

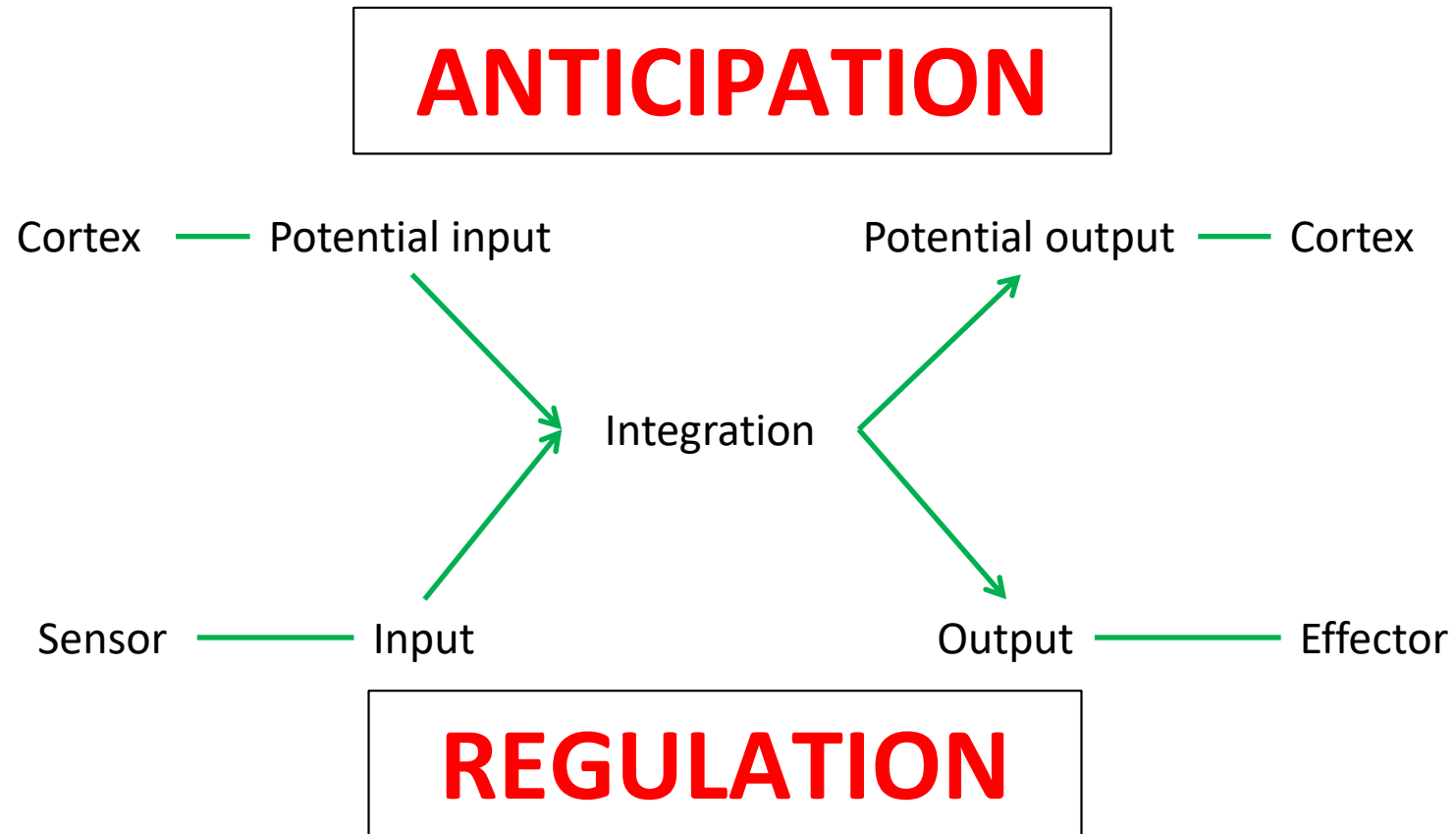
M U N I

M E D

**Autonomic nervous system**  
**Limbic system**  
**Neocortex**

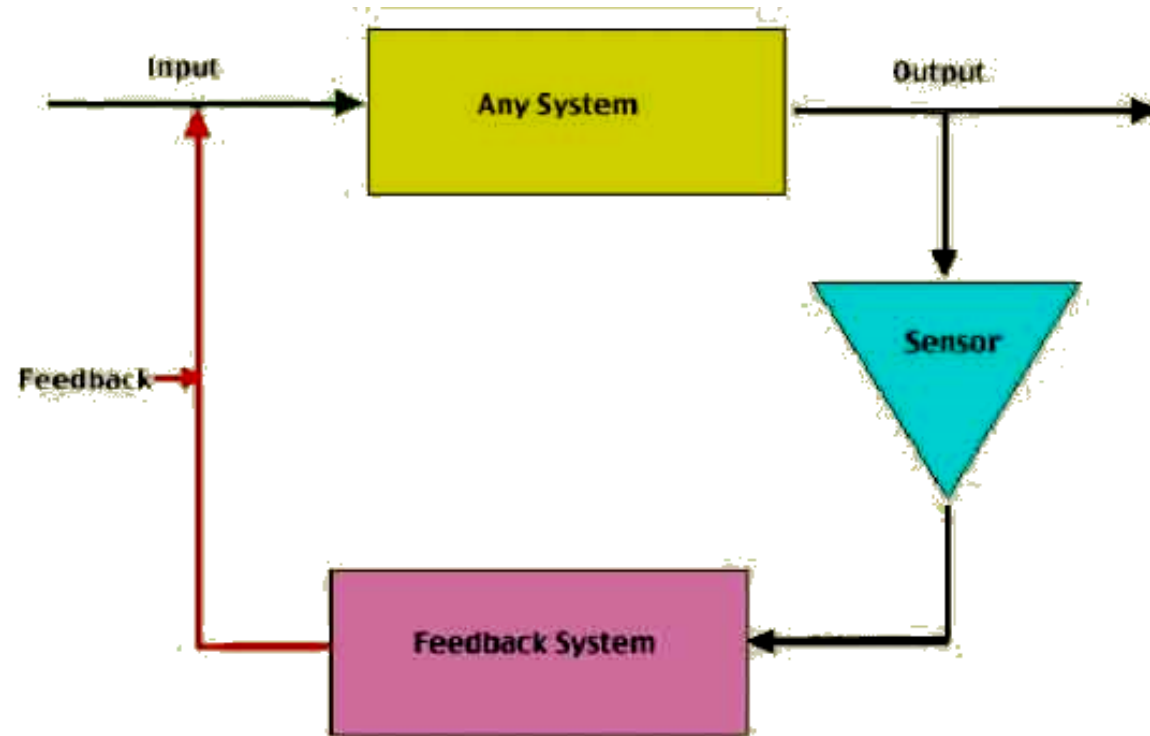
# **Autonomic nervous system**

# The role of nervous system



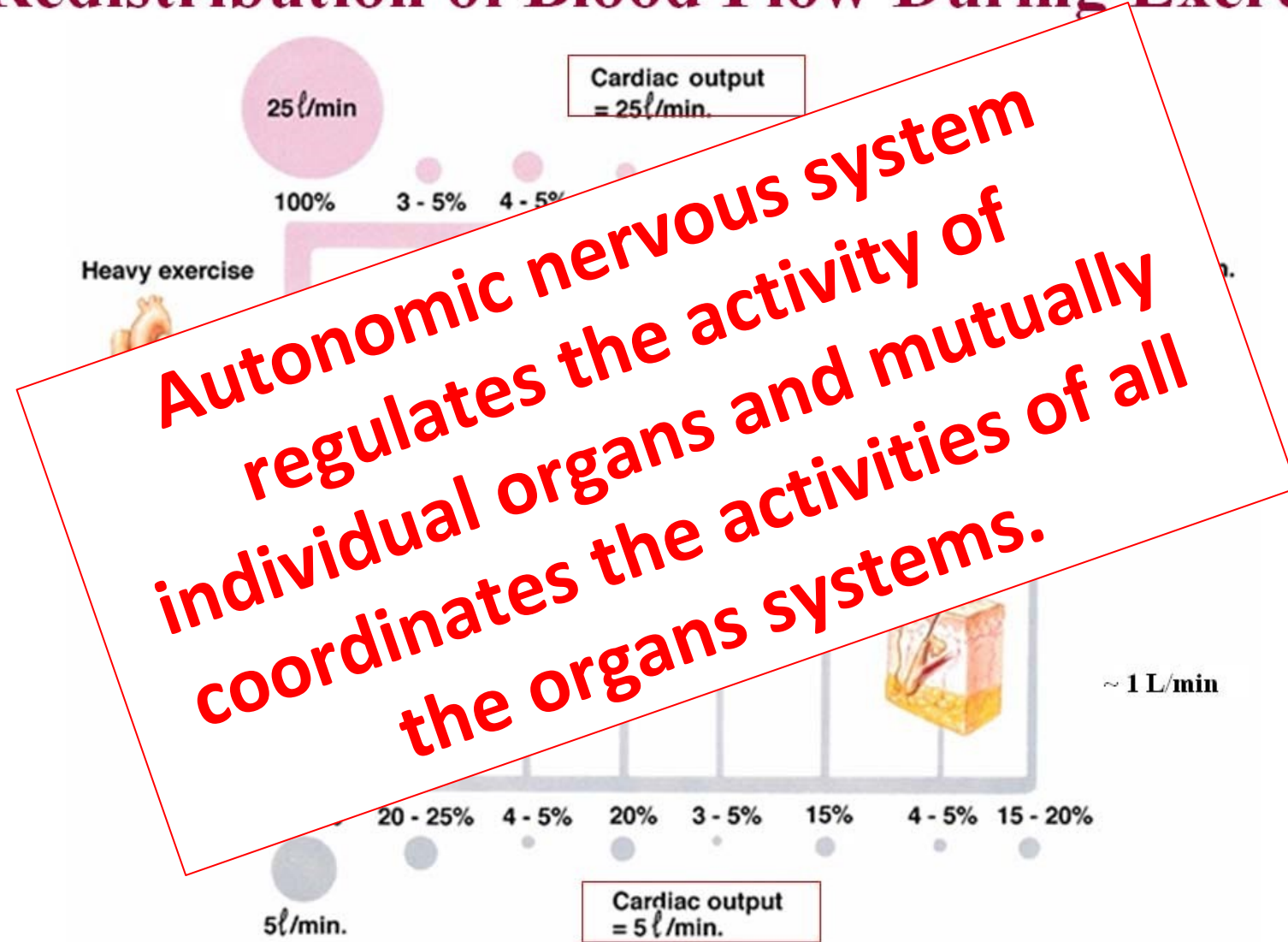


# Feedback regulation

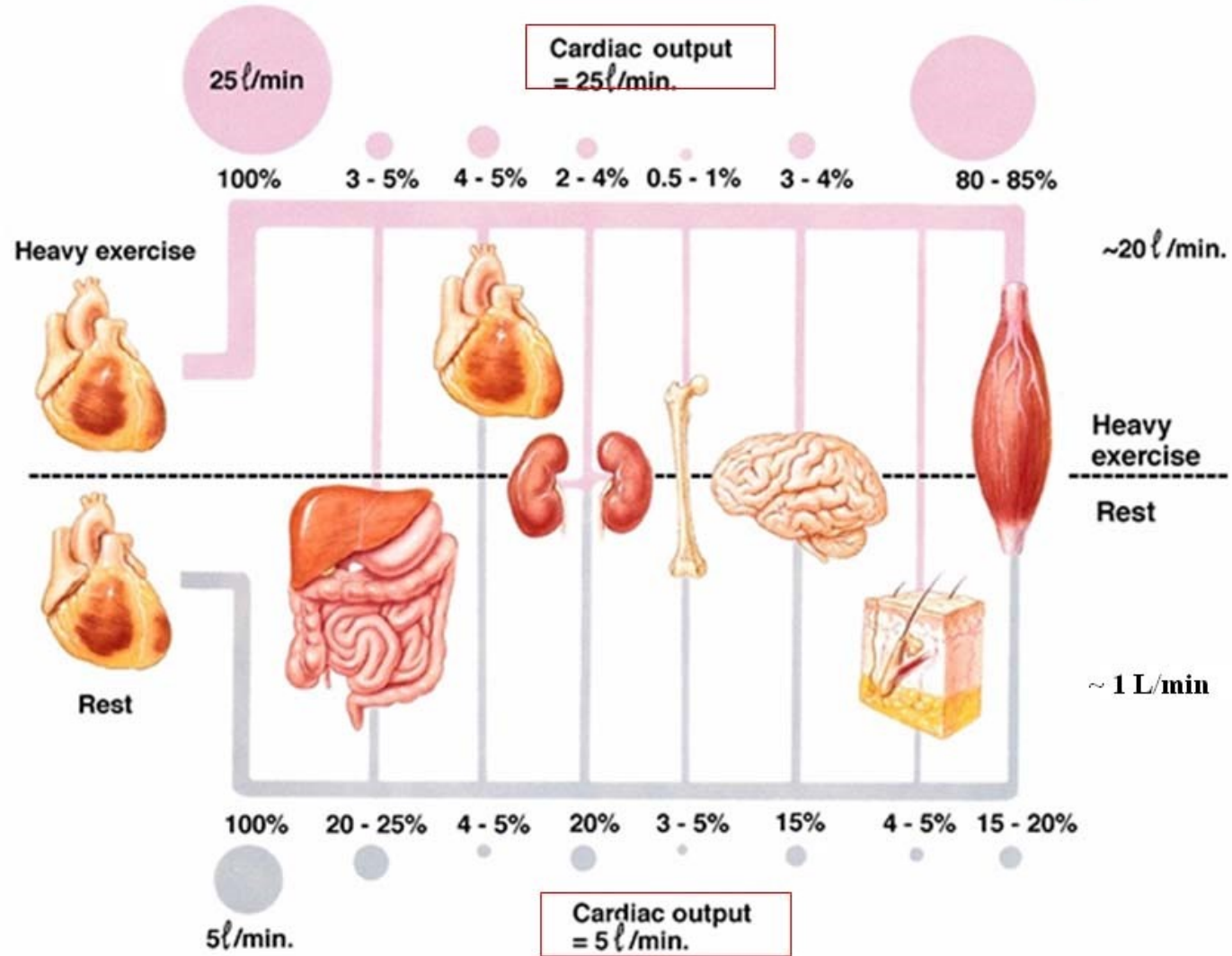


**Simple Feedback Loop**

# Redistribution of Blood Flow During Exercise



# Redistribution of Blood Flow During Exercise



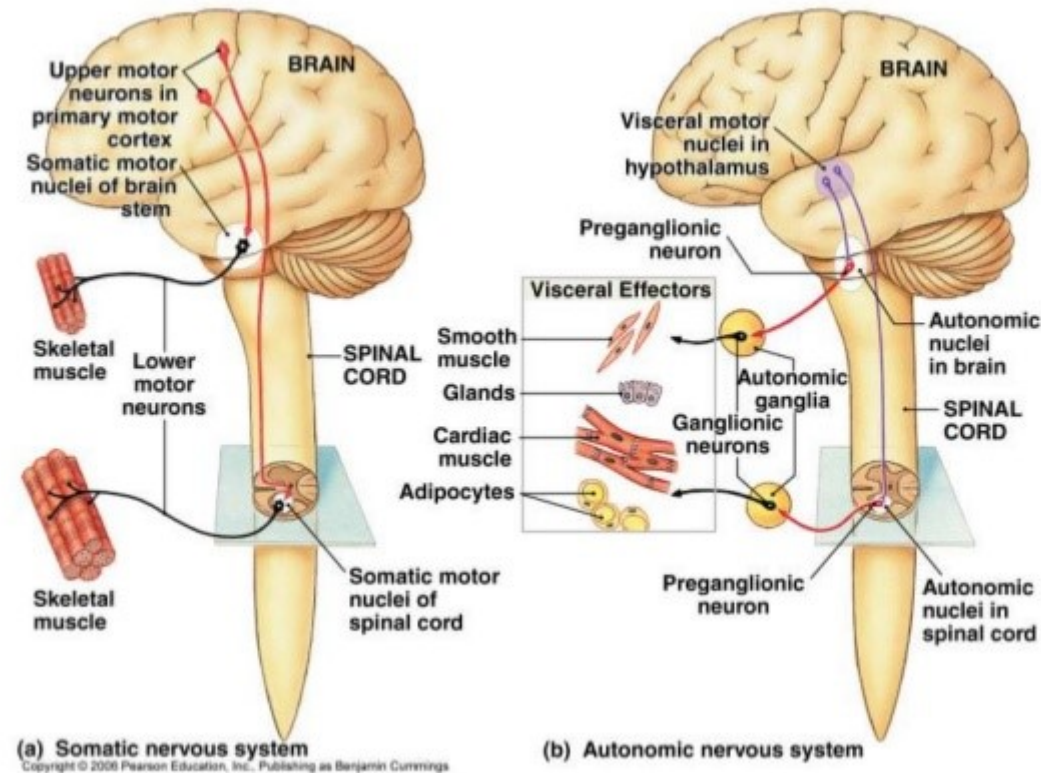
# Somatic a autonomic nervous system

➤ „Voluntary“

✓ Skeletal muscle

■ Direct connection between CNS and effector

## Somatic vs. Autonomic



➤ „Involuntary“

✓ Cardiomyocyte  
✓ Visceral muscle  
✓ Gland

■ Autonomic ganglion inserted between CNS and effector

# Somatic a autonomic nervous system

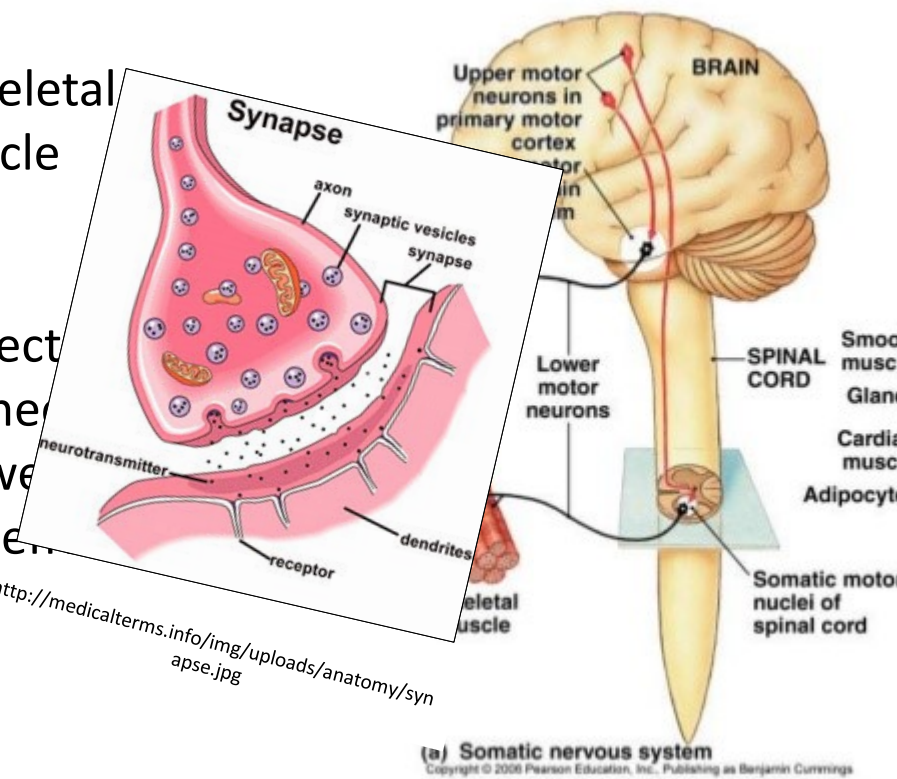
➤ „Voluntary“

## Somatic vs. Autonomic

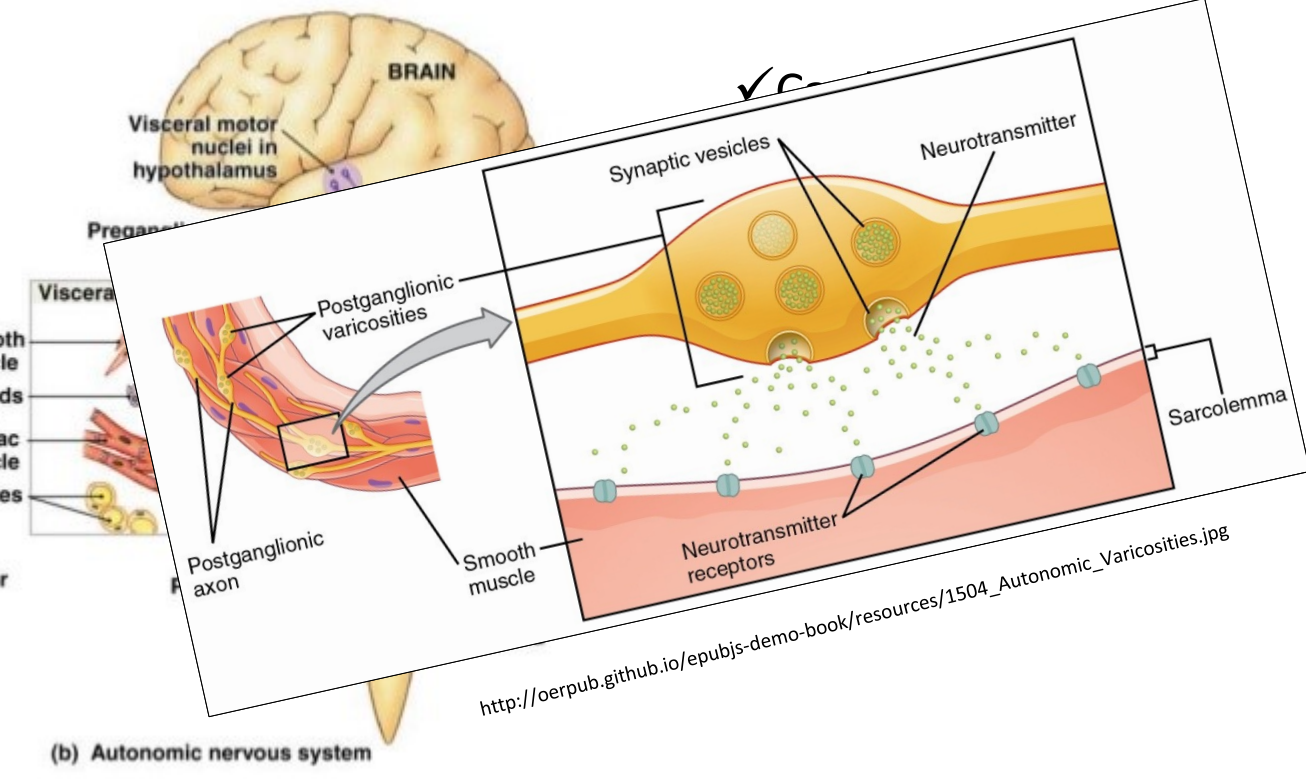
➤ „Involuntary“

✓ Skeletal muscle

▪ Direct connection between brain and effector



<http://medicalterms.info/img/uploads/anatomy/synapse.jpg>

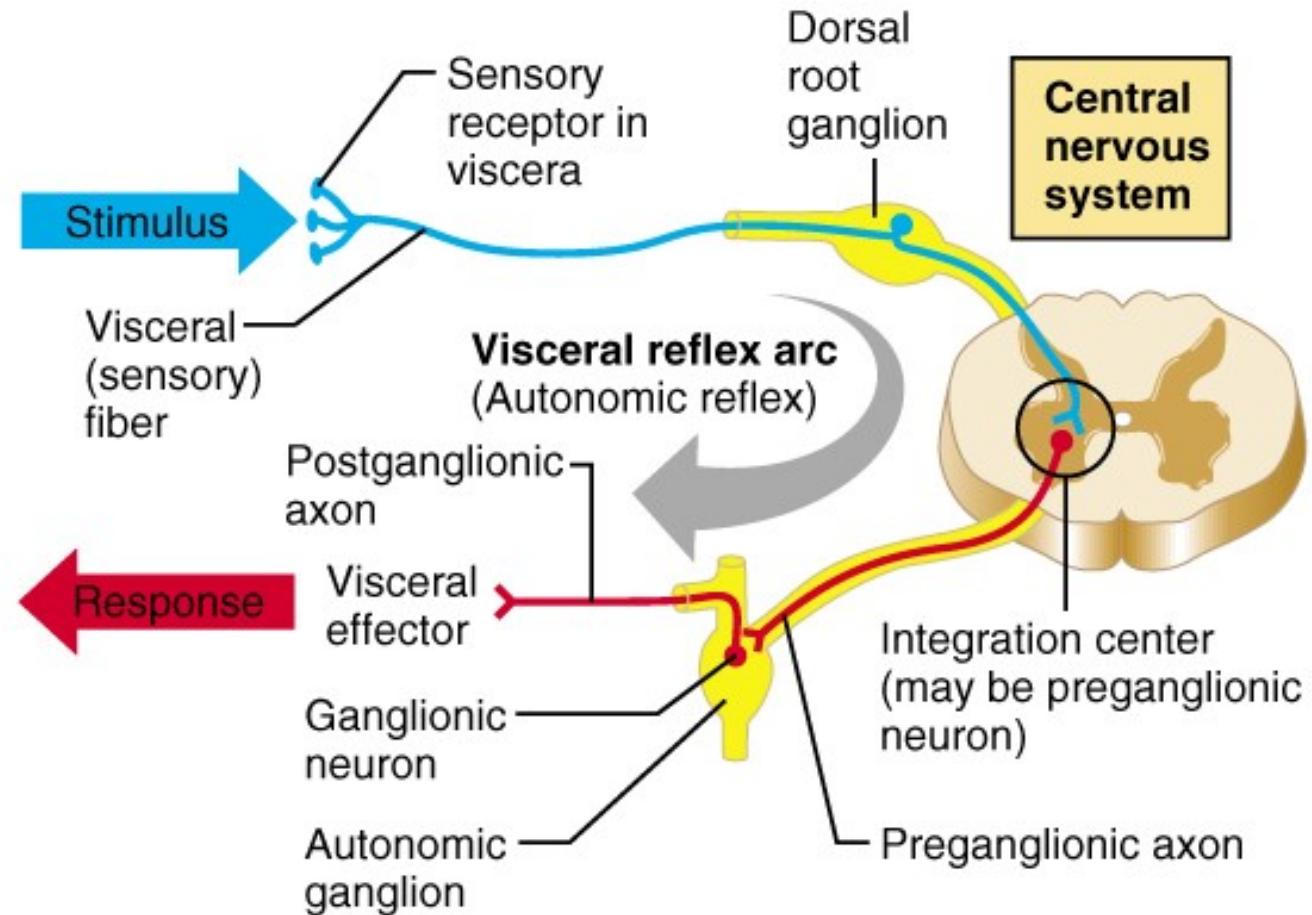


[http://oerpub.github.io/epubjs-demo-book/resources/1504\\_Autonomic\\_Varicosities.jpg](http://oerpub.github.io/epubjs-demo-book/resources/1504_Autonomic_Varicosities.jpg)

<http://image.slidesharecdn.com/ans-130217134747-phapp01/95/central-nervous-system-the-autonomic-nervous-system-7-638.jpg?cb=1361108947>

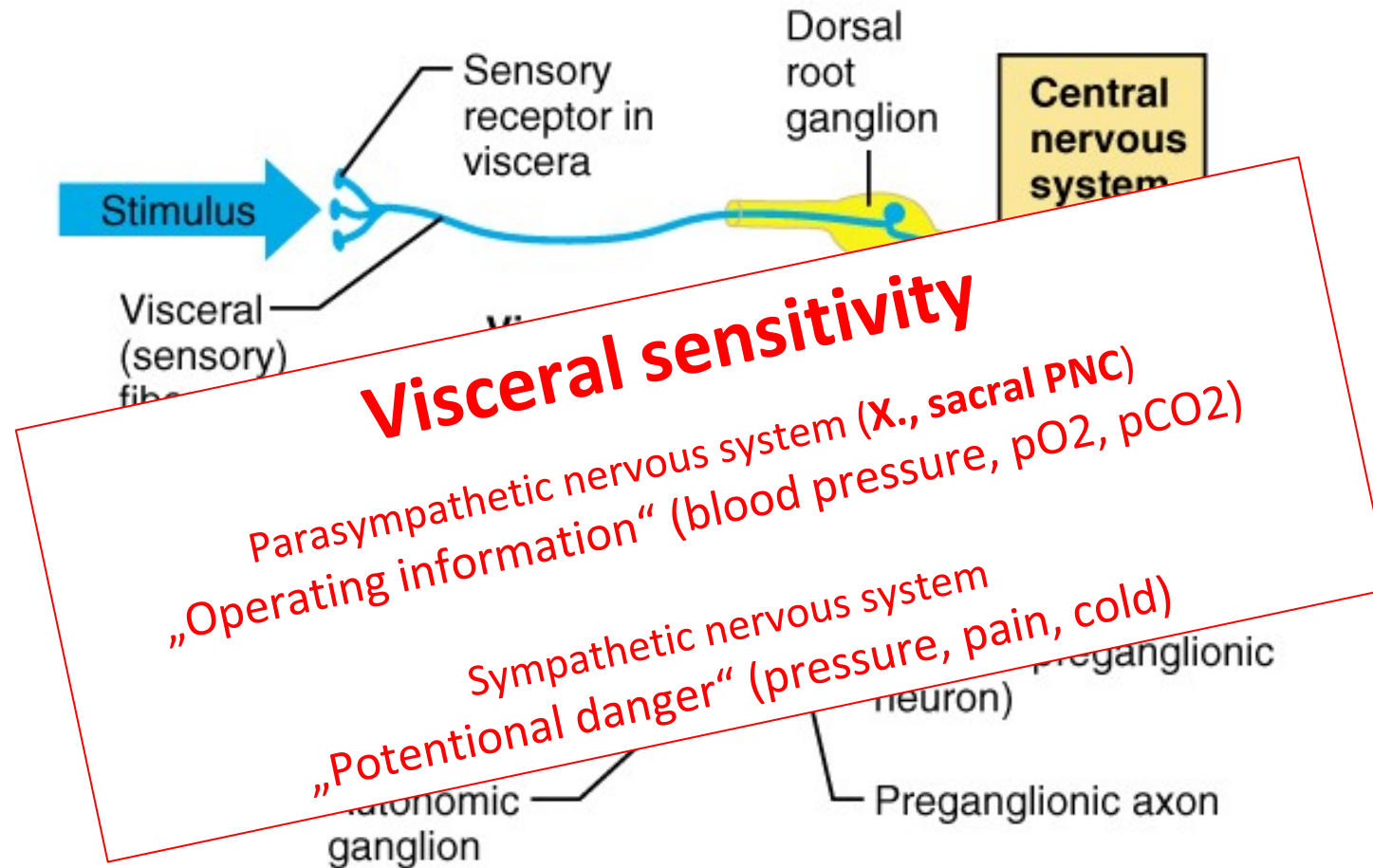


# Visceral reflex loop



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# Visceral reflex loop

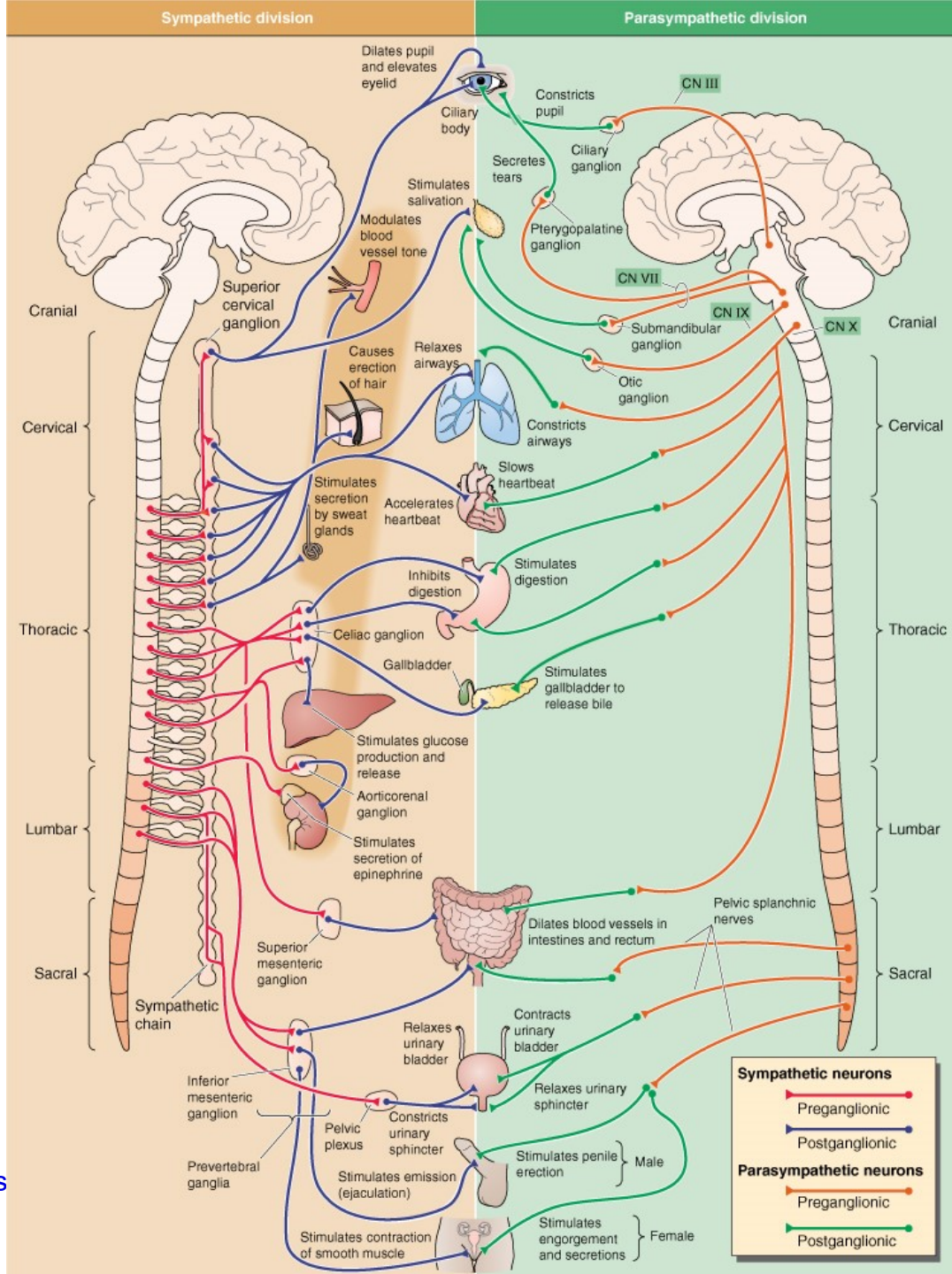


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# Sympathetic nervous system

Fight or flight response

Energy/store consumption



# Parasympathetic nervous system

Rest and digest response

Energy conservation/energy store production



# Sympathetic nervous system

Fight or flight response

Energy/store consumption

Preganglionic neuron

– Spinal cord

-Thoraco - lumbar system

Ganglia *Paravertebral*

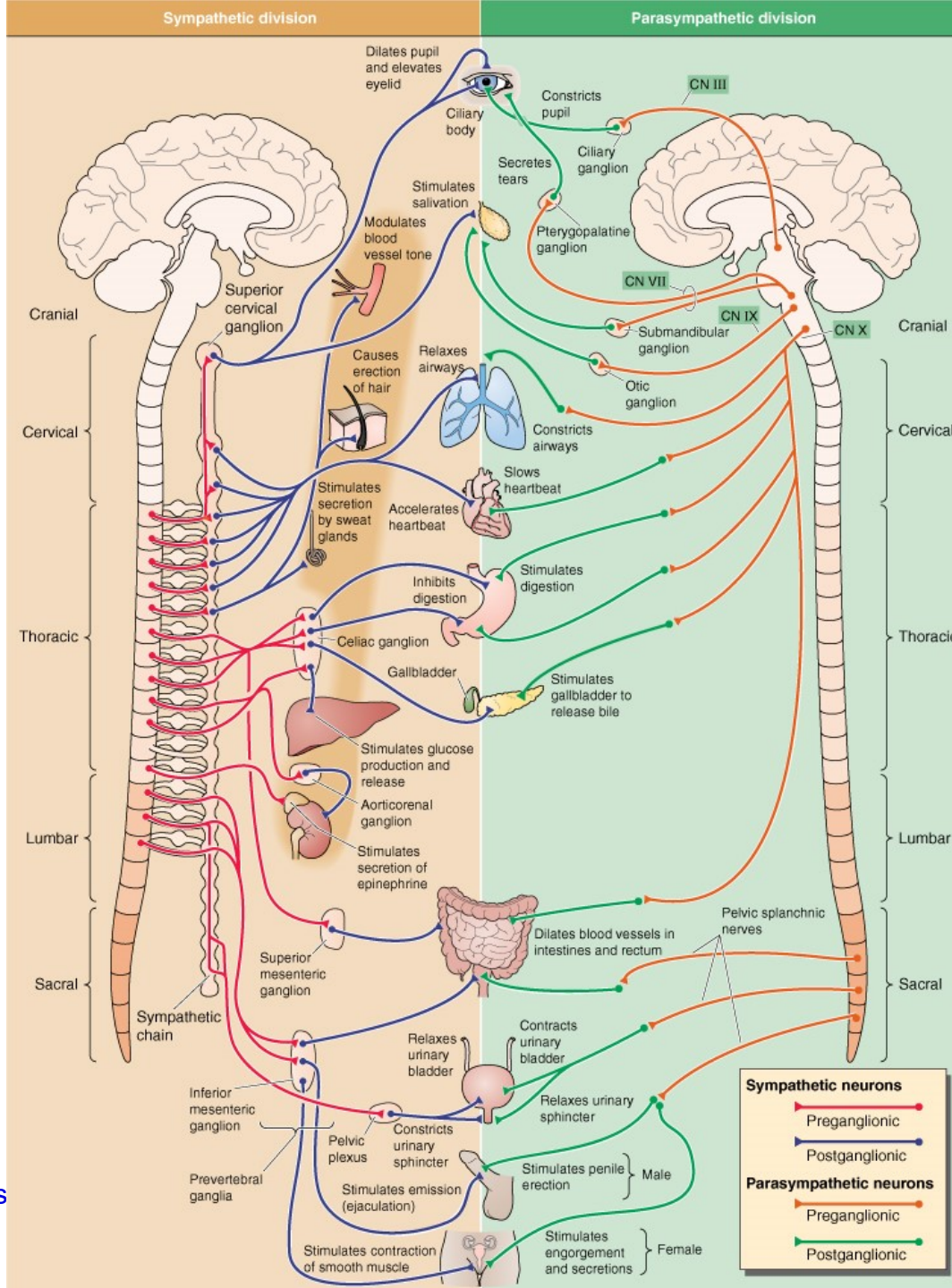
-Truncus sympathicus

- Majority

*Prevertebral*

-Plexus aorticus

Mostly diffuse effect



# Parasympathetic nervous system

Rest and digest response

Energy conservation/energy store production

Preganglionic neuron

– Brain stem and spinal cord

– cranio-sacral system

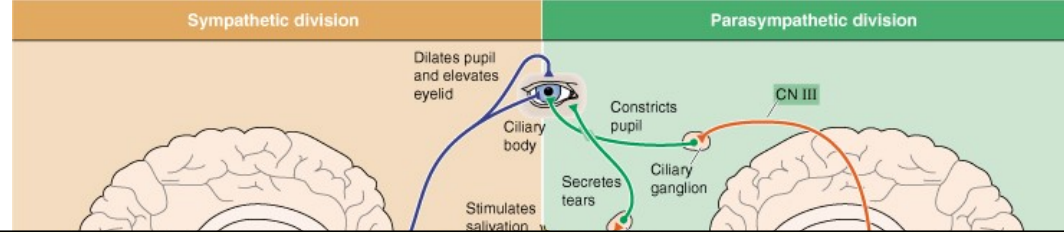
Ganglia

*Close to target organs or intramurally*

Mostly local effect

# Sympathetic nervous system

# Parasympathetic nervous system



System/function	Parasympathetic	Sympathetic
Cardiovascular	Decreased cardiac output and heart rate	Increased contraction and heart rate; increased cardiac output
Pulmonary	Bronchial constriction	Bronchial dilatation
Musculoskeletal	Muscular relaxation	Muscular contraction
Pupillary	Constriction	Dilatation
Urinary	Increased urinary output; sphincter relaxation	Decreased urinary output; sphincter contraction
Gastrointestinal	Increased motility of stomach and gastrointestinal tract; increased secretions	Decreased motility of stomach and gastrointestinal tract; decreased secretions
Glycogen to glucose conversion	No involvement	Increased
Adrenal gland	No involvement	Release epinephrine and norepinephrine

