Central Nervous System (CNS)

The CNS consists of the brain and spinal cord. Over the course of animal evolution, cephalization has occurred – there has been an increase in the development of the anterior portion of the CNS, and an increased number of neurons in the head.

**Embryonic Development** – The brain and spinal cord begin as a neural tube. The primary vesicles form at the anterior end and the spinal cord forms at the posterior end.

The brain grows faster than membranous skull so two major flexures develop – the midbrain and cervical flexures – which bend the forebrain toward the brain stem. The cerebral hemispheres are forced to grow posteriorly and laterally – they grow back over and envelop the diencephalon and midbrain. The continued growth of the cerebral hemispheres causes the surface to crease and fold ---- this increases the surface area to allow more neurons to occupy limited space.

**Regions and Organization**

The basic pattern of the CNS consists of a central cavity surrounded by a gray matter and an external white matter composed of myelinated fiber tracts. The brain has additional regions of gray matter not present in the spinal cord. The cerebral hemispheres and the cerebellum have an outer layer of gray matter consisting of neuron cell bodies called a **cortex**. This pattern changes through the brain stem --- the cortex disappears and scattered gray matter nuclei are within the white matter.
**Ventricles**

The ventricles are continuous with each other and with the central canal of the spinal cord. The hollow ventricles are filled with cerebrospinal fluid (CSF) and lined by ependymal cells. The paired ventricles in the cerebral hemispheres are separated by the septum pellucidum (thin membrane). The 3rd ventricle is in the diencephalon and the 4th ventricle is in the hindbrain. Each lateral ventricle communicates with the 3rd ventricle via the interventricular foramen (channel). The 3rd ventricle communicates with the 4th ventricle via the cerebral aqueduct. There are three openings on the walls of the 4th ventricles – lateral apertures and the median aperture. These apertures connect the ventricles to the subarachnoid space (fluid filled space surrounding the brain).

**Cerebral Hemispheres**

Nearly the entire surface of the cerebral hemispheres has elevated ridges of tissue called gyri which are separated by hallow grooves called sulci. Deeper grooves are called fissures --- these grooves separate larger regions of the brain.

- **Longitudinal fissure** – separates the hemispheres
- **Transverse fissure** – separates the cerebrum and cerebellum
- **Central sulcus** – separates the frontal and parietal lobes
- **Parieto-occipital sulcus** – separates the occipital and parietal lobes
- **Lateral sulcus** – outlines the temporal lobes

**Note that fissures are very deep grooves, sulci are less deep grooves**
Several sulci divide each hemisphere into five lobes—frontal, parietal, temporal, occipital, insula. The insula is buried deep within the lateral sulcus and forms part of its floor. The insula is covered by portions of the temporal, parietal and frontal lobes. There are three basic regions in each cerebral hemisphere: superficial cerebral cortex of gray matter, internal white matter and basal nuclei (islands of gray matter situated deep within the white matter).

**Cerebral Hemispheres**

(a) Superior view

**Cerebral Cortex – GRAY MATTER**

The cortex is the site of our conscious mind—enables awareness, sensory perception, voluntary motor initiation, communication, memory storage and understanding. The cerebral cortex is composed of gray matter—neuron cell bodies, dendrites, glia and blood vessels, but no fiber tracts.

- It is only 2-4 mm thick, accounts for 40% of total brain mass. It contains billions of neurons arranged in layers. Its many convolutions triple the surface area.
- The cerebral cortex contains 3 kinds of functional areas: motor area (controls voluntary movement), sensory areas (conscious awareness of sensation), and association areas (integrate diverse information).
- Each hemisphere is concerned with the contralateral (opposite) side of the body
- The two hemispheres are not equal in function—Lateralization (specialization) of cortical function in hemispheres.
- No functional areas of the cortex work alone—conscious behavior involves entire cortex in some way.
**MOTOR AREAS**

**Primary motor areas** – This area is located in the precentral gyrus of the frontal lobe. Large neurons called pyramidal cells allow us to consciously control precise voluntary movement of our skeletal muscles. The long axons, which project to the spinal cord, form the massive voluntary motor tracts called pyramidal (corticospinal) tracts of spinal cord. The entire body is represented spatially in the primary motor cortex of each hemisphere. *Motor homunculi* - upside-down caricatures represent contralateral motor innervation of body regions. The left primary motor gyrus controls muscles on the right side of the body and vice-versa.

