Behavioral Neuroscience Notes

PSYC 360

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CHAPTER 3

STRUCTURE OF THE NERVOUS SYSTEM

3.1 Neuroanatomy

Neuroscience is the study of the nervous system. Behavioral neuroscience is understanding the nervous system's underlying behavior.

3.1.1 Nervous System Structure

Structural Nervous System

How are neurons organized into systems?

- **Central Nervous System (CNS)**
  - Brain
  - Spinal Cord
- **Peripheral Nervous System (PNS)**

Functional Nervous System

What are the 'jobs' of the nervous system?

- *Somatic Nervous System*
  - Skeletal Muscles (Striated)
  - Sensory information in
  - Voluntary motion out
- *Autonomic Nervous System*
  - Uses smooth muscles
  - Glands
  - Sympathetic Nervous System
    - Fight or Flight
    - Heart rate, blood pressure, respiration, and alertness.
  - Parasympathetic Nervous System
    - Rest and Digest
  - *Enteric Nervous System*

- A mesh-like system of neurons that governs the function of the gastrointestinal system.
- AKA: 'Second Brain'
- GI problems are correlated with psychological disorders.
- The GI track houses a lot of our microbiota.
- Fecal Microbiota Transplant
  - Rat studies showed that when a skinny rat has a fecal transplant from a fat rat, the skinny rat becomes fat. This works in reverse too.
  - Therefore, the microbiota change the *behavior* of the rat.
- Elevated Plus Maze
  - A test to measure anxiety in rats.
  - The rats with the fecal transplant from the anxious rats were more anxious.
  - **This is huge!** This shows that the microbiota can change if a rat is anxious or not!

3.2 Meninges

- Cover the outside of the nervous system.
  - Three for the CNS and two for the PNS.
  - The PNS does not use the arachnoid mater.
- *Dura Mater*
  - "Hard Mother"
  - The outermost layer.
  - Tough and fibrous.
  - Contains blood vessels.
  - Early anatomists called it "pachymeninges" because similar to elephant skin.
- *Arachnoid Mater* = "Spider Mother"
  - Middle layer.
  - Web-like structure.
  - Contains blood vessels.
  - Subarachnoid Space
    - Between the arachnoid and Pia mater.
    - Contains cerebrospinal fluid (CSF).
  - Arachnoid trabeculae

        - Web-like structures that connect the arachnoid mater to the Pia mater.
        - Allows for the subarachnoid space to be filled with CSF.
- *Pia Mater* = "Soft Mother"
    - Innermost layer.
    - Thin and delicate.
    - Flows over every sulcus (grooves), fissure (deep indentations), and gyri (bumps).
    - Follows the contours of the brain and spinal cord.
- *Meningitis*
    - Inflammation of the meninges.
    - Can cause symptoms such as headache, fever, a stiff neck, or hallucinations.

3.3 Cerebrospinal Fluid (CSF)

- Similar to blood plasma.
- Functions of CSF
    - Protection
        - Failures:
            - Brain is injured.
            - AND even Contrecoup–when the brain is injured on the opposite side of the impact–injuries.
            - *Chronic Traumatic Encephalopathy (CTE)*
                - Old name: Dementia Pugilistica (boxer's dementia).
                - Symptoms (not exhaustive): Memory loss, confusion, impaired judgment, impulse control problems, aggression, depression, Parkinson's-like symptoms, insomnia, and progressive dementia.
                - Causes ventricular enlargement. In other words, the larger your ventricles, the less brain matter you have.
                - Also causes atrophy of the fornix. The fornix is a C-shaped bundle of nerve fibers in the brain that acts as the major output tract of the hippocampus.
                - Tau are abnormally phosphorylated aggregate into tangles. They accumulate both inside neurons and even released into extracellular space.
    - The CSF also moves neurotransmitters, waste, hormones, nutrients, and other substances from one place to another.
        - For example, the CSF moves β-amyloid (in-between cells) from the brain to the blood.

- *Choroid Plexus*
  - *Ependymal cells*
    - Lines the lateral ventricles.
    - These are the cells that produce the CSF.
  - If the choroid plexus is not working properly, it can cause hydrocephalus.
  - *Hydrocephalus*
    - "Water on the brain"
    - Swelling of the brain due to the accumulation of CSF.
  - Derives from the Pia mater.

3.3.1 Flow of CSF

- *Lateral ventricles*
  - CSF is produced here and flows through the interventricular foramen.
- *Third Ventricle*
  - Looks like a duck's head.
  - Is connected to the *pituitary gland* through the *infundibulum*.
- The CSF routed through the medial longitudinal fissure and into the *Superior Sagittal Sinus*.
- *Interperducular Fossa*
  - The space between the two cerebral peduncles.
- *Interventricular Foramen*
  - Connects the lateral ventricles to the third ventricle.
- *Cerebral Aqueduct*
  - Connects the third and fourth ventricles.
- *Central Canal*
  - Connects the fourth ventricle to the spinal cord.
  - For remembering purposes, the *cerebral* aqueduct is in the *brain* and the central canal is in the spinal cord.
- *Subarachnoid Space*
  - Foramen of Magendie (Medial) and Luschka (Lateral)
    - Two tiny little holes in the fourth ventricle.

3.3.2 Dumping of CSF

- Arachnoid Villi/Granulations
  - Absorbed into blood stream from the superior sagittal sinus.

3.3.3 Getting Some CSF Out -or- Putting Something Into It

- Where would you have them stick that needle?
  - *Dural Sac*
    - Enlarged space in the lumbar region.
    - Testing and introduction of anesthetic agents.
    - Epi = Something in
  - *Lumbar Puncture*
    - AKA: Spinal Tap.
    - Tap = Taking something out

3.4 Cranial Nerves

#	Name	Type	Information Carried
I	Olfactory	S	Smell
II	Optic	S	Vision
III	Oculomotor	M	Eye movement, pupil constriction
IV	Trochlear	M	Eye movement
V	Trigeminal	B	Touch to face, motor control of mandibles
VI	Abducens	M	Eye movement
VII	Facial	B	Taste and facial expression
VIII	(Vestibulocochlear)	S	Hearing
IX	Glossopharyngeal	B	Taste and swallowing
X	Vagus	B	Taste and sensation from neck, thorax, abdomen, swallowing, control of larynx, parasympathetic nerves to heart and viscera
XI	Spinal Accessory	M	Movement of shoulders
XII	Hypoglossal	M	Movement of tongue

3.4.1 Mnemonic for Cranial Nerves

Old **Op**ie **oc**casionally **t**ries **tri**gonometry **a**nd **f**eels **ve**ry **gloo**my, **vague**, **a**nd **hypo**active.

3.5 Terms

- Santiago Ramon y Cajal (1911)
  - Used the Golgi stain to show that neurons are separate cells.
- *Soma* – Cell Body
- *Dendrites* – "Branches"
  - Purpose is to increase the surface area of the neuron, so it can receive the most amount of information.
- *Axon terminal botton* – The ends of the neuron that send information.
- *Glial cells* – Support cells by insulating the axon for better communication.
- *Myelin sheath* – Insulates the axon.
- *Nodes of Ranvier* – Gaps in the myelin sheath.
- *Unmylinated axons* are called grey matter.
- *Ganglion* – A collection of cell bodies in the PNS.
- *Nerve* – A collection of axons in the PNS.
- *Nucleus* – A collection of cell bodies in the CNS.
- *Tract* – A collection of axons in the CNS.

Grey Matter	White Matter
Cell bodies Dendrites Unmyelinated axons	Myelinated axons

Table 3.1: Gray vs. White Matter

	Gray Matter	White Matter
Location	**Cell Bodies**	**Axons**
CNS	Nucleus	Tract
PNS	Ganglion	Nerve

Table 3.2: Differentiation of Gray and White Matter in the CNS and PNS

3.6 Brainstem

3.6.1 Hindbrain

- *Myenlencephalon*
  - *Medulla Oblongata*
    - Enlargement of the cord.
    - Lots of gray matter.
    - *Reticular Formation*
      - A network of nuclei.
      - Regulates sleep, wakefulness, and arousal.
      - Also regulates heart rate, blood pressure, respiration, and skeletal muscle tone.
    - *Pyramids*
      - Two ridges on the ventral surface.
        - Voluntary motor system.
    - *Olives*
      - Audition and motor learning.
      - Located on the lateral surface.
- *Metencephalon*
  - *Pons* – "Bridge"
    - White matter on the outside and gray on the inside.
    - *Locus Coeruleus*
      - Produces norepinephrine.
      - The norepinephrine is sent to the forebrain.
  - *Cerebellum*
    - Caudal portion of the brain.
    - Balance, hand/eye coordination, soothes movements.
    - Shifting attention between vision and hearing, sensory timing (judging rhythms), language, emotional control, and reward valuation.
    - Cerebellar agenesis – the cerebellum is not developed.

3.6.2 Midbrain

Mesencephalon

- *Techtum* = "Roof"
  - *Superior Colliculus* – Visual Reflexes

        - Pupils opening and closing in response to light.
    - *Inferior Colliculus* – Auditory Reflexes
    - Colliculus = "Little Hill"
    - *Pineal Gland* – Melatonin
- *Tegmentum* = "Floor"
    - *Substantia Nigra* = "Black substance."
        - Get its black coloring from the creation of dopamine.
        - Clearly, this brain structure makes a majority of dopamine (1 of 3).
    - *Red Nucleus* – Motor coordination.
        - Get its red color from iron oxidation.
        - Connects to the cerebellum for that motor coordination.
    - *Periaqueductal Gray Area* – Opioids.
        - Peri = around, so peri-aqueductual = around-the cerebral aqueduct.
        - Handles endogenous pain relief.

3.6.3 Forebrain

Diencephalon

- *Thalamus*
    - Massa Intermedia = intermediate mass. This connects the two halves together.
    - Made up of many specific relay nuclei.
        - *Lateral Geniculate Nucleus* – Vision
        - *Dorsal Medial Nucleus* – Pain
            - Routes the pain from the thalamus to the prefrontal cortex.
    - . . . and of non-specific relay nuclei.
        - *Nucleus Reticularis* – Promotes wakefulness.
            - Goes to different parts of the brain, not just one specific part like the specific relay nuclei.
- *Hypothalamus*
    - Irregular shape, size of a thumbnail.
    - Encases the ventral part of the third ventricle.
    - **Survival of the individual**
        - Eating
        - Drinking (water)
            - Salt regulation

- *Suprachiasmatic Nucleus*
  - Circadian rhythms
  - Daily fluctuations of temperature
- **Survival of the species**
  - Territoriality
  - Sexual activity
  - Reproduction
- **Integration of information**
  - Endocrine system
  - Autonomic nervous system

Telencephalon

- *Corpus callosum*
  - Connects the two hemispheres.
  - Remember that the neurons in this structure go from lateral to lateral, and not from dorsal to ventral.
  - Creates the roof of the lateral ventricles.
  - Agenesis of the cc
    - AKA: Callosal Agenesis
    - Vision impairments,
    - hypotonia,
    - poor motor coordination,
    - delays in motor milestones,
      - (Such as sitting and walking.)
    - cognitive disability,
      - (Disability in complex problem solving.)
    - and social difficulties.
      - (Missing subtle social cues maybe cause of impaired fair processing.)
  - *Corpus Callosotomy* – Split brain surgeries.
    - Used to treat epilepsy.
    - Gives information about lateralization of hemispheres.
    - **Left Hemisphere**
      - language
      - serial events
    - **Right Hemisphere**
      - creativity

- synthesis

- *Basal Ganglia*
  - **Function:**
    - Initiation of Voluntary Movements.
    - Click here for Parkinson's continuation.
  - Curls laterally around the thalamus.
  - *Striatum*
    - *Caudate Nucleus* = "Nucleus with a Tail"
      - Obsessive Compulsive Disorder (OCD)
        - MIXED RESULTS
          - Too much activity, too large.
      - Romantic Love
        - Fisher, Aron, and Brown
          - Anthropologist used fMRI with a picture of neutral and romantic partners.
          - The CN activity was increased for loved one.
      - Larger in folks with incredible episodic memories (superior autobiographical memory).
        - How large? 7-8 SDs larger.
    - *Putamen* = "Shell"
    - *Nucleus Accumbens*
      - Nucleus Accumbens Septi = "Nucleus leaning against the septum."
        - Where the head of the caudate and the most anterior portion of the putamen come together.
        - Plays an important role in reinforcement, pleasure, and addiction.
  - *Globus Pallidus* = "Pale Globe"
  - *Note:* When people mention the putamen and the globus pallidus, they call it the lentiform nucleus.

