The Cyprus International Institute for the Environment and Public Health
In collaboration with the Harvard School of Public Health

Lecture 3

Sherwood, Human Physiology

The Central Nervous System
(131-157, 163-166, 168-179)

Excluded: molecular mechanisms of memory, habituation, potentiation, permanent synaptic connections, sleep

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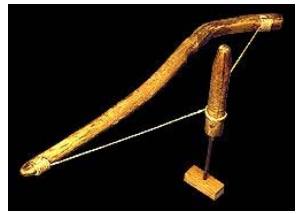
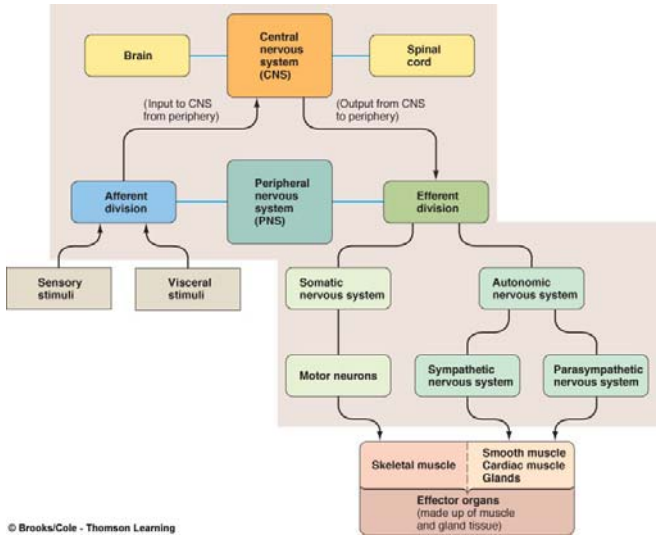
Evidence of Prehistoric Neurosurgery

- **Trepanation (or trephination)**
  - First neurosurgery → 20 000 BC
  - What was it good for?
    - Remove evil spirits
    - Epilepsy
    - Mental Disorders
    - Migraines
  - State of the art technology
    - Wooden drills with stone or bone tips
    - Arrow
  - Some of the patients actually survived!
  - Still performed today!

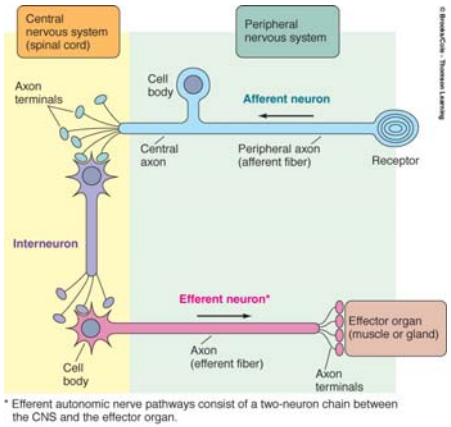


Organization of the Nervous System



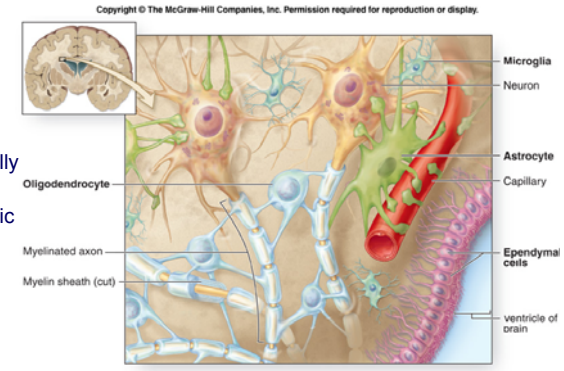
Organization of the Nervous System

- **Afferent neurons**
  - Inform CNS about conditions in both the external and internal environment
- **Efferent neurons**
  - Carry instructions from CNS to effector organs – muscles and glands
- **Interneurons**
  - Found entirely within CNS
  - Responsible for
  - Integrating afferent information and formulating an efferent response
  - Higher mental functions associated with the “mind”



Glial Cells

- **A.k.a. neuroglia**
- **90 % of cells in the CNS (50 % of the volume)**
- **Communicate with chemical signals (no electrical impulses)**
- **Role**
  - Support neurons physically and metabolically
  - Actively modulate synaptic function (major role in learning and memory)
- **Types**
  - Astrocytes
  - Oligodendrocytes
  - Microglia
  - Ependymal Cells

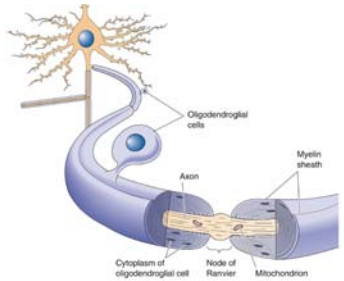


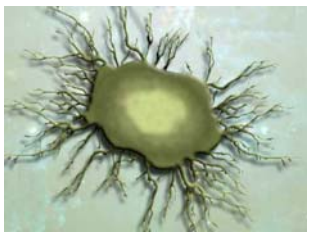
Glial Cells

- **Astrocytes**
  - Hold neurons together at proper distances and relationships
  - Guide neurons, as a scaffold, to the right location during fetal development
  - Induce blood vessels to form blood-brain barrier
  - Repair injuries and form scars in the CNS
  - Uptake and degrade glutamate and GABA, thus limiting their activity
  - Uptake excess K+ (from high activity) maintaining the ECF
  - Communicate chemically (gap junctions and receptors) with each other and with neurons and play a role in memory and learning

Glial Cells

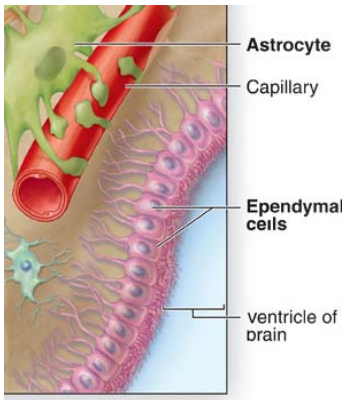
- **Oligodendrocytes**
  - Form myelin sheaths
  - Remember saltatory propagation?
- **Microglia**
  - Immune defense cells of the CNS
    - When activated become round and mobile and attack with destructive chemicals
    - Overactive microglia may be involved in neurodegenerative disorders
  - Secrete *Nerve Growth Factor* which helps neurons and other glial cells thrive





