Behavioral Neuroscience Notes

PSYC 360

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TABLE OF CONTENTS

3 Structure of the Nervous System **5**
- 3.1 Neuroanatomy . . . 5
  - 3.1.1 Nervous System Structure . . . 5
- 3.2 Meninges . . . 6
- 3.3 Cerebrospinal Fluid (CSF) . . . 7
  - 3.3.1 Flow of CSF . . . 8
  - 3.3.2 Dumping of CSF . . . 9
  - 3.3.3 Getting Some CSF Out -or- Putting Something Into It . . . 9
- 3.4 Cranial Nerves . . . 9
  - 3.4.1 Mnemonic for Cranial Nerves . . . 9
- 3.5 Terms . . . 10
- 3.6 Brainstem . . . 11
  - 3.6.1 Hindbrain . . . 11
  - 3.6.2 Midbrain . . . 11
  - 3.6.3 Forebrain . . . 12
- 3.7 Parkinson's Disease . . . 17
- 3.8 Alzheimer's Disease . . . 17

5 Methods and Strategies of Research **18**
- 5.1 Experimental Ablation . . . 18
  - 5.1.1 Terms . . . 18
  - 5.1.2 Evaluating the Behavioral Effects of Brain Damage . . . 20

6 How Neurons Process Information **21**
- 6.1 The Neuron . . . 21
  - 6.1.1 Structure of the Neuron . . . 21
  - 6.1.2 Support cells in the Nervous System . . . 22
  - 6.1.3 Are Glial Cells Contributing to Alzheimer's Disease? . . . 23
- 6.2 Different Kinds of Neurons . . . 23
  - 6.2.1 Structural Classification of Neurons . . . 23
  - 6.2.2 Functional Classification of Neurons . . . 23
- 6.3 Neural Communication . . . 24
  - 6.3.1 Binary System ("Off" and "On") . . . 24
  - 6.3.2 Conduction of Action Potential in Unmyelinated Axons . . . 26
  - 6.3.3 Conduction of Action Potential in Myelinated Axons . . . 26
- 6.4 Conversion from Electrical to Chemical Signals . . . 27
- 6.5 Conversion from Chemical to Electrical Signal . . . 28
  - 6.5.1 Two Kinds of Post Synaptic Potentials . . . 28
  - 6.5.2 What Happens to Excess or Used Neurotransmitters? . . . 28

6.5.3 Two Types of Chemically Gated Channels . . . 28
6.5.4 *Ionotropic Synapse* . . . 28
6.5.5 *Metabotropic Synapse* . . . 29
6.5.6 Who Cares About Metabotropic Synapses? . . . 29
6.5.7 Eletrical Synapse (Gap Junctions) . . . 30
6.6 Somatic vs. Autonomic (Revisited) . . . 30
6.7 Sensory Systems . . . 31
6.7.1 Why Study Sensory Systems in Psychology? . . . 32
6.8 What is Color? . . . 32
6.8.1 Language and Color . . . 33
6.8.2 Motivation Influences Visual Perception . . . 33

7 Psychopharmacology 34
7.1 Overview — Unit 3 . . . 34
7.1.1 Psychopharmacology in Detail . . . 34
7.1.2 Other Ways of Agonist and Antagonist . . . 35
7.2 What Do These Chemicals Between Neurons Do? . . . 36
7.3 Classes of Neurotransmitters (Revisited from Lab) . . . 36
7.4 Acetylcholine (ACh) . . . 37
7.4.1 ACh Synthesis and Metabolism . . . 38
7.4.2 Two Types of Cholinergic Receptors . . . 39
7.5 MORE Drugs and Toxins Affecting ACh . . . 39
7.6 New Drug for Schizophrenia . . . 41
7.7 Catecholamines . . . 41
7.7.1 Dopamine (DA) . . . 41
7.8 Schizophrenia in Focus . . . 45
7.8.1 General Description . . . 45
7.8.2 Theory behind Negative and Positive Symptoms** . . . 45
7.8.3 Negative Symptoms and Brain Damage . . . 47
7.8.4 Which Parts of the Brain are Affected? . . . 48
7.9 Positive Symptoms and Dopamine . . . 49
7.9.1 New Drug Treatment . . . 50
7.9.2 Phencyclidine Theory of Schizophrenia . . . 51
7.10 Norepinephrine . . . 52
7.10.1 Adrenergic Receptors . . . 52
7.10.2 Function . . . 53
7.10.3 Synthesis and Metabolism . . . 53
7.10.4 Depression . . . 54
7.11 Seratonin 5-HT . . . 56
7.11.1 Where It Is . . . 56
7.11.2 Receptors . . . 56
7.11.3 Function . . . 56
7.11.4 Synthesis . . . 57
7.11.5 Metabolism . . . 57
7.11.6 Function . . . 57

