BIEN500 – Lecture 57-60

- Cerebral Cortex
- Intellectual Functions of the Brain
- Learning and Memory
- Neurohormonal control
- Limbic System and the Hypothalamus
- Sleep & Epilepsy;
- Autonomic Nervous System

Cerebral Cortex

- Largest part of the nervous system
- Functional part: 2 – 5 mm thick layer of neurons
- Total area ~ 1 $m^{2,}$ ~ 100 billion neurons
- Three types of cells
  - Granular (or stellate)
  - Fusiform
  - Pyramidal
- Each area of the cortex is connected to a specific part of the thalamus.
- When thalamic connection is lost cortical function stops.
- All sensory pathways pass through the thalamus with the exception of the olfactory tract.

Histological Structure of the Cerebral Cortex

Short horizontal connections

I.Molecular Layer

II. External Granular Layer

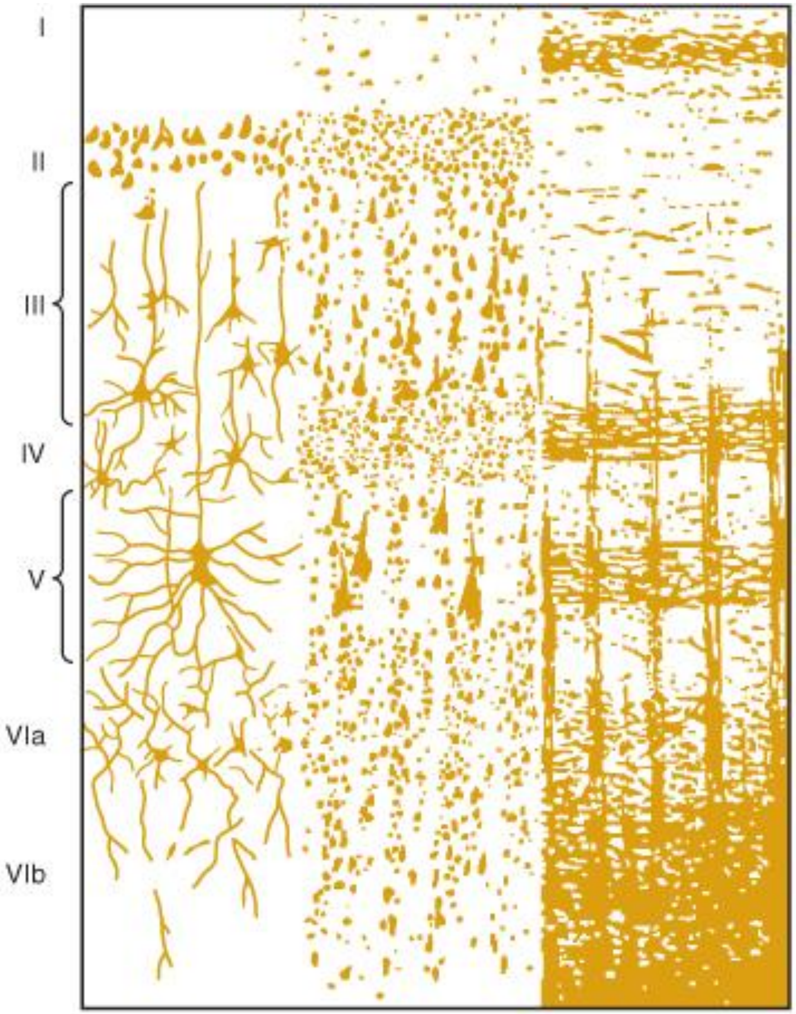
III.Pyramidal Cells

IV. Granular Cells, Output fibers to thalamus

V. Large fibers to brain stem and cord

VI. Fusiform or polymorphic cells

VII. Output signals



Granular Cells

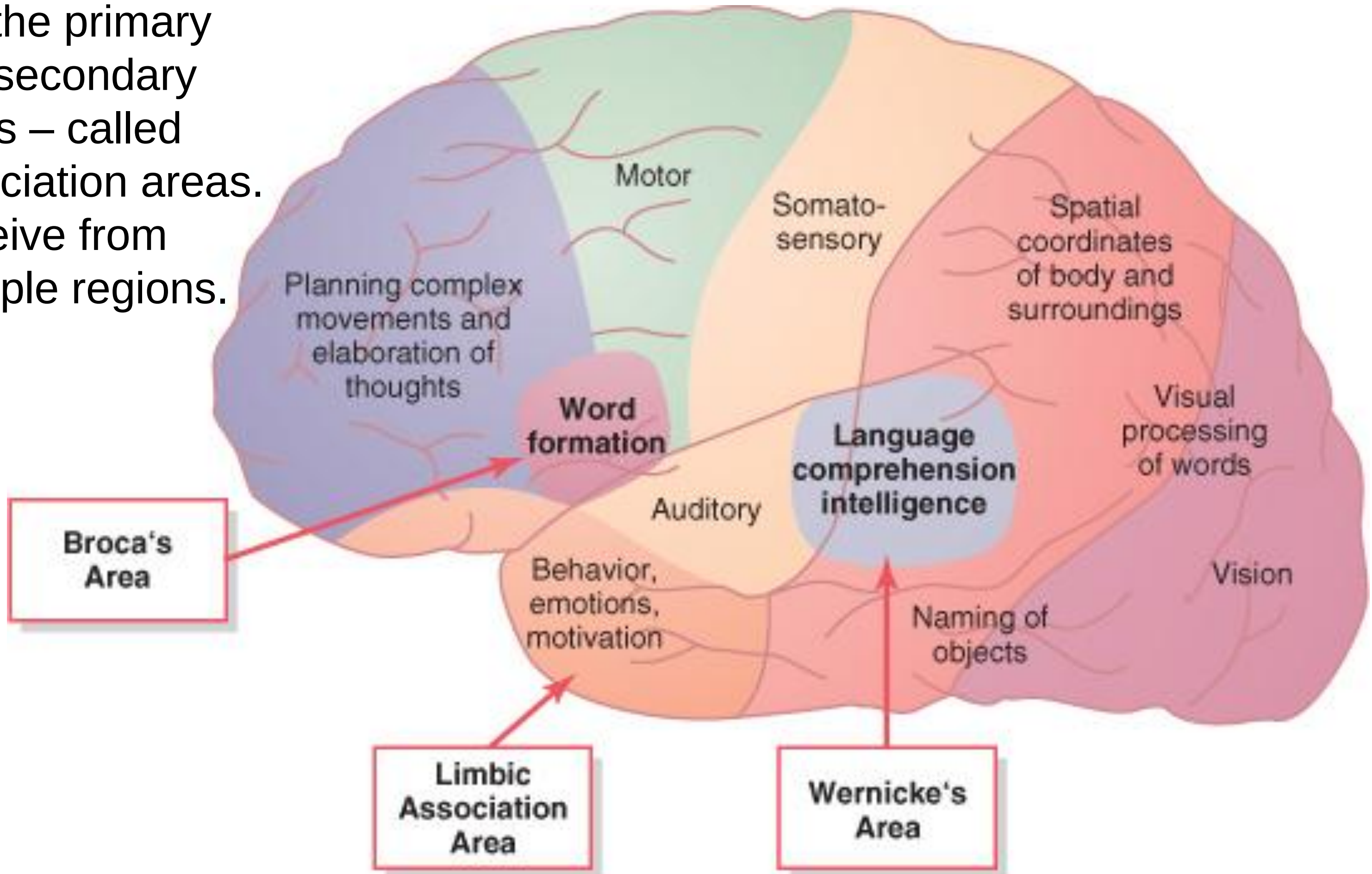
- Short axons – function as intracortical neurons
- Large concentration in the sensory and association areas.
- Excitatory – Glutamate
- Inhibitory - GABA

Pyramidal Cells

- Pyramidal in shape
- Source of output fibers
- Larger, more numerous than fusiform cells
- Nerve fibers go down to spinal cord.
- Fibers also connect major regions of the brain.
- Fusiform cells provide similar functions.