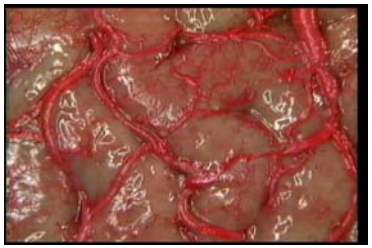
Glial Cells

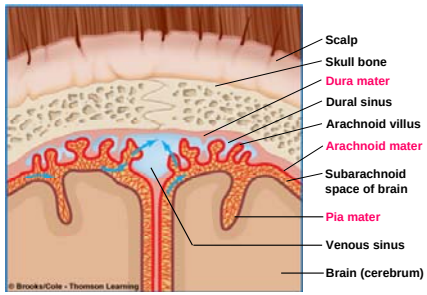
- **Ependymal Cells**
  - Line the cerebrospinal fluid (CSF) cavities (ventricles and central canal)
  - Form the CSF
  - Beating of cilia contributes to CSF flow
  - Precursors (stem cells) for glial cells and neurons in the hippocampus
- **Glial cells are the origin of most neural tumor (gliomas)**
  - Neurons can not divide



Meninges and the CSF

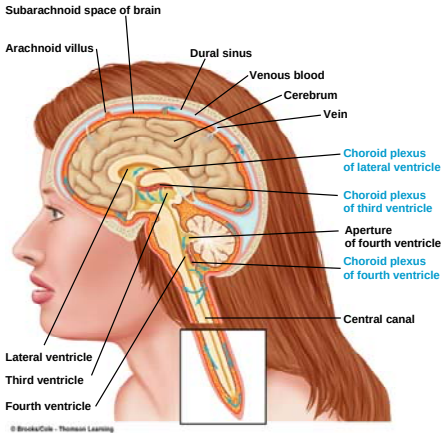
- **Protection of the CNS**
  - Hard bony structures (cranium and vertebral column) protect it
  - Three membranes (the meninges) protect and nourish it
  - The brain floats in the cerebrospinal fluid (CSF)
  - The blood-brain barrier (highly selective) limits access to harmful blood born substances
- **Meningial Membranes**
  - Dura matter
    - Two layers mostly attached
    - Dural and Venous sinuses return venous blood and CSF
  - Arachnoid matter
    - Richly vascularized layer
    - Arachnoid villi (CSF reabsorbed into venous circulation here)
  - Pia matter
    - Layer closer to the brain and ependymal cells





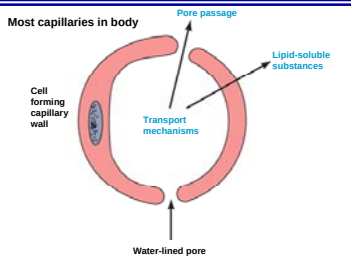
Meninges and the CSF

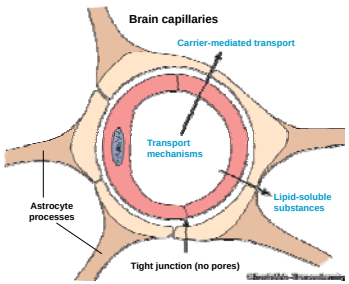
- **Cerebrospinal Fluid (CSF)**
  - Characteristics
    - Same density as brain →Brain floats in and is cushioned by the CSF
    - CSF and interstitial fluid of the brain cells are free to exchange materials → CSF composition must be carefully regulated
  - Formed by ***choroid plexuses*** in the ventricles
    - Richly vascular cauliflower-like masses
    - Selective and regulated transport
    - Differs from plasma (e.g. lower K^+ and higher Na^+)
    - 125-150 ml per day
  - Flow
    - Through the ventricles → 4th ventricle → Out to subarachnoid space → Over the entire brain → Top of the brain → Subarachnoid villi → Reabsorbed into the dural sinuses
  - Pressure
    - 10 mm Hg.
    - Even small reduction (e.g. during spinal tabs) can lead to severe headaches



Meninges and the CSF

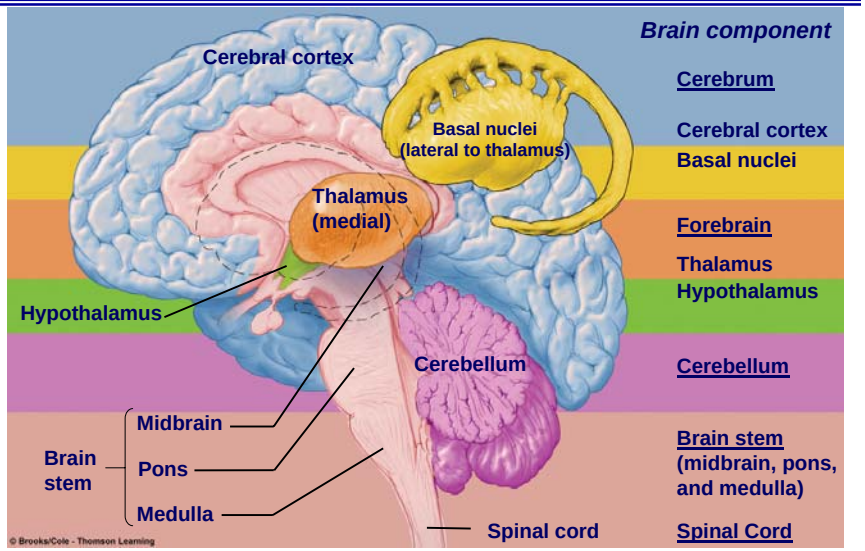
- **Blood-Brain Barrier (BBB)**
  - Tight junctions between endothelial cells of brain capillaries (anatomical restriction)
  - Few materials allowed to freely diffuse
    - Lipid soluble substances (O_2, CO_2, alcohol, steroid hormones
    - Water
  - Careful and controlled exchange between blood and CSF for everything else
  - Advantage
    - Brain shielded from changes in the ECF and harmful blood borne materials
  - Disadvantage
    - Limited types of drugs can pass through BBB
- **Brain Nourishment**
  - Brain can only use glucose and can only metabolize aerobically (O_2 present)
  - Highly dependent on blood supply
  - Very sensitive to blood supply variations
    - Damage if O2 deprived for > 4-5 mins