7.12 Return to Major Depressive Disorder . . . 57
7.12.1 Evidence for 5-HT . . . 58
7.12.2 Wellbutrin . . . 59

I Behavioral Neuroscience Lab Notes 60

8 Lab 1: History of Neuroscience 61
8.1 Prehistoric . . . 61
8.2 7000 Years Ago . . . 61
8.3 5000 Years Ago . . . 61
8.4 Ancient Greece–4th Century, BC . . . 61
8.4.1 *Hippocrates* . . . 61
8.4.2 *Aristotle* . . . 61
8.5 Roman Empire–*Galen* 2nd Century, AD . . . 62
8.6 Analysis by Analogy–17th Century . . . 62
8.7 *René Descartes*–1596-1650 . . . 62
8.8 The Mind/Body Problem . . . 63
8.9 The Scientific Method–17th and 18th Century . . . 63
8.10 Electricity . . . 63
8.11 The Great Debate . . . 64
8.12 Same Resolution? . . . 65
8.13 Analysis . . . 65

9 Lab 2: Psychophysiology 68
9.1 Physiological Psychology (Video Lab) Experiment . . . 72
9.1.1 Good Introductions . . . 72
9.2 Classes of Neurotransmitters . . . 72
9.2.1 Peptides—Opioids . . . 73
9.2.2 Antagonists . . . 73
9.2.3 New NonOpioid Pain Relievers . . . 73
9.3 Opioid Receptors . . . 73
9.4 Functions of Opioids . . . 74
9.4.1 Pain is Good . . . 74
9.5 NSAIDs . . . 75
9.6 Opioid Systems at Work? . . . 75
9.7 Carefully Plan Some Hypotheses . . . 76
9.7.1 Nonspecific Effects . . . 76
9.7.2 Results . . . 77

10 Lab 3: Sleep Lab 78
10.1 What Do We Know About Sleep? . . . 78
10.2 What is Sleep? . . . 79
10.3 Two States of Consciousness . . . 79
10.3.1 Being Awake . . . 79

10.3.2 Being Asleep 80
10.4 Sleep Architecture: The Hypnogram 81

II Behavioral Neuroscience Practice Exams 83

SKIP CHAPTER 2
Most of the content from Chapter 2 has been blended with Chapter 3.

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 6

HOW NEURONS PROCESS INFORMATION

NEW NOTES FOR 02/26/25

6.1 The Neuron

- Definition: Basic information processing unit of the NS.
- Similarities to an animal cell:
  - *Cell membrane*: Separates the inside of the cell from the outside environment.
  - *Nucleus*: Contains the genetic material of the cell.
  - *Organelles*: Carry out the basic functions of the cell.
    - *Mitochondria*: Produce energy for the cell.
    - *Endoplasmic Reticulum*: Synthesizes proteins.
    - *Golgi Apparatus*: Packages proteins for transport.
    - *Lysosomes*: Break down waste products.
  - Basic cellular processes.
- Differences:
  - Special "morphology" (shape).
  - Communicate through an electrochemical process.

6.1.1 Structure of the Neuron

(Mostly a recap of Terms)

- *Soma*
- *Dendrite*
- *Axon*
- *Terminal Arboriza* – Branches at the end of the axon.
- *Terminal Buttons* – End of the terminal arboriza.
- *Axon Hillock*
- *Myelin*

- Not all axons have it.
- Glial cells / 70% Lipid / Nodes of Ranvier.
- Mutliple Sclerosis (MS) – Demyelination.

6.1.2 Support cells in the Nervous System

- Glia/Glial Cells/ Neuroglia – Support cells.
  - Capable of cell division after birth/communication.
  - Make up half of the volume, but are 10-50 times more numerous. (The other half is made up of neurons.)
  - CNS:
    - *Macroglia* – Large glial cells.
      - *Astrocytes* – Star-shaped cells that provide physical support to neurons, clean up debris, and provide nutrients to neurons.
        - *Note* that these cells do not help neurons grow when they are damaged. In fact, they inhibit growth by proliferating and forming a scar.
      - *Oligodendrocytes* – "few branches (in contrast to Astrocytes)" – *Form* myelin sheath around multiple axons in the CNS.
    - *Microglia* – Small cells that remove debris from injured or dead cells.
    - *Ependymal Glia* – Line the ventricles of the brain and spinal cord. (Remember the CSF?)
  - PNS:
    - *Satellite Cells* – Provide nutrients and physical support to neurons.
    - *Schwann Cells* – Form myelin sheath around axons in the PNS. These cells are monogamists; they wrap their arms around one axon.
      - Neuronal Regeneration.
  - The Myelin Sheath is composed of Oligodendrocytes in the CNS and Schwann Cells in the PNS.
  - *Phagocytosis* – When an injury occurs, the glial cells divide and eat the dead cells. (Done by Microglia and Schwann Cells.)
  - Maintenance of Internal Consistency.
    - When neurons undergo rapid firing, they release potassium ions. Astrocytes absorb these ions to maintain the internal consistency of the neuron, and dump them into the blood stream.