Functional Areas of the Cerebral Cortex

Areas that don’t fit into the primary and secondary areas – called association areas. Receive from multiple regions.

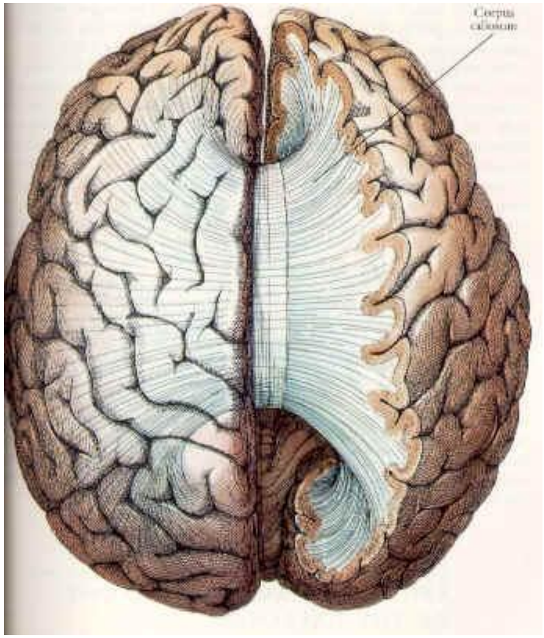


Interesting Brain Regions

- Broca’s Area
  - Word formation
  - Plans and motor patterns are initiated and executed
  - Learning of foreign language
- Wernicke’s Area
  - More developed in dominant side of brain
  - General interpretive area
  - Stimulation may produce complex visualization, hallucinations, complex statements, hearing a musical piece
- Limbic Association Area
  - Behavior and emotion
  - Motivational drive for learning
- Facial Recognition Area (large)

Dominant Hemisphere

- Wernicke's area more developed on one side.
  - Important for language, mathematics, logic. (Language comprehension)
- Left hemisphere more dominant for 95%
  - Wernicke's area >50% larger in >50% of neonates.
  - Other 5% is either dual- or right-dominant.
  - Related to right-handedness.
- Hemispheres communicate via corpus callosum



Non-Dominant Hemisphere

- Understanding/Interpreting music
- Nonverbal visual experiences
- Spatial relations with surroundings
- Interpretation of “body language”
- Interpretation of vocal intonation
- Somatic experiences
- Non-symbolic interpretation

“Dominant” in the sense of language-based intellectual function.

Effects of Prefrontal Lobotomy

Prefrontal cortex thought to be the locus of higher intellect.

- Inability to solve complex problems
- Inability to combine tasks to reach goals
- Inability to multitask
- Loss of aggressiveness/ambition
- Inappropriate social responses (w.r.t. morals/sex/body functions)
- Inability to produce trains of thought
- Rapid mood changes
- Normal motor function, but often without purpose

Pathways for Auditory Communication

5. activation of motor programs in Broca's area for control of word formation

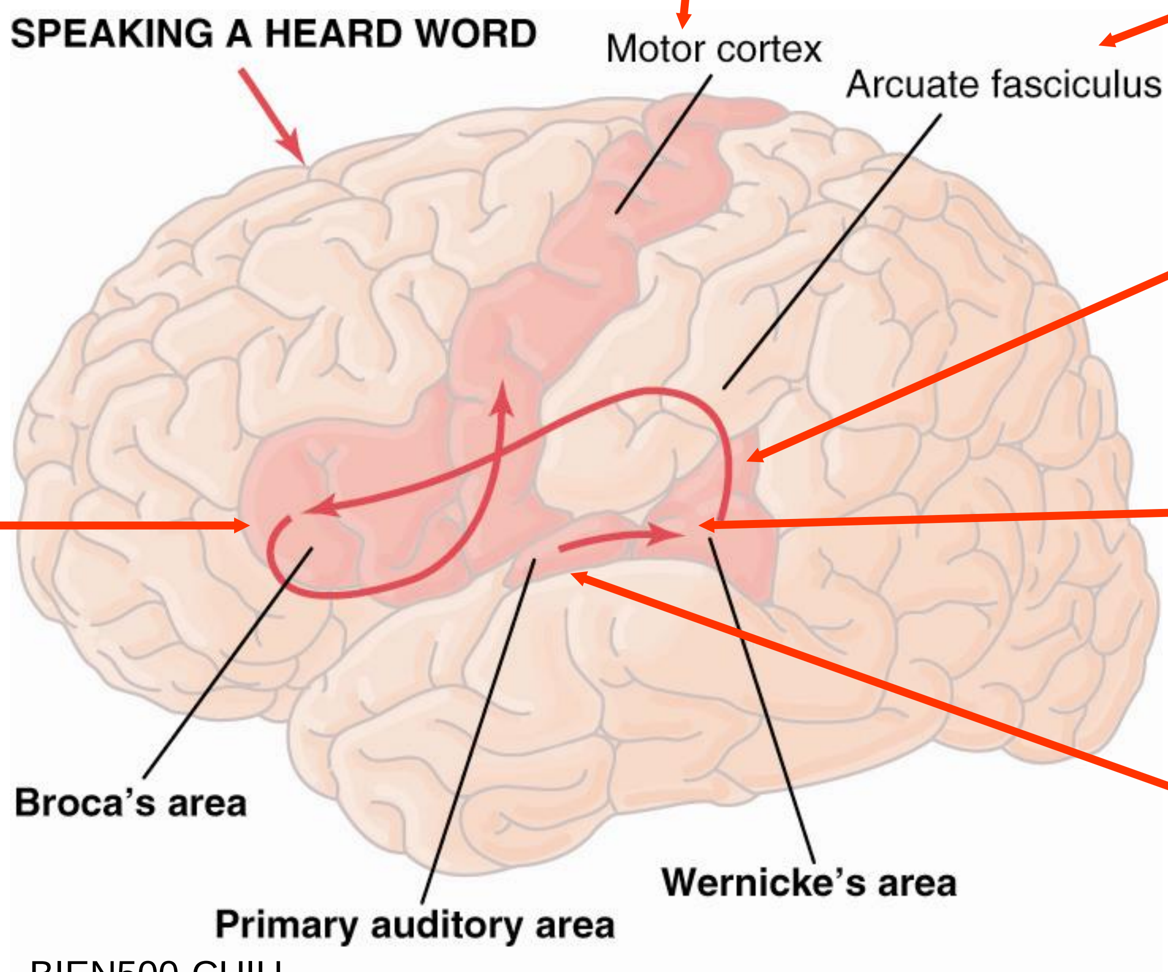
6. transmission of signals to motor cortex to control speech muscles

4. transmission via the arcuate fasciculus to Broca's area

3. formation of the word that expresses a particular thought

2. interpretation of the word and the thought that the word expresses in Wernicke's area

