

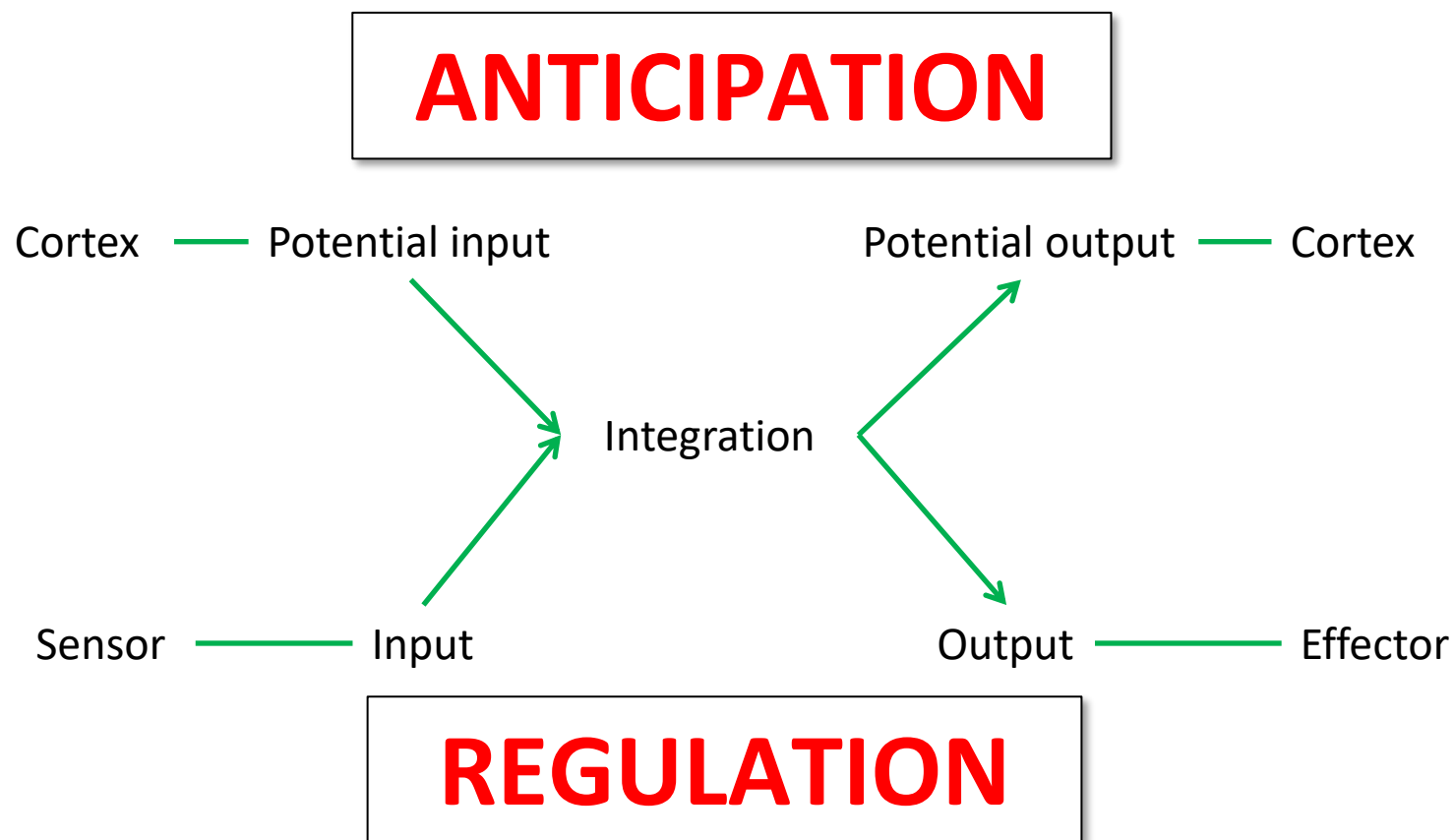
M U N I

M E D

Limbic system

Neocortex I

The role of nervous system



Hypothalamus

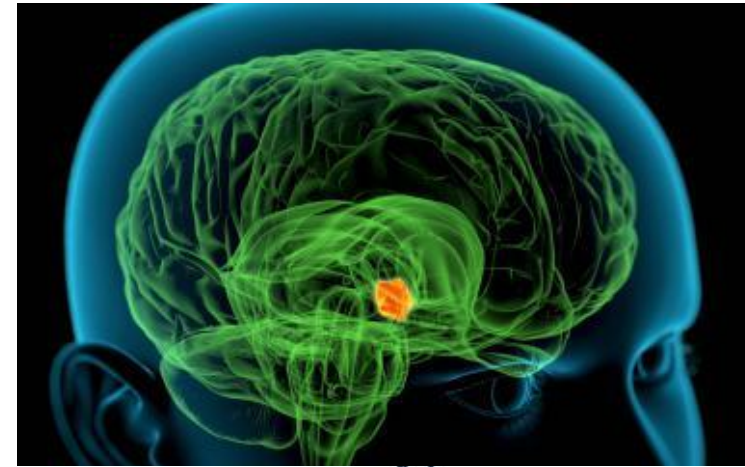
- Key center of autonomic regulations and coordination
- Integration of the information from inner and outer environment



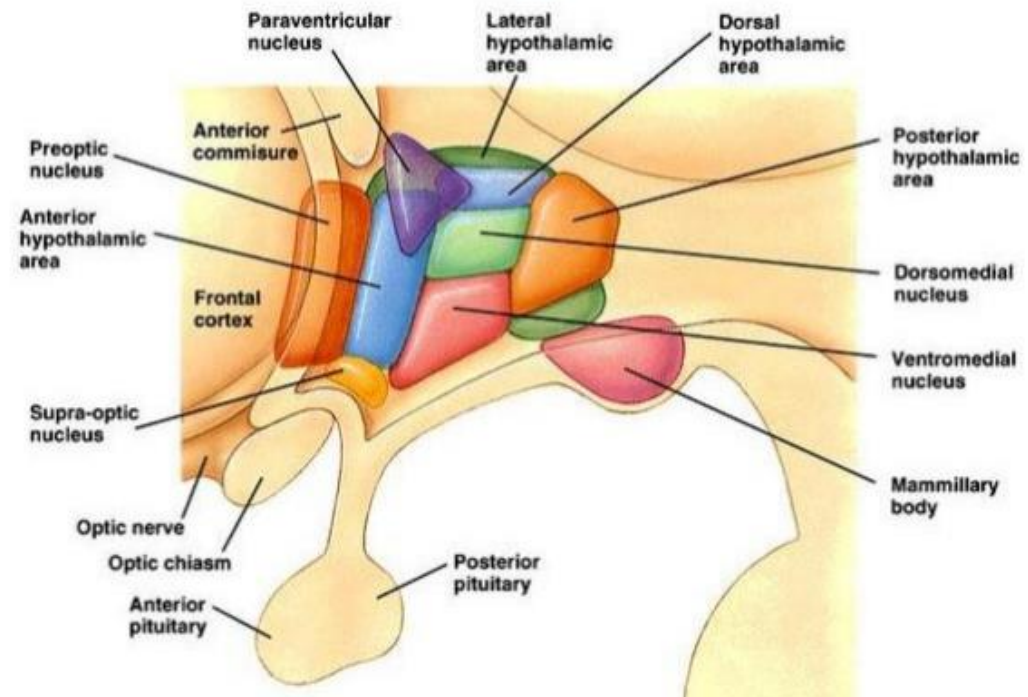
- Behavioral modulation
- Regulation of autonomic nervous system



- **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**

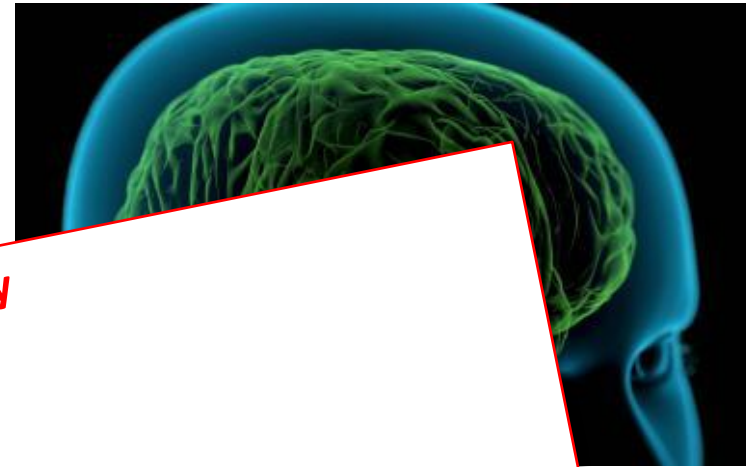
✓ **Regulation of body temperature**

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

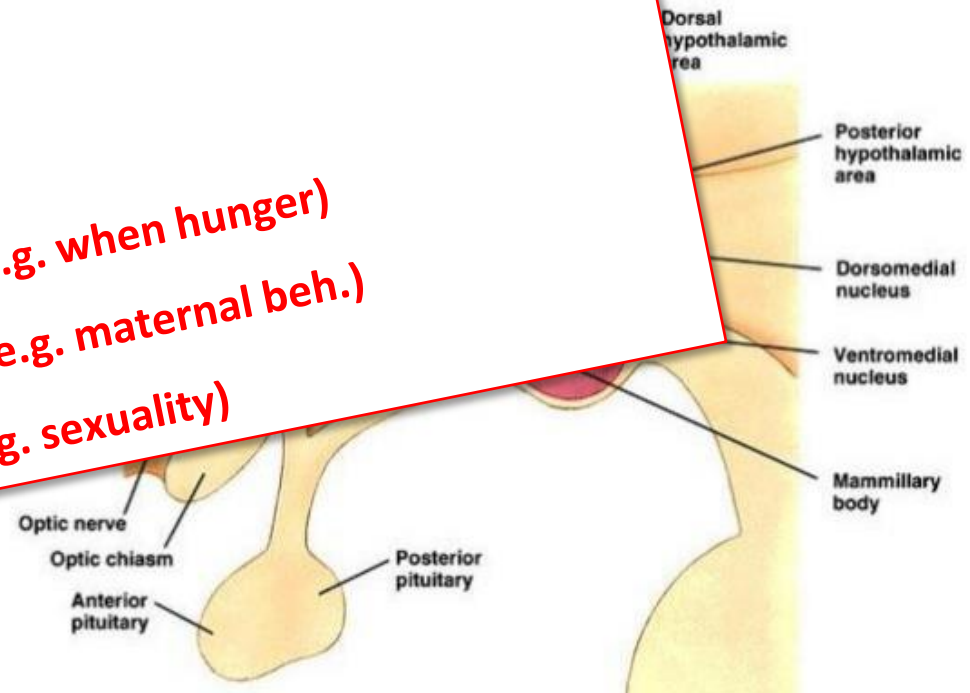
✓ **„Long-term“ behavior regulation (e.g. maternal beh.)**