**Premotor Cortex** – This region controls learned motor skills of a repetitious or patterned nature. It coordinates the movement of several muscle groups either simultaneous or sequential action by sending activating impulses to the primary motor cortex. This region is the staging area for skilled motor activities. It helps plan movements – using processed sensory information from cortical areas, it can control voluntary actions that depend on sensory feedback.

**Broca’s Area** – This area is present in one hemisphere (usually the left). It’s a special motor speech area that directs the muscles involved in speech production. Area is active in planning speech and voluntary motor activities.

**Frontal Eye Field** - Controls voluntary eye movements

**SENSORY AREAS**

**Primary Somatosensory Cortex** – receives general sensory information from skin, and proprioceptors of skeletal muscle, joints, and tendons. Capable of spatial discrimination: identification of body region being stimulated. *Somatosensory homunculus* - upside-down caricatures represent contralateral sensory input from body regions.

**Somatosensory Association Cortex** – integrates sensory input from primary somatosensory cortex to produce an understanding of object being felt. Area determines size, texture, and relationship of parts of objects being felt.
Visual Areas – The primary visual cortex receives visual information from the retinas. The visual association areas surround the primary visual cortex and uses past visual experiences to interpret visual stimuli (ex. Color, form, ability to recognize faces). Complex processing involves the entire posterior half of the cerebral hemisphere -- two visual streams: one handling spatial relationships and the other focusing on the object identity.

Auditory Areas – The primary auditory cortex interprets information from inner ear as pitch, loudness and location. The auditory association area is located posterior to the primary auditory cortex and stores memories of sounds and permits perception of sound stimulus.

Vestibular Cortex -- responsible for conscious awareness of balance (position of head in space)

Olfactory cortex – region of conscious awareness of odors

Gustatory Cortex – involved in perception of taste

Visceral Sensory Area – conscious perception of visceral sensations (ex. upset stomach)

Multimodal Association Areas
Most of the cortex is more complexly connected, receiving inputs from multiple senses and sending outputs to multiple areas. This area seems to be where sensation, thoughts and emotions become conscious – makes us who we are.

- Information flows from sensory receptors to appropriate primary sensory cortex then to a sensory association cortex and then on to the multimodal association cortex. Multimodal association cortex allows us to give meaning to the information received, store it in memory, link it to previous experiences/knowledge and decide what action to take. Once actions are determined, those decisions are relayed to the premotor cortex which communicates to the motor cortex.

Anterior Association Area (Prefrontal cortex) – This area is the most complicated cortical region. It is involved in intellect, cognition (complex learning activities), recall and personality. It contains working memory needed for abstract ideas, judgment, reasoning, persistence, and planning. This area matures slowly and the development is dependent on feedback from social environment.

Posterior Association Area – This are plays a role in recognizing patterns and faces, localizing us and our surroundings in space, and in binding different sensory inputs into a coherent whole. Many parts of this area (Wernicke’s area) are involved in understanding written and spoken language.

Limbic Association Area – provides emotional impact that makes scene important and helps establish memories. (part of the limbic system)

Lateralization of Cortical Functioning – We use both hemispheres for almost every activity and the hemispheres are almost identical. There is a division of labor between hemispheres (lateralization). One hemisphere dominates each task – cerebral dominance designates the hemisphere dominant for language (left hemisphere - 90% people). Hemispheres communicate almost instantaneously via fiber tracts and functional integration.

- Left hemisphere - Controls language, math, and logic
- Right hemisphere - Visual-spatial skills, intuition, emotion, and artistic and musical skills
**Cerebral White Matter**

The white matter deep to the cortical gray matter is responsible for communication between cerebral areas and between the cerebral cortex and lower CNS centers. White matter consists of myelinated fibers bundled into large tracts. These tracts are classified according to the direction in which they run – commissural, association, projection.