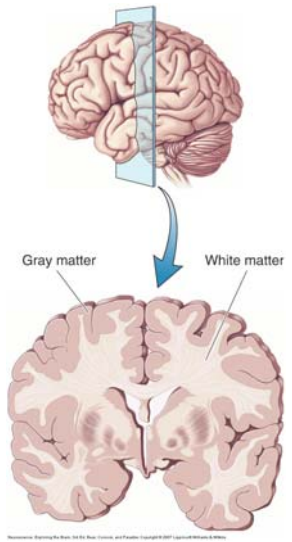
Overview of the CNS

Overview of the CNS



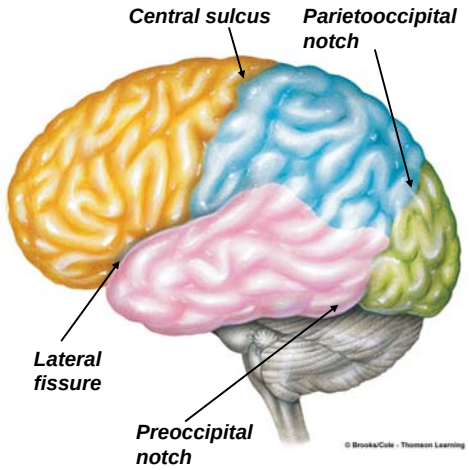
Cerebral Cortex

- **Cerebrum**
  - Left and right hemispheres
    - Gyri and sulci
  - Corpus callosum connects left and right
- **White matter (myelinated axons)**
  - Inner most layer
  - Interconnects
- **Cerebral cortex or Gray matter (cell bodies)**
  - Outermost layer
  - Organized in functional vertical columns (6 layers)
  - Each column is a team with distinct function
  - Differences are a result of different input/output and different layering patterns
  - Divided into four pairs of lobes

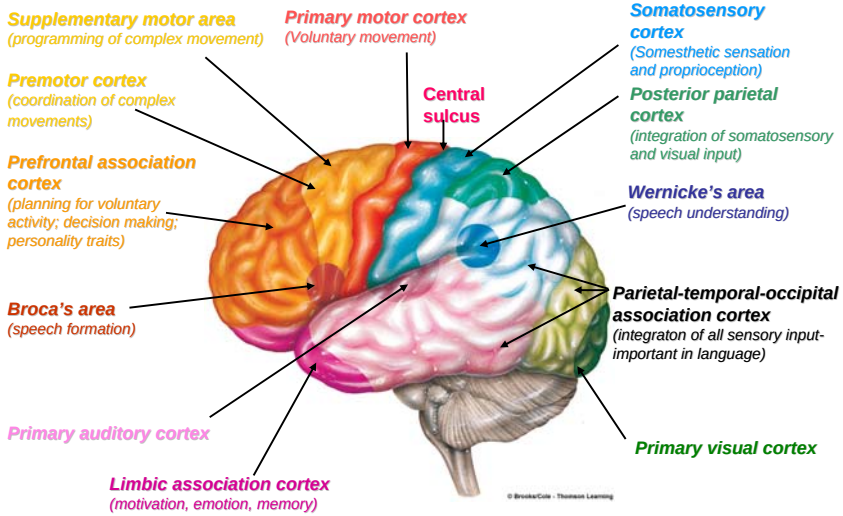


Cerebral Cortex

- **Cerebral cortex lobes**
  - Frontal
    - Voluntary motor activity, speaking ability, and elaboration of thought
    - Stimulation of different areas of its primary motor cortex moves different body regions, again primarily on the opposite side of the body.
  - Parietal
    - Somatosensory processing
    - Each region of its cortex receives somesthetic (feel) and proprioceptive (awareness of body position) input from a specific body area, primarily from the opposite body side.
  - Temporal
    - Receives sound sensation
  - Occipital
    - Initial processing of visual input

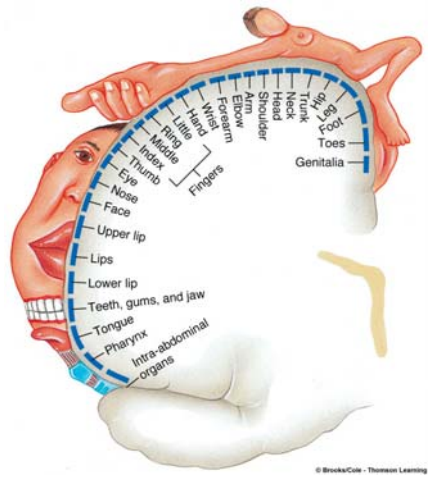


Cerebral Cortex

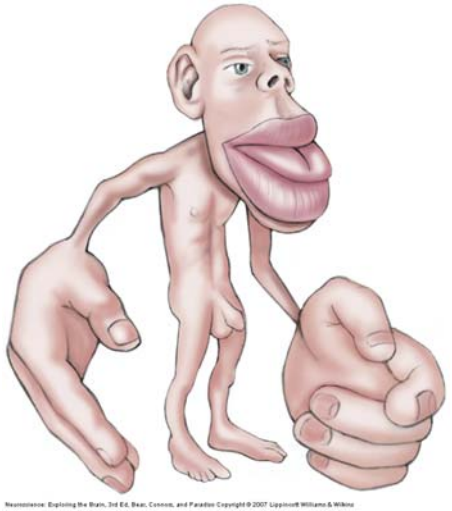


Cerebral Cortex

- **Parietal Lobe – Primary Somatosensory Cortex**
  - Somesthetic sensation → sensations from the surface of the body - touch, pain, pressure, heat and cold- and proprioception (awareness of body position)
  - Projected to the somatosensory cortex (initial cortical processing and perception)
  - Body regions are topographically mapped
    - Different parts of the body are not equally represented
    - Sensory Homonculus
    - Proportional to precision and sensitivity
  - Receives information from the opposite side of the body
    - damage on right side results in sensory loss on left side)