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

- Behavior
- Regulation of nervous system
- Maintenance of homeostasis

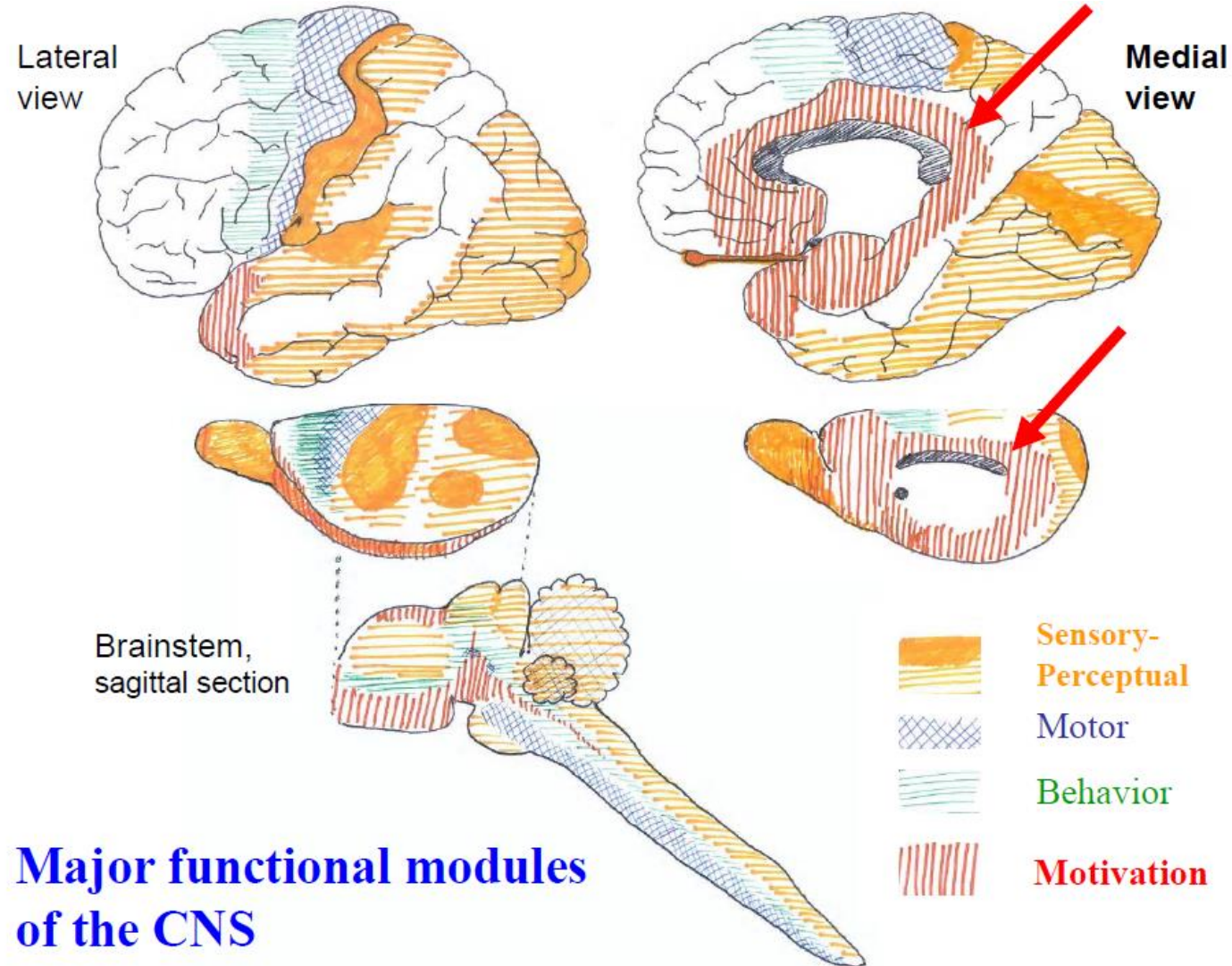


<http://biology.about.com/od/anatomy/pl/Hypothalamus.htm>



Limbic system

Limbus = border



Major functional modules of the CNS

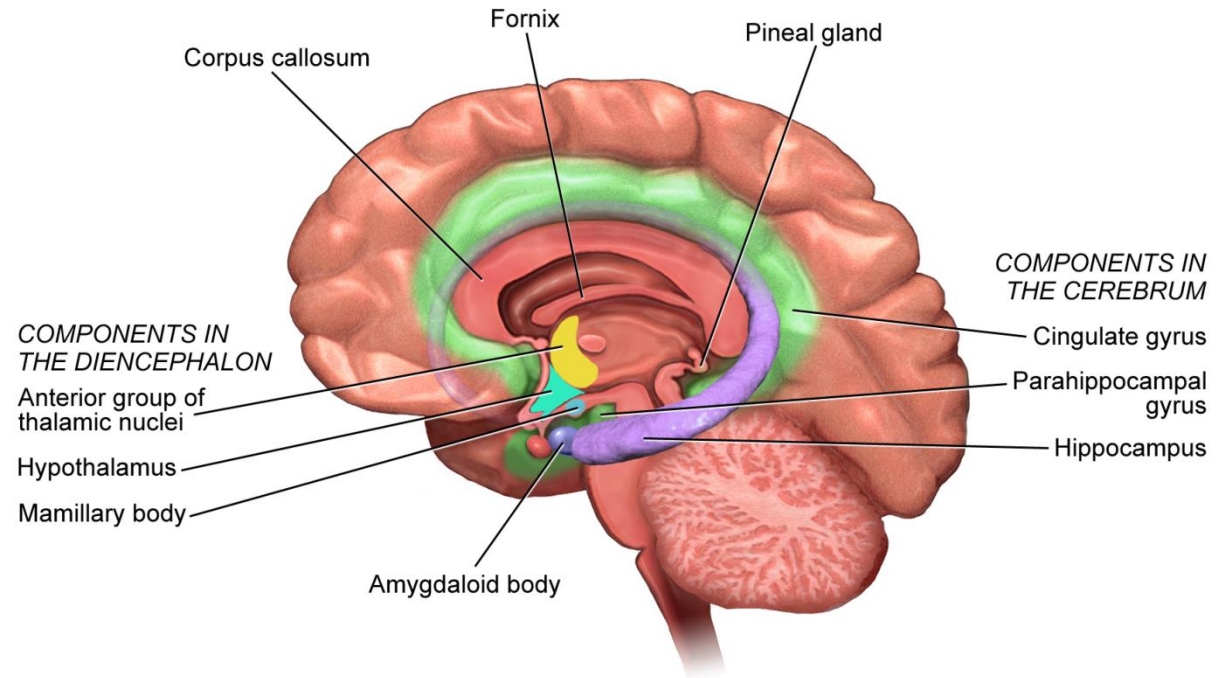
Concept of the limbic system

- Voluntary

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

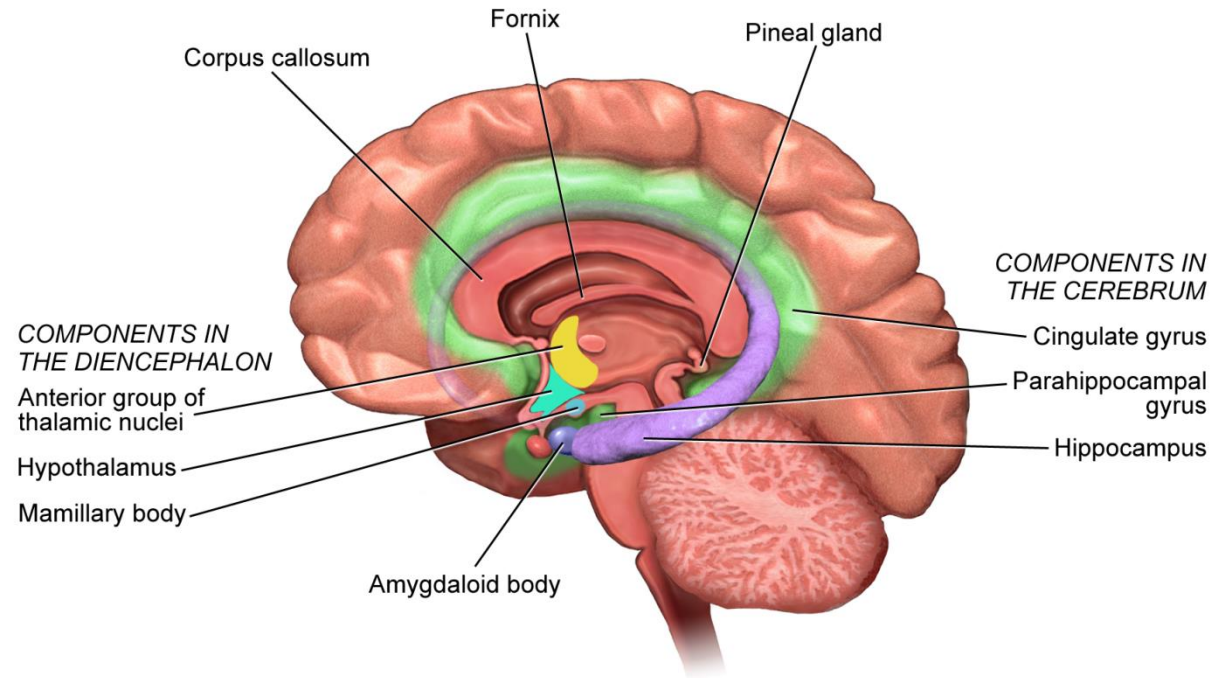
- Automatic

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

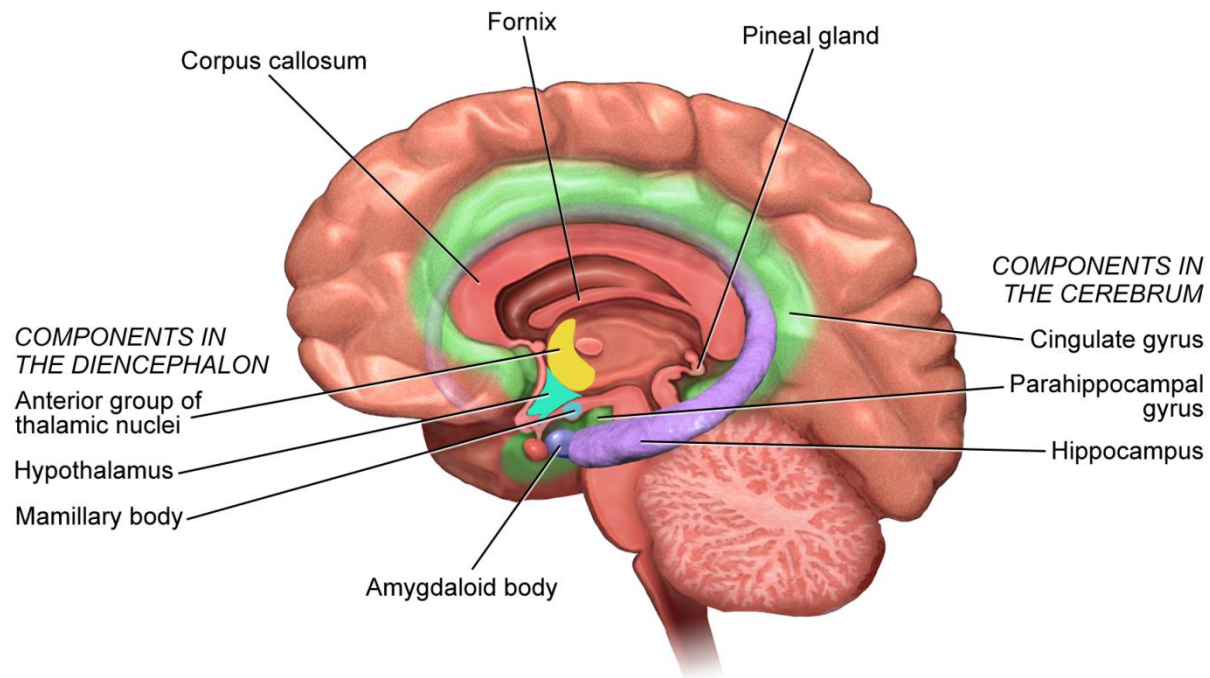
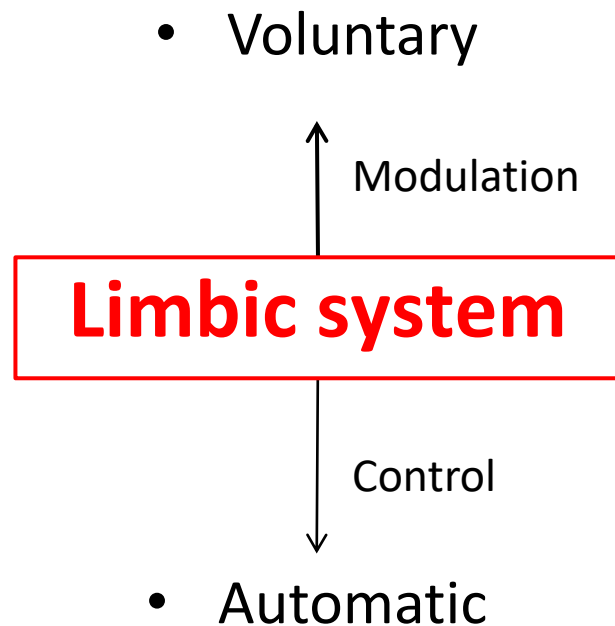


Concept of the limbic system

- Voluntary
- ↑
- Potential conflict
- ↓
- Automatic



Concept of the limbic system



Concept of the limbic system

- Voluntary

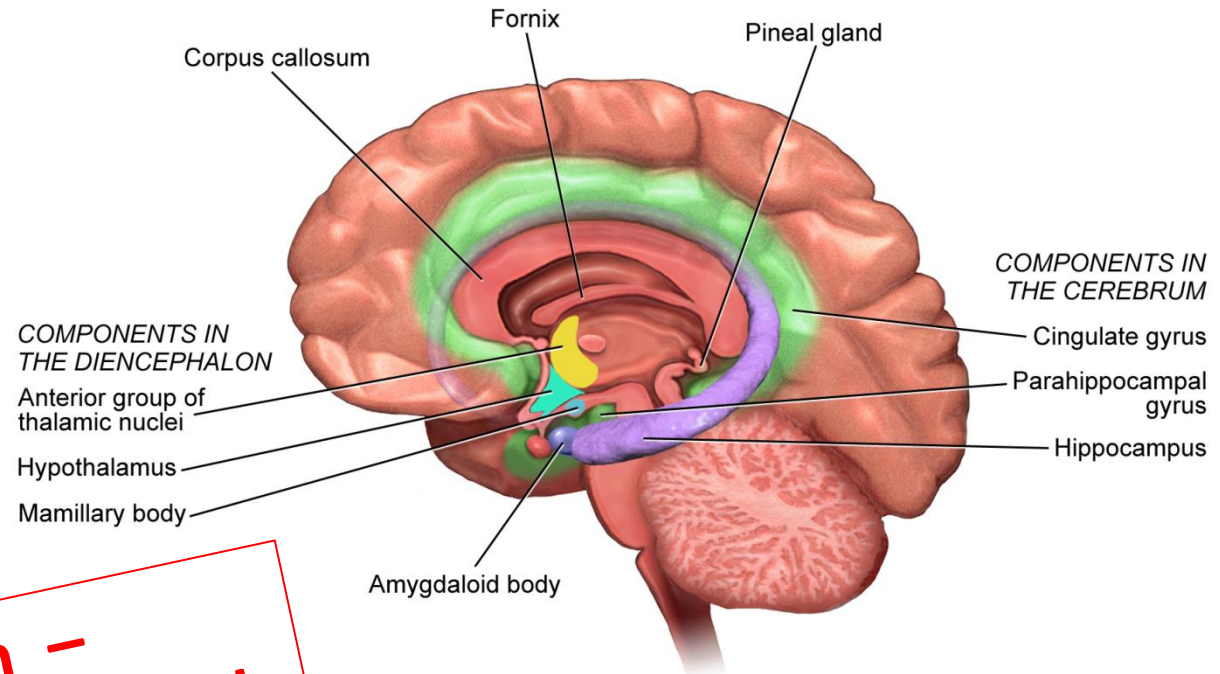
↑ Modulation

Limbic system

↓ Control

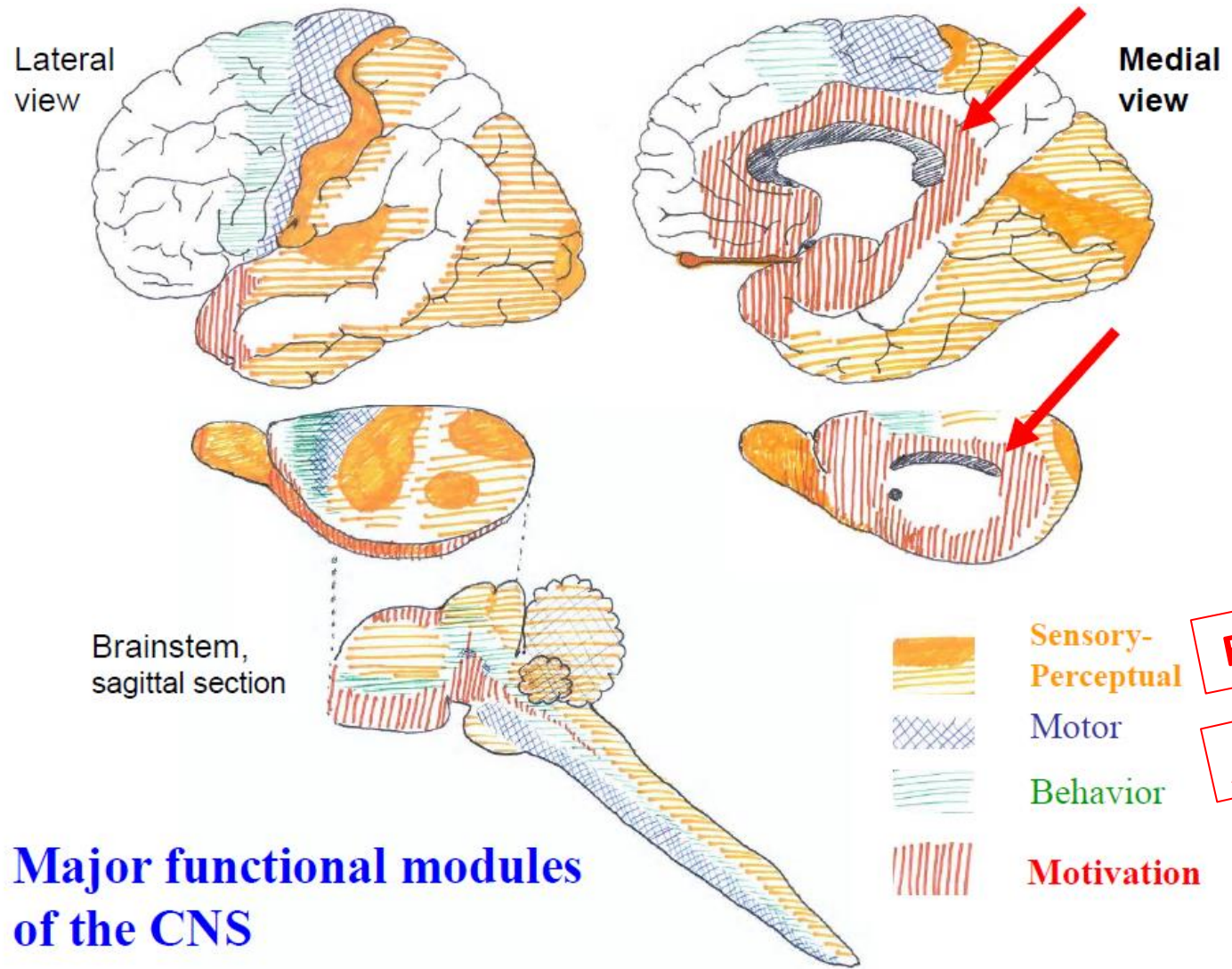
- Automatic

**Limbic system –
hypothalamus and related
structures**

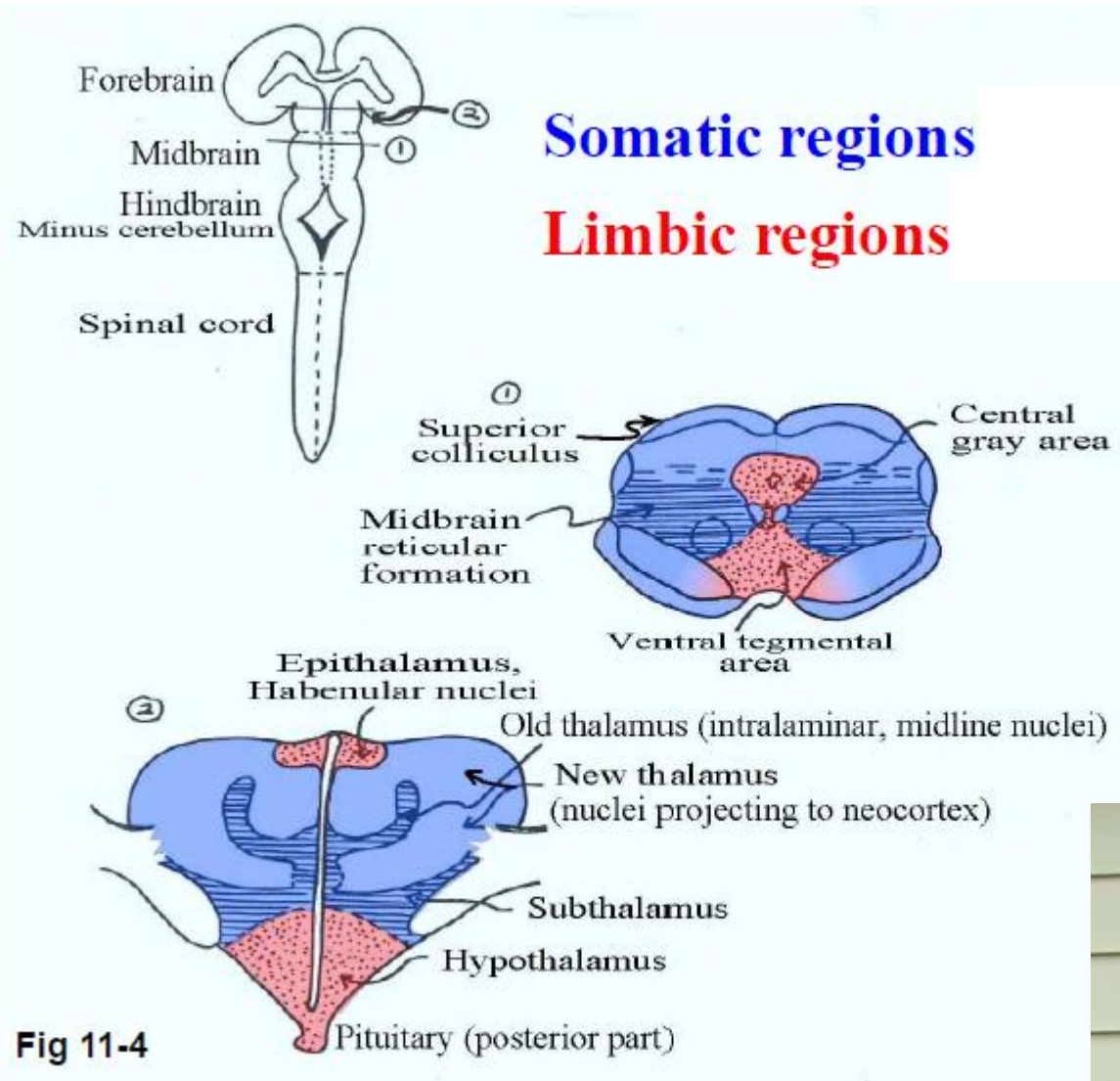


Limbic system

Limbus = border



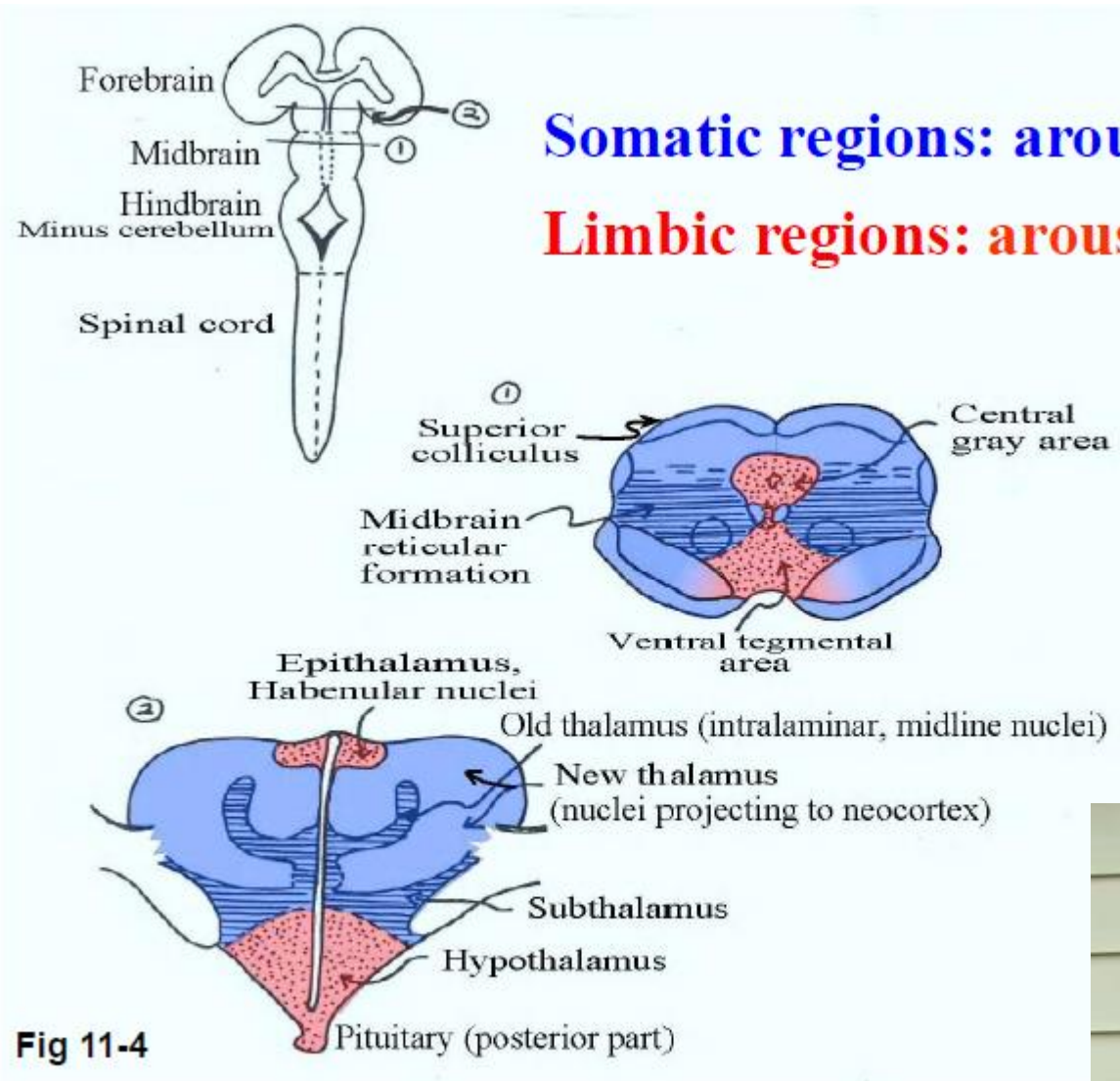
Major functional modules of the CNS



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Prof. Gerald Schneider



Somatic regions: arousal type 1

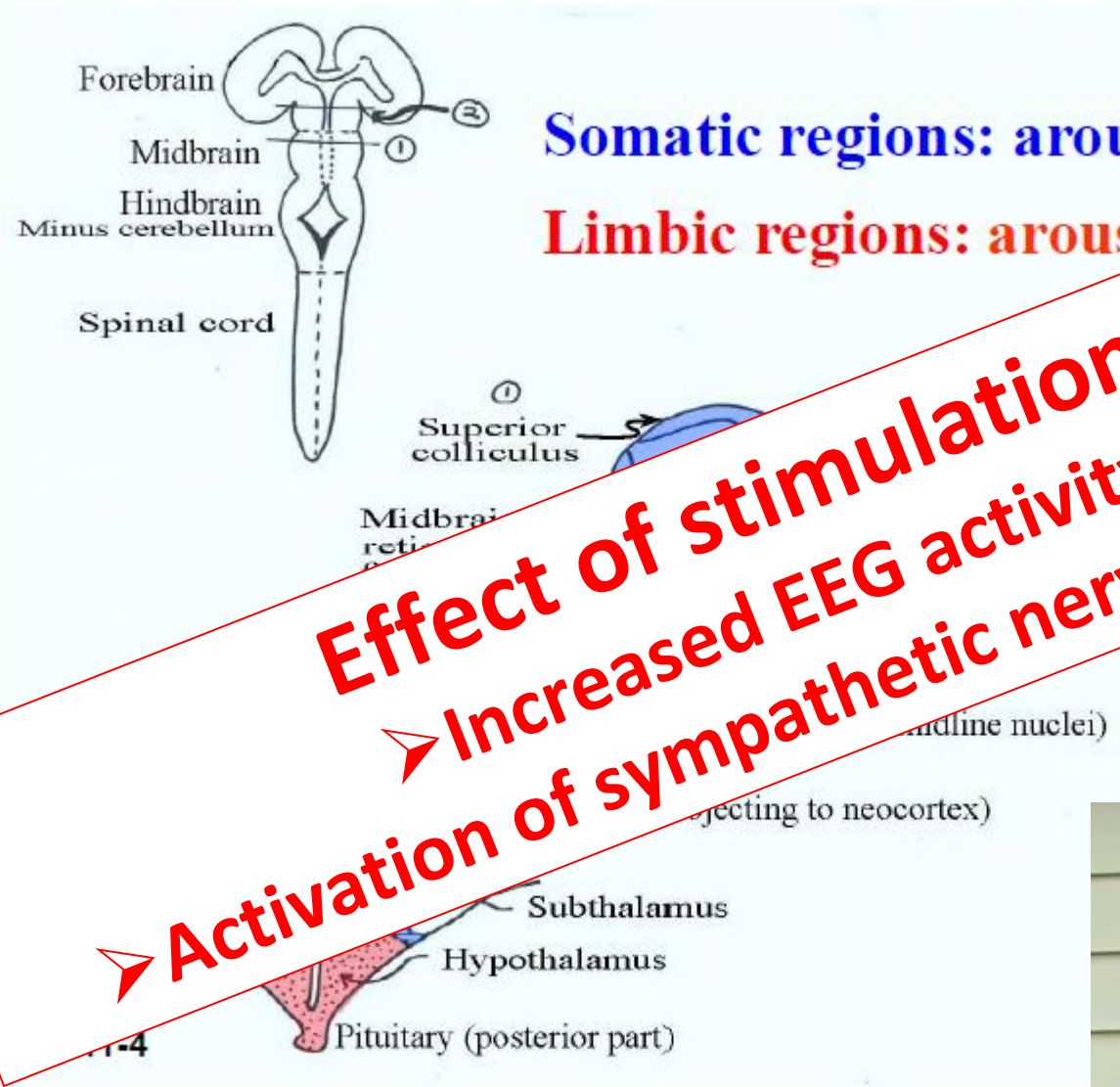
Limbic regions: arousal type 2

Fig 11-4

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Somatic regions: arousal type 1