Fight or flight resp

Energy/store consum

Preganglionic neu

- Spinal cord

- Thoraco - lumbar sys

Ganglia *Paraverte*

- Truncus sympathic

- Majority

*Prevertebral*

- Plexus aorticus

Mostly diffuse ef

and digest response

conservation/energy store production

Preganglionic neuron

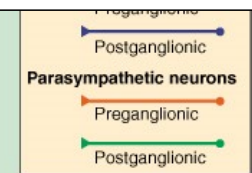
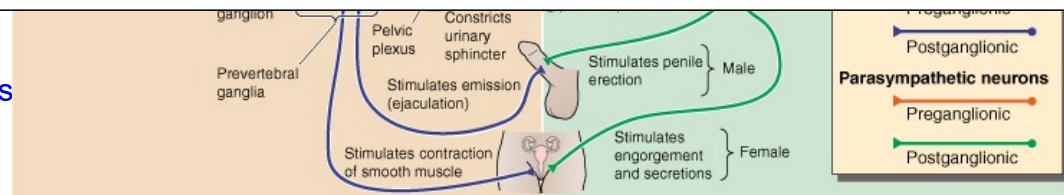
main stem and spinal cord

- cranio-sacral system

Ganglia

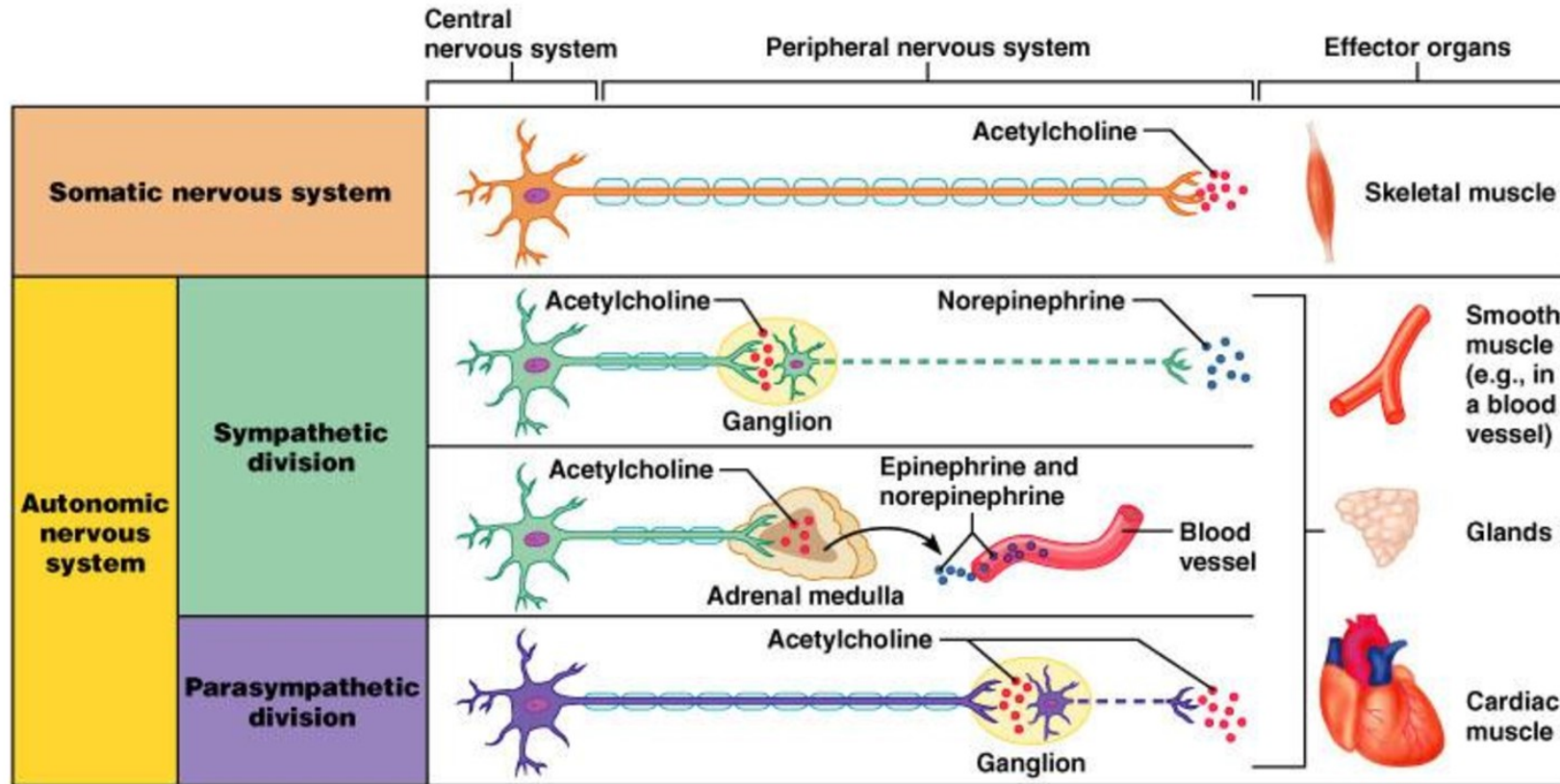
close to target organs or intramurally

Mostly local effect



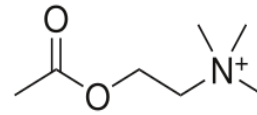


# Mediators of somatic and autonomic nervous system



**Key:**

— = Preganglionic axons (sympathetic)    
 - - - = Postganglionic axons (sympathetic)    
 = Myelination    
 — = Preganglionic axons (parasympathetic)    
 - - - = Postganglionic axons (parasympathetic)



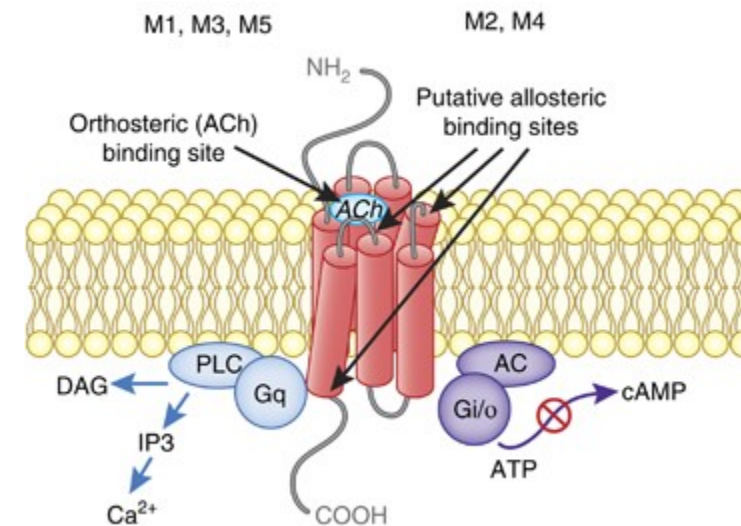
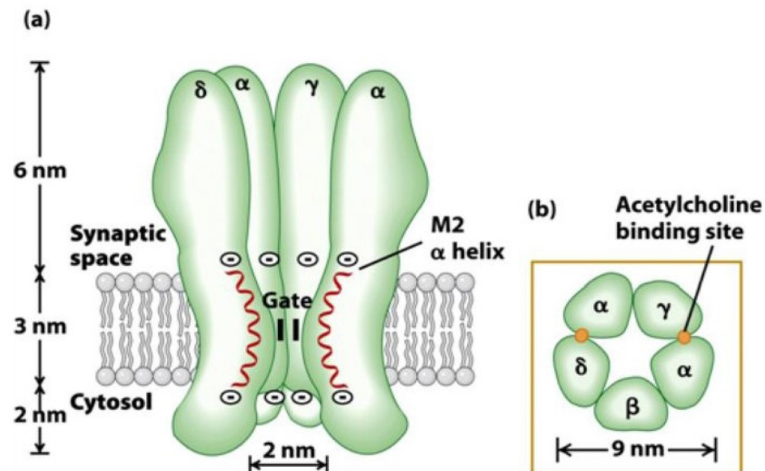
# Acetylcholine

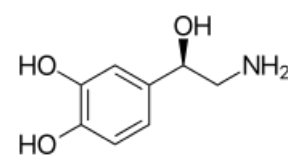
## Preganglionic fibers

- Sympathetic
- Parasympathetic
- ✓ Nicotinic receptor
  - Ligand-gated ion channels
  - Na<sup>+</sup>, K<sup>+</sup>, Ca<sup>2+</sup>
  - Neuronal (N<sub>N</sub>) and muscle (N<sub>M</sub>) type
  - Excitatory

## Postganglionic fibers

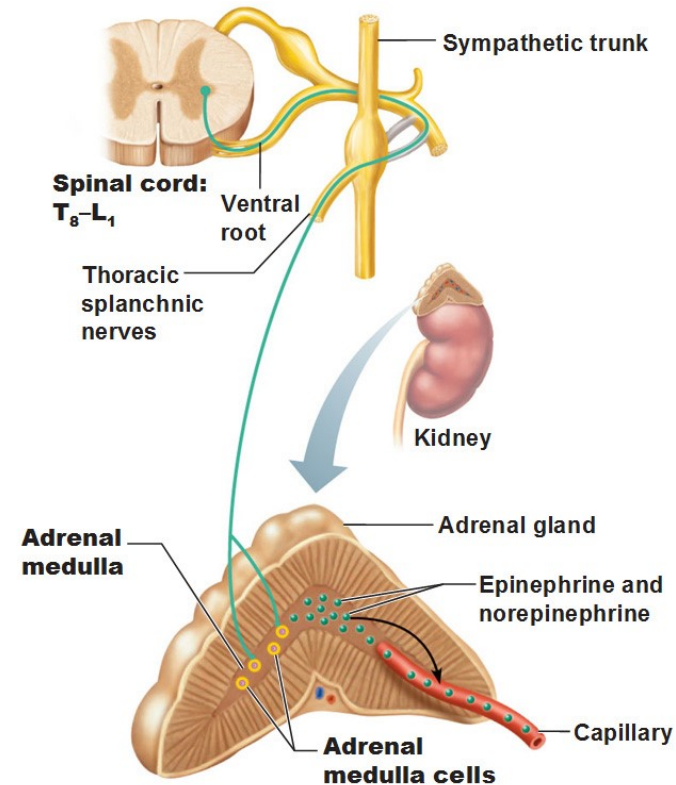
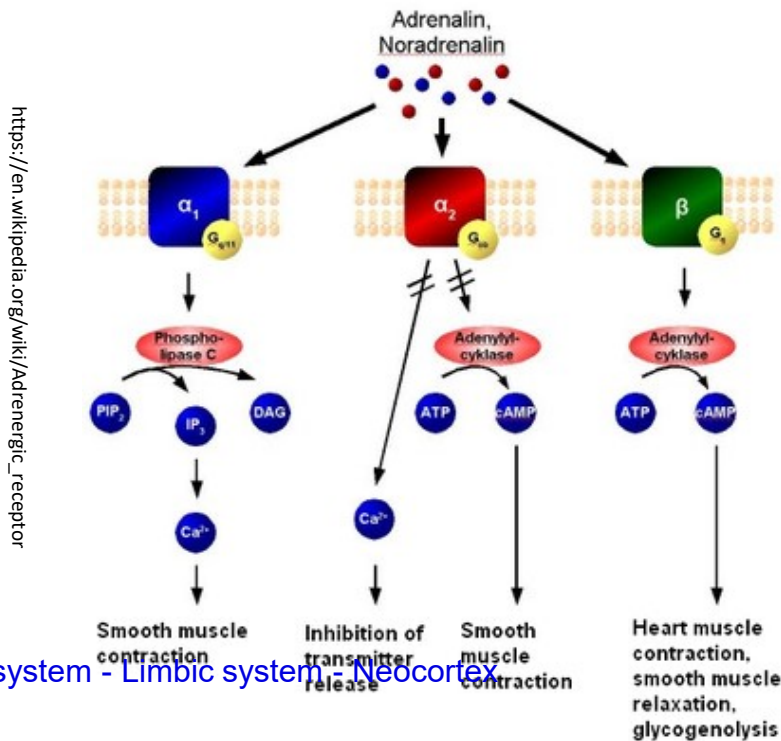
- Parasympathetic
- ✓ Muscarinic receptor
  - G-coupled
  - Excitatory
    - M1, M3, M5
  - Inhibitory
    - M2, M4



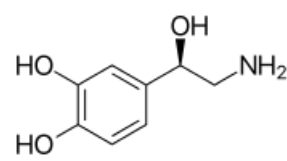


# Norepinephrine

- Postganglionic sympathetic fibers
- Adrenergic receptor
  - G-coupled
  - $\alpha$  type – generally excitatory (contraction) with an exception of GIT
  - $\beta$  type – generally inhibitory (relaxation) with an exception of !!! heart !!!
- Adrenal medulla
  - Modified sympathetic ganglion
  - „Transmitters“ (stress hormones) secreted into the blood stream
    - Norepinephrine
    - Epinephrine



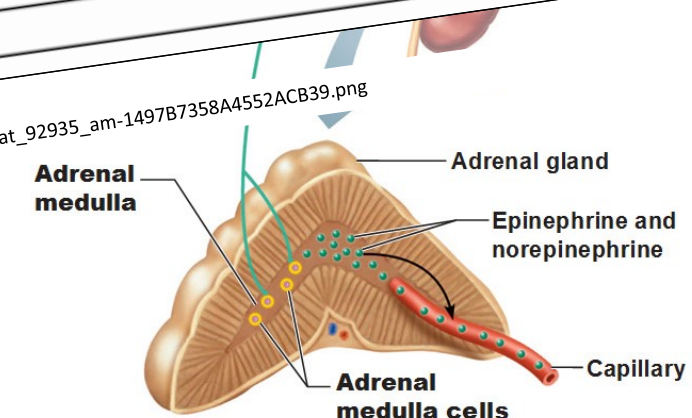
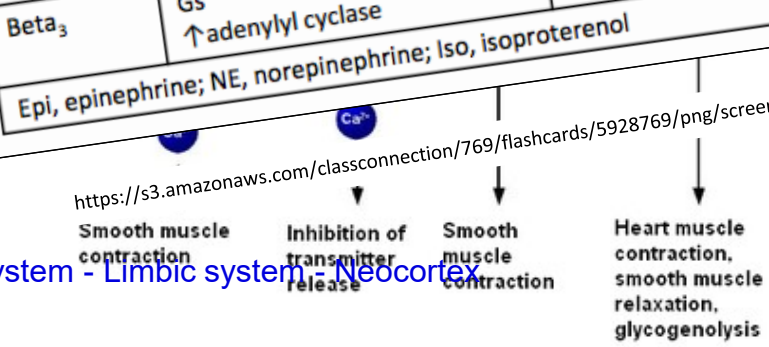
<http://antranik.org/wp-content/uploads/2011/11/the-adrenal-medulla-of-the-adrenal-gland-epinephrine-norepinephrine-splanchnic-nerves.jpg>



# Norepinephrine

- Postganglionic sympathetic fibers
- Adrenal medulla
- Adrenergic receptor
  - G-coupled

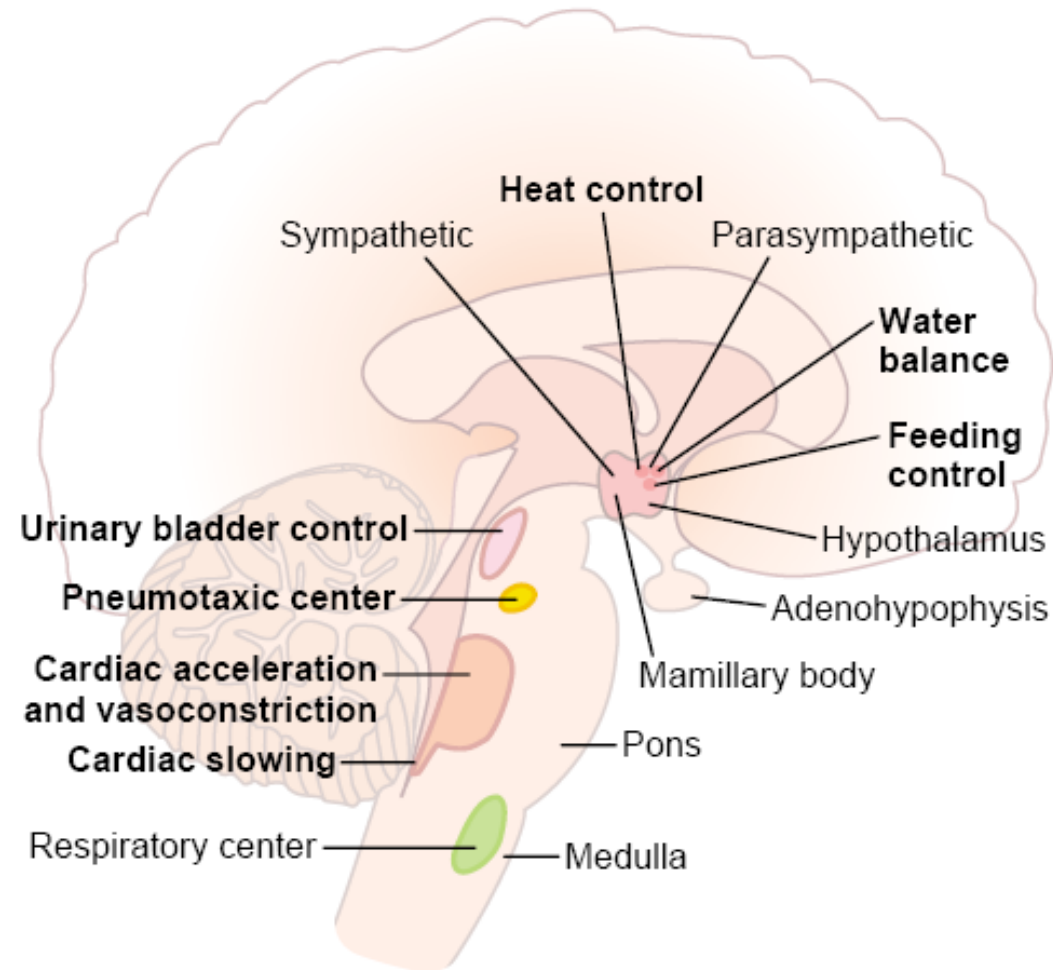
Receptor	G protein and effectors	Agonists	Tissue	Responses
Alpha <sub>1</sub>	Gq ↑phospholipase C, IP3 and DAG, intracellular Ca <sup>2+</sup>	Epi ≥ NE >> Iso Phenylephrine	Vascular, GU smooth muscle Liver Intestinal smooth muscle Heart	Contraction Glycogenolysis; gluconeogenesis Hyperpolarization and relaxation Increased contractile force; arrhythmias
Alpha <sub>2</sub>	Gi, Go ↓adenylyl cyclase ↓cAMP	Epi ≥ NE >> Iso Clonidine	Pancreatic islets (β cells) Platelets Nerve terminals Vascular smooth muscle	Decreased insulin secretion Aggregation Decreased release of NE Contraction
Beta <sub>1</sub>	Gs ↑adenylyl cyclase, cAMP, L- type Ca <sup>2+</sup> channel opening	Iso > Epi = NE Dobutamine	Juxtaglomerular cells Heart	Increased renin secretion Increased force and rate of contraction and AV nodal conduction velocity
Beta <sub>2</sub>	Gs ↑adenylyl cyclase	Iso > Epi >> NE Terbutamine	Smooth muscle (vascular, bronchial, GI, GU) Skeletal muscle	Relaxation Glycogenolysis; uptake of K <sup>+</sup>
Beta <sub>3</sub>	Gs ↑adenylyl cyclase	Iso = NE > Epi	Adipose tissue	Lipolysis



http://antranik.org/wp-content/uploads/2014/11/medulla-of-the-adrenal-gland-epinephrine-norepinephrine-splanchnic-nerves.jpg

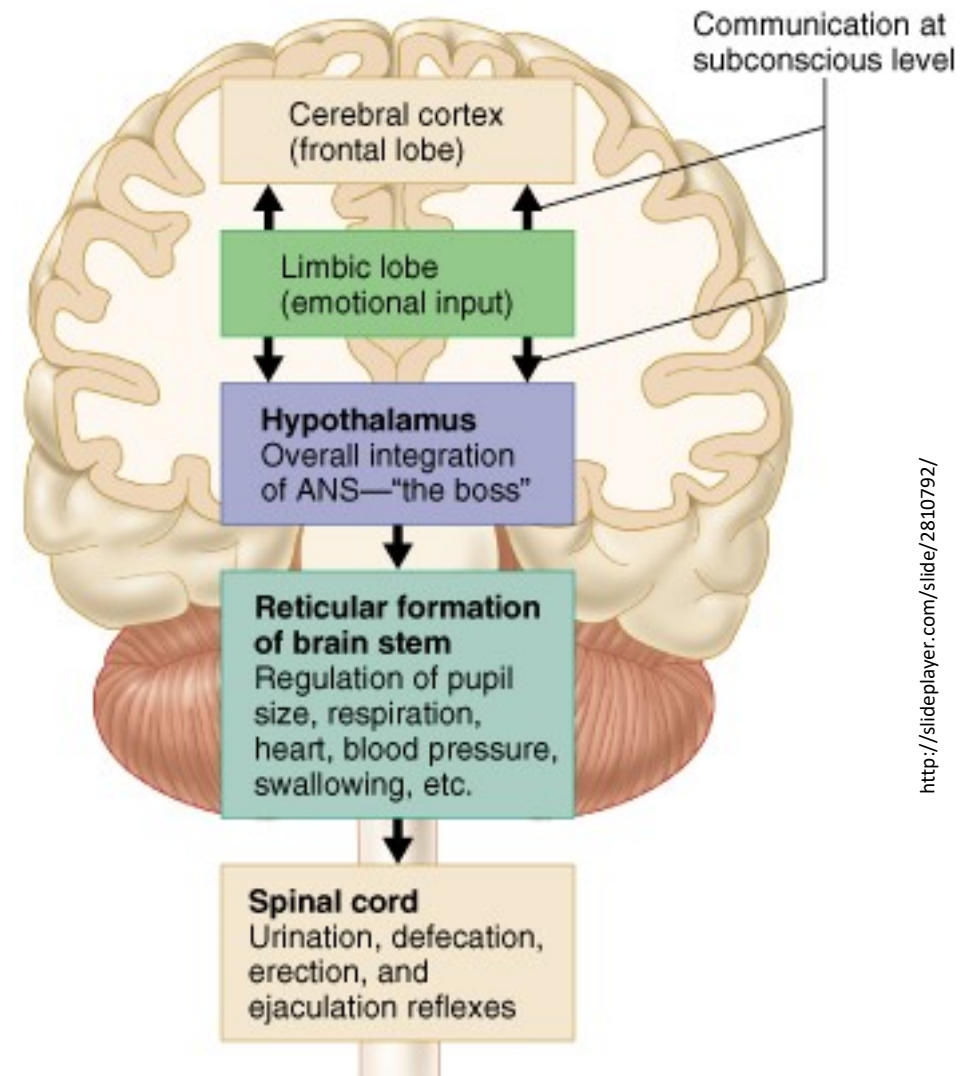


# Brain centers controlling autonomic nervous system



# Brain centers controlling autonomic nervous system

- Most of the regulations are unconscious and originate from the hypothalamus
- Strong emotional experiences or strong emotional memories can trigger autonomic response (usually sympathetic)





# Hypothalamus

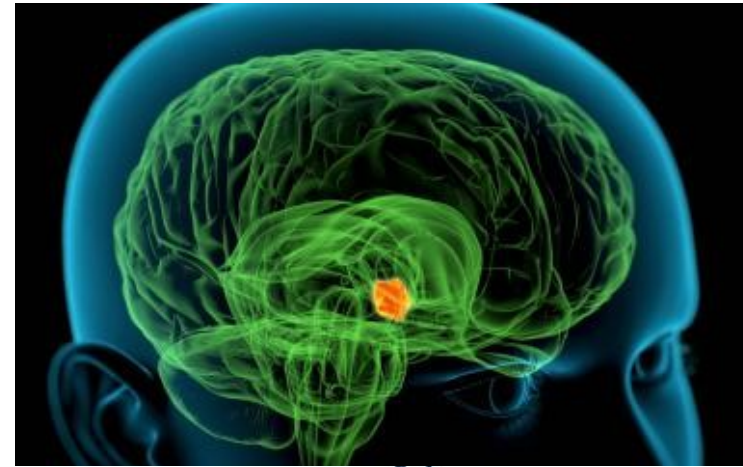
- Key center of autonomic regulations and coordination
- Integration of the information from inner and outer environment



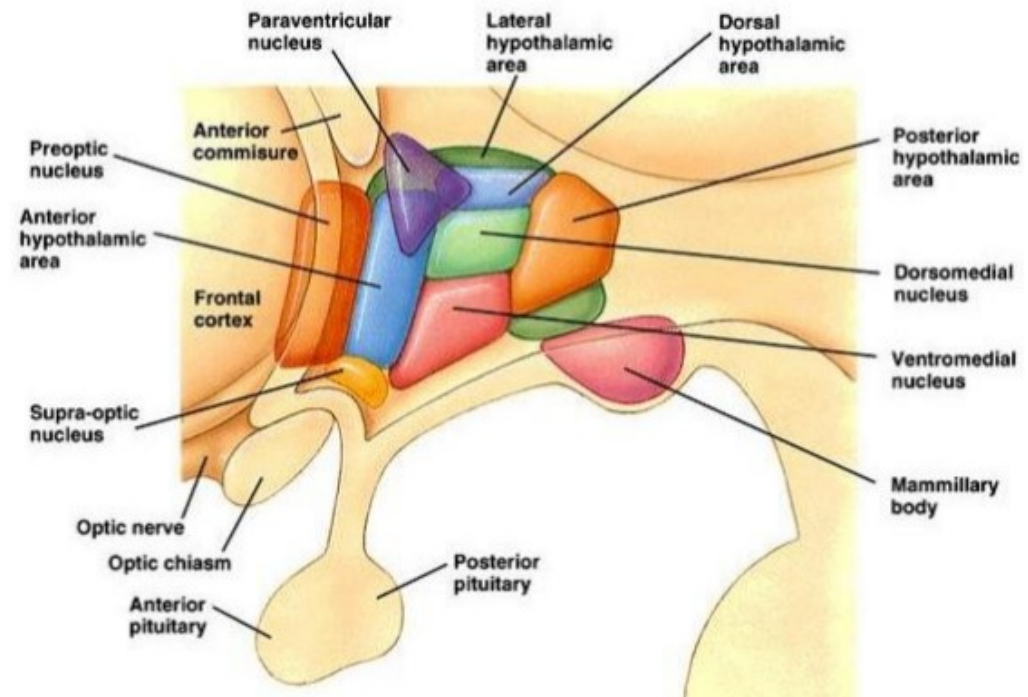
- Behavioral modulation
- Regulation of autonomic nervous system



- **Maintenance of homeostasis**



<http://biology.about.com/od/anatomy/pl/Hypothalamus.htm>



<http://www.slideshare.net/physiologymgmcri/hypothalamus-15-apr-2016>

# Hypothalamus

- Key center of autonomic regulations and coordination
- Integration of the information from inner and outer environment

✓ **Biological clock – circadian /seasonal activity**

✓ **Autonomic nervous system regulation**

✓ **Endocrine system regulation**

✓ **Food and water intake regulation**

✓ **Regulation of body temperature**

✓ **„Immediate“ behavior regulation (e.g. when hunger)**

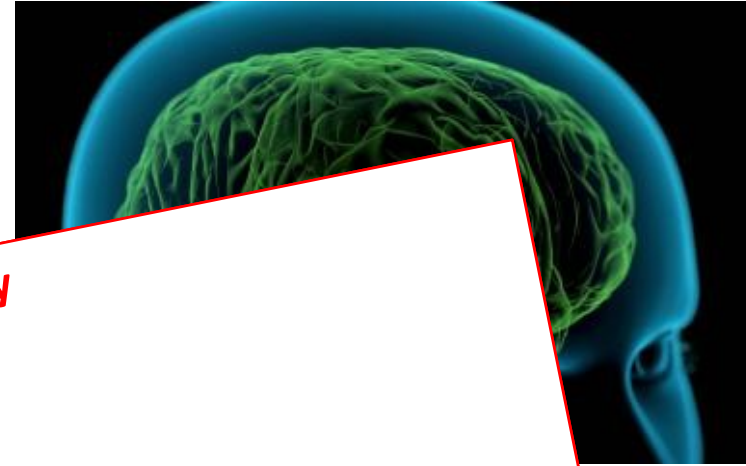
✓ **„Long-term“ behavior regulation (e.g. maternal beh.)**

✓ **Instinctive behavior regulation (e.g. sexuality)**

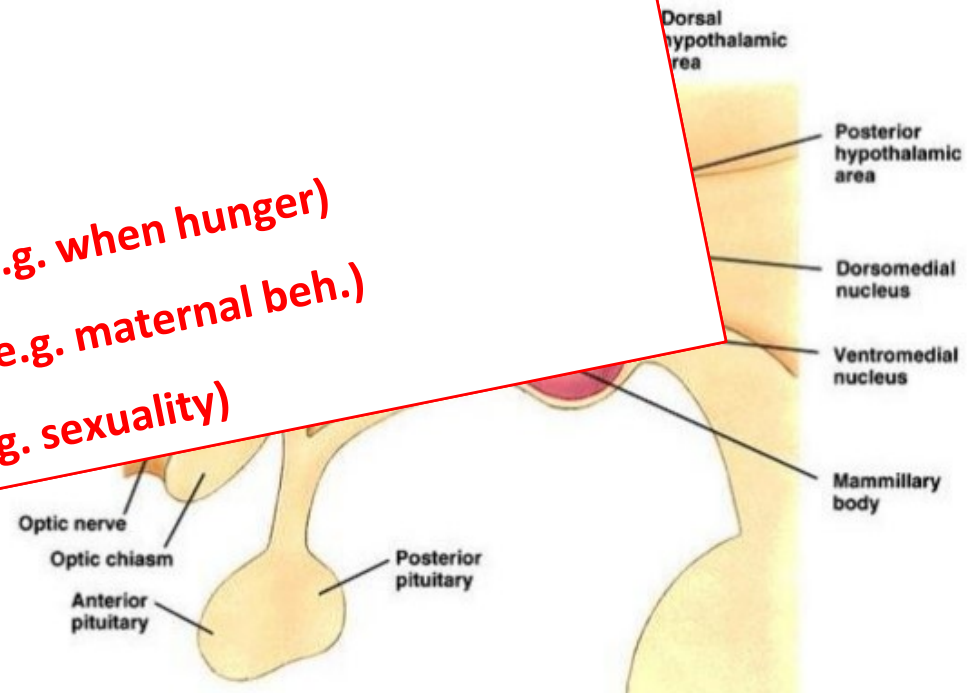
• Behavior

• Regulation of nervous system

• Maintenance of homeostasis

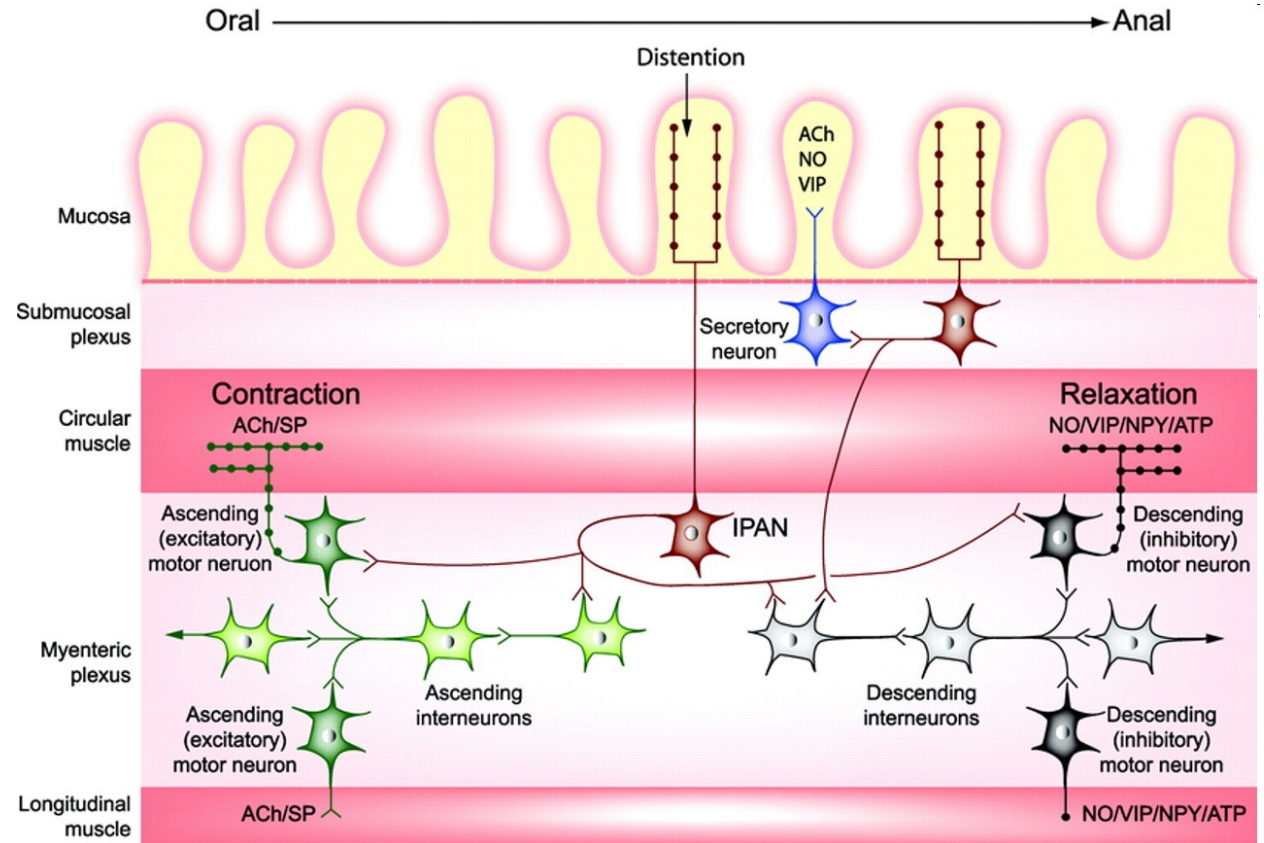


<http://biology.about.com/od/anatomy/pl/Hypothalamus.htm>



# Enteric nervous system

- aprox. 500 mil. neurons
  - (brain aprox. 100 bil.)
  - (spinal cord aprox. 100 mil.)
- Plexus myentericus
- Plexus submucosus
- Sensory component
- Executive component
- Interneurons
- High level of autonomy
  - „brain in the gut“



[http://www.slideshare.net/carmencrivii/central-nervous-system-the-autonomic-nervous-system?qid=d1502190-93fe-4b05-9d92-6a42e3ca72fc&v=&b=&from\\_search=8](http://www.slideshare.net/carmencrivii/central-nervous-system-the-autonomic-nervous-system?qid=d1502190-93fe-4b05-9d92-6a42e3ca72fc&v=&b=&from_search=8)

# Enteric nervous system

- Autonomy
  - Control of motility
  - Control of secretion
  - Control of blood flow
- Autonomic nervous system
  - Whole GIT regulation
  - Coordination of all organ systems activities

## The Brain in Your Gut

The gut's brain, known as the enteric nervous system, is located in sheaths of tissue lining the esophagus, stomach, small intestine and colon.

### SMALL INTESTINE CROSS SECTION

#### Submucosal plexus

Layer contains sensory cells that communicate with the myenteric plexus and motor fibers that stimulate the secretion of fluids into the lumen.

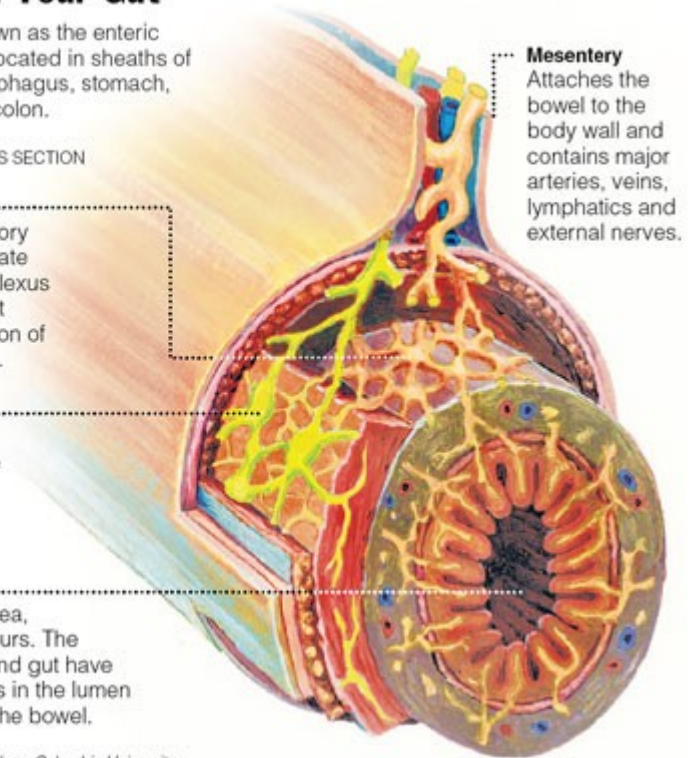
#### Myenteric plexus

Layer contains the neurons responsible for regulating the enzyme output of adjacent organs.

#### Lumen

No nerves actually enter this area, where digestion occurs. The brains in the head and gut have to monitor conditions in the lumen across the lining of the bowel.