- *Limbic System*
  - *Hippocampus*
    - In charge of moving memories from short-term to long-term.
    - Emotion, selective attention, learning, and memory.
  - *Amygdala*
    - In charge of emotions.
    - Fear and aggression, territoriality, odor processing, and sexual activity.
    - **Amygdala and Fear**

- 1930's.
- Lesions to amygdala in monkeys.
- Many things happened...
  - Exploratory behavior of objects (put in mouth–hyperorality).
  - Hypersexuality.
  - Loss of fear.
    - Freezing, increased heart rate, hair standing on end, etc.
    - Lost their fear of the human experimenters.
- *Kluver-Bucy Syndrome*
  - Damaging the anterior temporal lobes.
  - Herpes encephalitis and trauma.
  - Loss of normal fear and anger responses.
- Facial mimicry
  - Seeing fear in others lead to fear expression.
  - AND has amygdala activity.
- **Other things**
  - Social networks (Bickart et al., 2010)
    - Size and complexity of social network + correlated with amygdala size.
    - MAYBE: More effectively identify, learn about, and recognize socioemotional cues.
  - Political views (Rees et al., 2011)
    - Took extreme liberals and extreme conservatives and found that the more extreme conservatives had a larger amygdala than the extreme liberals.
- **How burnout is related to your brain...**
  - Worse at suppressing negative emotions.
  - Big amygdala & weak connection to frontal lobe.

- *Cingulate Gyrus*
  - Selective attention.
  - Love (like the cingulate gyrus)
    - Same studies show increased activity for loved ones.
  - Pain.
    - Serves as alarm for distress
    - Association of the emotional components and the sensory components of pain.
    - Sympathetic pain (empathy).
    - Social rejection.
      - Eisenberger (1990s)

- Cyberball
  - A computer game where you play catch.
  - The other players stop throwing the ball to you.
  - The cingulate gyrus lights up.
- *Fornix*
- *Mammillary Bodies*
- *Septal Nucleus*

Cerebral Cortex

- Cortex = "bark"
- Many convolutions
  - Sulci/fissures
  - Gyri
- Gray matter.
- 6 Layers
- Four lobes
  - *Frontal Lobe*
    - Executive functions, motor control, and language production (Broca's area).
  - *Parietal Lobe*
    - Lips, toes, and spacial awareness.
  - *Temporal Lobe*
    - Memory, hearing, and language comprehension (Wernicke's area).
  - *Occipital Lobe*
    - Vision
  - **How they are separated:**
    - Frontal ↔ Parietal: *Central Sulcus*
    - Parietal ↔ Occipital: *Parieto-Occipital Sulcus*
    - Temporal ↔ Frontal/Parietal: *Lateral Sulcus (Sylvian Fissure)*
- *Nucleus Accumbens*

3.7 Parkinson's Disease

- *Bradykinesia*
  - Slowness of movement.
- *Akinesia*
  - Difficulty initiating voluntary movements.
- *Rigidity*
  - Increased muscle tone.
- *Tremors*
  - Involuntary shaking of hands and jaw most prominent at rest.

3.8 Alzheimer's Disease

- Progressive memory loss.
- Affects the cortex and hippocampus.
- Suffers from both retrograde and anterograde amnesia.

CHAPTER 5

METHODS AND STRATEGIES OF RESEARCH

Behavioral neuroscience research involves the efforts of science in many disciples, including physiology, neuroanatomy, biochemistry, psychology, endocrinology, and histology. An enormous array of research methods is available to researchers in behavioral neuroscience. The goal of this chapter is to provide an overview of the most common methods used in the field.

This chapter will mainly focus on the following research methods:

- Experimental Ablation
- Recording and Stimulating Neural Activity
- Neurochemical Methods
- Genetic Methods

Each research method has a multitude of techniques that we will explore in detail for each section.

5.1 Experimental Ablation

5.1.1 Terms

EVALUATING THE BEHAVIORAL EFFECTS OF BRAIN DAMAGE

- *Experimental Ablation* – Destroying a part of the brain and evaluating an animal's subsequent behavior. (Synonymous with *lesion study*)
- *Lesion* – The damaged tissue.

PRODUCING BRAIN LESIONS

- *Kainic Acid* – An excitatory amino acid that kills neurons by stimulating them to death.
- *Cannula* – A small metal tube.
- *Excitotoxic Lesions* (*ek sigh tow tok sik*) – A brain lesion produced by intracerbral injection of an excitatory amino acid, such as kainic acid.
- *Sham Lesions* – A placebo procedure that duplicates all the steps of producing a brain lesion except the one that actually causes the brain damage.

STEREOTAXIC SURGERY

- *Sterotaxic Surgery* (*stair ee oh tak sik*) – Brain surgery using a stereotaxic apparatus to position an electrode or cannula in a specified position of the brain.
- *Steotaxic Atlas* – A collection of drawings of sections of the brain of a particular animal with measurements that provide coordinates for stereotaxic surgery.
- *Bregma* – The junction of the sagittal and coronal structures of the skull; often used as a reference point for stereotaxic brain surgery.
- *Stereotaxic Apparatus* – A device that permits a surgeon to position an electrode or cannula into a specific part of the brain.
- *Deep Brain Stimulation* – A technique using sterotaxic surgery to implant a permanent electrode in the brain; used to treat chronic pain, movement disorders, epilepsy, depression, and OCD.

HISTOLOGICAL METHODS

- *Histological Methods* – Methods of preparing and examining brain tissue to determine the effects of behavior, injury, or disease.
- *Formalin* (*for mal lin*) – The aqueous solution of formaldehyde gas; the most commonly used tissue fixative.
- *Fixative* – A chemical such as formalin; used to prepare and preserve body tissue.
- *Microtome* – An instrument that produces very thin slices of body tissue.
- *Cryostat* – An instrument used to prepare very thin slices of body tissue inside a freezer chamber.
- *Immunocytochemical Method* – A histological method that uses radioactive antibodies or antibodies bound with a dye molecule to indicate the presence of particular proteins of peptides.
- *Transmission Electron Microscope* – A microscope that passes a focused beam of electrons through thin slices of tissue to reveal minuscule details.
- *Scanning Electron Microscope* – A microscope that provides three-dimensional information about the shape of the surface of a small object by scanning the object with a thin beam of electrons.
- *Confocal Laser Scanning Microscope* – A microscope that provides high-resolution images of various depths of thick tissue that contains fluorescent molecules by scanning the tissue with light from a laser beam.

TRACING NEURAL CONNECTIONS

- *Anterograde Labeling Method* – A histological method that labels the axons and terminal buttons of neurons whose cell bodies are located in a particular region.

- *Retrograde Labeling Method* – A histological method that labels cell bodies that give rise to the terminal buttons that form synapses with cells in a particular region.

STUDYING THE STRUCTURE OF THE LIVING HUMAN BRAIN

- *Computerized Tomography (CT)* – The use of a device that employs a computer to analyze data obtained by a scanning beam of X-rays to produce a two-dimensional picture of a "slice" through the body.
- *Magnetic Resonance Imaging (MRI)* – A technique whereby the interior of the body can be accurately imaged; involves the interaction between radio waves and a strong magnetic field.
- *Diffusion Tensor Imaging (DTI)* – An imaging method that uses a modified MRI scanner to reveal bundles of myelinated axons in the living human brain.

5.1.2 Evaluating the Behavioral Effects of Brain Damage

An example of experimental ablation (or lesion study) would be if, after part of the brain is destroyed, an animal can no longer perform tasks that require vision, we can conclude that the damaged area plays some role in vision. (See Johannes Müller and the doctrine of specific nerve energies for relevant information.)

What makes lesion studies so important, is that, we can distinguish between brain function and behavior. For example, reading involves functioned required for controlling eye movements, focusing the lens of the eye, perceiving and recognizing words and letters, comprehending the meaning of words, and so on. Some of these functions also participate in other behaviors; for example, controlling eye movement and focusing are required for any task that involves looking, and brain mechanisms used for comprehending the meanings of words also participate in comprehending speech.

CHAPTER 7

PSYCHOPHARMACOLOGY

7.1 Overview — Unit 3

- Neurotransmitters and Neuromodulators
  - Psychopharmacology
  - Disorders
  - Pain

7.1.1 Psychopharmacology in Detail

- The scientific study of the effects of drugs on the nervous system and behavior.
- Psychopharmacology is the study of how drugs affect the mind and behavior.
  - Psychotherapeutic drugs
  - Better understanding of how things normally work.

Principles of Drug Action

- *Selective Action* — Drugs are selective in their action on the nervous system.
  - *Sites of Action* — The location at which a drug interacts with the body to produce its effects.
  - Side effects are often due to the drug acting on sites other than the intended target.
    - Thus, side effects are relative to what our preferred site of action is.
  - *Example*: Opioids primarily affect the opioid receptor system.
- Drugs don't CREATE effects, they *modulate* ongoing cellular activity.
  - That is, they affect behavior by affecting neural transmission in some way.
  - *Agonist* — A drug that mimics or enhances the **effects of a neurotransmitter**.
    - Facilitates post synaptic effects.
    - *Example*: Morphine mimics endorphins, which are natural painkillers.
  - *Antagonist* — A drug that blocks or inhibits the effects of a neurotransmitter.
    - Inhibits post synaptic effects.
    - *Example*: Naloxone blocks the effects of opioids, reversing their effects.
  - Agonistic effects can become antagonistic if the drug is taken in excess.
    - *Example*: I make a neuron fire a neurotransmitter, but I also block the reuptake of that neurotransmitter.

Basic Process

- *Precursor* — A substance from which another substance is formed. AKA, the ingredients used to make a neurotransmitter.
- $$\text{Precursor} \xrightarrow{\text{Synthetic Enzyme}} \text{NT} \xrightarrow{\text{Metabolic Enzyme}} \text{Inactive Metabolite}$$
  - *Synthesis* — The process of creating a neurotransmitter from its precursors.
  - Sometimes, we break down the precursor to build the neurotransmitter.

7.1.2 Other Ways of Agonist and Antagonist

- Block Ca^{2+} channels from opening (antagonist)
- *Mimetic* — Mimics the action of a neurotransmitter.
  - *Direct Agonist* — Binds to the same receptor as the neurotransmitter and mimics its effects.
  - *Indirect Agonist* — Binds to a different site on the receptor and enhances the effects of the neurotransmitter.
- Blocking agent
  - Competitive
    - *Direct Antagonist* — Binds to the same receptor as the neurotransmitter and blocks its effects.
  - Non-competitive
    - *Indirect Antagonist* — Binds to a different site on the receptor and blocks the effects of the neurotransmitter.
  - *Inverse Agonist* — Binds to the same receptor as the neurotransmitter and produces the opposite effect.
- *Depolarizing* or *Desensitizing Agent* — A drug that causes the AP to stay in a depolarized state; refusing to let the neuron go through another AP, and it stays in the absolute refractory period. (Antagonist)
- Interfere with vesicles (leaky or transporter proteins). (Antagonist)
- Interfere with docking proteins. (Antagonist)
- Selectively deactivate autoreceptors. (Agonist)
- Selectively activate autoreceptors. (Antagonist)

7.2 What Do These Chemicals Between Neurons Do?

- Transmit information.
  - Glutamate
  - GABA
  - Glycine
- Modulate information.
  - Every other neurotransmitter.

