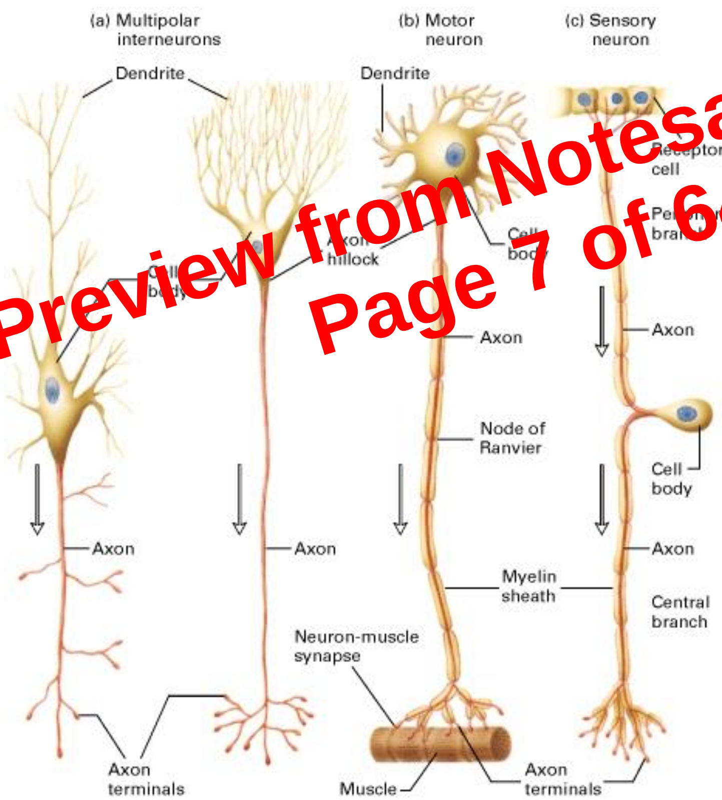
- o Cell differentiation
  - ▪ Once in place, chemical signals in the local environment cause cells to differentiate into the type of cell appropriate for that region
- o Synaptogenesis
  - ▪ The fourth stage: the establishment of synaptic connections as axons grow and dendrites grow
  - ▪ Forming synapses
- o Apoptosis
  - ▪ Cells that have not formed adequate synapses with other neurons will die
- o Synaptic restructuring
  - ▪ The last stage: the loss of some synapses and the development of others, to refine synaptic connections

- <u>Neuronal anatomy and communication</u>
- Sensory neurons: specialized to gather sensory information, directly affected by changes in the environment, such as light, odor, or touch
  - o Bring info into the CNS from the periphery
- Motor neurons: large and have long axons reaching out to synapse on muscles, causing muscular contractions
  - o Carry info from the CNS to the periphery
- Interneurons: receive input from and send output to other neurons, smaller axons
- Neuronal structure



  - o
- Input, integration, conduction, output zones
  - o Input: the part of a neuron that receives information from other neurons or from specialized sensory structures (dendrites)
  - o Integration zone: the part of a neuron that initiates nerve electrical activity (cell body or soma)
  - o Conduction zone: conducts the cells output information in the form of electrical impulses away from the cell body (axon or nerve fiber)
  - o Output zone: transmit the cells signals across synapses to other cells (axon terminals)
- Neuronal classifications (multipolar, bipolar and unipolar)
  - o Multipolar: many dendrites and a single axon. Most common type. Motor and interneurons
  - o Bipolar: single dendrite and a single axon. Sensory systems only