Source: Dr. Michael D. Gershon, Columbia University

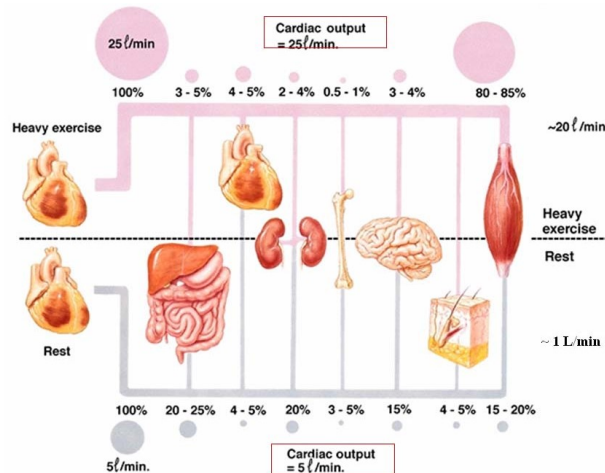


<https://kin450-neurophysiology.wikispaces.com/file/view/gut.jpg/187924395/gut.jpg>



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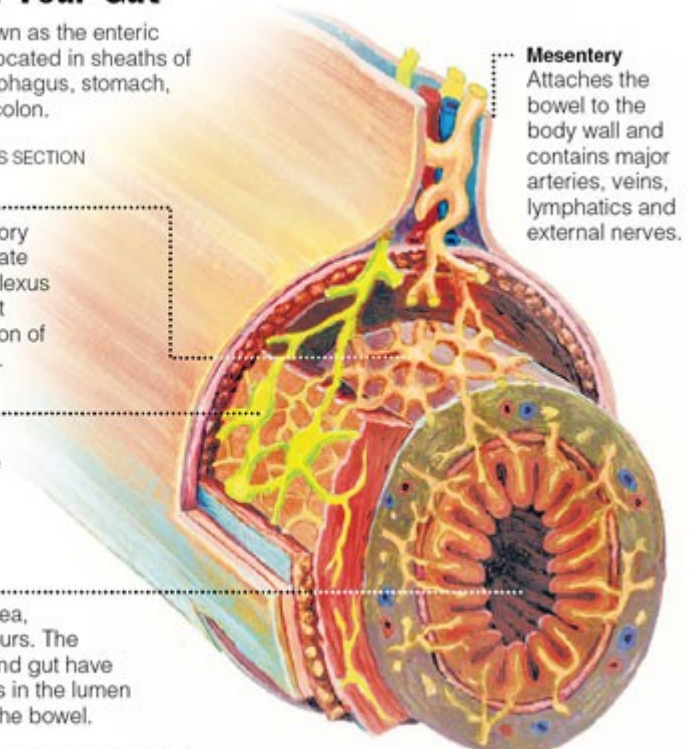
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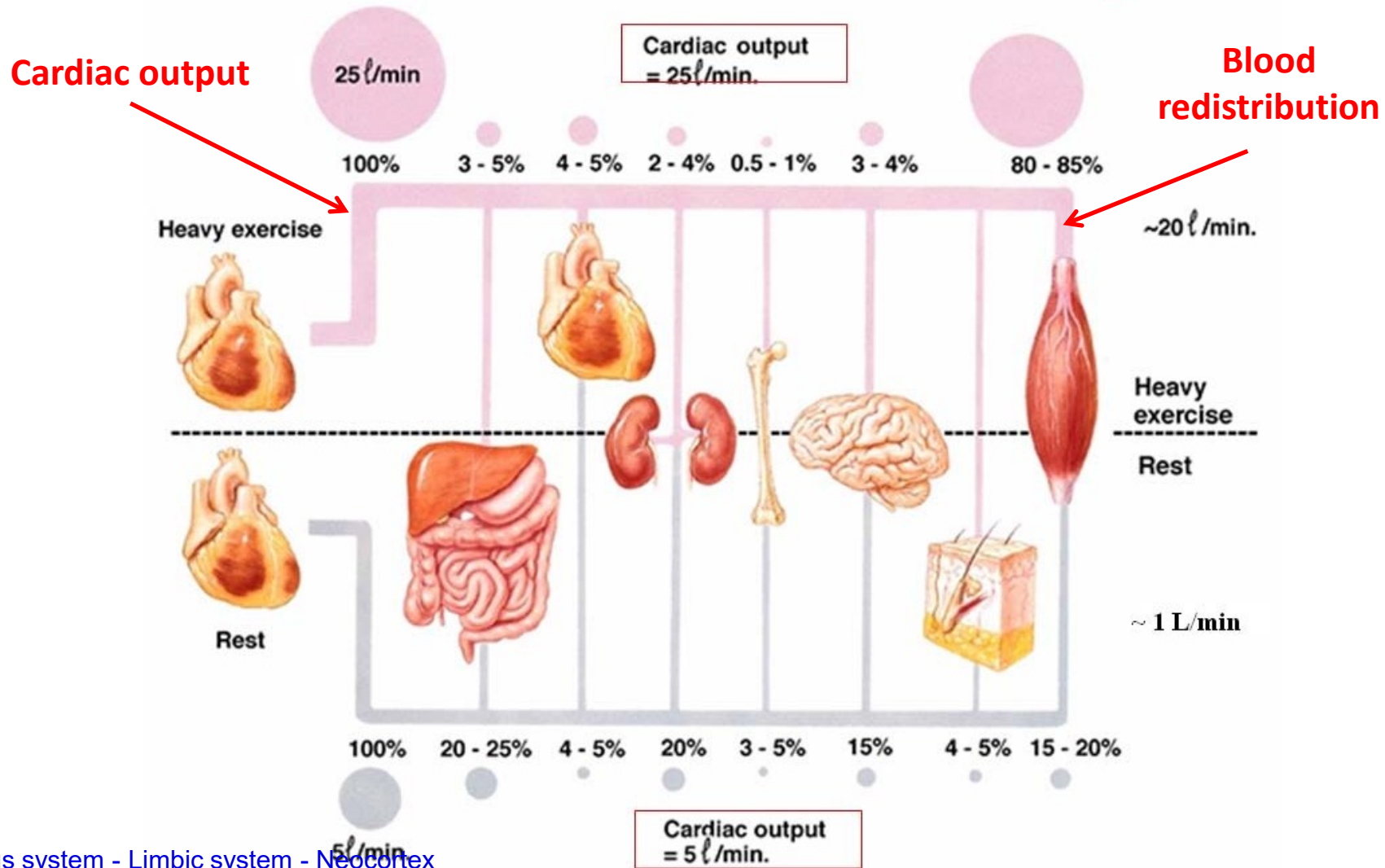
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<https://kin450-neurophysiology.wikispaces.com/file/view/gut.jpg/187924395/gut.jpg>

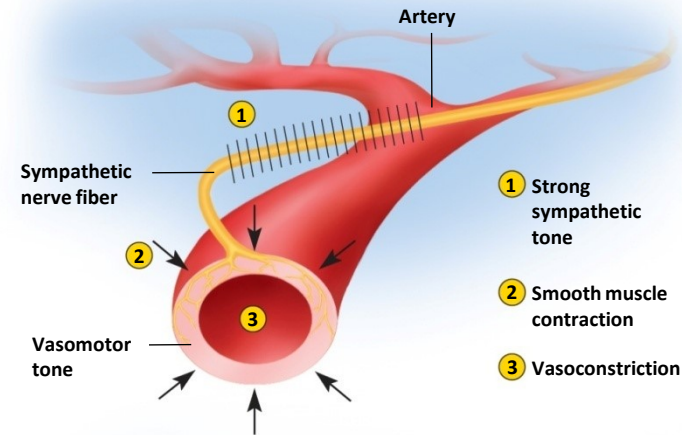
# ANS and cardiovascular system



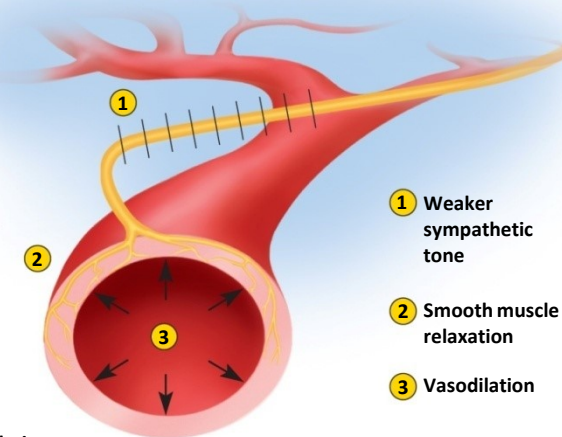
# ANS and cardiovascular system

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- Local regulatory mechanisms play major role in vasoreactivity
- Sympathetic regulation
  - Skin vessels contraction
  - Muscle vessels dilatation
- Parasympathetic regulation
  - GIT vessels dilation



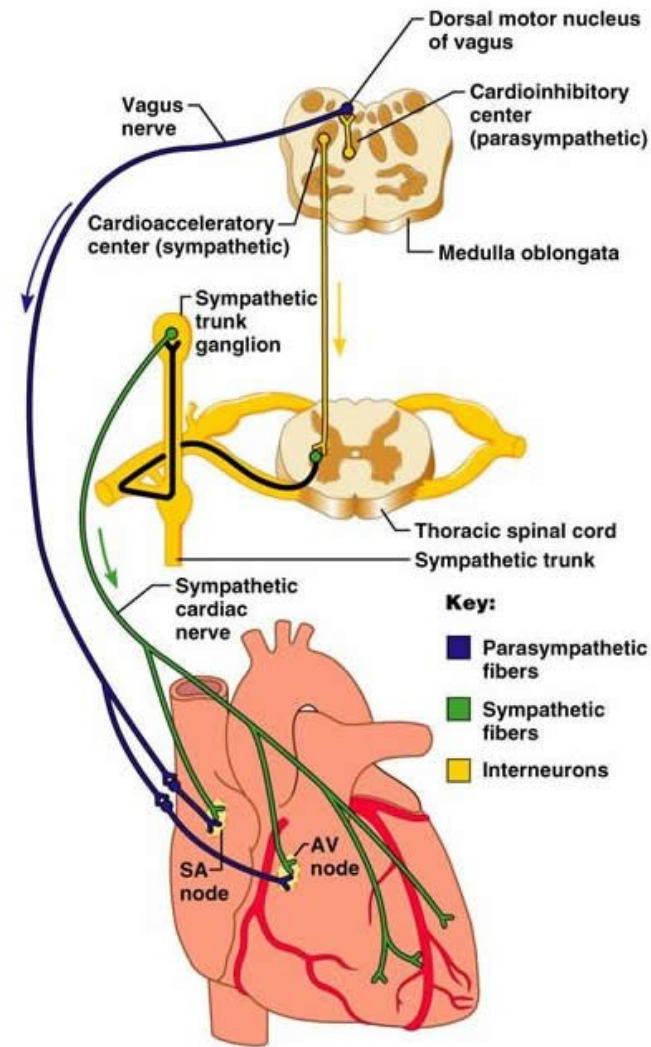
(a) Vasoconstriction



(b) Vasodilation

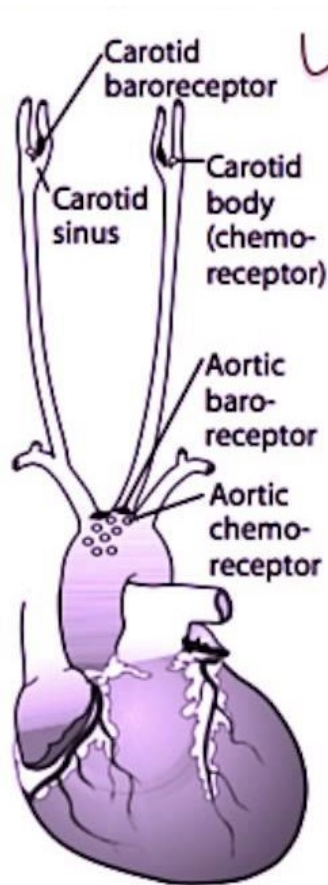
# ANS and cardiovascular system

- Sympathetic regulation
  - Heart rate increase
  - Contractility increase
  - Conductivity increase
- Parasympathetic regulation
  - Heart rate decrease
  - Contractility decrease
  - Conductivity decrease





# Baroreceptors a chemoreceptors



## Receptors:

1. Aortic arch transmits via vagus nerve to medulla (responds **only** to  $\uparrow$  BP)
2. Carotid sinus transmits via glossopharyngeal nerve to solitary nucleus of medulla (responds to  $\downarrow$  and  $\uparrow$  in BP).

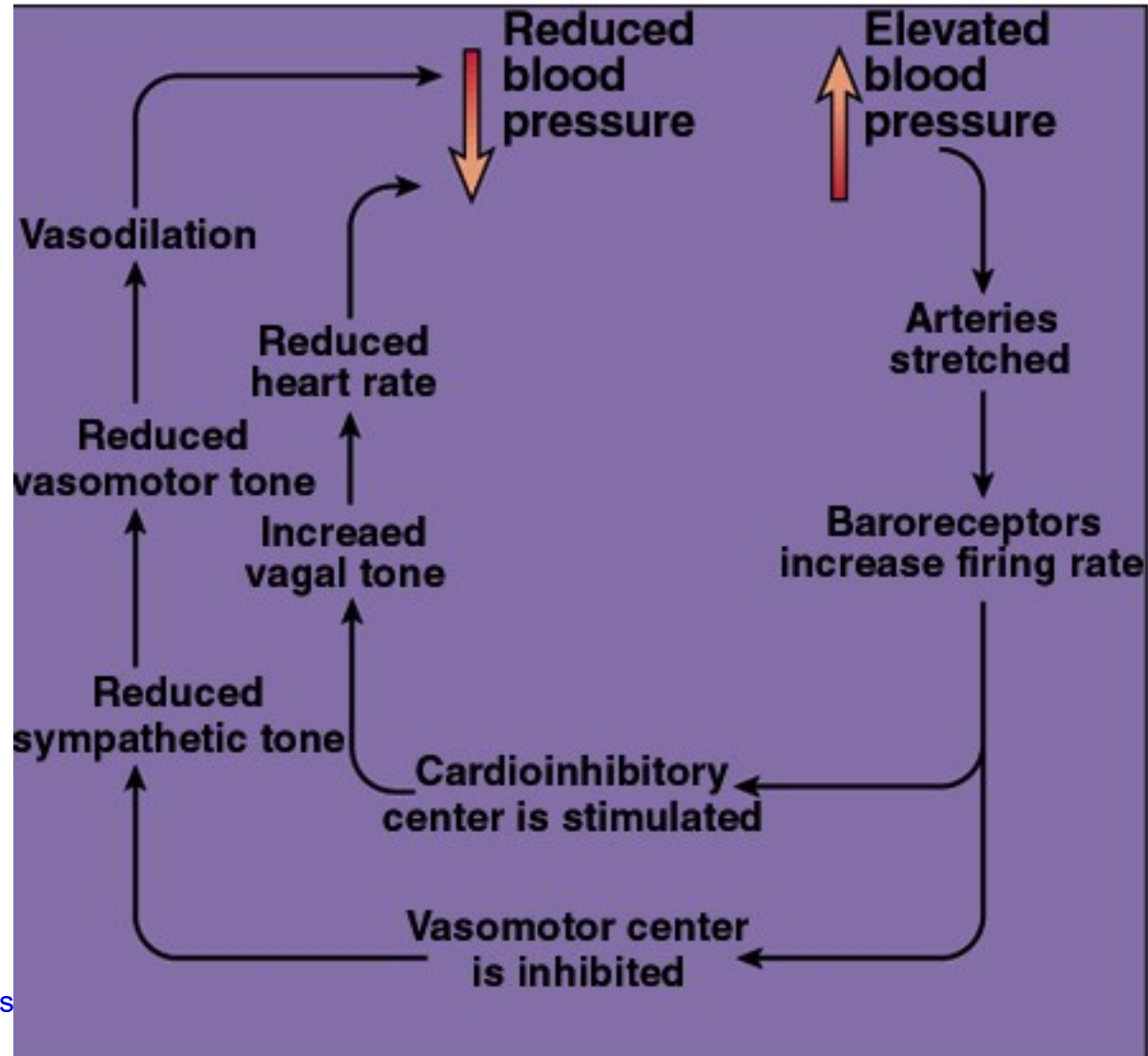
## Baroreceptors:

1. Hypotension —  $\downarrow$  arterial pressure  $\rightarrow$   $\downarrow$  stretch  $\rightarrow$   $\downarrow$  afferent baroreceptor firing  $\rightarrow$   $\uparrow$  efferent sympathetic firing and  $\downarrow$  efferent parasympathetic stimulation  $\rightarrow$  vasoconstriction,  $\uparrow$  HR,  $\uparrow$  contractility,  $\uparrow$  BP. Important in the response to severe hemorrhage.
2. Carotid massage —  $\uparrow$  pressure on carotid artery  $\rightarrow$   $\uparrow$  stretch  $\rightarrow$   $\uparrow$  afferent baroreceptor firing  $\rightarrow$   $\downarrow$  HR.

## Chemoreceptors:

1. Peripheral — carotid and aortic bodies respond to  $\downarrow$   $PO_2$  ( $< 60$  mmHg),  $\uparrow$   $PCO_2$ , and  $\downarrow$  pH of blood.
2. Central — respond to changes in pH and  $PCO_2$  of brain interstitial fluid, which in turn are influenced by arterial  $CO_2$ . Do not directly respond to  $PO_2$ . Responsible for Cushing reaction —  $\uparrow$  intracranial pressure constricts arterioles  $\rightarrow$  cerebral ischemia  $\rightarrow$  hypertension (sympathetic response)  $\rightarrow$  reflex bradycardia. Note: Cushing triad = hypertension, bradycardia, respiratory depression.

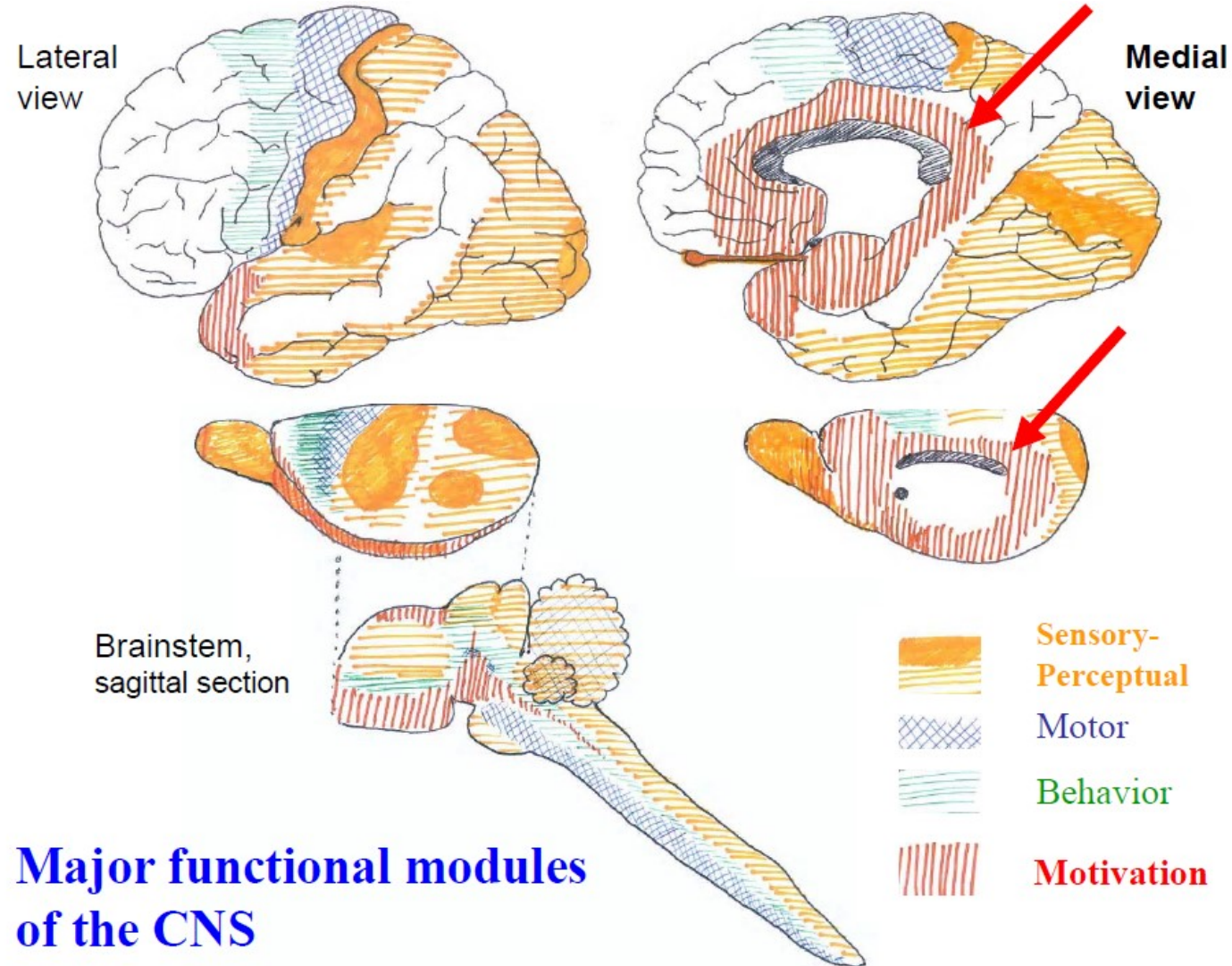
# Baroreflex



# **Limbic system**

# Limbic system

Limbus = border



## Major functional modules of the CNS



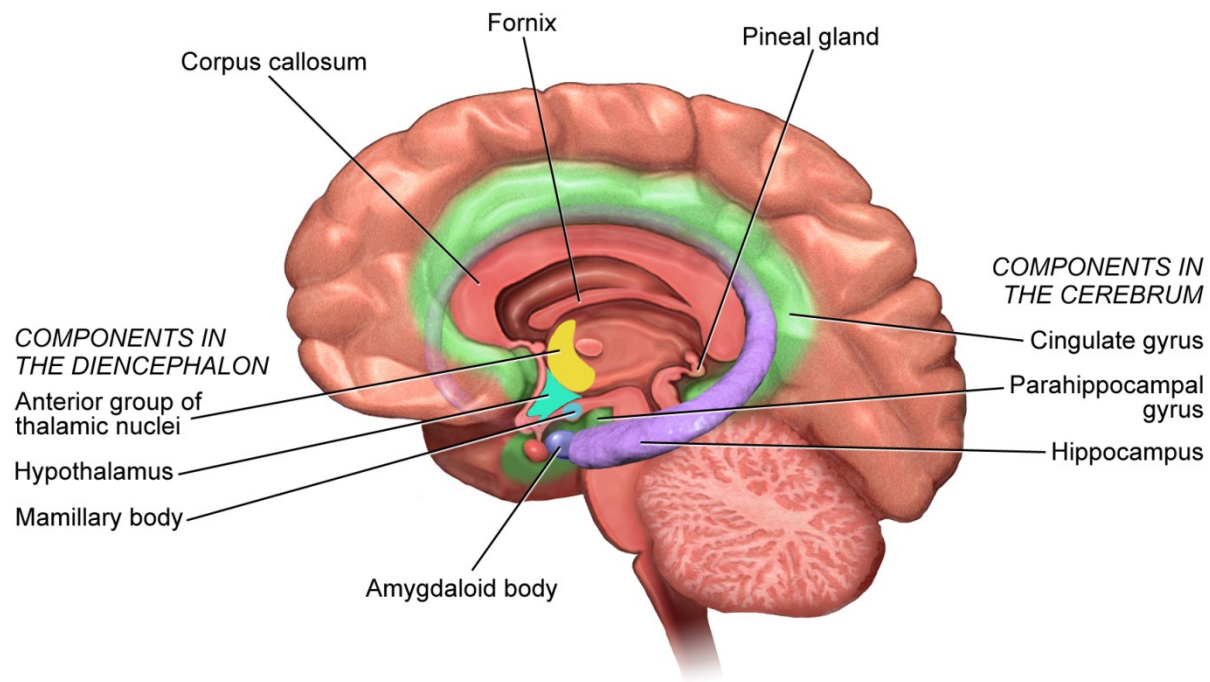
# Concept of the limbic system

- Voluntary

Somatic nervous system  
Inputs – mainly from outer environment  
Control – skeletal muscle

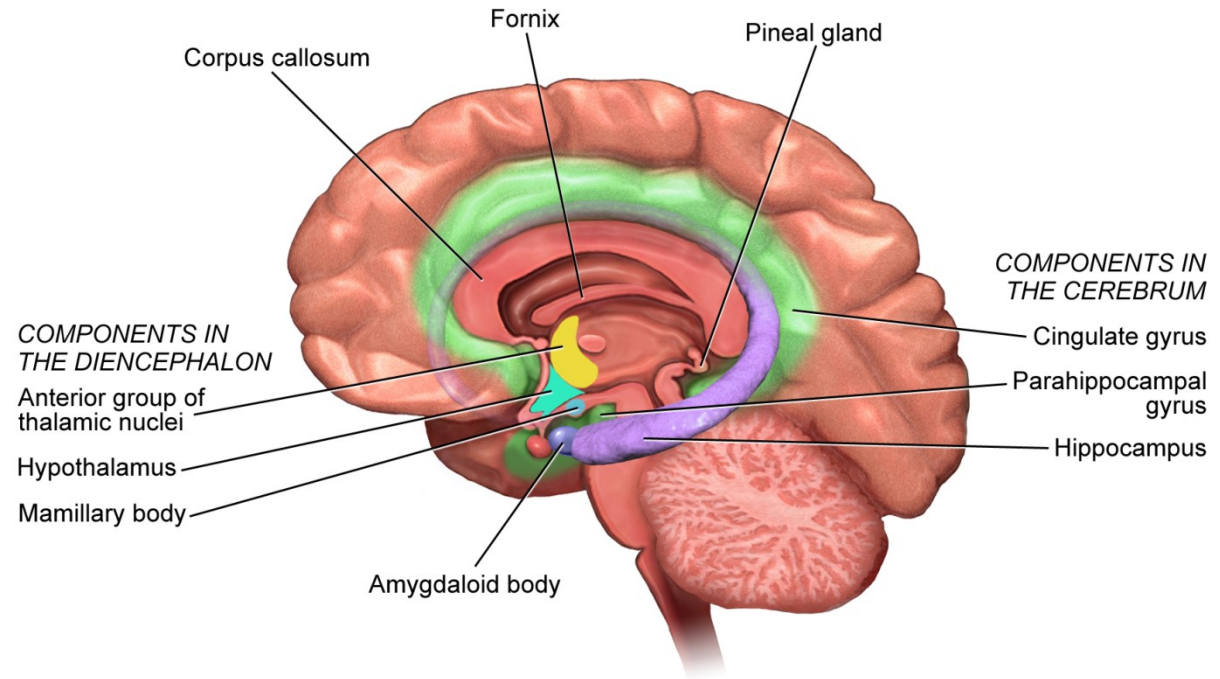
- Automatic

Autonomic nervous system  
Inputs – mainly inner environment  
Control – smooth/cardiac m., glands

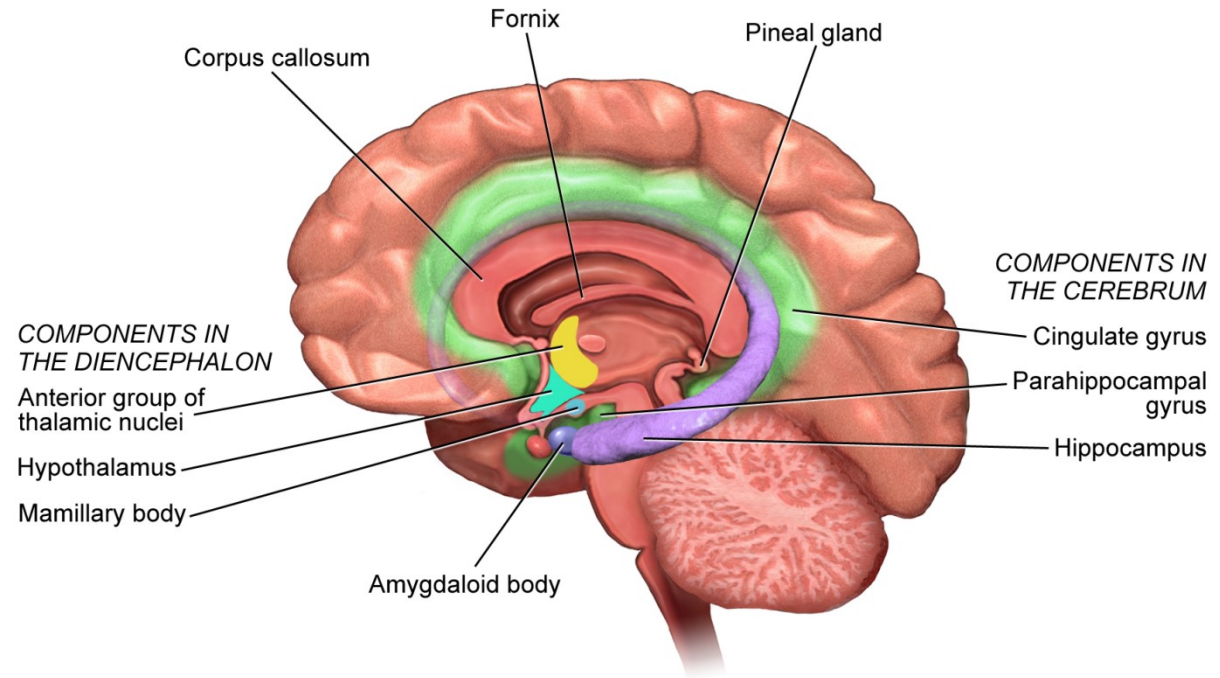
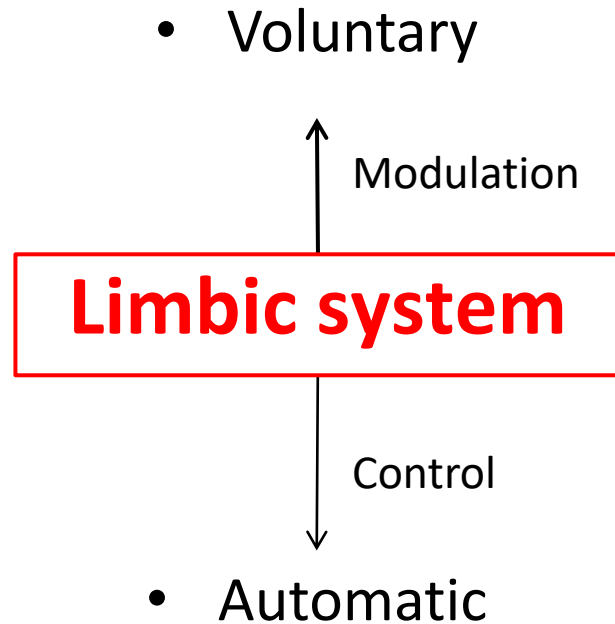


# Concept of the limbic system

- Voluntary
- ↑
- Potential conflict
- ↓
- Automatic



# Concept of the limbic system



# Concept of the limbic system

- Voluntary

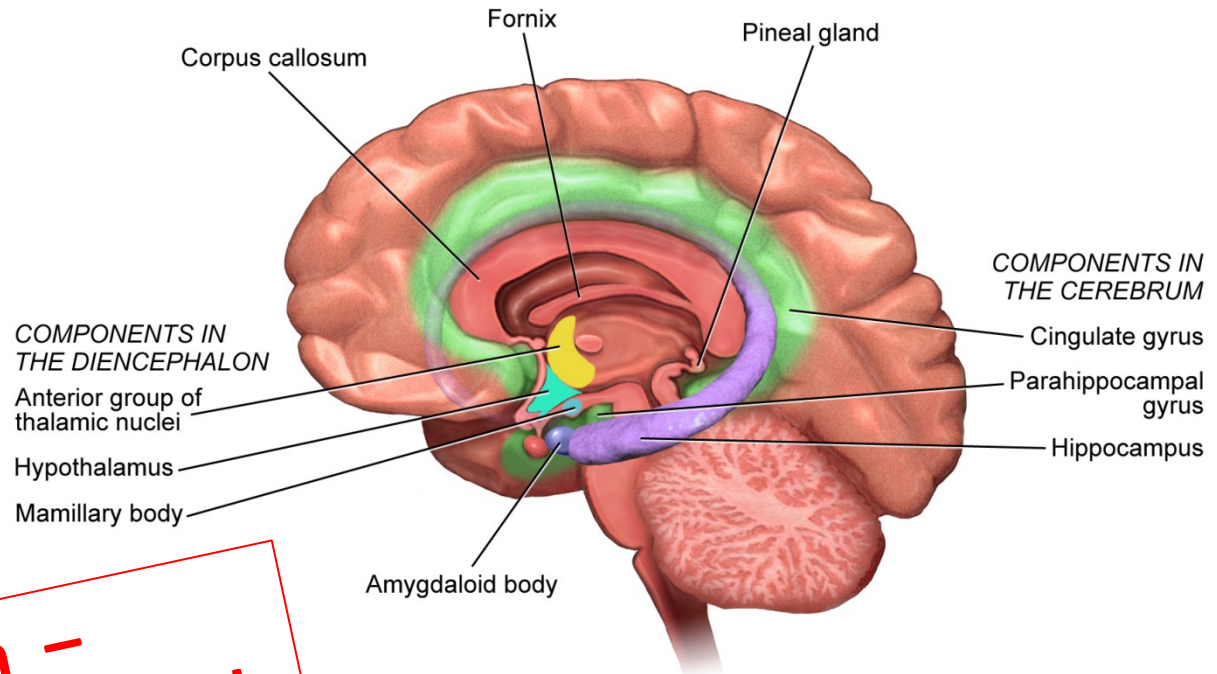
↑ Modulation

**Limbic system**

↓ Control

- Automatic

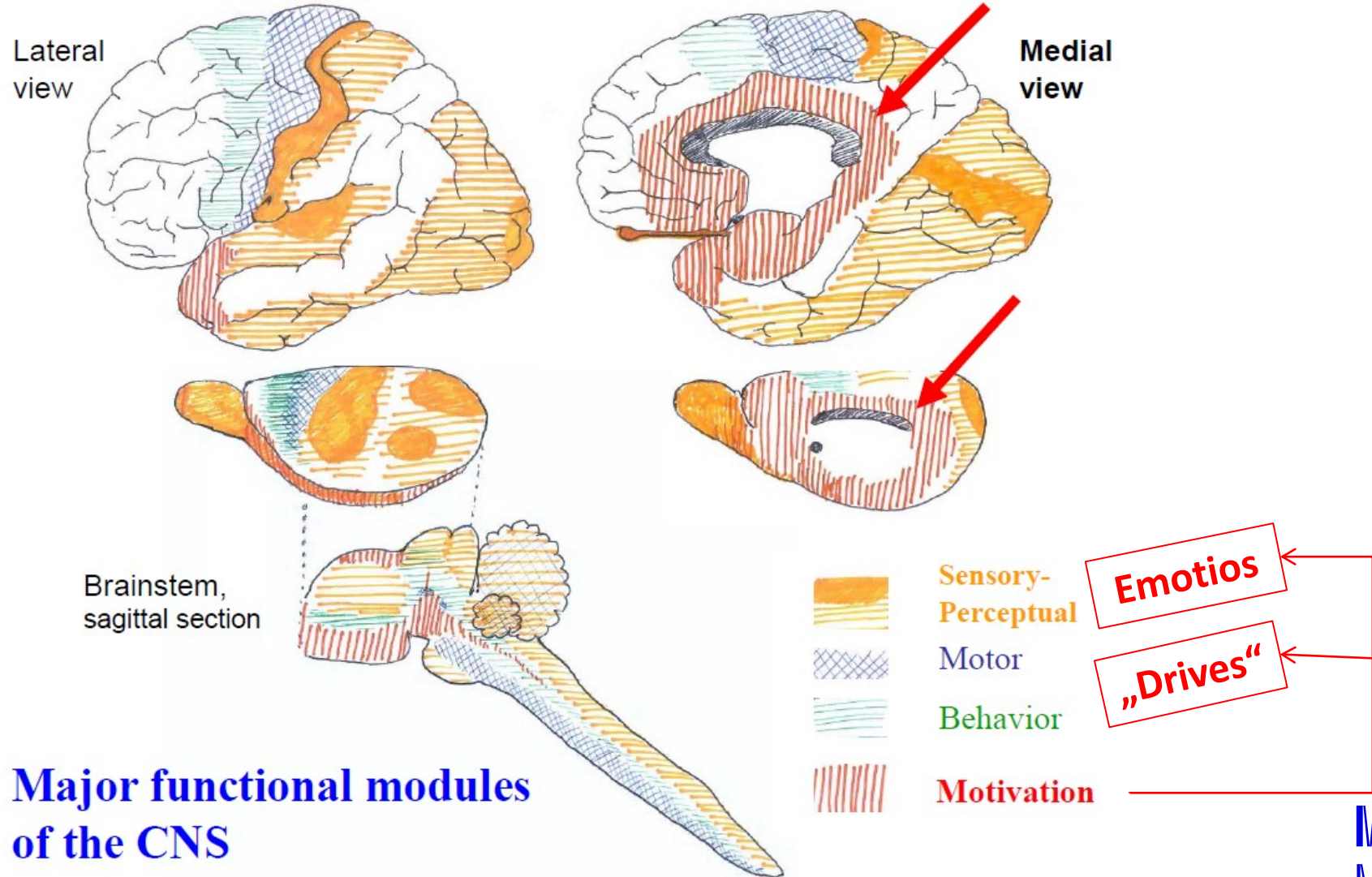
**Limbic system –  
hypothalamus and related  
structures**





# Limbic system

Limbus = border



## Major functional modules of the CNS

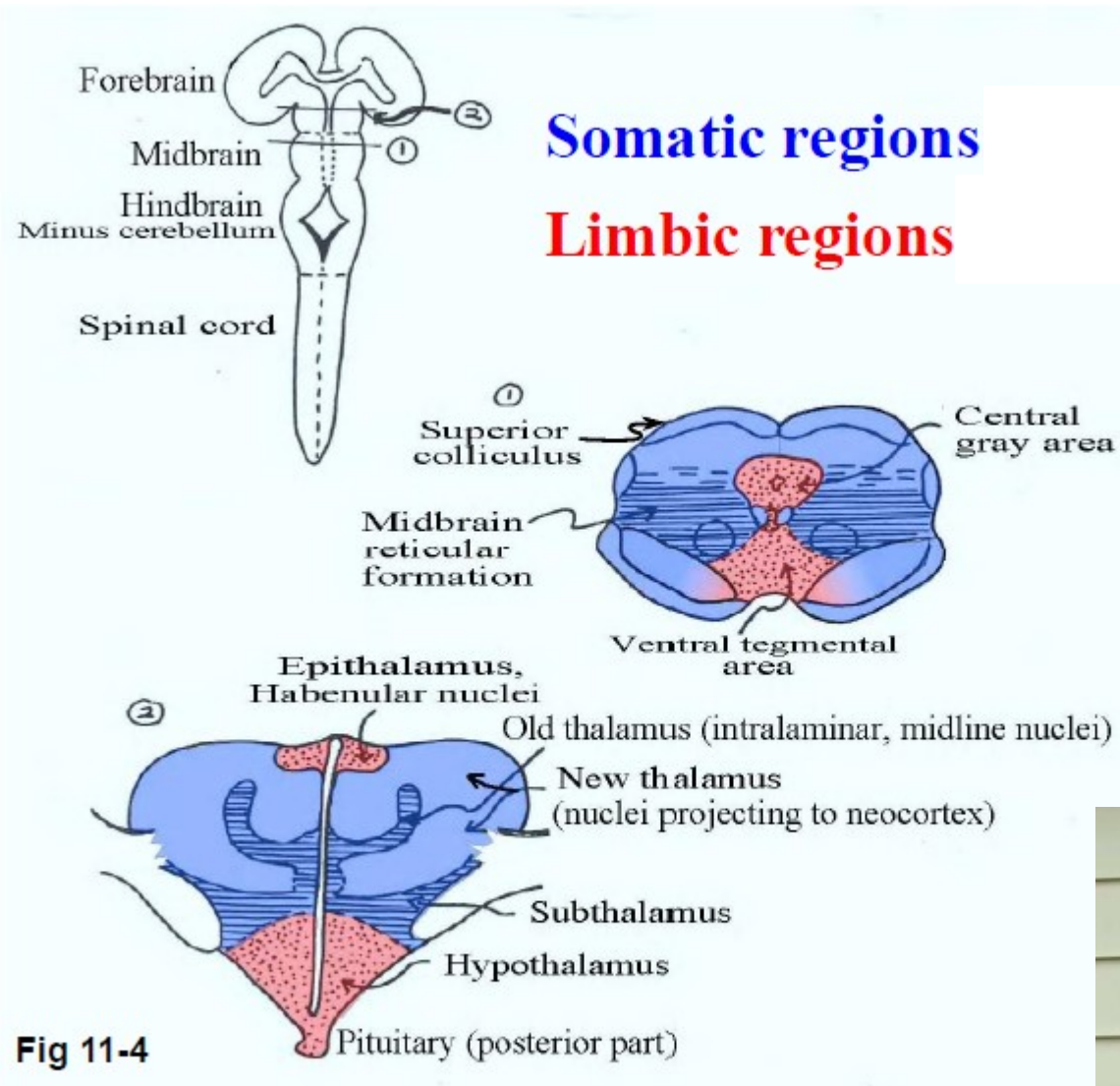
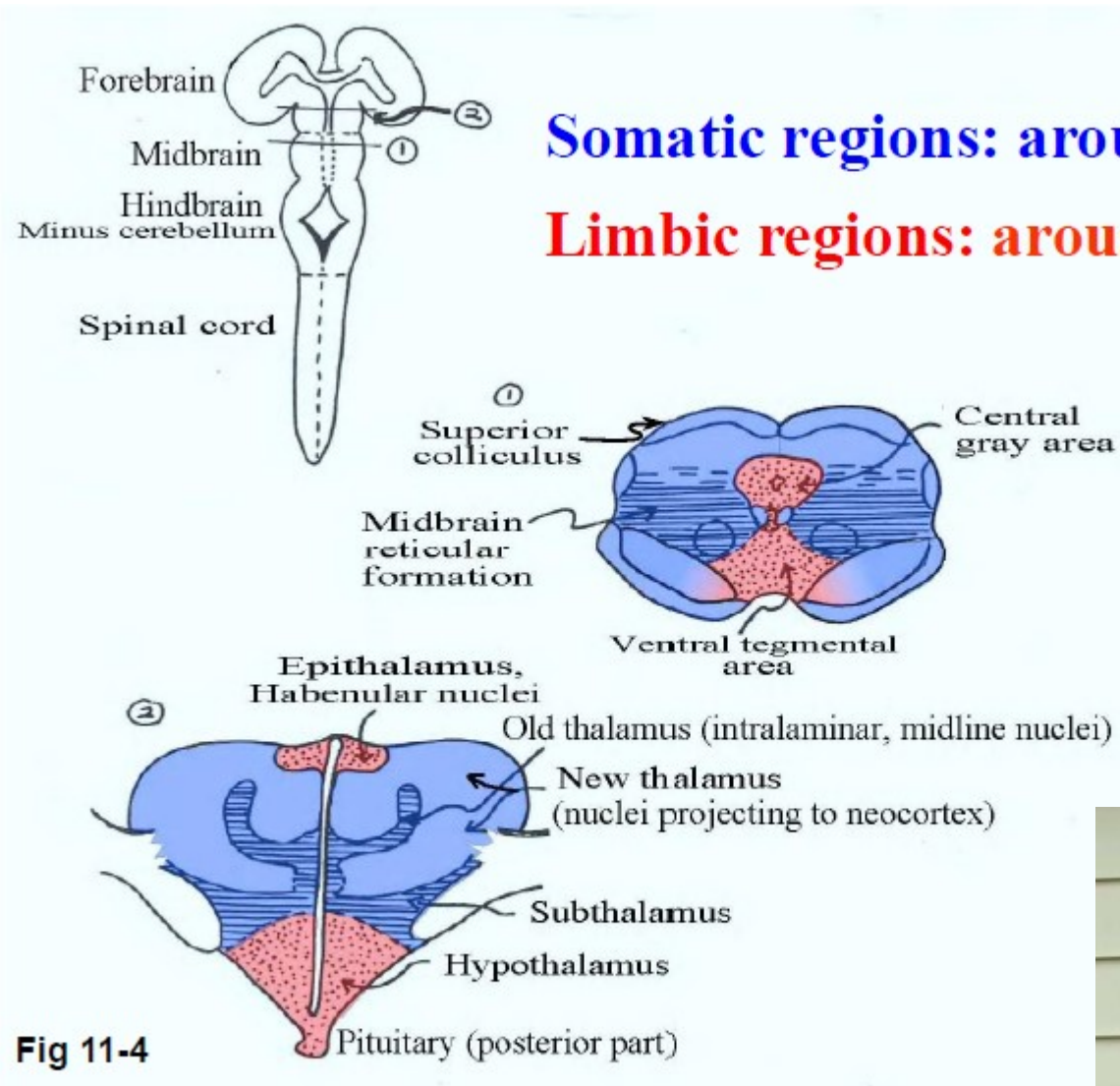


Fig 11-4

Courtesy of MIT Press. Used with permission.  
Schneider, G. E. *Brain Structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.