NEW NOTES FOR 02/28/25

6.1.3 Are Glial Cells Contributing to Alzheimer's Disease?

- Normally,
  - Beta amyloid cleared away through microglia.
- IF beta amyloid builds up too much, Tau INSIDE cells builds up.
- This leads to inflammation, which maybe leads to the problems of Alzheimer's.

6.2 Different Kinds of Neurons

- Based on Structure
- Based on Function

6.2.1 Structural Classification of Neurons

- *Unipolar/Pseudounipolar*
  - *The difference:* The axon and dendrite are fused together.
- *Bipolar*
- *Multipolar*

6.2.2 Functional Classification of Neurons

- Sensory Neurons (Afferent)
  - Carry information from the sensory receptors to the CNS.
  - Unipolar.
  - "Afferent" – "bearing or conducting inward"
- Interneurons
- Motor Neurons (Efferent)
  - Carry information from the CNS to the muscles and glands.
  - Multipolar.
  - "Efferent" – "conducting outward"
- Remember: Ad = towards Ex = from Ferro = I carry.

6.3 Neural Communication

- **2 Systems of Neuronal Communication:**
  - *Binary* – All or none (literally only 2 options).
  - *Analogue* –Graded, matter or degree.

NEW NOTES FOR 03/03/25 (kinda)
We added a lot to the notes that we already had, so there is new material springled throughout this section.

6.3.1 Binary System ("Off" and "On")

- *The Resting Membrane Potential (RMP)*: "OFF"
  - Click here for a diagram.
  - *Note:* Where the arrows land on either side of the cell membrane is supposed to represent the relative permeability of the cell membrane to different ions.
  - -70 mV (relative to the outside).
  - Understand the cell membrane.
    - *Phospholipid Bilayer* – Hydrophobic tails and hydrophilic heads.
    - *Semipermeability* – Some things can cross, others cannot.
      - Lipid, lipid soluble, small, and neutral.
    - *Embedded Proteins* – Channels and pumps.
      - **4 Jobs We Care About:**
        - *Receptors*
          - High specificity and affinity.
          - "Places where things can bind to the cell and cause a change."
        - *Channels*.
          - *Gated Channels*:
            - Passive movement. The cell itself does not expel any energy to move the ions.
            - Chemical (ligand) gated channels.
            - Voltage gated channels.
        - *Pumps* – Active transport.
        - *Enzymes* – Facilitates chemical reactions.
          - Breaking neurochemicals down or putting them back together.
  - **3 Determinants of the RMP**
    - *Differential Permeability* – The cell membrane is more permeable to some ions than others.

- For sodium, the membrane only allows a trickle of Na^+ into the cell.
- Conversely, the membrane is more permeable to K^+ and CL^-. (K^+ is the most permeable.)

- **Driving Forces**:
  - *Diffusion* – Ions move from high to low concentration (Concentration Gradient).
    - *Note:* The cell membrane is more permeable to potassium ions than sodium ions.
  - *Electrostatic Pressure* – Ions move towards the opposite charge (Electrical Gradient).
  - *Equilibrium Potential* – The charge the ion "perfers" if it were the only one and could pass freely through the membrane.
    - This answers the question: "Why doesn't the cell get more and more negative?"
    - Driving force in (influx) = Driving force out (efflux).
    - $K^+ = -80$ mV and $Na^+ = +55$ mV.
  - *Sodium-Potassium Pump* (Na^+/K^+ Pump)
    - 3 Na^+ out for every 2 K^+ in.
    - Costs 1 ATP.

- *The Action Potential (AP)*: "ON"
  - Click here for a diagram.
    - *Note:* The above diagram neglects to show that there can be *failed* attempts at an action potential wherein the threshold is not reached. In these cases, the charge of the cell can increase or decrease, but if it does not reach -55 mV, it will quickly settle back to its resting potential of -70 mV.
  - +40 mV (relative to the outside).
  - Thus, during an action potential, there is a total of 110 mV difference between the inside and outside the cell.

NEW NOTES FOR 03/05/25

- **Electrical Current**
  - *Depolarization*
    - A little
    - A lot
      - *Threshold of Excitation* = +15 mV.
      - Action potential
    - Even more.
  - *Repolarization*

- A little
- A lot
- Even more.

- *Refractory Period*
  - Cell is resistant to reexciation for a period after the AP peak.
    - *Absolute Refractory Period* – No amount of stimulation will cause another AP.
    - *Relative Refractory Period* – A stronger than normal stimulus is required to cause another AP. (This is because of hyperpolarization.)
  - **Three Questions:**
    - Why don't the Na^+ channels reopen during repolarization? ✓
      - *Answer:* Because of the refractory period.
    - How can an all or none signal convey analog information? ✓
      - *Answer:* The frequency of the APs can convey the intensity of the stimulus.
      - *Rate Law* – Variations in the intensity of a stimulus are represented by variations in the rate of firing.
    - Where does that signal come from that meets the threshold of excitation?
      - *Decremental Conduction* – The further the signal travels, the weaker it gets. (cable properties)
        - Analogue communication.
          - Degrading because for resistance and leakage.
        - *Passive Conduction* – No energy is expended.