7.3 Classes of Neurotransmitters (Revisited from Lab)

- Amino Acids
  - Glutamate, GABA, Glycine
    - *Glutamate* — Synthesized from precursor glutamine by an enzyme called *glutaminase*. It is the most common excitatory neurotransmitter in the brain.
      - Related closely with the *NMDA* receptor, which is a type of glutamate receptor that is important for synaptic plasticity and memory formation.
      - One drug that binds to this site, *Phencyclidine (PCP)* (direct antagonist), is a drug that blocks the NMDA receptor and causes hallucinations and dissociation. Another drug that is thought to bind here, *Ketamine* (direct antagonist), is a dissociative anesthetic that is used in surgery and is also being studied as a treatment for depression.
      - **Reuptake and Deactivation**
        - Reuptake is done by the *excitatory amino acid transporters (EAATs)*. These are important because it reduces the change of excitotoxicity, which is believed to be involved in damage to the brain in stroke and amyotrophic later sclerosis (ALS, Lou Gehrig's disease).
    - *GABA* — Synthesized from precursor glutamate by an enzyme called *glutamic acid decarboxylase (GAD)*. It is the most common inhibitory neurotransmitter in the brain.
- *Amines* (monoamines) — Derived from amino acids
  - Catecholamines
    - Contain catechol and derived from the amino acid tyrosine.
    - *Tyrosine* — Precursor for the catecholamines.
    - Dopamine (DA), Norepinephrine (NE), Epinephrine (Adrenaline)
    - Dopaminergic, Adrenergic, and Noradrenergic systems.
  - *Indolamines*

- *Serotonin* (5-HT)
- *Melatonin*

- Peptides (AKA: Neuropeptides)
  - Endogenous Opioids
- Acetylcholine (ACh)
- Lipids
  - *Anadamide* (Sanskrit for "bliss") — Endogenous cannabinoid.
  - These appear to be synthesized on demand; produced and released as needed and not stored in synaptic vesicles.
  - Anadamide is deactivated by the enzyme *fatty acid amide hydrolase (FAAH)*.
- **Two Other Classes**
  - Nucleosides
    - Adenosine
  - Soluble Gases
    - *Nitric Oxide (NO)* — Required for an erection.

7.4 Acetylcholine (ACh)

- First neurotransmitter discovered.
  - Otto von Loewy — Discovered ACh in 1921.
    - This guy took a frog heart and put it in saline. Then, he took simulated the parasympathetic part of the vagus nerve, and saw that the heart slowed down.
    - He then took the saline and put it in a different frog heart, and saw that the heart slowed down again.
    - "Vagusstoff" (ACh) — The chemical that was released from the vagus nerve that slowed the heart down.
    - Cholinergic — Referring to ACh.
- ***Some* Functions**
  - **Function in the ANS:**
    - Sympathetic
      - Spinal nerve leaves the cord and synapses in the paravertebral ganglion (ACh)
      - Then makes neuromuscular junction with smooth muscles and glands (NE)
        - *Neuromusclar Junction* — The synapse between a motor neuron and a muscle fiber.

        - *Paravertebral Ganglion* — A ganglion located next to the spinal cord.
        - Except sweat glands (ACh)
      - *Sympathetic Chain* — A chain of ganglia that runs parallel to the spinal cord. This is the reason for when you get anxious, ALL of your body gets anxious.
    - Parasympathetic
      - Spinal nerve leaves the cord and synapse in the parasympathetic ganglion (ACh)
      - Then makes neuromuscular junction with smooth muscles and glands (ACh)
    - The only NT in the parasympathetic branch.
    - NT of the preganglionic sympathetic branch.
  - **Function in the Somatic NS**
    - Excites the neuromusclar junction (ACh)
    - So, ACh is important for getting motor messages out to all kinds of muscles and glands.
  - **Function in the CNS**
    - ACh is important in:
      - Learning and alertness (*Basal Forebrain*)—-activates the cortex and facilitates learning.
        - *Nucleus Basalis* — Projects to the cortex
        - *Medial Septal Nucleus* and *Nucleus of Diagonal Band* — Projects to the hippocampus through the fornix.
      - Memory (*medial septal nucleus*)—-modulate the hippocampus
      - REM sleep generation (*Pedunculopontine nucleus (PPT)* and *Laterodorsal Tegmental Nucleus (LDT)*)—-projects to the pons and thalamus.
      - Reward system.
- **Synthesis and Metabolism**
- **Drugs and Disorders**

7.4.1 ACh Synthesis and Metabolism

- **Synthesis**
  - In a nutshell: A breakdown of lipids leads to Choline, which is the precursor for ACh. Acetate is the anion in vinegar (Acetic acid). Then, this is combined with Acetate to make ACh.
  - In more detail:
    - CoA attaches to an acetate ion (*Acetylcoenzyme A (acetyl-CoA)*).

- Then, *choline acetyltransferase (ChAT)* transfers the acetate from the acetyl-CoA to the choline molecule.
- Mnemonic: **ChAT**: From right to left: Transfers acetate to choline.

- **Metabolism**
  - ACh is broken down by the enzyme *acetylcholinesterase (AChE)* into acetate and choline. Nice and simple!
  - The choline is taken back up by active transport and reused, and the acetate is broken down and eliminated.

7.4.2 Two Types of Cholinergic Receptors

- Nicotinic Receptors
  - Agonist at low doses, but antagonist at high doses.
  - Iontropic.
  - Found at the Neuromusclar Function in the PNS.
  - *Curare* (direct antagonist) — A drug that blocks nicotinic receptors, causing paralysis.
    - Competitive blocking agent
    - Paralysis, surgery
- Muscarinic Receptors
  - Comes from a hallucinogenic mushroom (Amanita muscaria).
    - **Don't confuse with Serotonin's Mescaline: Cactus; nor Psilocybin: Mushroom.**
  - Vikings (probably took this drug before raiding) and Koryaks (Nordic people who used this mushroom in religious practices).
  - Metabotropic receptors.
  - Predominates in the CNS (although, both types are found in the CNS).
  - *Atropine* (direct antagonist) — A drug that blocks muscarinic receptors, causing pupil dilation and increased heart rate.
    - Competitive blocking agent
    - Belladonna alkaloids (deadly nightshade)

7.5 MORE Drugs and Toxins Affecting ACh

- *Botulinum Toxin* — A waste product of *Clostridium botulinum*, which are bacteria who grows without oxygen.

- Interferes with Ca^{2+} influx channels, preventing the release of ACh.
- Because Botox causes paralysis, it can interfere with emotional *expression* because it paralyzes muscles like the orbicularis oculi.
- Additionally, since we know that expression influences experience, when we paralyze these muscles, then the emotional *experience* is also negatively affected.
- **Does Botox Decrease Emotional Experiences?**
  - Population: Women who want wrinkles gone.
  - One IV: two levels: Botox or restylane (dermal filler).
  - Method: Everyone had wrinkle reduction. AND, Everyone watches some emotion evoking movies.
  - Results: Botox group had less emotional experience than the restylane group.
  - **Is this a good thing?**
    - Another study takes a sample of depressed people and gives them either Botox or a placebo.
    - Results: 15% of placebo had a decrease in depression, while 52% of the Botox group had a decrease in depression.
- Botox can also be used to treat migraines, cerebral palsy, and hyperhidrosis (excessive sweating).

- *Black Widow Spider Venom* — A neurotoxin that causes the release of ACh at the neuromuscular junction, causing continual release of ACh and paralysis.
- *Cobra and Krait Venom* — A neurotoxin that blocks the binding of ACh to nicotinic receptors, causing paralysis.
- *AchE Blockers* — Comes into contact with the enzyme that breaks down ACh, causing an increase in ACh in the synaptic cleft.
  - Irreversible
    - Insecticides (Parathion)
    - Nerve gas: DFP (Diisopropylfluorophosphate (don't need to know the whole name)) and Sarin.
      - Readily crosses the blood-brain barrier so PNS and CNS are affected.
      - Antidote?
        - *Atropine* — A drug that blocks muscarinic receptors, preventing the effects of excess ACh.
        - *Pralidoxime* — A drug that reactivates AChE, allowing it to break down ACh again.
  - Reversible
    - *Neostgmine* (**Prostigmin**) and *Physostigmine* (**Antilirum**) — Drugs that inhibit AChE, increasing the amount of ACh in the synaptic cleft.
      - Doesn't cross the blood-brain barrier, so it only affects the PNS.

- Used to treat *myasthenia gravis* (a disease that causes muscle weakness and fatigue).
  - Autoimmune disease that attacks nicotinic receptors at the neuromuscular junction.
- *Donepezil* (**Aricept**) and *rivastigmine* (**Exelon**) — These drugs do the same thing as the above drugs, but they cross the blood-brain barrier and are used to treat Alzheimer's disease and Parkinson's disease (only the cognitive part).

7.6 New Drug for Schizophrenia

- We'll talk about dopamine drugs later in this unit.
- This new drug now:
  - *Xanomelne and trospium chloride* (**Cobenfy**) — A drug that blocks the muscarinic receptors in the CNS, but not in the PNS.
  - Dopamine but also Ach!

7.7 Catecholamines

- Dopamine (DA)
- Norepinephrine (NE)
- Epinephrine (Adrenaline)

7.7.1 Dopamine (DA)

- Synthesis and Metabolism
- Function
- Drugs and Disorders

Dopamine Synthesis

- Tyrosine was first discovered from cheese (tyrosine = cheese).
  - Tyrosine is the precursor for DA, NE, and Epi.
  - *Tyrosine Hydroxylase* — The rate-limiting enzyme in the synthesis of catecholamines.
    - Converts tyrosine to L-DOPA.
    - L-DOPA is the precursor for DA, NE, and Epi.
  - L-DOPA is converted to DA by the enzyme *DOPA decarboxylase*.

Dopamine Metabolism

- DA is broken down by the enzyme *Monoamine Oxidase (MAO)* into *Dihydroxyphenylacetric acid (DOPAC)*.
- Then, *Catechol-O-methyltransferase (COMT)* converts DOPAC into *Homovanillic acid (HVA)*.
- Also, starting from DA, we can use COMT to convert it to 3-methoxytyramine (3-MT), then with MAO, we can convert it to HVA.

DA Function

- **Movement/Motor systems**
  - *Nigrostriatal System* — Starts in the substantia nigra and ends in the striatum (caudate nucleus and putamen).
  - Here's the route: We start at the striatum, which then sends an inhibitory GABA signal to the substantia nigra, who sends a reciprocal inhibitory DOPA signal back to the striatum nerve that sends an inhibitory GABA signal to the globus pallidus. Then, the globus pallidus excites the thalamus, who then excites the primary motor cortex, who then excites movement.
    - Note that if the inhibitory signal to the substantia nigra is limited, then the signal that the striatum sends to the globus pallidus is much stronger, which leads to a weaker signal to the thalamus, and thus to movements.
  - Parkinson's Disease symptoms:
    - Weakness,
    - Tremor at rest,
    - Muscle rigidity,
    - Problems with balance,
    - Abnormal gait,
    - Trouble learning
  - Treatment
    - *Reserpine* (**Raudixin**) for ↓ **BP** (Not in use anymore because it caused Parkinson's-like symptoms)
      - 1960's
        - Blocks monoamine transporters
          - Developed Parkinson's symptoms
          - Can't fill vesicles and DA is lowered
      - Then, discovered Substantia Nigra was pale.
    - L-DOPA can be a direct treatment for Parkinson's as well.
    - *MPTP* — Neurotoxin for DA cells in the Nigrostriatal System (which is not endogenous).

- **History of MPTP — or why you shouldn't use illicit drugs**
  - 1982 — young California heroin users
  - Had used what they THOUGHT was synthetic heroin
    - *MPPP* — Opioid analgesic drug
      - Not used clinically
      - Illegally manufactured for recreational drug use
    - INSTEAD it was MPTP (oh no!)
      - They instantly developed Parkinson's-like symptoms
      - Bad for them, but good for us because we can study it.
        - Led to animal model development and possible treatment ideas.
  - We don't know why Parkinson's patient's cells are dying, but maybe something similar.
  - MPTP is converted to the chemical *MPP+* by the enzyme MAO (which is what breaks down DA), which is what damaged the cells.
    - Question: Could MAO-I improve Parkinson's?
    - Yes!
    - *Deprenyl*, also called *selegiline* (**Eldepryl**, **Jumex**) — A drug that inhibits MAO, can slow down progression of the disease.
- New treatment
  - Molecule keeps proteins from misfolding
  - *Lewy Bodies* — Misfolded proteins that are found in the brains of people with Parkinson's.
    - These are toxic to DA cells
- *Huntington's Chorea* — A genetic disorder that leads to uncontrolled movements and cognitive decline.
  - Too little GABA from the Striatum to the Substantia Nigra causes an increase in dopamine back to the Striatum which, in turn, lessens the signal to the Globus Palidus, which increases overall movements.
  - *Tetrabenazine* (**Xenazine**) — Drug that inhibits the DA vesicle transporters.
  - *Pallidotomy* — A surgery that affects the Globus Pallidus to inhibit movement.
- *Choreoathetotic Movements* — too much movement
  - *Athetosis* — Slow continually writing movements
  - *Choreic* (to dance) — Rapid, purposeless, involvuntary movements

- **Behavioral Arousal and Attention**
  - Narcolepsy
    - *Methylphenidate* (**Ritalin**) — A drug that increases DA and NE in the brain, used to treat ADHD, but can also be used for narcolepsy.