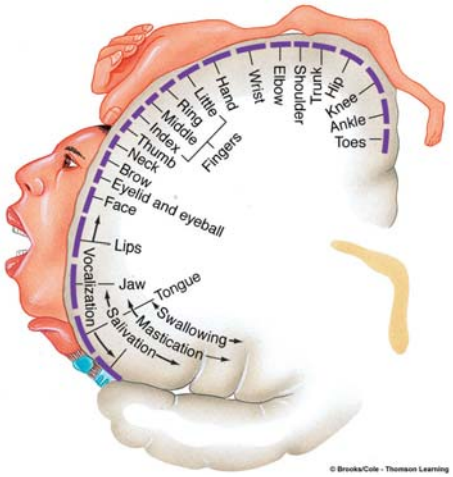


Cerebral Cortex



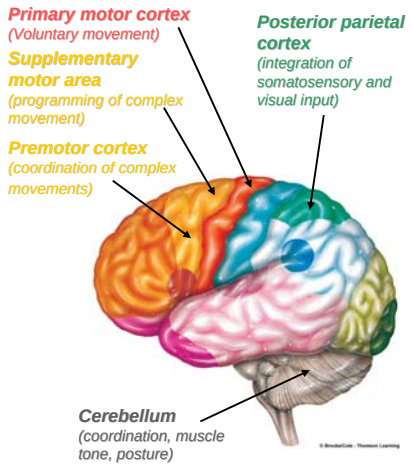
Cerebral Cortex

- **Frontal lobe – Primary Motor Cortex**
  - Voluntary control for muscle movement
  - Motor cortex on each side controls muscles on the opposite side of the body
    - Tracts originating in the cortex cross (at level of pyramids) before continuing down spinal cord to terminate muscle
  - Body regions are topographically mapped
    - Different parts of the body are not equally represented
    - Motor Homonculus
    - Proportional to precision and complexity of motor skills
  - Controls the opposite side of the body
    - Damage on right side results in motor deficit on left side



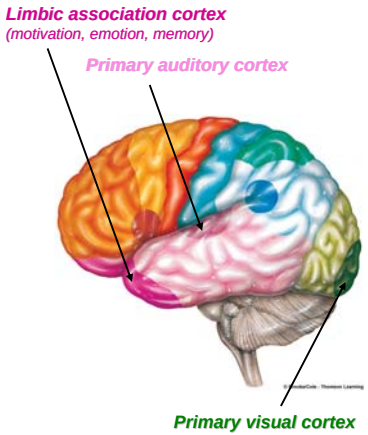
Cerebral Cortex

- **Movement**
  - The motor cortex itself does not initiate movement
  - Premotor cortex
    - Directs body orientation
    - Must be informed of body's position in relation to target
    - Acts in response to external cues
  - Supplementary motor cortex
    - Plays a preparatory role in programming complex sequences of movement
    - Responds to internal cues
  - Posterior parietal cortex
    - Posterior to the primary somatosensory cortex
    - Informs premotor cortex of position
  - Cerebellum
    - Motor coordination
    - (see more later)



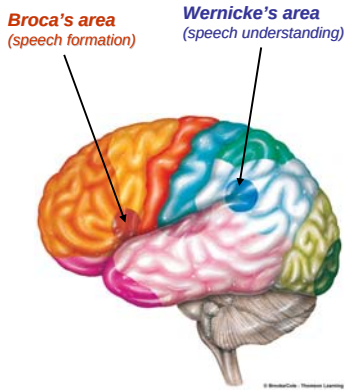
Cerebral Cortex

- **Occipital Lobe**
  - Primary visual cortex
  - Receives input from the eyes via optic nerve and optic projections to occipital lobe
  - Important for coordination of eye movements as well
- **Temporal Lobe**
  - Contains auditory centers that receive sensory fibers from the cochlea of each ear
  - Also involved in the interpretation and association of auditory and visual information
  - Temporal lobe contains the hippocampus and the amygdala
  - Involved in memory



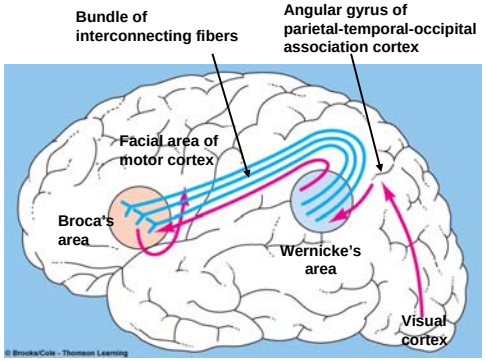
Cerebral Cortex

- **Language**
  - Areas responsible for language ability are found in only 1 hemisphere (usually the left)
  - Language involves the integration of 2 distinct capabilities
    - Expression (speaking ability)
    - Comprehension (understanding ability)
  - Broca's area
    - Responsible for speaking ability
    - Frontal lobe - in association with the motor area that controls the muscles necessary for articulation
  - Wernicke's area
    - Functions for language comprehension
    - Parietal-temporal-occipital association cortex - critical role in understanding both written and spoken language



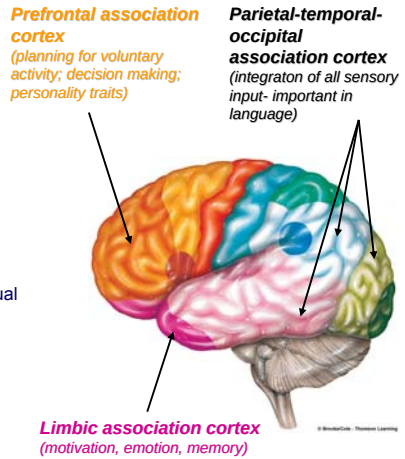
Cerebral Cortex

- **Language**
  - Damage to Broca's area → Expressive aphasia
    - Failure of word formation
    - The patient can still understand the spoken and written word
    - Know what they want to say but cannot express it
  - Damage to Wernicke's area → receptive aphasia
    - Loss of understanding of words seen or heard
    - Can speak fluently, but their words make no sense
    - Cannot attach meaning to words nor choose appropriate words to express thoughts
  - Concept of words
    - Originating in Wernicke's area
    - Must be communicated to Broca's area - via the arcuate fasciculus
    - Broca's area then sends fiber to the motor cortex to control muscles necessary for speech production
  - Damage to the arcuate fasciculus → Conduction aphasia
    - Fluent but nonsensical speech



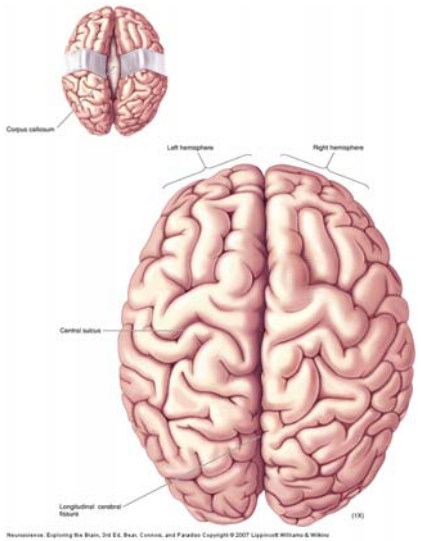
Cerebral Cortex

- **Cortical Association areas**
  - Prefrontal association cortex
    - Planning for voluntary activity, decision-making, creativity, and developing personality traits.
    - Site of operation of working memory
      - Temporary storage and active manipulation of information used in reasoning and planning
    - Deficits result in personality changes
  - Parietal-temporal-occipital association cortex
    - Integration of somatic, auditory, and visual sensations from the three lobes
    - Assign Meaning
    - Involved in connecting Broca's and Wernicke's area
  - Limbic association cortex
    - Motivation, emotion, and memory