6.3.2 Conduction of Action Potential in Unmyelinated Axons

NEW NOTES FOR 03/07/25

- *All or Nothing Law* – AP occurs or not once triggered, always the same size.
- *Active Regeneration* – The AP is regenerated at each point along the axon.
  - Takes a lot of time ($<$ 1–10 meters/second).
  - Takes a lot of energy.

6.3.3 Conduction of Action Potential in Myelinated Axons

- *Saltatory Conduction* = "To jump" – AP jumps from node to node.
  - Decremental conduction in the myelinated portions.
    - No extracellular fluid.

- Almost absent Na^+ channels.
- Active regeneration at Nodes of Ranvier.
  - High density of Na^+ channels.
  - AP is regenerated.
- **Advantages:**
  - Economic
    - Much less work for the Na^+/K^+ pump.
  - Speed
    - in excess of 100 m/s (225 mph) (not as fast as electricty's 300 million m/s).
  - So why not evolve 1 long myelin sheath?
    - *Answer:* The AP would be too weak from the decremental conduction by the time it reached the end.
- Think of how this applies to multiple sclerosis: The myelin sheath is destroyed, and the AP can no longer jump from node to node. This results in a loss of sensation and motor control.

6.4 Conversion from Electrical to Chemical Signals

- Occurs at the synapse (Greek: "syn" = together, "haptein" = to clasp).
  - Synaptic cleft (20 angstroms (Å) across). *Note:* 10^7 Å= 1 mm.
  - Pre-synaptic membrane
    - *Golgi bodies* – Synthesize neurotransmitters and package them into vesicles.
    - *Synaptic vesicles* – Contain neurotransmitters.
      - In the pre-synaptic cell, the golgi bodies
    - *Docking proteins* – Hold the vesicles in place.
      - Full synaptic vesicles migrate to membrane and attach.
    - Voltage gated *Ca^{2+} channels* open.
    - Once the AP arrives at the synapse, the docking proteins release the vesicles and the neurotransmitters are released into the synaptic cleft (this is due to the Ca^{2+} channels opening).
  - Post-synaptic membrane
    - *Receptors* – Bind to the neurotransmitters.

NEW NOTES FOR 03/10/25

6.5 Conversion from Chemical to Electrical Signal

6.5.1 Two Kinds of Post Synaptic Potentials

- *Excitatory Post Synaptic Potentials* (ESPSs)
  - Bring the cell closer to firing.
  - i.e., opening of Na^+ channels.
- *Inhibitory Post Synaptic Potentials* (ISPSs)
  - Take the cell further from firing.
  - i.e., opening of K^+ channels (and potassium leaves).
- Thus, post synaptic into action potential by summing up of the EPSPs and IPSPs at the axon hillock.

6.5.2 What Happens to Excess or Used Neurotransmitters?

- **Three things can occur:**
  - *Active Reuptake* – The neurotransmitter is taken back up into the pre-synaptic cell.
  - *Metabolism* – The neurotransmitter is broken down by enzymes.
  - *Bound to Autoreceptors* – The neurotransmitter binds to autoreceptors on the pre-synaptic cell.
    - This inhibits the release of more neurotransmitters.

6.5.3 Two Types of Chemically Gated Channels

2 Kinds of Synapse: *ionotropic* and *metabotropic*.

6.5.4 *Ionotropic Synapse*

- No change in metabolism. (No ATP expended.)
- Direct change of ions.
- Fixed duration (rapid and short).
- 1 neurotransmitter binds to 1 receptor.
- **Example:** Acetylcholine (ACh) binds to a receptor and opens a Na^+ channel.

6.5.5 *Metabotropic Synapse*

- Actual change in cellular metabolism.
- Indirect exchange of ions.
- Variable duration (can be very long).
- At least 2 neuromodulator molecules bind to a receptor.
- **Example:** Dopamine binds to a receptor, which activates a G-protein, which activates an enzyme, which produces a second messenger, which opens a K^+ channel.
- **At the Metabotropic Synapse:**
  - Neuromodulator binds and initiates process.
  - Alpha subunit of *G-Protien* binds to *Adenylate Cyclase*.
    - Activating adenylate cyclase to convert ATP to *cAMP* (cyclic adenosine monophosphate).
  - cAMP activates *Protein Kinase A*.
    - Causing 2 subunits to dissociate.
    - Catalytic portion is no longer inhibited.
    - Allowing it to convert ATP to ADP.
      - This produces a phosphate group.
    - To end this process:
      - Neuromodulator dissociates to end cAMP production.
      - Enzymes
        - *Phosphodieterase* – Metabolizes residual cAMP
        - *Phosphoprotein phosphatase* – Removes the phosphate and resets the channel.