Prof. Gerald Schneider

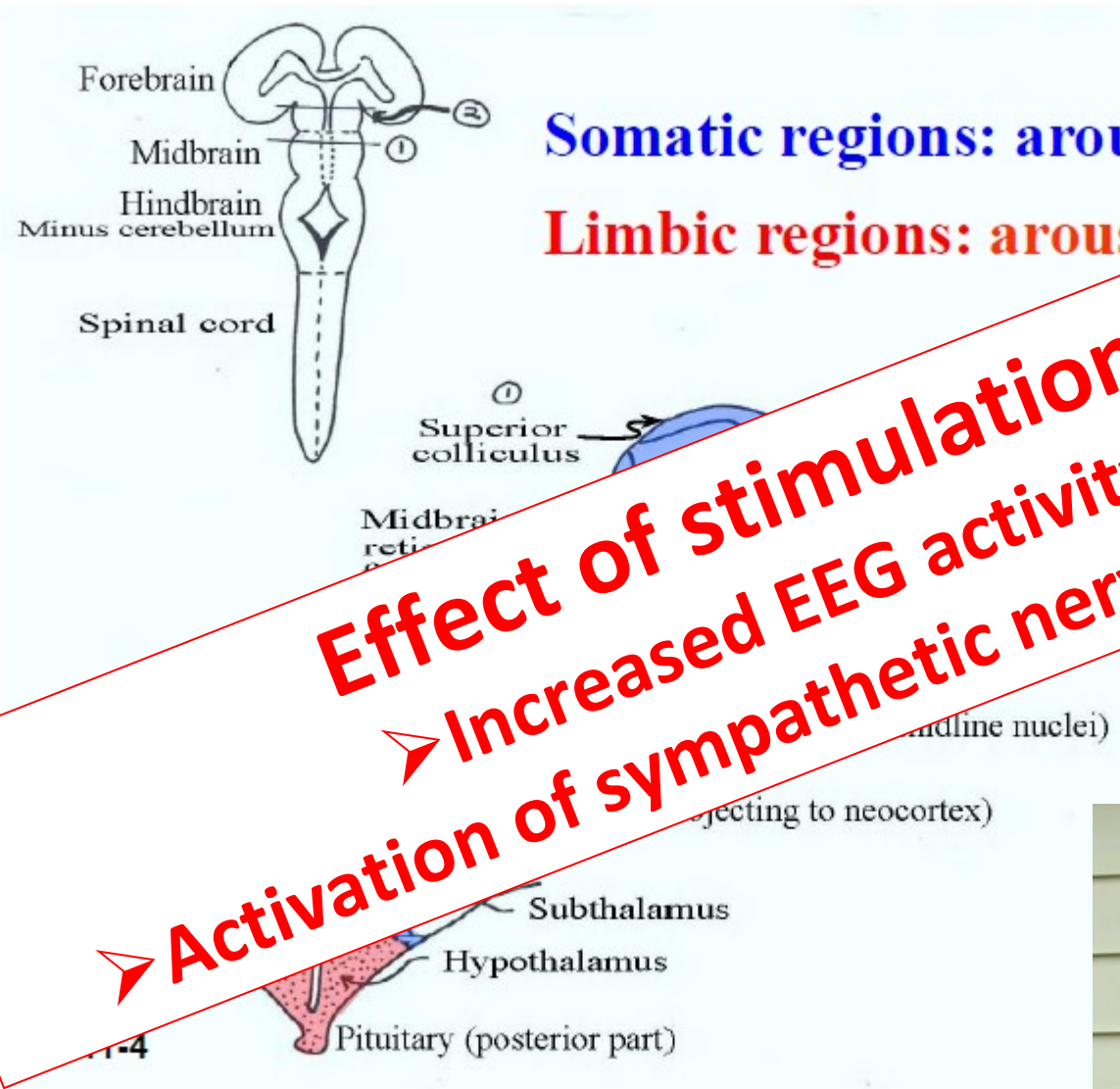


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Prof. Gerald Schneider





**Somatic regions: arousal type 1**

**Limbic regions: arousal type 2**

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Schneider, G. E. *Brain Structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.



Prof. Gerald Schneider



## Arousal type 1 (somatic)

### ARAS (ascendent retikulation activation system)

- Effect of stimulation
  - Habituation
  - Minimal activation of „reward/punishing“ system

## Arousal type 2 (limbic)

- Effect of stimulation
  - Minimal habituation
  - Strong activation of „reward/ punishing“ system
    - Central gray area –CGA - negative
    - Ventral tegmental area – VTA – positive

## Arousal type 1 (somatic)

### ARAS (ascendent retikulation activation system)

- Effect of stimulation
  - Habituation
  - Minimal activation of „reward/punishing“ system
- Ascendent connections
  - Somatosensetivity, visual s., auditory s., vestibular s., cerebellum
- Descendent connections
  - Neocortex, corpus striatum, thalamus

## Arousal type 2 (limbic)

- Effect of stimulation
  - Minimal habituation
  - Strong activation of „reward/ punishing“ system
    - Central gray area –CGA - negative
    - Ventral tegmental area – VTA – positive
- Ascendent connections
  - Mainly viscerosenzitivity, pain
- Descendent connections
  - Hypothalamus and other limbic areas, amygdala

## Arousal type 1 (somatic)

ARAS (ascendent retikulation activation)

- EEG

### Effect of stimulation

- Increased EEG activity
- Activation of sympathetic nervous system

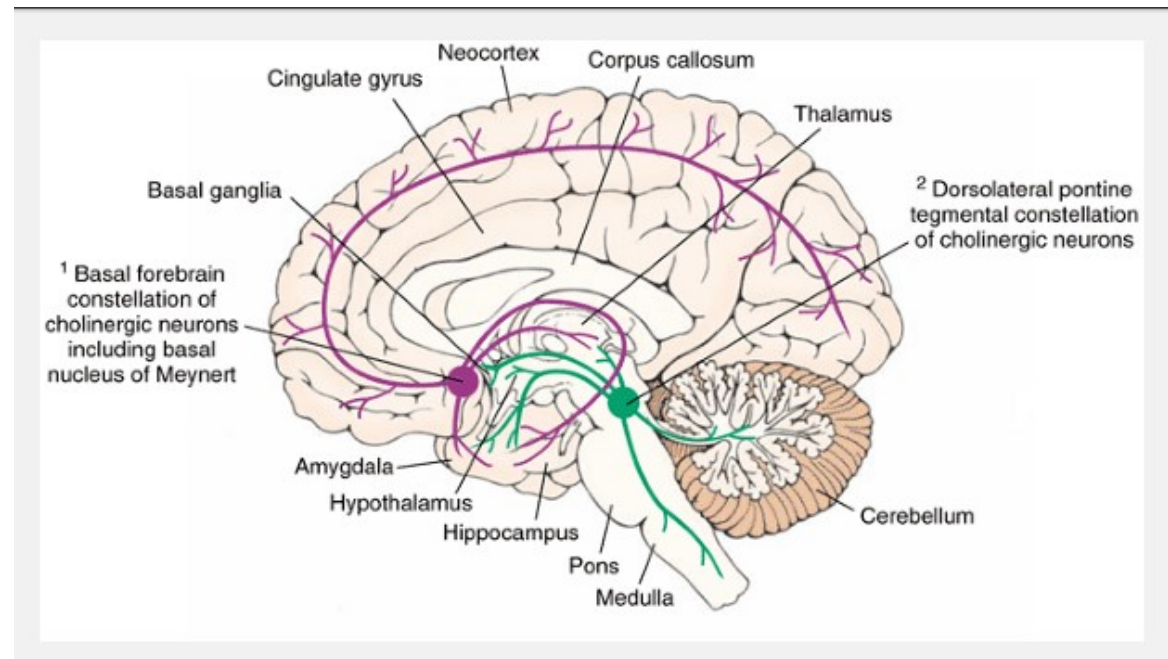
Cooperation of both systems is a key to maintaining consciousness (through neuromodulation)

- Ascending connections  
Neocortex, corpus striatum, thalamus

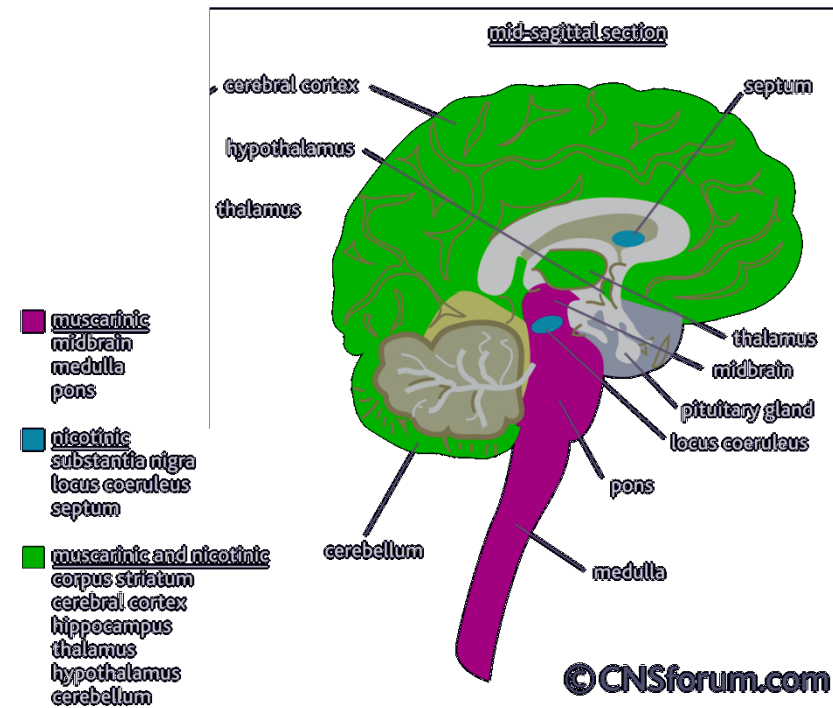
- Descendent connections
  - Hypothalamus and other limbic areas, amygdala

# Acetylcholine

- Nucleus basalis (Meynerti) and other nuclei
- Nicotin receptors
- Muscarin receptors
  
- Sleep/wake regulation
- Cognitive functions
- Behavior
- Emotions



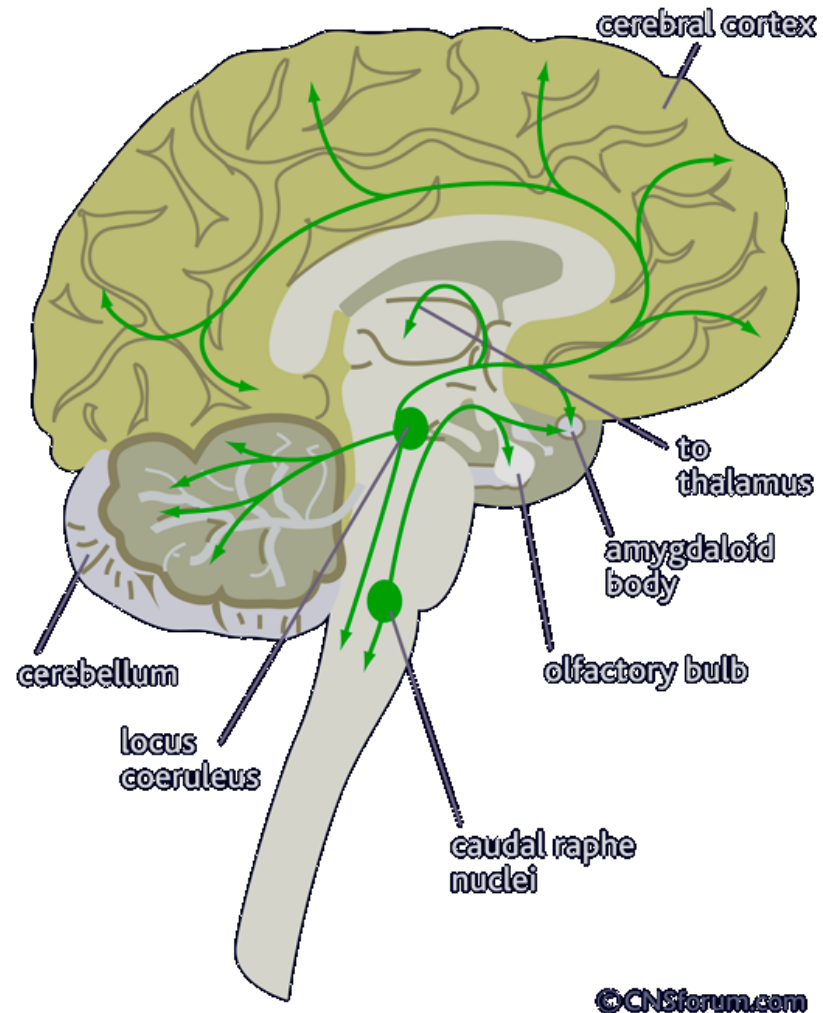
<http://www.slideshare.net/drpsdeb/presentations>





# Norepinefrine

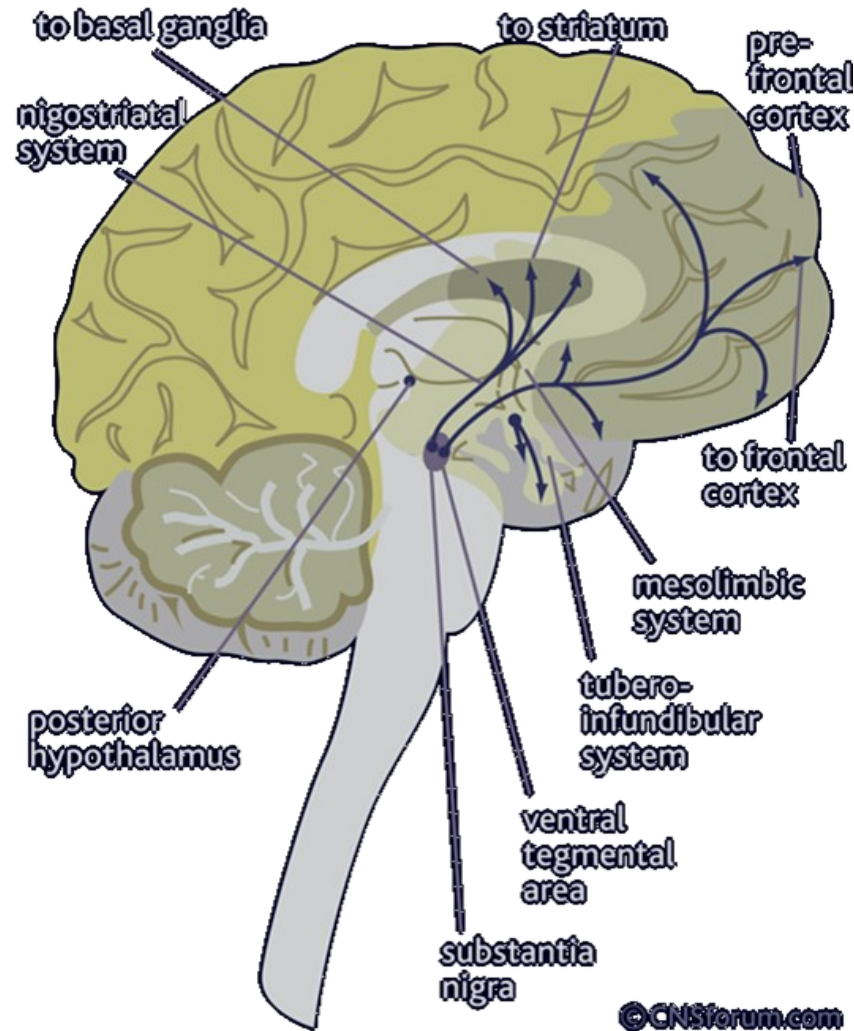
- Locus coeruleus
- Nuclei raphe caudalis
  
- Vigilance
- Responsiveness to unexpected stimuli
- Memory
- Learning



<http://www.slideshare.net/drpsdeb/presentations>

# Dopamine

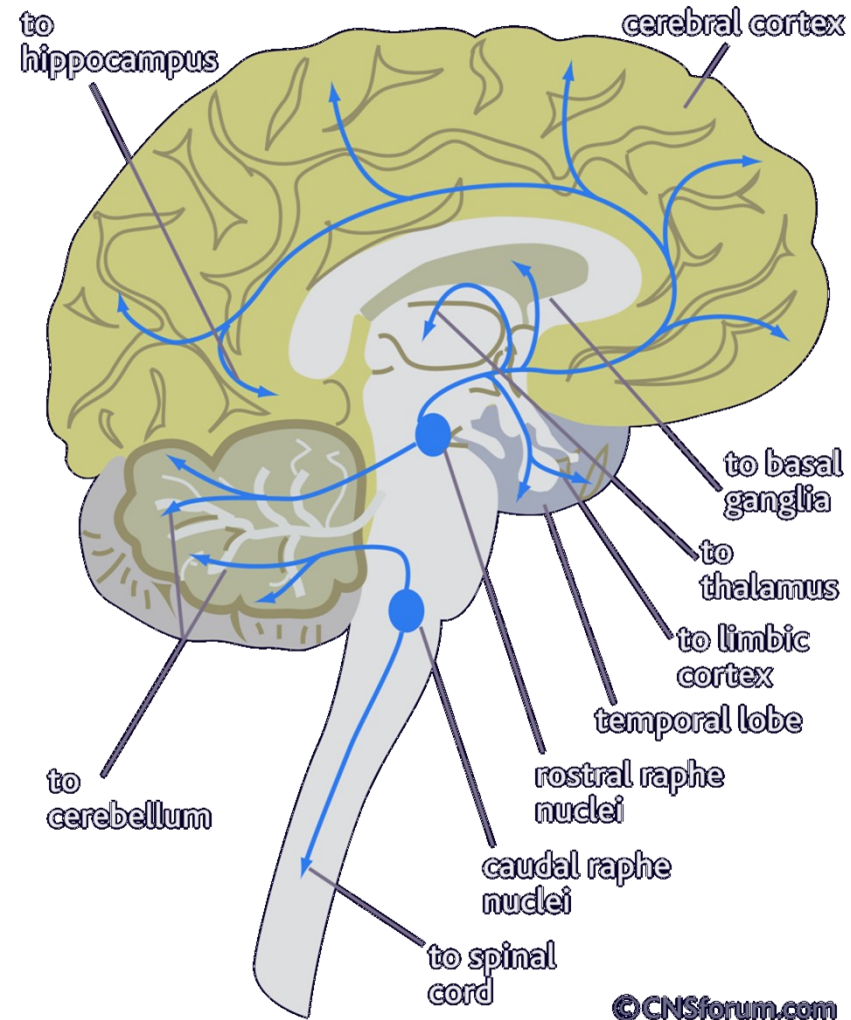
- Nigrostriatal system
  - Movement
  - Sensory stimuli
- Ventro- tegmentno-mesolimbic-frontal system
  - Reward
  - Cognitive function
  - Emotional behavior
- Tubero-infundibular system
  - Hypothalamic-pituitary regulation
- D1 receptors – excitatory
- D2 receptors - inhibitory



<http://www.slideshare.net/drpsdeb/presentations>

# Serotonin

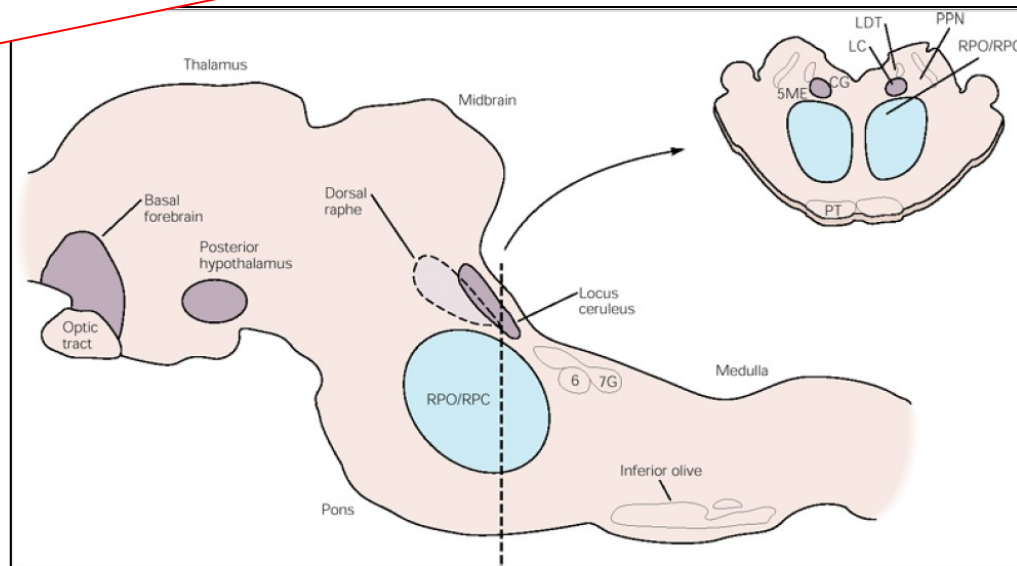
- Nuclei raphe rostralis
- Nuclei raphe caudalis
  
- Anxiety/relaxation
- Impulsive behavior
- Sleep



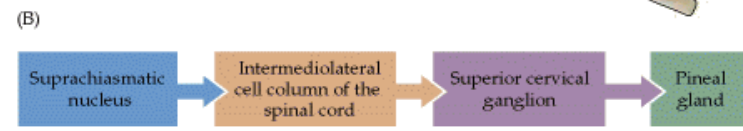
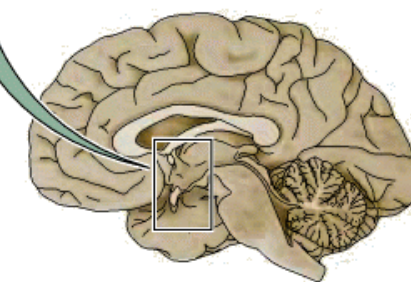
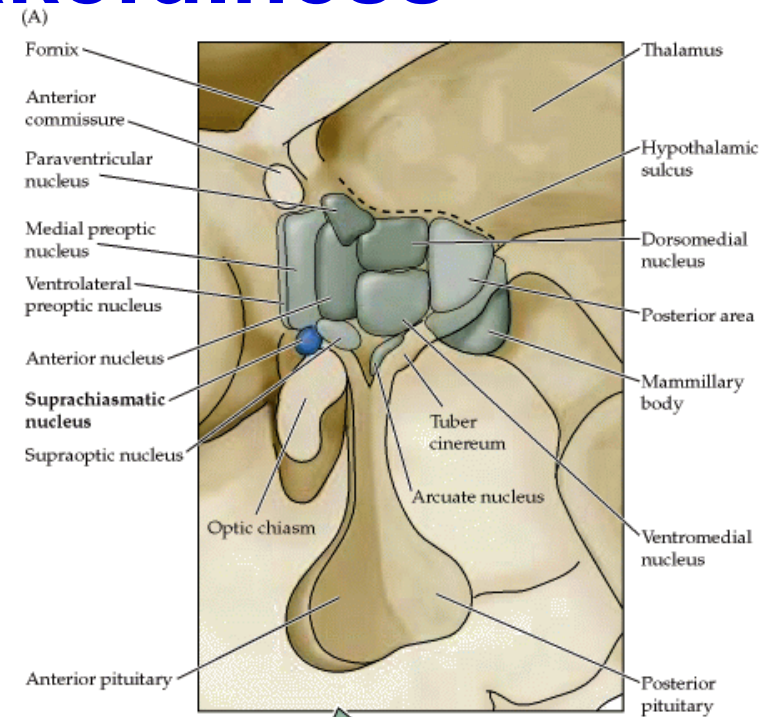
<http://www.slideshare.net/drpsdeb/presentations>

# Sleep and wakefulness

**Cooperation of ARAS and limbic activating system**



48 Autonomic nervous system - Limbic system - Neocortex





# Sleep

## The sleep cycle

There are two very different types of sleep:

1. Rapid Eye Movement or REM sleep, which is associated with fast brain activity and active dreaming; and
2. Non-REM sleep, which is associated with slower brain activity and divided into 4 stages:
  - » Stages 1-2 light sleep
  - » Stages 3-4 deep slow-wave sleep.

All these combine to make the non-REM/REM sleep cycle, which is about 90 minutes long on average, but can be up to 120 minutes.

For most people, a good night's sleep is around 4 – 5 cycles long.

Good quality sleep requires both non-REM and REM sleep in uninterrupted cycles.

### REM SLEEP

- › Eyes move rapidly under closed eyelids
- › Most dreaming occurs here
- › Brain is active, muscles are relaxed
- › Can't move voluntarily – signals from the brain to the postural muscles are blocked

### DEEP NON-REM SLEEP

- › Stages 3-4
- › Difficult to wake up
- › Sleep inertia when woken

## Rapid Eye Movement (REM)

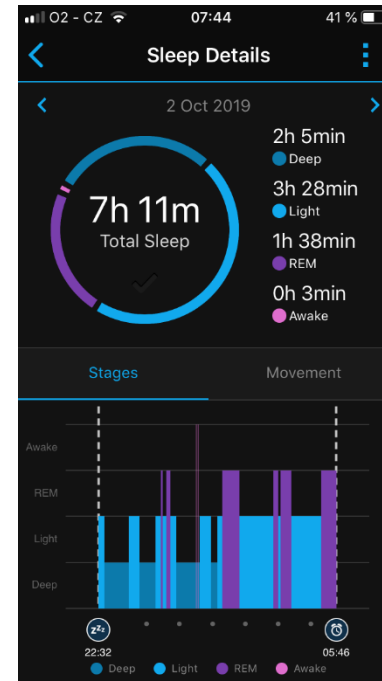
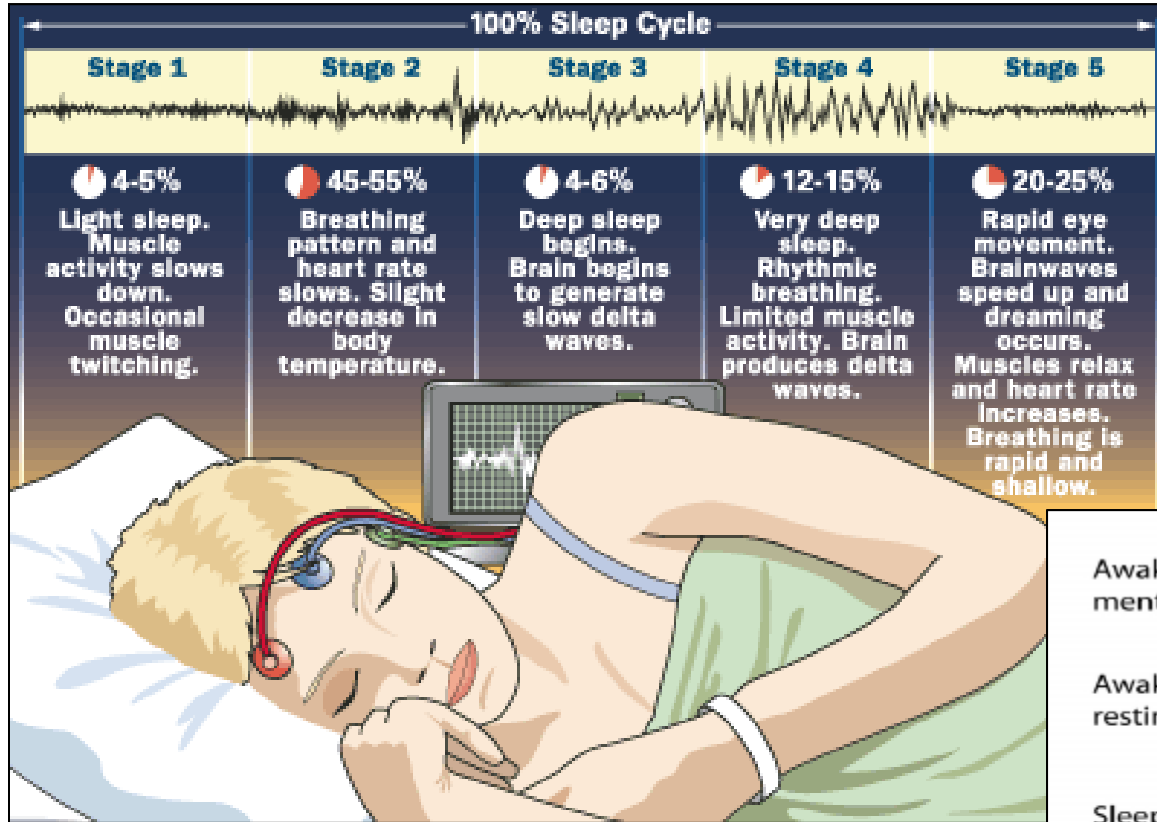
### LIGHT NON-REM SLEEP

- › Stages 1-2
- › May drift in and out of sleep several times at the start
- › Easy to wake up, disturbs easily

4 to 5 sleep cycles make a good night's sleep

# Sleep

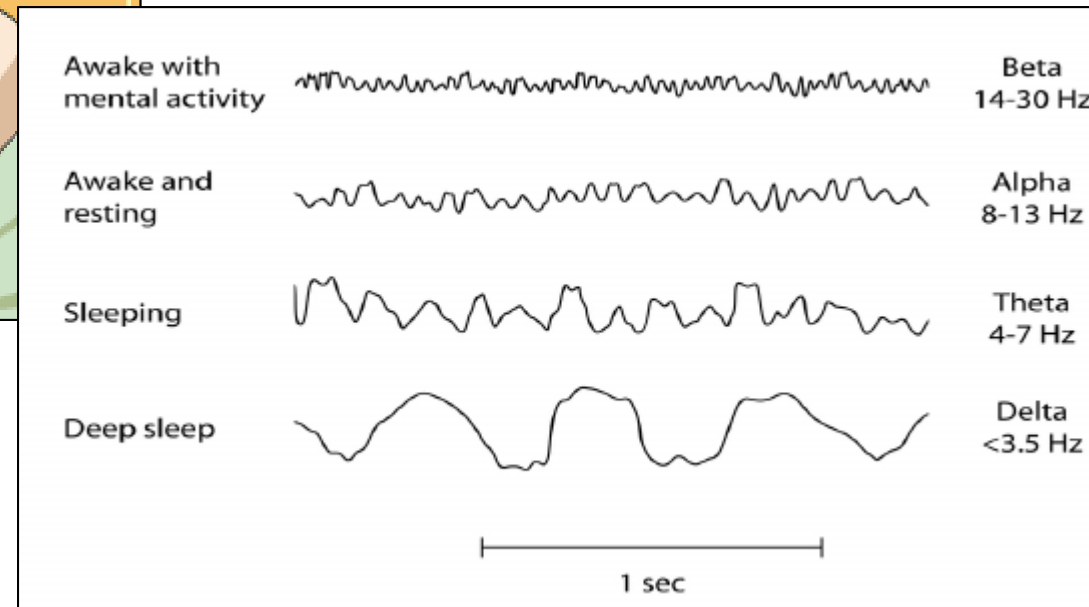
http://www.slideshare.net/dripsdeb/presentations



https://connect.garmin.com/modern/



LIGHT NON-REM SLEEP	DEEP NON-REM SLEEP	REM SLEEP
<ul style="list-style-type: none"> <li>Stages 1-2</li> <li>May drift in and out of sleep several times at the start</li> <li>Easy to wake up, disturbs easily</li> </ul>	<ul style="list-style-type: none"> <li>Stages 3-4</li> <li>Difficult to wake up</li> <li>Sleep inertia when woken</li> </ul>	<ul style="list-style-type: none"> <li>Eyes move rapidly under closed eyelids</li> <li>Most dreaming occurs here</li> <li>Brain is active, muscles are relaxed</li> <li>Can't move voluntarily – signals from the brain to the postural muscles are blocked</li> </ul>



https://www.researchgate.net/profile/Priyanka\_Abhang3/publication/281801676/figure/fig4/AS:305025248186371@1449735094401/fig-4-EEG-waves-for-different-signals.png

http://www.dailymail.co.uk/sciencetech/arti-cle-3042230/Sleeping-habits-world-revealed-wakes-grumpy-China-best-quality-shut-eye-South-Africa-wakes-earliest.html

# Sleep and wakefulness

## Brainstem nuclei responsible

## Neurotransmitter

## Activity state

### *WAKEFULNESS*

Cholinergic nuclei of pons-midbrain junction

Acetylcholine

Active

Locus coeruleus

Norepinephrine

Active

Raphe nuclei

Serotonin

Active

### *NON-REM SLEEP*

Cholinergic nuclei of pons-midbrain junction

Acetylcholine

Decreased

Locus coeruleus

Norepinephrine

Decreased

Raphe nuclei

Serotonin

Decreased

### *REM SLEEP ON*

Cholinergic nuclei of pons-midbrain junction

Acetylcholine

Active

Raphe nuclei

Serotonin

Inactive

### *REM SLEEP OFF*

Locus coeruleus

Norepinephrine

Active

# Hypothalamus

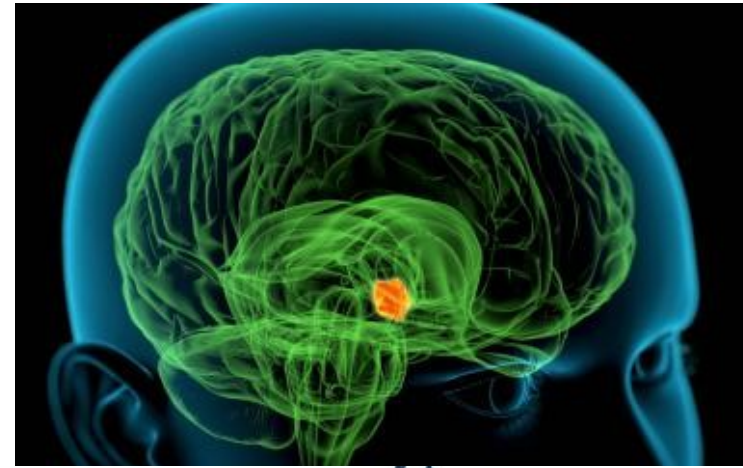
- Key center of autonomic regulations and coordination
- Integration of the information from inner and outer environment