Limbic regions: arousal type 2

Effect of stimulation
➤ Increased EEG activity
➤ Activation of sympathetic nervous system



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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)

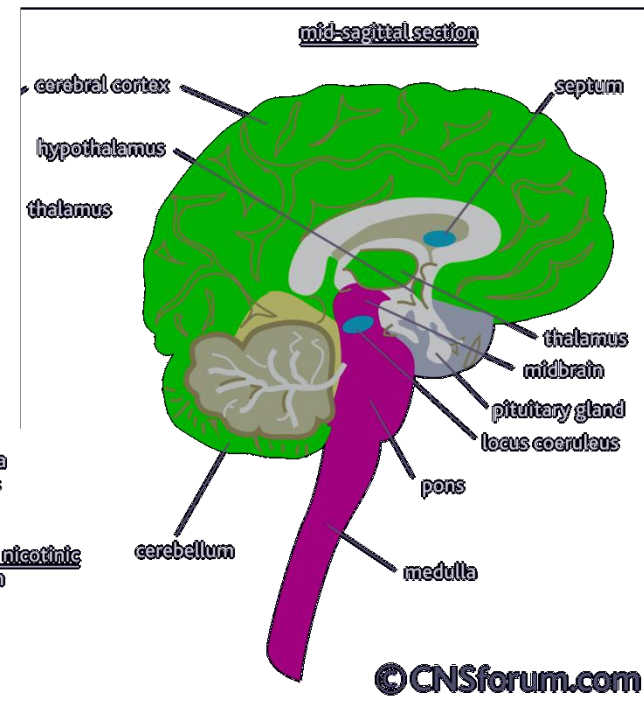
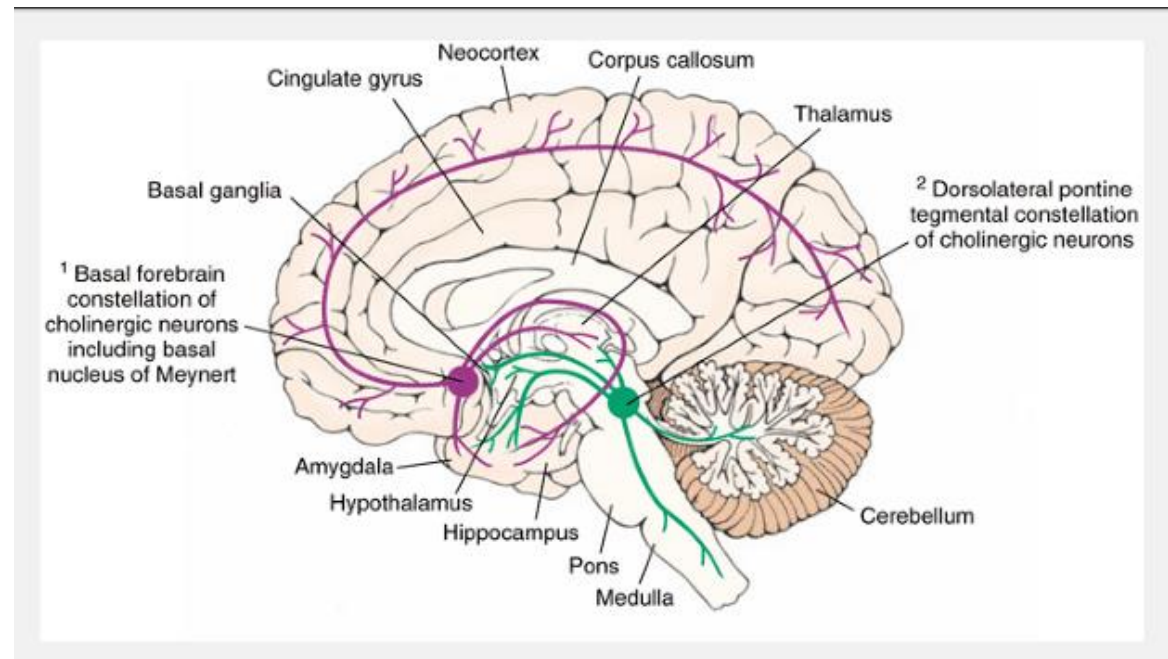
- Ascendent connections
 - Neocortex, corpus striatum, thalamus

- Descendent connections
 - Hypothalamus and other limbic areas, amygdala

Acetylcholine

- Nucleus basalis (Meynerti) and other nuclei
- Nicotin receptors
- Muscarin receptors

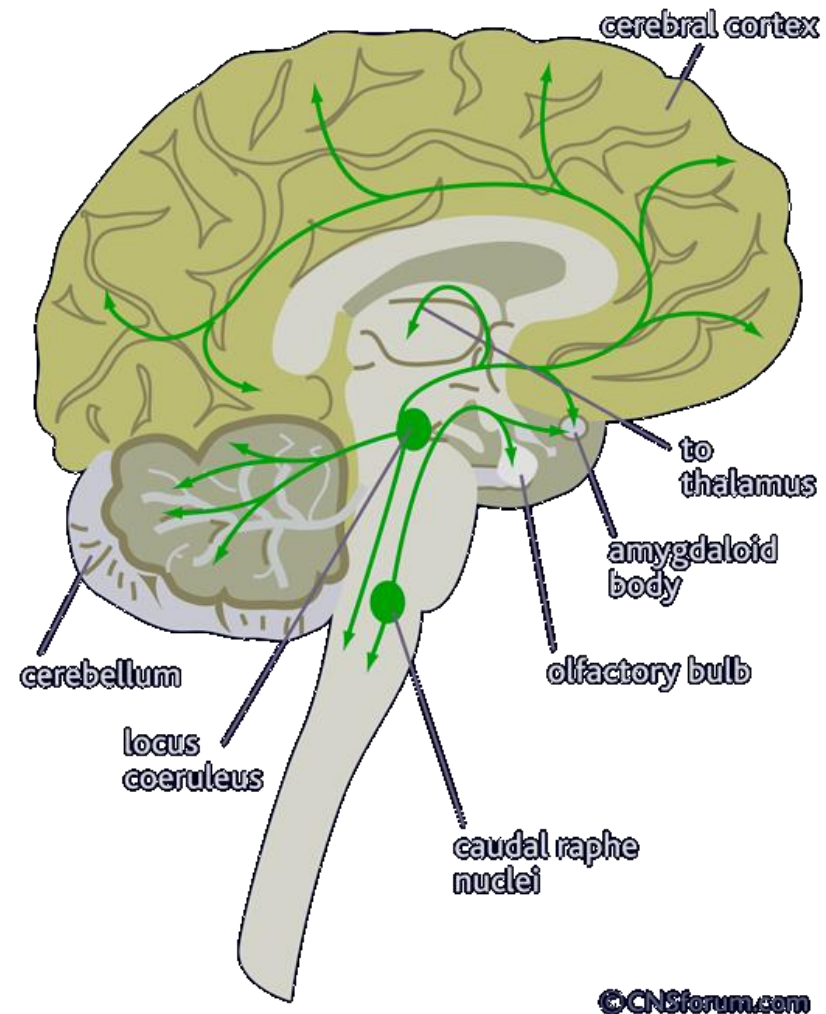
- Sleep/wake regulation
- Cognitive functions
- Behavior
- Emotions



Norepinefrine

- Locus coeruleus
- Nuclei raphe caudalis

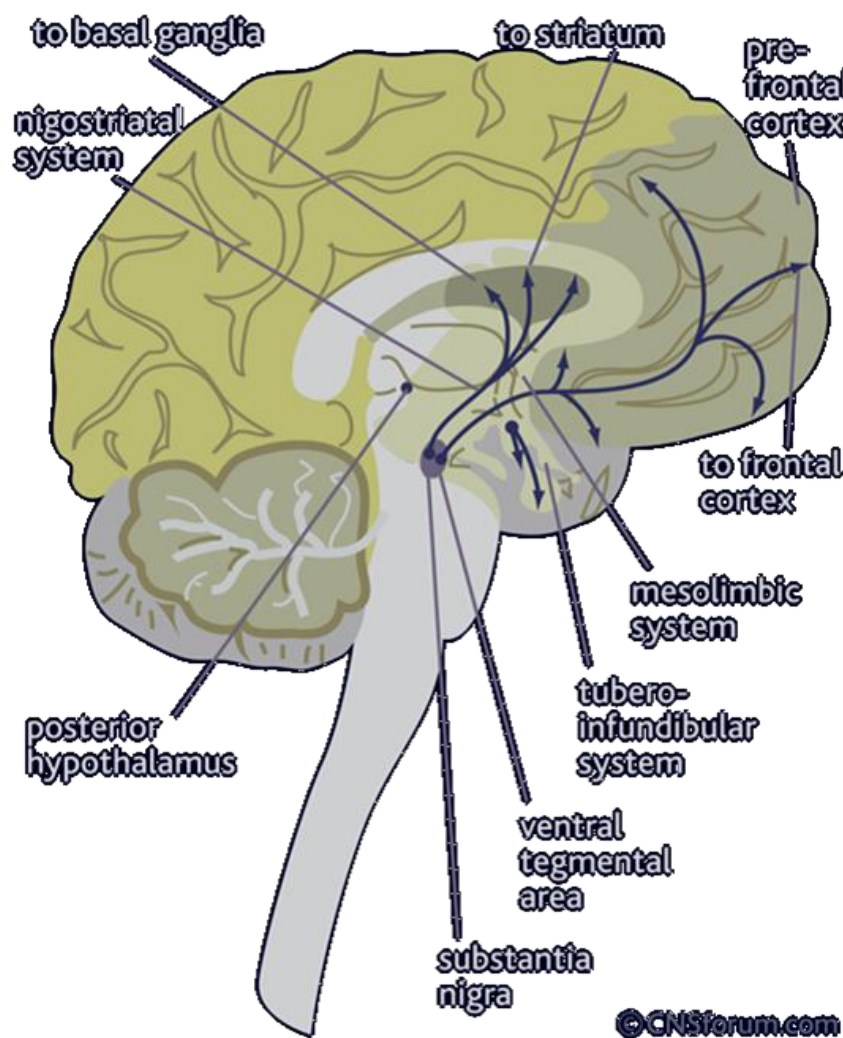
- Vigilance
- Responsiveness to unexpected stimuli
- Memory
- Learning



<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

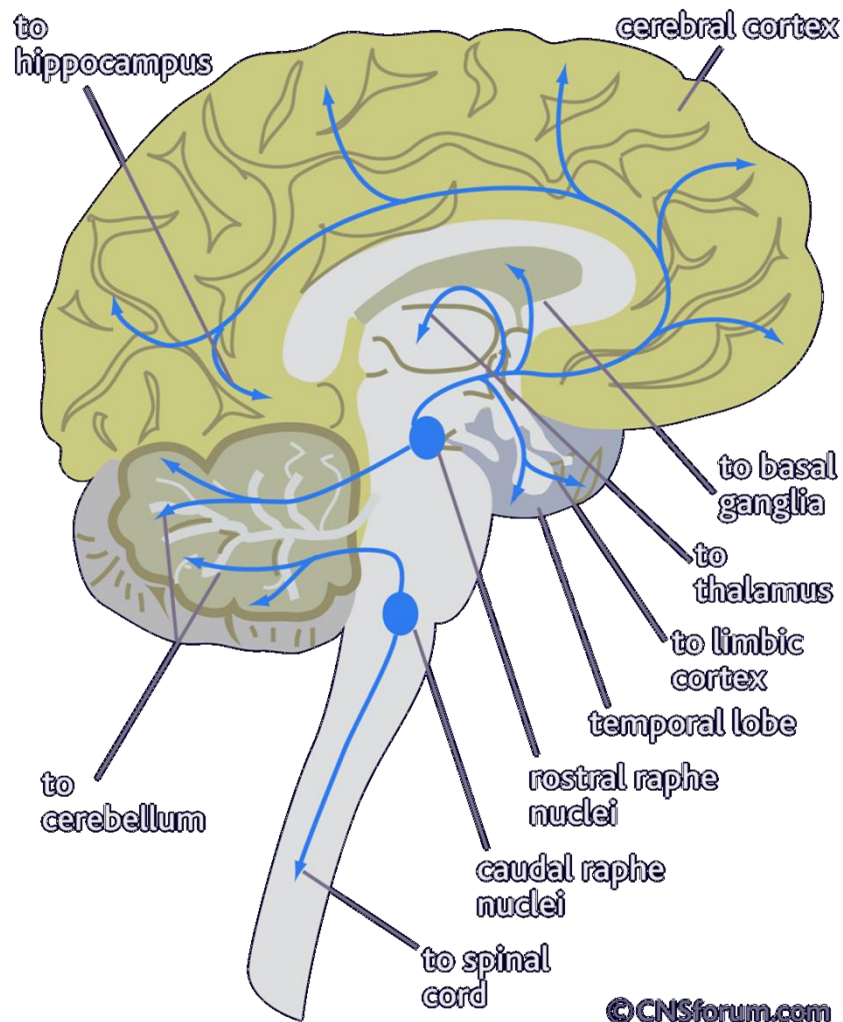


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Serotonin

- Nuclei raphe rostralis
- Nuclei raphe caudalis

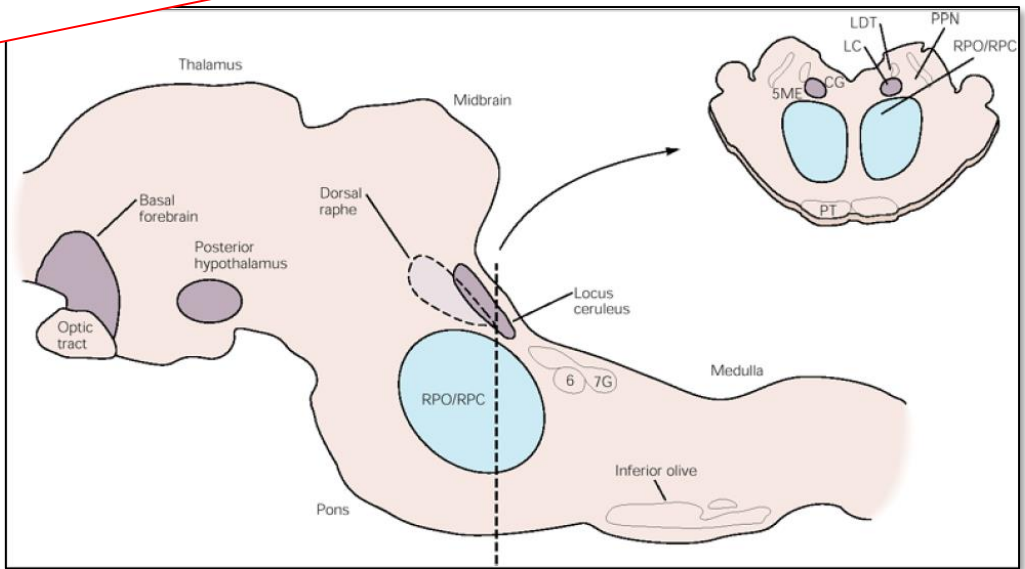
- Anxiety/relaxation
- Impulsive behavior
- Sleep



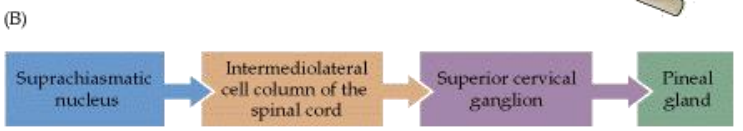
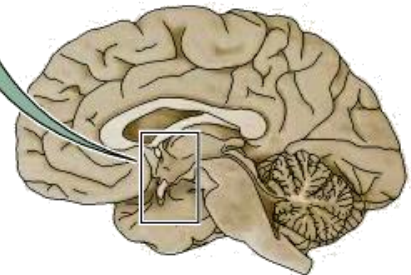
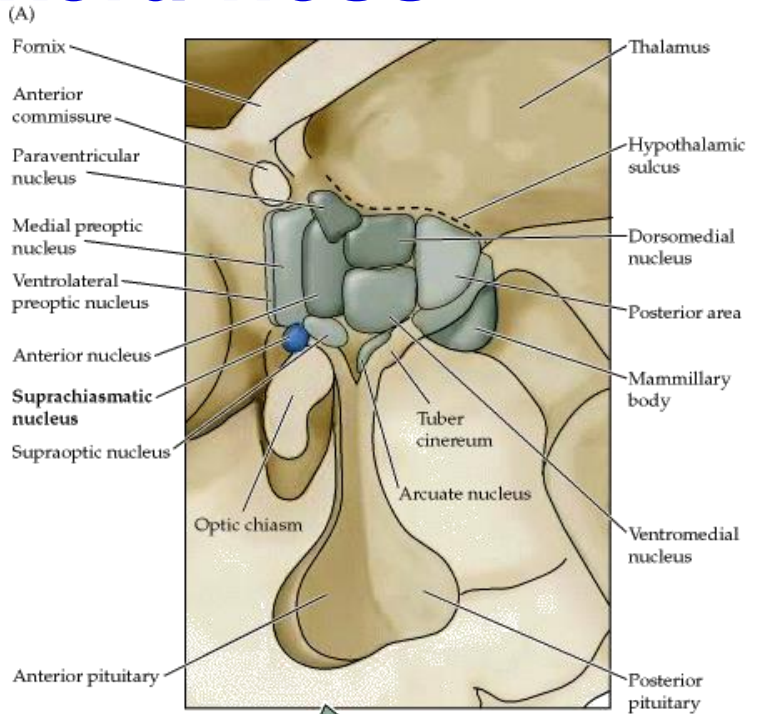
<http://www.slideshare.net/drpsdeb/presentations>

Sleep and wakefulness

Cooperation of ARAS and limbic activating system



22 Limbic system - RPO/RPC - nucleus reticularis pontis oralis/caudalis



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)