- **Commissures** – composed of commissural fibers that connect corresponding gray areas of the two hemispheres, enabling them to function as a coordinated whole. The largest commissure is the **corpus callosum**. Less prominent examples are anterior and posterior commissures.
- **Association fibers** connect different parts of the same hemisphere.
- **Projection fibers** connect hemispheres with lower brain or spinal cord. Fibers run vertically.

**Basal Nuclei** – Influence muscle movements - important in starting, stopping and monitoring the intensity of movements executed by the cortex; regulate intensity of slow or stereotyped movements (ex. swinging arms during walking); inhibits antagonistic or unnecessary movement. It also plays a part in regulating attention and in cognition.
**Diencephalon**
These gray matter areas are surrounded by the cerebral hemisphere and enclose the 3rd ventricle. It consists largely of three areas – thalamus, hypothalamus, and epithalamus.

**Thalamus** – Nuclei that form the superolateral walls of the 3rd ventricle. The nuclei are connected at the midline by the interthalamic adhesion – serval nuclei; nuclei project fibers to and receive fibers from the cerebral cortex.
- Gateway to the cerebral cortex – sorts, edits and relays ascending input.
- Afferent impulses from all senses and all parts of the body converge on the thalamus and synapse with at least one of its nuclei. Within the thalamus, information is sorted and edited.
- Mediates sensation, motor activities, cortical arousal, learning, and memory

**Hypothalamus** – Nuclei that form the inferolateral walls of the 3rd ventricle. The hypothalamus extends from the optic chiasma to the posterior margin of the mammillary bodies. Mammillary bodies are paired anterior nuclei that serve as relay stations for olfactory pathways. The infundibulum is a stalk of hypothalamic tissue that connects the pituitary gland to the base of the hypothalamus.
- Controls autonomic nervous system (e.g., blood pressure, rate and force of heartbeat, digestive tract motility, pupil size)
- Physical responses to emotions (limbic system) - perception of pleasure, fear, and rage, and in biological rhythms and drives
- Regulates sleep-wake cycles -- suprachiasmatic nucleus (biological clock)
- Controls endocrine system -- controls secretions of anterior pituitary gland and produces posterior pituitary hormones
- Regulates body temperature – sweating/shivering
- Regulates hunger and satiety in response to nutrient blood levels or hormones
- Regulates water balance and thirst

**Epithalamus** – Nuclei that form the roof of the 3rd ventricle. It contains the pineal gland which secretes melatonin to regulate sleep-wake cycles.
**Brain Stem**

The brain stem regions are the midbrain, pons and medulla oblongata. The organization of the brain stem is similar to the spinal cord – deep gray matter surrounded by white matter fiber tracts. The brain stem has nuclei of gray matter embedded in the white matter, not found in the spinal cord. Brain stem centers control automatic behaviors necessary for survival and contain fiber tracts connecting higher and lower neural centers. The brain stem nuclei are associated with 10 of the 12 pairs of cranial nerves.

**Midbrain** – On its ventral side, the cerebral peduncles contain large pyramidal motor tracts descending toward the spinal cord. Running through the midbrain is the cerebral aqueduct – channel connecting the 3rd and 4th ventricles. Midbrain nuclei function to:

- Periaqueductal gray matter – involved in pain suppression; links fear-perceiving amygdala and ANS pathways for ‘fight-or-flight’ response; contains nuclei that controls cranial nerves III (oculomotor) and IV (trochlear)
- Corpora quadrigemina – four dorsal protrusions; superior colliculi contain visual reflex centers and inferior colliculi contain auditory reflex centers
- Substantia nigra – functionally linked to the basal nuclei
- Red nucleus – relay nuclei for some descending motor pathways that effect limb flexion; part of reticular formation

**Pons** – Composed of conduction tracts that run in both directions --- deep fibers complete that pathway between higher brain centers and the spinal cord and superficial fibers relay impulses between motor cortex and the cerebellum. Several cranial nerves issue from pons nuclei -- cranial nerves V (trigeminal), VI (abducens), and VII (facial). Some pons nuclei are part of the reticular formation and some help the medulla oblongata maintain normal rhythm of breathing.