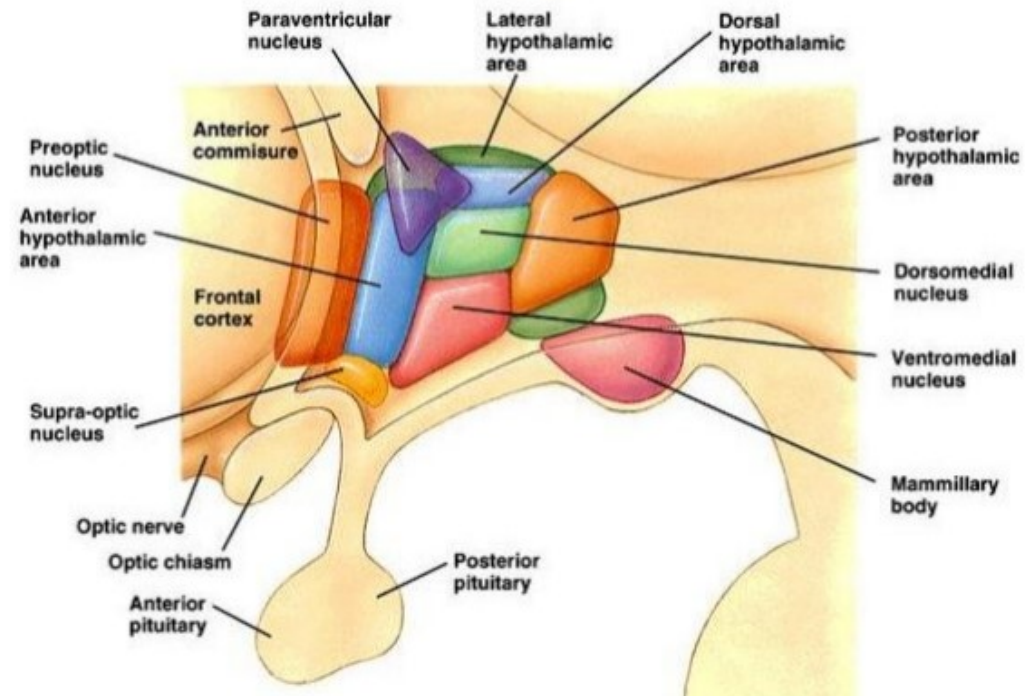
- Behavioral modulation
- Regulation of autonomic nervous system



- **Maintenance of homeostasis**



<http://biology.about.com/od/anatomy/pl/Hypothalamus.htm>



<http://www.slideshare.net/physiologymgmcri/hypothalamus-15-apr-2016>



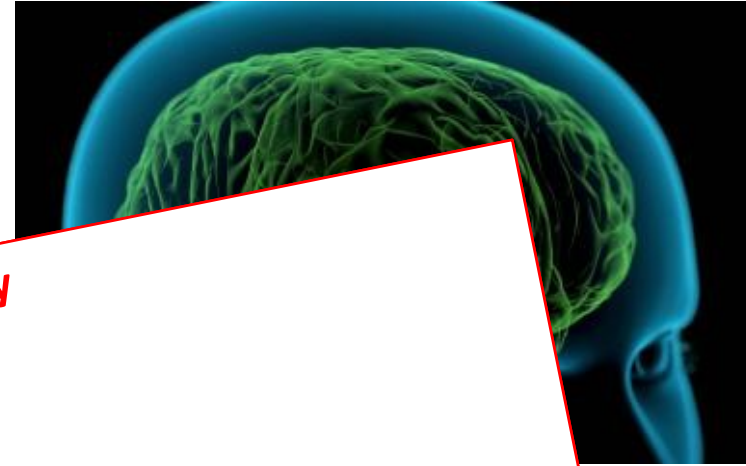
# Hypothalamus

- Key center of autonomic regulations and coordination
- Integration of the information from inner and outer environment

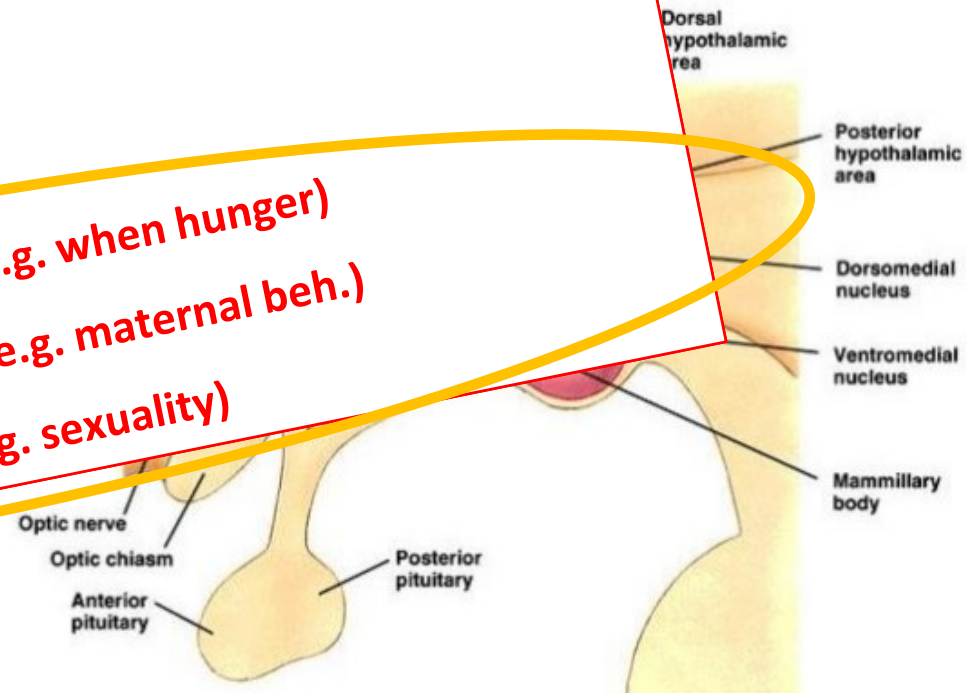
- Behavior
- Regulation of nervous system

- Maintenance of homeostasis

- ✓ Biological clock – circadian /seasonal activity
- ✓ Autonomic nervous system regulation
- ✓ Endocrine system regulation
- ✓ Food and water intake regulation
- ✓ Regulation of body temperature
- ✓ „Immediate“ behavior regulation (e.g. when hunger)
- ✓ „Long-term“ behavior regulation (e.g. maternal beh.)
- ✓ Instinctive behavior regulation (e.g. sexuality)

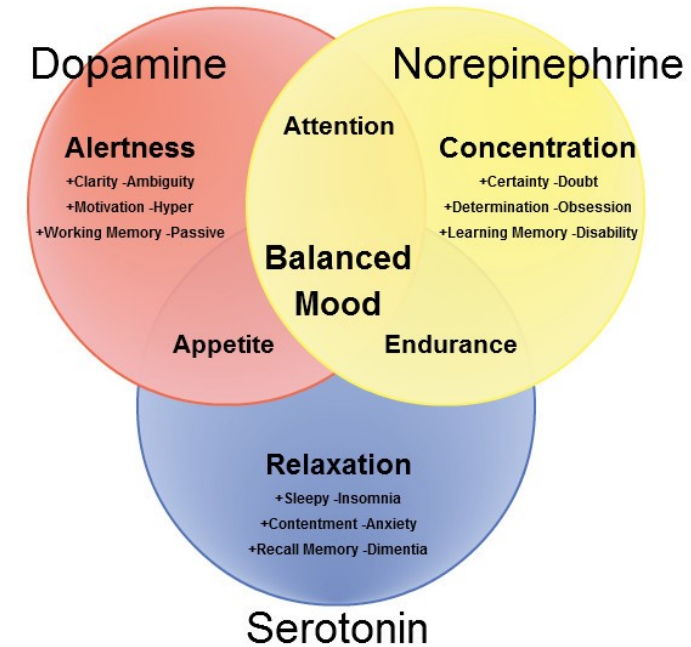


<http://biology.about.com/od/anatomy/pl/Hypothalamus.htm>



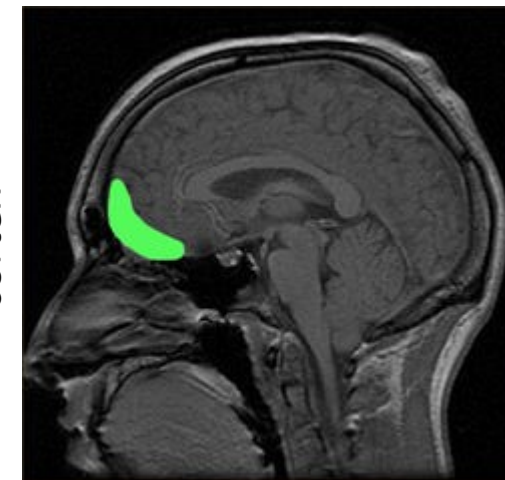
# Influence of hypothalamus on neocortex

- Via neuromodulating systems
  - Consciousness (see above)
  - Mood
- Via thalamus
  - Via nucleus mediodorsalis to orbitofrontal cortex (influence on decision making)
  - Influence gating function of other thalamic nuclei
- Papez circuit



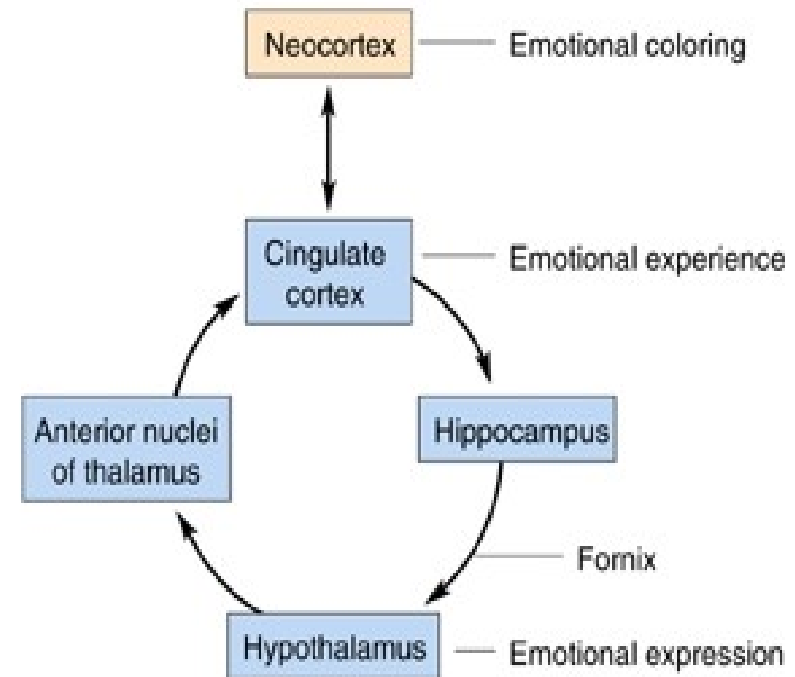
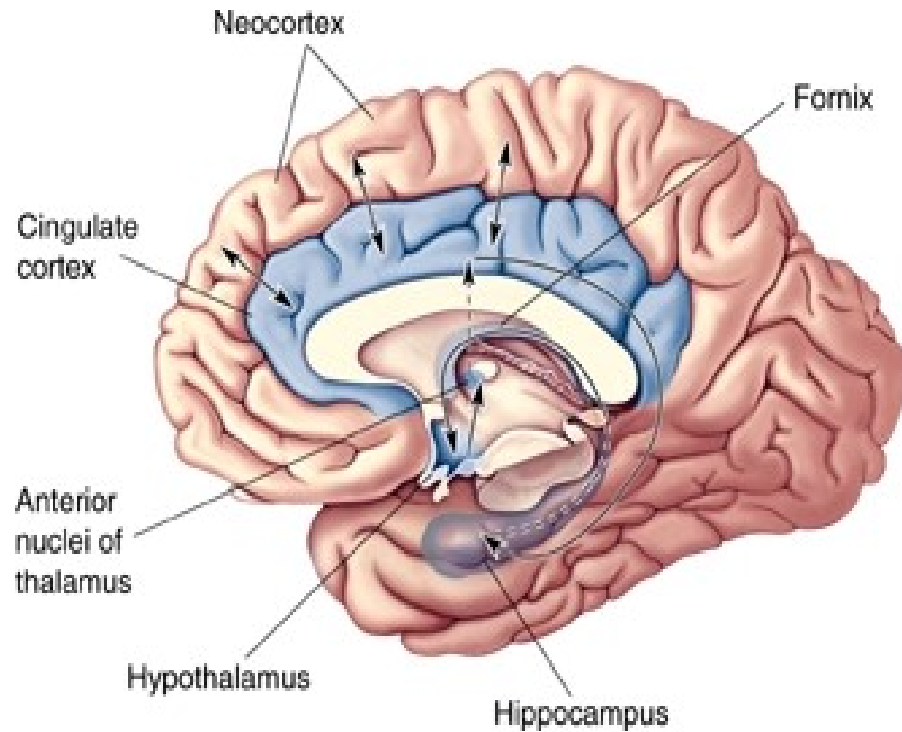
[http://ausm.org.uk/wp-content/uploads/2015/02/Dopamine\\_Norepinephrine\\_Serotonin.jpg](http://ausm.org.uk/wp-content/uploads/2015/02/Dopamine_Norepinephrine_Serotonin.jpg)

Orbitofrontal cortex



[https://en.wikipedia.org/wiki/Orbitofrontal\\_cortex](https://en.wikipedia.org/wiki/Orbitofrontal_cortex)

# Papez circuit



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<http://www.slideshare.net/drsunilsuthar/neurobiology-of-emotion>

# Papez circuit

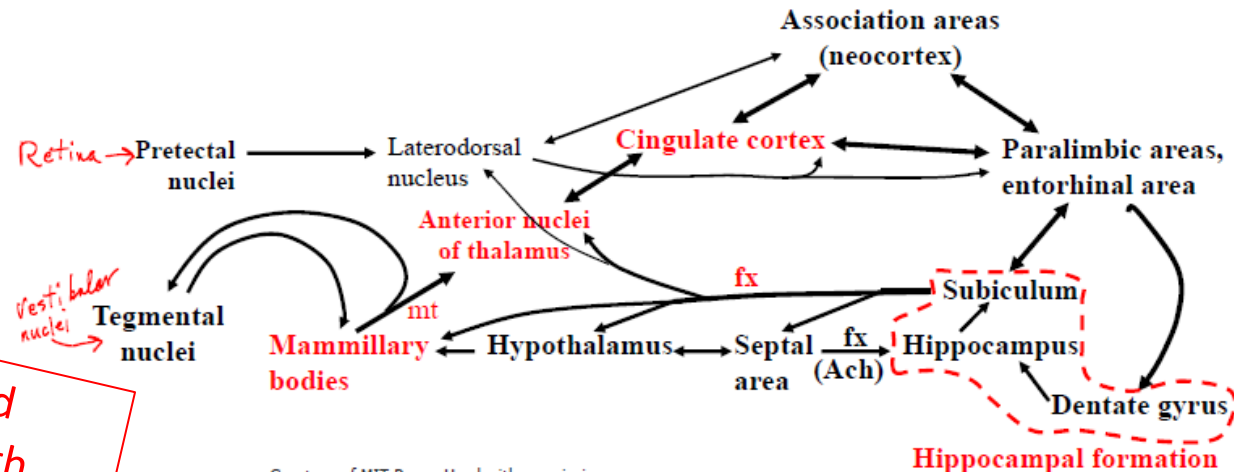
Gerald Schneider. 9.14 Brain Structure and Its Origins, Spring 2014. (Massachusetts Institute of Technology: MIT OpenCourseWare), <http://ocw.mit.edu> (Accessed). License: Creative Commons BY-NC-SA



Prof. Gerald Schneider

- *Suggestion: the ascending axons of this circuit are continuously activating memories of places that lie ahead, in the direction indicated by the current direction of the head.* Thus, decisions about direction of locomotion are influenced by memories of those places, including their good or bad values.
- *Axons in the Papez circuit are of more than one type. Only the ones signaling head direction have been characterized.*
- *What is the hippocampus sending to other parts of the hypothalamus? It may alter motivational levels according to remembered information about locations in the current frame of reference.*

mt = mammillothalamic tract  
fx = fornix bundle



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Schneider, G. E. Brain Structure and its Origins: In the Development and in Evolution of Behavior and the Mind. MIT Press, 2014. ISBN: 9780262026734.



# Papez circuit

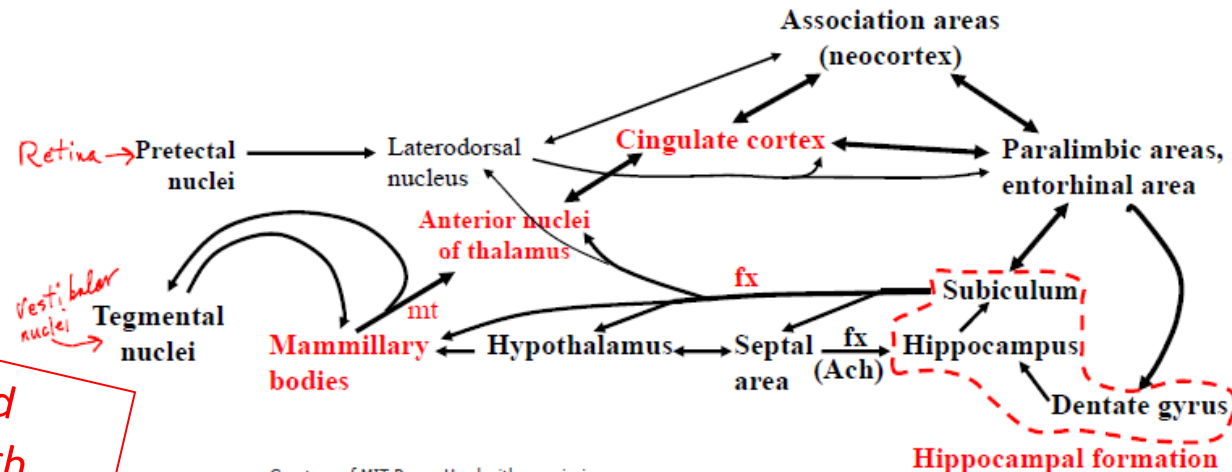
Gerald Schneider. *9.14 Brain Structure and Its Origins, Spring 2014*. (Massachusetts Institute of Technology: MIT OpenCourseWare), <http://ocw.mit.edu> (Accessed). License: Creative Commons BY-NC-SA



Prof. Gerald Schneider

- Origins of endbrain: Structures underlying olfaction
- Two major links between olfactory system and the motor systems of the midbrain
  - 1) Through the ventral endbrain, which became corpus striatum and basal forebrain (including much of the septal area)
    - Outputs to hypothalamus, (epithalamus, subthalamus), midbrain
    - These outputs affected locomotion and orienting movements
    - The links were plastic, so habits were formed according to rewarding effects mediated, e.g., by taste effects.
  - 2) Through the medial part of the dorsal endbrain, which became medial pallium—the hippocampal formation
    - Outputs to ventral striatum, hypothalamus, epithalamus
    - The links were plastic, but the “habits” formed were different: The association of place with good or bad consequences of approach.

mt = mammillothalamic tract  
fx = fornix bundle



Spatial orientation and emotions associated with particular place

# Papez circuit

Gerald Schneider. *9.14 Brain Structure and Its Origins, Spring 2014*. (Massachusetts Institute of Technology: MIT OpenCourseWare), <http://ocw.mit.edu> (Accessed). License: Creative Commons BY-NC-SA



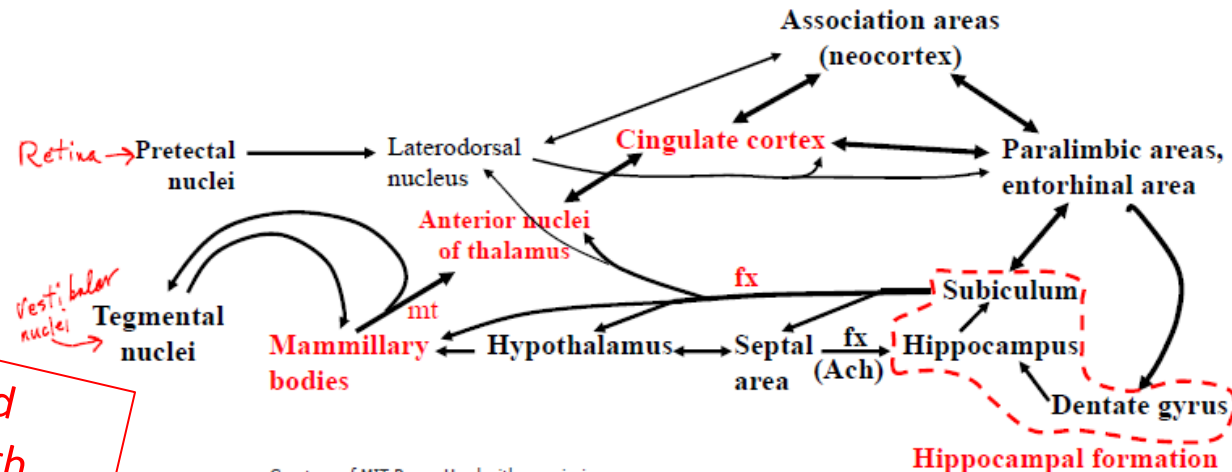
Prof. Gerald Schneider

Object oriented...

Location oriented...

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Spatial orientation and emotions associated with particular place

# Learning and memory

- Connections of striatum and hippocampus are plastic
- Plasticity is a base of learning
- Learning is a forming of long- term memory

**Working/Short term  
memory**  
– „RAM“

**Long term memory**  
– „Hard disk“

# Learning and memory

- Connections of striatum and hippocampus are plastic
- Plasticity is a base of learning
- Learning is a forming of long- term memory
- Declarative memory (explicit)
  - Based on hippocampus
  - Explicit information is stored and later recollected
  - „Construction of the maps (relationships)“ – spatial or abstract



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  - Habitual learning – motor skills, but also social habits
  - „Construction of the algorithms“

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**Location oriented:**  
Where am I and what has happened here?

**Object oriented:**  
Can I eat it and how to eat it?

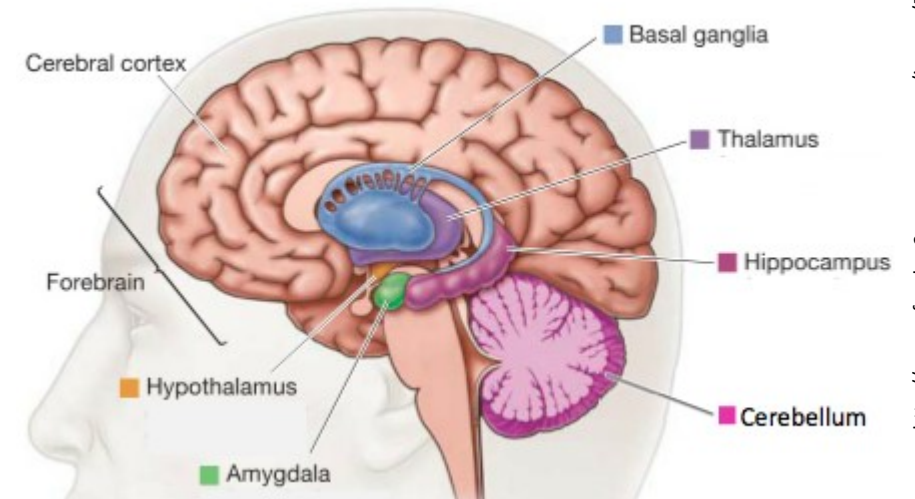
# Amygdala

*Corticomedial: Inputs from olfactory bulbs, hypothalamus & lateral amygdala; outputs to hypothalamus, amygdala, ANS*

*Basolateral: Inputs from thalamus, neocortex, hippocampus; outputs to prefrontal cortex, ventral striatum, other amygdala nuclei*

*Central: Intra-amygdalar inputs; outputs through stria terminalis (see later slides)*

- Connections to all major cortical and subcortical structures
- Modified corpus striatum
- Plasticity – memory formation



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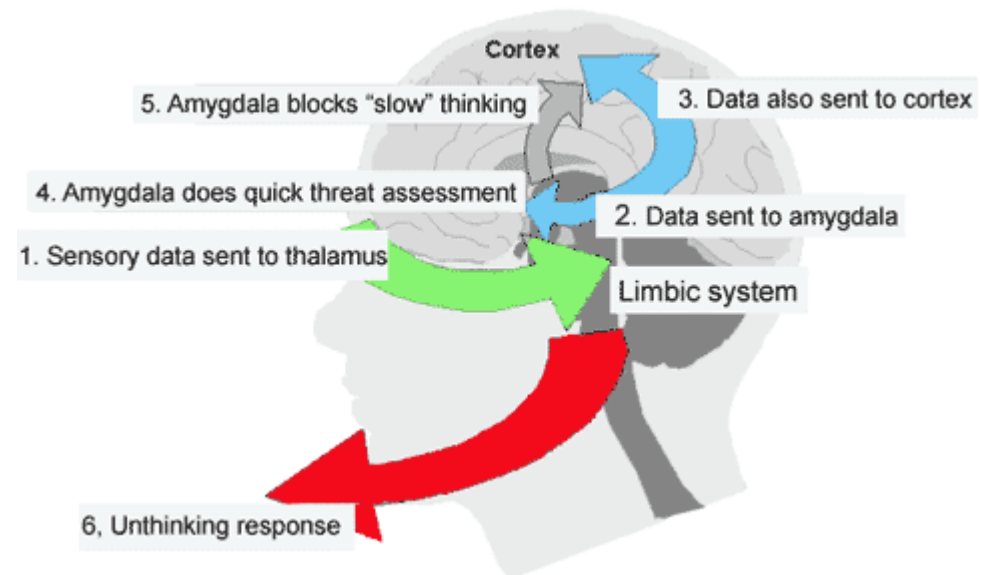
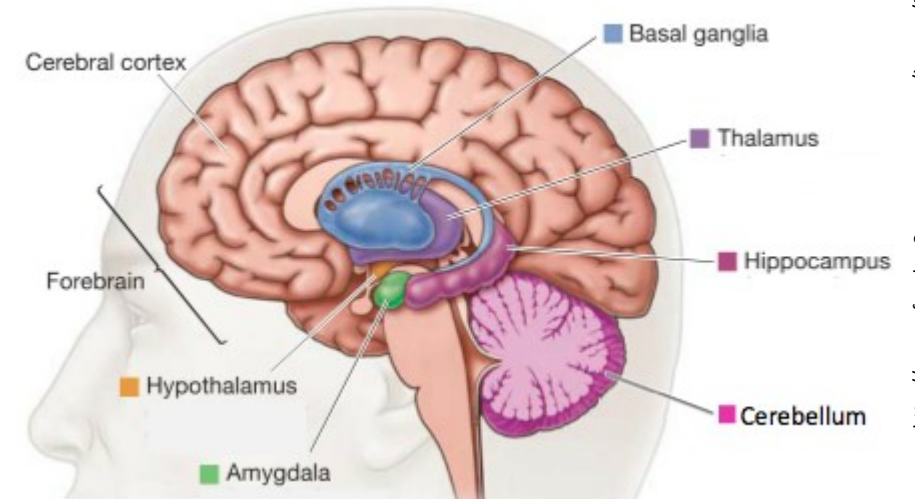
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- Connections to all major cortical and subcortical structures
- Modified corpus striatum
- Plasticity – memory formation
- „Influence of information from outer environment on limbic system“
- „Amygdala hijack“
- „Affective tags“
  - Both positive and negative
  - Higher responsiveness to negative



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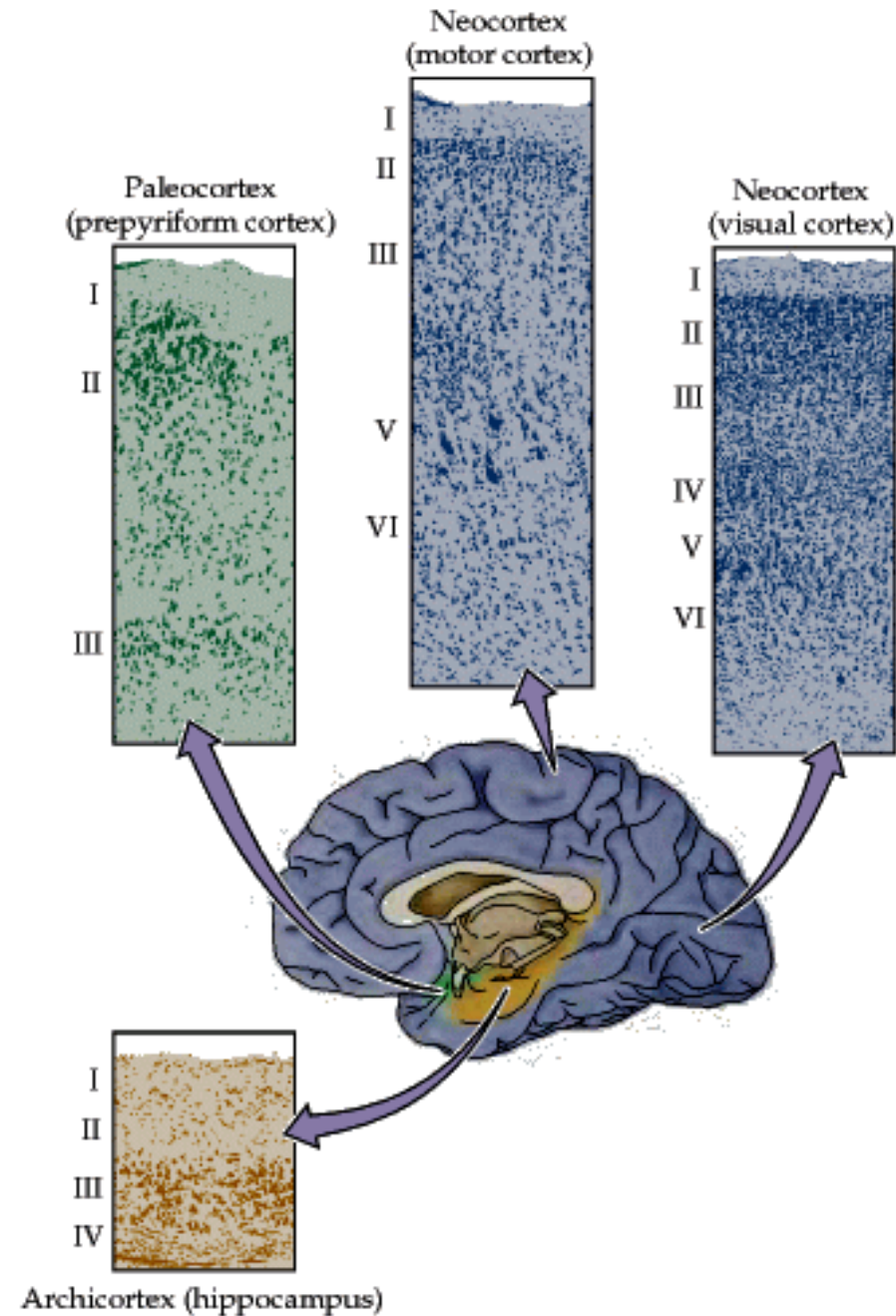
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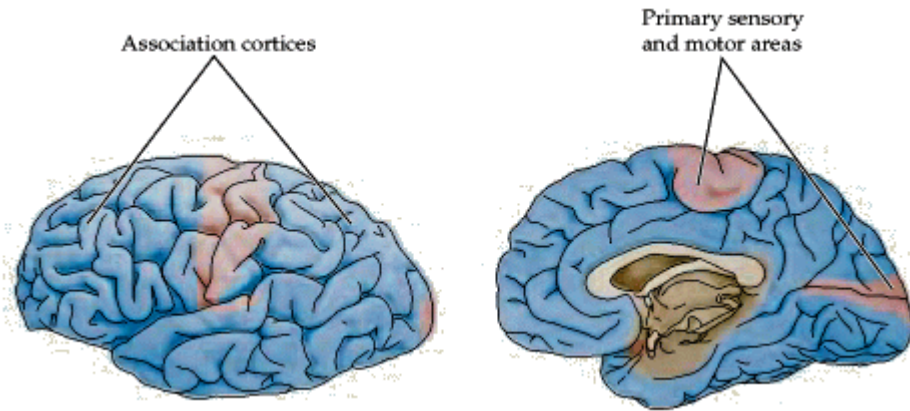
# **Neocortex**

# Cerebral cortex

- Paleocortex (1%)
  - 3 layers
  - rhinencephalon
- Archicortex (4%)
  - 3-4 layers
  - hippocampus
- Neocortex
  - 6 layers



# Neocortex

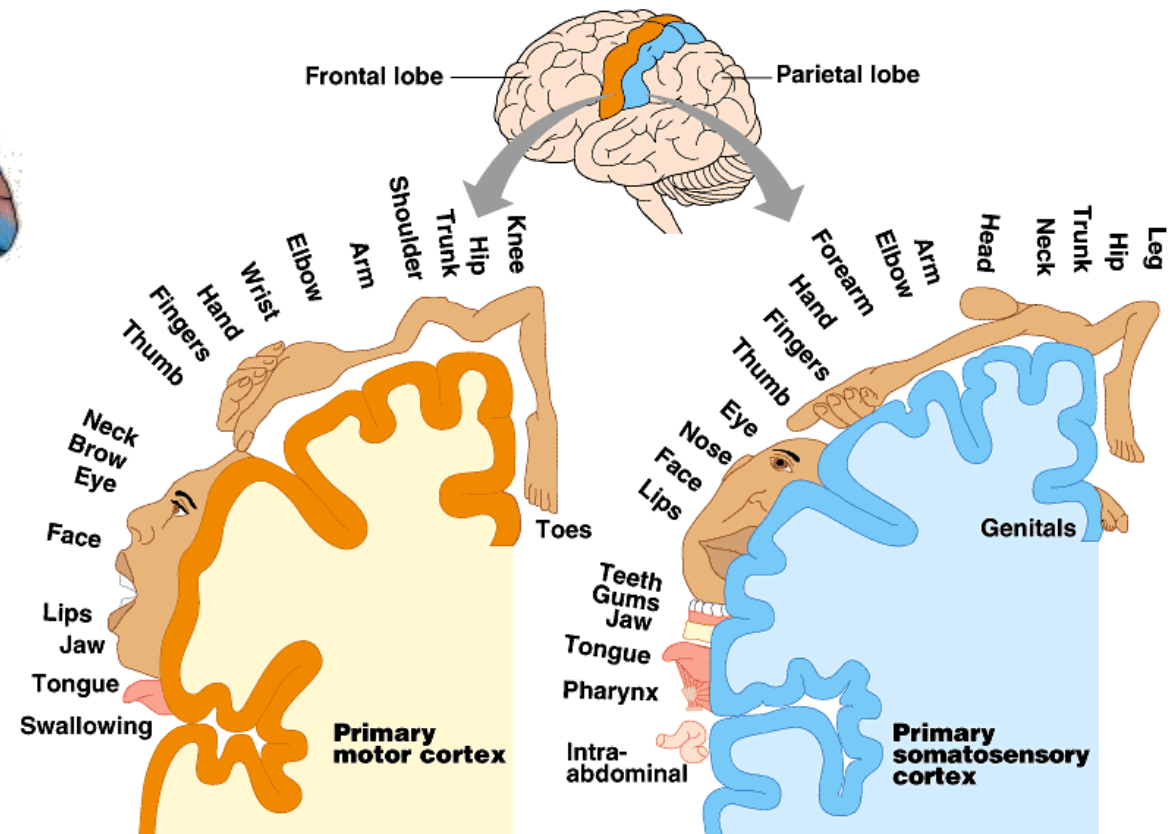


## Primary areas

- ✓ Somatotopic organization

## Association areas

- ✓ No somatotopic organization
- ✓ Unimodal
- ✓ Polymodal
- ✓ Association areas are thought to be the anatomical substrates of the highest brain functions—conscious thought, perception, and goal-directed action

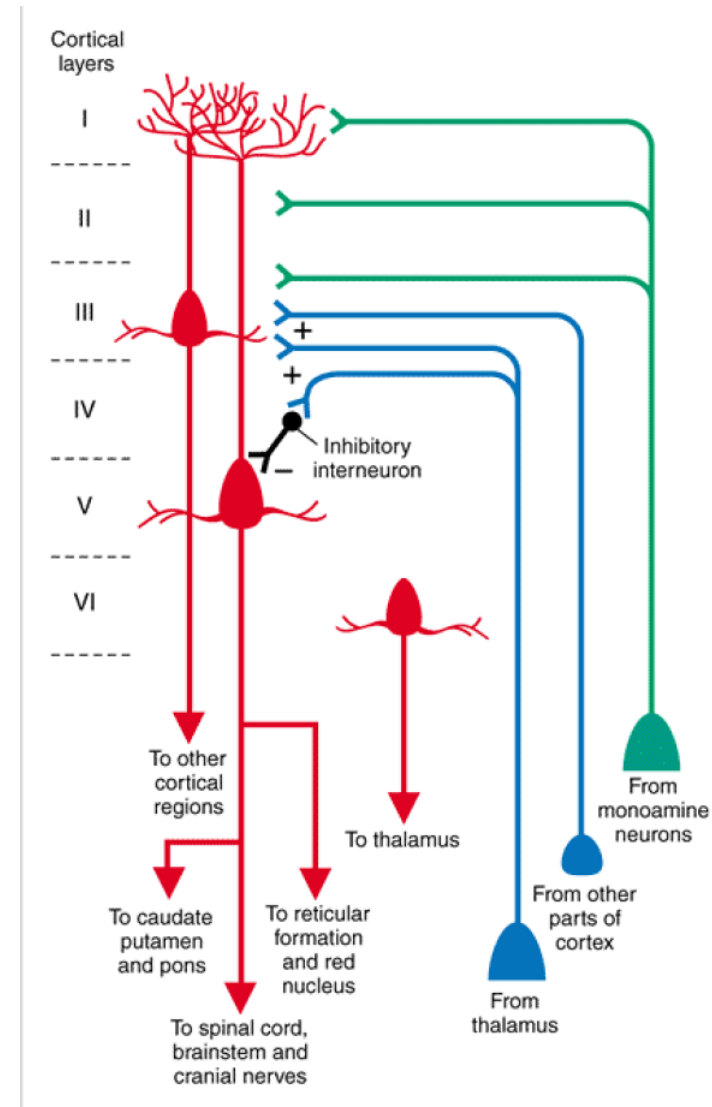


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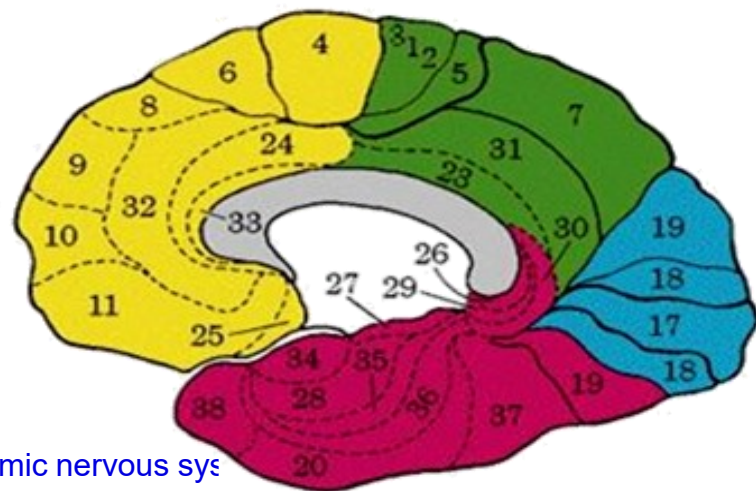
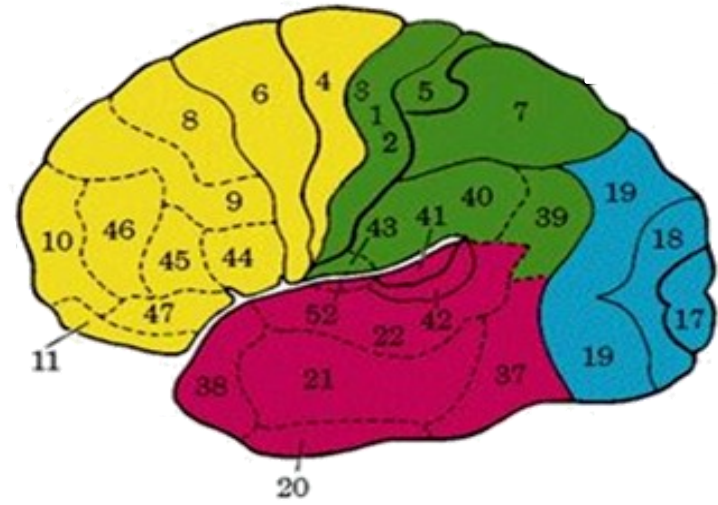
# Organization of neocortex

- Specific inputs/outputs to/from each layer
- Vertical and horizontal connections in each layer
- Each layer usually contains cells with similar functions
- Local differences in cytoarchitecture were used by Brodmann for construction of the map of brain areas





# Brodman areas

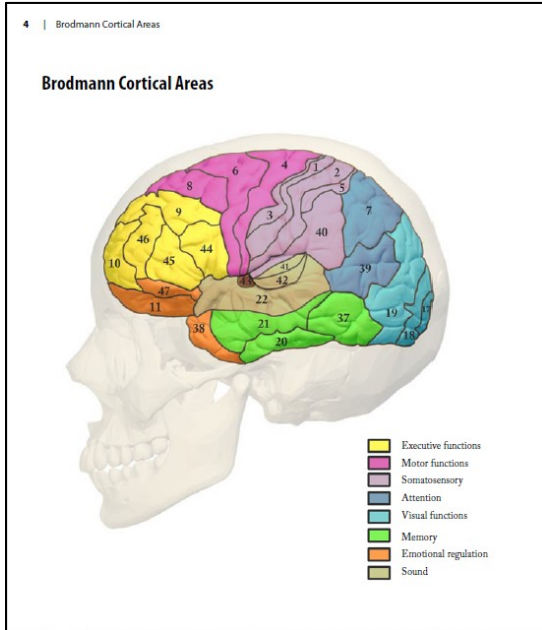


Brodman's #	NAME	FUNCTION
17	Occipital Lobe	Visual Projection Cortex
18		Visual Association Cortex
19	Posterior Parietal Lobe	Visual Association Cortex
37	Temporo-parietal-occipital area	General Sensory Association Cortex
39	Angular Gyrus	Word Recognition
40	Supramarginal Lobe	Somatosensory Association Cortex
1,2,3	Postcentral Gyrus	Somatosensory Projection Cortex
5, 7	Superior Parietal Lobule	General Sensory Association Cortex
41, 42	Middle 1/3 of Superior Temporal Cortex	Auditory Projection Cortex
22	Superior Temporal Gyrus	Auditory Association Cortex
21, 20, 38	Inferior Temporal Cortex	General Sensory Association Cortex
4	Precentral Gyrus	Primary Motor Cortex
1,2,3	Postcentral Gyrus	Somatosensory Projection Cortex
6,8,9	Premotor Cortex	Motor Association Cortex
41, 42	Middle 1/3 of Superior Temporal Cortex	Auditory Projection Cortex
44,45,46	Broca's Area	Motor Association Cortex - Specific to speech
10	Prefrontal Cortex	General Motor Association Cortex
11	Orbital Gyri	General Motor Association Cortex

Cortical Functions

REFERENCE

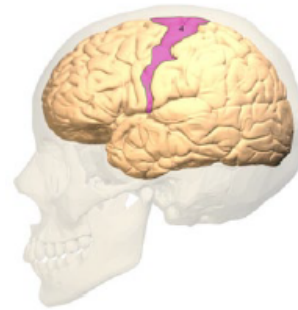
Trans Cranial Technologies



12 | Brodmann Cortical Areas

### Area 4 – Primary Motor Cortex

The human primary motor cortex is located on the anterior wall of the central sulcus. It also extends anteriorly out of the sulcus partly onto the precentral gyrus. Anteriorly, the primary motor cortex is bordered by a set of areas that lie on the precentral gyrus.