1. primary auditory area recognition of the sound as a word



Pathways for Visual Communication

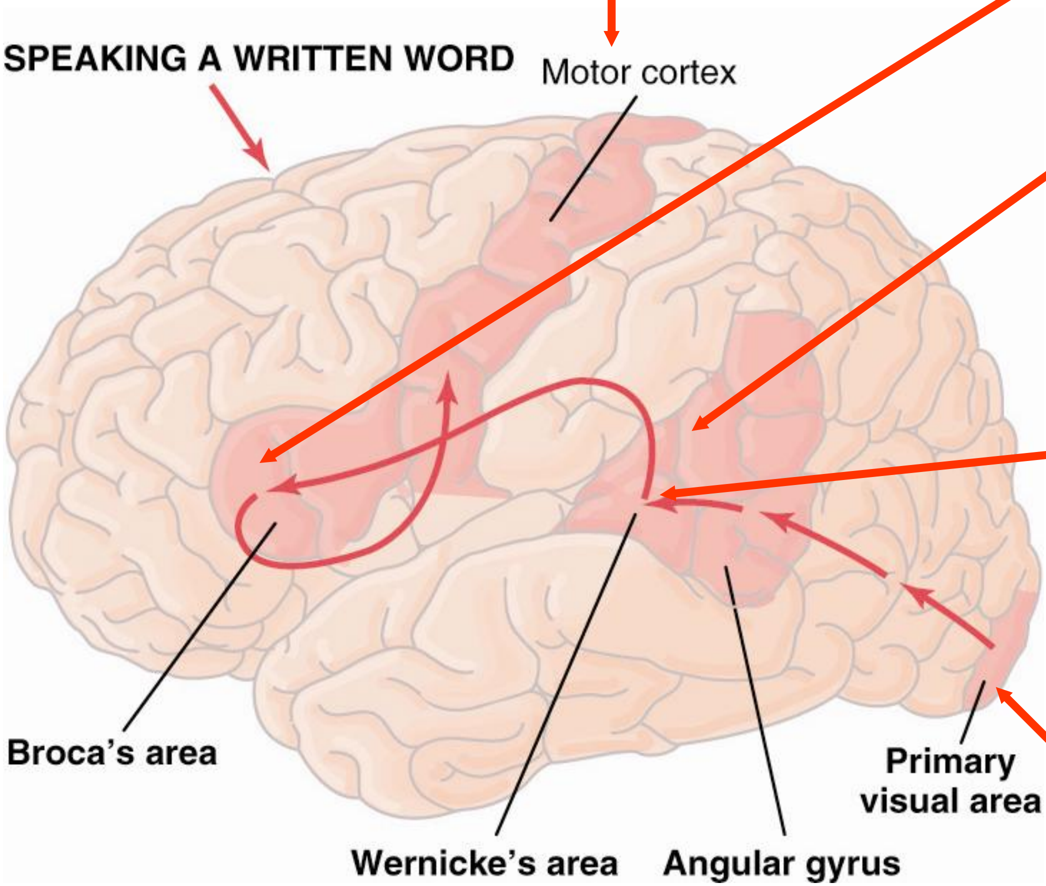
5. transmission of signals to motor cortex to control speech muscles

4. then to Broca's area for motor formation of the word

3. visual input reaches full level of interpretation in Wernicke's area

2. processing of the visual information in the parietal-temporal-occipital association cortex, the angular gyrus region

1. receive the visual input in primary visual area



Corpus Callosum

- Transfers information from Wernicke’s area to contralateral motor cortex
- Prevents somatosensory information from contralateral hemisphere from reachig Wernicke’s area
- If severed
  - Can still perform subconscious motor functions on the same side
  - May do things without knowing why
- Required for superficial subconscious level
- Anterior commissure unifies emotional response (because of amygdala)

Kim Peek (the Rain Man)

- Savant syndrome (Down’s syndrome)
- Music, art and mathematics
- Photographic memory
- Missing corpus callosum, anterior and posterior commissure.
- Malformed cerebellum – poor coordination

- Q: does the brain compensate or does the damage allow latent abilities?

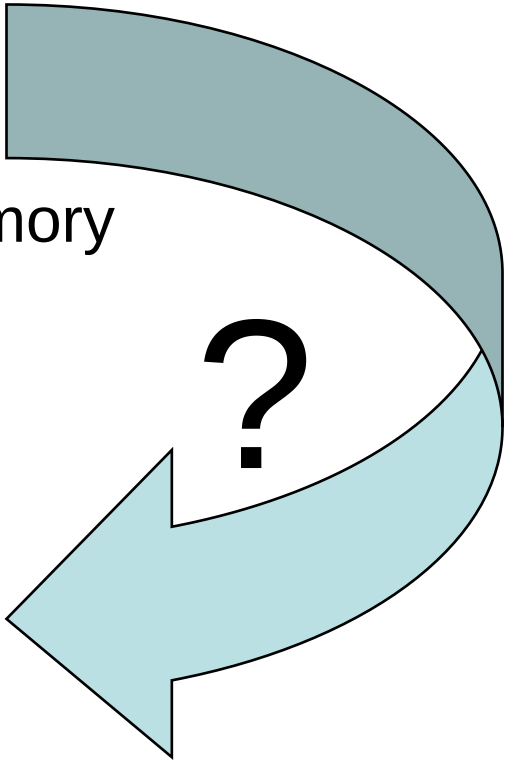
Thoughts and Memory

- Neural mechanism for thought is not known.
- Most likely a specific pattern of simultaneous neural activity in many brain areas.
- Destruction of cerebral cortex does not prevent one from thinking.
  - However, depth of thought and level of awareness may be less.

Memory

- Change in the capability of synaptic transmission from neuron to neuron as a result of prior stimulation.
- Memory trace is a specific pattern or pathway of signal transmission.
- Once established they can be activated by the thinking mind to reproduce the pattern and thus the memory.

Memory: classification by duration



- Short term
  - Last seconds or minutes
  - May be converted to long-term memory
  - Classic example – phone number
- Intermediate long-term
  - Last days to weeks, but fade
- Long-term
  - Can be recalled years later
  - Pathways to complex memories may be difficult to find
- Working memory: (like RAM – used then deleted)

Mechanism of Memory

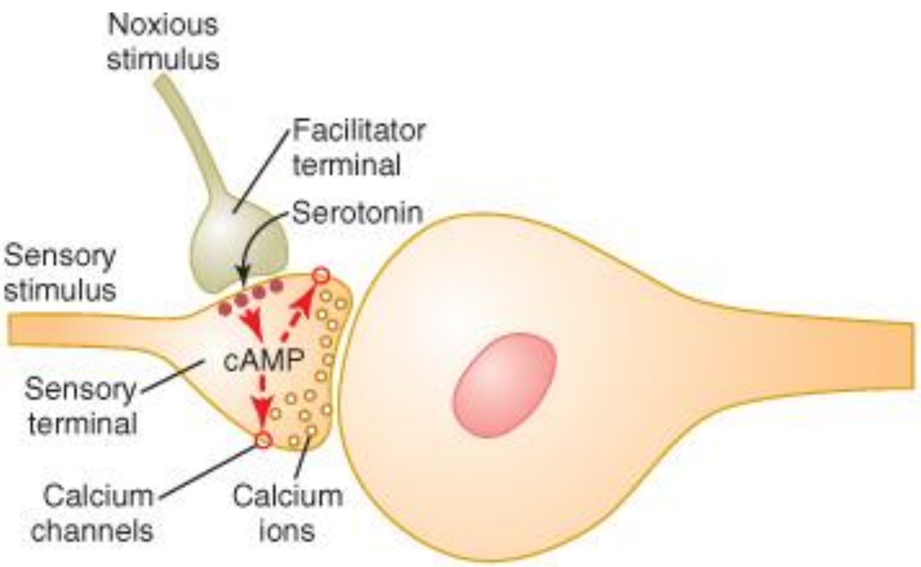
- Immediate memory may result from synaptic potentiation through the accumulation of calcium in the presynaptic membrane.
  – would promote neurotransmitter release
- Short-term memory may result from a temporary physical or chemical change in the pre- or postsynaptic membrane.