**Medulla Oblongata** – Blend into the spinal cord at the foramen magnum of the skull. The medulla and the pons help form the ventral wall of the 4th ventricle – the dorsal wall is formed by a thin capillary-rich membrane called the choroid plexus which forms the cerebrospinal fluid. In the midline, pyramids are formed by two large pyramidal tracts descending from the motor cortex. Most of these fibers cross over at the decussation of the pyramids. The inferior olivary nuclei are fold of gray matter that serve as relay sensory information from muscles and joints to cerebellum. Cranial nerves VIII, IX, X, and XII are associated with medulla. Vestibular nuclei (pons and
medulla) mediate responses that maintain equilibrium. Several nuclei (e.g., nucleus cuneatus and nucleus gracilis) serve to relay sensory information. Medulla is an autonomic reflex center --- functions overlap with hypothalamus --- hypothalamus relays instructions via medulla. Important visceral motor nuclei found in the medulla include:

- Cardiovascular center – cardiac center adjusts force and rate of heart contractions.
- Vasomotor center adjusts blood vessel diameter for blood pressure regulation.
- Respiratory centers – generate respiratory rhythm; control rate and depth of breathing
- Additional centers regulate – vomiting, hiccupping, swallowing, coughing, sneezing

**Cerebellum**

Receives and processes input from the motor cortex, brain stem and sensory receptors to allow for smooth, coordinated movements. The cerebellum provides precise timing and appropriate patterns of skeletal muscle contraction for smooth, coordinated movements and agility.

- The cerebellum has two cerebellar hemispheres connected by the vermis. Surface is highly convoluted with deep fissures which divide each hemisphere into three lobes – anterior, posterior, flocculonodular lobes. There is a thin outer cortex of gray matter and a treelike pattern of cerebellar white matter called the arbor vitae.
- Three paired fiber tracts – the cerebellar peduncles – connect the cerebellum to the brain stem. Cerebellum receives impulses from cerebral cortex of intent to initiate voluntary muscle contraction. Signals from proprioceptors and visual and equilibrium pathways continuously "inform" cerebellum of body's position and momentum. Cerebellar cortex calculates the best way to smoothly coordinate muscle contraction. "Blueprint" of coordinated movement sent to cerebral motor cortex and brain stem nuclei.
- The cerebellum recognizes and predicts sequences of events so it can adjust for complex movements.
- It plays a role in thinking, language and emotion.
Functional Brain Systems

Functional brain systems are networks of neurons that work together but span relatively large distances in the brain – the limbic system and reticular formation.

Limbic System – structures on medial aspects of cerebral hemispheres and diencephalon. It’s the emotional or affective brain – two parts involved in emotion.
- **Amygdala (amygdaloid body)**—recognizes angry or fearful facial expressions, assesses danger, and elicits fear response
- **Cingulate gyrus**—role in expressing emotions via gestures, and resolves mental conflict
- Odors trigger emotional reactions and memories this area puts emotional responses to odors.
- Extensive connections between the limbic system and other brain regions allow the system to integrate and respond to a variety of stimuli – most output is relayed through the hypothalamus.
- Limbic system interacts with prefrontal lobes – establishes a relationship between feelings and our thoughts. As a result, we react emotionally to things we consciously understand to be happening and are consciously aware of emotional richness in our lives.
- They **hippocampus** and amygdala body play a role in memory