- *Hypocretine* — A neuropeptide that is involved in the regulation of sleep and wakefulness.
  - Created by the lateral hypothalamus.
  - Hypocretine: *Hypo* for *hypo*thalamus, *cretine* for *secretin* (a hormone).
  - *Orexin* — Another name for hypocretine; makes you want to eat.
- From hypocretine, researchers developed an antagonist for the orexin receptor, which is used to treat insomnia. This drug is called *Suvorexant* (**Belsomra**).
- **Treatment**
  - *TAK-994* — OX2R (Orexin-2 receptor) Agonist
  - *Hcrt-1* — Intranasal hypocretine-1 (orexin-1) agonist
  - Hypocretine Cell Transplant
  - Gene Therapy: *introduce* preprohypocretin gene into the brain to make more hypocretine.
  - Opiates (exogenous) can increase the number of hypocretin-producing cells in the brain.
  - Indirect role for opiate agonists in treating narcolepsy.

- ADHD
  - Uses Methylphenidate for selective attention.
- *Mesocortical System*
  - From ventral tegmental nucleus to prefrontal cortex, limbic CORTEX, hippocampus, all frontal lobes, and association areas of parietal and temporal lobes in primates.
  - Short-term memories, planning, and problem-solving are all associated with this system.

- **Reinforcement and Reward**
  - *Mesolimbic System (MLS)* — Responsible for reward and reinforcement.
    - From vental tegmental nucleus to limbic system
      - Amygdala, hippocampus, and nucleus accumbens.
      - Opioids cause the release of dopamine at the nucleus accumbens, which is the pleasure center of the brain.
  - James Olds & Peter Milner (1954)
    - They asked: "Does electrical stimulation of the reticular formation facilitate learning?"
    - James Olds visits a conference and listens to Neal Miller, who says electrical stimulation is aversive, so it should be avoided.
    - One lone rat was put in a box with a lever, and when the rat pressed the lever, it would get a shock to the reticular formation. He ended up pressing the level 700 times per hour.

- More studies of this
  - Skinner box
    - Rats press 2000 times per hour for a shock to the MLS.
    - Monkeys press 8000 times per hour for a shock to the MLS.
    - Starving animals will choose the MLS over food 80% of the time.
    - They also press the button for these conditions too:
      - Thirsty,
      - Getting shocked (at their feet),
      - Mother instincts.
- Delgado (1969) — For people who were getting their brain stimulated for seizures, this researcher also asked them about what they thought of the stimulation. They all thought that it was pleasurable.

NEW NOTES FOR 04/16/25

7.8 Schizophrenia in Focus

7.8.1 General Description

- *Dementia Praecox* — A term used to describe a group of disorders characterized by a decline in cognitive function and emotional regulation. Found by Emil Kraepelin, a German psychiatrist (1887).
  - Premature deterioration of the mind.
- Age of onset: Late teens to mid 30s.
- *Schizophrenia* — Same definition as before, duh. Found by Eugen Bleuler, a Swiss psychiatrist (1911).
  - Split of the mind from reality, not split personalities.

7.8.2 Theory behind Negative and Positive Symptoms**

**(and Cognitive Symptoms)

- "Positive" and "Negative" are not used in the traditional sense. Instead, they are used to describe the presence or absence of certain symptoms.
  - Positive symptoms are the presence of abnormal behaviors, while negative symptoms are the diminution or absence of normal behaviors.
  - Cognitive symptoms are the presence of cognitive deficits.

Positive Symptoms (Escalation over normal functioning)

- *Hallucinations* — Perception of something that does not have a basis in reality.
  - Auditory (most common), visual, tactile, olfactory, and gustatory.
- *Delusions* — A false belief that is resistant to reason or confrontation with actual fact. Actually built on reality, but misinterpreted.
  - Patently unrealistic.
  - For example:
    - *Referential* — Believing that something is meant for you (e.g., the TV is talking to you).
    - *Persecutory* — Believing that someone is out to get you (e.g., the government is watching you).
    - *Grandiose* — Believing that you are more important than you are (e.g., you are the king of the world).
    - *Control* — Believing that someone is controlling your thoughts or actions (e.g., the government is controlling your mind).
  - On the difference between an *illusion* and a *delusion* is that everyone can experience and illusion (not unique and based on manipulations of our nervous systems), whereas a delusion is unique to the person experiencing.
- *Disorganized Speech* — A pattern of incoherent or illogical speech that is difficult to follow.
  - *Derailment* — A pattern of speech in which the speaker jumps from one topic to another without any logical connection between them.
  - *Tangentiality* — A pattern of speech in which the speaker goes off on tangents and does not return to the main topic.
  - *Word Salad* — A pattern of speech in which the speaker uses words that are not related to each other in any meaningful way.
- *Grossly disorganized behavior* — A pattern of behavior that is inappropriate for the situation or that is not goal-directed. It is unpredictable and unprovoked.
- *Catatonic behavior* — A pattern of behavior in which the person is unresponsive to the environment and does not move or speak.
  - Maintaining a rigid or bizarre posture.
  - Purposeless excessive motor activity.
    - For example, continuously spinning your hair in circles or pacing back and forth.

Negative Symptoms

- *Affective Flattening* — Restricted range of emotional expression, including facial expressions, voice tone, and body language.
- *Alogia* — A lack of speech or a decrease in the amount of thought, which is reflected in a decrease in speech produced.
- *Avolition* — A lack of motivation or a decrease in the ability to initiate and persist in activities.
- *Anhedonia* — A lack of pleasure or a decrease in the ability to experience pleasure from activities that are normally pleasurable.
- Notice that these negative symptoms are shared with a lot of other disorders, including depression and anxiety, or even brain damage.

Positive versus Negative (Summary)

- Positive
  - Relatively unique and historically easier to treat.
- Negative
  - Common in a number of disorders.
  - Less responsible to treatment.
  - Usually emerge first.

NEW NOTES FOR 04/18/25

7.8.3 Negative Symptoms and Brain Damage

- *Discordant Twins* — Twins that are discordant for a disorder, meaning that one twin has the disorder and the other does not.
- Brain atrophy is larger than normal ventricles and cortical sulci.
- Abnormal neurological systems (physiological tests that are used to assess the function of the nervous system).
  - Jerky or non-existent visual pursuit, and cannot do it without moving their head.
  - Absence of a blink reflex.
  - Poor pupillary light reactions.
  - Unusual facial expressions.
  - Continuous elevation of the eyebrows.

- *Cytoarchitectual Abnormalities* — Abnormalities in the structure of the brain cells and their organization.
  - **Hippocampus** — Cell bodies are aligned with healthy people, but not aligned for people with schizophrenia. It indicates that this is a developmental disorder.
  - List of reasons for why these abnormalities **MIGHT** occur:
    - Exposure to a virus during pregnancy (e.g., influenza).
      - Either the literal virus or the immune response to the virus from your mom.
      - *Seasonality Effect* — The idea that people born in late winter/early spring months are more likely to develop schizophrenia than those born in the summer months.
        - 2nd trimester of pregnancy is important to brain development.
          - In Finland 1957, there was a flu epidemic in the winter months
          - *Note:* Flu is not the only virus that can cause this. Measles, polio, and chicken pox can also cause this.
        - The seasonality is more pronounced in cities.
        - Other disorders that are affected by this include autism, bipolar disorder, narcolepsy, and depression.
    - Vitamin D deficits
      - *Latitude effect* — The idea that people who live in higher latitudes (further from the equator) are more likely to develop schizophrenia than those who live closer to the equator.
    - Stress?
      - Huttunen and Niskanen (1978) — Studied people who were born in Finland during the war and found that they had a higher incidence of schizophrenia than those who were not born during the war.
        - When the mother's husbands were away, the mothers became much more stressed and their babies had a higher incidence of schizophrenia.
    - Babies who have pre or perinatal complications (e.g., low birth weight, hypoxia, and obstetric complications) are more likely to develop schizophrenia than those who do not have these complications.

7.8.4 Which Parts of the Brain are Affected?

- *Dorsolateral Prefrontal Cortex (DLPFC)* — The part of the brain that is responsible for organization, motor planning, regulation, self-reflection, directed thought, and attention.
  - Activity here
    - Low
      - Blood flow and cerebral metabolism

- Post mortem studies
  - Deterioration of DA neurons here
  - Lower D_1 receptors
    - Correlated with severe negative symptoms
    - *D1 Receptors* — A type of dopamine receptor that is involved in the regulation of movement and cognition.
- Destroy DA input for D_1 receptors
  - *Hypofrontality* — A decrease in metabolic activity in the prefrontal cortex, which is associated with negative symptoms of schizophrenia.
  - Amphetamine?
    - Increased blood blow and increased frontal lobe tasks.
- Why does it take so long to develop?
  - Don't notice until synaptic pruning occurs (around 18-25 years old).

NEW NOTES FOR 04/21/25

  - Something about hormone changes (estrogen and testosterone) that may be involved in the development of schizophrenia.
  - Maybe not so long to develop, but rather a long time to be diagnosed.
    - This could be due to the fact that parents do not think that their children have abnormal behavior until they reach teenage years. With the advent of cameras, we are able to video children when they are younger, and are able to see that people with schizophrenia have abnormal behavior when they are younger.
    - Such as: more negative affect, poorer social adjustment, abnormal movements

- Other places: Hippocampus (memory), amygdala (emotion), lateral temporal cortex (auditory processing), and thalamus (sensory processing).

7.9 Positive Symptoms and Dopamine

- 1950s neuroleptics (antipsychotic drugs) were used to treat schizophrenia. (Old name: major tranquilizers)
  - *Chlorpromazine* (**Thorazine**)
  - *Haloperidol* (**Haldol**)
  - Both of these drugs block post synatpic DA receptors and block the release of DA from presynaptic membrane.
  - *Dopamine Hypothesis* — The idea that schizophrenia is caused by an overactivity of dopamine in the brain.

- **Strengths of DA Hypothesis**
  - Better antagonists are more effective at treating symptoms.
  - *Amphetamine Psychosis* — DA Agonists (e.g., amphetamines) can cause positive symptoms in healthy people.
    - Agonists include:
      - Cocaine
      - Amphetamines
      - L-Dopa
  - Neurological symptoms in patients with Schizophrenia like excessive blinking led researchers to further believe that DA was involved in the disorder.
- **Post Mortem Studies in HVA**
  - Given the dopamine hypothesis, we would expect to see an increase in HVA in the brains of people with schizophrenia, but this is not the case.
    - *The Revised Dopamine Hypothesis* — Instead of an increase in dopamine, we see an increase in the number of dopamine receptors in the brains of people. However, this was also not true.
  - *Modified Dopamine Hypothesis* — The idea that schizophrenia is caused by an imbalance of dopamine in the brain, rather than an increase or decrease in dopamine levels.
    - What you need to know first:
      - Prefrontal neurons inhibit subcortial DA activity.
        - Lesion studies of the DLPFC result in an increase in HVA for mesolimbic areas.
    - The hypothesis:
      - Loss of neurons in the brain leads to a decrease of dopamine input in the DLPFC, which leads to hypofrontality.
        - This leads to negative symptoms.
        - And an increase in dopamine in the mesolimbic system, which leads to positive symptoms.
      - Overview: Too little dopamine in the mesocortial system leads to an increase in dopamine in the mesolimbic system, which leads to positive symptoms.

7.9.1 New Drug Treatment

- From the prior section, we know that Schizophrenia needs
  - An agonist in the mesocortical system (where there is too little dopamine)
  - An antagonist in the mesolimbic system (where there is too much dopamine)
  - **A partial agonist could do this.**

Atypical Antipsychotics

- *Clozapine* (**Clozaril**)
- *Olanzapine* (**Zyprexa**)
- *Cariprazine* (**Vraylar**)
- *Risperidone* (**Risperdal**)
- *Arirpiprazole* (**Abilify**)
- *Brexpiprazole* (**Rexulti**)

- These drugs are all used to treat schizophrenia and are partial agonists at the D2 receptor.
- An increase in treatment for positive and negative symptoms.
- Partial agonists are responsible for a decrease in dopamine in the mesolimbic system, and an increase in dopamine in the mesocortical system.
- A decrease in Tardive Dyskinesia
- *Tardive Dyskinesia* — Rapid involuntary movements of the tounge, jaw, trunk, or extremities developed in association with the use of neuroleptics (20% - 30% of long-term users).
- Drugs that impact serotonin receptors: Mescaline (from cactus) and Psilocybin (from mushrooms).
- Also impact serotonin receptors (increase in 1A, decrease in 2A).
  - *Dopamine-Serotonin Interaction Hypothesis* —

NEW NOTES FOR 04/23/25

7.9.2 Phencyclidine Theory of Schizophrenia

- Deficit of Glutamate?
  - People with Schizophrenia have 1/2 as much glutamate in their brains as healthy people.
  - Then how are DA antagonists helping?
    - Dopamine is a direct antagonistic to glutamate. That is, DA inhibits the release of Glutamate.
    - Think: Major tranquilizers (antipsychotics) are antagonists of DA, which leads to an increase in glutamate.
- Evidence?
  - *PCP (Phencyclidine)* — Glutmate antagonist that blocks NMDA receptors (a type of glutamate receptor).