Explanations of Short-Term Memory

- continual neural activity resulting from nerve signals that travel around and around a temporary memory trace in a *circuit of reverberating neurons*
- *Presynaptic facilitation or inhibition*: at synapses on terminal nerve fibrils immediately before fibrils synapse with a subsequent neuron.
- Enhanced *synaptic conduction*
- Accumulation of *calcium*

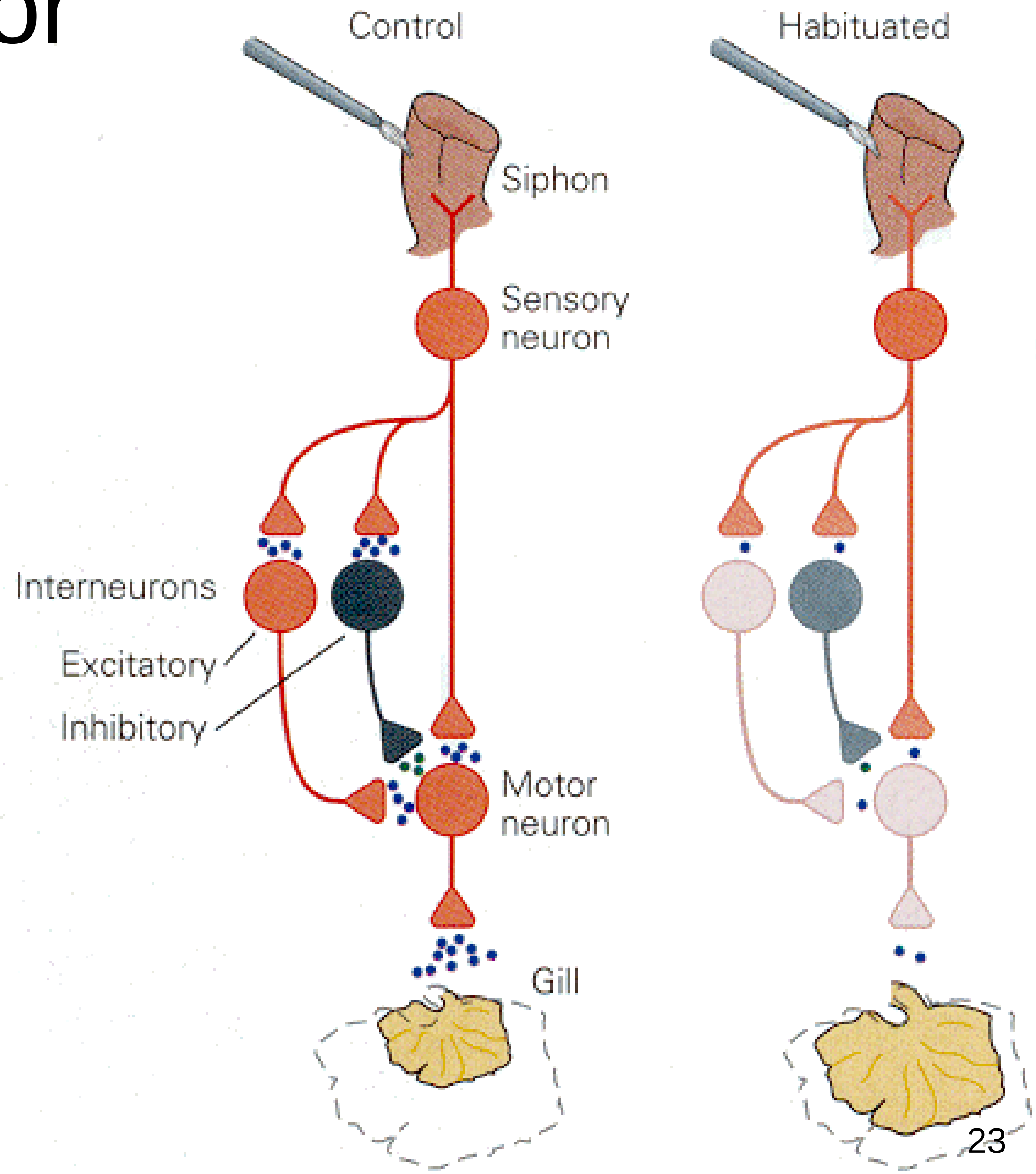
Mechanism for Intermediate Memory

- *Habituation* – signal transmission of repeated stimulation becomes less intense.
- Noxious stimulus causes the ease of transmission to become stronger and stronger – *Facilitation*.



Mechanism for Habituation

Habituation caused by closure of Ca++ channels

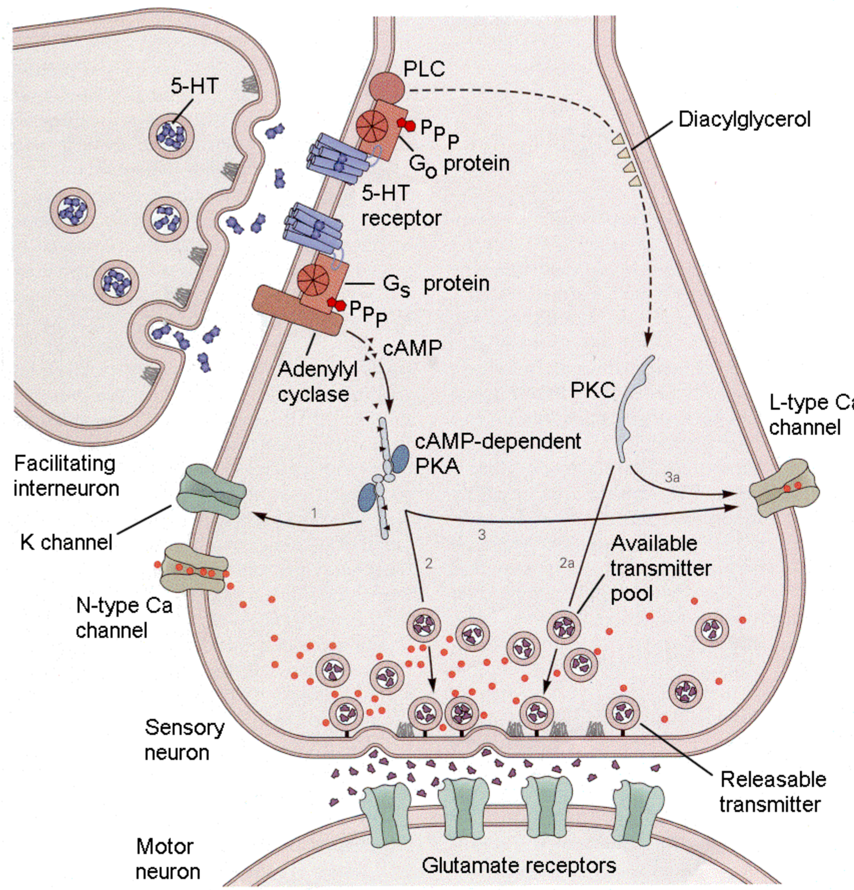


The control condition is shown on the left, the habituated condition on the right.

(Kandel, ER, JH Schwartz and TM Jessell (2000) Principles of Neural Science. New York: McGraw-Hill.)