#### Clinical significance

Lesions of the precentral gyrus result in paralysis of the contralateral side of the body (facial palsy, arm-/leg monoparesis, hemiparesis).

#### Notes

According to functional neuroimaging techniques area 4 participates in three different groups of functions: Motor, somatosensory, and "others" ("verbal encoding during a non-semantic process", "attention to action", and "motor memory for visual landmarks").

Motor function is the traditional function, and occasionally it has been reported that the primary motor cortex reacts to sensory stimulation. Nonetheless, in these cases the primary motor activation is found in addition to a more extensive pattern of activation, obviously including sensory areas; that is, area 4 may some times be included in a brain circuitry supporting sensory perception; area 4 activation may reflect in those cases the implicit representation of a potential movement.

This implicit representation of movements can also account for "attention to action" and "motor memory".

The participation in "verbal encoding during a non-semantic process" is probably tangential, considering that it becomes activated (in addition to frontal and

temporal networks) only during "successful encoding", suggesting a certain role in the attentional process (increased muscle tone).

### Associated Functions

#### Motor

- Contralateral finger, hand, and wrist movements (Dorsal)
- Contralateral lip, tongue, face, and mouth movement (Lateral)
- Swallowing / laryngeal movement
- Contralateral lower limb (knee, ankle, foot, toe) movement (Mesial)
- Motor imagery
- Learning motor sequences
- Volitional breathing control
- Control of rhythmic motor tasks (i.e. bicycling)
- Inhibition of blinking / voluntary blinking
- Horizontal saccadic eye movements

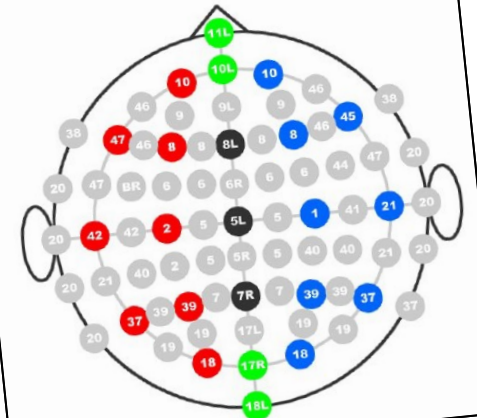
#### Somatosensory

- Kinesthetic perception of limb movements
- Vibrotactile frequency discrimination
- Finger proprioception
- Thermal hyperalgesia (contralateral)
- Response to touch/observed touch (Left)

#### Other

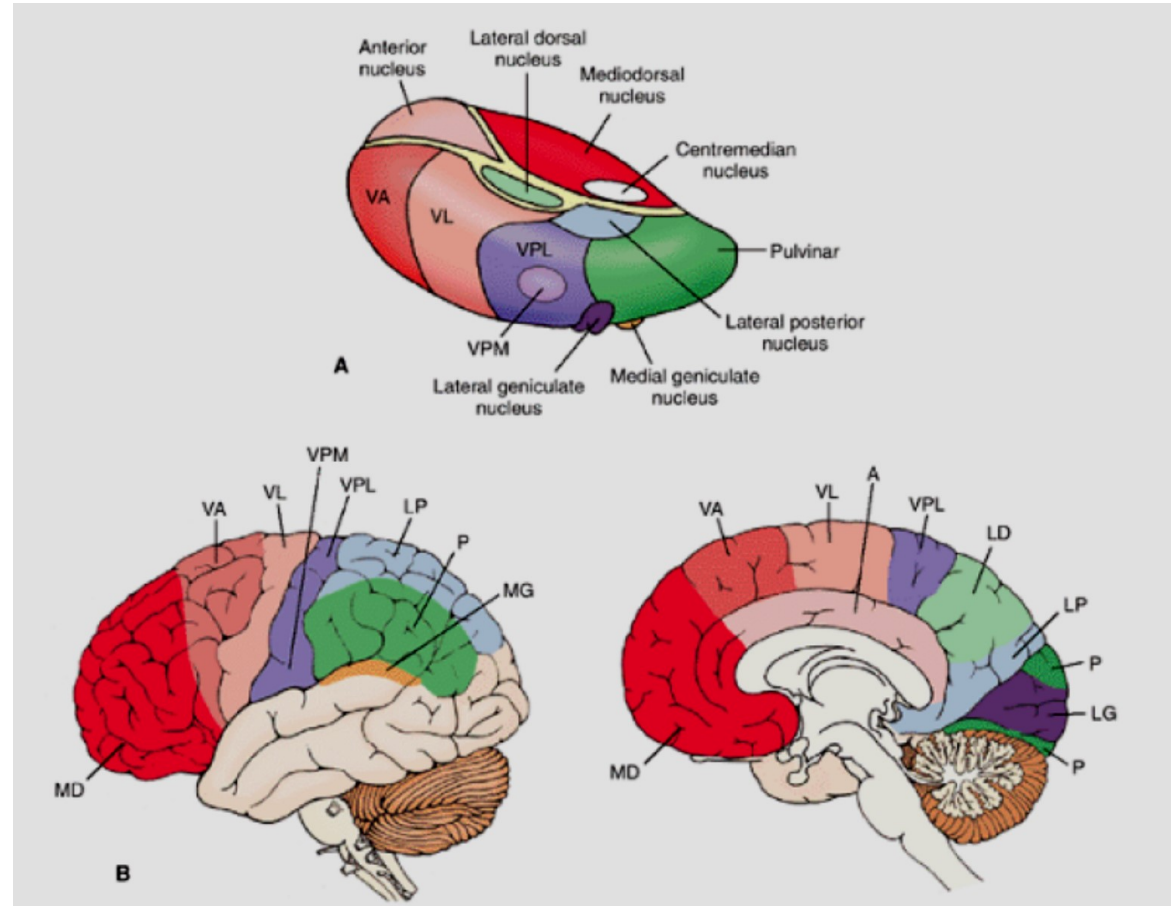
- Verbal encoding during a non-semantic process (Right)
- Attention to action (posterior)
- Topographic memory (motor memory) for visual landmarks

### Corresponding Brodmann Areas



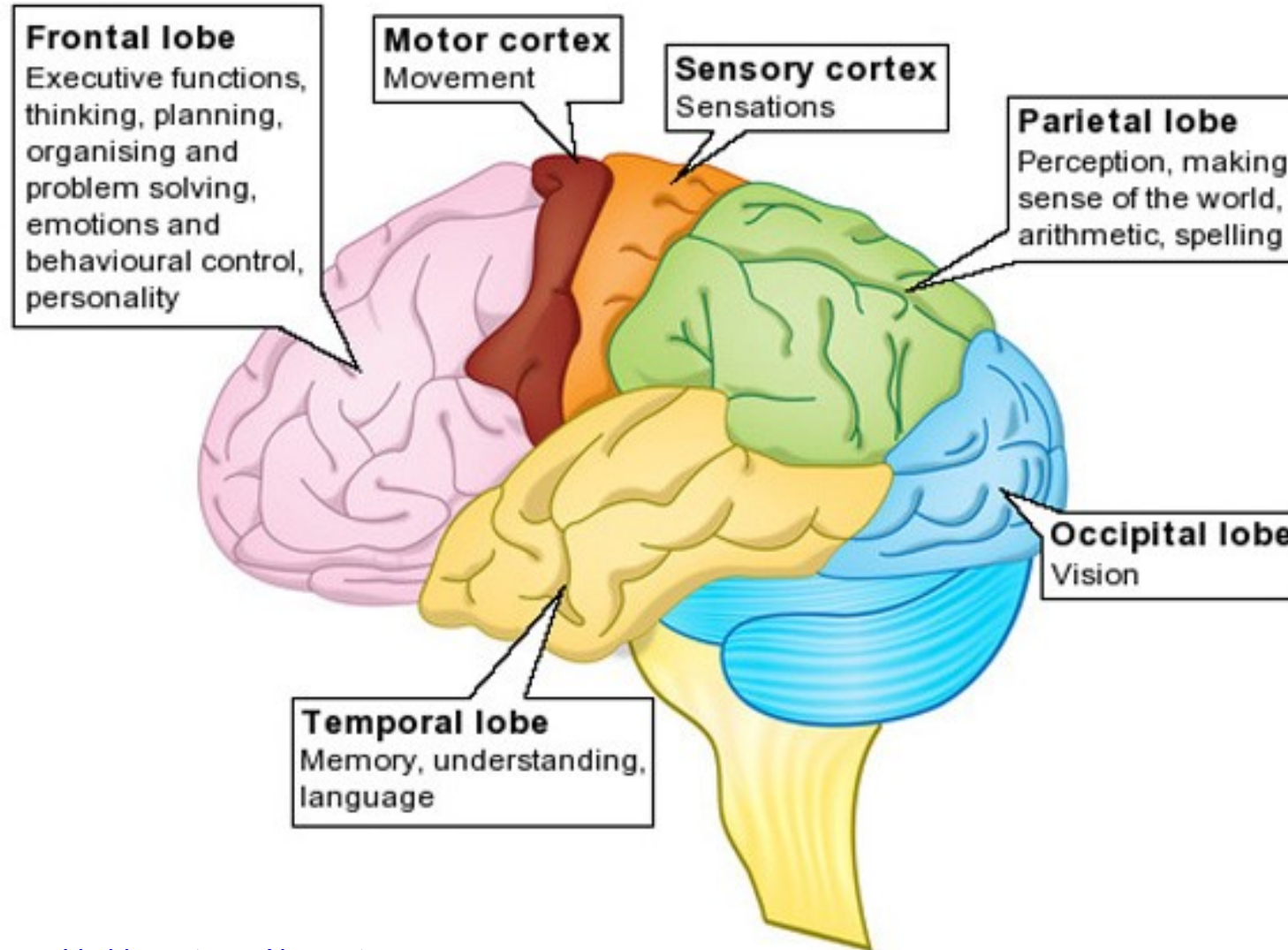
# Cerebral cortex and thalamus

- Close cooperation between cerebral cortex and thalamus
- Bilateral connections
- Almost all sensory information reaching cerebral cortex is gated by thalamus
- Exception - olfaction



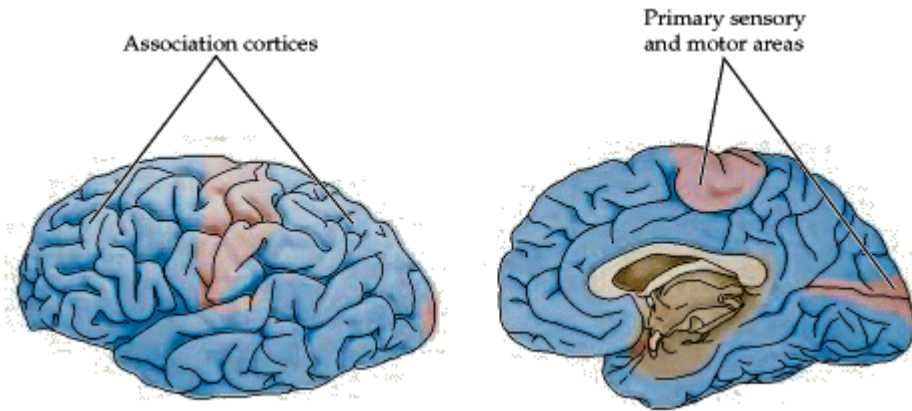
<http://www.slideshare.net/drpsdeb/presentations>

# Cortical functions

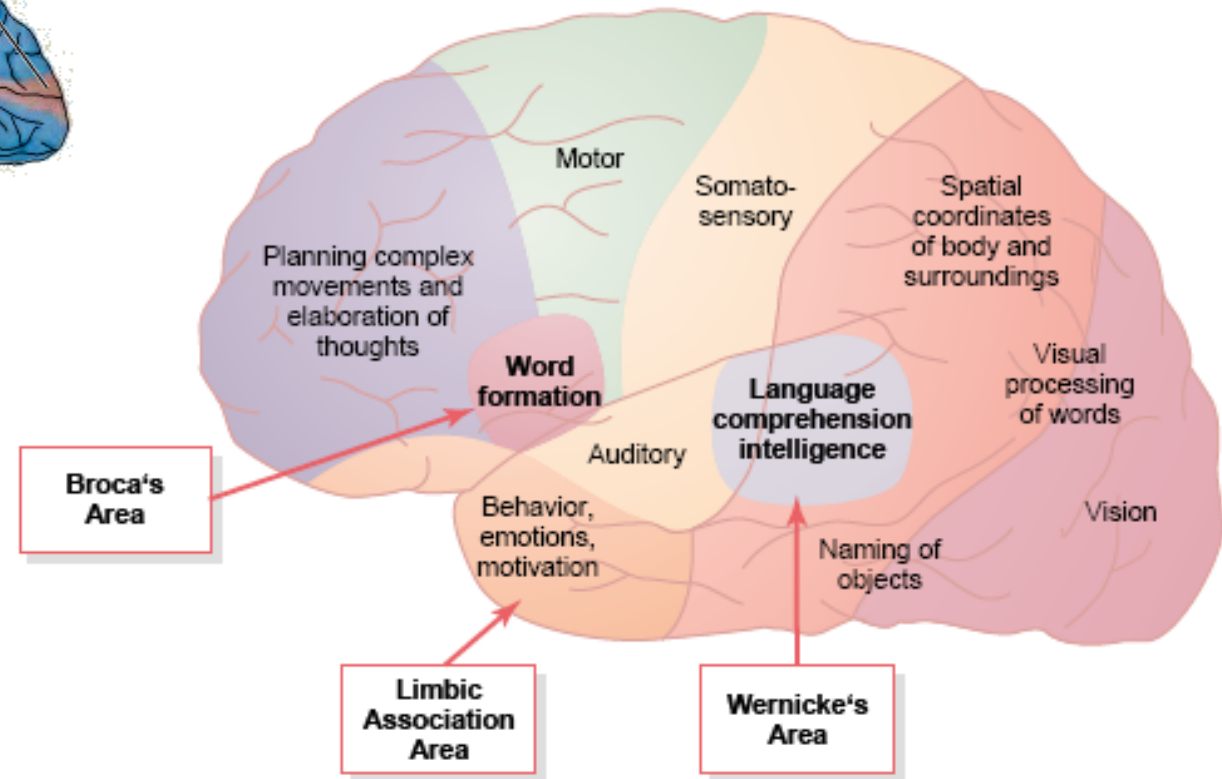




# Association areas

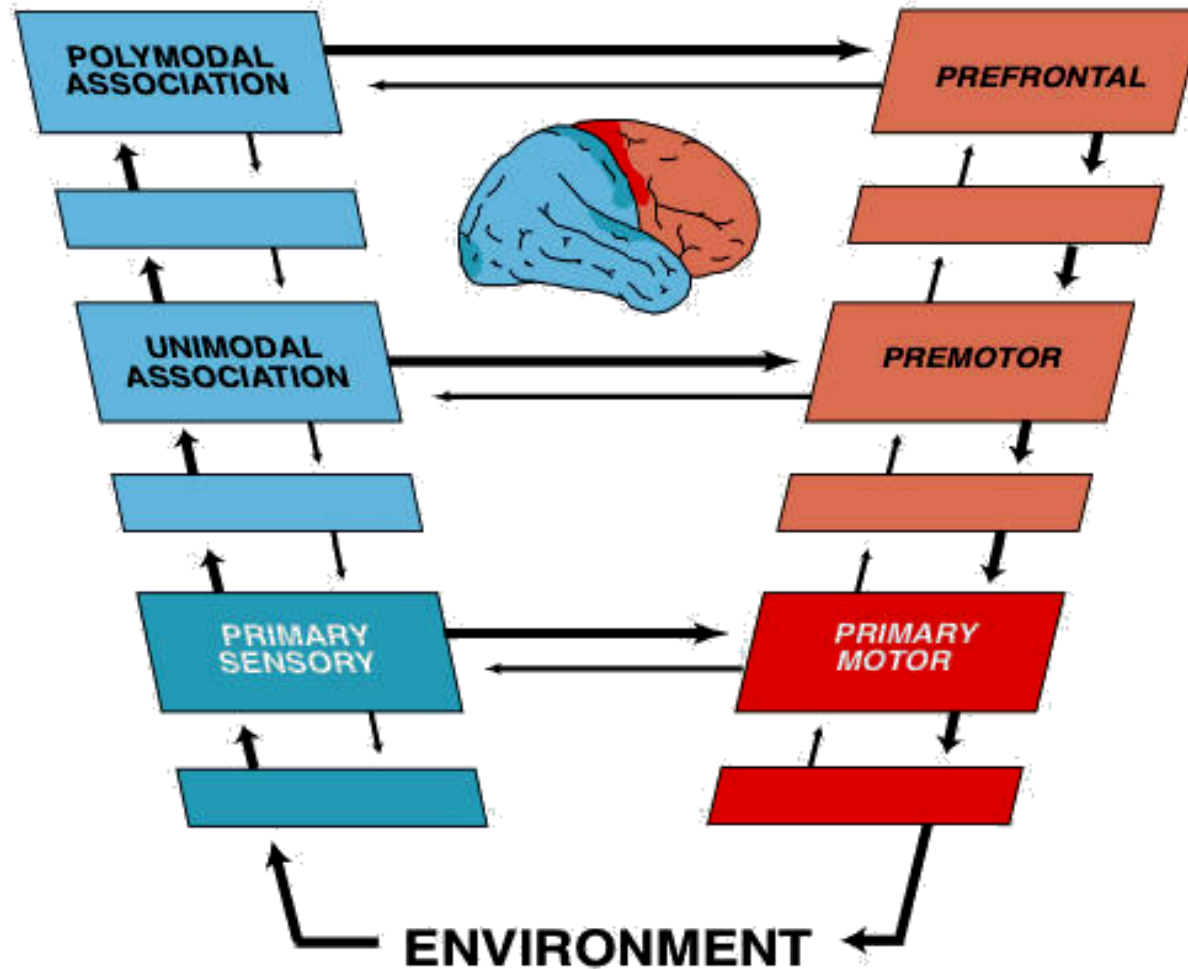


- Neither receptive
- Nor effector
- Integrative function
- Limbic
- Parieto-occipito-temporal
- Frontal



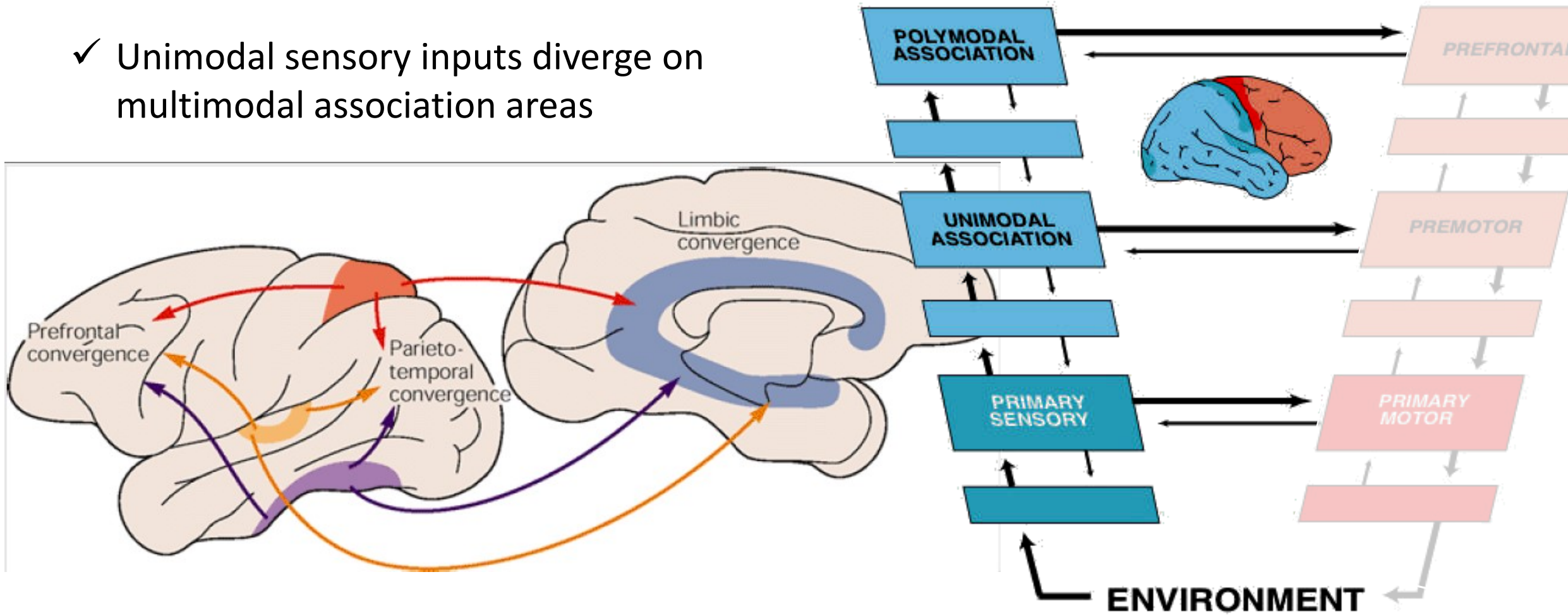


# Signal processing algorithm

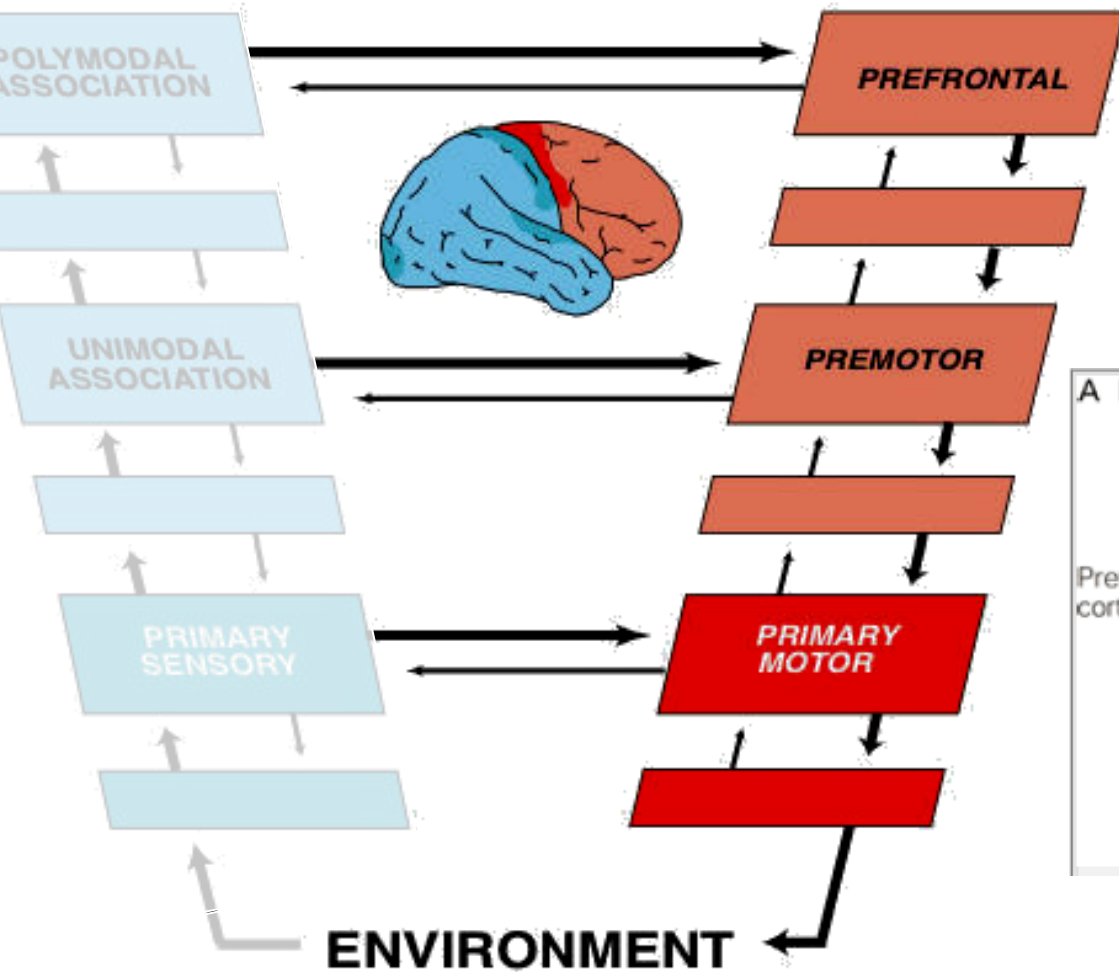


# Aferentation

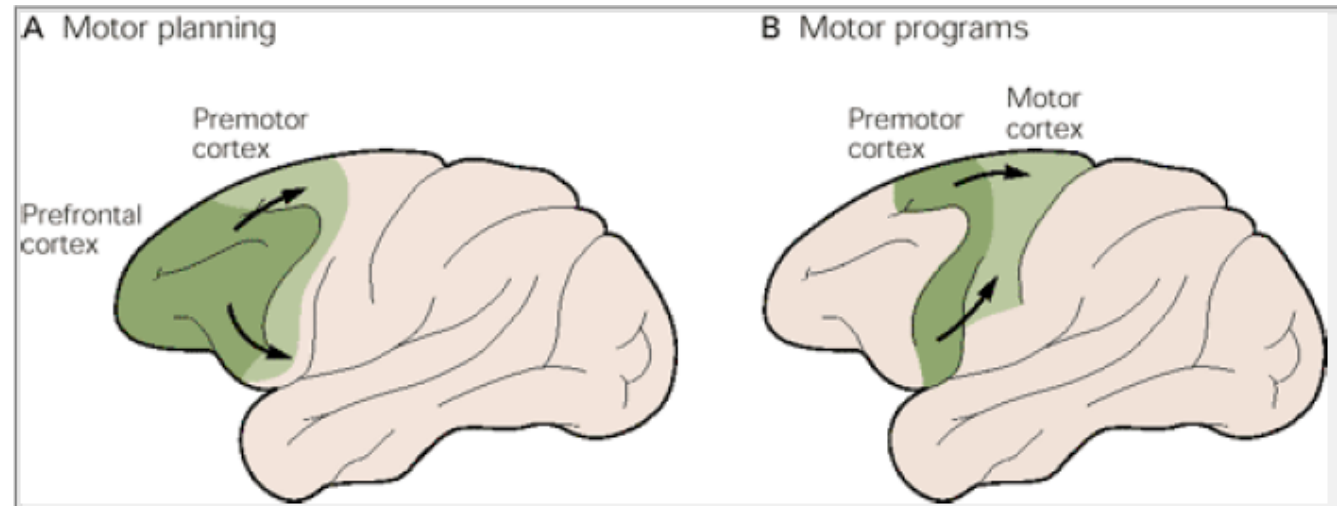
- ✓ Unimodal sensory inputs diverge on multimodal association areas



# Efferentation



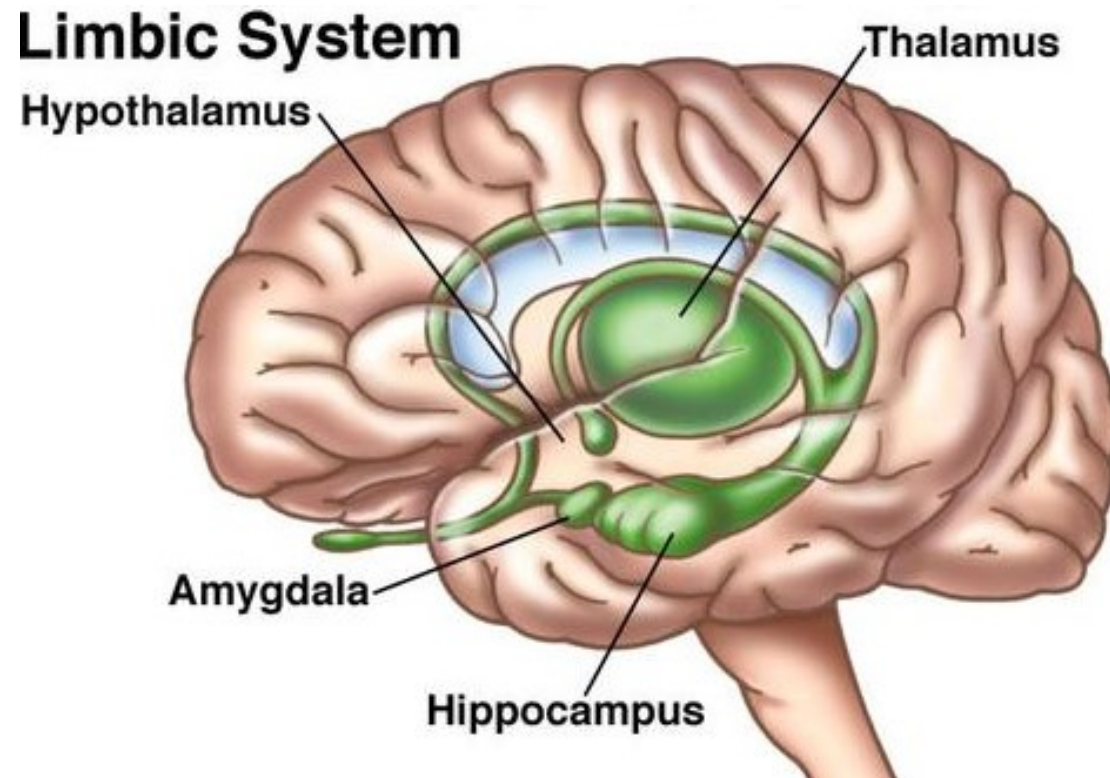
✓ The Sequence of Information processing Is Reversed in the Motor System



<http://www.slideshare.net/drpsdeb/presentations>

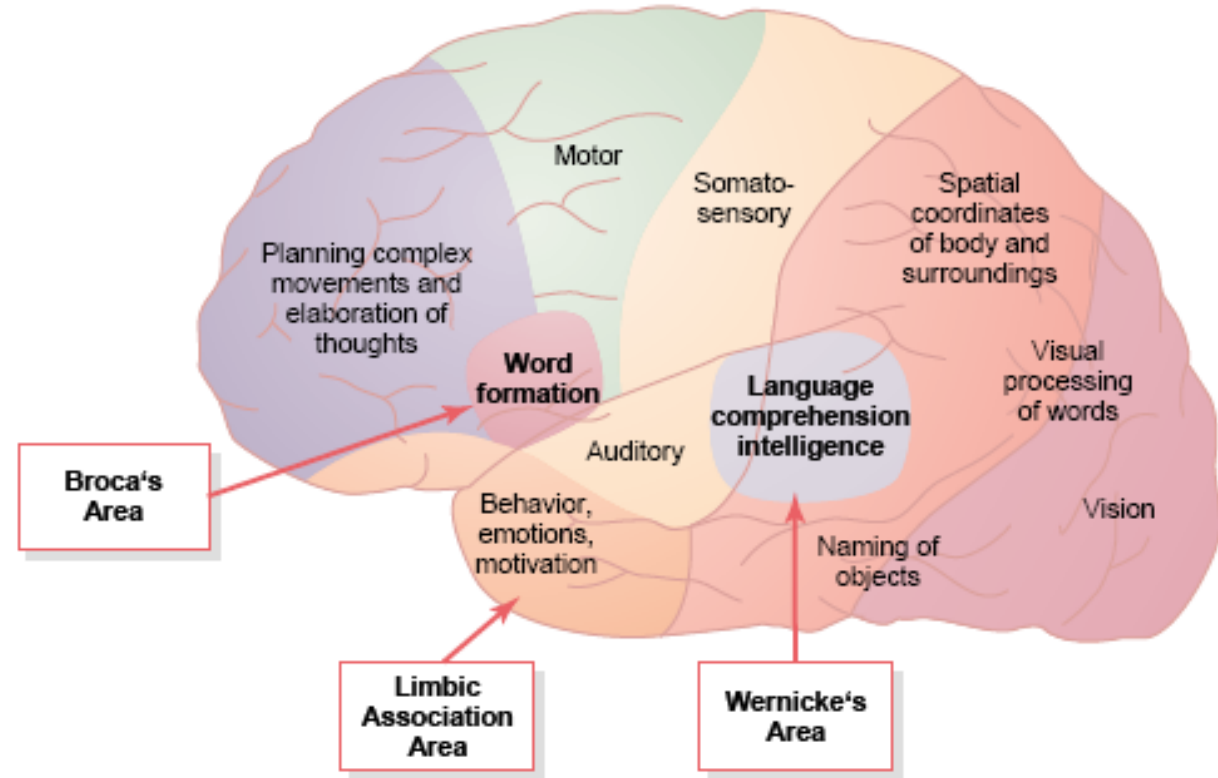
# Limbic association area

- Integration of information from inner and outer environment
- Hypothalamus
- Emotions
- Motivation
- Instinct behavior



# Parieto-occipito-temporal association area

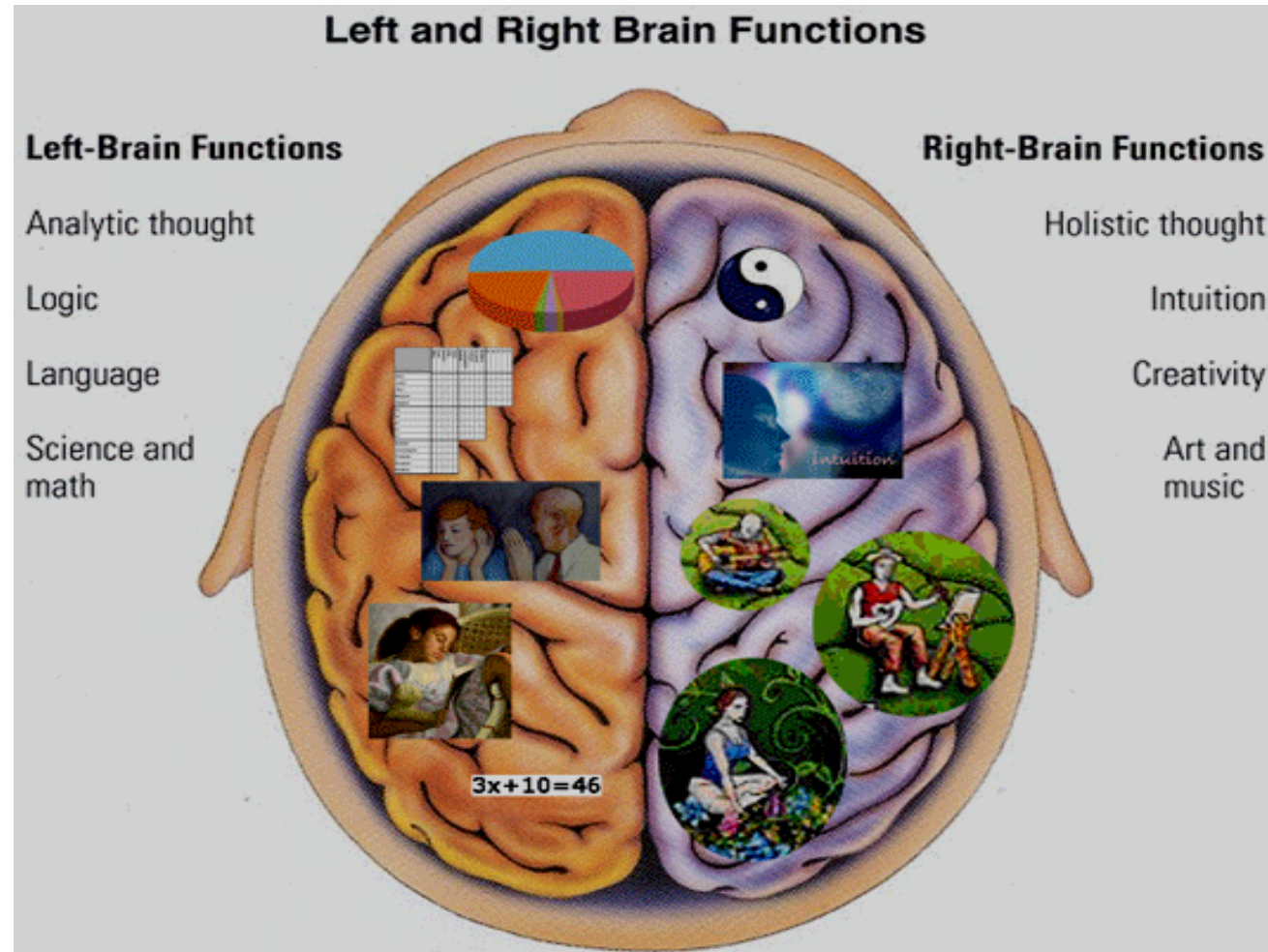
- Linkage and interpretation of information from several sensory modalities
- Visual – acoustic – sensory analysis
- Object recognition and categorization
- Language comprehension
- Attention