- Hallucinations
- Depersonalization
- Cognitive disorganization
- Negative and hostility
- Frontal lobe impairments

- Chronic PCP use leads to a decrease in DA and metabolic activity in the DLPFC.
- *Ketamine (antagonist)* — Anesthetic for children and nonhuman animals NOT adults.
  - Causes psychotic reactions in adults (but not children).
- Treatment possibility?
  - Direct agonists cause seizures and brain damage, so we want to avoid those.
  - However, indirect agonists, such as gylcine leads to a decrease in symptomns.
  - *Lumateperone* (**Caplyta**) — Though this drug is used to treat schizophrenia, the mechanism of action is not well understood. However, we do know that this drug DOES work on Serotonin, dopamine, and glutamate receptors.

7.10 Norepinephrine

- Cell bodies in the pons, medulla, and some in the thalamus.
- *Locus Coeruleus (LC)* — The main source of norepinephrine in the brain. It is located in the pons and is involved in arousal, attention, and the sleep-wake cycle.
- The plan for this section is to go over:
  - Receptors
  - Functions
  - Synthesis and metabolism
  - Depression

7.10.1 Adrenergic Receptors

- *α Receptors* — Strong affinity for norepinephrine, but epinephrine can also bind to them (so far only found in the brain).
- *β Receptors* — Strong affinity for epinephrine, but norepinephrine can also bind to them.
- Agonists increase BP
  - α agonist = vasoconstriction
  - β agonist = force and rate of cardiac contractions
- Inversely, β-blockers and α-blockers decrease BP.

- *Doxazosin* (**Cardura**) — α-blocker that is used to treat high blood pressure and benign prostatic hyperplasia (BPH).
- *Metaprolol* (**Lopressor**) — β-blocker that is used to treat high blood pressure and heart failure.

NEW NOTES FOR 04/25/25

7.10.2 Function

- Increases vigilance, arousal, selective attention, and orienting.
  - With amphetamines, they increase levels of dopamine, but also norepinephrine, which leads to increased orientation.
    - Works by blocking reuptake and causes the transporters to work in reverse.
  - *Atomoxetine* (**Strattera**) — (ADHD tx) Reuptake inhibitor especially in the PFC.
  - *Guanfacine* (**Intuniv**) — (ADHD tx) α-2A-agonist reduces activity in the sympathetic nervous system.
    - Binds to autoreceptors and improves PTSD along with anxiety.
- Feeding
  - Antagonists and agonists can increase feeding.
- Stress response
  - Used in the neuromuscular junction of sympathetic nervous system.

Anxiety

- β-blockers used to be used to treat anxiety.
  - *Propranolol* (**Inderal**) — A non-selective β-blocker that is used to treat high blood pressure and anxiety.
- Now,
  - We use antidepressants and benzodiazepines to treat anxiety.

7.10.3 Synthesis and Metabolism

Synthesis

- Most NT synthesized in terminal button cytoplasm, then stored in synaptic vesicles.
- **NE is Different!**
- In a nutshell, it follows from the synthesis of dopamine. The rest of the process is on the handout.

Metabolism

- On the handout.

NEW NOTES FOR 04/28/25

7.10.4 Depression

- Some symptoms
  - Depressed or irritable mood
  - Slowed walking and talking
  - Disturbed sleep
  - Disturbed eating
  - Avolition, apathy, anhedonia
- Two types
  - Major depressive disorder
  - Bipolar (Manic-depressive disorder)

Major Depressive Disorder

- Low levels of NE (and serotonin... but wait)
  - Evidence?
    - Low levels of VMA and MHPG
    - Antagonist
      - Reserpine (Raudixin) (Remember from DA?)
      - Decreased blood pressure but produce depressive sxs in 15%
    - Agonists
      - Treatment
- Agonists as Treatments (about 30 years ago)
  - Trycyclic antidepressants
  - *Amitriptyline* (**Elavil**)
  - *Clomipramine* (**Anafranil**)
  - *Desipramine* (**Norpramin**)
  - *Imipramine* (**Tofranil**)
  - Block reuptake (5-HT too, didn't know about the 5-HT back then)
  - Lots of side effects

        - Dry mouth, blurred vision, constipation, difficulty with urination, hyperthermia, drowsiness, anxiety, restlessness, cognitive and memory difficulties, confusion, dizziness, hypersensitivity reactions, increased appetite with weight gain, sweating, decrease in sexual ability and muscle twitches, weakness, nausea and vomiting, hypotension, tachycardia, and rarely, irregular heart rhythms (she wants us to know four: sleep, sex, eating, easy to OD).
    - MAO inhibitor (MAO breaks down NE and 5-HT)
        - People took MAO inhibitor (isoniazid) for Tuberculosis and had improved mood
        - *Isocarboxazid* (**Marplan**)
    - NE, DA, and 5-HT
    - Cheese effect
        - Really: cheese, yogurt, wine, yeast breads, chocolate, some fruits and nuts
- Pressor amines
    - Sympathetic reaction
        - As bad as intracranial bleeding, cardiovascular collapse
    - Normally broken down by MAO

More Treatments

- COMT Inhibitor
- Sleep Deprivation
- ECT
    - 1930's Cerletti and Bini
        - Gave people seizures to treat depression.
    - NOW
        - Memory loss is very short
        - Tx effectiveness in 80-90% vs. 67% (works well in 80-90% of people who get it, but only treatment resistant people are really getting it) (67% effectiveness from drug treatment)
        - Seizures, Schizoaffective PD, Parkinson's, Bipolar
        - How does it work
            -
- Deep brain stimulation (one area ventral striatum)
- Vagus nerve stimulation
- Ketamine

- Bright light
- Transcranial magnetic stimulation

NEW NOTES FOR 04/30/25

7.11 Seratonin 5-HT

- Sero = blood; tonus = tension
  - Vasoconstriction
- Where it is
- Receptors
- Function
- Synthesis
- Metabolism

7.11.1 Where It Is

- Most of it is produced in the raphe nuclei of the midbrain, pons, and medulla.
  - "Raphe" = seam; the middle part of the reticular formation.

7.11.2 Receptors

- Metabotropic
- At least 12 different receptors.
  - They all follow the same pattern of 5-$\text{HT}_{\text{Number,Letter}}$.

7.11.3 Function

- Mood (emotionally stable, happy, calm).
- Sleep and dreams (increase before bed, decrease in the morning)
- Can cause hallucinations (mescaline, psilocybin).
  - Remember:
    - Mescaline — From cactus (Psychoactive)
    - Psilocybin — From mushrooms (Psychoactive)

7.11.4 Synthesis

- *Tryptophan* — An amino acid that is the precursor to serotonin (and melatonin).
  - *Tryptophan hydroxylase (TPH)* — The enzyme that converts tryptophan to 5-hydroxytryptophan (5-HTP).
  - *5-HTP decarboxylase* — The enzyme that converts 5-HTP to 5-HT (5-hydroxytryptamine, or serotonin).

7.11.5 Metabolism

- May be taken back into the cell with no metabolism
- Order of events:
  - 5-HT $\xrightarrow{\text{MAO}}$ 5-hydroxy-indolacet-aldehyde $\xrightarrow[\text{Dehydrogenase}]{\text{Aldehyde}}$ 5-hydroxy-indole-acetic acid (5-HIAA)

7.11.6 Function

- Mood (emotionally stable, happy, calm).
  - Emotional closeness, elevated mood, and empathy
  - Triggers hormones that affect sexual arousal and trust
- Sleep and Dreams (Increased before bed - decreased in the morning)
- Satiety
- Regulation of Pain
- Sensory Perception
  - Some indigenous Americans
    - *Peyote Cactus* – Mescaline
  - LSD and MDMA (ecstasy and molly)

7.12 Return to Major Depressive Disorder

- Monoamine Theory of Unipolar Depression
  - Low levels of NE and 5-HT
    - Used to say "Probably not DA"
      - Agonists elevate mood in folks without depressive symptoms
      - But not in folks who have symptoms of depression

- Now, maybe yes to DA
  - *Pramipexole* (**Mirapex**)
    - Relatively selective D3 receptor agonist
    - D3 Receptors implicated in the motoric and hedonic deficits of depression

7.12.1 Evidence for 5-HT

- 5-HIAA
  - Low in people with depression
- Antagonist
  - *Resperpine* (**Raudixin**)
  - Trptophan depletion procedures
  - Become more depressed
- Agonists
  - SSRIs
    - *Fluoxetine* (**Prozac**)
    - *Paroxetine* (**Paxil**)
    - *Sertraline* (**Zoloft**)
    - *Escitalopram* (**Lexapro, Cipralex**)
  - SNRIs
    - *Duloxetine* (**Cymbalta**)
    - *Desvenlafaxine* (**Pristiq**)
  - Triple uptake inhibitors (SNDRIs)
  - 5-HT, NE, and DA
    - *Venlafaxine* (**Effexor**) (originally thought to be SNRI)
  - Not new (1980's-1990's)
    - Looking for 5-HT drugs at the time
  - In development and clinical trials now (e.g. Ruoxinlin (Ansofaxine))
    - Some didn't make it
      - Not effective or too addictive
      - *Nefazodone* (**Serzone**) – Liver problems

Ketamine Helps with Depression

- Ketamine, Phencyclidine are what?
  - Glutamate antagonists
  - *Geniprone* (**Exxua**) – New glutamate antagonist that fine-tunes glutamate.
- BUT also
  - *SNDRAs* – Serotonin Norepinephrine Dopamine Releasing Agents

7.12.2 Wellbutrin

- *Buproprion* (**Wellbutrin**)
  - Weak NDRI
  - Increases release of both
  - Nicotinic antagonist (decreases smoking)
  - Very common alone and in combination with SSRI
  - Cool
    - Decreased weight gain, sleepiness, sexual dysfunction

CHAPTER 8

LAB 1: HISTORY OF NEUROSCIENCE

8.1 Prehistoric

- A million years or more, people have been interested in the brain. Archaeological evidence shows that skulls are bashed in (jagged, not precise). As a result, the person dies, and therefore the brain is vital to life.

8.2 7000 Years Ago

- New holes in the brain, but these holes show signs of healing. Therefore, these new holes are intended to help the person who is suffering. The fancy name is trephination.
- The theory for these holes is that they were drilled to cure the person. In other words, to relieve a person of a wicked spirit.

8.3 5000 Years Ago

- *Egyptian* physicians show that they were aware of brain damage through their writings.
- Complications arise because they thought the heart contained the soul–you need it to live and emotions effect it.

8.4 Ancient Greece–4th Century, BC

8.4.1 *Hippocrates*

- Ponder the correlation between structure and function. Now, extend this thought to the brain/head.
- The brain is the place where sensation and intelligence reside. Not the heart.

8.4.2 *Aristotle*

- Clung to the idea of the heart being the one in charge.
- Figured the brain was a radiator. That is, we would send heated blood to the brain for it to be cooled off. This "heated blood" arose from our emotions. Thus, humans are more rational because we have a lot of cooling when compared to other animals.

8.5 Roman Empire–*Galen* 2nd Century, AD

- Galen is a physician to gladiators.
- Thought the cerebellum was for motor control (because the cerebellum is hard, like muscles) and the cerebrum is for memory because it is soft, and you can "write on it."
- Noticed there were large spaces (called "ventricles," or "spaces") that were filled with fluid.
- From here, we get the four humors (fluids).
- Galen thought that these fluids are what control the brain, NOT the brain structure itself. Think of the purpose of canned vegetables. The tin container does not actively contribute to the liquid / vegetables; rather, it is disposable.
- These ideas were jumpstarted by the invention of aqueducts. The movement of water was so important from aqueducts, so the idea this idea was extended to the brain.