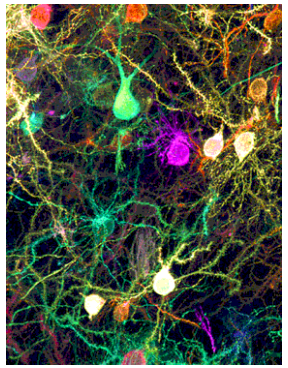
Cerebral Cortex

- **Lateralization/dominance of the cerebral hemispheres**
  - Each cerebral hemisphere receives information from both sides of the body due to connections via the corpus callosum
  - The left cerebral hemisphere excels in performing logical, analytical, sequential, and verbal tasks
    - Better at describing facial appearances
  - The right cerebral hemisphere excels in spatial perception and artistic and musical talents
    - Better at recognizing faces



Cerebral Cortex

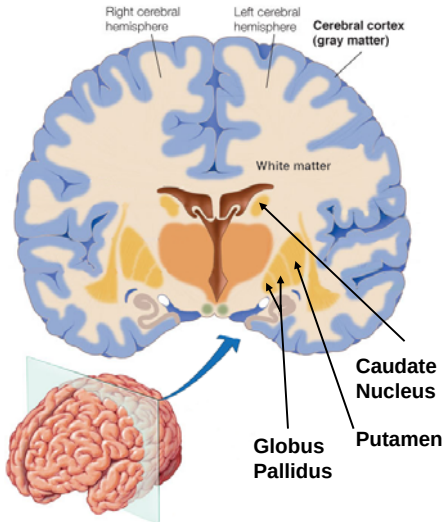
- **Brain plasticity**
  - Somatotopic maps
    - Vary slighlty between individuals
    - Dynamic, not static
      - Use-dependent competition
  - Plasticity
    - Functional remodeling of brain
    - More pronounced in early developmental years
    - Adults retain some plasticity
  - Brain injuries
    - Other regions adapted to cover deficits



http://saturn.med.nyu.edu/research/mn/ganlab/

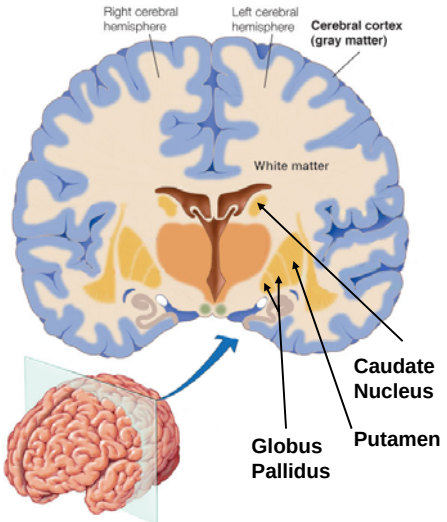
Basal Nuclei

- **A.k.a. basal ganglia**
- **Masses of grey matter deep inside the white matter**
- **Act by modifying ongoing activity in motor pathways**
  - Inhibit muscle tone
    - Proper tone - balance of excitatory and inhibitory inputs to motor neurons that innervate skeletal muscle
  - Select and maintain purposeful motor activity while suppressing unwanted patterns of movement
  - Monitor and coordinate slow and sustained contractions
    - Especially those related to posture and support



Basal Nuclei

- **Parkinson's disease**
  - Damage to basal ganglia neurons and a deficiency in dopamine
    - Increased muscle tone or rigidity
    - Resting tremors (eg unwanted movements
    - Slowness in initiating and carrying out motor behaviors



Diencephalon

- **Diencephalon**
  - Thalamus
  - Hypothalamus
- **Thalamus**
  - A relay station
  - A synaptic integrating center for processing sensory input on its way to the cerebral cortex.
    - Directs attention (e.g. when a baby cries parents wake up)
  - Also integrates information important for motor control
  - Receives sensory information from different areas of the body
  - Information is processed by specific thalamic nuclei

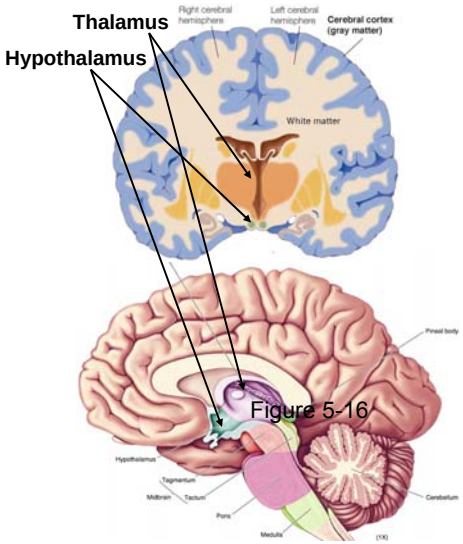


Figure 5-16

Diencephalon

- **Hypothalamus**
  - Homeostatic control
    - body temperature
    - thirst and urine production
    - food intake
    - anterior pituitary hormone secretion
    - production of posterior pituitary hormones
    - uterine contractions and milk ejection
  - Serves as an ANS coordinating center
  - Plays a role in emotional and behavioral patterns
  - Participates in sleep-wake cycle