Reticular Formation – Loosely clustered neurons running the length of the brain stem that form three broad columns (raphe nuclei, medial group, and lateral group). Individual reticular neurons project axonal connections with the hypothalamus, thalamus, cerebral cortex, cerebellum, and spinal cord → can govern brain arousal.
- **Reticular activating system (RAS)** - sends impulses to cerebral cortex to keep it conscious and alert; filters out repetitive, familiar, or weak stimuli (~99% of all stimuli).
- RAS is inhibited by sleep centers, alcohol, drugs; severe injury results in permanent unconsciousness (coma).
- **Motor function** – Some of its motor nuclei project motor neurons to spinal cord via reticulospinal tract and help control coarse limb movement. Other motor nuclei are reticular autonomic centers that regulate visceral motor functions -- vasomotor centers, cardiac center and respiratory centers.
Higher Mental Functions

Brain Wave Patterns and the EEG (electroencephalogram)

An EEG records electrical activity that accompanies brain function—measures electrical potential differences between various cortical areas. The pattern of neuronal electrical activity is recorded as brain waves—pattern is generated by synaptic activity of cortex. Each person’s brain wave is unique and can be grouped into 4 classes based on frequency of hertz (Hz) – alpha, beta, theta and delta waves.

- **Alpha waves (8–13 Hz)**—regular and rhythmic, low-amplitude, synchronous waves indicating an "idling" brain
- **Beta waves (14–30 Hz)**—rhythmic, less regular waves occurring when mentally alert
- **Theta waves (4–7 Hz)**—more irregular; common in children and uncommon in awake adults
- **Delta waves (4 Hz or less)**—high-amplitude waves of deep sleep and when reticular activating system is damped as during anesthesia; indicate brain damage in awake adult

Brain waves change with age, sensory stimuli, brain disease, and chemical state of body. EEGs are used to diagnose and localize brain lesions, tumors, infarcts, infections, abscesses, and epileptic lesions. Flat EEG (no electrical activity) is clinical evidence of brain death.

**Epilepsy** - victims may lose consciousness, fall stiffly, and have uncontrollable jerking. Not associated with intellectual impairments and aura (sensory hallucination) may precede seizure. Epilepsy occurs in 1% of population

- **Absence seizures** (formerly petit mal) - mild seizures of young children; expression goes blank for few seconds
- **Tonic-clonic** (formerly grand mal) **seizures** - most severe; last few minutes; victim loses consciousness, bones broken during intense convulsions, loss of bowel and bladder control, and severe biting of tongue
- Control of epilepsy - Anticonvulsive drugs; vagus nerve stimulator or deep brain stimulator implanted -- deliver pulses to vagus nerve or directly to brain to stabilize brain activity; research into brain electrode implants to detect and prevent oncoming seizures

**Consciousness** – Encompasses conscious perception of sensation, voluntary initiation and control of movement and capabilities associated with higher mental processing. Loss of brain consciousness signals that brain function is impaired. Clinically, consciousness is defined on a continuum that grades behavior in response to stimuli as: alertness, drowsiness (lethargy), stupor and coma. The current suppositions about consciousness are: (1) involves simultaneous activity of large cortical areas; (2) superimposed on other neural activities; (3) it is holistic and totally interconnected.

**Sleep and Sleep-Wake Cycles** – Sleep is a state of partial unconsciousness from which person can be aroused by stimulation. There are two major types of sleep (defined by EEG patterns) -- non-rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep.

- Pass through first two stages of NREM and into stages 3 and 4 (slow-wave sleep) during the first 30–45 minutes of sleep.
At ~ 90 minutes, after fourth stage, REM sleep begins abruptly. In REM, the EEG changes and there is an increase in heart rate, respiratory rate, blood pressure, and a decrease in GI motility change. Oxygen use is greater in REM than during the awake state. Eye’s move rapidly, but skeletal muscles are inhibited and go limp – temporary paralysis.

* Sleep Patterns - alternating cycles of sleep and wakefulness reflect natural circadian (24-hour) rhythm. RAS activity inhibited during, but RAS also mediates sleep stages. Suprachiasmatic and preoptic nuclei of hypothalamus time sleep cycle. Typical sleep pattern alternates between REM and NREM sleep.