  - Unipolar: single extension that branches in two directions after leaving the cell body. One end is the input zone with dendrites, the other end the output zone. From body into spinal cord, sensory
- Innervate
  - To provide neural input to
  - Most neurons have an axon hillock from which the axon projects, this hillock gathers and integrates information from the synapses and converts them into a code of electrical impulses that race down the axon toward targets
- **Glial** cells in the adult brain – (astrocytes, oligodendrocytes/Schwann cells, microglia) & functions of each
  - Glial cells outnumber neurons
  - Oligodendrocytes (in the brain and spinal cord) and Schwann cells: wrap around axons to provide myelin, a fatty insulating substance (improves the speed at which nerve impulses are conducted)
  - Nodes of Ranvier: gap between successive segments of myelin sheath where the axon membrane is exposed
  - Astrocytes: weave around and between neurons with tentacle-like extensions, controlling local blood flow to increase the amount of blood reaching more-active brain regions, modulate neural activity and formation of synapses, forming outer membranes that swaddle the brain
    - Nourishment and support
    - Problem when they swell in response to injury
  - Microglial: tiny and mobile, contain and cleanup site of injury
    - Glial scars
- Problems associated with glial cells (MS, glial scars, swelling)
  - MS: interferes with myelin
  - They continue to divide into adulthood, can give rise to deadly brain tumors, and can create glial scars that create a wall, problem especially in the spinal cord
  - Respond to brain injury by changing size, leading to swelling (edema)
- Blood brain barrier – structure and function
  - The mechanisms that make the movement of substances from blood vessels into brain cells more difficult than exchanges in other body organs, thus affording the brain greater protection from exposure to some substances found in the blood
  - Capillaries in the brain are highly resistant to the passage of large molecules across their walls and neighboring regions
  - Composed of tightly packed cells and astrocytes
  - Semipermeable: drugs, hormones
- Withdrawal reflex
  - Sensory neuron detects the pain stimulus
  - Message is sent to the terminal buttons on the spinal cord
  - Message is passed to an interneuron inside the spinal cord
  - Interneuron passes the message to a motor neuron
  - Motor neuron sends a message to contract the muscle
- Membrane potential
  - The difference in electrical charge between the inside and outside of a cell
- Polarization: a difference in electric charge between the inside and outside of a cell. All living cells are more negative on the inside than on the outside, so we say they are polarized
- Resting potential: a difference in electrical potential across the membrane of a never cells during an inactive period
  - A neuron at rest exhibits a resting potential of about- 50 / -80 thousandths of a volt
  - Inside of a neuron is negatively charged relative to the outside
  - <u>Outside of the cell: positively charged sodium ions and negatively charged chloride ions</u>
  - <u>Inside of the cell: positively charged potassium ions and negatively charged organic anions</u>
- **Concentration gradients of ions**
  - Sodium (Na+) and chloride (Cl–) ions are at high concentrations in the extracellular region, and low concentrations in the intracellular regions. These concentration gradients provide the potential energy to drive the formation of the membrane potential. This voltage is established when the membrane has permeability to one or more ions.
- Electrostatic forces

- The propensity of charged molecules or ions to move, via diffusion, toward areas with the opposite charge
- Diffusion: force that causes molecules of a substance to spread from regions of high concentration to regions of low concentration
- Go towards equal concentration
- So, cations like potassium are attracted to the negatively charged interior of the cell, and anions are repelled
- Positive exterior attracts anions, repels cations