8.6 Analysis by Analogy–17th Century

- *French* developed hydraulically controlled machines.
- Again, this is adding to the idea that liquids (which can flow through things and cause movements) are responsible for the brain's functionality.

8.7 *René Descartes*–1596-1650

- Believed that non-humans—what he called animals—are controlled by fluid.
- From this, he posited that the human body is a material entity functioning as a machine (like animals)–these are known as reflexes.
- But, the mind is nonmaterial and free from the laws of the universe and was uniquely human.
- Question: How does the nonmaterial part of the body (the mind) communicate with the material part of the body? Through the pineal gland! This gland would move around like a joystick and would manipulate the fluid that came from the third ventricle.

8.8 The Mind/Body Problem

- What is the basic relationship between mental events and physical events?
- *Dualism*–The mind exists independently of the brain and exerts some control over it.
- Strengths: Commonsense view.
- Weaknesses: The universe is composed of matter or energy.
- Modern neuroscientific explanation: Everything the body does rests on the events taking place in specific, definable parts of the nervous system–the "mind" is the product of the nervous system activity.

8.9 The Scientific Method–17th and 18th Century

- A new world view at the end of the Renaissance.
  - Replace *Rationalism* with *Scientific Method*.
- Closer look at the substance of the brain:
  - Gray and white matter change the way we look at the brain. That is, why would these parts of the brain that are clearly different, be different if the brain is used just to move fluids around.
  - Also, everyone has the same brain structure, so these bumps and groves must mean something.

8.10 Electricity

- *Isaac Newton* showed it is possible to electrically stimulate nerves.
- Then, *Luigi Galvani* and *Emil du Bois-Reymond* showed that electricity can make muscles contract.
- Later on, *Hermann von Helmholtz* showed that the speed of nerve conduction is not instantaneous.
- This important distinction shows that these nerves are not like wires–such as *Luigi Galvani* and *Emil du Bois-Reymond* thought.
- *Bell* and *Magendie* showed that the dorsal nerve root and the ventral nerve root are different.
  - Specifically, Bell showed that the ventral nerve root is for motor information, and Magendie showed that the dorsal nerve root is for sensory information.

- The dorsal nerve root is for sensory information, and the ventral nerve root is for motor information.
- *Dorsal* = *Sensory*: Think of the dorsal fin of a shark sensing vibrations in the water.
- *Ventral* = *Motor*: Think of a vent (like a car exhaust) pushing out movement.
- *Johannes Müller* came up with the doctrine of *Specific Nerve Energies*.
  - This doctrine states that the nature of a sensation depends on which nerve is stimulated, not on how the nerve is stimulated.
  - For example, if you stimulate the optic nerve, you will see something. If you stimulate the auditory nerve, you will hear something.
- Spawned the *Great Debate*: Is the brain a homogenous mass or is it made up of different parts?

8.11 The Great Debate

- *Franz Joseph Gall* and *Johann Spurzheim* thought the bumps and groves on the head were due to the size of the brain parts.
- They concluded that the size of the brain parts was correlated to the use of that part.
- This is known as *phrenology*.
- *Localization of Functions*–brain function can be localized to regions, pathways, or neurons.
  - Basically, if you cut out a piece of brain, and the animal (a pigeon) is no longer able to do a specific task, then that part of the brain is responsible for that task.
  - However, it turns out that these pigeons were able to relearn the task, so the brain is not as localized as we thought (this research is from Flourens).
- *Aggregate Field Theory*–the brain is a homogenous mass.
  - Complex brain functions emerge from the collective interactions of numerous simple neuronal activities.
  - Unlike localizationist models, this theory emphasizes the distributed nature of cognitive processes across neural networks.
- *Pierre Flourens* (1794–1867)
  - Studied the effect of brain damage with pigeons and supported the Aggregate Field Theory.
- *Paul Broca* (1824–1880)

- Found a patient who *could speak* but could *not understand language*.
- After the patient died, Broca found a lesion in the *left frontal lobe*.
- This area is now known as *Broca's area*.
- This area is responsible for *speech production*.
- These results put us back into the realm of Localization of Function.

- In comes *Carl Wernicke* (1874)
  - Found a patient who *could understand language* but could *not produce language*.
  - After the patient died, Wernicke found a lesion in the *left temporal lobe*.
  - This area is now known as *Wernicke's area*.
  - This area is responsible for *language comprehension*.
- Then, we have *Gustav Fritsch* and *Eduard Hitzig* (1870)
  - Similarly to *Luigi Galvani* and *Emil du Bois-Reymond*, they electrically stimulated the brain.
  - They found that the *motor cortex* is responsible for *movement*.
- *Shepherd Ivory Franz* (in D.C. from 1907–1924)
  - Found that people are able to relearn tasks after brain damage.

8.12 Same Resolution?

- *Modified Aggregate Field Theory*
  - *Karl S. Lashley* (1890-1958)
    - *The Principles of Mass Action*
      - Complex behavior–such as learning–is dependent on the total mass of the brain.
    - *Equipotentiality*
      - Specialization of function is not tied to specific brain regions.
      - All parts of the cortex contribute equally to complex behavior.
    - *Vicarious functioning*
      - If one part of the brain is damaged, another part can take over.

8.13 Analysis

1. **Prehistoric**: Recognition of the brain's vital role in life through skull injuries. No scientific theories yet.

2. **7000 Years Ago**: Trephination (skull drilling) practiced to release "evil spirits," indicating early medical intervention.

3. **5000 Years Ago**: Egyptians documented brain damage but prioritized the heart as the seat of the soul.

4. **Ancient Greece—Hippocrates (4th Century BCE)**: Proposed the brain as the center of sensation/intelligence, countering heart-centric views.

5. **Ancient Greece—Aristotle**: Defended the heart as the command center, viewing the brain as a blood-cooling "radiator."

6. **Roman Empire—Galen (2nd Century CE)**: Linked cerebellum to motor control and cerebrum to memory; emphasized ventricular fluids (humors) over brain structure.

7. **17th Century (Analysis by Analogy)**: Hydraulic systems inspired fluid-based brain theories.

8. **René Descartes (1596–1650)**: Dualism (mind vs. body); proposed pineal gland as the mind-body interface.

9. **17th–18th Century (Scientific Method)**: Shift to empirical study; recognition of gray/white matter differences.

10. **Electricity Discoveries**: Newton (nerve stimulation), Galvani/du Bois-Reymond (muscle contraction via electricity), Helmholtz (nerve conduction speed), Bell/Magendie (sensory/motor nerve roots), Müller (specific nerve energies).

11. **The Great Debate**:

    Table 8.1: Key Figures in the Great Debate: Localization vs. Aggregate Theory

Localization	Aggregate Theory
Johannes Müller	Pierre Flourens
Franz Joseph Gall	Shepherd Ivory Franz
Paul Broca	
Carl Wernicke	
Gustav Fritsch	
Eduard Hitzig	

12. **Modified Aggregate Theory**: Karl Lashley emphasized mass action and equipotentiality.

Table 8.2: Key Scientists and Contributions

Scientist	**Contributions**
Hippocrates	Brains as seat of sensation/intelligence
Aristotle	Heart as command center; brain as radiator
Galen	Cerebellum (motor), cerebrum (memory); humors
René Descartes	Mind-body dualism; pineal gland
Isaac Newton	Early nerve stimulation via electricity
Luigi Galvani	Electricity-induced muscle contraction
Emil du Bois-Reymond	Same as Galvani
Hermann von Helmholtz	Measured nerve conduction speed
Charles Bell	Ventral nerve = motor
François Magendie	Dorsal nerve = sensory
Johannes Müller	Doctrine of specific nerve energies
Franz Joseph Gall	Phrenology (brain localization)
Johann Spurzheim	Promoted phrenology
Pierre Flourens	Aggregate theory
Paul Broca	Localized speech production (Broca's area)
Carl Wernicke	Localized language comprehension (Wernicke's area)
Gustav Fritsch	Mapped motor cortex
Eduard Hitzig	Same as Fritsch
Shepherd Ivory Franz	Relearning post-brain damage
Karl S. Lashley	Mass action, equipotentiality

CHAPTER 9

LAB 3: SLEEP LAB

NEW NOTES FOR 04/10/25

9.1 What Do We Know About Sleep?

- Sleep is an active process.
- Sleepiness and alertness are controlled in part by a biological clock.
- Things can go wrong
  - There are whole books that discuss sleep disorders.
- *Suprachiasmatic nucleus (SCN)* is the master clock of the body.
  - The SCN is located in the hypothalamus and is responsible for regulating circadian rhythms.
  - Note the name of the SCN, it is *above* the *chiasm* of the optic nerve.
- *International Classification of Sleep Disorders (ICSD)* – A system for classifying sleep disorders.
- Three kinds of rhythms:
  - *Ultradian* rhythms: cycles shorter than 24 hours (e.g., heart rate, respiration).
  - *Circadian* rhythms: cycles of about 24 hours (e.g., sleep-wake cycle, body temperature).
    - Our circadian rhythm is an endogenous clock that is influenced by exogenous factors.
    - *Free-running* is when the circadian rhythm is not influenced by external cues (e.g., light, temperature).
    - It is about 24.2 hours in humans.
  - *Infradian* rhythms: cycles longer than 24 hours (e.g., menstrual cycle, seasonal changes).
- *Zeitgeber* is a stimulus that helps to regulate the biological clock (e.g., light, temperature).
- Human clocks run long when left free running. Rats are short.

9.2 What is Sleep?

- For regular people, sleep is behaviorally defined as a state of reduced movement, species specific posture, reduced response to stimuli, and reversibility.
- For sleep researchers, they take a more physiological definition of sleep.
  - *Polysomnography (PSG)* is a method of recording various physiological signals during sleep, including:
    - **Electroencephalography (EEG):** measures electrical activity in the brain.
    - **Electromyogram (EMG):** measures muscle activity.
    - **Electrooculogram (EOG):** measures eye movements.
    - Rechtschaffen and Kales (1968) defined sleep stages based on EEG patterns.
    - In 2007, the American Academy of Sleep Medicine (AASM) updated the sleep stage criteria.

Name	Frequency	Amplitude	Description	State
Beta β	12 – 50 Hz (variable)	Lower and Variable	Desynchronous	Awake and Paying Attention
Alpha α	8 – 12 Hz	50 Microvolts	Synchronous	Relaxed Wakefulness (eye closed, not fully attending, and usually largest occipitally)
Theta θ	3.5 – 7.5 Hz	Low in voltage Microvolts	Synchronous	Drowsy, Light Sleep (Stage 1)
Delta δ	1 – 3.5 Hz	20 – 200 Microvolts	Synchronous	Deep Sleep (Stages 3 and 4)

Table 9.1: Summary of EEG Wave Characteristics

9.3 Two States of Consciousness

9.3.1 Being Awake

- Physiological definition of wakefulness:
  - Supposed to be awake for $\frac{2}{3}^{\text{rd}}$ of the day.

- $< 5\%$ of the day is spent in REM sleep.
- Predominantly alpha and beta waves in the brain when drowsy.
- Muscle activity – high muscle tone when awake.
  - Lose muscle tone when you are sleeping.
    - EMG is high when awake
- Variability in the eye movement

9.3.2 Being Asleep

- Delta waves and theta waves predominantly.
- EMG is low
- Slow rolling eye movements everytime you fall asleep.
- *Hypnic Jerk* – a sudden muscle contraction that occurs when falling asleep.
- *NREM Sleep* – non-rapid eye movement sleep, which is divided into three stages:
  - *N1* – light sleep, theta waves, low EMG, and slow rolling eye movements (5-10% of the night).
    - Transition between wakefulness and sleep.
    - Hypnic jerks can occur in this stage.
    - Muscle tone is reduced, but not completely lost.
  - *N2* – light sleep, theta waves, sleep spindles, K-complexes, low EMG, and slow rolling eye movements (45-55% of the night).
    - Sleep spindles and K-complexes are characteristic of this stage.
    - Muscle tone is further reduced compared to N1.
  - *N3* – deep sleep, delta waves (3-8%), low EMG, and slow rolling eye movements (10-15% of the night).
    - Characterized by high-amplitude delta waves.
    - Muscle tone is at its lowest in this stage.
- *REM Sleep* – rapid eye movement sleep.
  - Aserinsky (1952): Discovered 70% in infants, 20-25% for healthy adults
  - Characteristics:
    - EEG – Low voltage, random, fast with sawtooth waves.
    - Fast activity, low amplitude, and desynchronous.
    - EMG – atonia (loss of muscle tone).
    - Paradoxical sleep: brain is active, but body is paralyzed.
    - Intercostal muscles are paralyzed, but not the diaphragm (obviously).