**Sleep Disorders**

Narcolepsy - abrupt lapse into sleep from awake state; often have cataplexy - sudden loss of voluntary muscle control; Orexins ("wake-up" chemicals from hypothalamus) destroyed by immune system

Insomnia – chronic inability to obtain amount or quality of sleep needed; may be treated by blocking orexin action

Sleep apnea - temporary cessation of breathing during sleep; causes hypoxia

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**Importance of Sleep**

- Slow-wave sleep (NREM stages 3 and 4) presumed to be restorative stage
- People deprived of REM sleep become moody and depressed
- REM sleep may be reverse learning process where superfluous information purged from brain
- Daily sleep requirements decline with age
- Stage 4 sleep declines steadily and may disappear after age 60

**Language** – practically all the association cortex on the left side is involved. Two regions critical to language is the Broca’s area and Wernicke’s area. Broca’s area, Wernicke’s area and basal nuclei form a single system that analyzes incoming words and produces outgoing word sounds and grammatical structures. The corresponding areas on right side are involved with nonverbal language components – ‘body language’.

**Memory** – The storage and retrieval of information – essential to learning, incorporating our experiences into behaviors and part of our consciousness. Two stages: Short-term memory (STM, or working memory)—temporary holding of information; limited to seven or eight pieces of information; Long-term memory (LTM) has limitless capacity.
Factors affecting transfer from STM to LTM --
- Emotional state—best if alert, motivated, surprised, and aroused
- Rehearsal—repetition and practice
- Association—tying new information with old memories
- Automatic memory—subconscious information stored in LTM

Categories of Memory & Brain Structures --
1. Declarative (fact) memory - explicit information; related to conscious thoughts and language ability; stored in LTM with context in which learned
   - Hippocampus and surrounding temporal lobes function in consolidation and access to memory. ACh from basal forebrain is necessary for memory formation and retrieval.

2. Nondeclarative memory - less conscious or unconscious; acquired through experience and repetition; best remembered by doing; hard to unlearn; includes procedural (skills) memory, motor memory, and emotional memory
   - Procedural memory -- Basal nuclei relay sensory and motor inputs to thalamus and premotor cortex; dopamine from substantia nigra is necessary. Motor memory—cerebellum; Emotional memory—amygdala

Molecular Basis of Memory - during learning
- Changes: neuronal RNA altered; newly synthesized mRNA moved to axons and dendrites; dendritic spines change shape; extracellular proteins deposited at synapses involved in LTM; number and size of presynaptic terminals may increase; presynaptic neurons release more neurotransmitter
- The result of these changes is long-term potentiation (LTP) -- Increase in synaptic strength crucial. Long-lasting synaptic strength increases underlie memory formation.
Protection of the Brain

1. **Meninges** – connective tissue membranes that (1) covers and protects the CNS, (2) protects blood vessels and encloses venous sinuses, (3) contains cerebrospinal fluid (CSF) and (4) forms partitions in the skull. Three layers –
   - Dura Mater – strongest meninges; two layers of fibrous connective tissue (around brain) separate to form dural venous sinuses. Dural septa limit excessive movement of brain.
   - Arachnoid Mater – middle layer with weblike extensions; separated from dura mater by **subdural space**. **Subarachnoid space** contains CSF and largest blood vessels of brain. **Arachnoid villi** protrude into superior sagittal sinus and permit CSF reabsorption.
   - Pia Mater – delicate vascularized connective tissue that clings tightly to brain