- Sodium/potassium pump
  - Energetically expensive mechanism that pushes sodium ions out of a cell, and potassium ions in
  - Pumps three sodium ions out for every two potassium ions pumped in
  - Buildup of K ions inside the cell, but K ions can leave the interior, moving down their concentration gradient and causing a net buildup of negative charges inside the cell, exerting electrostatic pressure to pull positively charged K ions back inside, leading to equilibrium potential: any further movement of K into the cell is matched by movement out
- Selective permeability
  - The property of a membrane that allows some substances to pass through, but not others
  - Some ion channels stay open all the times, but the cell membrane of a neuron contains many such channels that selectively allow only potassium ions to cross the membrane
- Voltage-gated ion channels
  - Ion channels are pores in the cell membrane that permits the passage of certain ions through the membrane when the channels are open
  - A Na selective channel that opens or closes in response to changes in the voltage of the local membrane potential; it mediates the action potential
  - When the cell membrane becomes depolarized the threshold level, the gates channel changes, opening the gate to allow Na ions through
  - Voltage gated K channels then allow K ions to rush out quickly, restoring the resting potential
  - Regenerated along the length of the axon, so normally goes in only one direction, because leaves in its wake refractory membrane
  - Charge: electrical: within
- **Ligand-gated ion channels**
  - Sodium and potassium
  - Chemical: between
  - Open in response to a ligand binding to them
- Depolarization
  - A decrease in membrane potential (the interior becomes less negative) –moving the membrane potential closer to zero
- Hyperpolarization
  - An increase in membrane potential (the interior of the neuron becomes more negative) –making the potential even farther from zero
- EPSPs (depolarization)
  - A depolarizing potential in the postsynaptic neuron that is caused by excitatory presynaptic potentials. Increase the probability that the postsynaptic neuron will fire an action potential
  - Stimulation of the excitatory presynaptic neuron, releases transmitter, postsynaptic cell depolarizes, Na channels open to let the positive ions in. this depolarization is known as EPSP, because it pushes the postsynaptic cell a little closer to the threshold for an action potential
  - <u>Increase in the charge inside of the cell reduces resting potential (less polarized, closer to zero)</u>
- IPSPs (hyperpolarization)
  - A hyperpolarizing potential in the postsynaptic neuron that is caused by inhibitory connections. Decrease the probability that the postsynaptic neuron will fire an action potential
  - Inhibitory leads to postsynaptic membrane becoming even more negative, decreasing the probability of an action potential
  - Usually result from opening of channels that permit chloride ions to enter the cell
  - <u>Decrease in the charge inside the cell increases resting potential (more polarized, more negative)</u>
  - Inhibits communication within a cell
- Spatial & temporal summation

        - Contain synaptic vesicles, containing molecules of neurotransmitter, the chemical the pre uses to communicate with the post, where there are matching neurotransmitter receptors
    - Post: specialized membrane on the surface of a nerve cell that receives information by responding to neurotransmitter from a presynaptic neuron
    - Synapse: synaptic cleft is the gap
    - When the action potential reaches the end of an axon, it causes the axon to release a chemical, called a neurotransmitter
        - When released, briefly alters the membrane potential on the other side of the synapse
        - Brief changes are called postsynaptic potentials
- Vesicles
    - When an action potential reaches a presynaptic terminal, it causes hundreds of synaptic vesicles near the presynaptic membrane to fuse with the membrane and discharge their contents into the synaptic cleft (neurotransmitter)
        - Influx of calcium ions into the axon terminal
- **Transporter molecule**
    - Class notes:
    - Synaptic transmission
        - Neurotransmitter is released from pre neuron, diffuses across the synapse to the post
        - Pre synaptic membrane
            - Terminal button
            - Contains vesicles carrying neurotransmitter
            - Transporter molecules
        - Synaptic cleft
        - Postsynaptic membrane
            - On the dendrite, soma, axon
            - Contains receptors, ligand gated ion channels, opened up by ligands
- Receptors: a protein that captures and reacts to molecules of a neurotransmitter or hormone
- **Binding sites**
    - Specialized region in the post-synaptic receptor molecule
    - Uniquely shaped
- Ligands: a substance that binds to receptor molecules, such as a neurotransmitter or drug that binds postsynaptic receptors
    - Molecule that fits into a specific binding site
        - Endogenous ligands
            - Neurotransmitters
            - Neuromodulators and hormones
        - Exogenous ligands
            - Drugs
    - Key in a lock
- Steps of synaptic firing
    - The action potential arrives at the presynaptic axon terminal
    - Voltage gated calcium channels in the membrane of the axon terminal open, and calcium ions enter the axon terminal
    - Calcium causes the synaptic vesicles filled with neurotransmitter to fuse with the presynaptic membrane and rupture, releasing the transmitter molecules into the synaptic cleft
    - Some transmitter molecules bind to special receptor molecules in the postsynaptic membrane, leading to the opening of an ion channels in the postsynaptic membrane. The resulting flow of ions creates a local EPSP or IPSP in the postsynaptic neuron
    - The IPSP and ESPS in the postsynaptic cell spread toward the axon hillock (if the sum of it all depolarizes the hillock enough to reach threshold, an action potential will arise)
    - Synaptic transmission is rapidly stopped, so the message is brief and accurately reflects the activity of the presynaptic cell
    - Synaptic transmitter may also activate presynaptic receptors, resulting in a decrease in transmitter release
    - Class
        - Action potential arrives at the terminal button