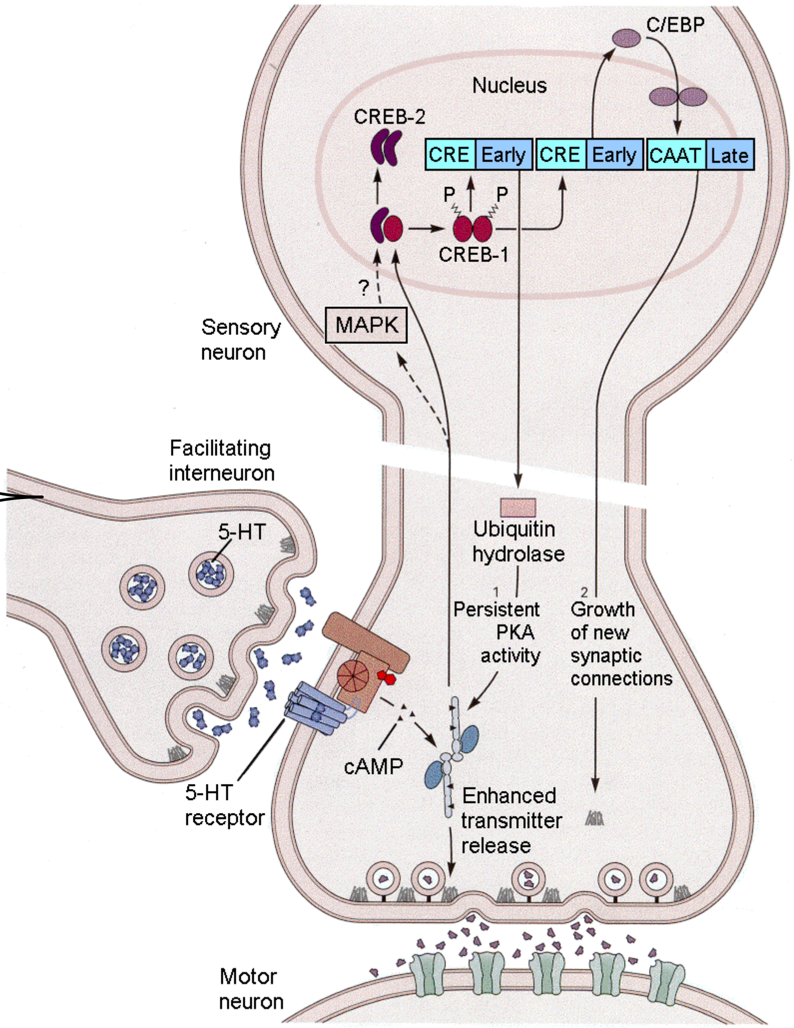
Mechanism for Facilitation

- Serotonin (or 5HT) activates adenylcyclase, forms cAMP.
- cAMP activates protein kinase, blocks K+ conductance (up to several weeks), prolongs action potential (AP).
- Prolonged AP releases large amounts of Ca^{++}.
- Facilitatory neuron can also act on post-synaptic membrane



Long-Term Memory

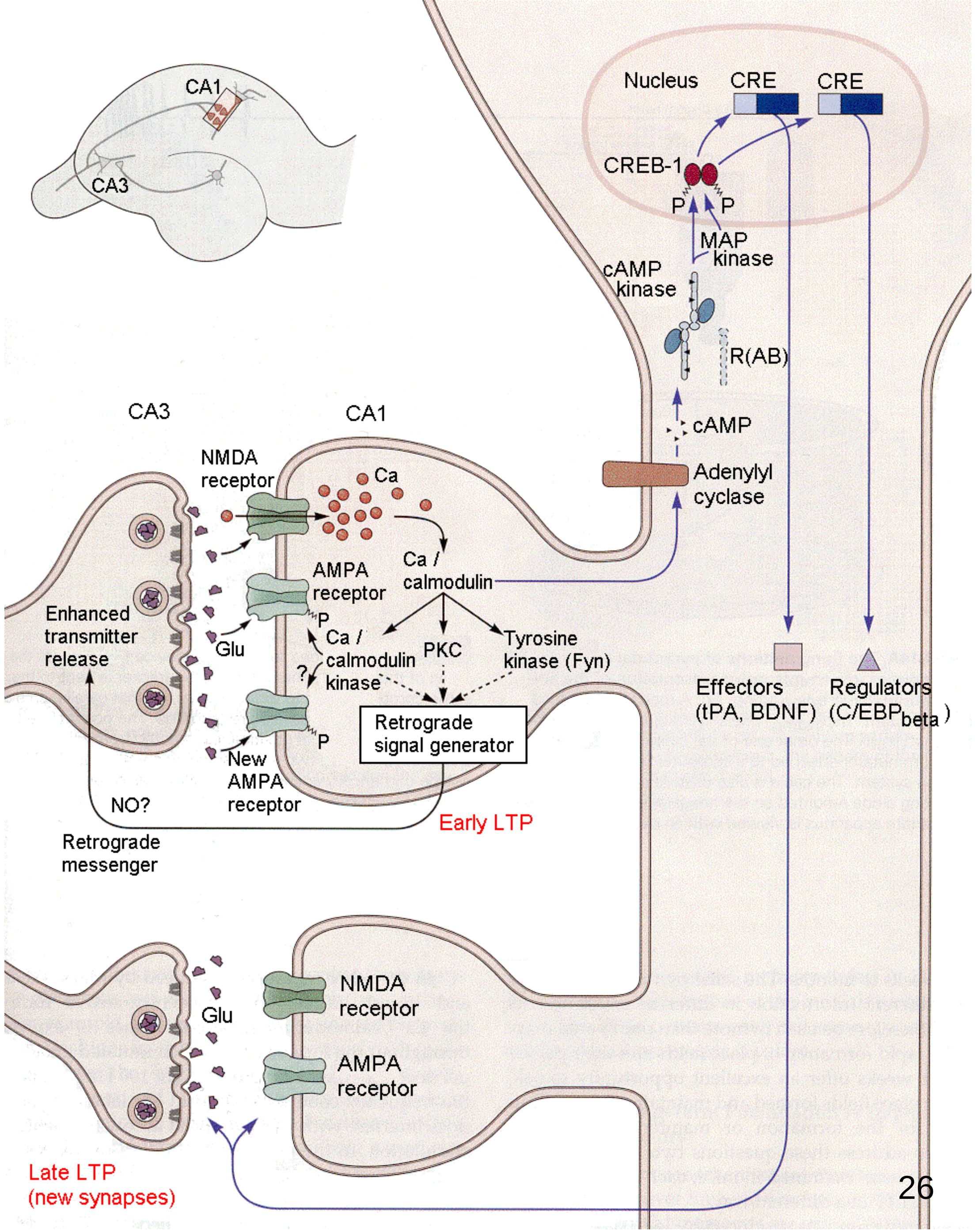
- Caused by structural changes.
  – Increase in no. of neural transfer vesicles
  – Increase in no. of neural transfer vesicle release sites
  – Increase in no. of presynaptic terminals/length of dendrites



- Long-Term Potentiation (LTP)

LTP

leads to changes in protein synthesis and to formation of new synaptic connections



Role of Thalamus in Memory

- Damage may cause retrograde amnesia without anterograde amnesia
  - Forget things
  - Forget recent things more than older things
- Thalamus may affect memory “search.”

Role of Hippocampus in Memory

- Hippocampus output is reward/punishment
- Removal of hippocampus
  - Inability to form new long term verbal/symbolic memories
    - Referred to as anterograde (ante=before) amnesia
    - You do not “forget” things.
    - You just cannot remember new things.
  - Can also cause some retrograde amnesia
- Not important in reflexive learning (e.g. sports)

Case study: HM

- Surgically removed the medial temporal lobe on both sides of his brain (2/3 of hippocampal formation, parahippocampal gyrus, entorhinal cortex and amygdala).
- Cannot commit new episodic memory into long-term.
- (researcher's frustration)
- Can commit new procedural memory into long-term.
- Able to do motor learning, and do it well. (But can't remember that he had learnt it.)

