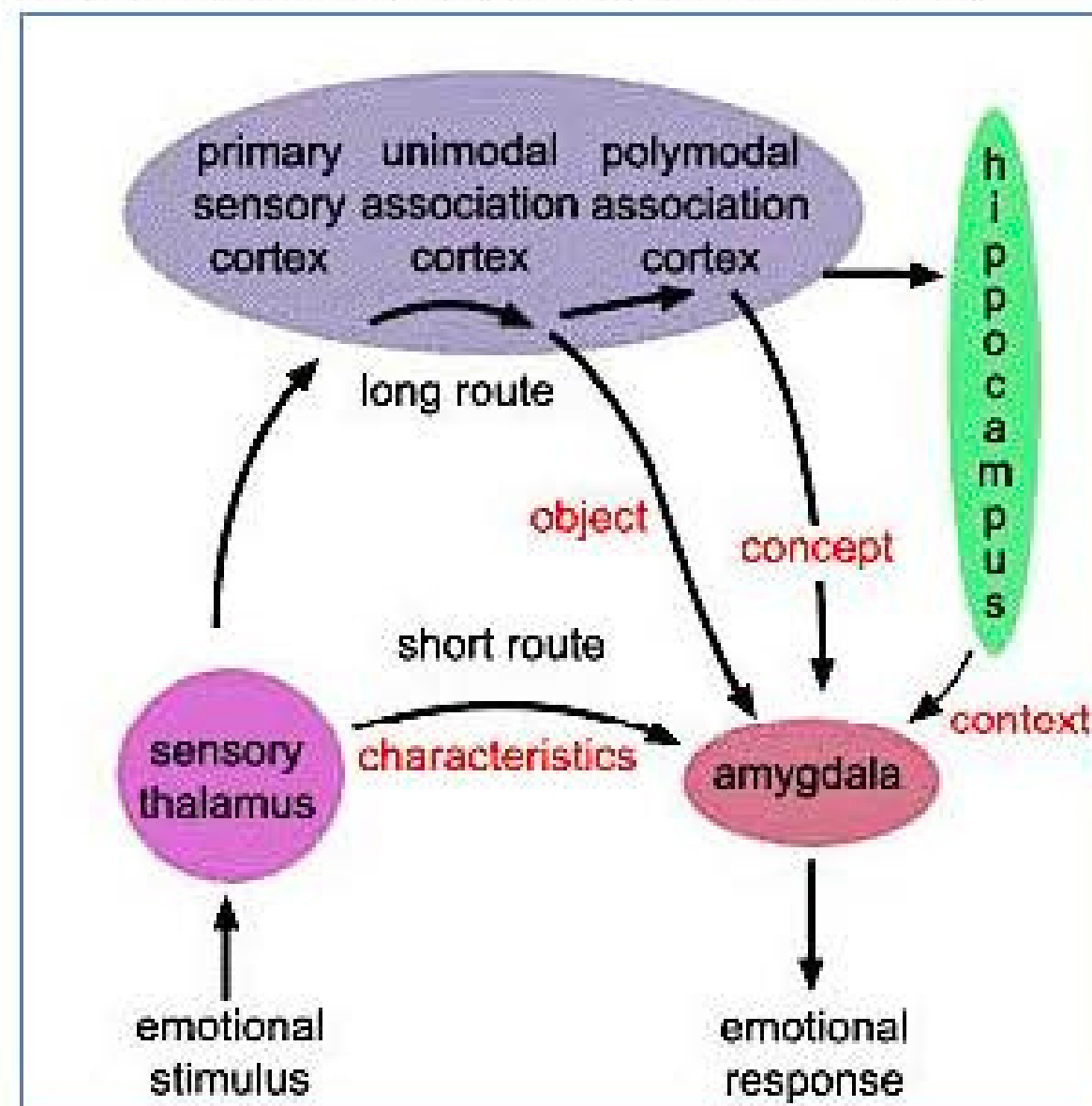
- Reduces Anxiety

- **Acetylcholine:**

- **Released By:**
 - Basal & Septal Nuclei of Meynert
- **Regulates:**
 - Cognitive Processing
 - Arousal & Attention

The Emotion of Fear:

- **Brain Structures Involved:**
 - o Thalamus →
 - Amygdala
 - o Thalamus →
 - Primary Sensory Cortex
 - Association Cortices
- **Long & Short Pathways:**
 - o **Long:**
 - Info processed by higher brain centres & Hippocampus.
 - Results in a more complex response
 - o **Short:**
 - Info sent straight to Amygdala
 - Results in a basic response (Recoil from stimulus/Freeze)
 - **Advantage** = No cortical processing means quicker reaction times → ↑Survival.
- **Process of Fear:**
 - o 1. Sensory Info enters brain → Thalamus
 - o 2. Thalamus Sends info to Amygdala (Via Long/Short Route)
 - o 3. Amygdala activates Visceral Responses through Hypothalamus
 - o 4. Amygdala Activates Ventromedial Pre-Frontal Cortex (Allows conscious recognition of the Emotion)
 - o 5. Visual Cortex also inform Prefrontal Cortex about the Threat.



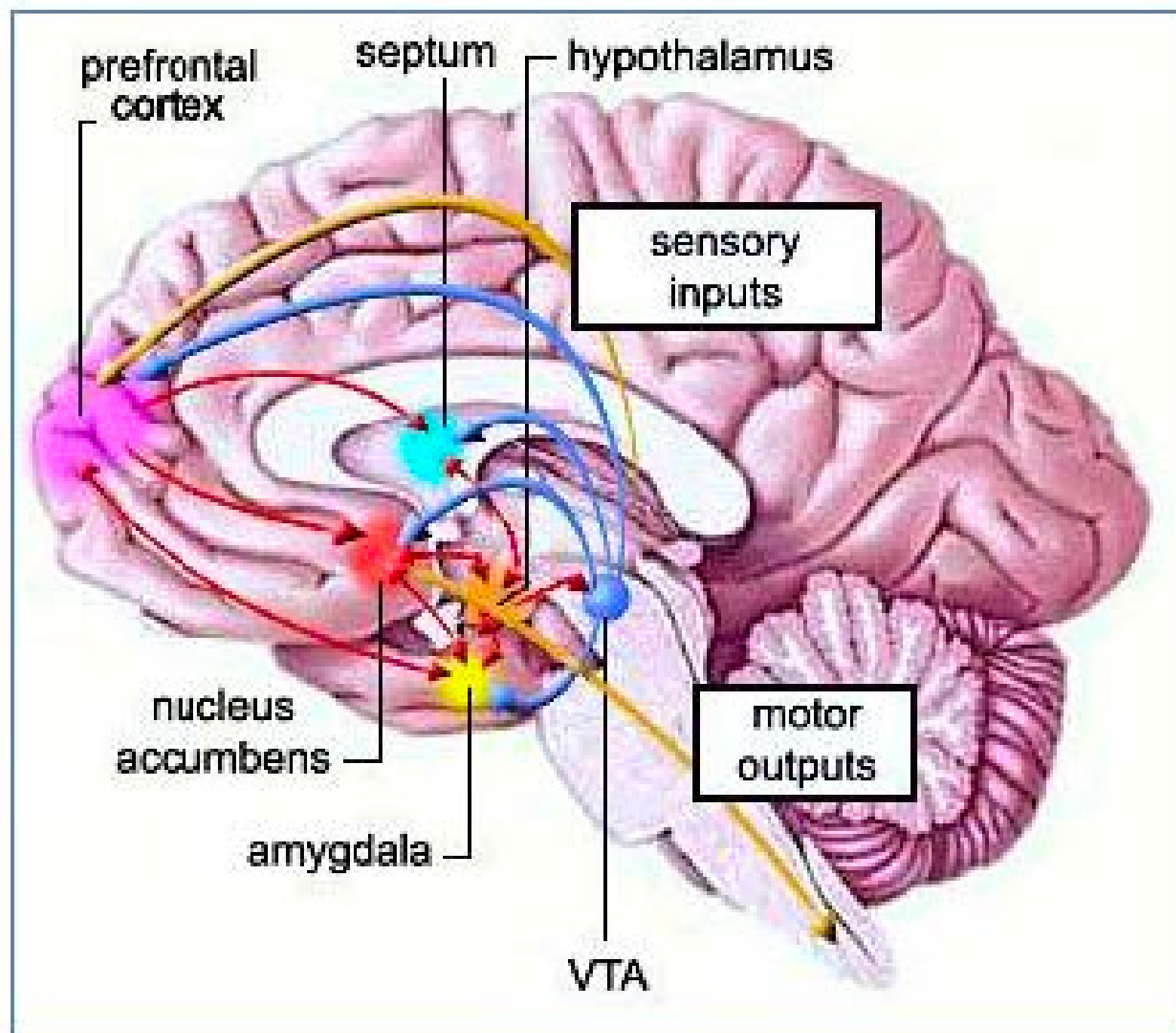
https://thebrain.mcgill.ca/flash/a/a_04/a_04_cr/a_04_cr_peu/a_04_cr_peu.html