- EOG – Bursts of rapid eye movements

NEW NOTES FOR 04/17/25

9.4 Sleep Architecture: The Hypnogram

- *Hypnogram* – a graphical representation of the stages of sleep over time. (Basically a histogram of sleep stages.)
- Enter sleep through NREM sleep.
- Healthy adults trend gradually from N1 to N3, then back to N2, and then REM sleep. After $\approx$ 90 minutes of sleep, you hit REM, and then the cycle repeats.
- 4-6 cycles per night.
- As then night progresses, the amount of time spent in N3 decreases, while the amount of time spent in REM sleep increases.
- The first half of the night is dominated by NREM sleep, while the second half is dominated by REM sleep.
- *Voluntary Sleep Curtailment* – when you sleep less than your body needs, you will spend more time in N3 and REM sleep to make up for the lost sleep.
  - *REM Debt* – the amount of REM sleep that is lost due to sleep deprivation.
  - As a consequence of not getting enough REM, you are at risk of these conditions because REM **forces** you to get the pay your debt:
    - *Hypnagogic Hallucinations* – vivid, dream-like experiences that occur when falling asleep.
    - *Hypnopompic Hallucinations* – vivid, dream-like experiences that occur when waking up.
    - *Sleep paralysis* – a temporary inability to move or speak when waking up or falling asleep.
- Infants, people with sleeping disorders, and people with sleep deprivation all experience this sleep curtailment in one way or another.
- When healthy adults are sleep-deprived, their mood is worsened. However, for people with depression, their mood is improved when they are sleep-deprived.
  - In fact, REM disruption is actually a treatment for depression.
- *Sleep Efficiency* – the ratio of total sleep time to total time spent in bed.
  - Sleep researchers consider 85% or better for sleep efficiency to be good. Anything lower is considered poor.

- *Wake after sleep onset (WASO)* – This is the amount of time spent awake after initially falling asleep.
- *Sleep Latency (SL)* – This is the amount of time it takes to fall asleep after getting into bed.
- Time spent in deep sleep and time it takes to get to deep sleep are both important for sleep quality.
- Also, time spent in REM sleep.
- *Latency to Persistent Sleep (LPS)* – This is the amount of time it takes to fall asleep after getting into bed and staying asleep for a certain period of time (e.g., 20 minutes).
- *Time Spent out of Bed (TSOB)* – Self-explanatory.
- *Total Sleep Time (TST)* – Also self-explanatory.

- Assign the following to either owls, larks, or neither:
  - Better on IQ tests; more likely to procrastinate; less conscientious; more open; better at baseball; more sexual partners; more likely to be unfaithful; poorer diet; smoke and drink more; more positive affect.

Characteristics	Larks	Neither	Owls
Better on IQ Tests:			✓
More Likely to Procrastinate:			✓
Less Conscientious:			✓
More Open:			✓
Better at Baseball:	✓		
More Sexual Partners:			✓
More Likely to be Unfaithful:			✓
Poorer diets:			✓
Smoke and Drink More:			✓
More Positive Affect:	✓		
More Social Jet Lag:			✓

Table 9.2: Chronotypes

EXAM 1B

1.1

Directions: For short answer questions, write your response in the space provided. Most of the short answer questions should be only a sentence or two long. For multiple choice questions, circle the letter of the correct response. For fill-in-the-blank questions, write your response in the space provided. For matching questions, write the letter of the correct response in the space to the right. For true or false questions, write "True" if the statement is true, and if the statement is false, *explain why* the statement is false. Lastly, the sections (1.1, 1.2, etc.) are provided to break the exam into smaller parts. Good luck!

Q1.1.1 **Short Answer:** Define neuroscience.
Answer:

Q1.1.2 **True or False:** Behavioral neuroscience involves understanding the nervous system's underlying behavior.
Answer:

Q1.1.3 **Fill in the Blank:** The Central Nervous System (CNS) is composed of the _____ and the _____.

Q1.1.4 **Matching:** Match the following systems with their primary functions.

Choices

(i) Voluntary motor control and sensory input.

(ii) Involuntary control of the gastrointestinal system.

(iii) Involuntary control of smooth muscle and glands.

(a) Somatic Nervous System ..... _____

(b) Autonomic Nervous System ..... _____

(c) Enteric Nervous System ..... _____

Q1.1.5 **Fill in the Blank** The autonomic nervous system regulates the body's _____ AND _____ response.

Q1.1.6 Short Answer: How does the flight-or-flight response affect your body?
Answer:

Q1.1.7 Fill in the Blank: In the fecal microbiota transplant study, researchers found that the microbiota change the _____ of the mice.

Q1.1.8 Fill in the Blank: In the elevated plus maze study, researchers found that the anxious mice were more willing to _____ after the fecal microbiota transplant.

1.2

Q1.2.1 Short Answer: What is the primary function of the meninges?
Answer:

Q1.2.2 Multiple Choice: Which of the following is the middle meningeal layer?

(A) Arachnoid Membrane
(B) Dura Mater
(C) Pia Mater
(D) Subarachnoid Space

Q1.2.3 Short Answer: Why did early anatomists call the outermost meningeal layer "pachymenginges"?
Answer:

Q1.2.4 Fill in the Blank The Peripheral Nervous System uses _____ layer(s) of the meninges.

Q1.2.5 Fill in the Blank: Arachnoid _____ are web-like structures that connect the Arachnoid Membrane to the *pia mater*

Q1.2.6 Multiple Choice: Which combination of symptoms is LEAST consistent with a diagnosis of acute bacterial meningitis?

(A) Fever, headache, and nuchal rigidity.
(B) Photophobia, vomiting, and altered mental status.
(C) None of the above.

Q1.2.7 Fill in the Blank: The subarachnoid space is filled with _____.

Q1.2.8 **Short Answer:** What is meningitis?
Answer:

1.3

Q1.3.1 **Short Answer:** List two functions of CSF.
Answer:

Q1.3.2 **True or False:** CSF is similar in composition to blood plasma.
Answer:

Q1.3.3 **Fill in the Blank:** CSF is produced by the _____ cells lining the lateral ventricles.

Q1.3.4 **Fill in the Blank:** A contra-coup injury is an injury that occurs on the _____ side of the brain from the impact site.

1.4

Q1.4.1 **Matching:** Match the location with its description.

Choices

(i) Connected to the pituitary gland via the infundibulum.

(ii) Production of CSF and connection to the third ventricle via the interventricular foramen.

(iii) Connects the third and fourth ventricles.

(a) Lateral Ventricles ..... _____

(b) Third Ventricle ..... _____

(c) Cerebral Aqueduct ..... _____

Q1.4.2 **True or False:** The central canal connects the fourth ventricle to the spinal cord.
Answer:

1.5

Q1.5.1 Short Answer: Where is CSF absorbed into the bloodstream?
Answer:

Q1.5.2 Fill in the Blank: _____ is caused by swelling of the brain due to a blockage in the CSF flow.

Q1.5.3 True or False: The *Interventricular Foramen* connects the lateral ventricles to the third ventricle.
Answer:

1.6

Q1.6.1 Fill in the Blank: The term "*epi*" means _____ and the term "*tap*" means _____.

Q1.6.2 Multiple Choice: A lumbar puncture is sometimes called a:

(A) Brain Tap
(B) Spinal Tap
(C) CSF Drain
(D) Ventricular Tap

Q1.6.3 Fill in the Blank: The needle for a lumbar puncture is typically inserted into the _____ sac in the lumbar region.

1.7

Q1.7.1 True or False: Cranial nerve IV controls pupil constriction and eye movement.
Answer:

Q1.7.2 Short Answer: What is the function of cranial nerve X?
Answer:

Q1.7.3 Fill in the Blank: There are _____ cranial nerve(s) that modulate eye movements, and _____ cranial nerve(s) that control the sense of vision.

Q1.7.4 Matching: Match the cranial nerve number with its function.

Choices

(i) Facial sensation or motor control of the mandible

(ii) Vision

(iii) Smell

(a) I ..... _____

(b) II ..... _____

(c) V ..... _____

Q1.7.5 True or False: The term "*glossal*" means "taste".
Answer:

Q1.7.6 Fill in the Blank: For the following table, fill in the blanks with the correct name.

Cranial Nerve	Name	Cranial Nerve	Name
I	_____	VII	_____
II	_____	VIII	_____
III	_____	IX	_____
IV	_____	X	_____
V	_____	XI	_____
VI	_____	XII	_____

1.8

Q1.8.1 Short Answer: What does the term *Soma* refer to?
Answer:

Q1.8.2 True or False: The term "*nucleus*" refers to a collection of cell bodies in the PNS.
Answer:

Q1.8.3 Fill in the Blank: Fill in the following table for the terms that match its definition.

Term	Definition
Tract	_____
_____	The ends of the neuron that send information.
_____	Extends surface area of the neuron.
_____	A collection of axons in the PNS.

Q1.8.4 True or False: *Ganglion* are collections of axons.
Answer:

Q1.8.5 Short Answer: What is the function of the myelin sheath?
Answer:

1.9

Q1.9.1 Short Answer: Name two principal structures of the hindbrain.
Answer:

Q1.9.2 Short Answer: What vital functions are regulated by the Reticular Formation in the Medulla Oblongata?
Answer:

Q1.9.3 Short Answer: Describe the role of the Pons in the brainstem.
Answer:

Q1.9.4 Fill in the Blank: Pons directly translates to _____ in Latin.

Q1.9.5 Fill in the Blank: The _____ (specific) is a structure in the pons that produces norepinephrine.

Q1.9.6 True or False: The norepinephrine produced by the Locus Coeruleus is sent primarily to the hind brain.
Answer:

Q1.9.7 Short Answer: What is the primary function of the cerebellum?
Answer:

Q1.9.8 ***Bonus* Short Answer:** Can you name every function of the cerebellum? (There's 8!)
Answer:

Q1.9.9 **Fill in the Blank:** The rare malformation wherein the cerebellum is not developed is called _____.

Q1.9.10 **Multiple Choice:** Which of the following midbrain structures is primarily responsible for visual reflexes?
(A) Olives (B) Pyramids (C) Superior Colliculus (D) Substantia Nigra

Q1.9.11 **Fill in the Blank:** The _____ in the midbrain is critical for motor coordination.

Q1.9.12 **Short Answer:** What does the *periaqueductal gray area* produce?
Answer:

Q1.9.13 **True or False:** The medulla oblongata contains the reticular formation which regulates vital functions like heart rate and respiration.
Answer:

Q1.9.14 **Fill in the Blank:** The midbrain's _____ Colliculus is important for visual reflexes, while the _____ Colliculus is involved in auditory reflexes.

Q1.9.15 **Multiple Choice:** The *substantia nigra* is known for its role in:

(A) Serotonin production
(B) Dopamine production
(C) GABA production
(D) Acetylcholine production

1.10

Q1.10.1 **Short Answer:** What is the role of the thalamus in the brain?
Answer:

Q1.10.2 **Short Answer:** What does it mean to be a non-specific relay nuclei?
Answer:

Q1.10.3 Multiple Choice: The thalamic nucleus responsible for pain routing sends those signals to the:

(A) Prefrontal Cortex
(B) Primary Somatosensory Cortex
(C) Primary Motor Cortex
(D) Amygdala

Q1.10.4 Fill in the Blank: Fill in the following table with the correct terms.

Thalamic Relay Nuclei	Role
_____	Vision
_____	Pain
_____	Promotes wakefulness

Q1.10.5 Fill in the Blank: The *Massa Intermedia* connects the left _____ half with the right half.

Q1.10.6 Multiple Choice: Which of the following is NOT a function of the hypothalamus?

(A) Survival of the individual
(B) Survival of the species
(C) Regulation of endocrine system
(D) Integration of information

Q1.10.7 True or False: The hypothalamus is involved in both individual survival functions (like eating and drinking) and species survival functions (such as reproduction).
Answer:

Q1.10.8 True or False: The *Suprachiasmatic Nucleus* is responsible for circadian rhythms.
Answer:

Q1.10.9 Fill in the Blank: The *Corpus Callosum*'s neurons go from _____ to _____ and not from _____ to _____. (Your answers should directions.)