Emotional Effects of Hypothalamus

- Lateral hypothalamus
  - Thirst, eating
  - Increased activity level
  - Rage and fighting
- Ventromedial nucleus
  - Reward centers
  - Opposite of lateral hypothalamus
- Thin zone of periventricular nuclei & central gray area of mesencephalon
  - Fear and punishment
- Anterior & Posterior regions (and others)
  - Sexual drive

Lesion causes opposite effect of stimulation

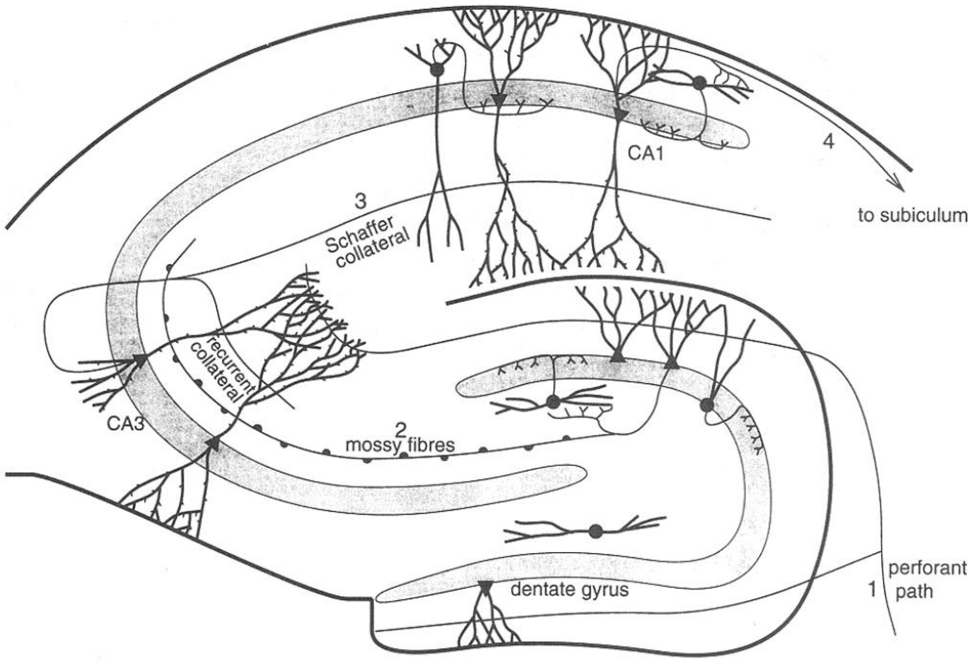
Function of Other Limbic Areas

- amygdala
  - receives input from other areas of limbic system as well as most areas of the cortex
  - sends output back to cortex as well as into hippocampus, septum, and hypothalamus
  - functions in behavioral awareness at the semiconscious level
  - projects into limbic system one's status with respect to the surroundings and current thoughts
  - helps pattern behavior appropriate for the each occasion

Function of Other Limbic Areas

- hippocampus
  - originated as part of the olfactory cortex
  - in lower animals the sense of smell is an important determinant of behavior (is it good to eat, does it smell like danger, is it sexually inviting)
  - therefore, the early hippocampus was involved in decision making by determining the importance of the incoming information

Hippocampus



- Three nerve cell layers instead of six.
- Filtering of incoming sensory information
- Originally part of olfactory cortex.
- Smells important to eating & sex drive.
- Stimulation – rage, passivity & sex drive
- can become hyper-excitable
- A very common seizure model
- Consolidation – repeating signals.

Types of Sleep

- Slow-wave sleep
  - The largest proportion of a given sleep period
  - Deep, restful
- Rapid-eye-movement (REM) sleep [Paradoxical or Desynchronized Sleep]
  - Occur periodically (ca. every 90 minutes for 5-30 minutes)
  - About 25% of time for young adult
  - Associated with vivid dreaming
  - Duration increases as person becomes less tired.

Slow Wave Sleep

- Decrease in body functions (10 – 30%)
  - Peripheral vascular tone
  - Blood pressure
  - Respiratory rate
  - Basal metabolic rate
- Dreams & sometimes nightmares *do* occur.
  - Less likely to be remembered.
  - Consolidation of dreams in memory does not occur.

REM Sleep

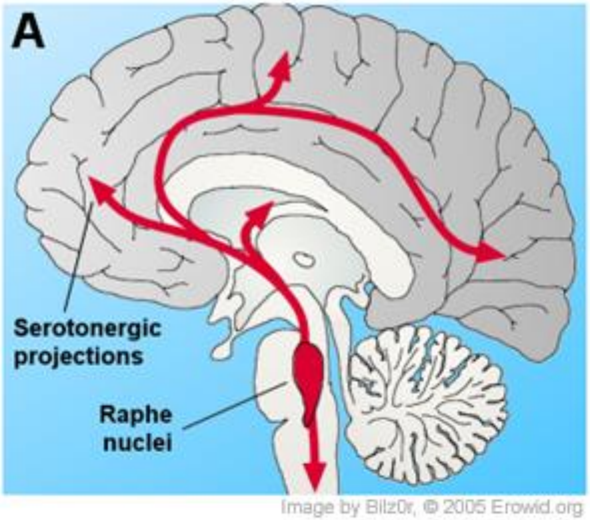
- Usually associated with dreaming
- Harder to wake subject, yet …
- People usually awaken naturally during REM
- Strong suppression of muscle tone (but not the eye muscles, obviously).
- Irregular heart rate/respiratory rate
- Increase of brain metabolism of ~20%.
- EEG patterns similar to wakefulness
- Brain is active, just not connected to the world

Theories of Sleep

- Passive theory (old)
  - Brain becomes fatigued and inactive
- Active theory (new)
  - Brain is actively inhibited
  - Experiment: transecting brain stem in the midpon region prevents cortex from going to sleep (based on EEG)
  - I.e., inhibiting operator in the brain.

Areas where stimulation causes sleep

- Raphe nuclei in medulla & lower half of pons
  - Nerve fibers extend to reticular formation, thalamus, neocortex, hypothalamus & limbic system.
  - Can inhibit incoming pain signals
  - Release serotonin
    - If serotonin formation is blocked, no sleep but …
    - Serotonin levels are *decreased* during sleep.
  - Melatonin and sleep?
- Parts of nucleus of the tractus solitarius
  - Region of medulla & pons for visceral signals
  - Depends on presence of raphe nuclei
- Regions of diencephalon



Causes of REM Sleep

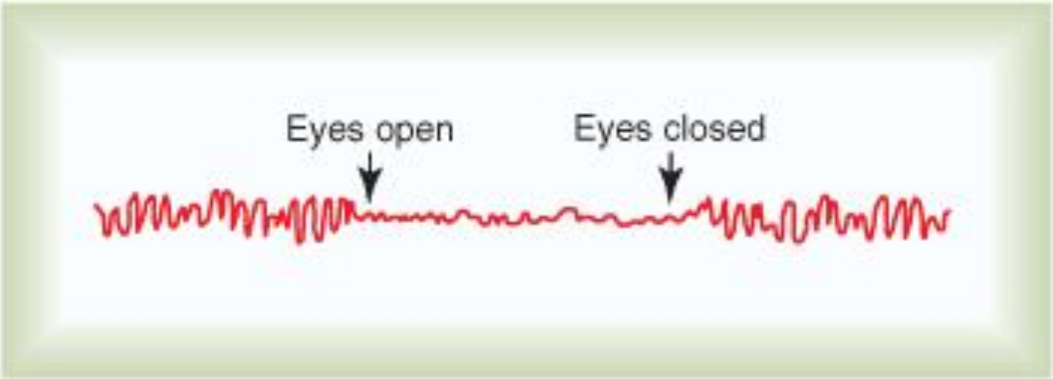
- Possibly associated with acetylcholine from upper brain stem reticular formation.
- Cyclic behavior of sleep not well understood.