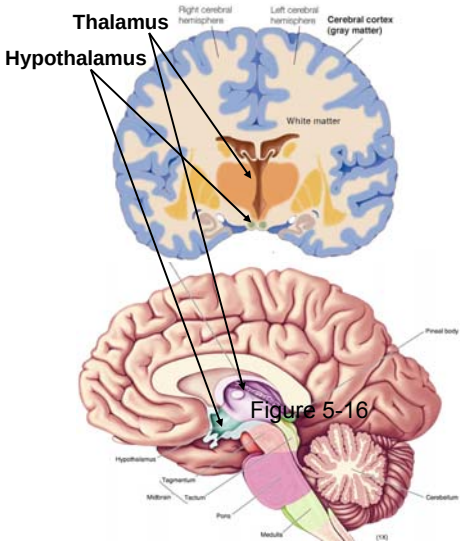
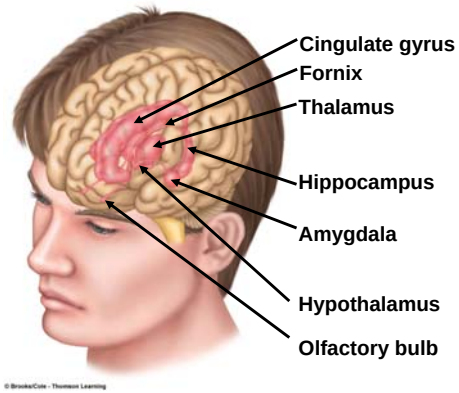


Figure 5-16

Limbic System

- **Several forebrain structures that function together**
  - Cortex (limbic association cortex)
    - Cingulate gyrus
    - Hippocampus
    - Amygdala
  - Basal Nuclei
  - Thalamus
  - Hypothalamus
- **Plays a role in**
  - Emotional state and basic behavioral patterns
  - Learning and memory



Limbic System

- **Emotion**
  - Subjective feelings and moods
  - Elicited by stimulation of specific regions, e.g.
  - Aggression
    - Lesions of amygdala → docility
    - Stimulation of amygdala → rage and aggression
  - Fear
    - Ablation of amygdala and hypothalamus→ absence of fear
    - Stimulation of amygdala and hypothalamus → fear

Limbic System

- **Basic behavioral pattern**
  - Individual survival
    - Attack
    - Search for food
  - Perpetuation of the species
    - Sociosexual behaviors of mating
- **Hypothalamus**
  - Involuntary responses which prepare the body's response
  - E.g. in attack
    - ↑ heart rate, respiratory rate, blood pressure and blood supply to skeletal muscles
- **Higher Cortex**
  - Executes the behavioral pattern
    - Stereotypical (pre-programmed) "gut" reactions, e.g. smile
  - Modify behavioral patterns based on planning, strategy and judgment
    - E.g. not smile when socially inappropriate

Limbic System

- **Reward and Punishment Centers**
  - Throughout the limbic system
  - Stimulation → pleasant or unpleasant feelings
    - Experimental animals self-deliver up to 5000 stimulations per hour!
  - Most in regions related o eating, drinking and sexual activity
- **Motivated behaviors**
  - Goal oriented
    - Homeostatic drives → aimed to fulfill bodily needs
  - Influenced by experience, learning, habit and culture
  - Complex interaction of reward and punishment centers
    - May accept punishment (exercise) to receive reward (win a race)

Learning and Memory

- **Learning**
  - Acquisition of new knowledge and skills
  - Reward and punishment plays a role
  - Learning → avoid punishment and seek reward
- **Memory**
  - Storage of knowledge for later recall
  - Stored as a ***memory trace***
  - Three types of memory
    - Short-term
    - Long-term
    - Working memory

Learning and Memory

- **Short-term memory**
  - Stores new information
  - Immediately after acquisition
  - Limited storage capacity
  - Last for seconds to hours
  - Rapid retrieval
  - Transient modification in the function of pre-existing synapses
    - E.g. alteration of neurotransmitter released
- **Memory permanently forgotten unless *consolidated* in long-term memory**
  - Consolidation enhanced by active practice or re-cycling through short-term mode (Cramming for an exam doesn't work!)
    - Enhancement of both pre- and post-synaptic neuron activity
    - Can last for days or even weeks

Learning and Memory

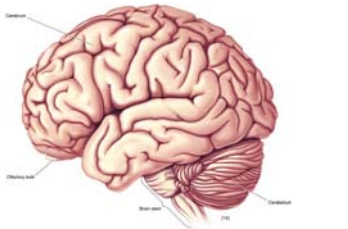
- **Long-term memory**
  - Stores memories through consolidation
  - Very large storage capacity
  - Last for days to years
  - Slow retrieval (except for memories thoroughly ingrained through years of practice)
  - Functional or structural changes between existing neurons
    - Formation of new synapses
    - Synthesis of new proteins
- **Amnesia**
  - Inability to recall whole portions of memory
  - Retrograde
    - Inability to recall recent events
    - Usually after trauma
  - Anterograde
    - Inability to store memories for long-term use

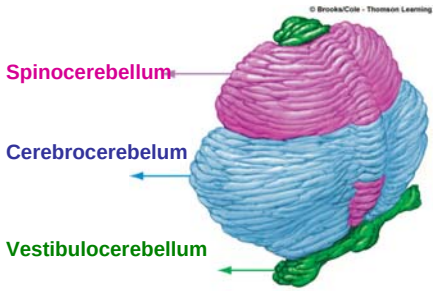
Learning and Memory

- **Memory location**
  - Several areas of the brain
  - Hippocampus
    - Declarative memories (e.g. specific people, places, objects, facts and events)
    - Damaged in Alzheimer's disease
  - Cerebellum
    - Procedural memories (e.g. motor skills gained through repetitive training
  - Prefrontal Cortex
    - Working memory (temporary space for recently recalled memories)
    - Involved in planning, judging, organizing and problem solving
    - More working memory → higher intelligence?

Cerebellum

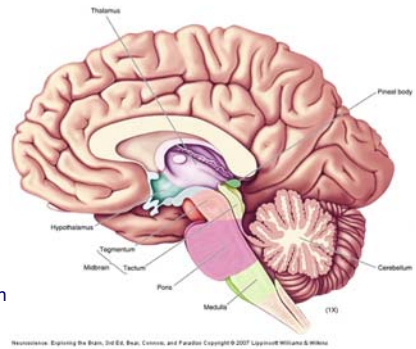
- **Highly folded, posterior, part of brain**
- **Important in**
  - Balance
  - Planning and executing voluntary movement
- **Activities**
  - Maintenance of balance, control of eye movements
  - Regulation of muscle tone (enhancement, opposite of basal nuclei), coordination of skilled voluntary movement
  - Planning and initiation of voluntary activity
- **Cerebellar disease**
  - Intention tremor → present only during voluntary activity