NEW NOTES FOR 03/12/25

6.5.6 Who Cares About Metabotropic Synapses?

- Fine tuning of electrical signals is done through presynaptic inhibition and facilitation.
  - *Presynaptic Inhibition* – The release of neurotransmitters is inhibited.
    - Example: One synapse can modulate another that causes it to have some of its—normally opening—Ca^{2+} channels closed.
  - *Presynaptic Facilitation* – The amount of neurotransmitters released is increased.
    - Think of this like, instead of 3 APs, it would seem like 4 APs.

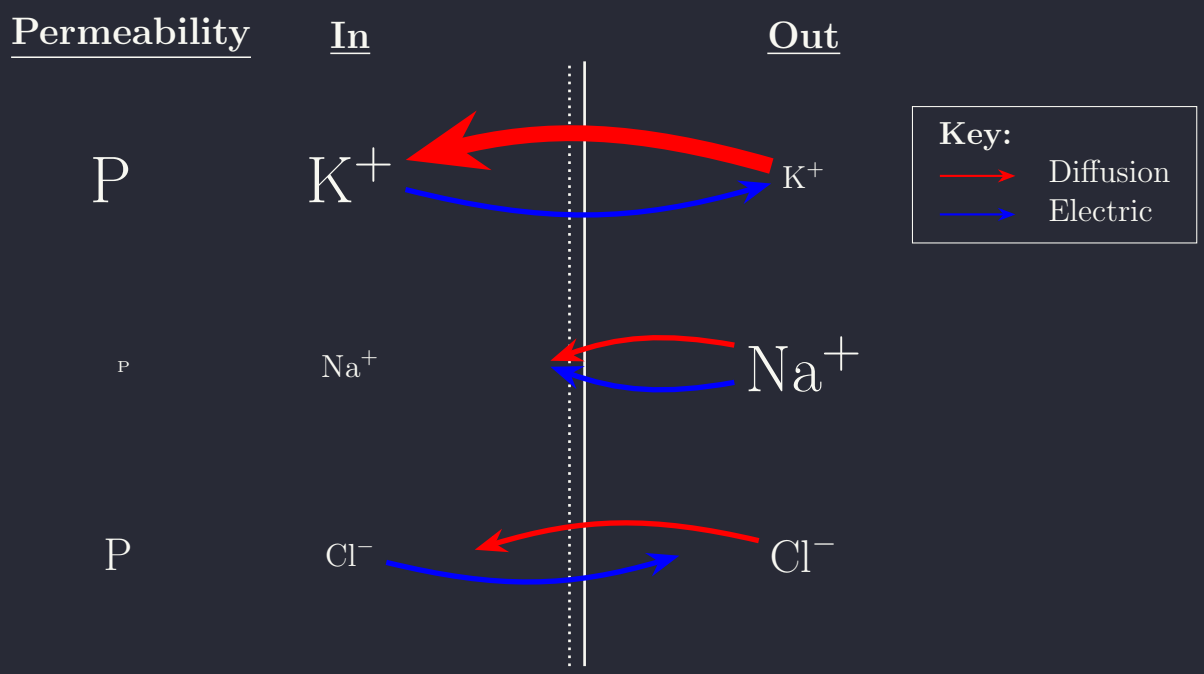

Figure 6.1: The Resting Membrane Potential (RMP) of a Neuron

6.5.7 Eletrical Synapse (Gap Junctions)

- No neurotransmitters, no neuromodulator.
- Channels cross the synapse.
- Very fast.
- Rare in mammalian brain, common in some fish (simpler CNS).
- No facilitation or inhibition is possible.

6.6 Somatic vs. Autonomic (Revisited)

- *Somatic Nervous System*
  - Voluntary control.
  - Sensory and motor neurons.
  - Innervates striated muscles.
  - More differentiated.
- *Autonomic Nervous System*
  - Relatively involuntary.