Aggression:

- **Affective Aggression Vs Predatory Aggression:**
 - o Predatory aggression is related to feeding behaviour & isn't accompanied by sympathetic physiological response with which affective aggression is associated.
- **Associated Structures:**
 - o Cerebral Cortex
 - o **Amygdala**
 - o **Hypothalamus**
 - o Periaqueductal Grey-Matter (PAG)
 - o Ventral Tegmental Area (VTA)
 - IE. "Aggression is controlled by a neural pathway from the Amygdala through the Hypothalamus, PAG & VTA.
- **Neurotransmitter:**
 - o Serotonin
- **Possible Hormonal Link:**
 - o Adenosine

Pleasure & Reward: The 'Reward Circuit':

- Brain Structures Involved:
 - o **Ventral Tegmental Area (VTA)*
 - o **Nucleus Accumbens*
 - o Amygdala
 - o Pre-Frontal Cortex
 - o Thalamus
- Neurotransmitters Involved:
 - o **Dopamine* - VTA & Nucleus Accumbens



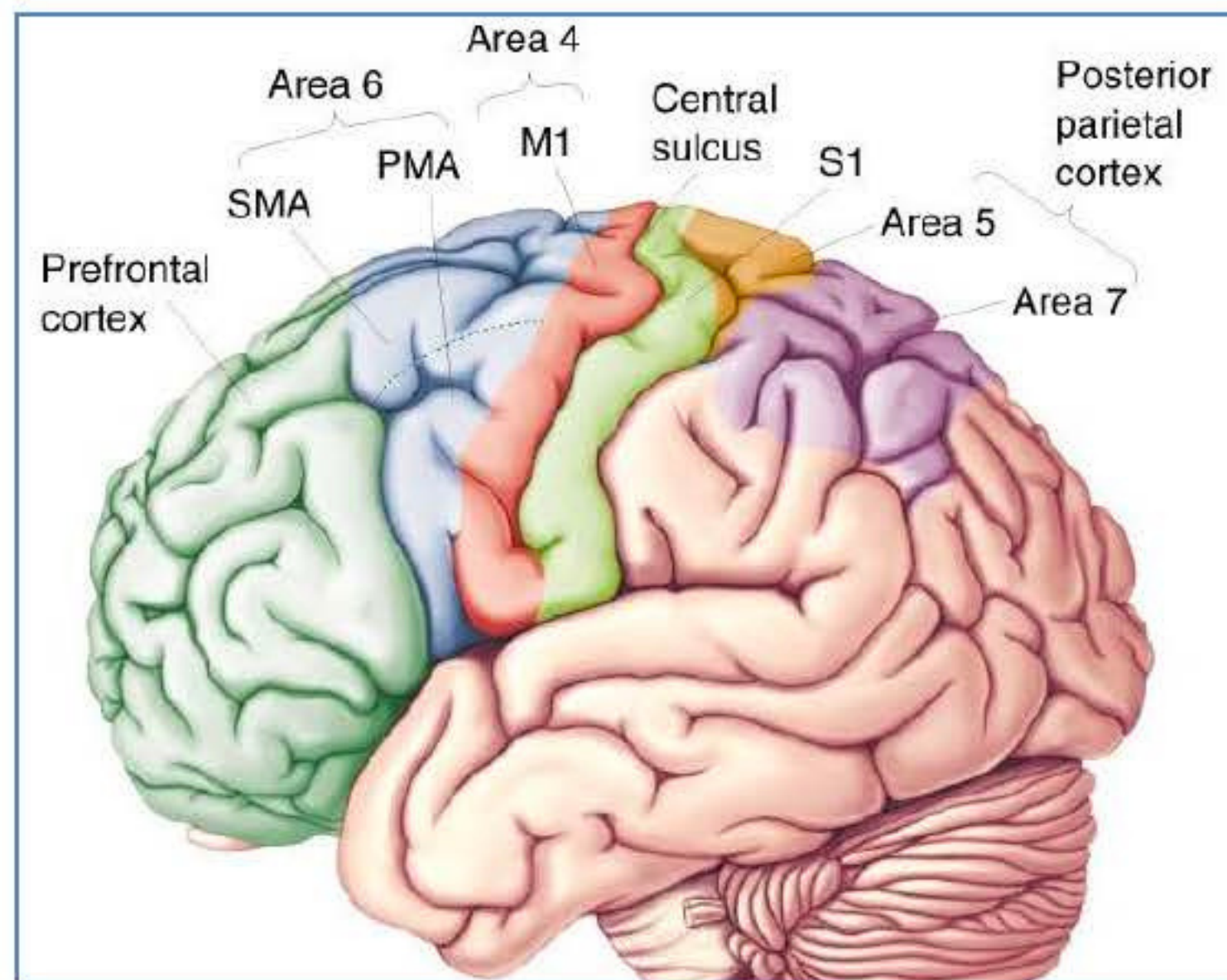
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MOTOR PROCESSING:

MOTOR PROCESSING

Motor Processing Hierarchy of Structures - The Levels of Motor Control:

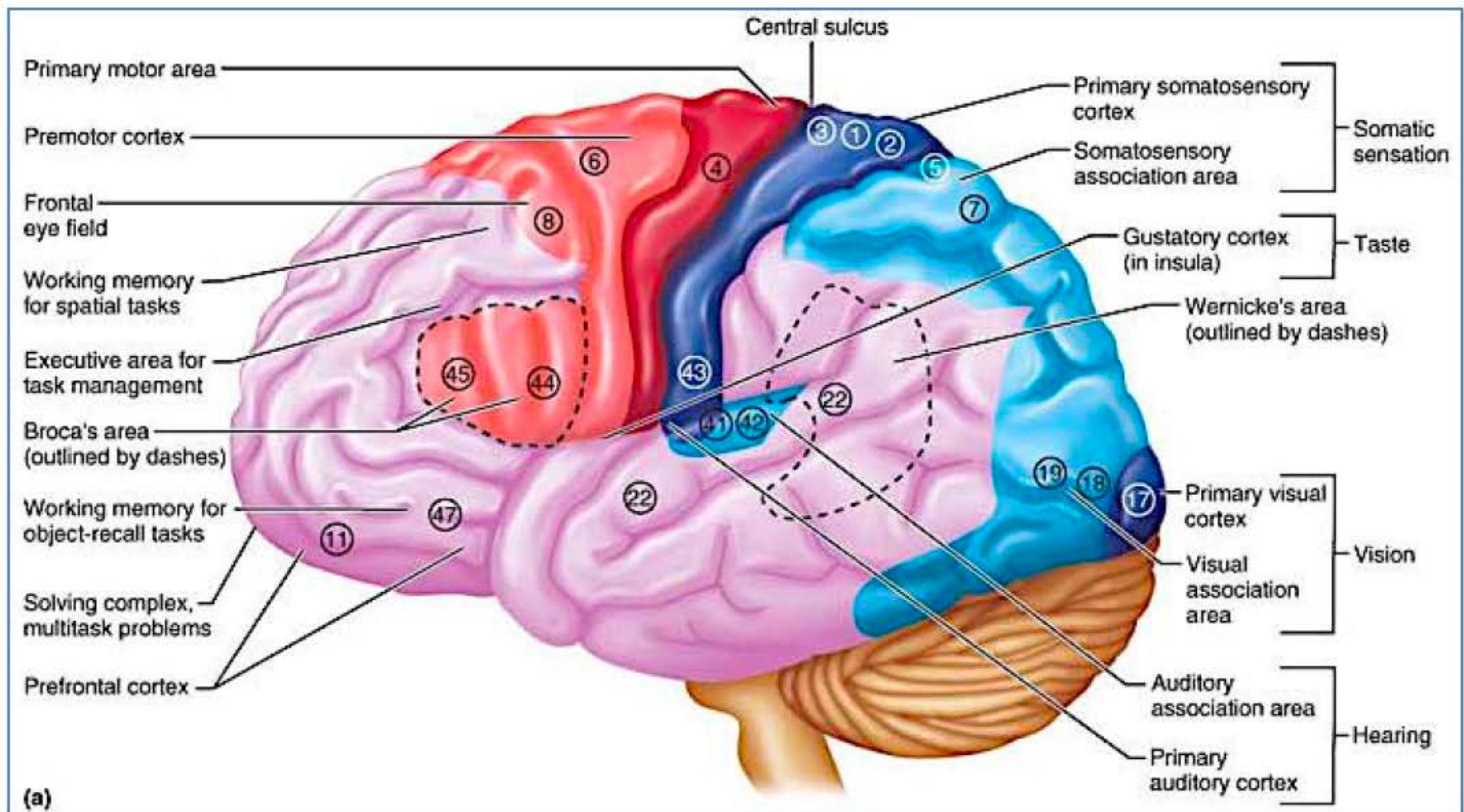
- **1. Ready (Strategy) – Deciding ‘What to do’:**
 - o Prefrontal Cortex
 - o Somatosensory Association Cortex (Area 5)
 - o Basal Ganglia (Note: Basal Ganglia are the interface between ‘Strategy’ & ‘Tactics’.)
- **2. Set (Tactics) – Deciding ‘How to do it’:**
 - o Basal Ganglia
 - o Pre-Motor Area (PMA)
 - o Supplementary Motor Area (SMA)
- **3. Go (Execution) – ‘Action’:**
 - o Primary Motor Cortex (M1)
 - o Cerebellum
 - o Brainstem
 - o Descending Tracts
 - o Spinal Nerves
 - o Peripheral Motor Neurons



Berg-Johnsen, J., Høgestøl, E.A. Supplementary motor area syndrome after surgery for parasagittal meningiomas. *Acta Neurochir* **160**, 583–587 (2018). <https://doi.org/10.1007/s00701-018-3474-3>

Roles of these Brain Regions (In Motor Processing):

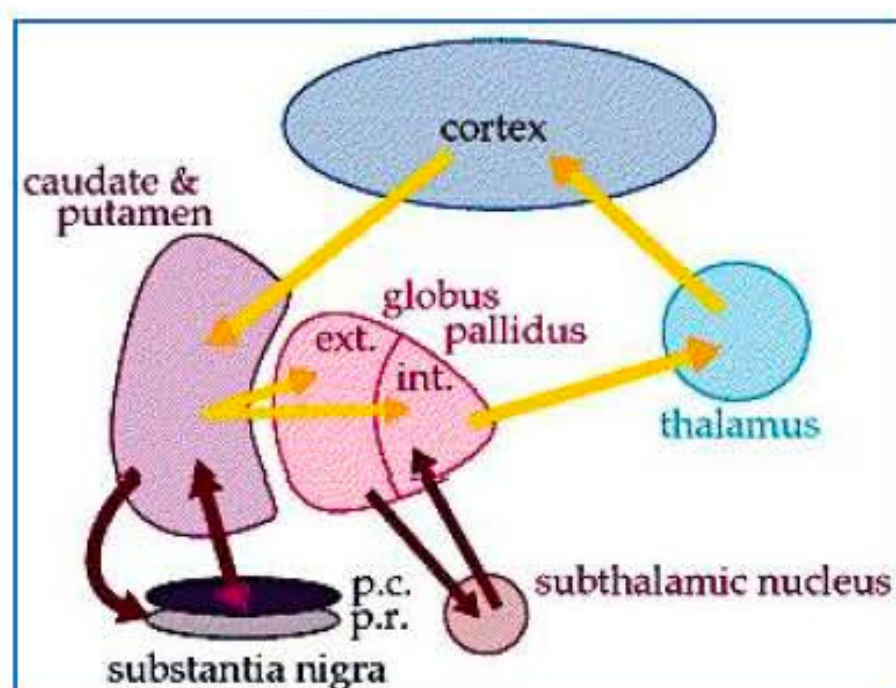
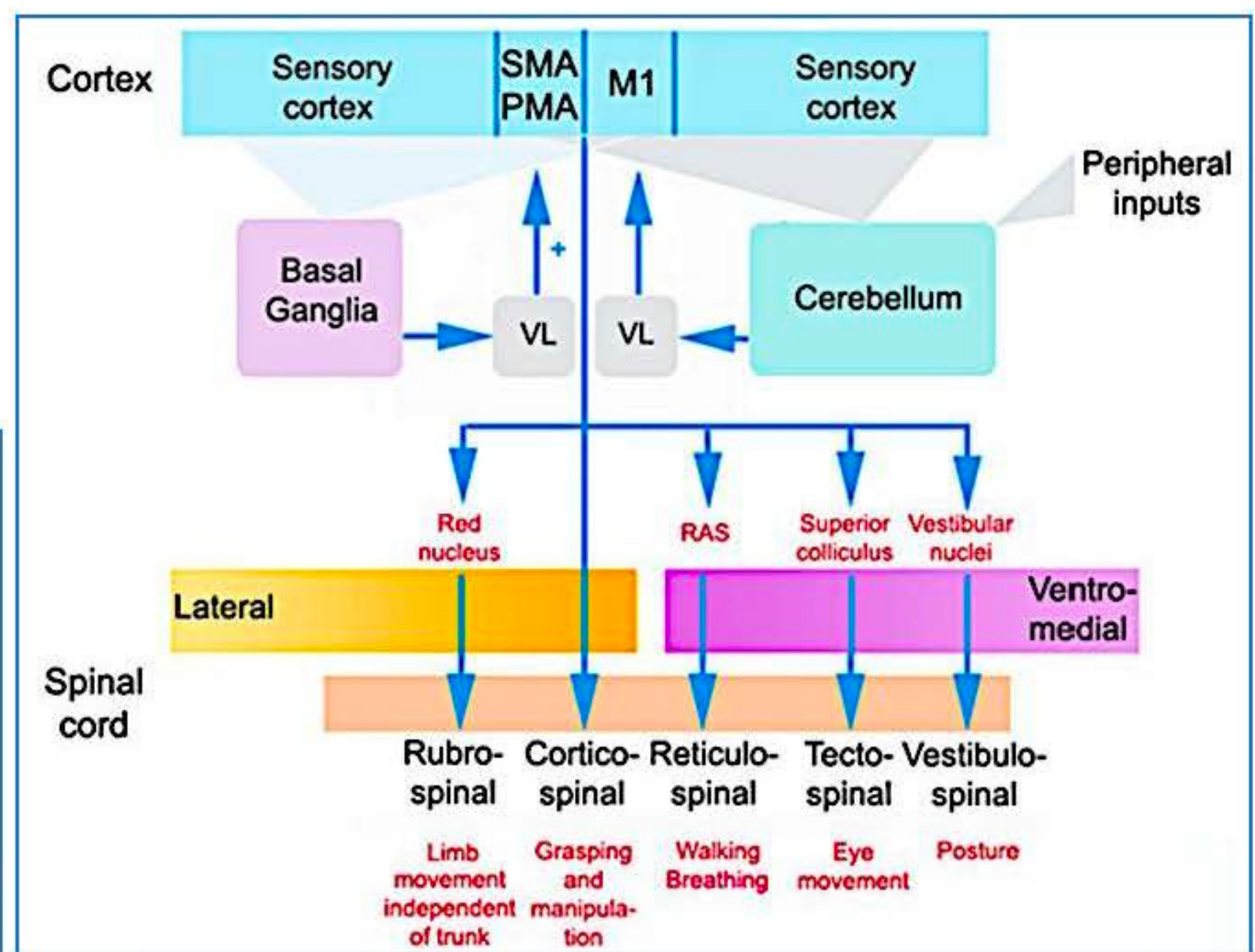
- **Pre-Frontal Cortex:**
 - o Consciously Decides ‘what movement’ is required for the desired outcome. (Managerial Function)
- **Somatosensory Association Areas:**
 - o Tells the brain where the body is in space (Proprioception)
- **Pre-Motor Area & Supplementary-Motor Areas:**
 - o Plans ‘how to do the movement’.
 - o Is also the *memory bank* of Complex, Patterned & Highly Skilled Learned Movements.
- **Primary Motor Cortex (M1):**
 - o ‘Initiates the movement’ (Typically precise or skilled voluntary movement)
 - o Note: M1 also exhibits **Somatotopy** – The Bigger the Cortical Area, The More Precise the Movements
 - o **Receives Direct & Indirect Inputs:**
 - **Direct** – From: Prefrontal Cortex, SMA/PMA, Somatosensory Areas
 - **Indirect** – From: Cerebellum (Via Thalamus)
 - o **Broca’s Area** – Area of M1 that controls the Muscles responsible for speech (Tongue/Jaw/Lips/Face)