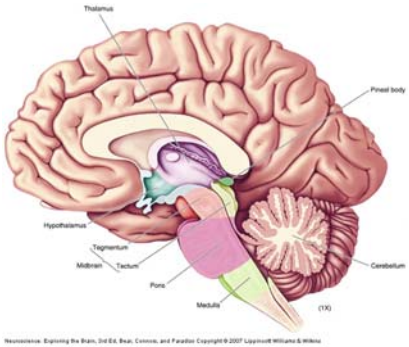
Brain Stem

- **Critical connecting link between rest of brain and spinal cord**
- **Functions**
  - Most of cranial nerves arise from brain stem
  - Neuronal clusters within brain stem control heart and blood vessel function, respiration, and many digestive functions
  - Plays role in regulating muscle reflexes involved in equilibrium and posture
  - Reticular formation within brain stem receives and integrates all incoming sensory synaptic input
    - Plays a role in modulating sensitivity of spinal reflexes and regulating transmission of sensory info (esp pain) into ascending pathways
  - Centers that govern sleep are in brain stem (evidence suggests center promoting slow-wave sleep lies in hypothalamus)

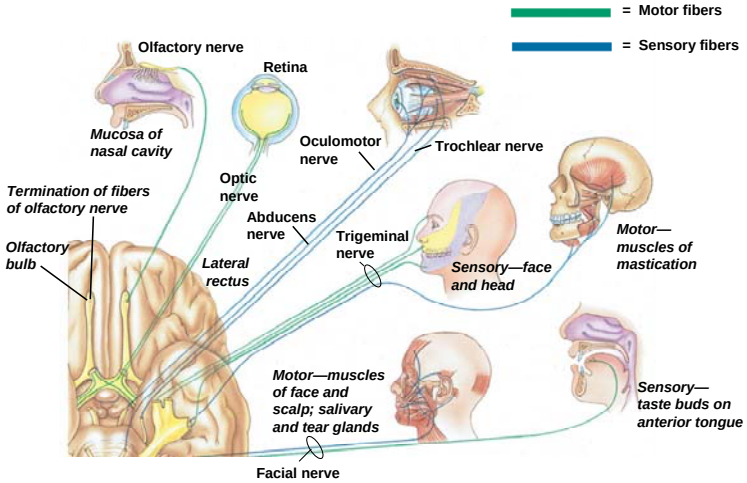


Brain Stem

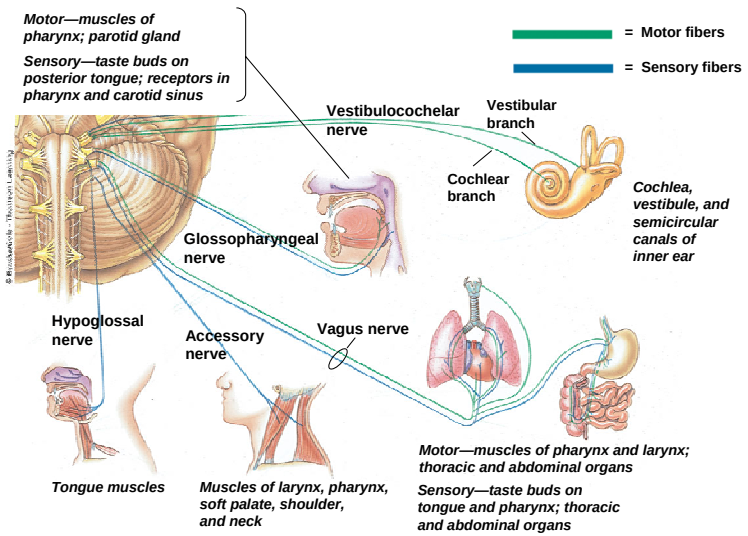
- **Consists of**
  - Midbrain
    - Nerve pathway of cerebral hemispheres
    - Auditory and Visual reflex centers
    - Cranial Nerves III, IV
  - Pons
    - Respiratory Center
    - Cranial Nerves V-VIII
  - Medulla
    - Crossing of motor tracts
    - Cardiac Center
    - Respiratory Center
    - Vasomotor (nerves having muscular control of the blood vessel walls) Center
    - Centers for cough, gag, swallow, and vomit
    - Cranial Nerves IX-XII



Cranial Nerves

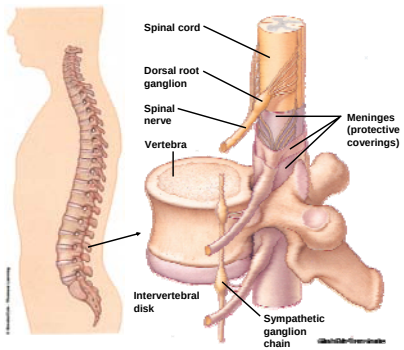


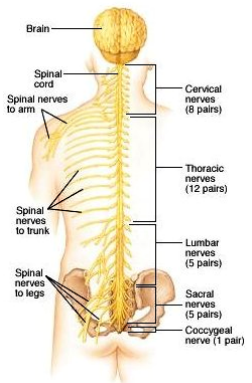
Cranial Nerves



Spinal Cord

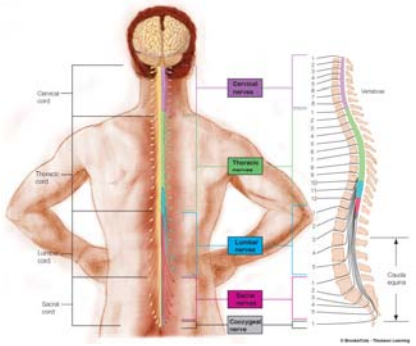
- **Extends from brain stem through vertebral canal**
  - Below L2 turns into a bundle of nerves
    - *Cauda equina*
    - Spinal tabs are taken below this point
- **Two vital functions**
  - Neuronal link between brain and PNS
  - Integrating center for spinal reflexes

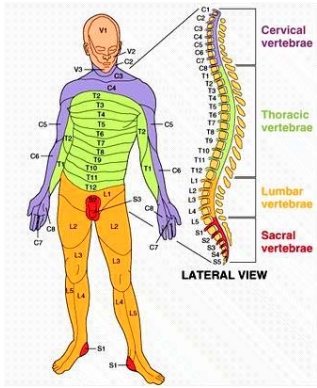




Spinal Cord

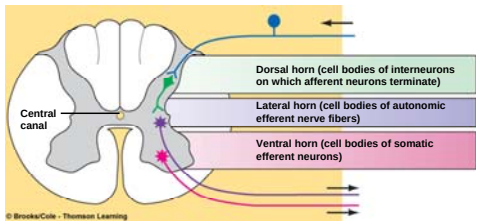
- **31 pairs of spinal nerves emerge from spinal cord through spaces formed between arches of adjacent vertebrae**
  - Named for region of vertebral column from which they emerge
    - 8 pairs cervical (neck) nerves
    - 12 pairs thoracic (chest) nerves
    - 5 pairs lumbar (abdominal) nerves
    - 5 pairs sacral (pelvic) nerves
    - 1 pair coccygeal (tailbone) nerves