n. Agonist in both NE and DA symptoms would likely to:
   i. Euphoria, arousal, and energy, low appetite: meth!!!

o. Inocbye rimosa
   i. Muscarine [Symbol] convulsions

p. Neuromodulators: modulation mean change, neuro means

q. Alcohol affects CNS

- <u>Visual system</u>
- Sensory transduction
  - The process of transferring physical stimuli into neural signals
  - Physical stimuli act on **sensory receptors** in the periphery and alter their membrane potential
- Receptor potential
  - Change in membrane potential results in change in neurotransmitter released
  - Receptor cells lack an axon, no action potential!!! Only local potentials
- Eyeball anatomy
  - Light passes through:
    - Conjunctive: mucous membrane
    - Cornea: transparent outer layer
      - Refracts light
    - Pupil: hole regulated by contractions of the iris (pigmented ring of muscle)
    - Lens: transparent layer
      - Refracts light to focus it on the retina
      - **Accommodation:** adjustment of the lens by ciliary muscles to focus on near or distant objects
- Retinal anatomy
  - Light is focused on the retina: lining at the back of the eye; contains photoreceptors
    - Rods (**scotopic**): respond to dim light, mediate low resolution vision
    - Cones (**photopic**): respond to bright light and color; mediate high resolution vision
    - Fouea is the region of the retina that contains only cones; mediates acute vision
    - Optic desk: location on the retina where axons exit the retina and enter the optic nerve
      - Blind spot: no receptors
- Retinal cells function
  - Photoreceptor layer: contains rods and cones
  - Bipolar layer
    - Bipolar cells: connect the photoreceptors to the ganglion cells
    - **Horizontal and amacrine cells:** combine information from adjacent photoreceptors
  - Ganglion cells layer: axons carry visual information into the brain through the optic nerve
    - Form the optic nerve
    - Do conduct action potentials
- Photoreceptors
  - Contain molecules of photopigments
    - Each molecules consists of an opsin and a retinal
  - Steadily released glutamate in the dark
  - Light exposure causes the photopigments to break apart, causing a hyperpolarization of the receptor membrane
  - Hyperpolarization decreases the amount of glutamate that is steadily released by photoreceptors
  - Effect of decreased photoreceptor glue release on **bipolar cells** (with light on)
    - On center bipolar cells: inhibited by glutamate
      - Less glutamate is depolarizing
      - Cells release less glutamate
    - Off center bipolar cells: excited by glutamate
      - Less glutamate is hyperpolarizing