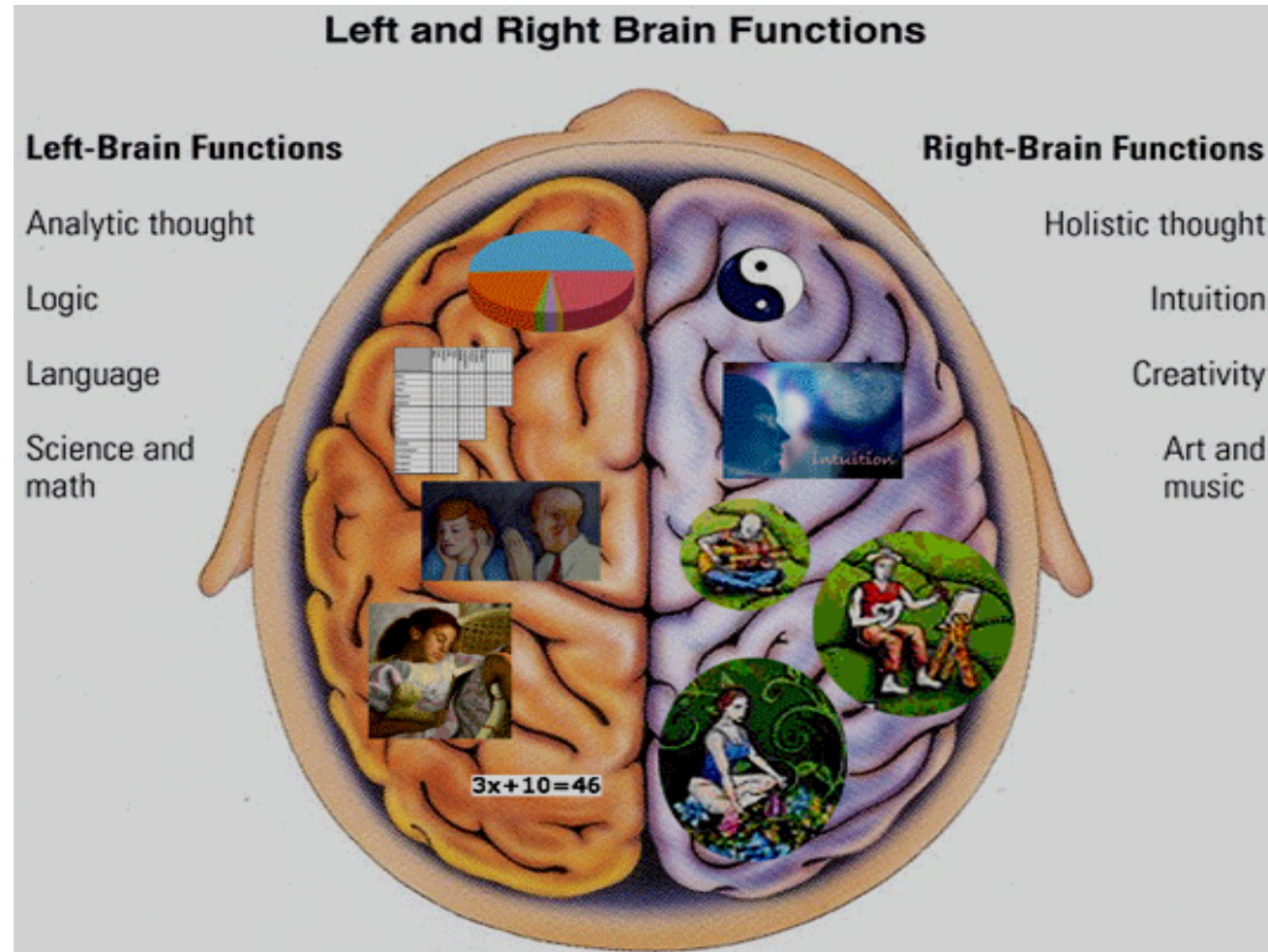
<http://www.slideshare.net/drpsdeb/presentations>



# Lateralization of cerebral functions



# Lateralization of cerebral functions



Aphasia

Acalculia

Tactile agnosia

Conceptual apraxia

Ideomotor apraxia

Orientation disorders

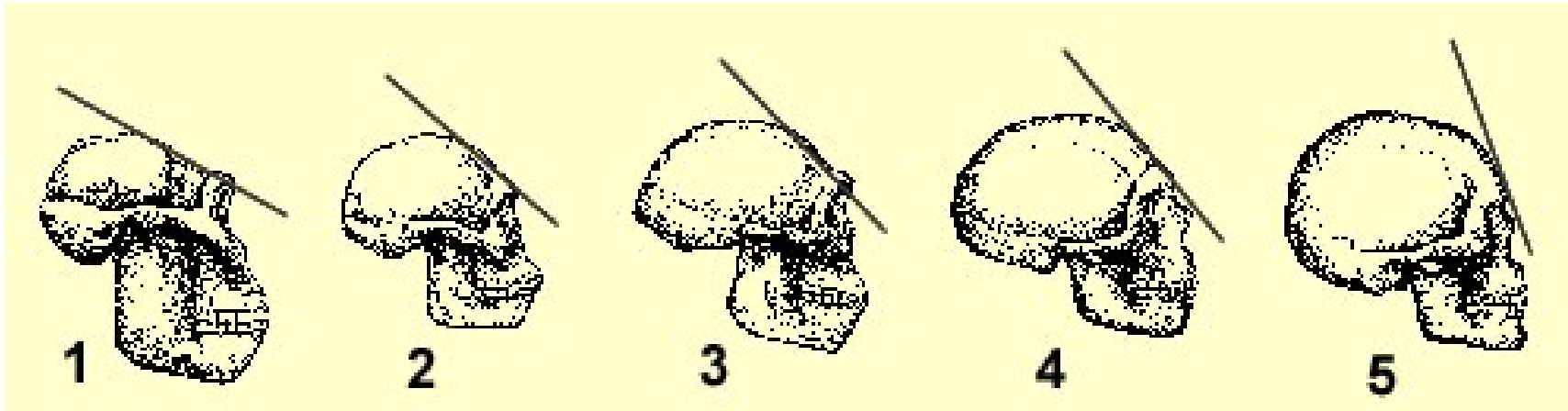
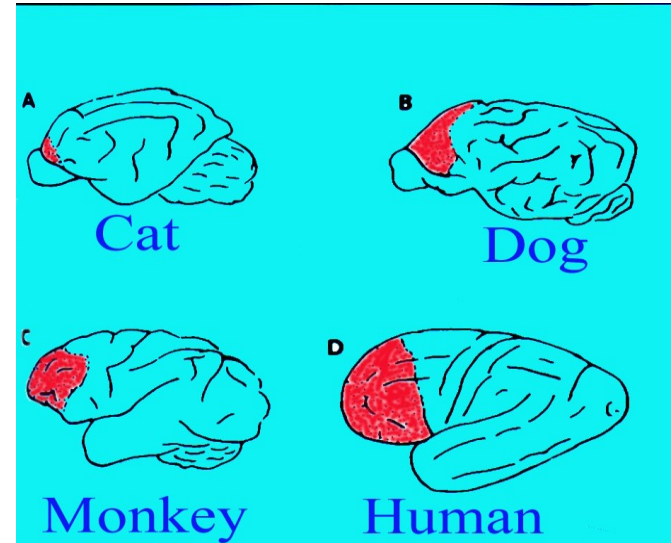
Constructional apraxia

Anosognosia

Neglect syndrome

# Frontal association area

- Executive function
  - Motor / behavioral
  - Cognitive
- Mostly developed in human

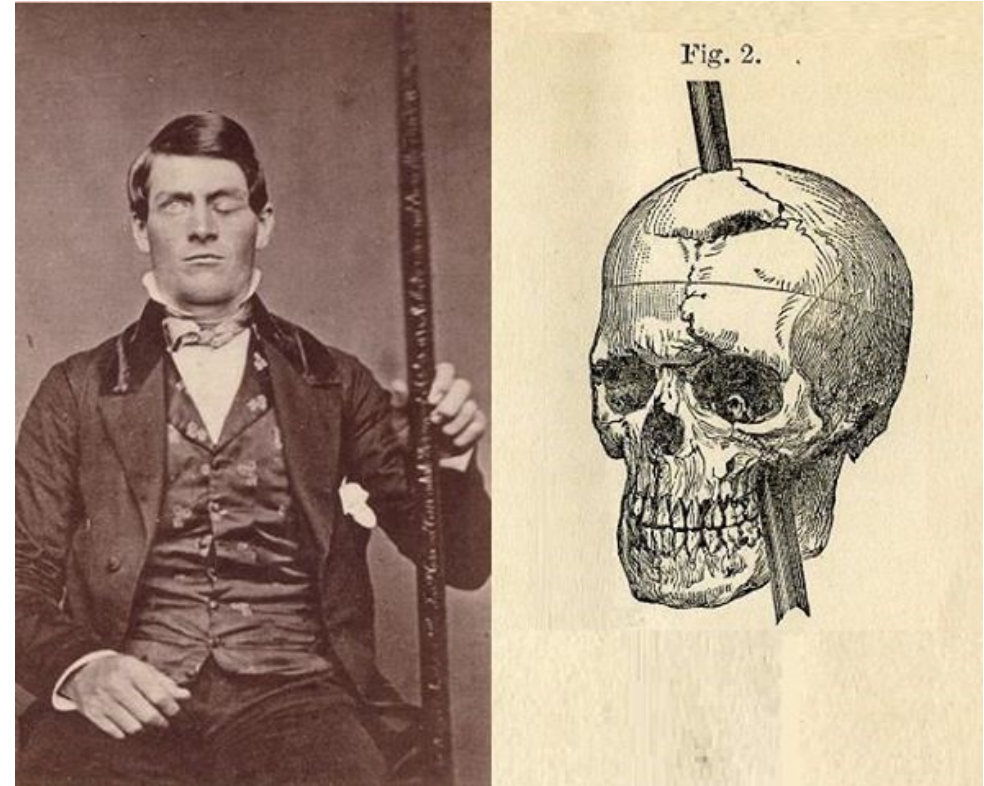


- Autonomic nervous system - Limbic system - Neocortex
- 1. *Australopithecus robustus* 2. *Homo habilis* 3. *Homo erectus*
  - 4. *Homo sapiens neanderthalensis* 5. *Homo sapiens sapiens*

<http://www.slideshare.net/drpsdeb/presentations>

# Phinease Gage (1823 – 1860)

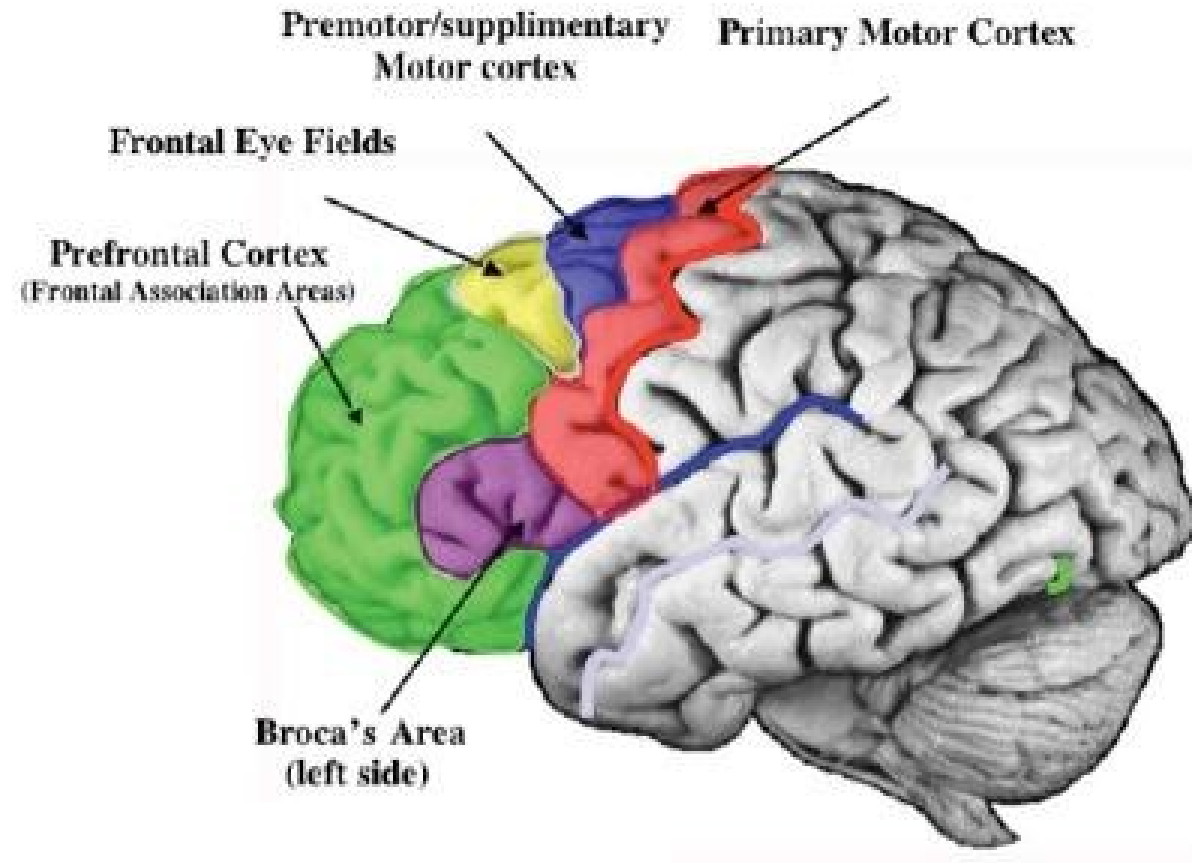
- 1848 – work injury
- Before injury
  - Reliable
  - Friendly
  - Responsible
  - Polite
- After injury
  - Unreliable
  - Hostile
  - Irresponsible
  - Rude
- 1860 – died from status epilepticus



[http://65.media.tumblr.com/553d3c3f3f579f57273b8598ec6739ab/tumblr\\_o11oqt0MUK1uaq7mqo1\\_1280.jpg](http://65.media.tumblr.com/553d3c3f3f579f57273b8598ec6739ab/tumblr_o11oqt0MUK1uaq7mqo1_1280.jpg)



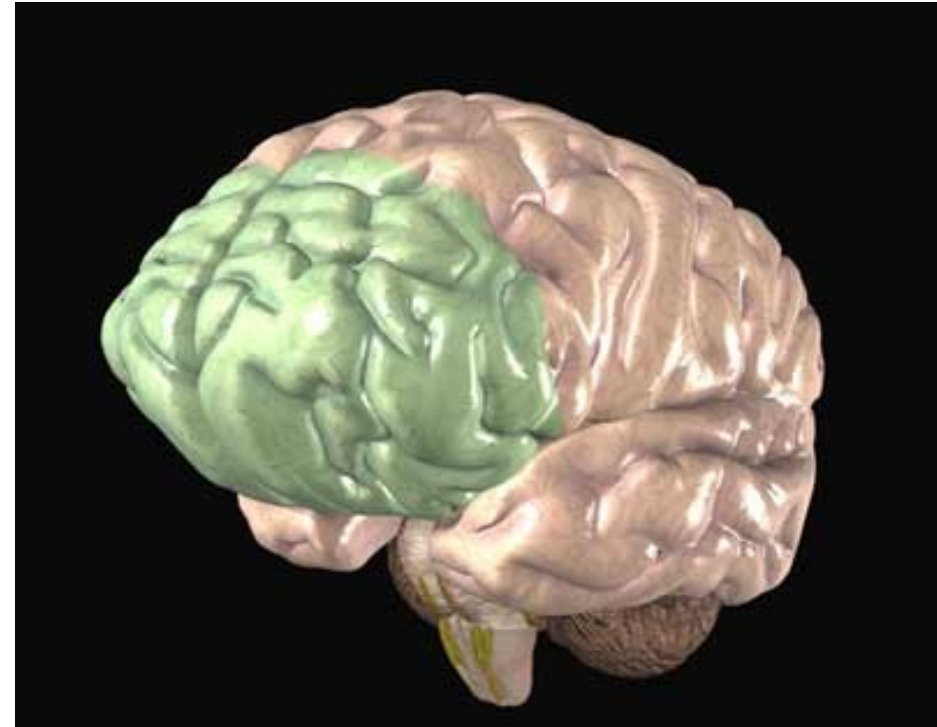
# Frontal lobe





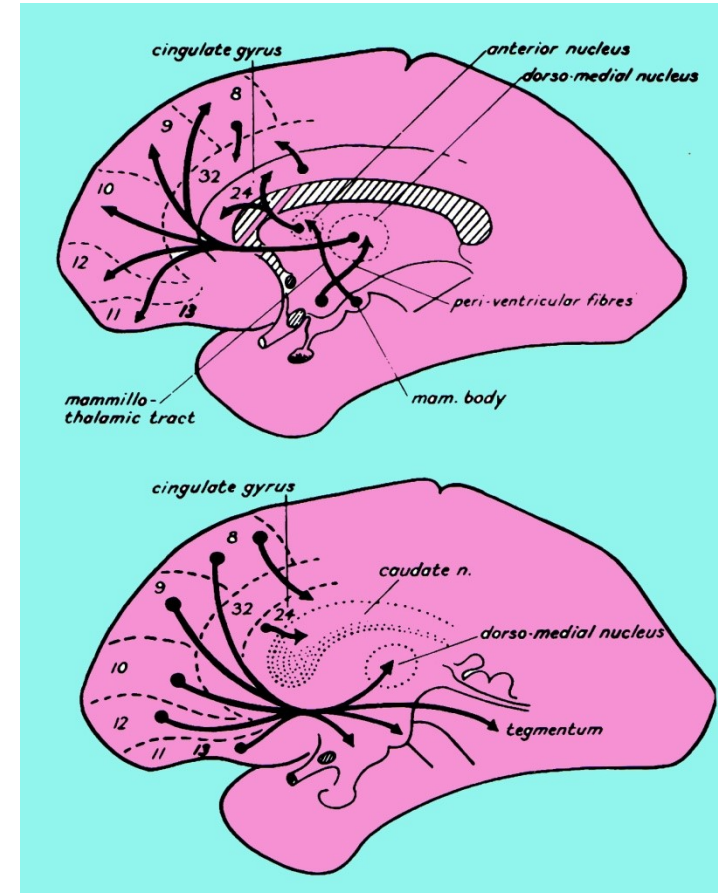
# Frontal association area

- ~ 1/3 of neocortex
- One of the evolutionary youngest cortical areas
- Late development in ontogeny
  - Differentiation during the 1st year of life
  - Mostly developed around the 6th year of life
  - ? End of maturation around the 20th year of life?



# Frontal association area

- Input from association cortex
  - P-O-T association area
  - Limbic association area
- Reciprocal connections:
  - prefrontal processing modulates perceptual processing
  - „Loops“
- Input to premotor areas



<http://www.slideshare.net/drpsdeb/presentations>

# Functions of frontal association area

- Motor/non-motor planning/organization - strategy - anticipation

- Thinking – mental models processing

- Attention – „information filtering“

- Behavioral control
  - Facilitation of „wanted“
  - Inhibition of „unwanted“



<http://thenextweb.com/wp-content/blogs.dir/1/files/2015/03/jerry1.jpg>



<http://thenextweb.com/wp-content/blogs.dir/1/files/2015/03/jerry1.jpg>

# Frontal lobe and mental arousal

- Right frontal lobe
  - Bilateral influence
  - Inhibition
- Left frontal lobe
  - Unilateral influence
  - Activation
- Left frontal lobe damage
  - Reduced spontaneous activity
  - Reduced self-control; impulsive instinct behavior



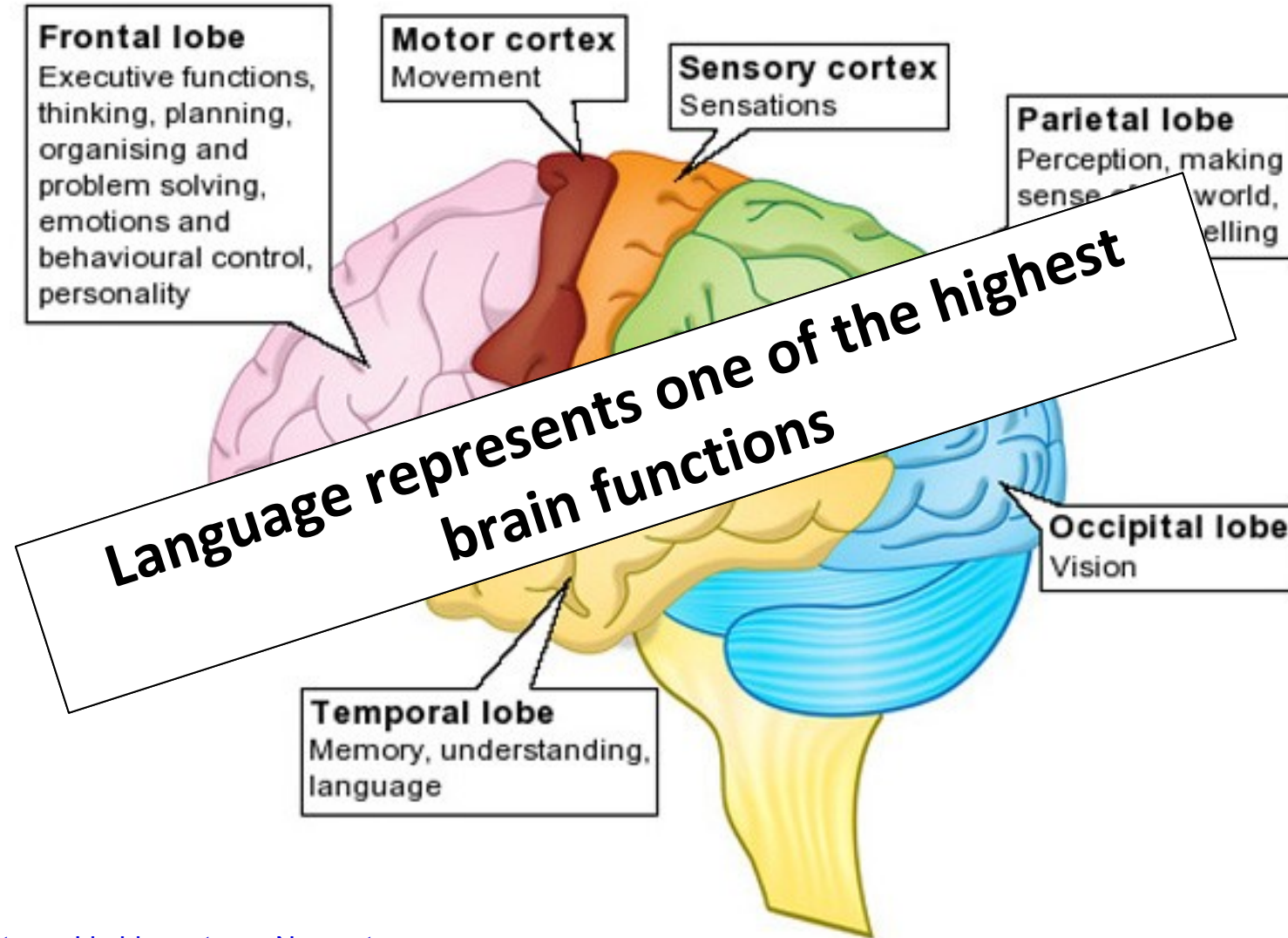
<http://www.anna-om-line.com/BRAIN-GRAPHICS-by-annaOMline.jpg>

# Frontal lobe functions

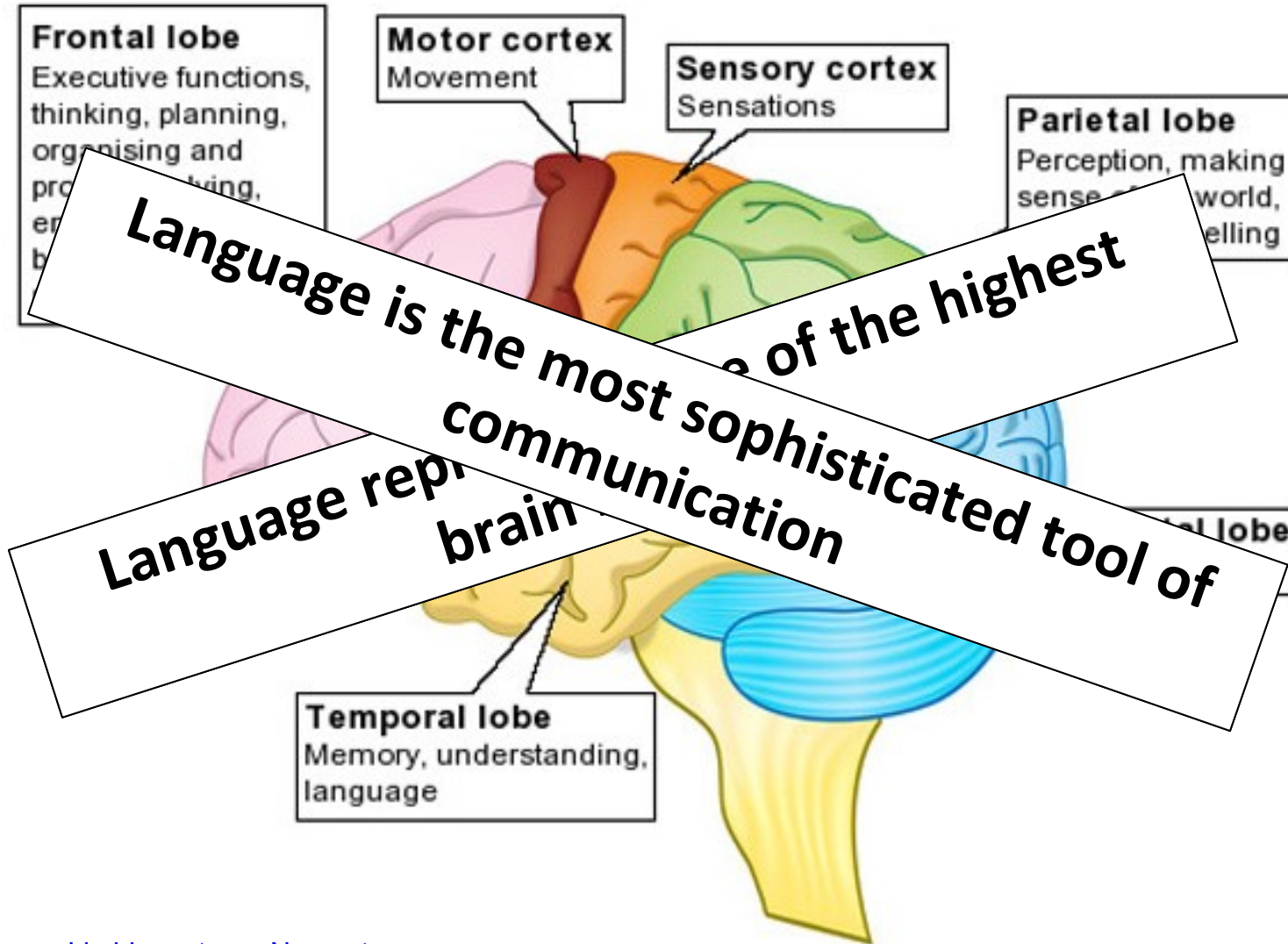
<b>Motor</b>	<b>Cognitive</b>	<b>Behavior</b>	<b>Arousal</b>
Voluntary movements	Memory	Personality	Attention
Language Expression	Problem solving	Social and sexual	
Eye movements	Judgment	Impulse control	
Initiation	Abstract thinking	Mood and affect	
Spontaneity			



# Cortical functions

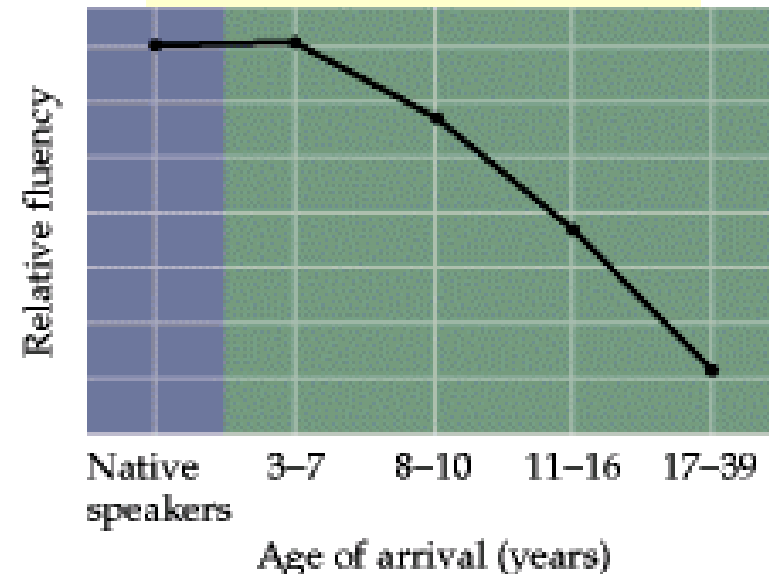
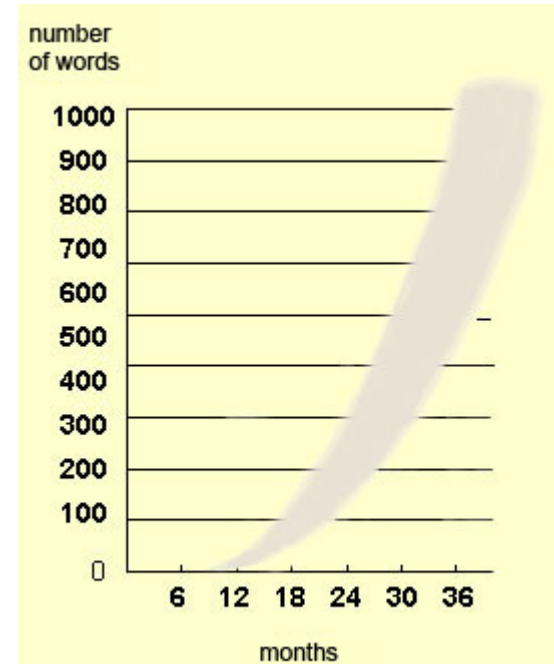


# Cortical functions



# Learning to speak

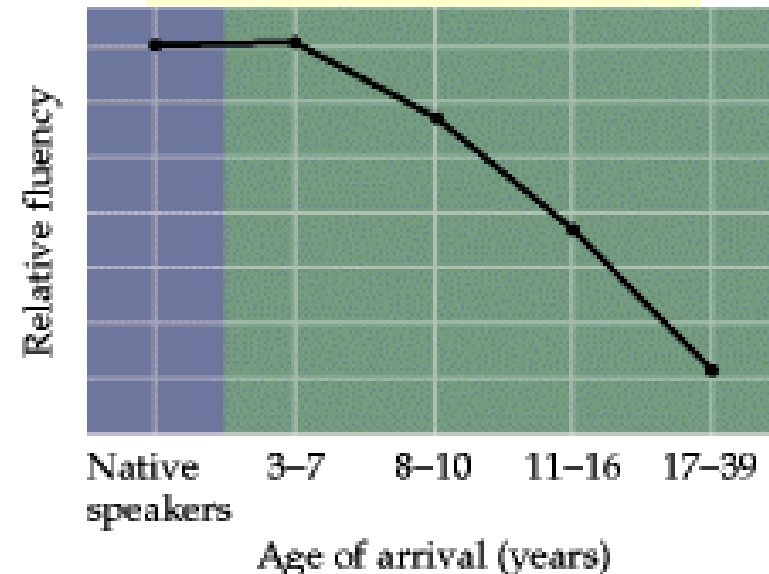
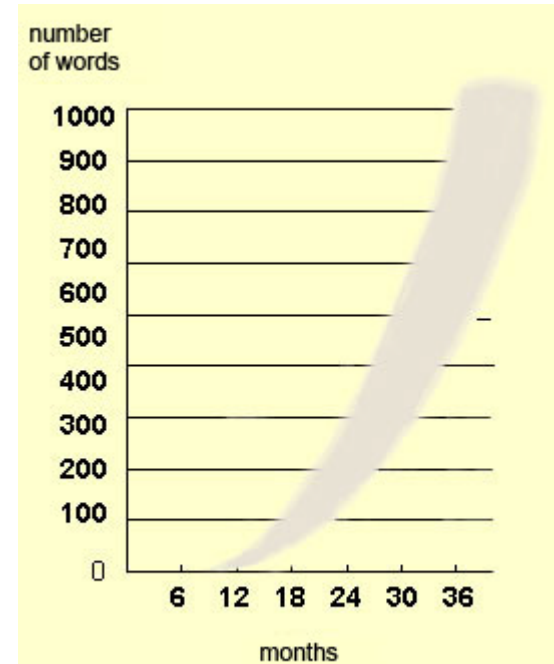
- Learning to speak takes a long time period
  - Understanding – „sensoric“
  - Speaking – „motor action“
- 7.-12. month – baby begins to understand simple orders
- 1. year – baby uses a couple of words
- 2.-5. years – baby masters syntax rules
- 6. years – child uses around 2500 words



<http://www.slideshare.net/drpsdeb/presentations>

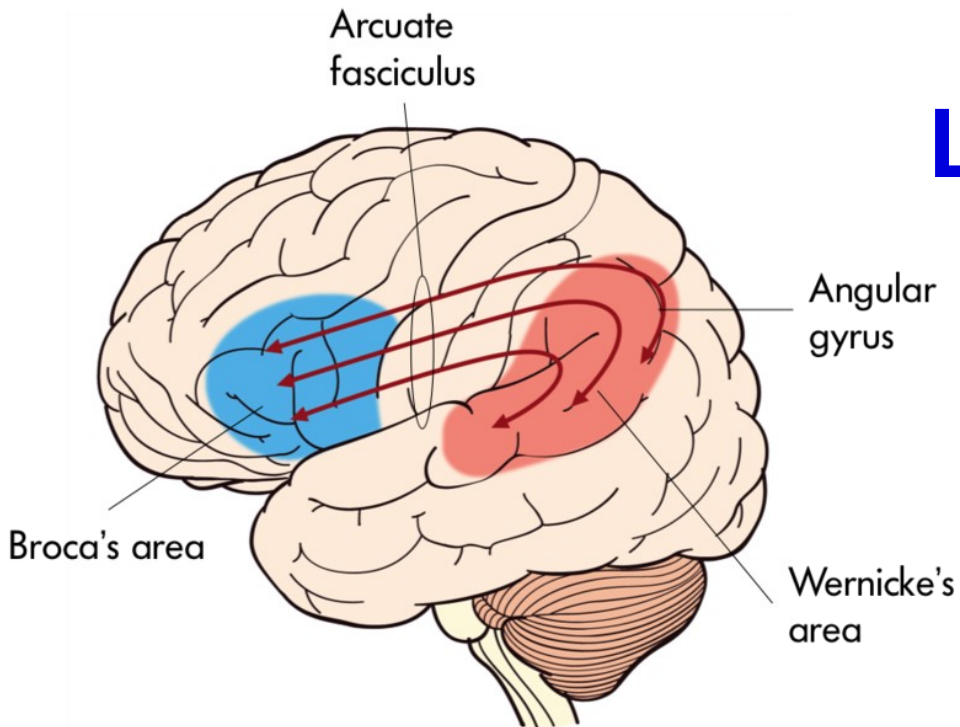
# Learning to speak

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- 6. years – child uses around 2500 words
- Adult vocabulary
  - Active: 3000 -10 000 words
  - Passive: 3-6x higher than active v.



<http://www.slideshare.net/drpsdeb/presentations>

# Language areas



<http://www.slideshare.net/CsillaEgri/presentations>

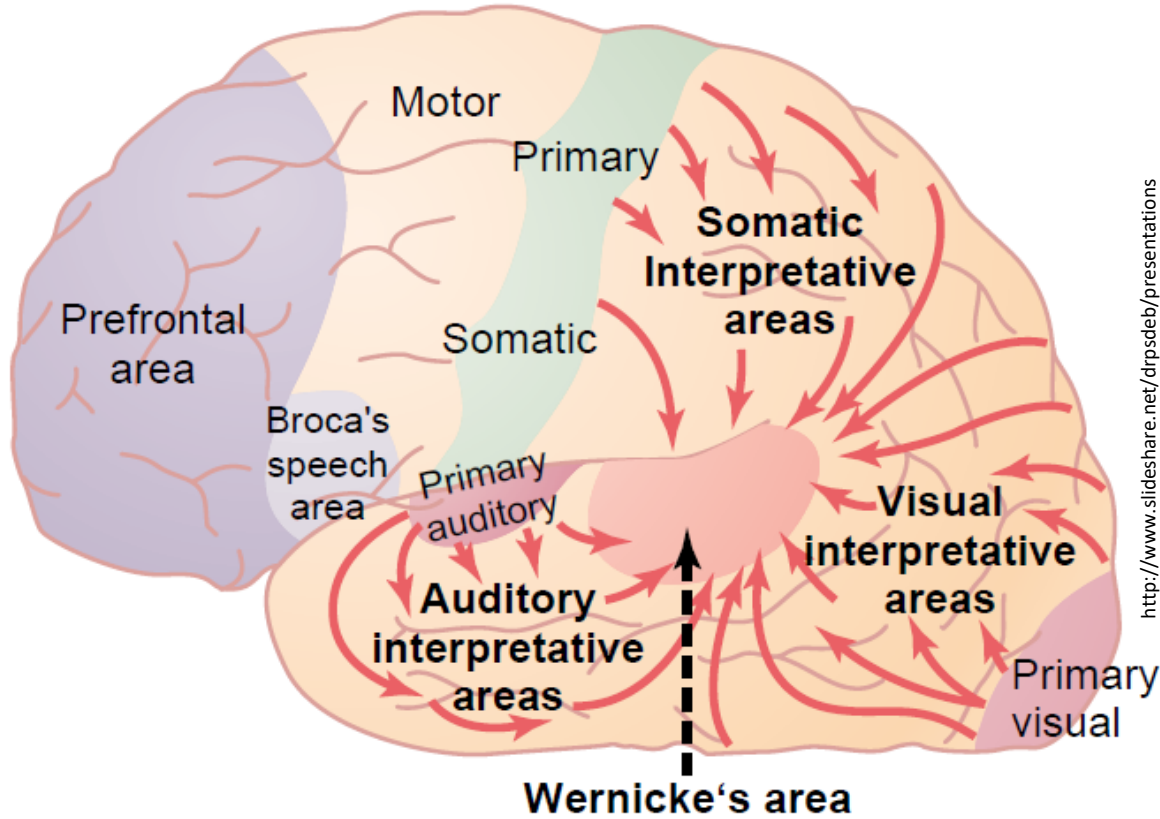
## There are two main language areas

- Broca's area (motor)
  - ✓ Close to motor cortex
- Wernicke's area (sensor)
  - ✓ Close to auditory cortex
- Fasciculus arcuatus

- Broca's aphasia
  - ✓ Motor, expressive
  - ✓ Comprehension preserved, speech unarticulated
- Wernicke's aphasia
  - ✓ perceptive, sensor
  - ✓ Comprehension damaged, speech fluent, but not meaningful
- Conduction aphasia
  - ✓ Damage of fasc. arcuatus
  - ✓ Speech fluent, comprehension preserved
  - ✓ Problem with repeating words and sentences
- Dysarthria
  - ✓ Problem with articulation
  - ✓ For example, damage of vocal cord ...