<https://medicoapps.org/m-functional-areas-of-cerebral-cortex/>

Basal Ganglia:

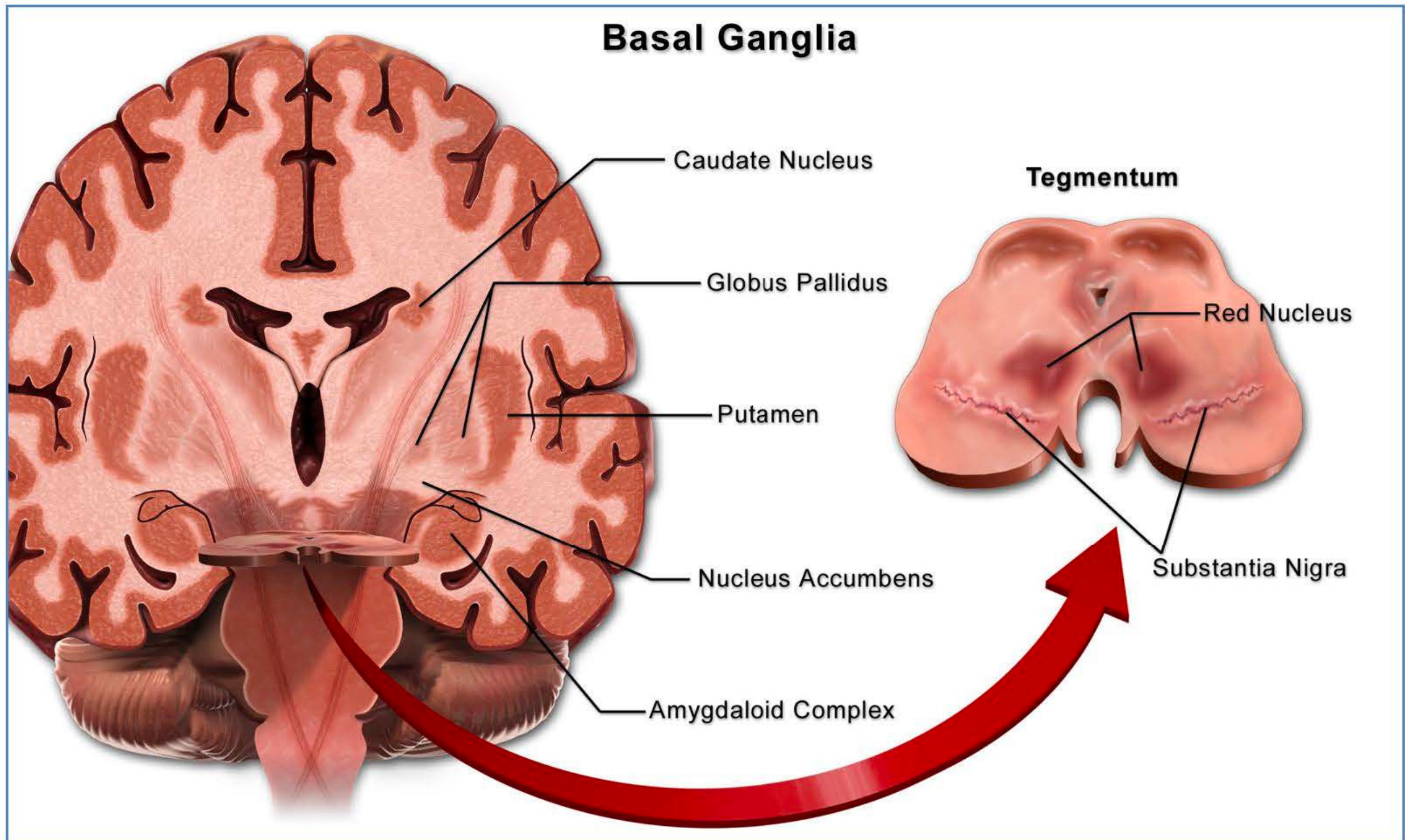
- **Involved in** Action-Selection & Initiation of Voluntary & Patterned Movements (Eg: Walking)
 - Motor Control & Motor Learning
 - Note: Also has a role in Cognition & Memory
- **A Loop Exists** between the Cortex → Basal Ganglia → Thalamus → Pre-Motor Cortex → Cortex
 - Receives inputs from the Entire Cortex. (SMA/Prefrontal Cortex/Sensory Cortex/M1)
 - **Info travels through Basal Ganglia in This Order: Striatum→Globus Pallidus.**
 - Sends info to the PMA & *SMA via the (Ventral-Lateral Nucleus of the) Thalamus (VLo)



Note: The GLOBUS PALLIDUS is Spontaneously Active:

Globus Pallidus → Thalamus (Inhibits Thalamic-SMA Activity → Keeps the SMA 'Quiet')