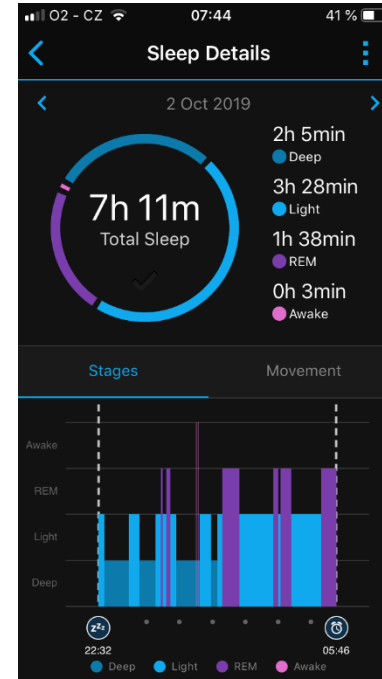
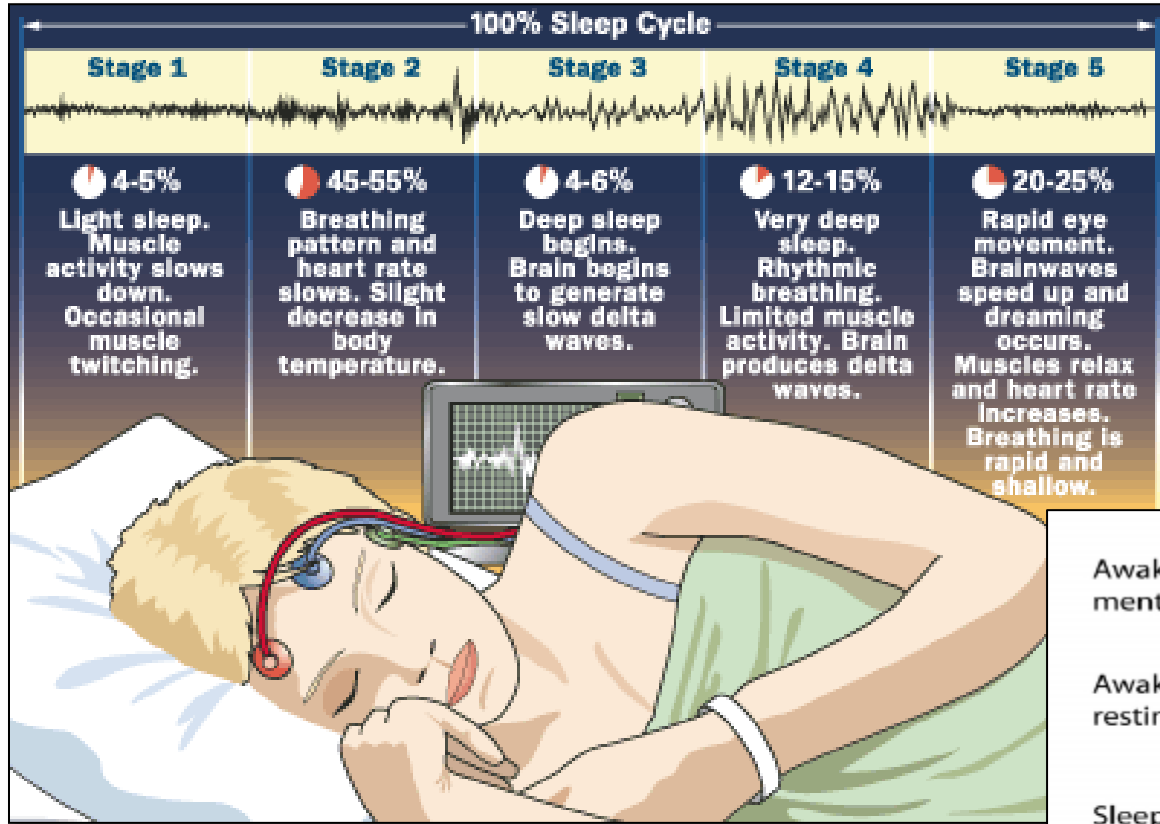
4 to 5 sleep cycles make a good night's sleep

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

Sleep

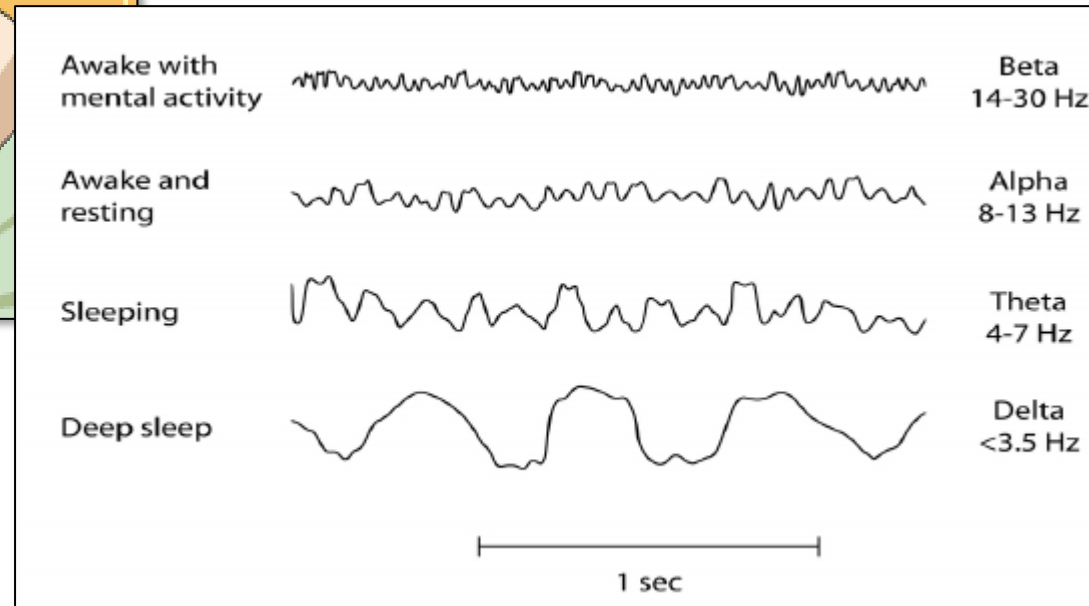
http://www.slideshare.net/dipsdeb/presentations



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



LIGHT NON-REM SLEEP	DEEP NON-REM SLEEP	REM SLEEP
<ul style="list-style-type: none"> Stages 1-2 May drift in and out of sleep several times at the start Easy to wake up, disturbs easily 	<ul style="list-style-type: none"> Stages 3-4 Difficult to wake up Sleep inertia when woken 	<ul style="list-style-type: none"> 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



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/article-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

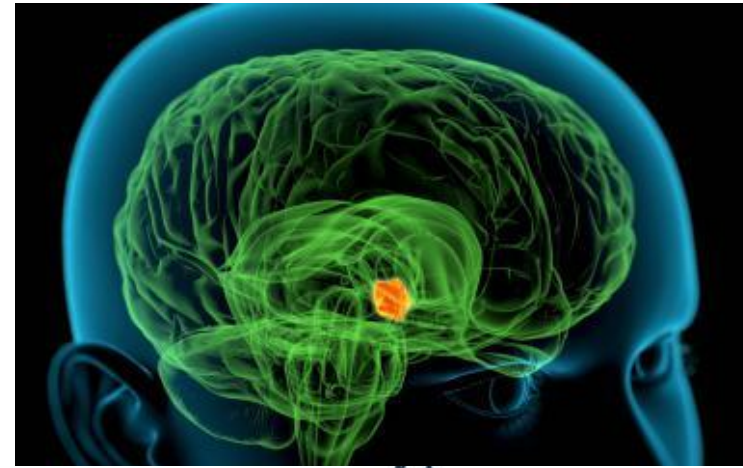
- Key center of autonomic regulations and coordination
- Integration of the information from inner and outer environment



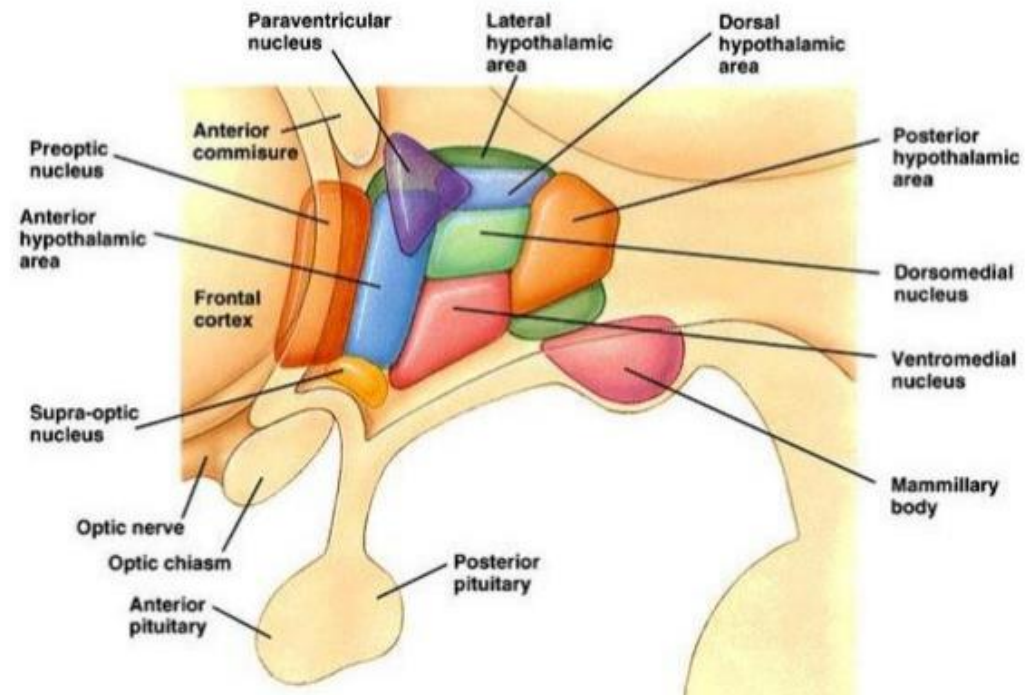
- Behavioral modulation
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- **Maintenance of homeostasis**



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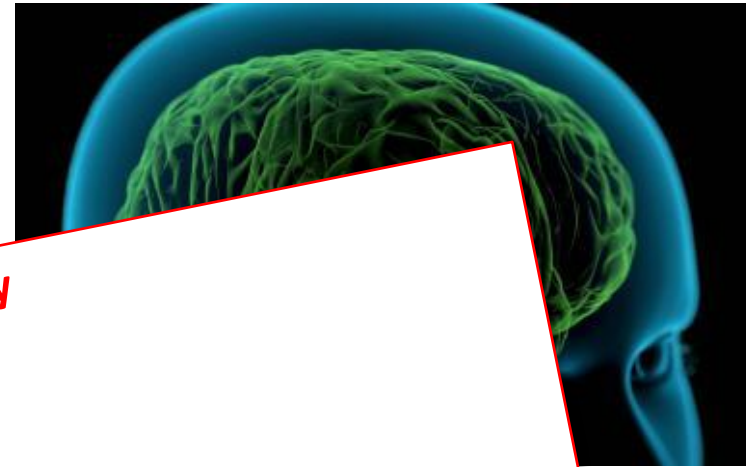
Hypothalamus

- Key center of autonomic regulations and coordination
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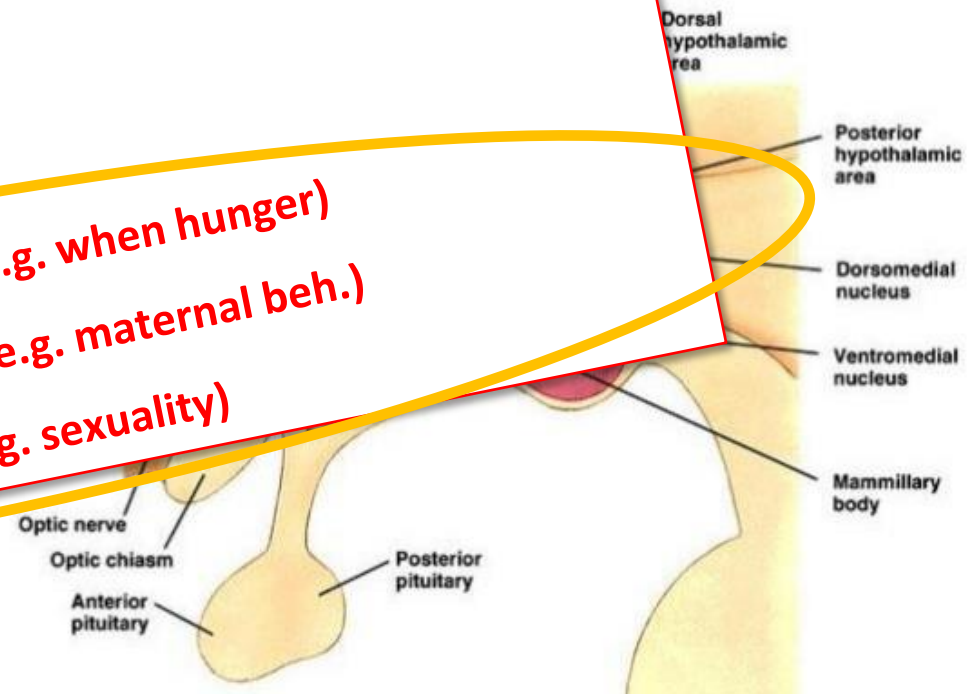
- Behavior
- Regulation of nervous system

- 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)

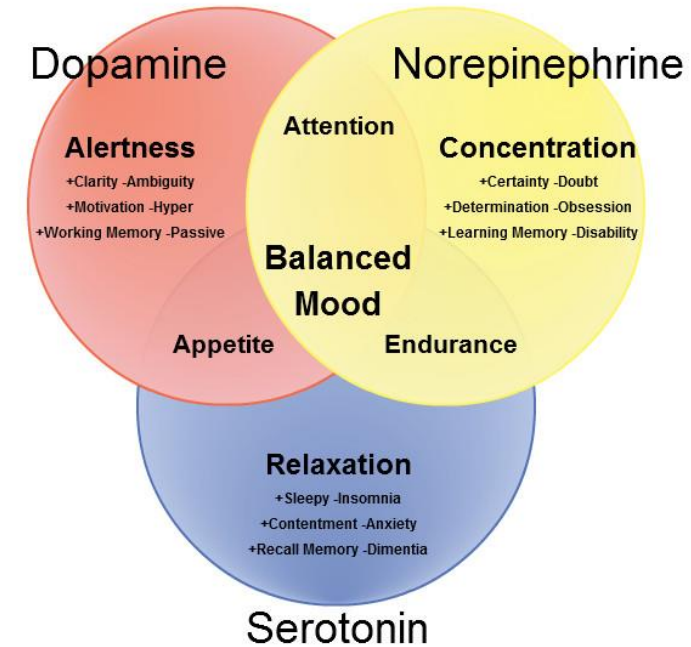


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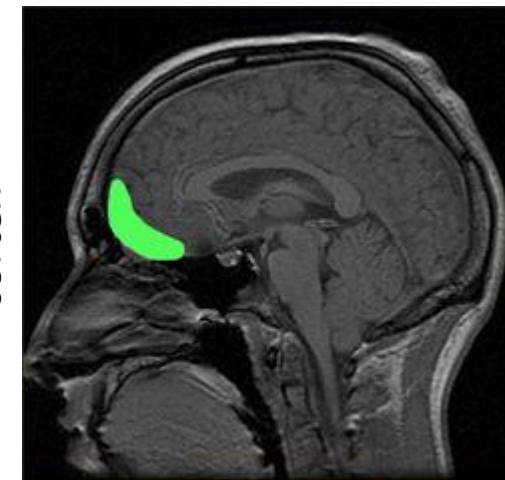
Influence of hypothalamus on neocortex

- 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



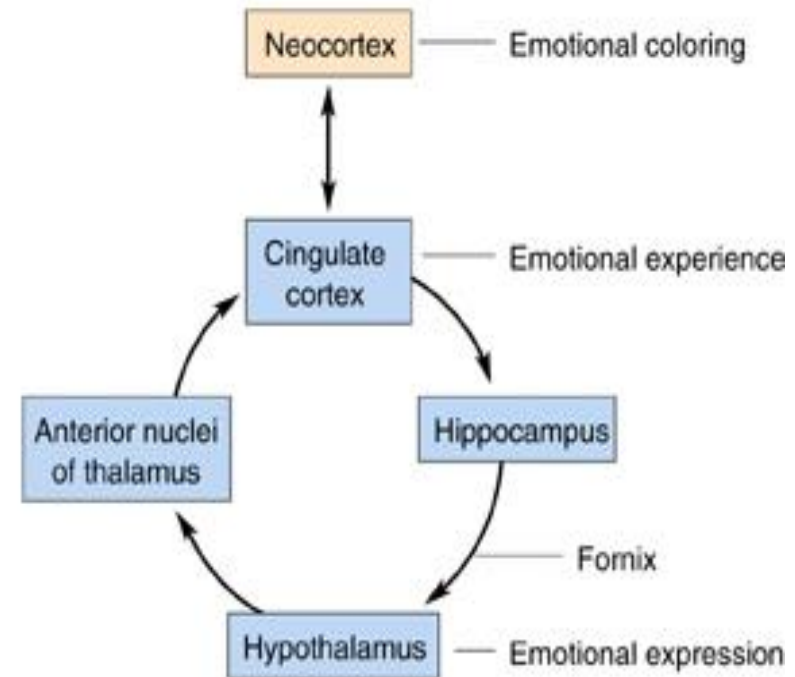
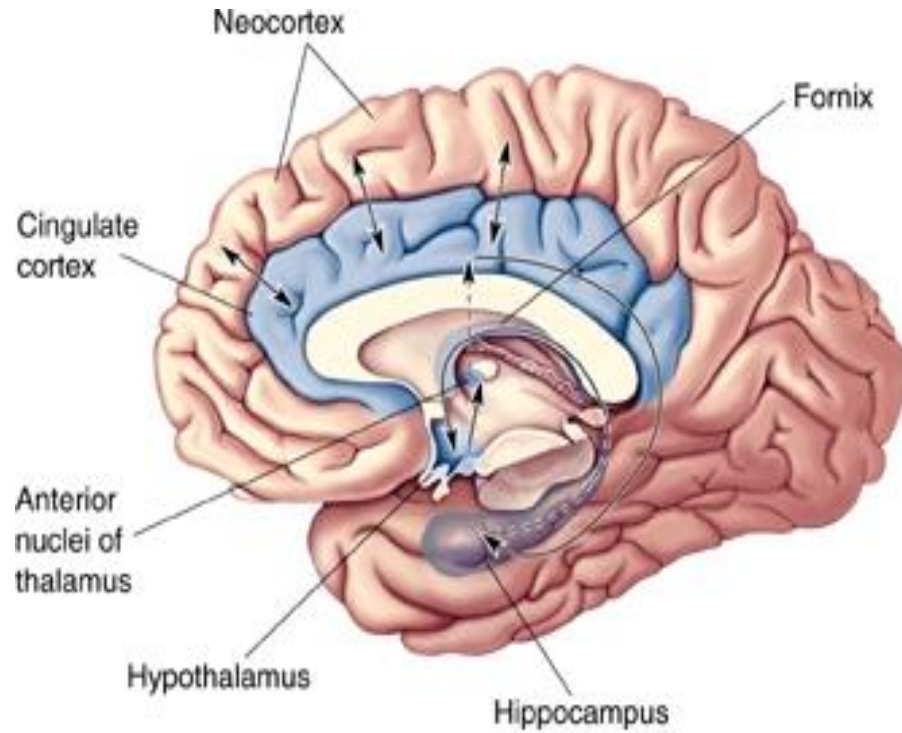
http://ausm.org.uk/wp-content/uploads/2015/02/Dopamine_Norepinephrine_Serotonin.jpg