2. **Cerebrospinal Fluid (CSF)** – forms a watery cushion that gives buoyancy to the CNS structures. The CSF reduces brain weight by 97% and prevents brain from crushing under its own weight. It protects the CNS from blows and other trauma. CSF helps nourish the brain and carries chemical signals from one part of the brain to another. CSF is a water solution formed from blood plasma, but contains less protein and different ion concentration than plasma (more Na, Cl and H; less Ca and K).
   - **Choroid Plexus** – a cluster of capillaries enclosed by the pia mater and a layer of ependymal cells. Plexus hangs from roof of each ventricle and produces CSF at a constant rate and is kept in motion. Ependymal cells use ion pumps to control composition of CSF and help cleanse CSF by removing waste. Normal volume of CSF ~ 150 ml; replaced every 8 hours
   - **Hydrocephalus** – obstruction blocks CSF circulation or drainage; unfused skull bones of newborn allow enlargement of head; brain damage in adult due to rigid adult skull; treated by draining with ventricular shunt to abdominal cavity
3. **Blood-brain barrier** - refers to the least permeable capillaries that selectively diffuse materials to neurons. It helps maintain a stable environment for the brain and separates neurons from some blood-borne substances. It’s a selective barrier that allows nutrients to move by facilitated diffusion -- allows any fat-soluble substances to pass, including alcohol, nicotine, and anesthetics. Metabolic wastes, proteins, toxins, most drugs, small nonessential amino acids, K\(^+\) denied access. Barrier is absent in some areas, e.g., vomiting center and hypothalamus, where necessary to monitor chemical composition of blood.

**Homeostatic Imbalances of the Brain**

1. Traumatic brain injuries
   - Concussion—temporary alteration in function
   - Contusion—permanent damage
   - Subdural or subarachnoid hemorrhage—may force brain stem through foramen magnum, resulting in death
   - Cerebral edema—swelling of brain associated with traumatic head injury

2. Cerebrovascular accidents (CVAs or strokes) – occurs when tissue is deprived of blood supply and brain tissue dies (ischemia – deprivation of blood supply); Most common cause is blockage of cerebral artery by a blood clot.
   - Transient ischemic attacks (TIAs)—temporary episodes of reversible cerebral ischemia

3. Alzheimer’s disease (AD): a progressive degenerative disease of brain that results in dementia; memory loss, short attention span, disorientation, eventual language loss, irritable, confused, hallucinations; plaques of beta-amyloid peptide form in brain and brain shrinks

4. Parkinson’s disease - degeneration of dopamine-releasing neurons of substantia nigral → basal nuclei deprived of dopamine become overactive → tremors at rest. Cause is unknown.

5. Huntington’s disease - fatal hereditary disorder caused by accumulation of protein huntingtin → leads to degeneration of basal nuclei and cerebral cortex. Symptoms include jerky movements, mental deterioration and treatments include drugs that block dopamine effects.
Spinal Cord
The spinal cord is a continuation of the brain stem with a two-way conduction pathway to & from the brain and serves as a reflex center. It extends from the foramen magnum of the skull to about the 2nd lumbar vertebrae. The spinal cord is protected by bone, meninges and CSF. The single layered spinal dura mater is not attached to the bony walls of the vertebral column. Between the vertebrae and the dural sheath is the epidural space filled with fat and a network of veins. CSF fills the subarachnoid space between the arachnoid and pia mater. The dural and arachnoid membrane extend to sacrum, beyond end of cord at L1 and L2 – site of lumbar puncture or tap. The spinal cord terminates in the conus medullaris – tapered cone-shaped structure. The filum terminale, a fibrous extension of the conus covered by pia mater extends to coccyx – where it anchors the spinal cord. Denticulate ligaments are extensions of the pia mater that secure the cord to the dura mater.

31 pairs of spinal nerves attach to the cord by paired roots. Each nerve exits from the vertebral column via the intervertebral foramina and travels to the body region it serves. Cervical and lumbosacral enlargements are due to emergence of nerves serving the upper and lower limbs. Cauda equine are collection of nerve roots at inferior end of vertebral canal.
Cross-Section Anatomy
Two lengthwise grooves partially divide the cord into right and left halves – ventral median fissure and dorsal median sulcus. The gray commissure connects masses of gray matter and encloses the central canal.