Effects of Lack of Sleep

- Sluggishness
- Irritability
- Psychosis

Electroencephalogram and brain waves

- EEG measures activities from a population of neurons.
- Frequency - synchronous firing or artifacts?



- Frequency reflects varying levels of cerebral activity. (problem with average frequency)

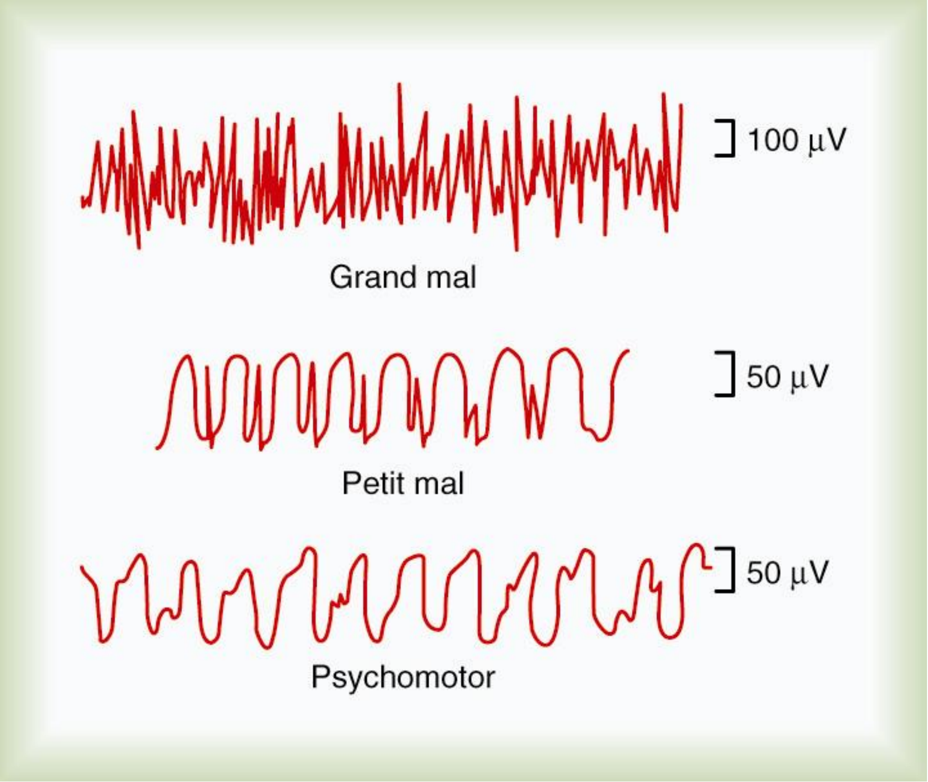
Brain Waves

- Alpha:
  - 8-13Hz
  - Quiet resting state
  - Occipital region
  - 50uV
- Beta:
  - 14-80Hz
  - Asynchronous
  - Lower-voltage
- Theta:
  - 4-7Hz
  - Parietal, temporal regions
  - Emotional stress
- Delta:
  - <3.5Hz
  - 2-4 x larger in magnitude
  - Cortex independent activities

Epilepsy

- Characterized by hyper-excitability

  - Grand Mal Epilepsy (high voltage)
  - Petit Mal Epilepsy (spike & dome pattern)
  - Focal Epilepsy (localized reverberation)



Petit Mal Epilepsy

- Probably involves thalamocortical brain activating system
- 3 to 30 seconds of unconsciousness or diminished consciousness
- Twitching, blinking
- Remains conscious afterwards
- Onset in late childhood, disappear at ~ age of 30.
- May trigger Grand Mal

Focal Epilepsy

- Can occur anywhere in the brain
- Usually caused by localized lesion
- E.g. when occurs in motor cortex, causes “progressive march of muscle contractions on contralateral side (jacksonian epilepsy)
- May trigger Grand Mal
- Interesting case – psychomotor seizure (involves the limbic portion of the brain)

Psychomotor Seizure

- May involve
  - Short period of amnesia
  - Attack of abnormal rage
  - Sudden anxiety, fear, discomfort
  - Moment of incoherent speech, mumbling trite phrase.
  - Motor act (attack, rub face)
- Conscious but unable to control
- Subject may not remember activities
- May remember he/she did them, but not know why.