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

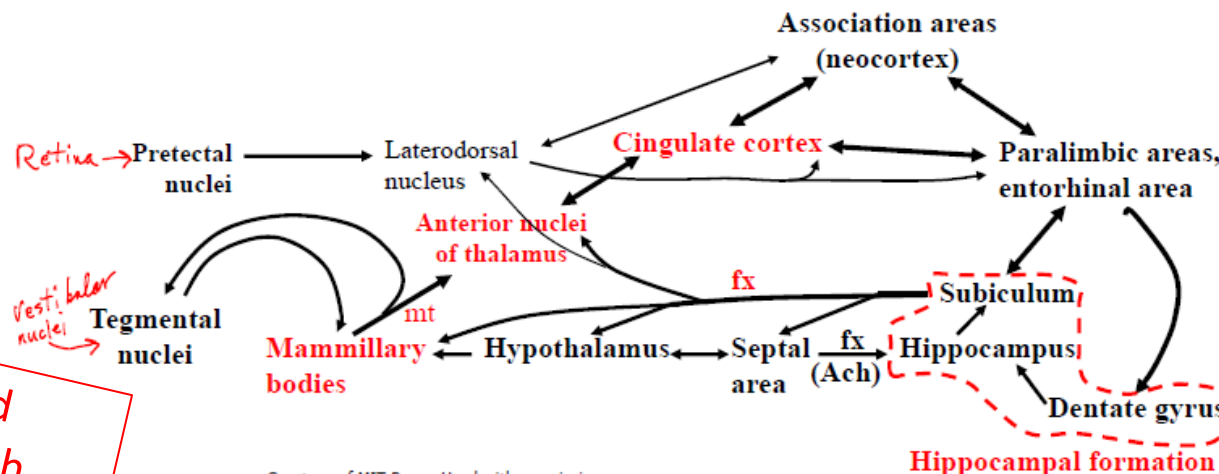
Gerald Schneider. *9.14 Brain Structure and Its Origins, Spring 2014*. (Massachusetts Institute of Technology: MIT OpenCourseWare), <http://ocw.mit.edu> (Accessed). License: Creative Commons BY-NC-SA



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- *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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Spatial orientation and emotions associated with particular place

Papez circuit

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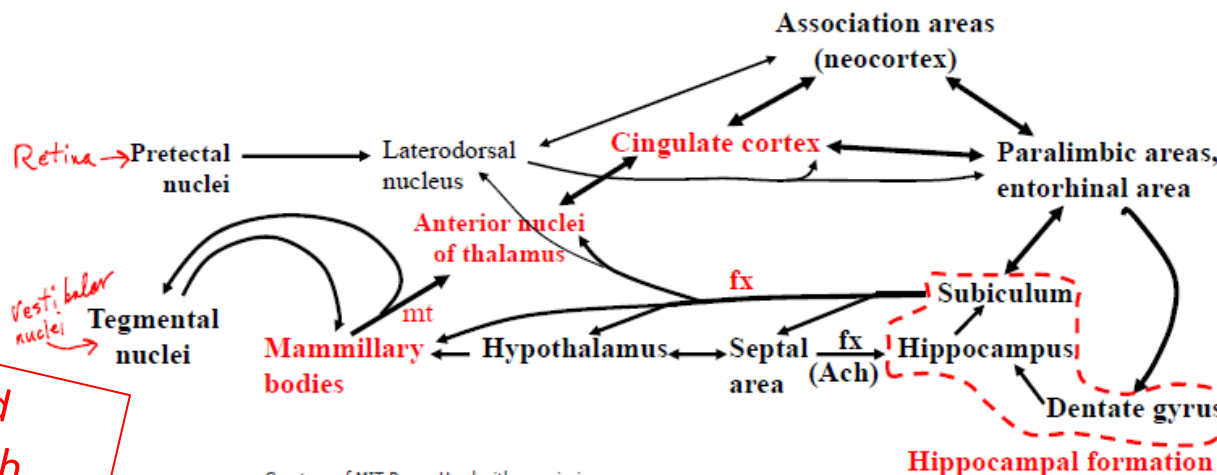


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Spatial orientation and emotions associated with particular place

- 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.

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Papez circuit

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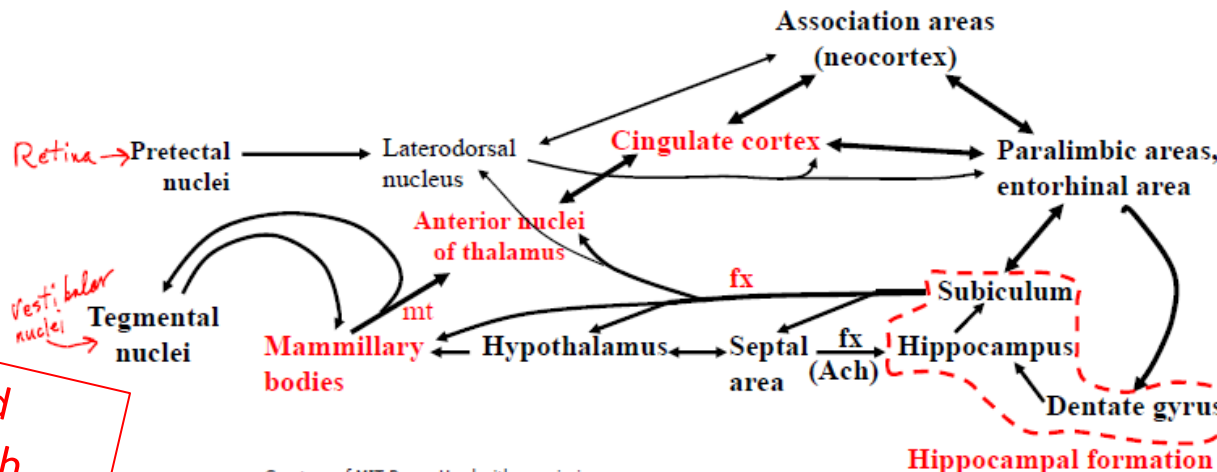
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Object oriented...

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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 - Based on striatum
 - 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?

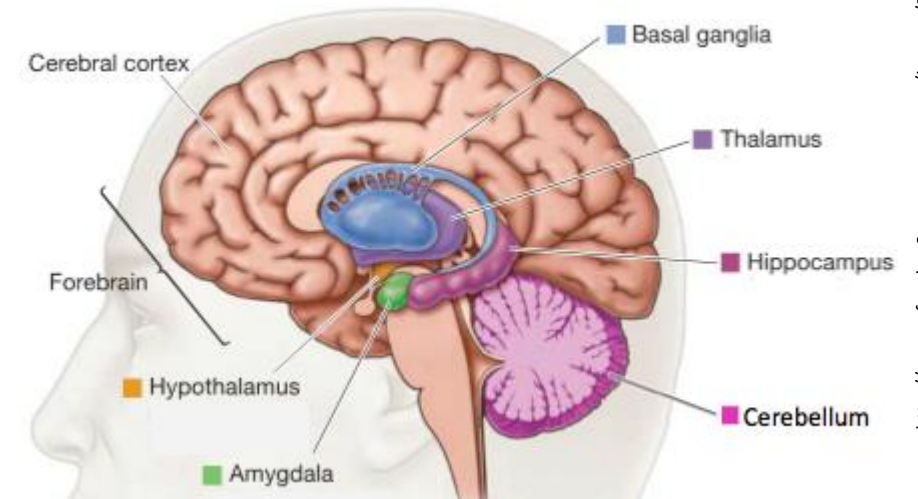
Amygdala

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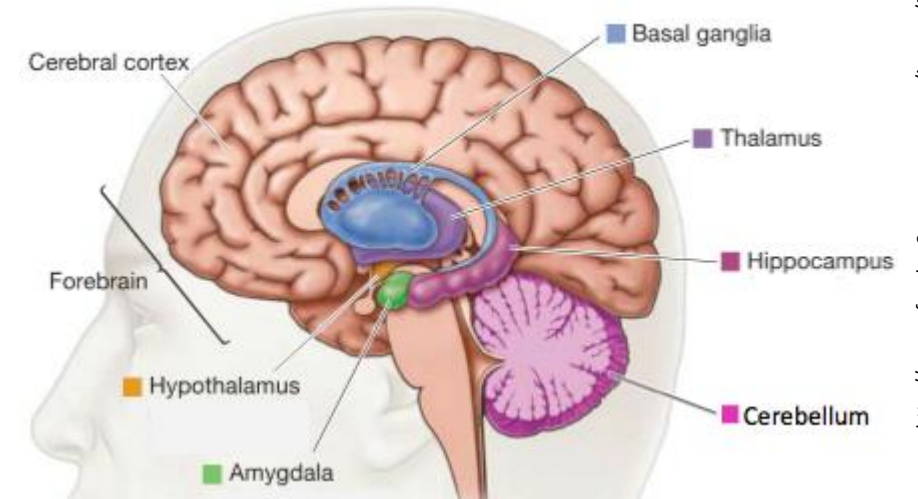
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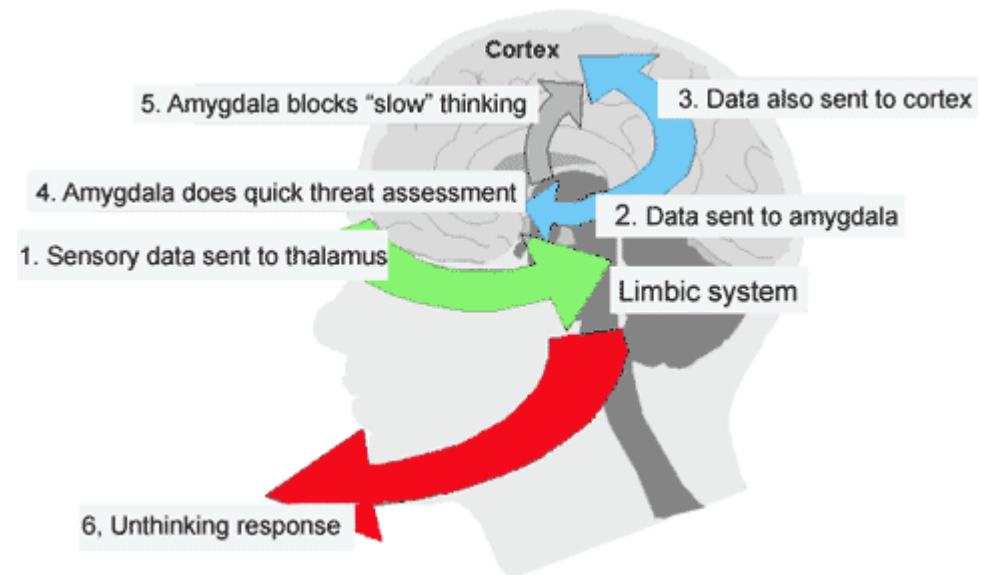
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- Connections to all major cortical and subcortical structures
- Modified corpus striatum
- Plasticity – memory formation
- „Influence of information from outer environment on limbic system“
- „Amygdala hijack“
- „Affective tags“
 - Both positive and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



http://proprofs-cdn.s3.amazonaws.com/images/FC/user_images/1406217/9806788916.png

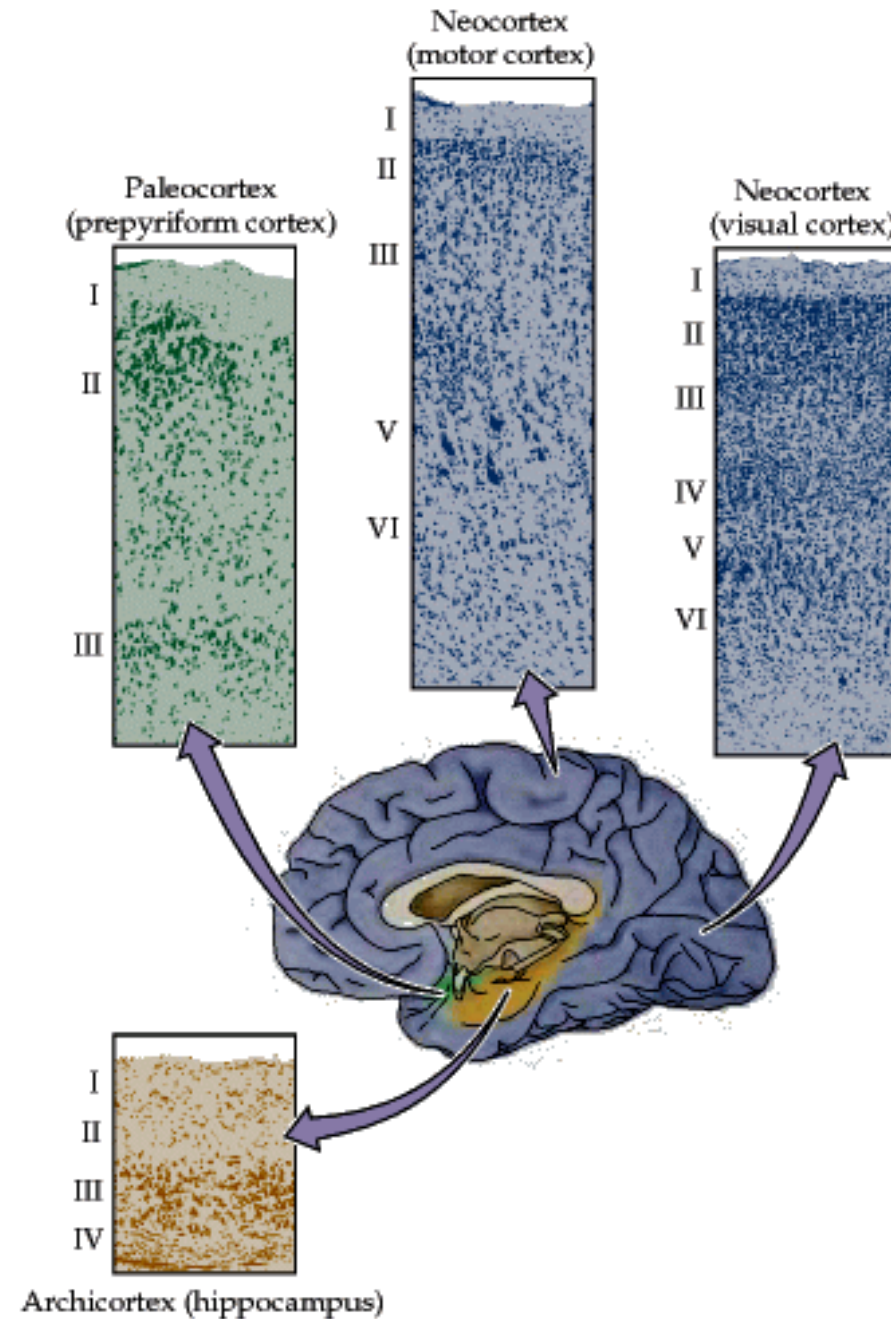


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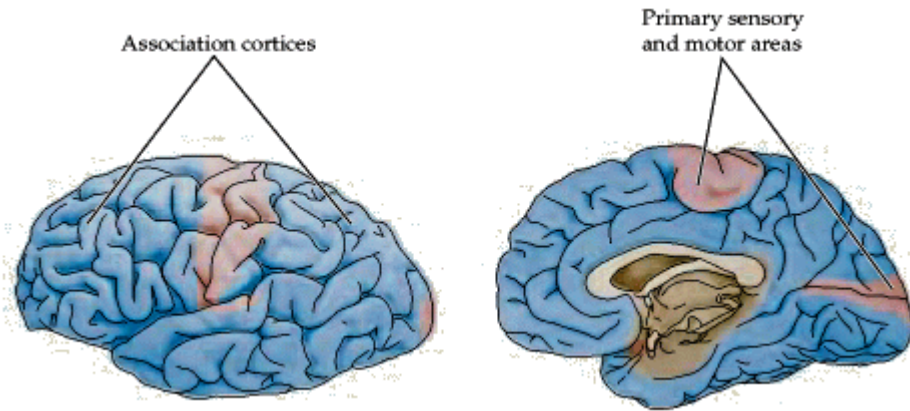
Neocortex