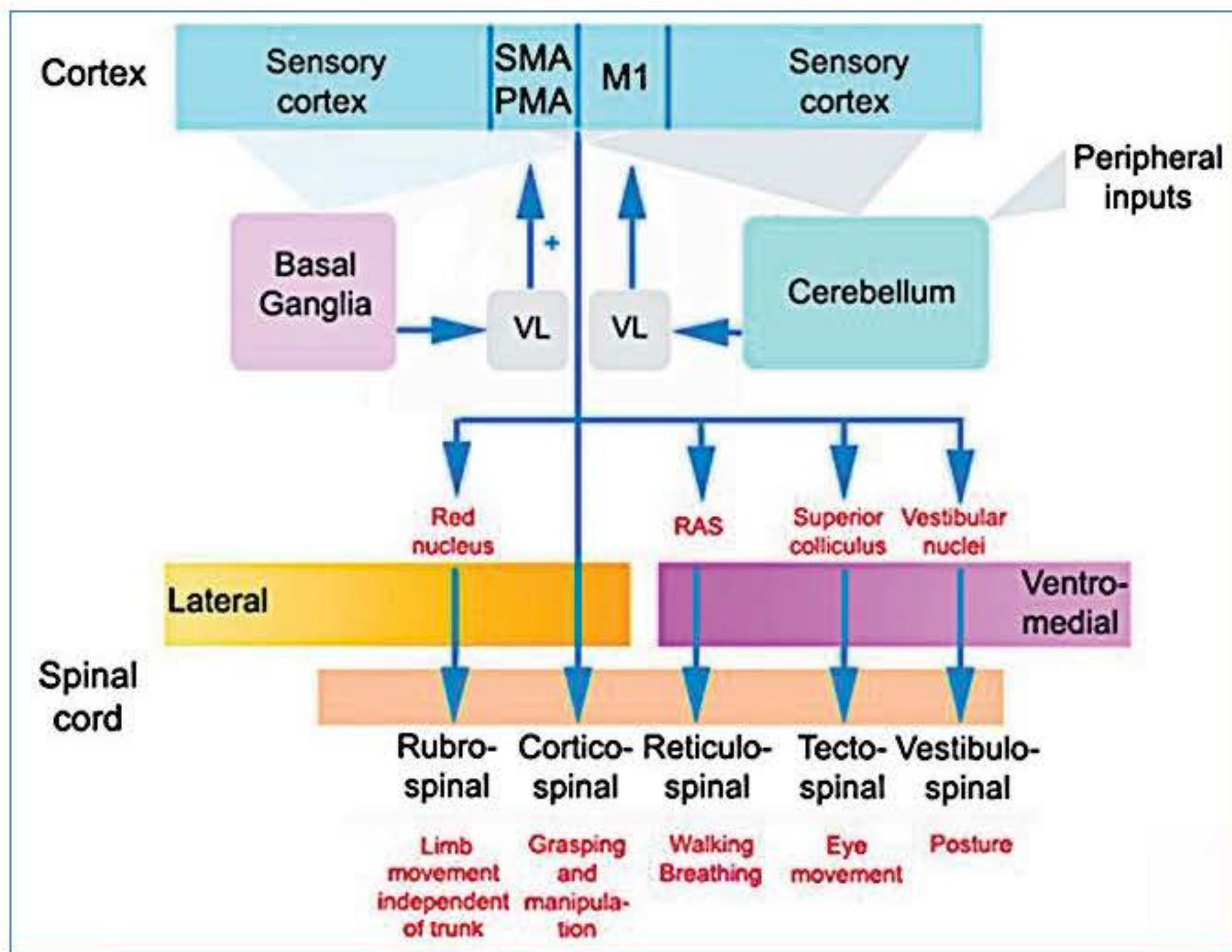
- **Basal Ganglia Consists of:**
 - **Striatum:**
 - **Caudate Nucleus:** Cognition & Behaviour
 - **Putamen:** Motor (Automatic performance of previously learned movements.)
 - **Globus Pallidus**
- **& Other Associated Structures:**
 - **Subthalamic Nuclei**
 - **Substantia Nigra:** Eye Movement, Motor Planning, (Reward Seeking, Learning, & Addiction)



Blausen.com staff (2014). "Medical gallery of Blausen Medical 2014". WikiJournal of Medicine 1 (2). DOI:10.15347/wjm/2014.010. ISSN 2002-4436., CC BY 3.0 <<https://creativecommons.org/licenses/by/3.0/>>, via Wikimedia Commons

- **Cerebellum:**

- **Functions:**
 - *Precise Timing & Appropriate Patterns* of Skeletal Muscle Contraction – Required for Smooth, Coordinated movements & agility needed for daily living (Driving/Typing/Playing Music/etc)
 - Involved in the *Correct Sequencing & Coordination* of Muscle Contractions.
 - Involved in Motor Learning – Compares intention with result & corrects for next time.
 - Balance & Posture
- **Note:** Cerebellar Activity is Subconscious (Ie: We have no awareness of its functioning.)
- **A Loop exists** between the Cortex → Pons → **Cerebellum** → Thalamus → M1 → Cortex.
 - Receives inputs from the Cerebral Cortex (M1, PMA, ***Somatosensory Areas**) via the Pons.
 - Also receives Proprioceptive Feedback
 - Sends info to the Primary Motor Cortex (M1) via the VentroLateral Nucleus of the Thalamus.
 - Informs Primary Motor Cortex (M1) about Direction, Force & Timing of Movements.
- **Output into Descending Pathways:**
 - **Vermis** → Ventromedial Pathways
 - **Hemispheres** → Lateral Pathways

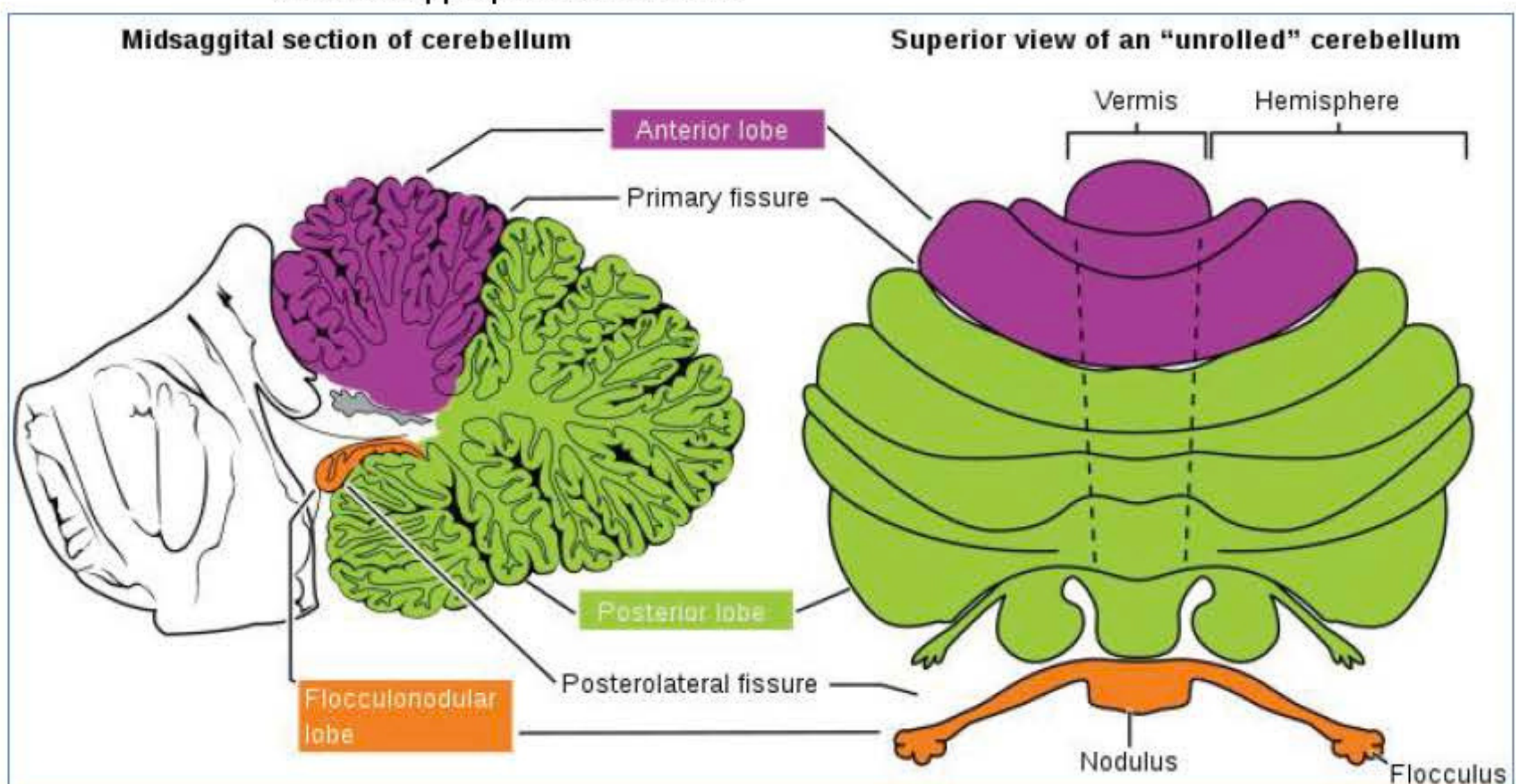


○ **Cerebellar Processing:**

- 1. Cortical Motor Areas Notify the Cerebellum (via 'relay nuclei' in the brainstem) of their **intent** to initiate voluntary muscle contractions.
- 2. Constant Proprioceptive Input (Muscle/Tendon Tension, Joint Position, etc) enables the cerebellum to evaluate the body's position & momentum.
- 3. Cerebellum calculates optimum Force, Direction & Extent of Muscle Contraction to ensure Smooth, Accurate & Coordinated Movements.
- 4. Cerebellum sends its "Blueprint" for coordinating movement to the Cerebral Motor Cortex via the Superior Peduncles. It also sends info to Brainstem Nuclei → Influences Motor Neurons of the Spinal Cord.