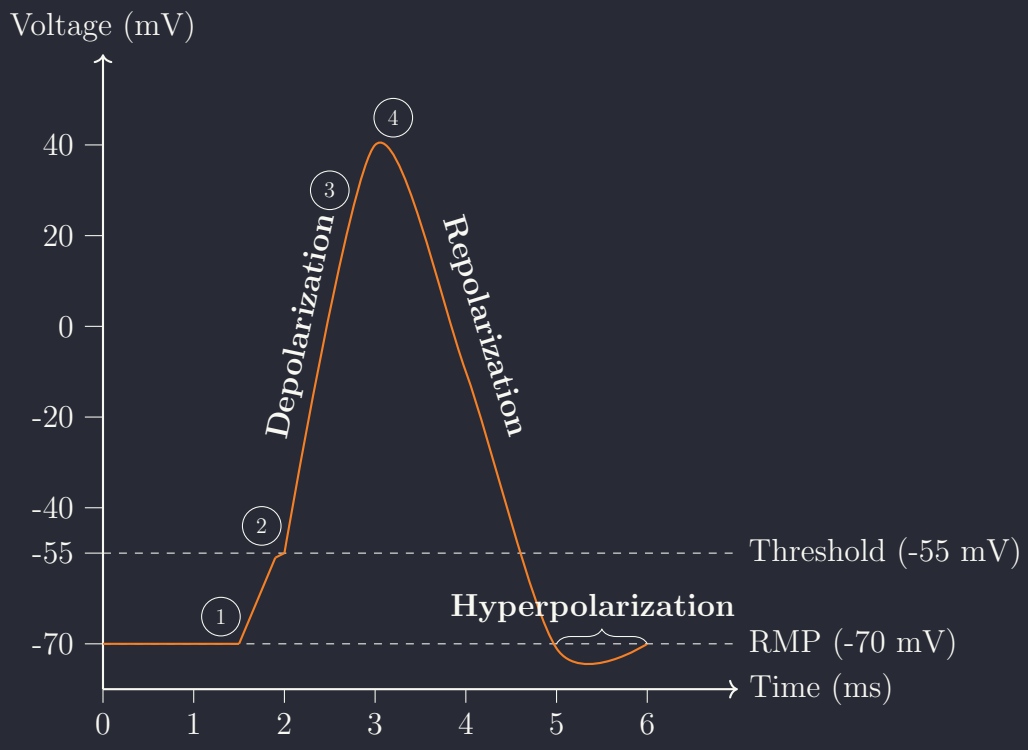

Figure 6.2: Action Potential Waveform

- Purely motor.
- Innervates smooth muscle, cardiac muscle, glands.
- Functions more as a whole.

6.7 Sensory Systems

- *Vision* – Light waves hit photoreceptors in the retina.
- *Audition* – Sounds waves vibrate hair cells in the cochlea.
- Chemical senses: *Olfaction* and *Gustation*. Where, for both, chemicals bind to receptors.
- *Somatosensory System*
  - *Proprioception* – Sense of body position.
  - *Cutaneous Senses* – Touch, temperature, pain.
  - *Kinesthesis* – Sense of movement.
  - *Vestibular Sensation* – Balance.

6.7.1 Why Study Sensory Systems in Psychology?

- Psychologists are interested in? The study of behavior
  1. Perceptions are the basis for behavior and mental processes.
     - "Why did you drive through that stop light?"
     - "Why did you shoot that unarmed man?"
     - The answer to both of these questions are that the person genuinely (sometimes genuinely, other times, they're lying) believed that the light was green, or the person had a gun.
  2. And those perceptions don't exactly match to the stimuli.
     - Get a physicist to measure stimulus.
     - BUT—a psychologist to measure perceptions.

NEW NOTES FOR 03/14/25

6.8 What is Color?

- *Electromagnetic Spectrum* – Energy radiated as waves that are produced by electric charges.
  - Measured in wavelengths.
  - Visible light (for humans)
    - ranges from 380 to 760 nanometers (10^{-9} m).
- *Rods* – Sensitive to low light levels.
  - These cannot differentiate color because there is only one type of rod.
- *Cones* – Sensitive to color.
  - 3 types: *Short* (Blue), *Medium* (Green), *Long* (Red).
- *The Problem of Univariance* – One cone type can't differentiate between different wavelengths of light. Thus, we need multiple cone types.
- *Trichromatic Color Theory* – 3 types of cones, each sensitive to a different wavelength of light.
- *Physiology* – From the sensory systems to the psychology systems (Bottom-up processing).
- *Top-Down Processing*
  - Expectation

  - Knowledge
  - Cognition of ALL sorts.
- *Background* – Changes your depth perception.
  - For example, a small circle surrounded by 6 large circles will appear larger than the same small circle surrounded by 6 smaller circles.

6.8.1 Language and Color

- Color perceptions influenced by language.
- Russians have 2 words for blue.
  - 'siniy' for dark blue and 'goluboy' for light blue.

6.8.2 Motivation Influences Visual Perception

- Radel and Clement-Guillotin (2012).
  - Hungry people see food words better.

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

Part I

Behavioral Neuroscience Lab Notes

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 2: PSYCHOPHYSIOLOGY

We're starting with three studies:

1. **Study 1:** Blinking:
    - Three levels of blinking:
        - Reflexive blinking. Ex: When a puff of air is directed at the eye.
        - Voluntary blinking. Ex: When you're asked to blink.
        - Endogenous blinking. Meaning: "originating from or due to internal causes."
    - *Endogenous blinking* is the focus of this study.
        - Endogenous blinks occur during reading or speaking and reflect changes of attention and changes in thought processes. The more attention required by a visual task; the fewer endogenous blinks occur.
        - More attention required is associated with fewer endogenous blinks. Especially for visual tasks.
        - **The harder the tasks → the fewer the blinks.**
        - Even when a task is not visual, there is a decrease in endogenous blink rate (EBR) during a difficult task followed by flurry of blinks when task is over.
        - **But wait!**
            - EBR has been shown to increase when a cognitive secondary task is performed concurrently, and the cognitive task does not involve visual attention.
        - **WHY?**
            - EB is a dopaminergic activity.
            - Dopamine plays a big role in selective attention.
    - Through this study, we learned that endogenous blinking (DV) is affected by cognitive load (IV)
2. **Study 2:** Cartoon Judgement:
    - Group 1 and 2 membership.
    - Follow group instructions then rate the 3 cartoons that follow on scale from 1-10.
        - 1 is NOT funny
        - 10 is VERY funny
        - Answers (Lips = Pen in lips; Teeth = Pen in teeth):

Groups	Pics 1	Pics 2	Pics 3	Average
Lips	3	3	4	$3\frac{1}{3}$
Teeth	4	4	3	$3\frac{2}{3}$
Stretch	4	5	6	5
J. Jacks	4	2	3	3

- **Facial Feedback Hypothesis**
  - Selective activation or inhibition of facial muscles has a strong impact on emotional responses to stimuli.
  - Zygomatic major muscle.
    - When we had the pen in our teeth, we were activating the zygomatic major muscle.
    - This muscle is responsible for smiling.
  - Our data supported this hypothesis with a probability of $p < 0.02$.
- **Arousal**
  - Increased heart rate in many emotions.
  - Heart rate and attraction
    - 1973 Dutton and Aron
      - Shaky high bridge vs. low stable bridge.
      - Woman on the other side who is asking questionnaire questions (faux DV).
      - She gave her phone number to the guys once they got done answering the questions.
      - The actual DV was the amount of phone calls she received and the sexual content in questionnaire answers.
      - The high bridge group had more sexual content in their messages.
    - 15 minutes of physical activity, then rate attractiveness of potential mates.

Psychophysiology: Behavioral, cognitive, emotional, and social events are all mirrored in physiological processes.

The idea is that we can get a peep into your psychology by looking at what your biology is doing.

Sleep: EEG (Electroencephalogram; measuring brain activity), EOG (Electrooculogram; measuring eye movement), EMG (Electromyography; measuring muscle movement), ERP (Event-Related Potential; measuring electrical activity in the brain in response to a stimulus).

When your brain is hooked up to the ERP and you are asked either task relevant-stimulus, important stimulus, or surprising stimulus, it will produce a higher p—300 amplitude compared to otherwise. Think about how this would be used for interrogating a suspect, for

example.

Then, there are n—350 amplitudes which are activated when we are asleep, and we hear our name, for example.

Notice the implications of this with sleeping: the more tired you are (or closer to falling asleep), the harder it will be to find the p—300 amplitude.

Omitted Stimulus Paradigm – Given a constant stimulus, this is the phenomena wherein there is a gap in the pattern. This will result in a higher p—300 amplitude.

Polygraph: Respiration, GSR (EDA), Blood flow, Blood pressure, and heart rate.

With a polygraph, we're looking at all the components of the peripheral nervous system. That is, when we're "looking at " a polygraph, we're not measuring lying, but all the physiological responses that are associated with lying.

EDA

- *Electrodermal Activity*
  - Old name: Galvanic Skin Response
  - Measuring sympathetic nervous system activity by detecting sweat gland activity by measuring the conductance of an electrical signal from one electrode to another.
  - More rapid conductance with more activity.
  - Particularly good for emotion.
  - Maybe attention.
  - This also is a good measure for the sympathetic nervous system because it is the only one that can enervate the sweat glands.

What if I Want to Know

- If you're lying
- Cognitive or emotional states when you're sleeping
- If you're attending to stimuli I'm presenting

Psychophysiology is different from Physiological Psychology. Note that Psychophysiology is where mind/behavior is the IV, and physiology is the DV. Similarly, Physiological Psychology uses the same IVs and DVs, but notice that we are manipulating the physiological psychology to measure psychology. Remember the independent variable is first (mnemonic).

Examples

- Present snake photo or not. Then measure effects on physiology that evidence fear.
- Presenting in-group and out-group photographs. Then measure effects on physiology that evidence prejudicial cognition.
- Drugs: Measure effects on psychology (behavior/aggression)
- Lesion: Measure effects on psychology (cognition/memory)
- Manipulate heart rate: (behavior/attractiveness ratings)
- Electrical Stim of Brain [tDCS (transcranial direct current stimulation)]: Measure effects on psychology (mood/emotion/depression)

EEG

- Activity in large groups of neurons.
- Difference in electrical activity at a reference point and site of interest.
- You get: Wavelike patterns.
- *International 10-20 system*.
  - Fz, Fp1, Fp2, F7, F8, F3, F4, T3, T4, Cz, C3, C4, T5, T6, Pz, P3, P4, O1, O2.
    - F = Frontal
    - T = Temporal
    - C = Central
    - P = Parietal
    - O = Occipital
    - Odd numbers = left hemisphere.
    - Even numbers = right hemisphere.
    - Z = Midline
- Researchers use *visual inspection* to look at the EEG data.
- Measurements
  - *Frequency* – $\frac{1}{\text{time}}$ (in Hz)
  - *Amplitude* – Height of wave (in μV)

Neurofeedback

- Learn to control your brain activity.
  - See the activity
  - Get reinforcement or punishment

- Make changes
- Even if you don't "know" what you're doing, you can still learn to control your brain activity.