Cerebral cortex

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



Neocortex

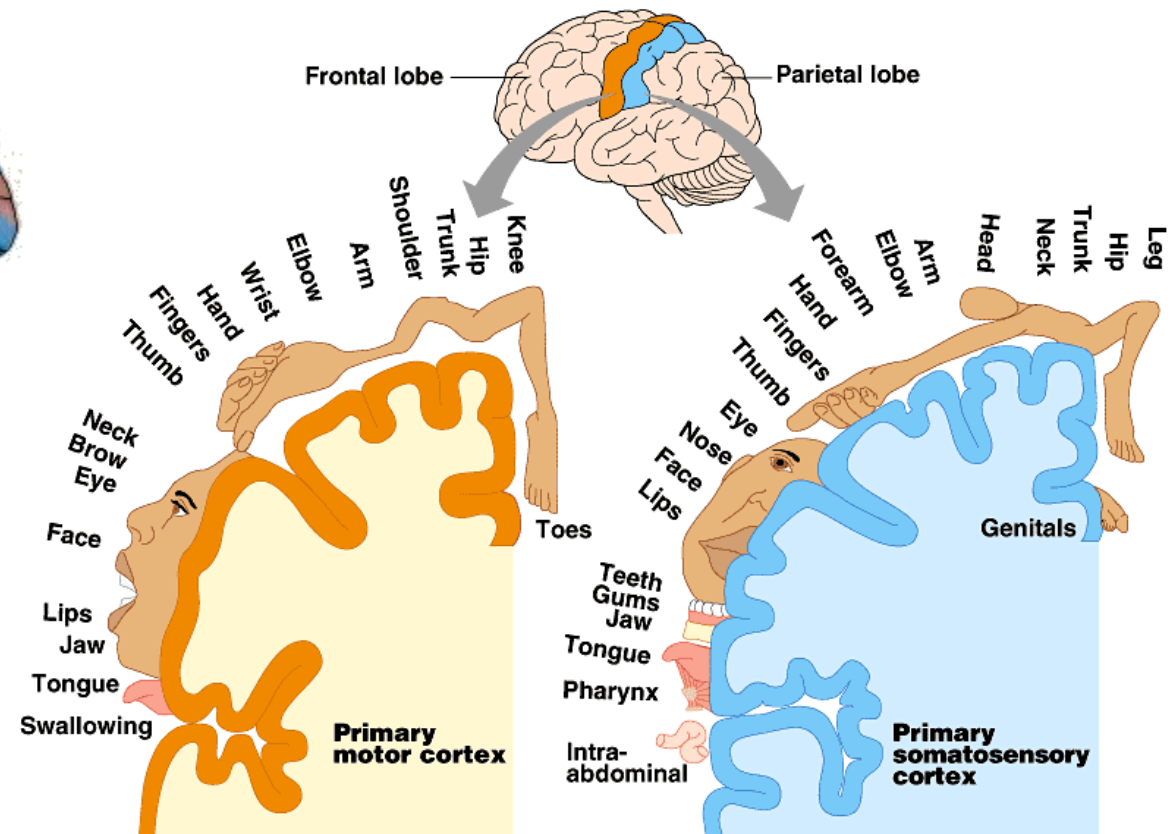


Primary areas

- ✓ 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

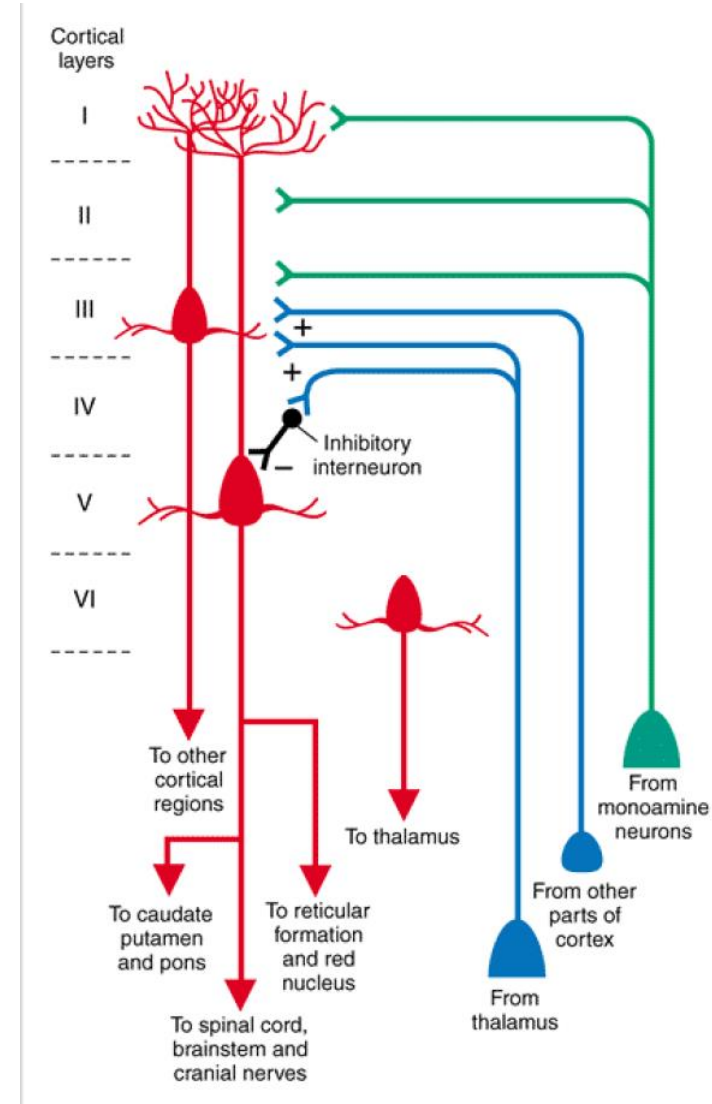


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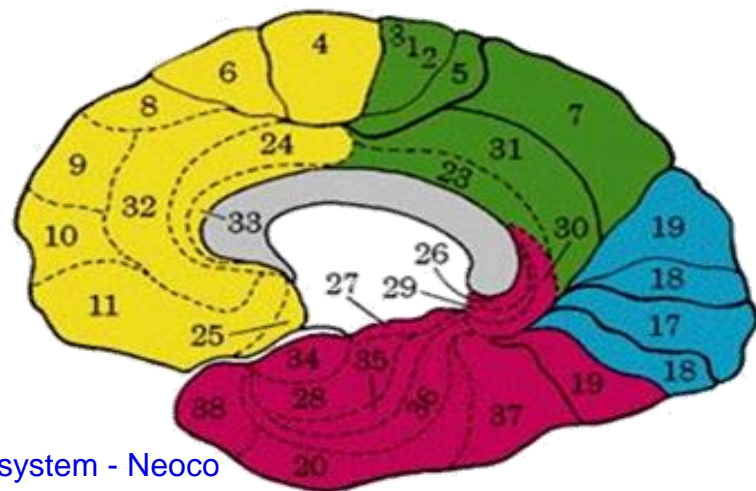
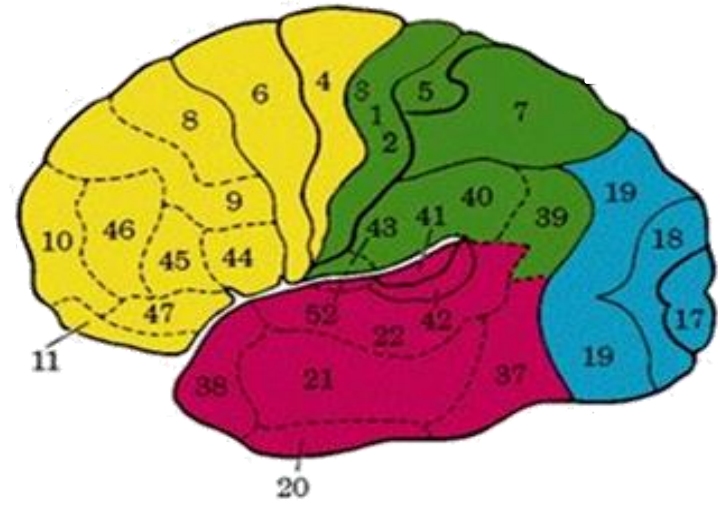
<http://www.emunix.emich.edu>

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

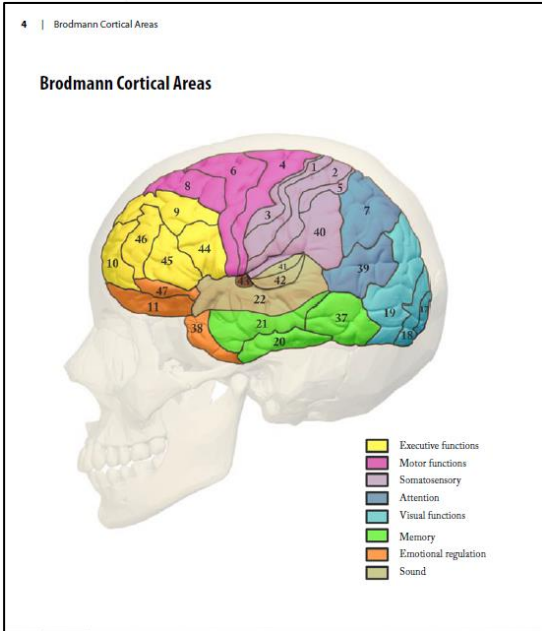
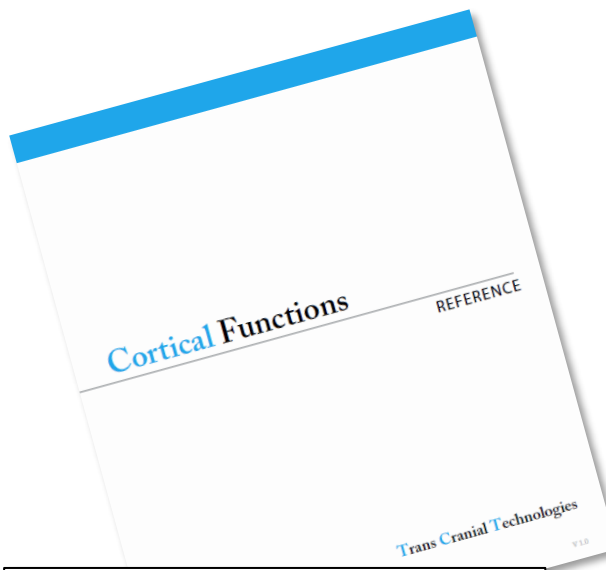


Brodman areas



Broadman'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

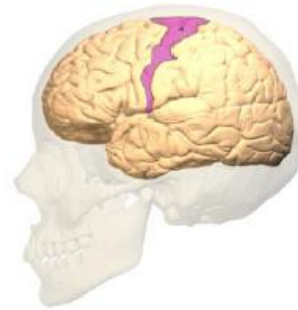
43 Limbic system - Neoco



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

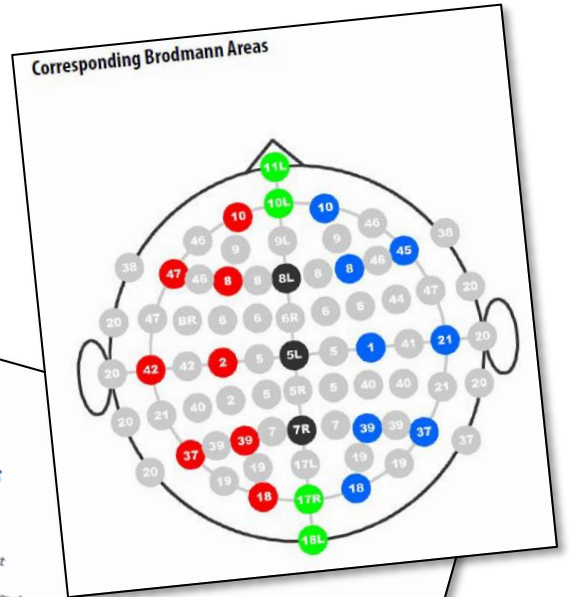
- Contralateral finger, hand, and wrist movements (Dorsal)
- Contralateral lip, tongue, face, and mouth movement (Lateral)
- Swallowing / laryngeal movement
- Contralateral lower limb (knee, ankle, foot, toe) movement (Mesial)
- Motor imagery
- Learning motor sequences
- Volitional breathing control
- 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)