    - Increased activity in this region while recalling spatial locations and navigating through an environment
- Hippocampal place cells
  - Hippocampus is not necessary for most simple stimulus response learning, it is critical for relational learning
  - Studied in the Morris water maze – measure of spatial learning
    - Animal model of relational learning
  - Animals and humans with hippocampal lesions
    - Can learn stimulus response tasks
    - Cannot learn spatial relationships and cannot navigate according to contextual cues
- Anterograde amnesia – definition, characteristics, development, brain regions, circuits and receptors involved
  - Loss of relational learning ability
  - New declarative memories are not formed
  - Stimulus- response, perceptual, and motor learning abilities remain intact
  - Most previously formed memories remain intact, though some retrograde amnesia is often seen
  - Results from bilateral damage to, or removal of, the medial temporal area
    - Contain the hippocampus—critical to memory formation
    - Unilateral damage may produce minor memory deficits
  - Famously studied in HM
    - Both medial temporal lobes were removed to treat epilepsy
    - Results in pervasive anterograde amnesia, accompanied by some retrograde amnesia
- Retrograde amnesia
  - Loss of previously formed declarative memories
- Short-term memory
  - Immediate and limited memory for recently perceived stimulus
    - Holds 5 to 7 items for a few moments
    - Indefinitely with rehearsal
- Long-term memory
  - Stable and unlimited memory for all learning
  - Consolidation: shifts information from STM to LTM
    - Hippocampus
- Hippocampus – role in memory
  - Not the location of long term memory storage
    - HM long term memory was intact
  - Not the location of short term memory storage
    - Able to answer questions and hold info in his mind as long as he rehearsed it
  - Involved in consolidation of long term memories
    - Unable to form declarative memories

Final Review

Final Exam Study Guide
In addition to the list below, be sure to review your reading from the textbook.
<u>Language and communication</u>

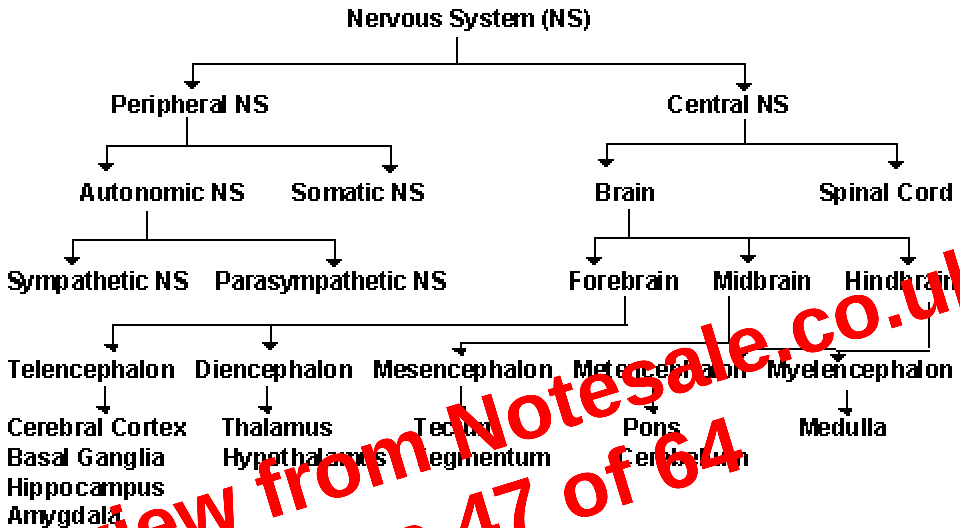
- Lateralization
  - Roles of left and right hemisphere in language
    - Left hemisphere
      - Sequential processing
      - Language production and comprehension
      - Damage to the left hemisphere → severe language impairments
    - Right hemisphere dominance
      - Global processing

        - Being a 2nd RH positive offspring
    - Genetic or biological predisposition combine with environmental stressors influence onset
    - Discordant rates of schizophrenia among monozygotic twins supports the precipitating stimulus theory
- Treatments
    - Antipsychotic drugs
        - Typical antipsychotics
            - Dopamine antagonists
                - Chlorpromazine
                - Haloperidol
                - Pimozide
        - Atypical
            - Works at a variety of post-synaptic receptors
                - Clozapine
                - Aripripzole
    - Psychotherapy