○ **Analogy:**

- Just as an 'Autopilot' compares a plane's instruments with its planned course, the Cerebellum continually compares the higher brain's intention with the body's performance & makes appropriate corrections.



Descending Tracts Involved in Motor Function:

Descending Motor Pathways:

- Lateral Pathways:

○ Roles:

- Both Tracts – Voluntary Movement of Distal Extremities (Particularly Hands & Feet)

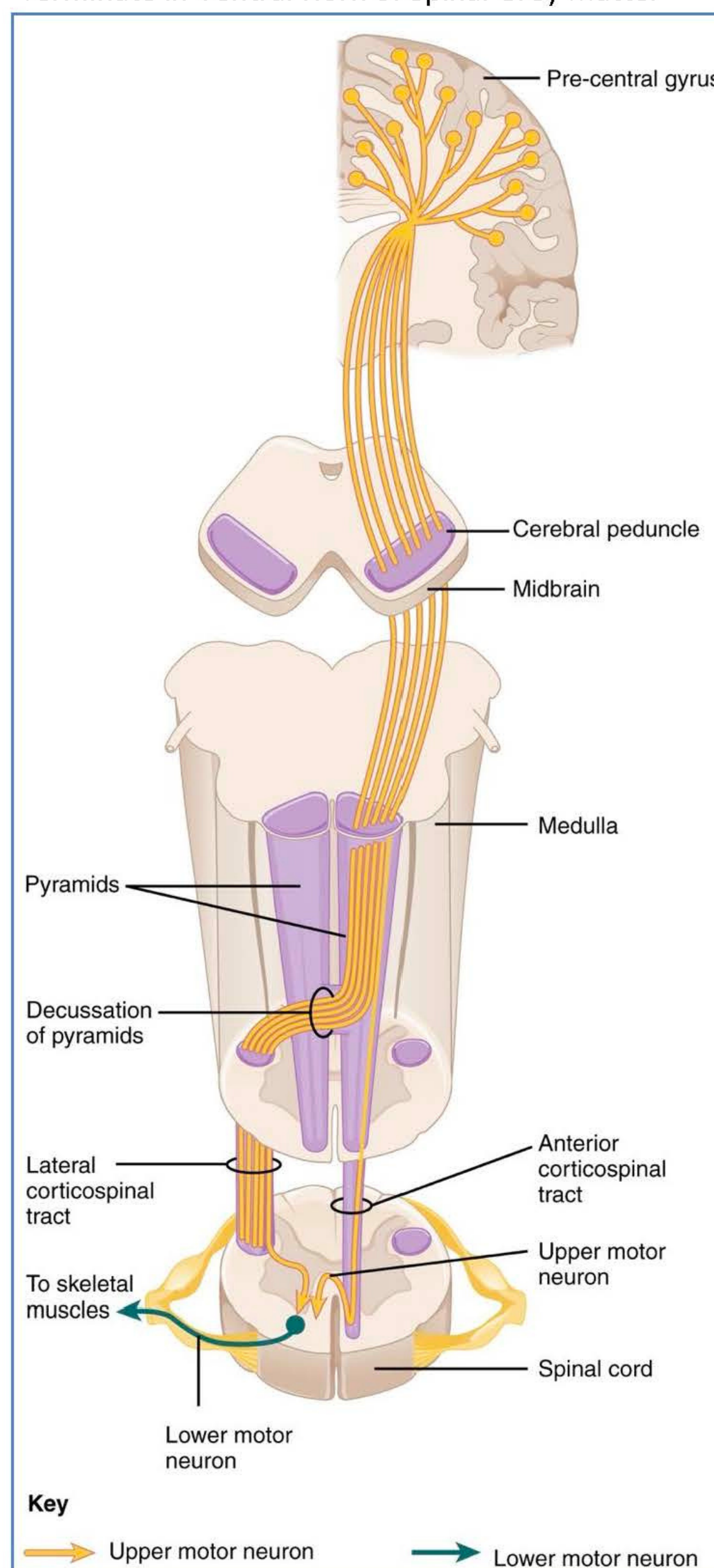
○ 2 Divisions:

▪ **Corticospinal Tract:**

- Originates in Primary Motor Cortex
- Run through the **Internal Capsule** to the Brainstem.
- **Decussate** in Medullary Pyramids (Medulla)

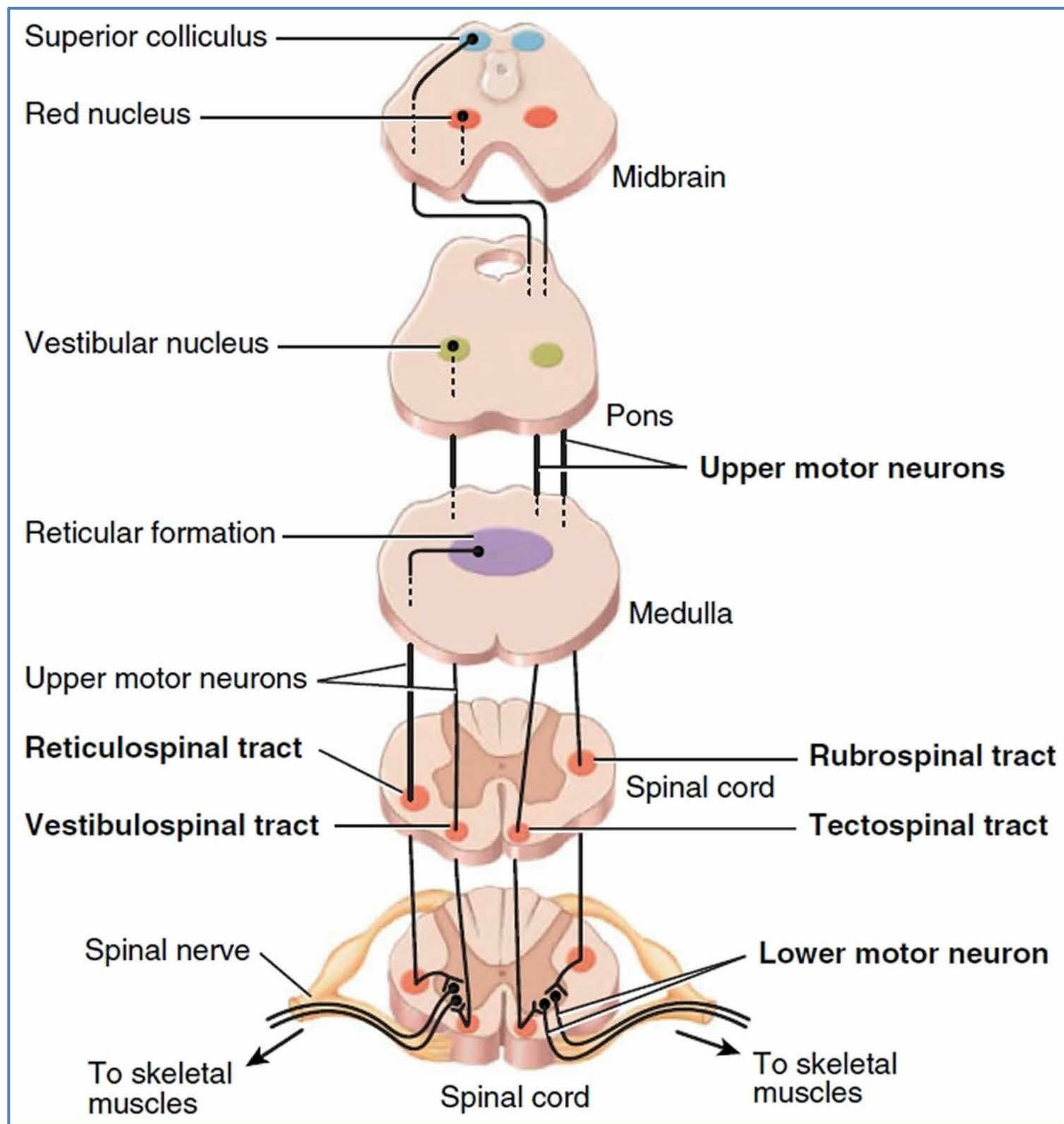
▪ **Rubrospinal Tract:**

- Originates in Red Nucleus of Midbrain.
- Decussate immediately below Red Nucleus (In the Pons)
→→
- Continue down the spinal cord in the Lateral White Matter.
- Terminate in Ventral Horn of Spinal Grey Matter