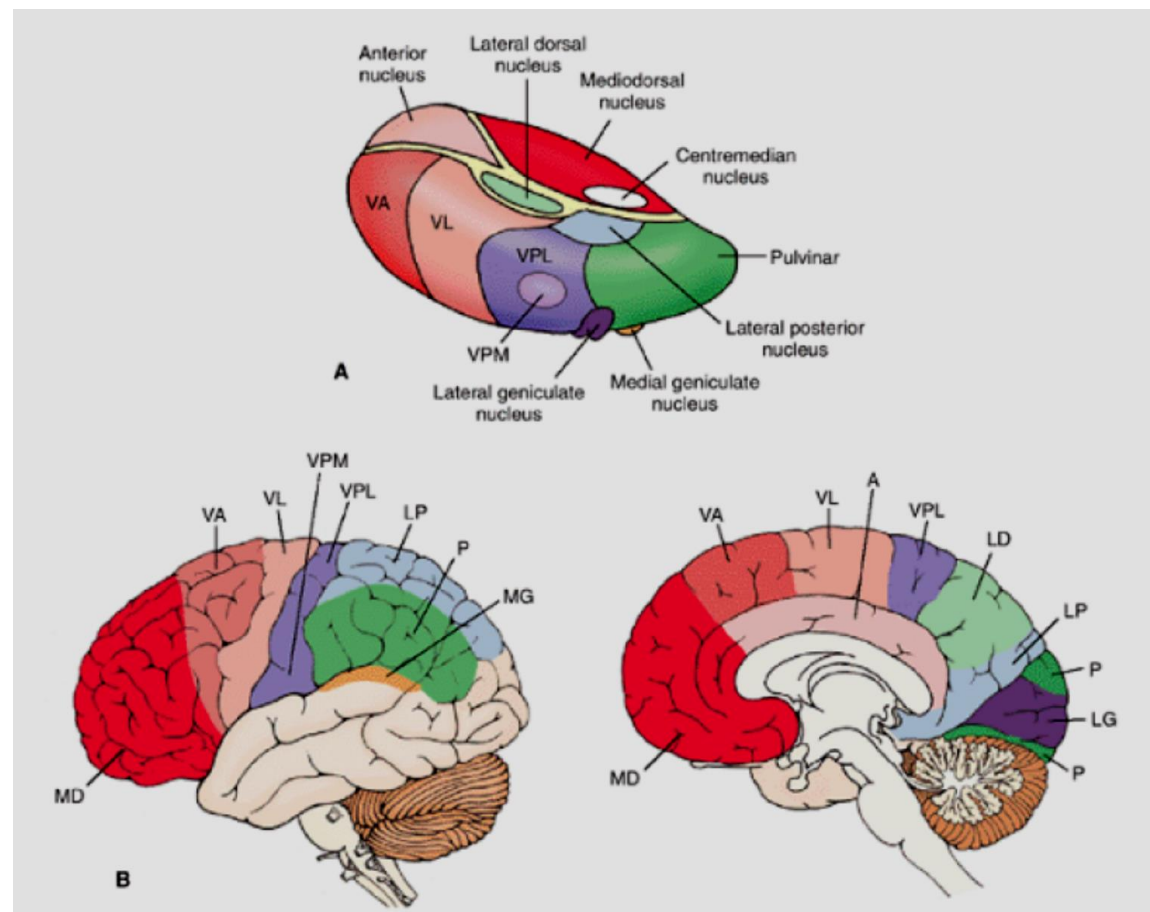
Other

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



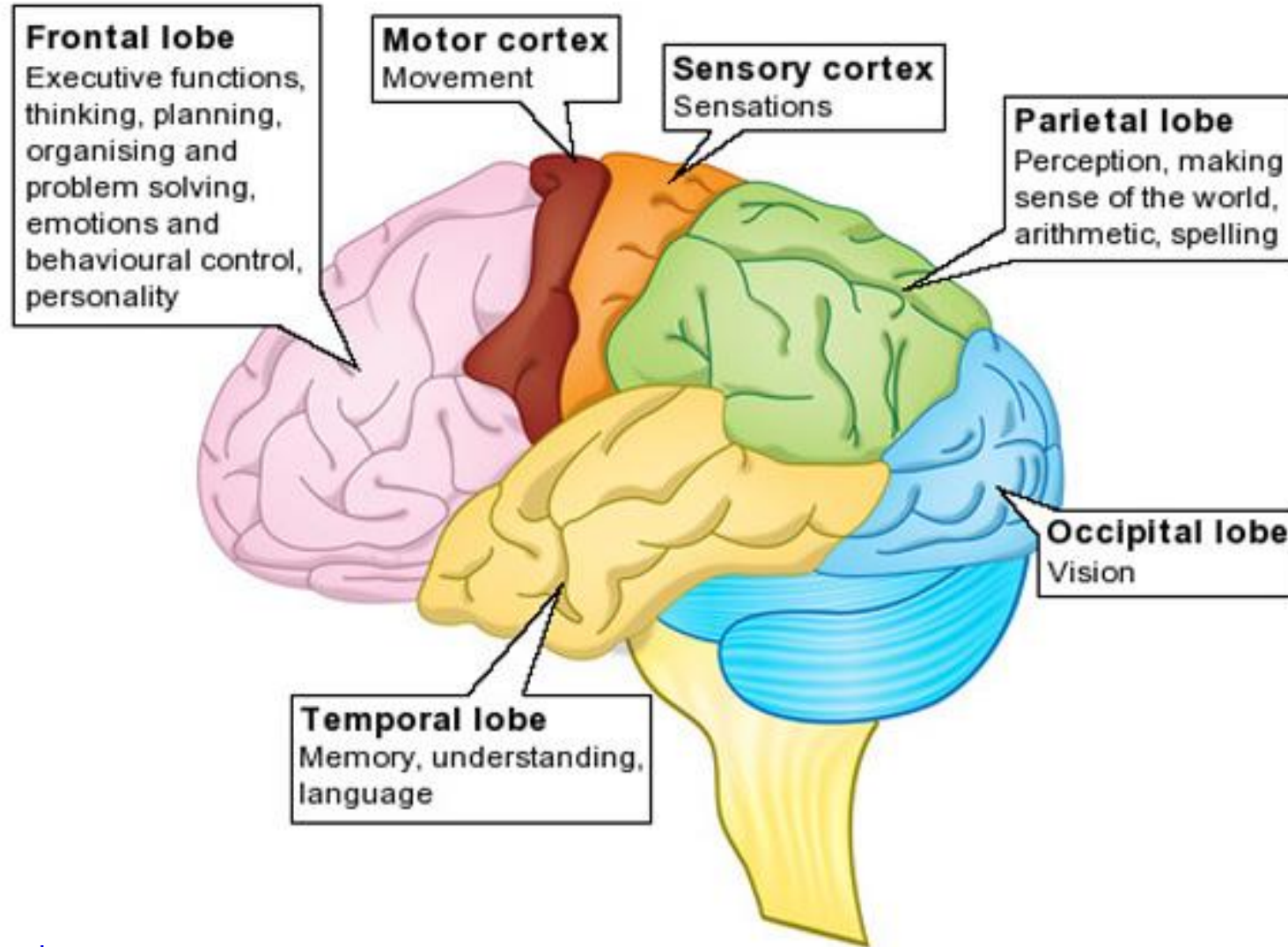
Cerebral cortex and thalamus

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

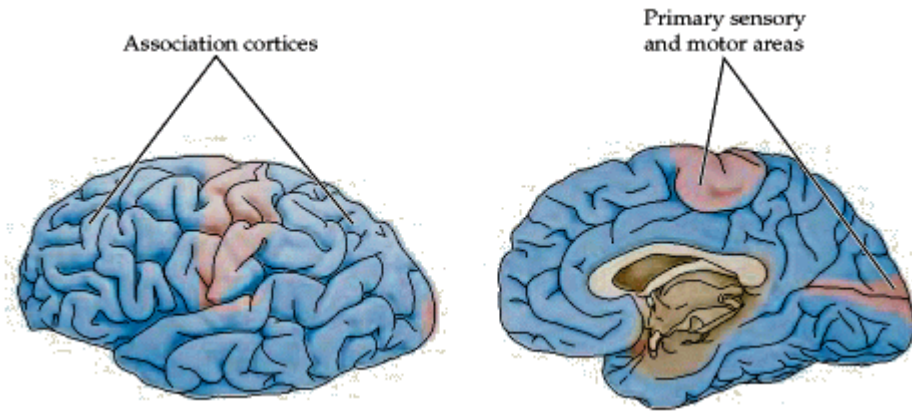


<http://www.slideshare.net/drpsdeb/presentations>

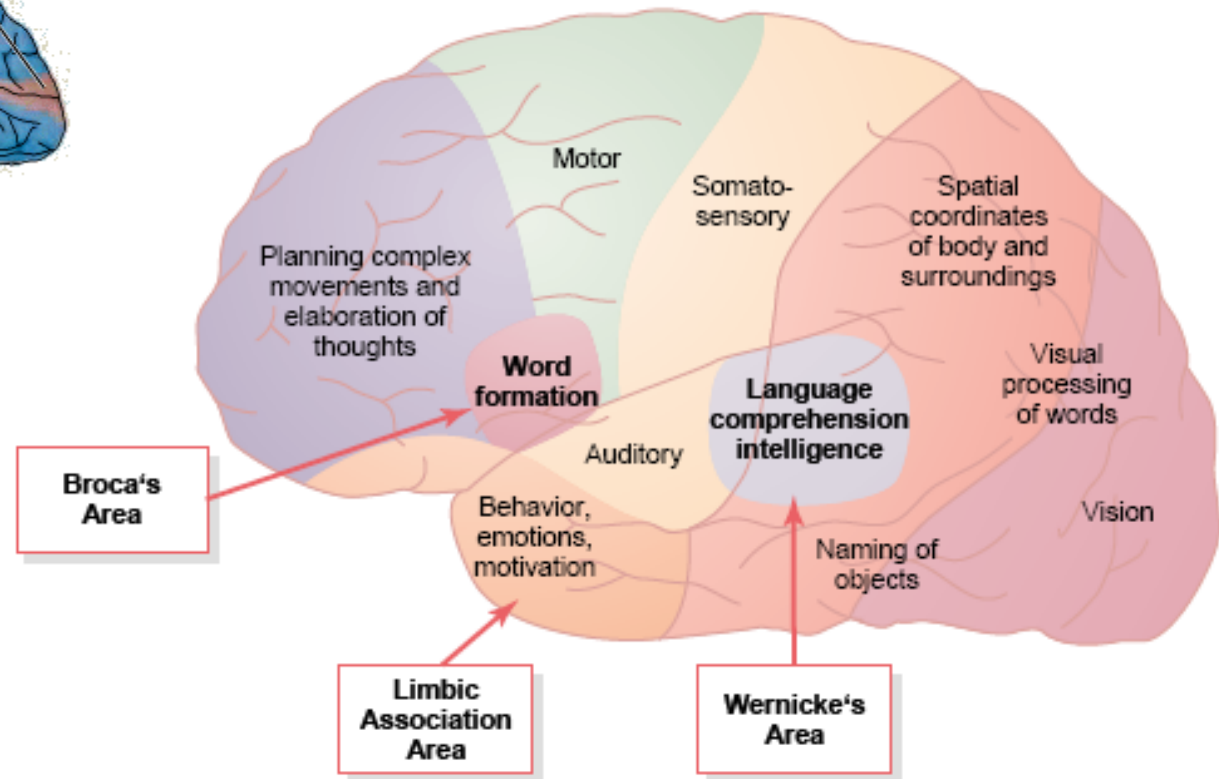
Cortical functions



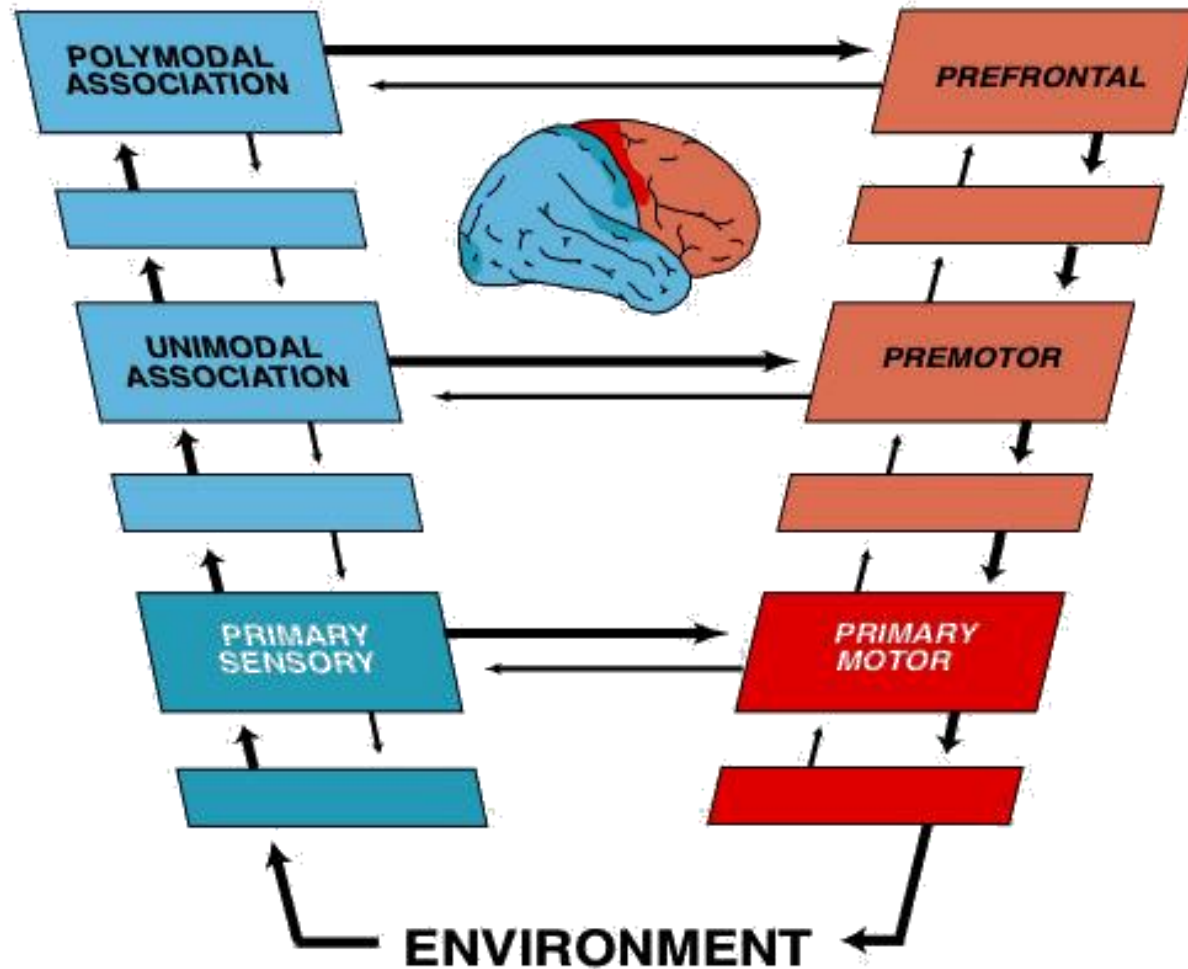
Association areas



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

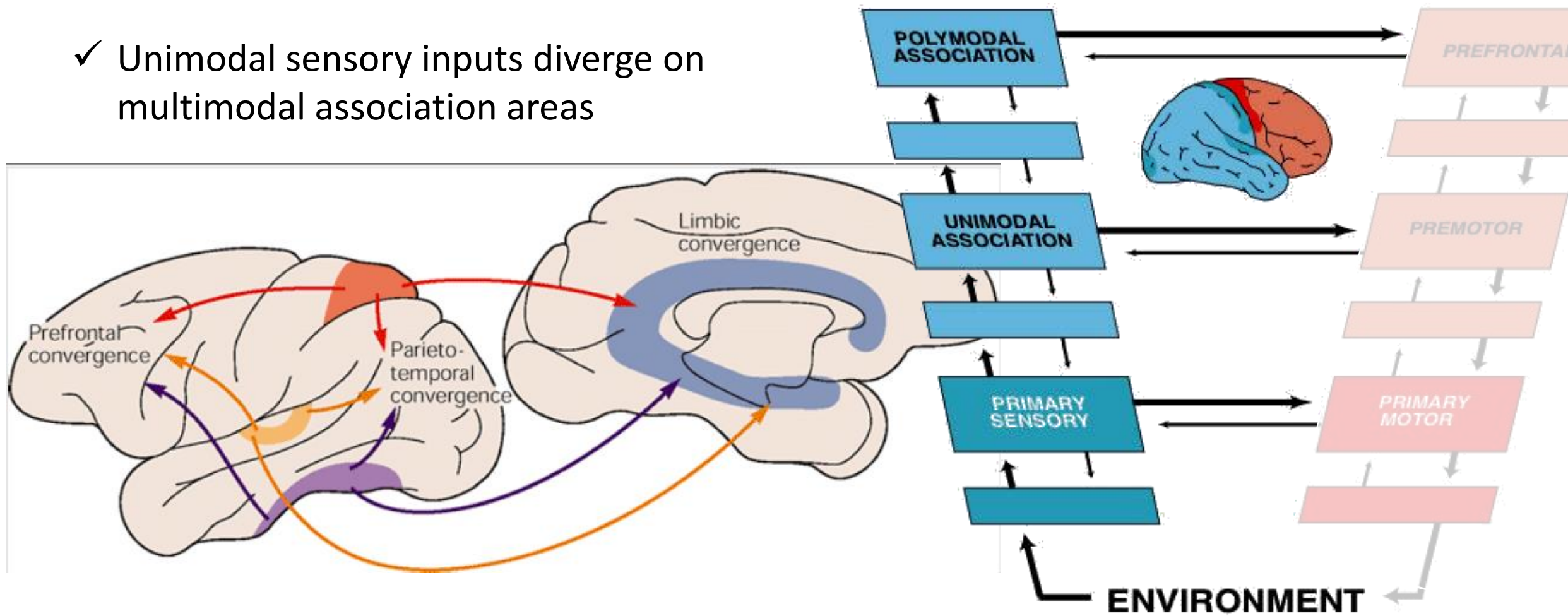


Signal processing algorithm

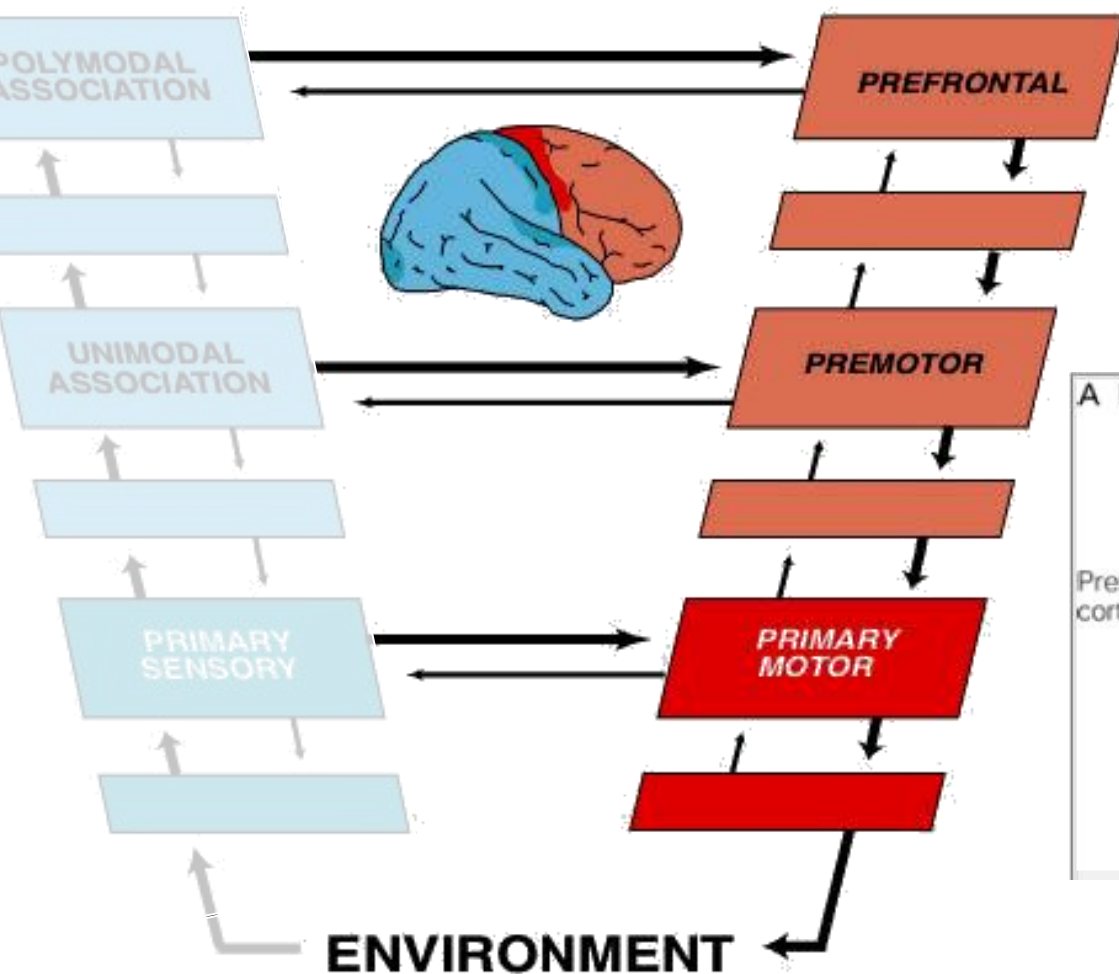


Aferentation

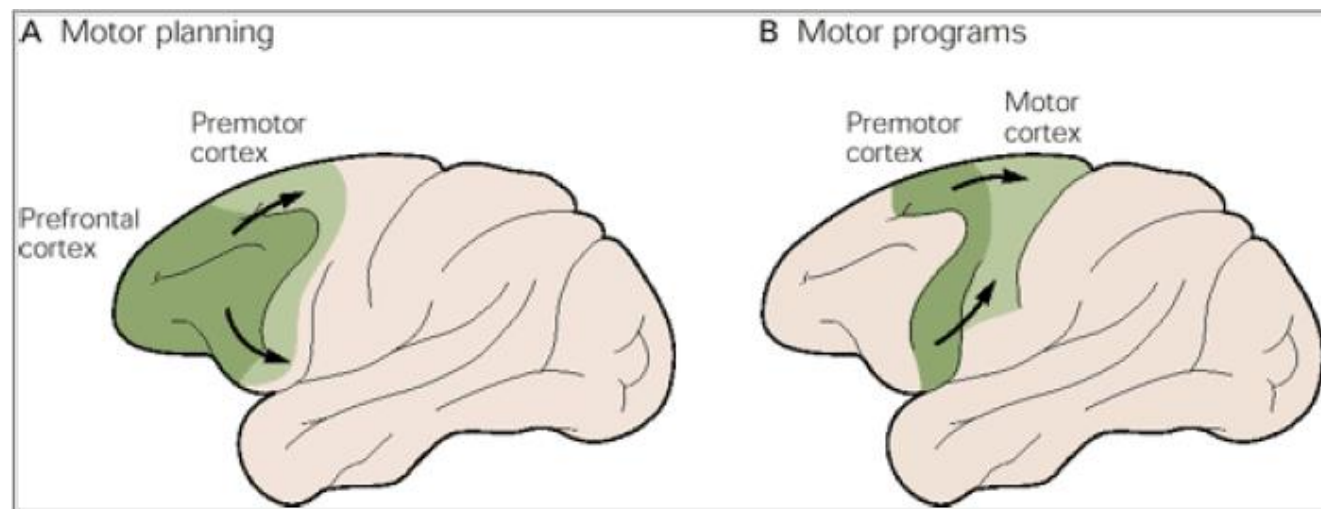
- ✓ Unimodal sensory inputs diverge on multimodal association areas



Efferentation



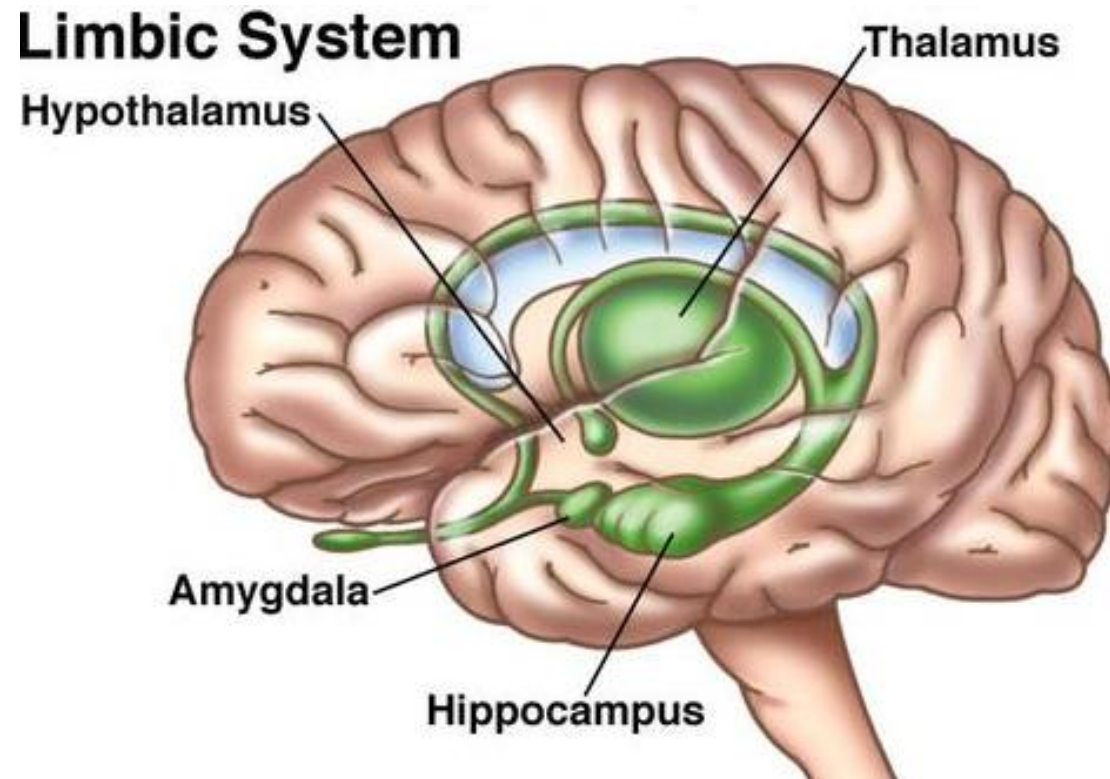
- ✓ The Sequence of Information processing Is Reversed in the Motor System



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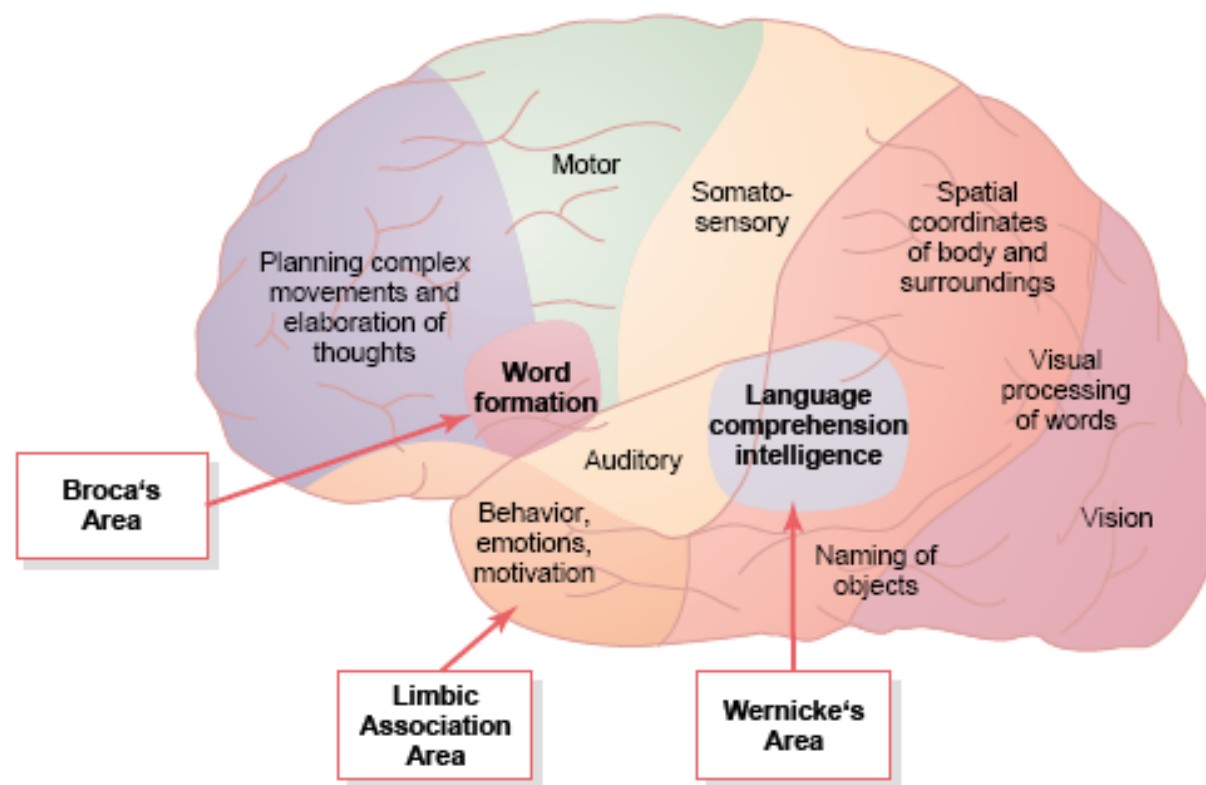
Limbic association area

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



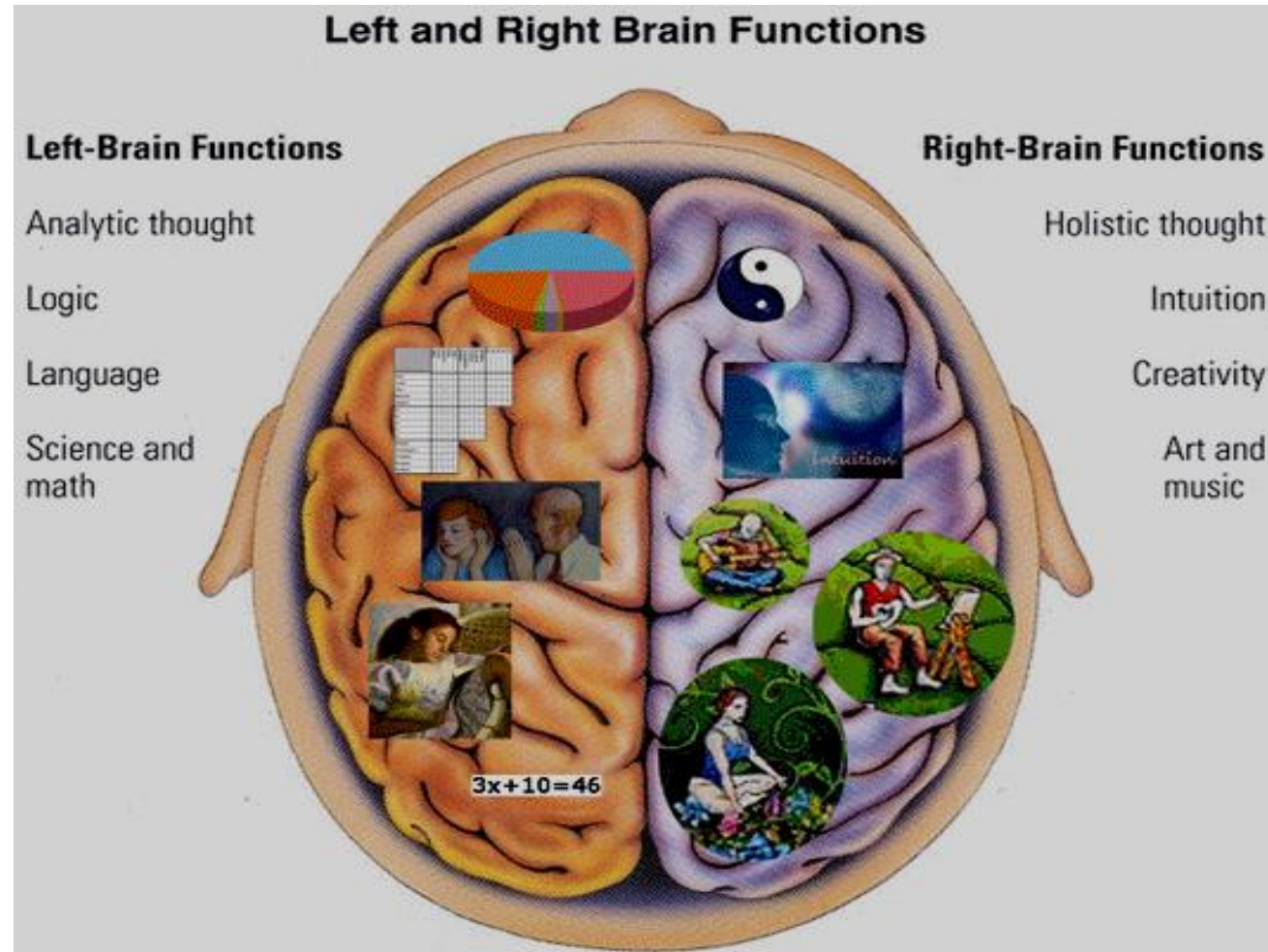
Parieto-occipito-temporal association area