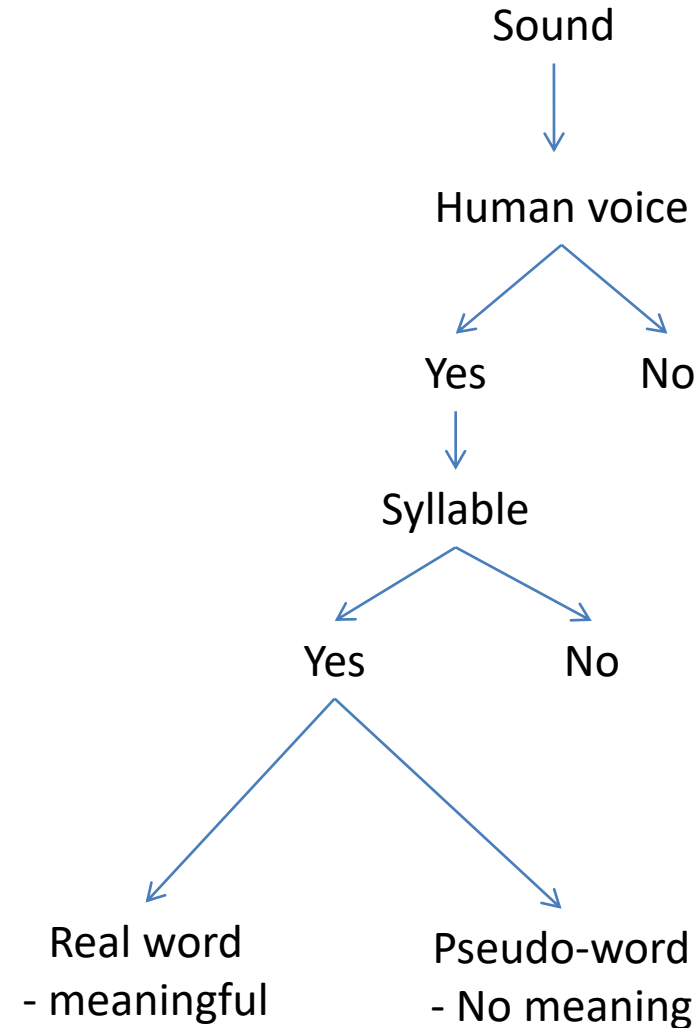


# Algorithm of sound processing

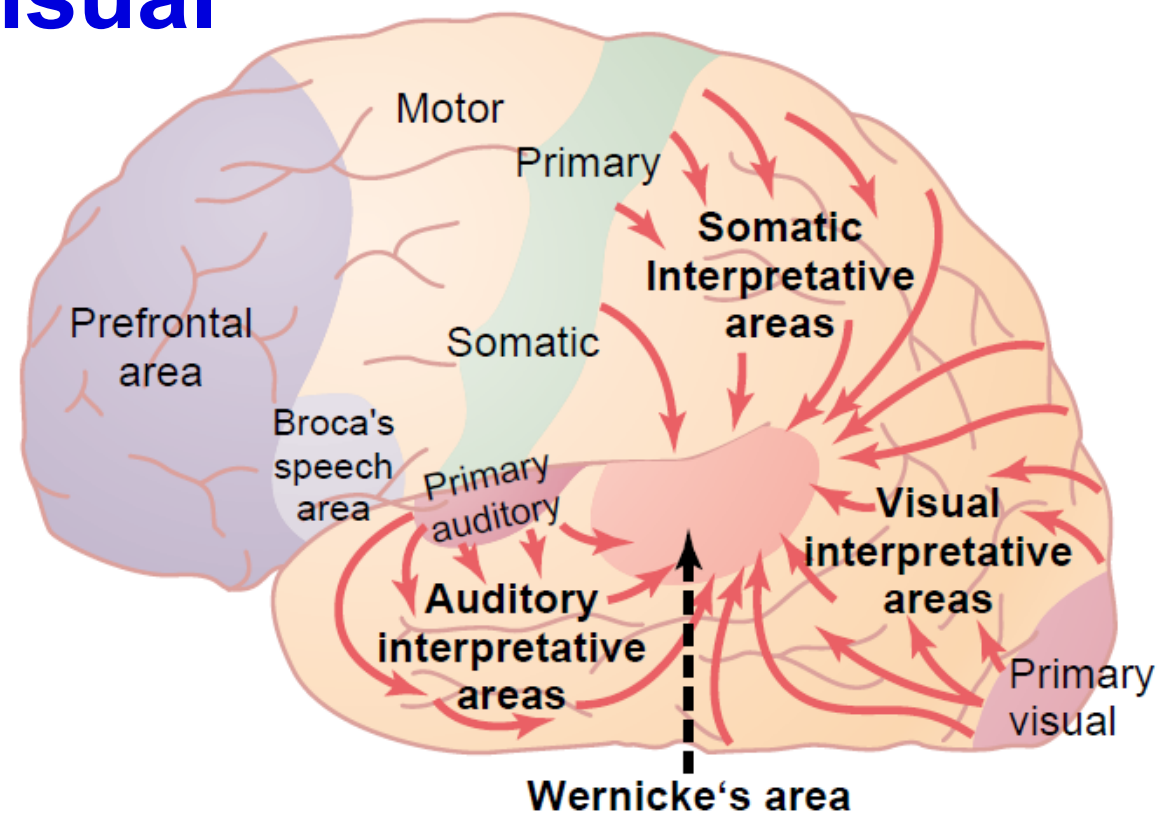


<http://www.slideshare.net/drpsdeb/presentations>

- ✓ Wernicke's area
- ✓ Broca's area
- ✓ P-O-T association cortex



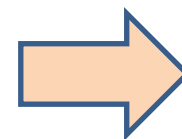
# Integration of auditory, visual and somatosensory information



**P - O - T association cortex**

**Lobulus parietalis inferior**

- Interpretation of sound
- Interpretation of visual signal
- Interpretation of somatosensation
- Interpretation of spoken/read word



**Categorization**

# Language functions lateralization

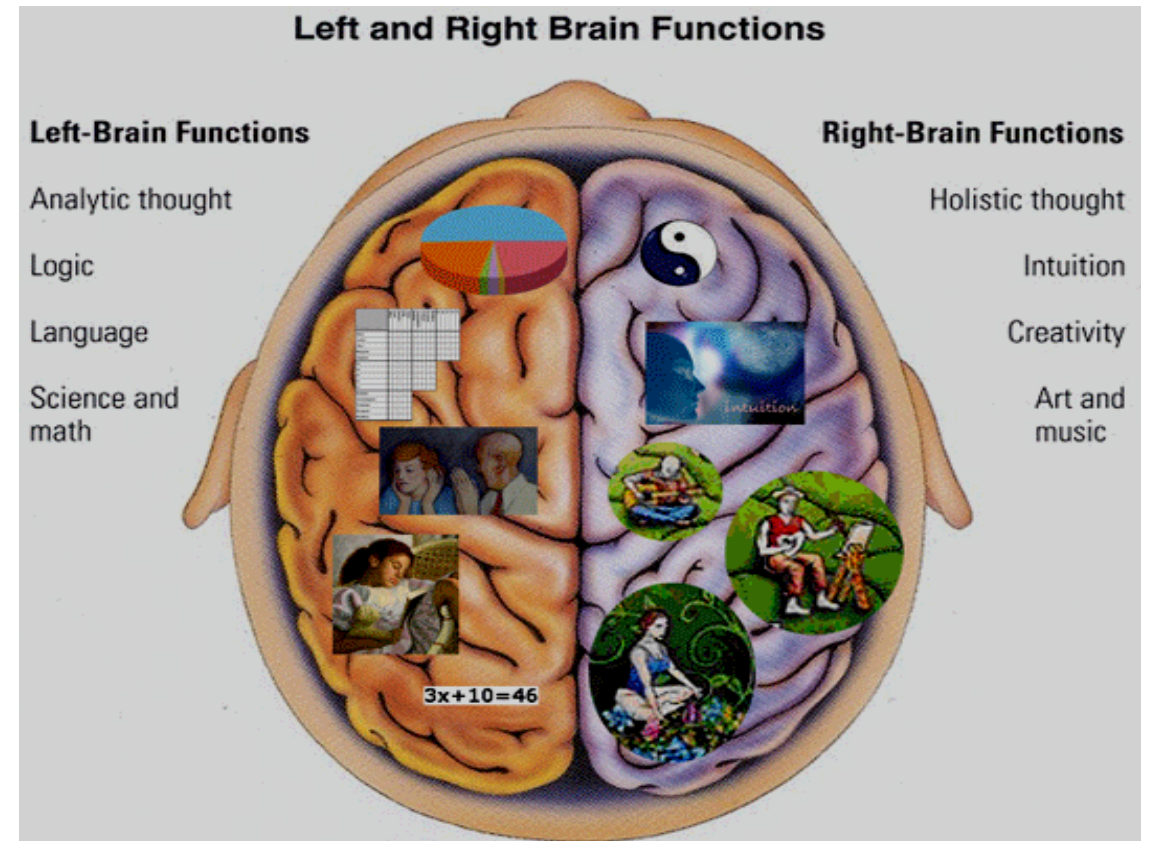
- Broca's and Wernicke's area is localized in the left hemisphere in 97% of people
- Localization of B-W areas is not fully linked to left/right hand lateralization
  - ✓ 90% of people are right handed
  - ✓ 95% of right handed people have B-W area in the left hemisphere
  - ✓ The majority of left handed people has B-W areas also in left hemisphere

# Language functions lateralization

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  - ✓ 90% of people are right handed
  - ✓ 95% of right handed people have B-W area in the left hemisphere
  - ✓ The majority of left handed people has B-W areas also in left hemisphere
- Some scientists suggest that the left hemisphere dominance for language evolved from this hemisphere's better motor control
- The language specialization develops in the left hemisphere, which matures slightly earlier

# Right hemisphere language functions

- Non-verbal aspect of language
  - ✓ Prosody – intonation, stress...
- Non-literal language aspects
  - ✓ Irony
  - ✓ Metaphors
- Understanding to discourse / complex speech
  - ✓ Lecture, discussion



<http://www.slideshare.net/drpsdeb/presentations>



# Women and language

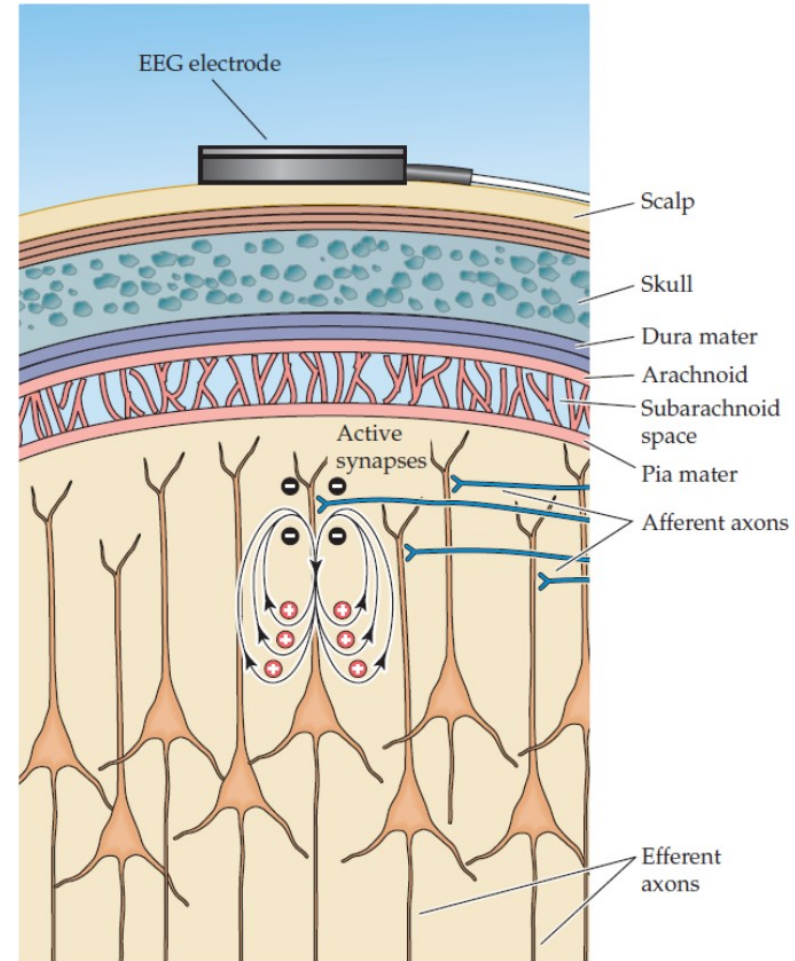
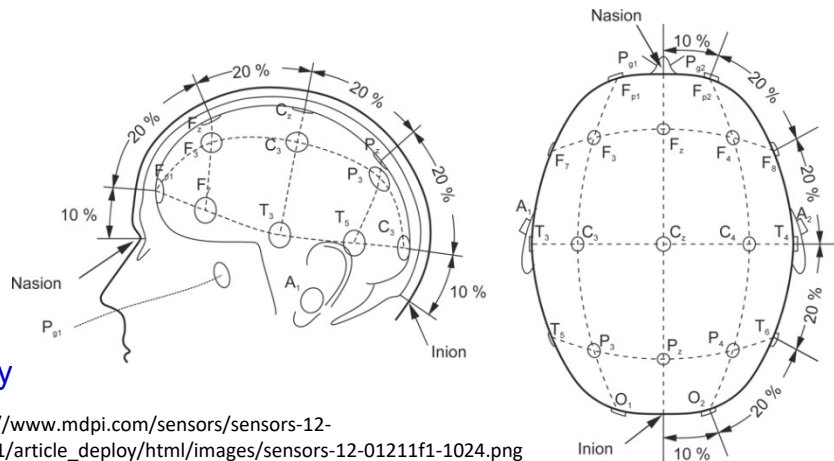
- Females' speech is more fluent
  - they can pronounce more words or sentences in a given amount of time
- Women have the reputation of being able to talk and listen while doing all sorts of things at the same time
- Women language is more widespread in both hemispheres while in men more left lateralized
  - more nerve fibers connecting the two hemispheres of their brains, which also suggests that more information is exchanged between them.
- The males' higher levels of testosterone, which delays the development of the left hemisphere
  - 4 times more boys than girls suffer from stuttering, dyslexia

# Functional diagnostic methods

- Detection of electrical activity
  - Higher neuronal activity - higher electrical activity
  - Electroencephalography (EEG)
- Detection of regional blood flow
  - Higher neuronal activity – increased blood flow
  - Single photon emission tomography (SPECT)
  - Positron emission tomography (PET)
  - Functional magnetic resonance imaging (fMRI)

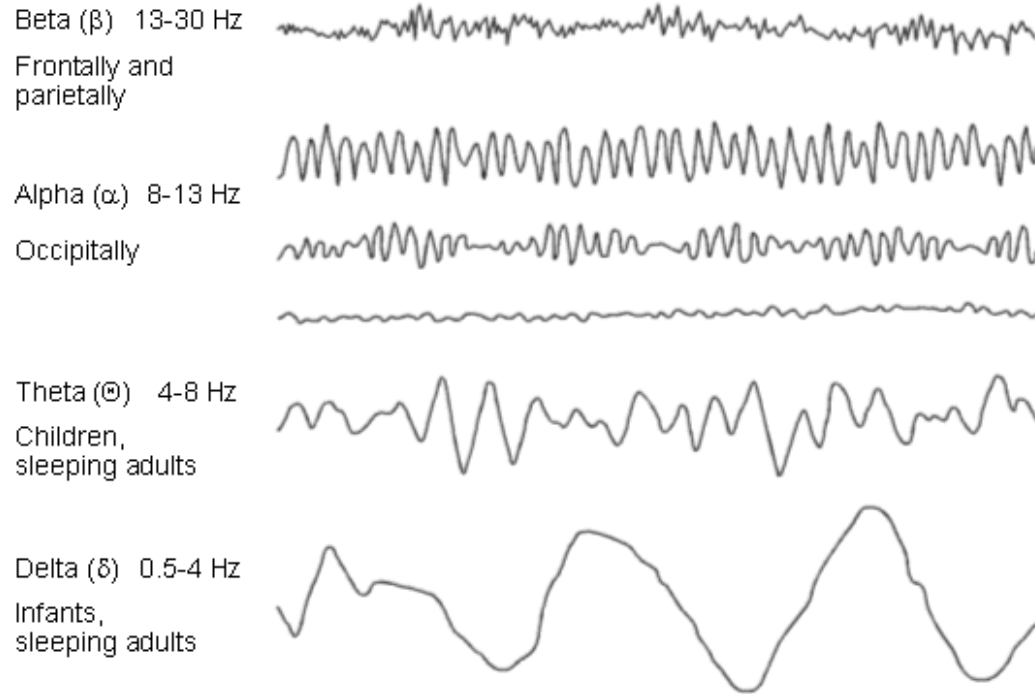
# EEG

- Detection of neuronal electrical activity
- monopolar arrangement:
  - active electrode
  - indifferent electrode= referential recording
- bipolar recording
  - lead (channel)
  - ground electrode
- EEG voltage in microvolts (vs. in mV in neurons)

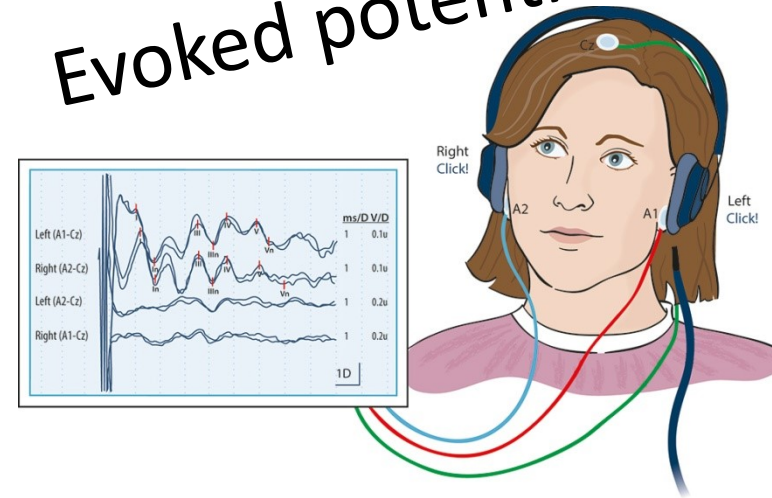


[http://www.slideshare.net/kj\\_jantzen/biophysical-basis-of-eeeg](http://www.slideshare.net/kj_jantzen/biophysical-basis-of-eeeg)

# EEG

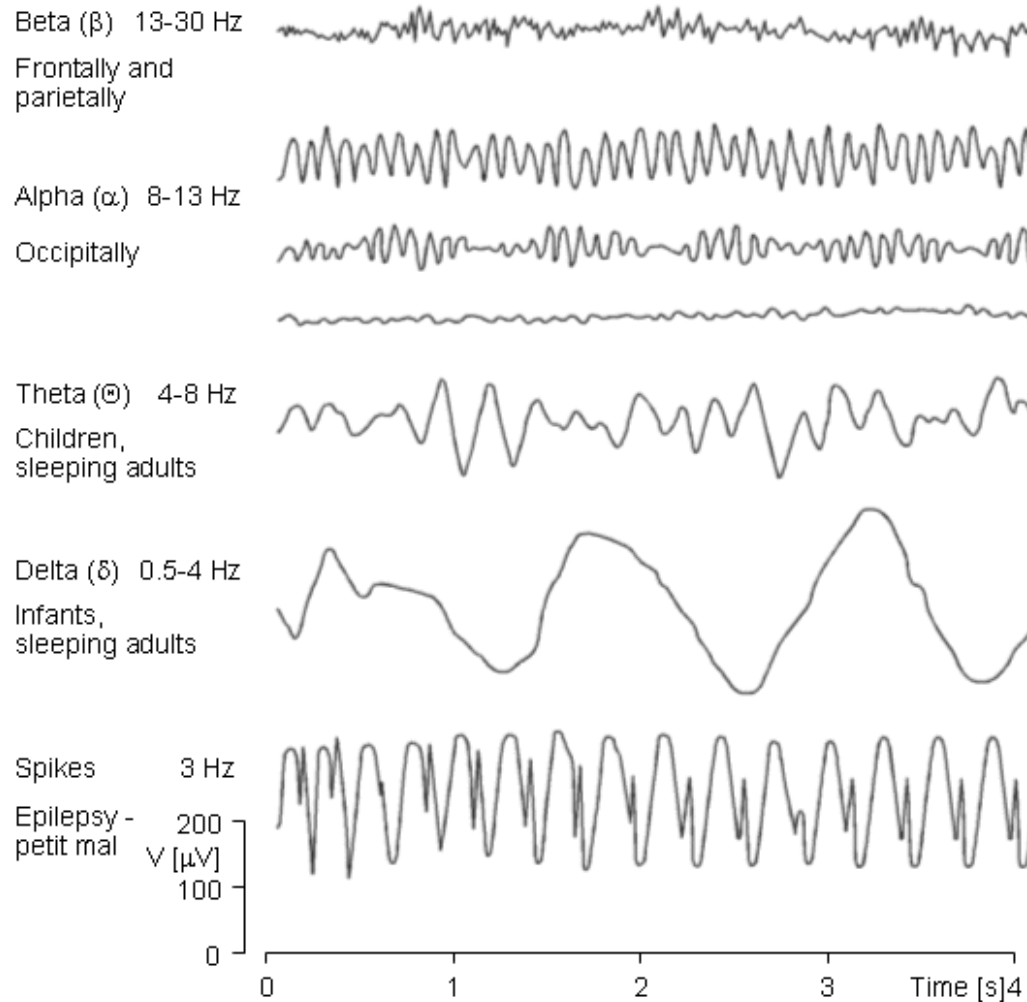


## Evoked potentials

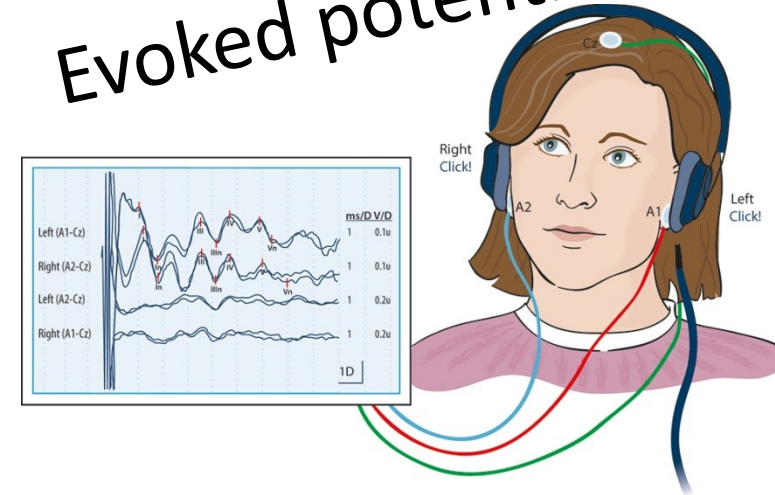


<http://tidsskriftet.no/2013/05/evoked-potential-tests-clinical-diagnosis>

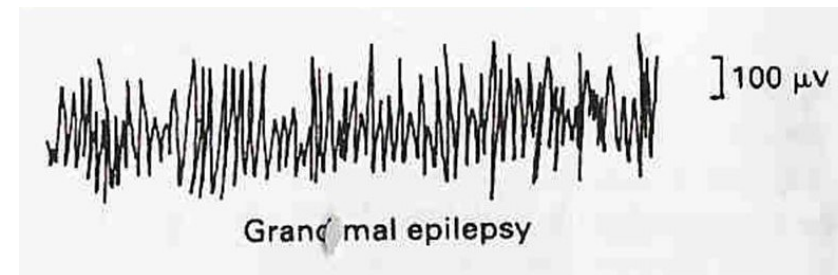
# EEG



## Evoked potentials



<http://tidsskriftet.no/2013/05/evoked-potential-tests-clinical-diagnosis>

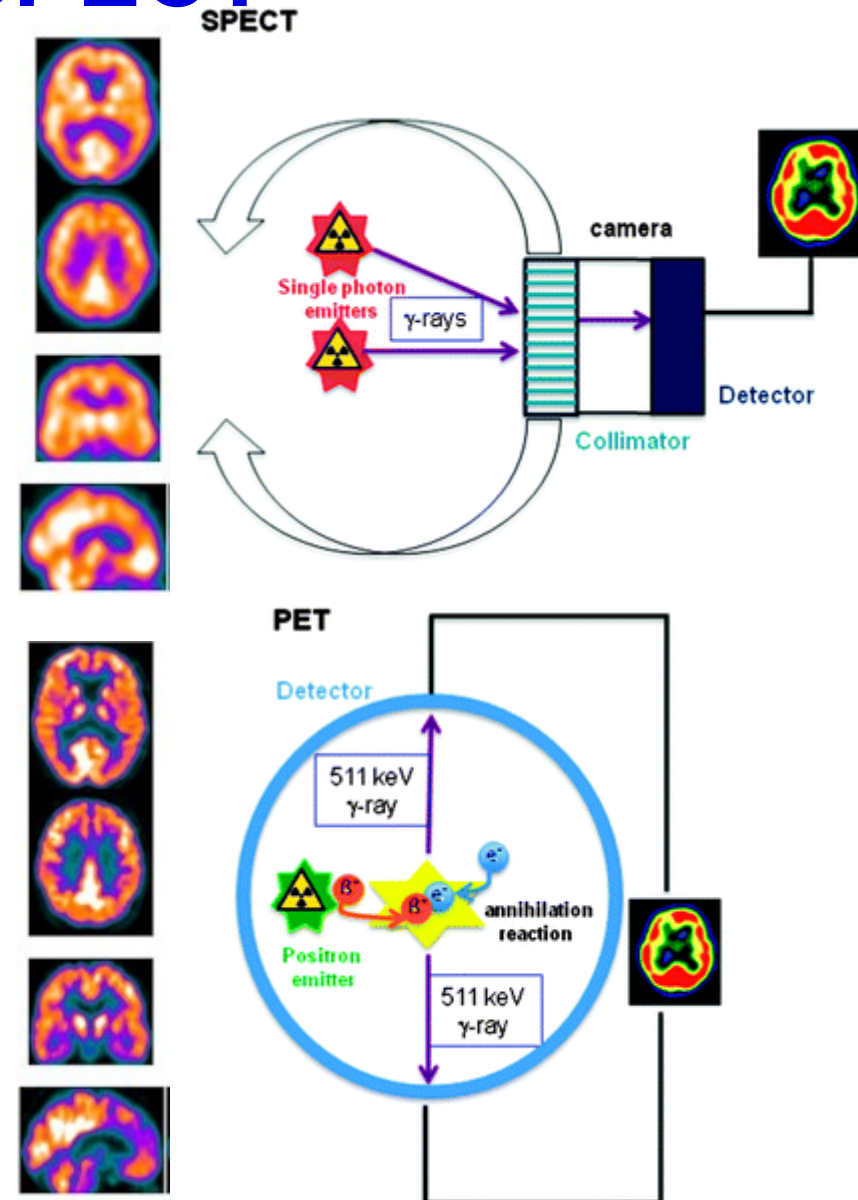


[https://www.google.com/search?q=GRAND+MAL+EEG&source=Inms&tbn=isch&sa=X&ved=0ahUKewjyr82Im6veAhUliaYKHfquClkQ\\_AUIDigB&biw=1222&bih=574#imgrc=nCNGCX88H3K7ZM](https://www.google.com/search?q=GRAND+MAL+EEG&source=Inms&tbn=isch&sa=X&ved=0ahUKewjyr82Im6veAhUliaYKHfquClkQ_AUIDigB&biw=1222&bih=574#imgrc=nCNGCX88H3K7ZM)



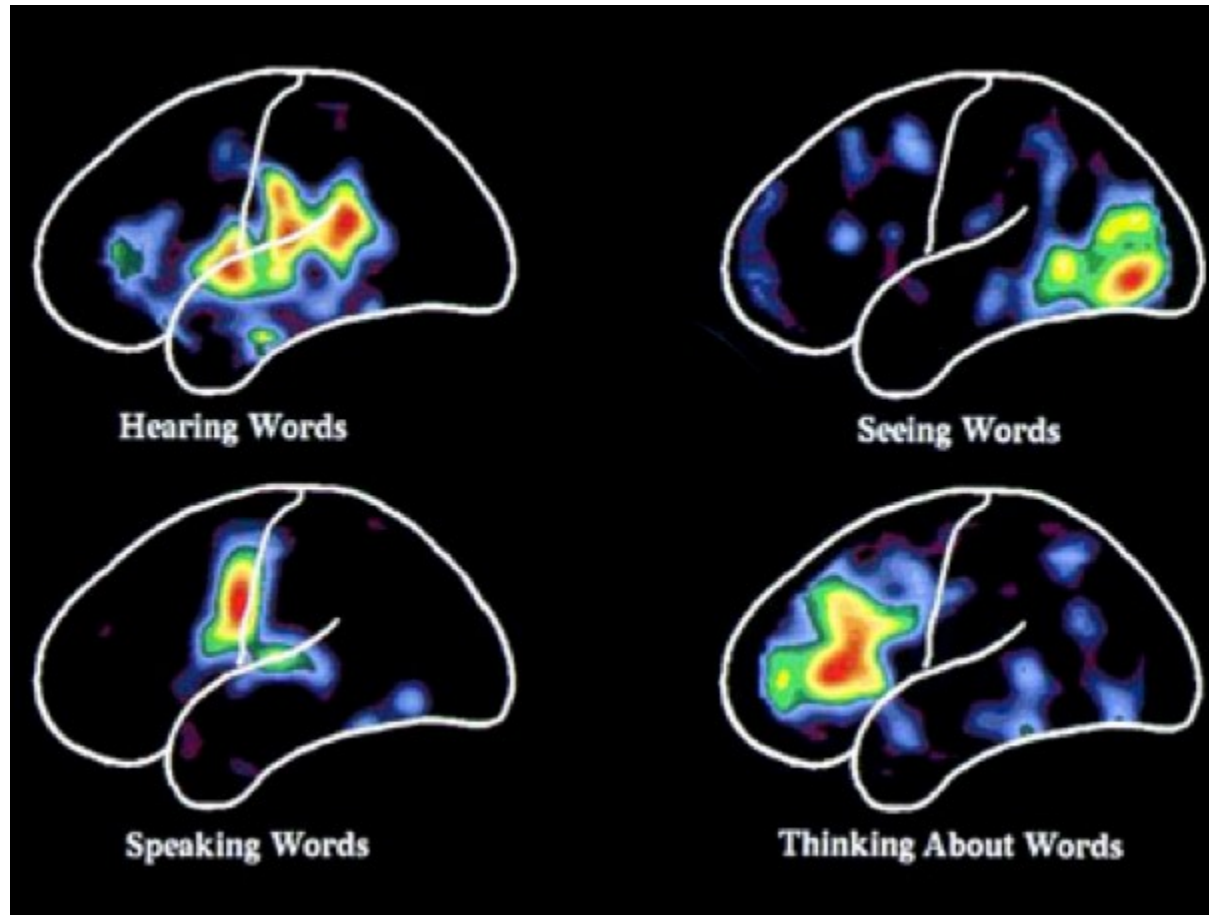
# PET a SPECT

- Injection of radionuclide labeled substances
- Short half live of radionuclide
  - Necessary to prepare shortly before application
  - Nuclear medicine department
- SPECT
  - Single photon emission computer tomography
  - radionuclide is the source of gamma rays
  - Low resolution (around 1 cm)
- PET
  - Positron emission tomography
  - radionuclide is the source of positrons
  - Positron annihilation produces two gamma photons – higher resolution (around 2mm)



<http://pubs.rsc.org/services/images/RSCpubs.ePlatform.Service.FreeContent.ImageService.svc/ImageService/ArticleImage/2013/CS/c3cs60086f/c3cs60086f-f4.gif>

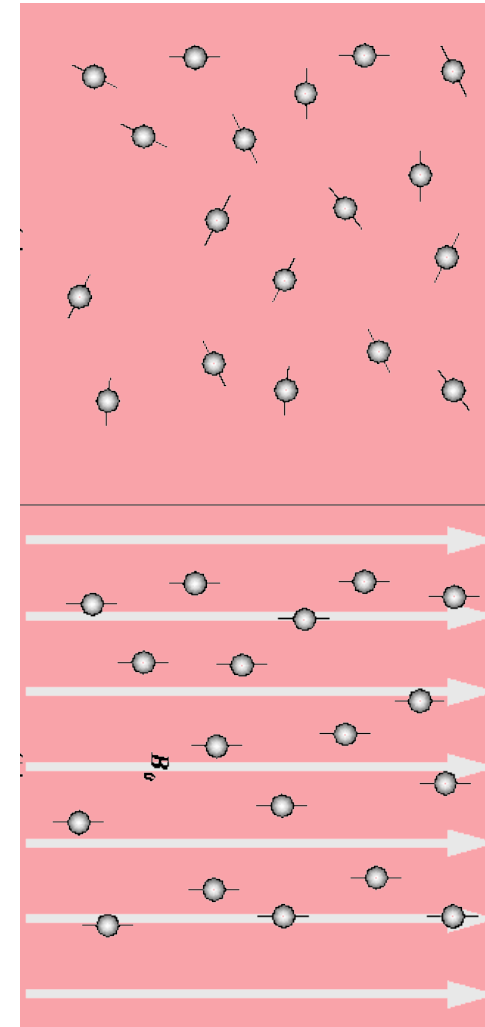
# Functional regions of the brain



<http://www.chroniclebooks.com/blog/wp-content/uploads/brain-scan.png>

# fMRI

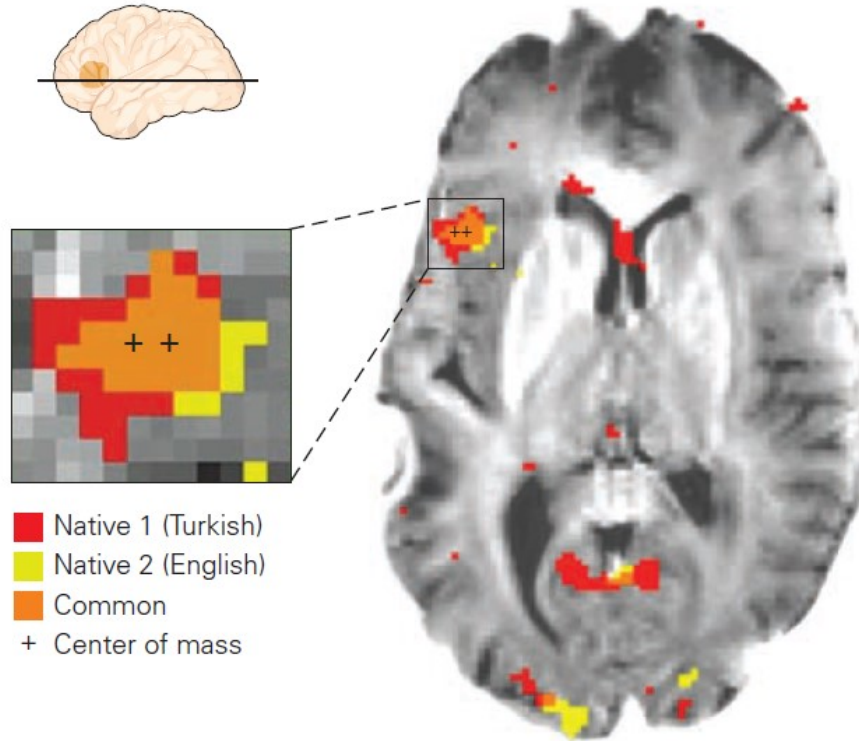
- Different atoms (nuclei) have various magnetic properties when exposed to strong magnetic field
- Hydrogen
- fMRI uses different magnetic properties of oxy- and deoxyhemoglobin
- reduced hemoglobin becomes paramagnetic, change the signal emitted by blood, we can measure the amount of oxy- and deoxyhemoglobin as an indicator of the blood flow
- High resolution (up to 1mm)
- No radiation



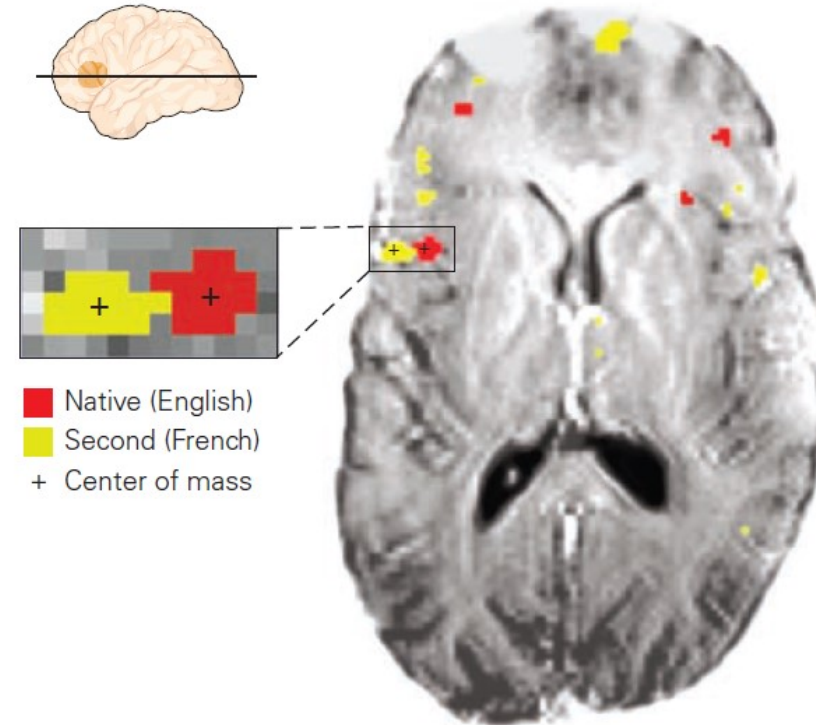
<https://www.cs.sfu.ca/~stella/papers/blairthesis/main/node11.html>

# fMRI

A Early bilingual



B Late bilingual



Kim, K. H. S., Relkin, N. R., Lee, K.-M. & Hirsch, J.  
Distinct cortical areas associated with native and  
second languages. *Nature* **388**, 171–174 (1997).

M U N I

M E D