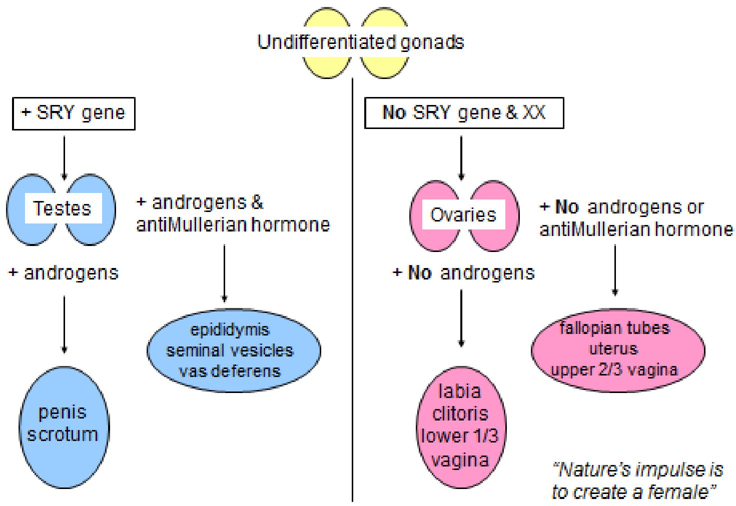
Major depression

- Symptoms
    - Most prevalent mood disorder
    - Sadness, anhedonia, pessimism, anxiety, rumination, loss of interest, change in appetite and sleep patterns, impaired cognitive functions, restlessness or torpor, possible suicidal ideation, gestures, or attempts
- Neural characteristics
    - Reduced function in serotonin and norepinephrine system
        - Drugs that increase 5HT and norepinephrine decrease symptoms
    - Increased activity in amygdala and prefrontal cortex
        - Decreased activity in the parietal, temporal, and anterior cingulate cortex
        - May explain impaired cognition, and increased anxiety and rumination
    - Thinner right cerebral cortex correlated with depression risk
        - Seen in subjects whose parents and or grandparents experience chronic or recurring depression
        - May be genetic, may be exacerbated by living with a depressed parent
    - Chronic depression leads to reduced hippocampal volume
        - Neurons are reduced in size, not necessarily lost
- Possible causes
    - Diathesis stress model
        - Genetic predisposition
        - Concordance rates 60%
        - Short allele for 5HT transporter gene increases sensitivity and susceptibility to depression
        - Stress leads to expression
            - Stress may disrupt monoamine function in susceptible individuals
    - Immune response
        - Prolonged release of cytokines by the immune system results in symptoms of depression
            - Rates of depression higher in people with chronic inflammatory conditions
            - May be mediated by reduced levels of tryptophan
- Treatments
    - Antidepressant drugs
        - Selective serotonin reuptake inhibitors
            - Prozac, paxil, Zoloft
        - Norepinephrine reuptake inhibitors
            - Strattera, Wellbutrin
    - Psychotherapy
        - Cognitive-behavioral therapy
    - SSRI's and CBT are most effective together
        - Alone, they are equally effective

            - Changes in the charge of the postsynaptic membrane
        - Neural **integration** is the summation of all post synaptic potentials
            - Spatial summation and temporal summation
            - Determines the absolute effect of the axon hillock
            - If the cell is depolarized to the threshold of excitation → an action potential fires
            - If the cell is hyperpolarized → nothing happens
        - Removal of NT from the synapse terminates PSPs
            - Reputake
                - Transporter molecules draw NT back into the cell
            - Enzymatic deactivation
                - Enzyme in the synapse breaks down NT molecules
- Major divisions of the nervous system from telencephalon to myelencephalon



- Corpus callosum: main band of axons that connects the two cerebral hemispheres
    - Coordinates sensory processing and motor output between hemispheres
- **Division of the central nervous system:**
    - Forebrain
        - Telencephalon
        - Diencephalon
    - Midbrain
        - Mesencephalon
    - Hindbrain
        - Metencephalon
        - Mylencephalon
- Forebrain: contains the telencephalon (cerebral hemispheres) and diencephalon
    - Telencephalon: cortex, basal ganglia, limbic system
        - Cerebral cortex: thick sheet of brain tissue, mostly neurons and their fibers
            - Surrounds the cerebral hemisphere
            - Divided into four lobes
                - Gyrus: ridges of tissue
                - Sulcus: crevices
                - Fissure: large grooves
            - Frontal lobe
                - Prefrontal cortex
                    - Higher cognitive functions
                - Motor association cortex
                    - Anterior to the PMC (in front of)
                    - Plans movement