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

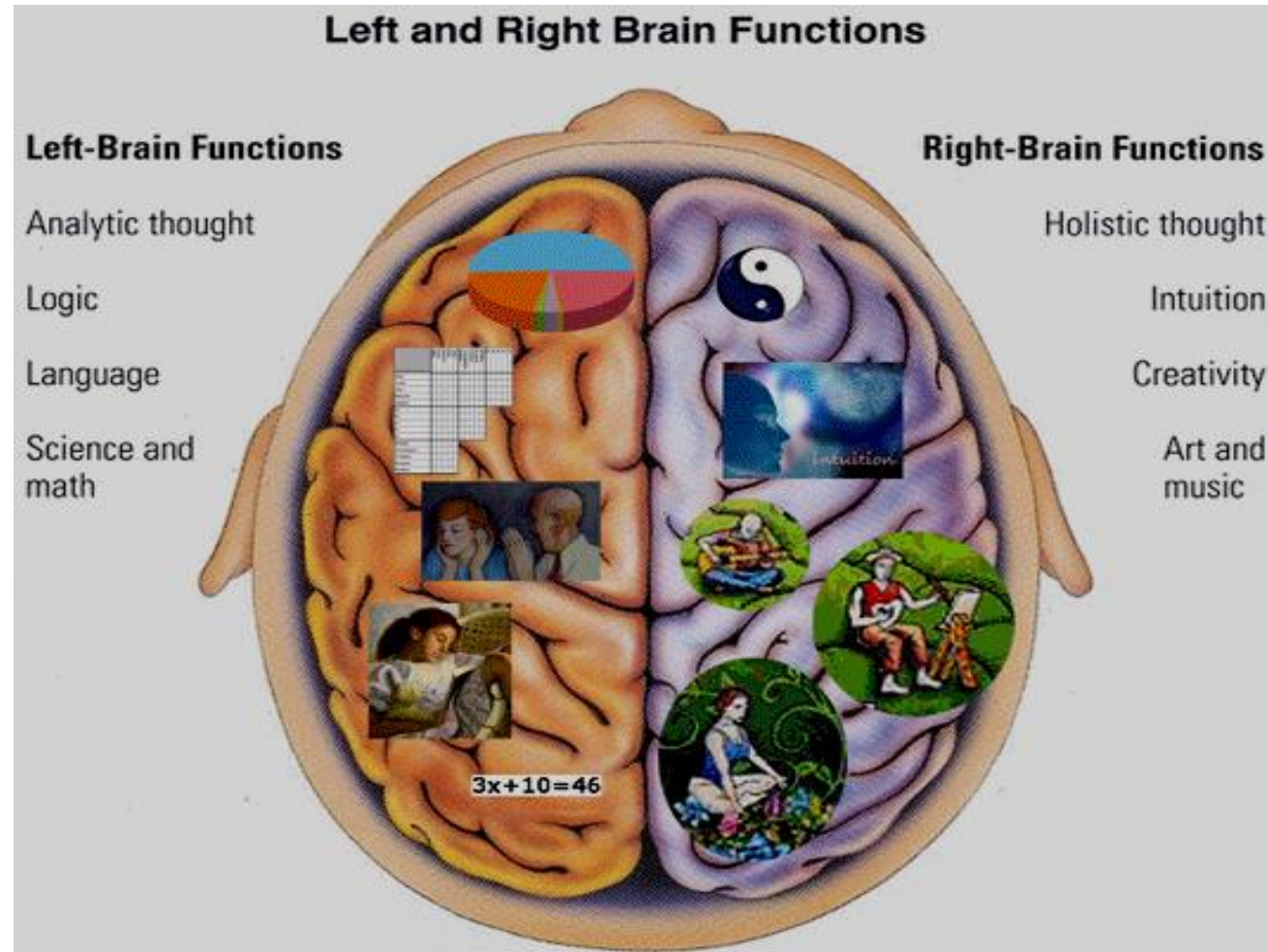


<http://www.slideshare.net/drpsdeb/presentations>

Lateralization of cerebral functions



Lateralization of cerebral functions



Aphasia

Acalculia

Tactile agnosia

Conceptual apraxia

Ideomotor apraxia

Orientation disorders

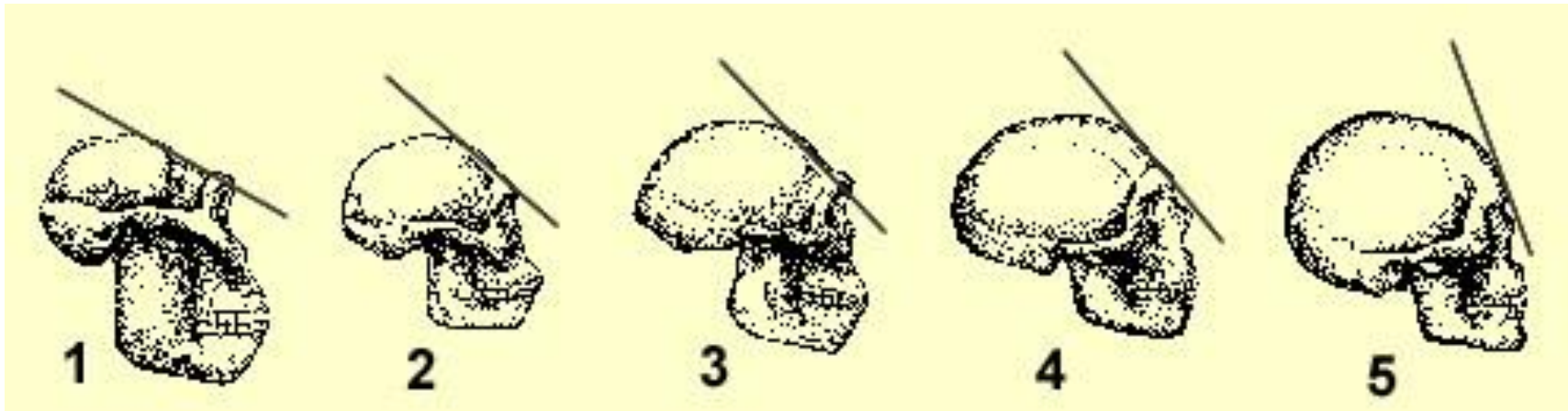
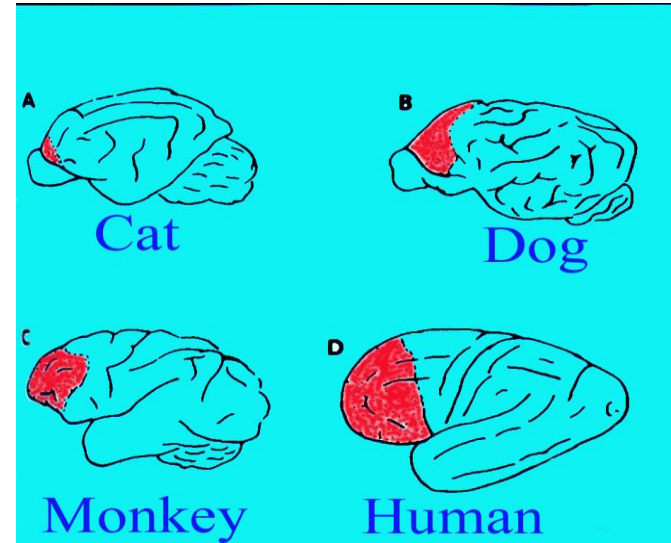
Constructional apraxia

Anosognosia

Neglect syndrome

Frontal association area

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



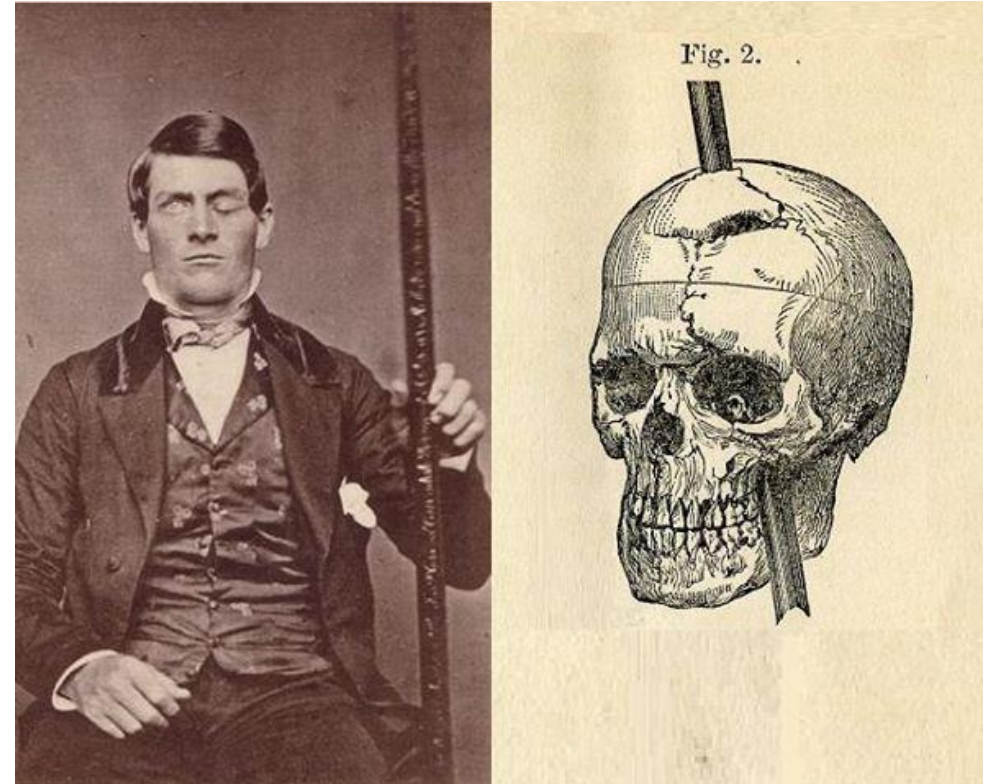
Limbic system - Neocortex 1

1. *Australopithecus robustus*
2. *Homo habilis*
3. *Homo erectus*
4. *Homo sapiens neanderthalensis*
5. *Homo sapiens sapiens*

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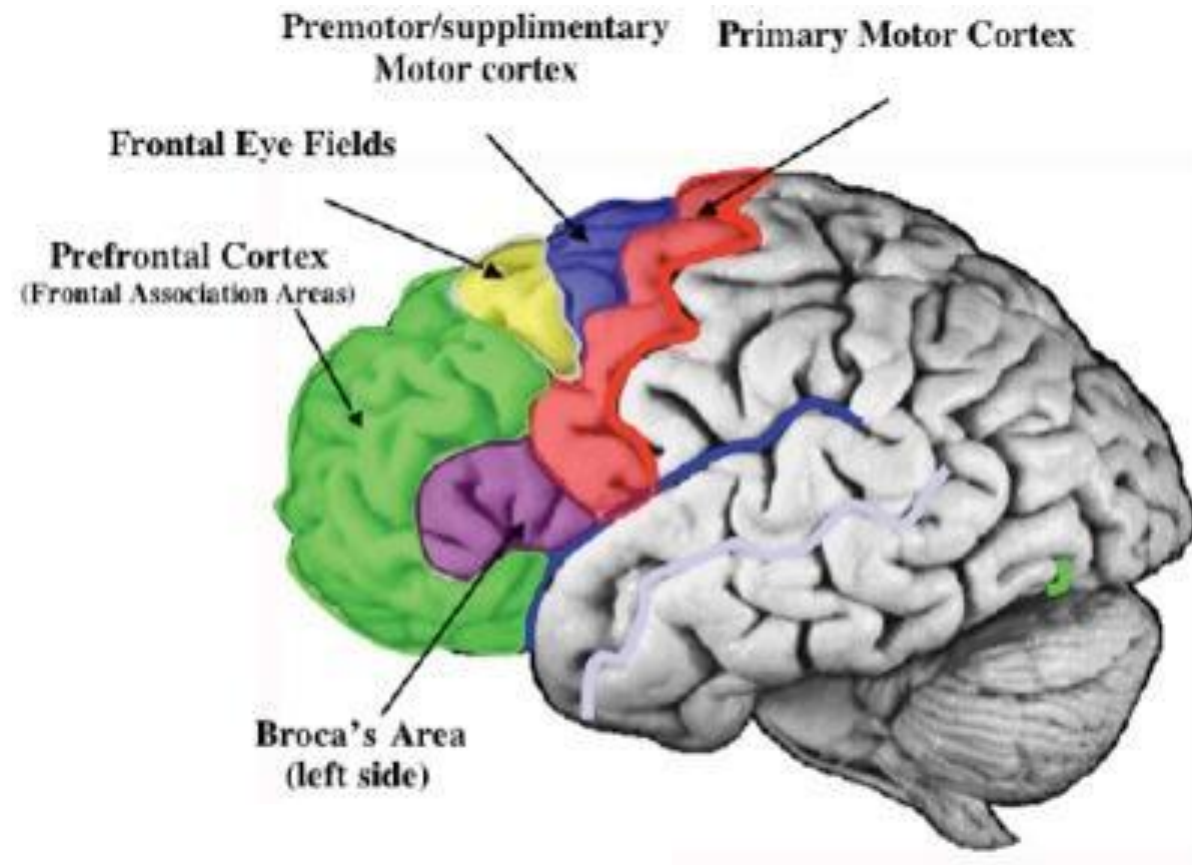
Phineas Gage (1823 – 1860)

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



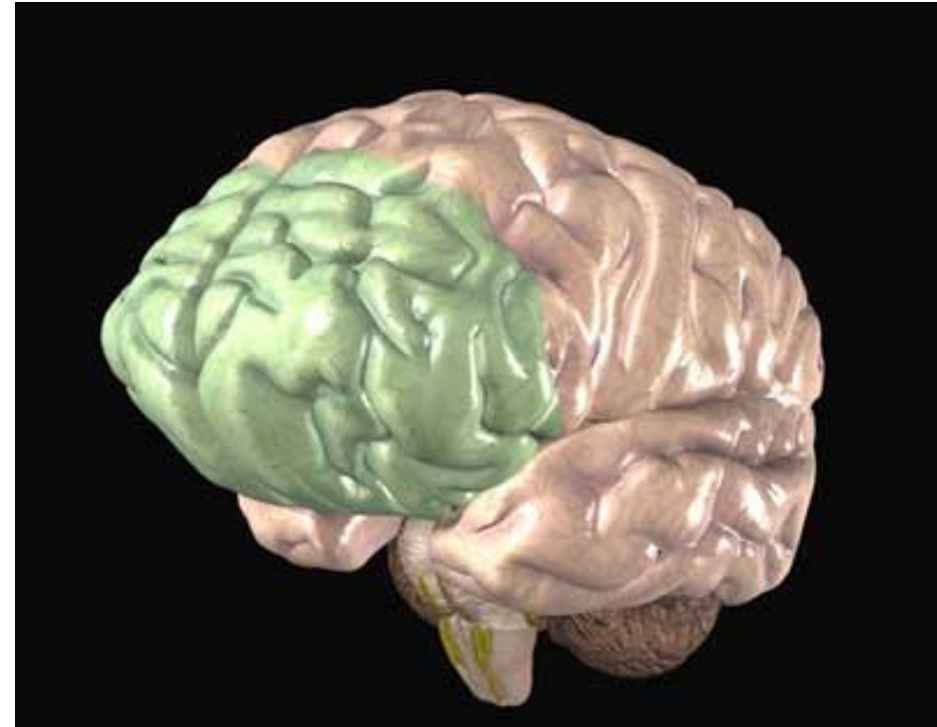
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Frontal lobe



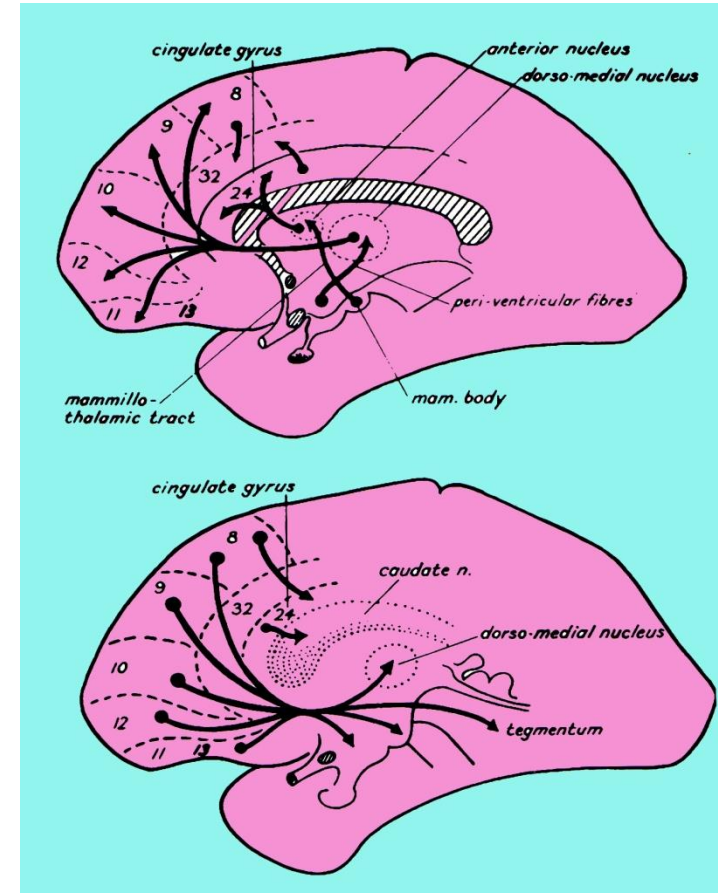
Frontal association area

- ~ 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>

1. Motor planning / organization

- Frontal association area
- Premotor area
- ✓ Close cooperation with motor cortex
- ✓ Planning and preparing of complex motor action (in cooperation with Basal ganglia)
- ✓ Close cooperation with P-O-T area which sends visual-acoustic-sensory-spatial information
- ✓ Voluntary motor control



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2. Thinking skills

- Organization
 - The ability to arrange information in a meaningful system
- Planning
 - The ability to create a strategy for reaching goals
- Time management
 - The ability to estimate time needed for reaching goals
- Working memory
 - The ability to hold information in awareness while performing a mental operation



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3. Attention

- Selective attention
 - The ability to filter information
- Sustained attention
 - The ability to actively attend to a task
- Divided attention
 - The ability to attend to two tasks at once
- Shifting attention
 - The ability to shift attention between two or more tasks



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4. Behavioral control

- Facilitation/ initiation of „wanted“ (re)action
- Inhibition of „unwanted“ (re)action
 - Anticipation
 - Self-regulation x procrastination
- Flexibility
 - The ability to revise plans when it is needed
- Goal-directed persistence
 - The ability to self-motivate
- Social brain
 - Mentalization
 - Empathy
 - Social behavior - frontal association area
 - Instinct behavior - limbic association area



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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

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

M U N I

M E D