Q1.10.10 Multiple Choice: Which of the following is NOT a symptom of Callosal Agenesis?

(A) Impaired motor coordination
(B) Impaired language comprehension
(C) Impaired spatial awareness
(D) Impaired executive functions

Q1.10.11 Fill in the Blank: The _____ is involved in the regulation of voluntary motor control.

Q1.10.12 **Fill in the Blank:** The *Striatum* consists of the _____, _____, and the _____. (*Note:* The *Globus Pallidus* is not a viable answer here.)

Q1.10.13 **True or False:** When people mention the Nucleus Accumbens and the Globus Pallidus, they call it the lentiform nucleus.
Answer:

Q1.10.14 **Matching:** Match the following telencephalic structures with their functions.

Choices

(i) Sensory integration and spatial awareness.

(ii) Executive functions, motor control, language production.

(iii) Memory, hearing, language comprehension.

(iv) Vision

(a) Frontal Lobe ..... _____

(b) Temporal Lobe ..... _____

(c) Parietal Lobe ..... _____

(d) Occipital Lobe ..... _____

Q1.10.15 **Fill in the Blank:** Participants in Rees et al.'s (2011) study showed extreme conservatives had a larger _____

Q1.10.16 **Short Answer:** How does the hippocampus have an impact upon memory?
Answer:

Q1.10.17 **Short Answer:** What is the left hemisphere of the brain responsible for? And the right hemisphere? (2 each.)
Answer:

Q1.10.18 **Multiple Choice:** In a study by Eisenberger (1990) called the Cyberball study, participants who were excluded from the game showed increased activity in the:

(A) Amygdala
(B) Hippocampus
(C) Anterior Cingulate Cortex
(D) Septal Nucleus

Q1.10.19 **Matching:** Arrange the following structures in the brain in the right order.

Choices

(i) Tectum

(ii) Medulla Oblogata

(iii) Limbic System

(iv) Hypothalamus

(a) Myelencephalon ..... _____

(b) Diencephalon ..... _____

(c) Telencephalon ..... _____

(d) Mesencephalon ..... _____

Q1.10.20 **Short Answer:** What is *Kluver-Bucy Syndrome*?
Answer:

Q1.10.21 **Fill in the Blank:** The _____ is involved in the regulation of emotions, memory, and motivation.

Q1.10.22 **Fill in the Blank:** Selective attention, love, and pain are all functions of the _____.

Q1.10.23 **Short Answer:** What lobes make up the *Cerebral Cortex*?
Answer:

Q1.10.24 **Short Answer:** We learned that the *Temporal Lobe* is responsible for language comprehension. Who was the scientist that discovered this? Similarly, we learned that the *Frontal Lobe* is responsible for language production. Who was the scientist that discovered this?
Answer:

Q1.10.25 Fill in the Blank: Fill out the following table with the correct terms.

Major Divisions	Ventricle	Subdivision	Principal Structures
Forebrain	_____	_____	_____ _____ _____ _____
	_____	_____	_____ _____
Midbrain	_____	_____	_____ _____ _____ _____
Hindbrain	_____	_____	_____ _____
		_____	_____

1.11

Q1.11.1 Multiple Choice: Which of the following is NOT a typical symptom of Parkinson's Disease?

(A) Bradykinesia (B) Rigidity (C) Tremors (D) Hyperactivity

Q1.11.2 Short Answer: Name one symptom associated with Alzheimer's Disease.
Answer:

Q1.11.3 True or False: Only retrograde amnesia is observed in Alzheimer's Disease.
Answer:

4.1

Q4.1.1 Short Answer: Describe the main difference between positive and negative symptoms of Schizophrenia.
Answer:

Q4.1.2 Short Answer: What is the Dorsolateral Prefrontal Cortex (DLPFC) responsible for?
Answer:

Q4.1.3 Short Answer: Other than the DLPFC, what are four other parts of the brain that are affected in people with Schizophrenia? *Answer:*

Q4.1.4 Multiple Choice: Which of the following best describes Hypofrontality?

(A) An increase in metabolic activity in the prefrontal cortex.

(B) A decrease in metabolic activity in the prefrontal cortex, associated with negative symptoms of schizophrenia.

(C) An overactivity of dopamine receptors in the frontal lobe.

(D) A blockage of NMDA receptors in the prefrontal cortex.

Q4.1.5 Multiple Choice: Tardive Dyskinesia is a potential side effect associated with long-term use of which type of medication?

(A) β-blockers

(B) Glutamate antagonists

(C) Neuroleptics

(D) Reuptake inhibitors

Q4.1.6 Fill in the Blank: The _____ suggests an imbalance: _____ dopamine in the meso_____ system (leading to negative symptoms and _____) causes a(n) _____ in dopamine in the meso_____ system (leading to positive symptoms).

Q4.1.7 Multiple Choice: Which of the following best describes the Revised Dopamine Hypothesis?

(A) Instead of an increase in dopamine, there was an increase in dopaminergic receptors.

(B) Instead of an increase of dopamine, there was a decrease of dopaminergic receptors.

(C) There is an imbalance of dopamine in the brain, rather than an increase or decrease in dopamine levels.

(D) Loss of neurons in the brain leads to a decrease of dopamine input in the DLPFC, which leads to hypofrontality.

Q4.1.8 Short Answer: According to the Modified Dopamine Hypothesis, how does a decrease of dopamine input in the DLPFC contribute to both negative and positive symptoms of schizophrenia?
Answer:

4.2

Q4.2.1 Short Answer: What is some evidence that support this finding in the previous problem?
Answer:

Q4.2.2 Short Answer: As a direct result of the previous question, there are medications that block these receptors. What are they, and which receptor do they respectively target?
Answer:

Q4.2.3 Multiple Choice: Amphetamines can lead to increased orientation and vigilance primarily by:

(A) Selectively increasing dopamine reuptake.

(B) Blocking norepinephrine reuptake and causing its transporters to work in reverse.

(C) Acting as an α-2A-agonist in the PFC.

(D) Potentiating the effects of glutamate.

Q4.2.4 Matching: Match the older antidepressant class with its characteristic or primary drug example.

Choices

(A) Associated with the "cheese effect" due to interaction with pressor amines.

(B) Blocks reuptake of NE and 5-HT, with side effects like dry mouth and drowsiness.

(C) Example: Isocarboxazid (Marplan).

(D) Example: Amitriptyline (Elavil).

(a) Tricyclic Antidepressants ..... _____

(b) MAO Inhibitors ..... _____

Q4.2.5 Short Answer: What are four common side effects associated with Tricyclic Antidepressants that patients should be aware of, particularly concerning overdose risk?
Answer:

Q4.2.6 Fill in the Diagram: Fill in each chemical for the synthesis of Norepinephrine:

Tyrosine $\xrightarrow[\text{Tyrosine-}]{\quad}$ _____ $\xrightarrow{\quad}$ _____ $\xrightarrow[\text{Dopamine-}]{\quad}$ Norepinephrine.

Q4.2.16 Fill in the Diagram: Fill in each chemical for the metabolism of Norepinephrine:

Norepinephrine $\xrightarrow{\quad}$ Normetanephrine $\xrightarrow{\quad}$

Normetanephrine aldehyde $\xrightarrow[\text{Aldehyde}]{\quad}$ _____

(OR $\xrightarrow[\text{Aldehyde}]{\quad}$ _____)

Q4.2.17 Multiple Choice: Which of the following symptoms is LEAST likely to be considered a primary symptom of Major Depressive Disorder?

(A) Avolition and apathy.

(B) Grandiose delusions.

(C) Disturbed sleep and eating patterns.

(D) Depressed or irritable mood.

Q4.2.18 Short Answer: How did the observation of patients taking isoniazid for tuberculosis contribute to the development of antidepressant medications? (Be sure to name the drug it helped make.)
Answer:

Q4.2.19 Fill in the Diagram: Fill in each chemical for the synthesis of 5-HT:

Trypotophan $\xrightarrow[\text{\_\_\_\_\_}]{\text{Tryptophan-}}$ _____ $\xrightarrow[\text{\_\_\_\_\_}]{\text{5-HTP}}$ 5-HT.

Q4.2.20 Fill in the Diagram: Fill in each chemical for the metabolism of 5-HT:

5-HT $\xrightarrow[\text{\_\_\_\_\_}]{\text{\_\_\_\_\_}}$ _____ $\xrightarrow[\text{\_\_\_\_\_}]{\text{Aldehyde}}$ _____ (5-HIAA)

Q4.2.21 Short Answer: What are the three functions of 5-HT?
Answer:

4.3

Q4.3.1 Short Answer: Why did researchers think that DA was not involved with depression?
Answer:

Q4.3.2 Multiple Choice: This drug is acts as a selective D3 recptor agonist.

(A) *Buproprion* (**Wellbutrin**)
(B) *Pramipexole* (**Mirapex**)
(C) *Geniprone* (**Exxua**)
(D) *Nefazodone* (**Serzone**)

Q4.3.3 Short Answer: List the functions of the other 3 drugs that were listed.
Answer:

Q4.3.4 Matching: Assign the correct drug with its corresponding drug class.

Choices

(a) *Paroxetine* (**Paxil**)
(b) *Duloxetine* (**Cymbalta**)
(c) *Sertraline* (**Zoloft**)
(d) *Venlafaxine* (**Effexor**)
(e) *Escitalopram* (**Lexapro, Cipralex**)
(f) *Ruoxinlin* (**Ansofaxine**)
(g) *Desvenlafaxine* (**Pristiq**)

(a) SSRIs ..... _____

(b) SNRIS ..... _____

(c) Triple uptake inhibitors (SNDRIs) ..... _____

4.4

Q4.4.1 Fill in the Blank: In the following table, put a checkmark next to the chronotype that fits the given characteristic.

Characteristics	Larks	Neither	Owls
Better on IQ Tests:			
More Likely to Procrastinate:			
Less Conscientious:			
More Open:			
Better at Baseball:			
More Sexual Partners:			
More Likely to be Unfaithful:			
Poorer diets:			
Smoke and Drink More:			
More Positive Affect:			
More Social Jet Lag:			

Q4.4.2 Multiple Choice: What is the suprachiasmatic nucleus (SCN) responsible for?

(A) Regulating the sleep-wake cycle.

(B) Producing melatonin.

(C) Controlling the release of norepinephrine.

(D) All of the above.

Q4.4.3 Fill in the Blank: A _____ is a stimulus that helps to regulate the circadian rhythm.

Q4.4.4 Short Answer: Where is the Suprachiasmatic Nucleus (SCN) located? (Hint: just read the name):
Answer:

Q4.4.5 Short Answer: What are the three kinds of rhythm cycles, and what are their respective time frames?
Answer:

Q4.4.6 **True or False:** Sleep is a state of unconsciousness.
Answer:

Q4.4.7 **Fill in the Blank:** A _____ is a method of recording various physiological measures during sleep. It consists of an _____, an _____, and an _____.

Q4.4.8 **Fill in the Blank:** For the following table, fill in each section that is left blank with the correct term. (The first one is filled out for you.)

Name	Frequency	Amplitude	Description	State
Beta β	12 – 50 Hz (variable)	Lower and Variable	Desynchronous	Awake and Paying Attention
_____	_____	50 Microvolts	_____	_____
_____	_____	_____	_____	_____
_____	_____	_____	_____	_____

Table 9.3: Summary of EEG Wave Characteristics

Q4.4.9 **Fill in the Blank:** What is the physiological definition of wakefulness? Predominantly _____ and _____ waves, _____ muscle tone, and _____ eye movements.

Q4.4.10 **Fill in the Blank:** What is the physiological definition of sleep? Predominantly _____ and _____ waves, _____ muscle tone, and _____ eye movements.

Q4.4.11 **Fill in the Blank:** What is the physiological definition of REM sleep? EEG: _____; EMG: _____; EOG: _____ and _____, which gets its name because brain activity is similar to that of being awake.

Q4.4.12 Matching: Match the following NREM stages with their characteristics (some answers may be used more than once).

Choices

(A) Light sleep
(B) Low EMG activity
(C) slow rolling eye movements
(D) Sleep spindles
(E) 10%-15% of sleep
(F) 45%-55% of sleep
(G) Delta waves
(H) 5%-10% of sleep
(I) K-complexes
(J) Medium muscle tone
(K) Lowest muscle tone
(L) Highest muscle tone

(a) N1 ..... _____

(b) N2 ..... _____

(c) N3 ..... _____