Gray Matter
- **Dorsal horns** - interneurons that receive somatic and visceral sensory input
- **Ventral horns** - some interneurons; somatic motor neurons; axons exit cord via ventral roots
- **Lateral horns** (only in thoracic and superior lumbar regions) - sympathetic neurons
- **Dorsal roots** – sensory input to cord
- **Dorsal root (spinal) ganglia**—cell bodies of sensory neurons

Zones of Spinal Gray Matter – per relative involvement in innervating somatic and visceral regions of body
White Matter – Composed of myelinated and nonmyelinated nerve fibers that allow communication between parts of spinal cord, and spinal cord and brain. These fibers run in three directions: Ascending (up to higher centers – sensory inputs), Descending (from brain to cord and lower cord levels – motor output), Transverse (from one side to other – commissural fibers). Ascending and descending tracts make up most of the white matter. White matter is divided into three columns (funiculi) on each side – dorsal, lateral and ventral. Each spinal tract is composed of axons with similar destination and functions.

- All major spinal tracts are part of multineuron pathways that connect the brain to the body periphery. Most pathways cross to the other side (deccussation), consist of two or three neurons (relay), exhibit precise spatial relationships (somatotopy) and pathways are paired symmetrically.

**Ascending Pathways – consist of three neurons**
- First-order neuron – conducts impulses from cutaneous receptors and proprioceptors to the spinal cord or brain stem, where they synapse with the 2nd order neuron
- Second-order neuron (interneuron) - transmit impulses via axons that extend to thalamus or cerebellum
- Third-order neuron (interneuron) - conduct impulses via axons extend to somatosensory cortex of the cerebrum
- Three main pathways – nonspecific and specific ascending pathways transmit impulses to the sensory cortex to provide discriminatory touch and conscious proprioception & spinocerebellar tracts terminate in the cerebellum and convey information about muscle or tendon stretch used to coordinate muscle activity.

**Descending Pathways** – deliver efferent impulses from brain to spinal cord and are divided into two groups – direct pathways (pyramidal tracts) and indirect pathways (all others). Motor pathways involve two neurons: upper motor neurons (pyramidal cells in primary motor cortex) and lower motor neurons (ventral horn motor neurons) innervate skeletal muscles.
- Direct pathways - impulses from pyramidal neurons in precentral gyri pass through pyramidal (corticospinal) tracts; axons synapse with interneurons or ventral horn motor neurons; direct pathway regulates fast and fine (skilled) movements
- Indirect pathways - includes brain stem motor nuclei, and all motor pathways except pyramidal pathways – these pathways are complex and multisynaptic. Pathways are mostly involved in (1) axial muscles maintaining balance and posture, (2) muscles controlling coarse limb movements, (3) head, neck, and eye movements that follow objects in visual field.
Spinal Cord Trauma & Disorders

Any localized damage to the spinal cord or its roots leads to some functional loss, either paralysis (loss of motor functions) or paresthesias (sensory loss).

- **Flaccid paralysis**—severe damage to ventral root or ventral horn cells; impulses do not reach muscles; there is no voluntary or involuntary control of muscles --- muscles atrophy
- **Spastic paralysis**—damage to upper motor neurons of primary motor cortex; spinal neurons remain intact; muscles are stimulated by reflex activity -- no voluntary control of muscles, muscles often shorten permanently
- **Amyotrophic Lateral Sclerosis** (ALS) - destruction of ventral horn motor neurons and fibers of pyramidal tract; caused by environmental factors and genetic mutations involving RNA processing – involves glutamate excitotoxicity. Symptoms include loss of ability to speak, swallow, and breathe. Death typically occurs within five years.

Developmental Aspects of CNS

- Gender-specific areas appear in both brain and spinal cord, depending on presence or absence of fetal testosterone
- Maternal exposure to radiation, drugs (e.g., alcohol and opiates), or infection can harm developing CNS
- Smoking decreases oxygen in blood, which can lead to neuron death and fetal brain damage
- Age brings some cognitive declines, but not significant in healthy individuals until 80s
- Shrinkage of brain accelerates in old age
- Excessive alcohol use and boxing cause signs of senility unrelated to aging process
- Hypothalamus one of last areas of CNS to develop -- premature infants poor body temperature regulation
- Visual cortex develops slowly over first 11 weeks
- Neuromuscular coordination progresses in superior-to-inferior and proximal-to-distal directions along with myelination