- Female: neural control of sexual behavior
  - Medial amygdala
    - Sexually dimorphic (smaller in females)
    - Receives:
      - Chemosensory, hormonal, somatosensory input
    - Projects to VMH and MPOA
  - Ventromedial nucleus of the hypothalamus (VMH)
    - Critical control of lordosis and sexual behavior
    - Activate by estradiol and progesterone
    - Projects to the PAG
  - Periaqueductal grey (PAG)
    - Projects to the spinal motor neurons, simulating sexual reflexes
  - Medial preoptic area (MPOA)
    - Critical to material behaviors
    - Activated by several reproduction-related hormones
- Males: neural control of sexual behavior
  - Medial amygdala
    - Sexually dimorphic (85 percent large in males)
    - Receives: chemosensory, hormonal, somatosensory input
    - Projects to the MPOA
  - Medial preoptic area (MPOA)
    - Critical to male sexual behavior
    - Activated by testosterone and other hormones
    - Projects to the PAG and PGI
  - Periaqueductal grey (PAG)
    - Region of the midbrain, stimulates the spinal cord sexual reflexes
    - Input from the MPOA activates these connections
  - Nucleus paragigantocellulans (PGI)
    - Located in the medulla, inhibits spinal cord and sexual reflexes
    - Input from the MPOA suppresses this inhibition
    - Stops constant sexual arousal
- VMH is critical in females/ MPOA is critical in males
- Female internal
  - absence of anti-mullerian hormones prompts it
- Ovaries do not produce luteinizing hormones
- Congenital adrenal hyperplasia: results from hypertrophy of the adrenal cortex and overproduction of androgen
- Posterior and anterior pituitary

- Oxytocin
- PGI
- Disorders
- What stimulates arousal?
    - Serotonin
    - Hypocretin
    - Norepinephrine
    - Adenosine
- Wakefulness (brain waves, behavioral characteristics, neural control)
    - Brain waves
        - Alpha: regular, medium frequency waves (typical of resting)
        - Beta: irregular, low amplitude waves (typical of alertness and active thinking)
    - Neural control of arousal
        - Wakefulness is characterized by cycles of varying arousal
        - Controlled by:
            - Acetylcholine (ACH)
                - ACH neurons in the pons and basal forebrain stimulate cortical arousal
            - Histamine
                - Excitatory NT involved in arousal
                - Neurons located in the tuberomammilary nucleus of the hypothalamus
                    - Project to the cerebral cortex and basal forebrain—increase cortical activation / arousal
                - Histamine agonists impair arousal
            - NE
                - Firing of NE neurons in the locus coruleus of the brainstem facilitates alertness
                - Disappears during sleep, increasing at waking
                - Drugs that increase NE and 5-HT impair sleep
            - 5-HT
                - Neurons in the brainstem raphe nuclei involved in
                    - Cortical arousal
                    - Tonic motor activity
                - Firing activity decreases with each stage of sleep to almost none during REM sleep
                    - REM sleep paralysis
                    - Returns at the end of a REM stage
            - Hypocretin
                - Excitatory NT released by cells in the lateral hypothalamus
                    - Axons synapse with cells in:
                        - The pons, basal forebrain, locus coreuleus, raphe nuclei, tuberomammillary nucleus
                    - Promotes wakefulness
- Non-REM sleep stages 1-4 (brain waves, length of time, behavioral characteristics, functions, importance, neural control)
    - Brain waves
        - Stage 1 sleep (ten minutes)
            - Theta waves: lower frequency
            - Transition from wakefulness to sleep
        - Stage 2 sleep (15 minutes)
            - Theta waves continue, marked by sleep spindles and k complexes
        - State 3 (15 to 20)
            - Beginning of slow wave sleep
                - Deep sleep
            - Combination of theta and delta activity