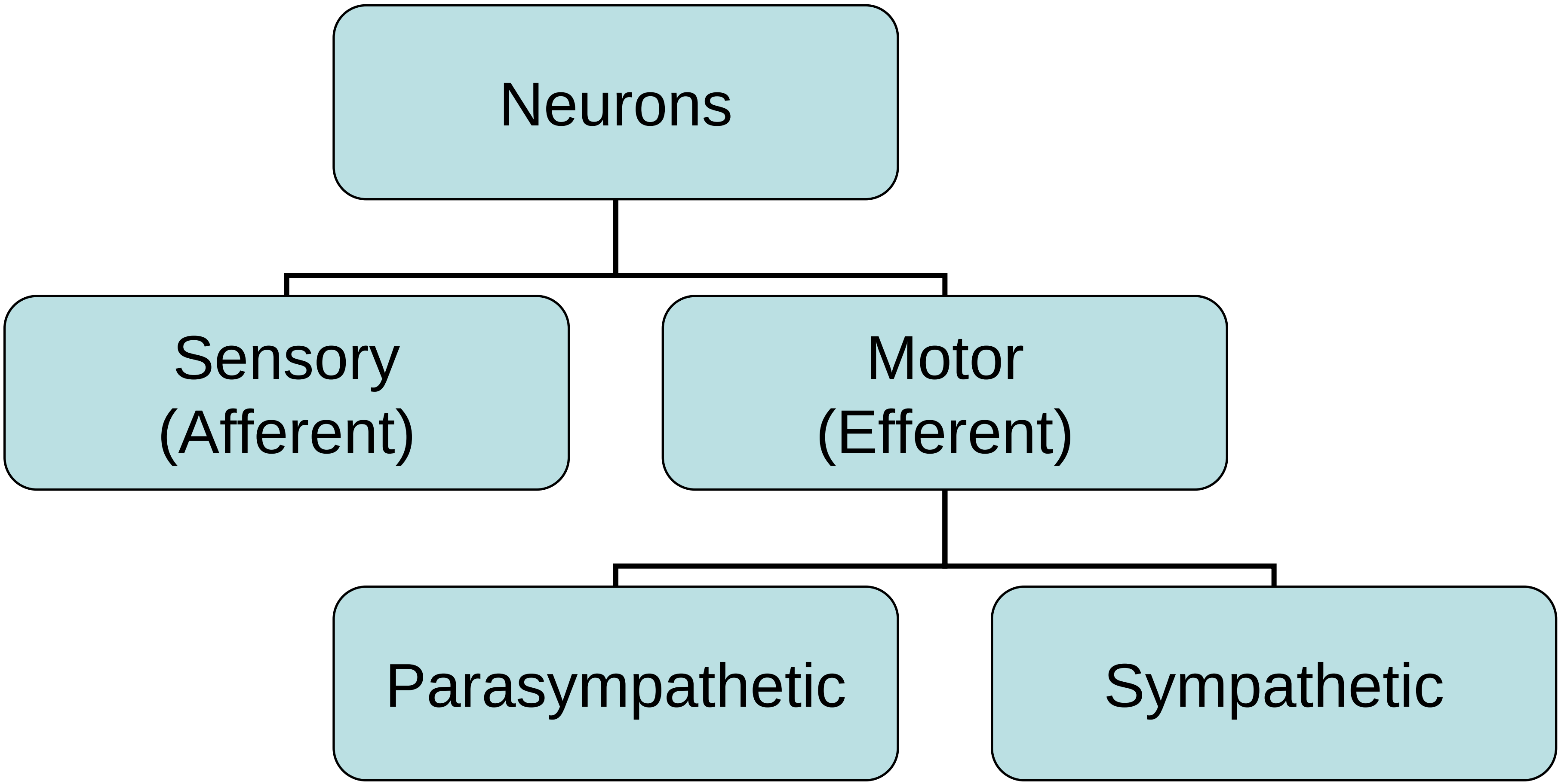
Depression

- disorder of **norepinephrine** secreting neurons in the **locus ceruleus**
- disorder of **serotonin** secreting neurons in the **raphe nucleus**
- drugs that block the uptake of these transmitters are helpful in treating depression
- presumed that norepinephrine and serotonin systems normally provide drive to the limbic system
  - increase sense of well being, create happiness, contentment, psychomotor balance
- pleasure and reward center of hypthalamus receive large input from norepi and serotonin systems - too much can lead to mania

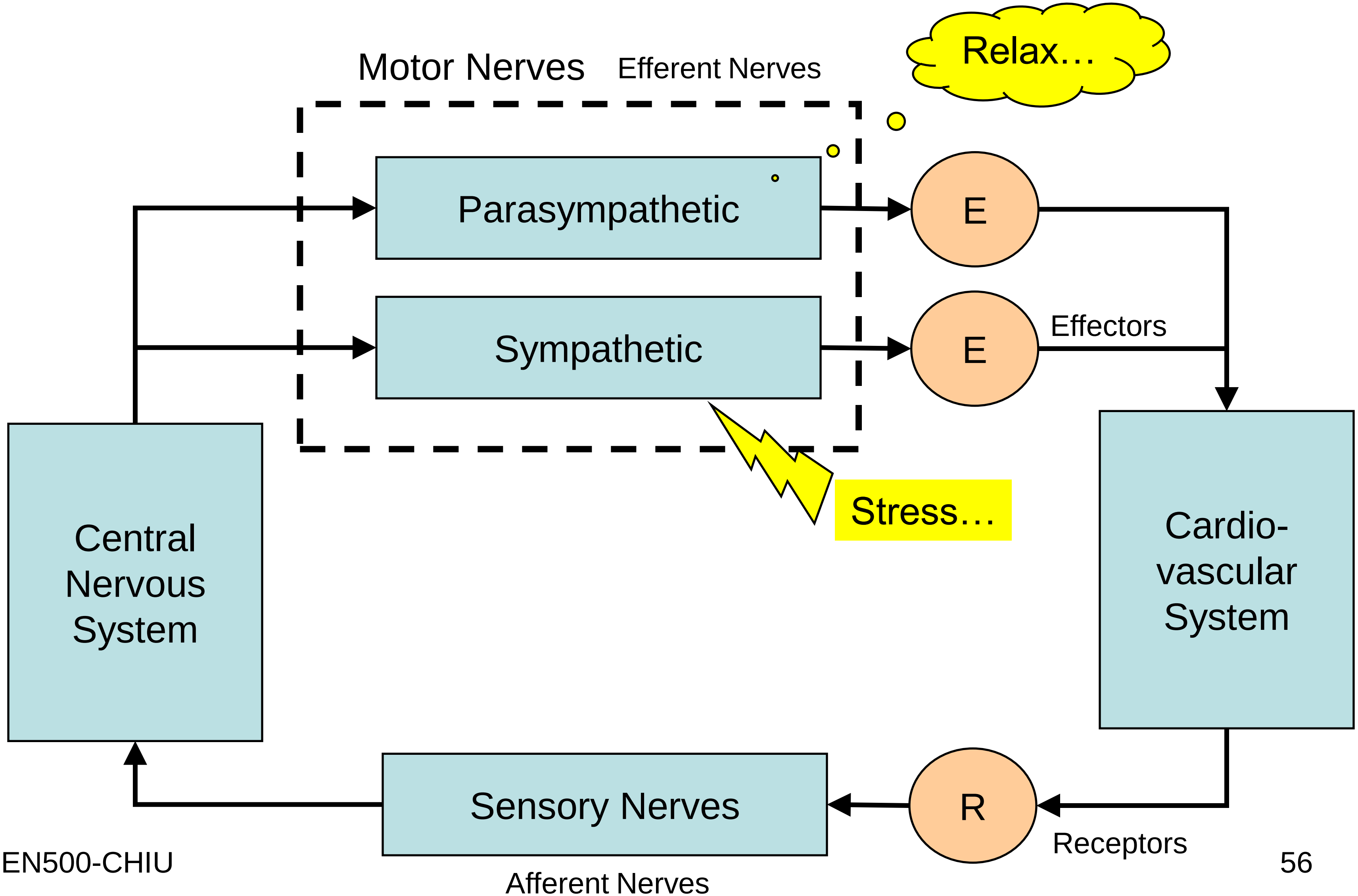
Schizophrenia

- disorder of the **mesolimbic dopaminergic system**.
  - dopaminergic projections to anterior and medial portions of limbic system - especially to hippocampus, amygdala, anterior caudate as well as portion of prefrontal lobes
  - too much dopamine
  - drugs that block the action of dopamine are effective in treating the symptoms of schizophrenia
- portion of hippocampus smaller on dominant side of brain

Autonomic Nervous System



e.g. How it relates to the heart?



The Autonomic Nervous System		
Structure	**Sympathetic Stimulation**	**Parasympathetic Stimulation**
Iris (eye muscle)	Pupil dilation	Pupil constriction
Salivary Glands	Saliva production reduced	Saliva production increased
Oral/Nasal Mucosa	Mucus production reduced	Mucus production increased
Heart	Heart rate and force increased	Heart rate and force decreased
Lung	Bronchial muscle relaxed	Bronchial muscle contracted
Stomach	Peristalsis reduced	Gastric juice secreted; motility increased
Small Intestine	Motility reduced	Digestion increased
Large Intestine	Motility reduced	Secretions and motility increased
Liver	Increased conversion of glycogen to glucose	
Kidney	Decreased urine secretion	Increased urine secretion
Bladder	Wall relaxed Sphincter closed	Wall contracted Sphincter relaxed
Penis	Ejaculation	Erection

"fight or flight" "rest and digest"

Table 60-2 in Guyton & Hall

- Sympathetic nerves release *norepinephrine.*
  - Norepinephrine stimulates *alpha* and *beta* adrenergic receptors.
  - Alpha receptors are located on blood vessels where they cause vasoconstriction.
  - Beta receptors are further divided into *beta*$_1$ and *beta*$_2$*.*
    - activation of beta$_1$ - causes an increase in heart rate and contractility
    - activation of beta$_2$ - causes bronchial dilation, dilation of blood vessels in skeletal muscles, calorigenesis, and glycogenolysis

- Parasympathetic nerves release *acetylcholine.*
  - Acetylcholine excites two types of receptors *nicotinic* and *muscarinic*.
  - Nicotinic receptors are found in synapses between the pre- and post- ganglionic neurons.
  - Muscarinic receptors are found on all effector cells stimulated by postganglionic parasympathetic fibers.

Adrenal Medulla

- Release epinephrine and norepinephrine when stimulated by sympathetic activation.
- Dual mechanism (direct stimulation of sympathetic nerve and hormones) – safety factor for substitution.
- Hormones affects cells that are not innervated by sympathetic fibers.