- **Ventromedial (Indirect/Extrapyramidal) Pathways:**

- **Tectospinal (AKA: Colliculospinal) Tract:**
 - Begins in the Superior Colliculus
 - Decussates between Midbrain & Pons
 - **Function:** Visual Tracking (Head/Eye Coordination)
- **Vestibulospinal Tract:**
 - Begins in the Vestibular Nuclei of the Medulla.
 - Does not decussate.
 - **Function:** Maintain Balance During Standing & Moving
- **Pontine & Medullary Reticulospinal Tracts:**
 - Begin in the Pontine Reticular Formation
 - Do not decussate
 - **Function:** Maintains Muscle Tone & Visceral Motor Functions



<https://healthjade.net/upper-motor-neuron/>

TABLE 12.3 Major Descending (Motor) Pathways and Spinal Cord Tracts

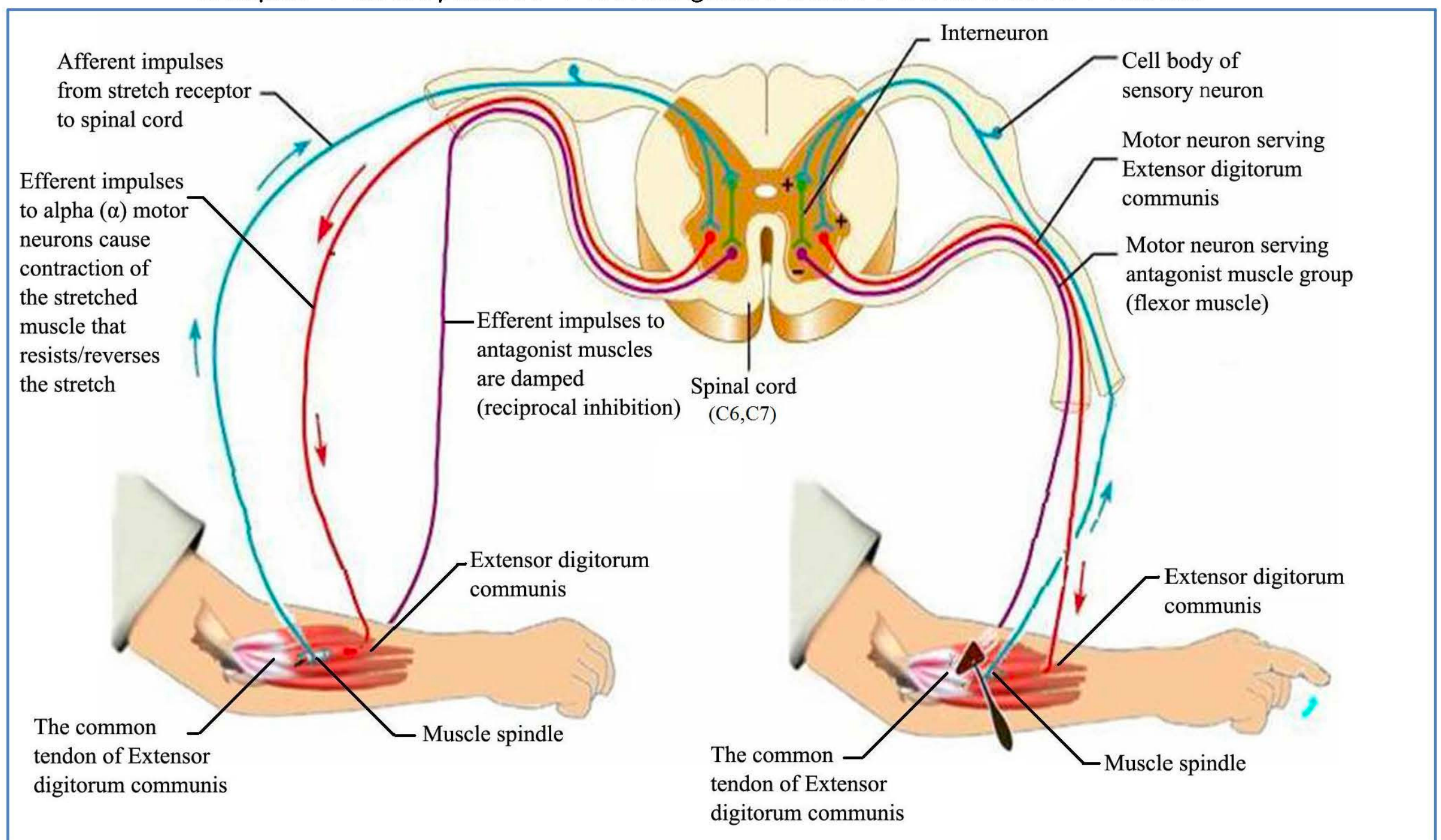
SPINAL CORD TRACT	LOCATION (FUNICULUS)	ORIGIN	TERMINATION	FUNCTION
DIRECT (PYRAMIDAL)				
Lateral corticospinal	Lateral	Pyramidal neurons of motor cortex of the cerebrum; decussate in pyramids of medulla	By synapse directly with ventral horn motor neurons and with ventral horn interneurons that influence motor neurons	Transmits motor impulses from cerebrum to spinal cord motor neurons (which activate skeletal muscles on opposite side of body); voluntary motor tract
Anterior corticospinal	Anterior	Pyramidal neurons of motor cortex; fibers cross over at the spinal cord level	Ventral horn (as above)	Same as lateral corticospinal tract
INDIRECT (EXTRAPYRAMIDAL) PATHWAYS				
Tectospinal	Anterior	Superior colliculus of midbrain of brain stem (fibers cross to opposite side of cord)	By synapse with ventral horn interneurons that influence motor neurons	Transmits motor impulses from midbrain that are important for coordinated movement of head and eyes toward visual targets
Vestibulospinal	Anterior	Vestibular nuclei in medulla of brain stem (fibers descend without crossing)	By synapse, directly with ventral horn motor neurons and with ventral horn interneurons that influence motor neurons	Transmits motor impulses that maintain muscle tone and activate ipsilateral limb and trunk extensor muscles and muscles that move head; in this way helps maintain balance during standing and moving
Rubrospinal	Lateral	Red nucleus of midbrain of brain stem (fibers cross to opposite side just inferior to the red nucleus)	Ventral horn (as above)	In experimental animals, transmits motor impulses concerned with muscle tone of distal limb muscles (mostly flexors) on opposite side of body; in humans, functions largely assumed by corticospinal tracts except for some upper limb movement
Reticulospinal (anterior, medial, and lateral)	Anterior and lateral	Reticular formation of brain stem (medial nuclear group of pons and medulla); both crossed and uncrossed fibers	Ventral horn (as above)	Transmits impulses concerned with muscle tone and many visceral motor functions; may control most unskilled movements

Source: Unattributable

- **Note: These Descending 'Upper Motor Neurons' Terminate in the Ventral Grey Horns of the Spinal Cord Grey Matter by Synapsing with either:**
 - **Spinal Interneurons – Enabling info to be sent to multiple outputs.**
 - Some Interneurons are '*Central Pattern Generators*' → generate timing for patterned movements (Eg: Walking)
 - **Or Lower Motor Neurons – That directly innervate skeletal muscle.**

Somatic Reflexes:

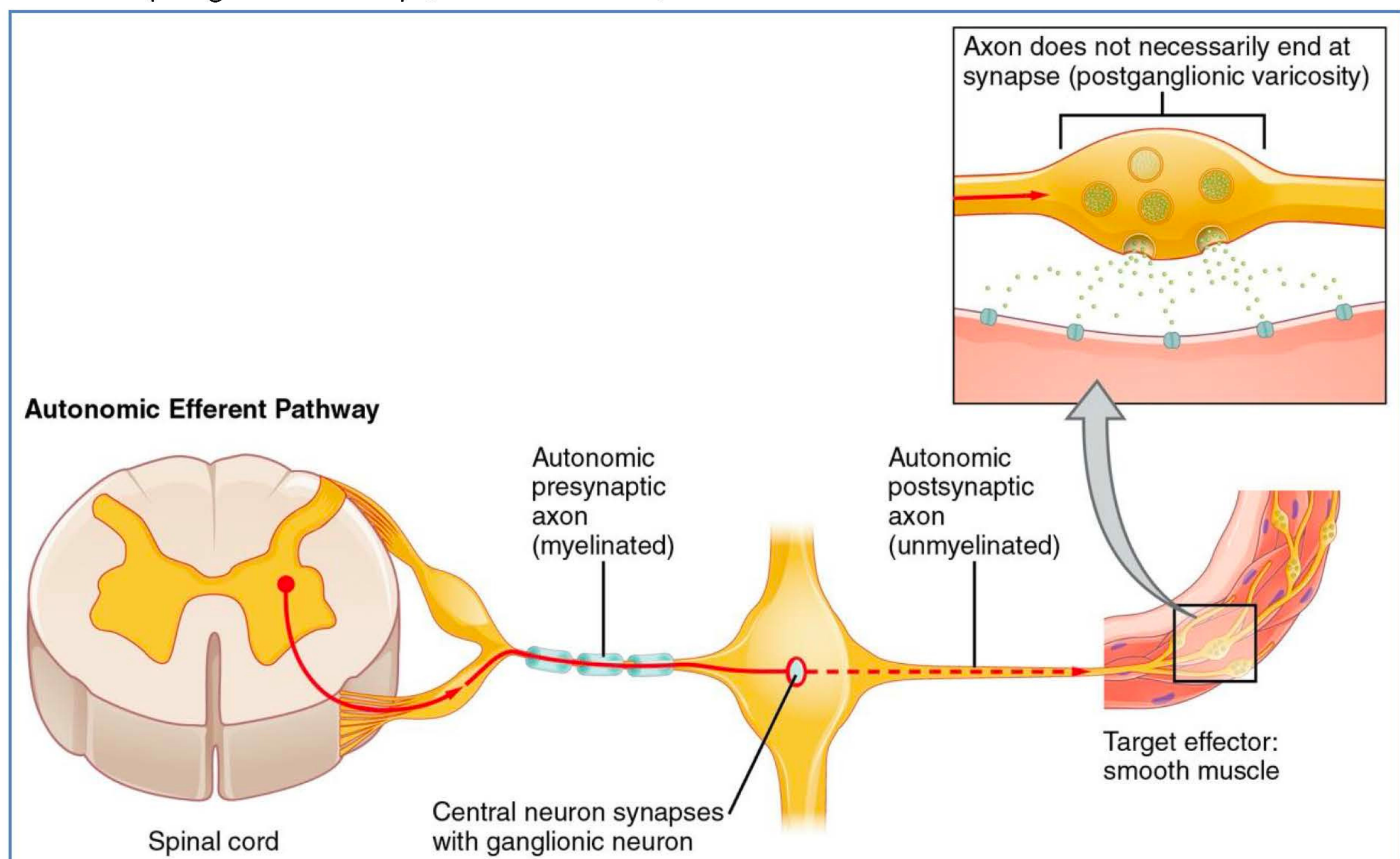
- Rapid, automatic responses to stimuli.
- Occur over neural pathways called **reflex arcs**.
- **Components of a reflex arc:**
 - Receptor → Sensory neuron → CNS integration centre → Motor neuron → Effector



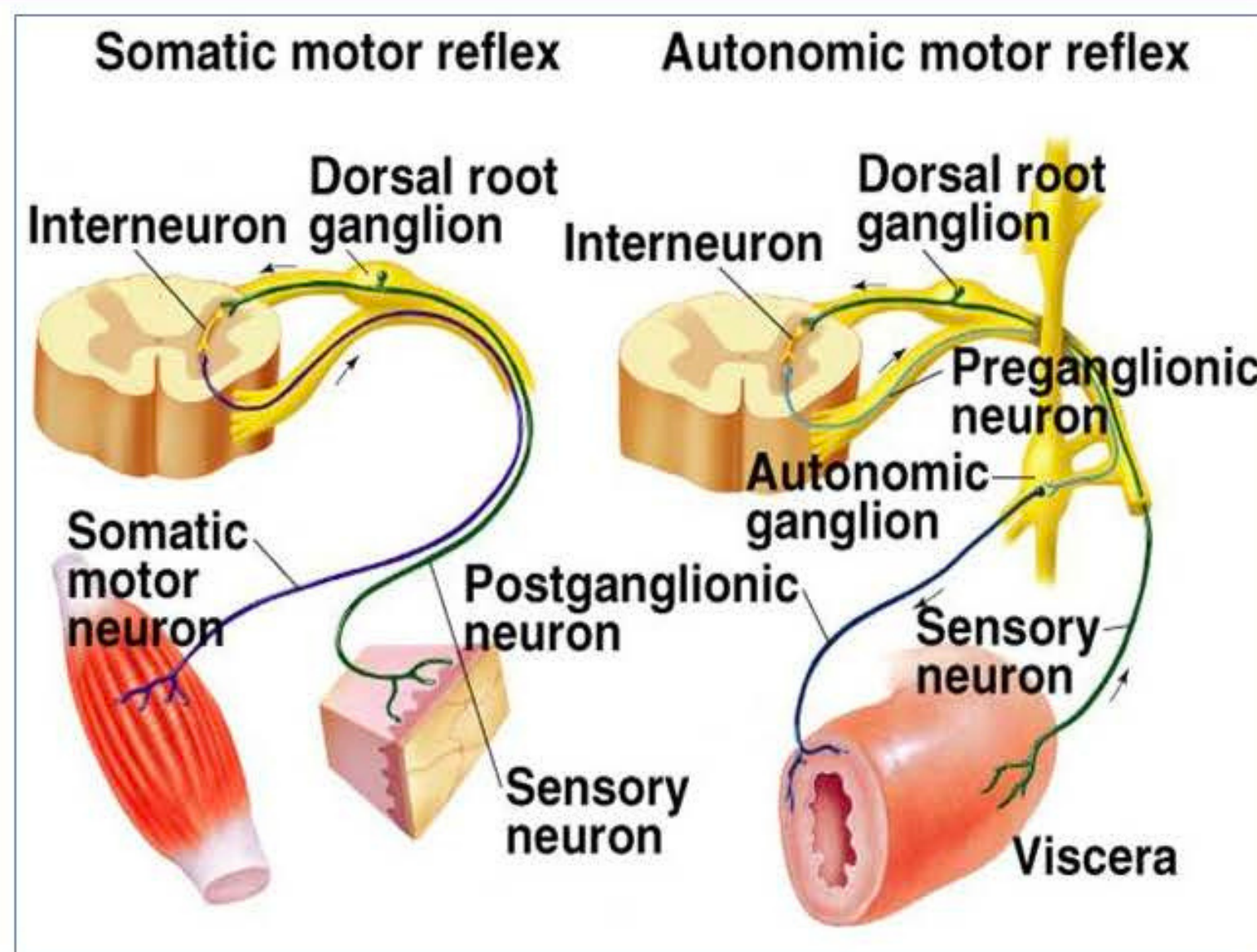
Zhang MJ, Zhu CZ, et.al, CC BY-SA 4.0 <<https://creativecommons.org/licenses/by-sa/4.0>>, via Wikimedia Commons

Visceral Reflexes:

- Similar to the Somatic-NS, the ANS also has reflex arcs;
- **Visceral Reflex Arcs Components:**
 - Visceral Sensory Neurons (Chemical Changes/Stretch/Irritation of Viscera) → Ganglionic Neuron (Integration Centre) → Motor Neuron → Effector



<https://open.oregonstate.edu/aandp/chapter/16-2-autonomic-reflexes-and-homeostasis/>



<https://www.austincc.edu/apreview/PhysText/PNSEfferent.html>