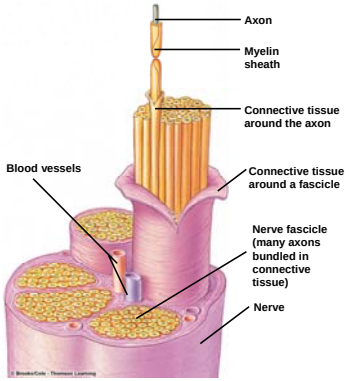




Spinal Cord

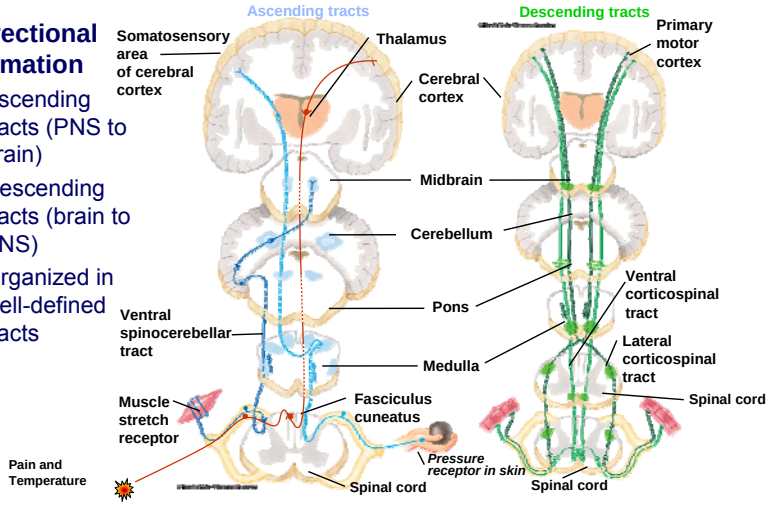
- **Fairly uniform cross-section**
  - Gray matter in the core
    - Cell bodies
    - Each horn houses different types of neurons
  - White matter in the outer segment
    - Axons organized into bundles
    - Bundles organized into tracts





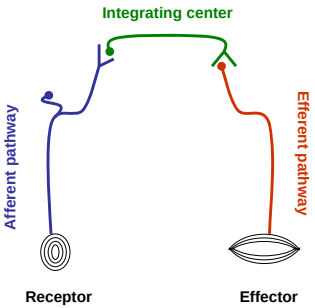
Spinal Cord

- **Bidirectional information**
  - Ascending tracts (PNS to brain)
  - Descending tracts (brain to PNS)
  - Organized in well-defined tracts

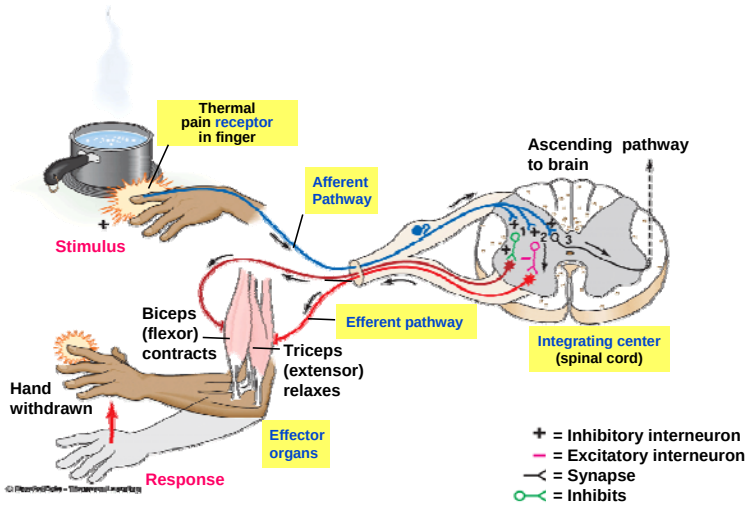


Spinal Cord

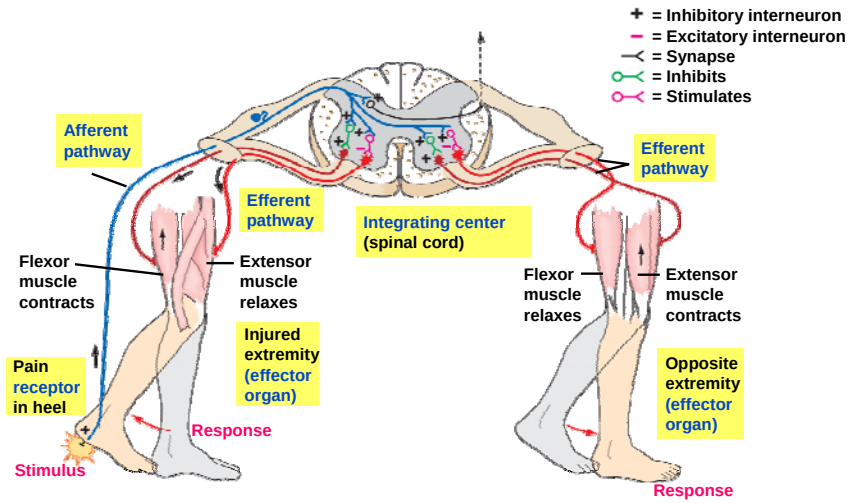
- **The spinal cord is an integrating center for many basic reflexes**
- **Reflex**
  - Any response that occurs automatically without conscious effort
- **Two types of reflexes**
  - Simple, or basic, reflexes
    - Built-in, unlearned responses
  - Acquired, or conditioned, reflexes
    - Result of practice and learning
- **Reflex Arc**
  - Neural pathway involved in accomplishing reflex activity
  - Five basic components
    - Receptor
    - Afferent pathway
    - Integrating center
    - Efferent pathway
    - Effector



Spinal Cord



Spinal Cord



Next Lecture …

Sherwood, Human Physiology

The Peripheral Nervous System (181-240)

Excluded: adaptation of pacinian corpuscle (185), labeled lines (186), acuity (186-187), phototransduction (200-203), on- off- center ganglion cells (205))