NEW NOTES FOR 03/20/25

9.1 Physiological Psychology (Video Lab) Experiment

Research Question: *Do opioids play a role in social behavior?*

- Pros of videoing:
  - Minimizes the effect of the experimenter.
    - Called "reactivity"
  - Permanent data record
  - Double blind procedures
    - Observer bias/experimenter effect

9.1.1 Good Introductions

- *Rationale* – Why is this study important?
  -
- *Questions* – What are you trying to answer?
- *Hypothesis* – What do you think will happen?
- *Support for Hypotheses* – Why do you think this will happen?
-

9.2 Classes of Neurotransmitters

- Peptides (AKA: Neuropeptides)
  - Endogenous opioids

9.2.1 Peptides—Opioids

- *Peptides* – Short chain of amino acids.
- **Opioid vs. Opiates:**
  - *Opioid*: Endogenous (from inside the body).
  - *Opiate*: Exogenous (from outside the body) morphine, codeine, heroin, percodan (*levorphanol*), opium, OxyCotin, fentanyl, etc.
    - All agonists.
  - Richard Deyo, the guy whose data we're going to be using says opiates are the ones derived by plants.

9.2.2 Antagonists

- NARCAN (Naloxone) – Opioid antagonist.
  - Reverses opiate intoxication.
- Vivitrol (Naltrexone) – Opioid antagonist.
  - Blocks euphoric effects but may not work that well on addiction because doesn't get rid of cravings.

9.2.3 New NonOpioid Pain Relievers

- VX-548 (January 2024—Late stage trials)
  - Acute post-surgical pain.
  - No addiction risk.
- Blocks Na^+ channels in peripheral (not CNS) pain pathways.
- Better than placebo but not as good as hydrocodone + acetaminophen.

9.3 Opioid Receptors

- 3 Kinds:
  - *Mu* (μ) – Analgesia and euphoria.
  - *Delta* (δ) – Analgesia
  - *Kappa* (κ) – *Colocalized* with certain *catecholamines*, learning and memory, emotional control, stress response and analgesia.
    - *Colocalized* – When two or more neurotransmitters are released from the same neuron.

- *Catecholamines* – Dopamine, norepinephrine, and epinephrine.

- [The process was] Discovered in early 1970s.
- Mid 1970s endogenous opioids were discovered.
  - *Endorphins* – Binds to mu receptors the most.
  - *Enkephalins* – Binds to delta receptors the most.
  - *Dynorphins* – Binds to kappa receptors the most.

9.4 Functions of Opioids

- Prevents diarrhea.
- Euphoria.
- Analgesia.
- Stress response, body temperature, emotions, feeding motivation, sexual behavior, learning (reinforcement), drowsiness.
- Social behavior?

9.4.1 Pain is Good

- Unpleasant sensory and emotional experience associated with actual or potential tissue damage.

Pain Pathway

- From face
  - Comes in via cranial nerve V (trigeminal nerve).
- From neck down
  - Cones in via a spinal nerve in one of 2 pathways:
    - Direct (fast pain pathway)
      - Sharp and well localized pain.
      - Immediate and brief.
      - *A-delta fibers* (myelinated) – Fast conducting fibers.
      - Mechanical (strong) and thermal (extreme temperature).
    - Indirect (slow pain pathway)
      - Slow pain.
      - Throbbing, aching and dull pain.

- Takes longer, but lingers.
- *C-fibers* (unmyelinated) – Slow conducting fibers.
- Chemical (inflammatory) pain.
- Receptors are sensitive to chemical simulation.
- *Prostaglandins* – Inactive until tissue damage occurs.
  - *Cyclooxygenase* (COX) – Enzyme that converts inactive prostaglandins to active prostaglandins.
- Pain arrives at the brain stem reticular formation (BSRF)
- After the BSRF:
  - Thalamus (Arousal)
  - Limbic system: Anterior Cingulate Cortex (ACC) (emotional)
  - Periaqueductal gray region (Opioids)
    - This is activated when there is too much pain.
    - For example, a person gets their finger cut off; instead of incapacitating the person, the periaqueductal gray region will activate and release opioids to help the person get away from whatever is causing the pain.
  - Frontal lobes (Association)
  - and others.

9.5 NSAIDs

- 2 Classes:
  - *Proprionic Acid Derivatives* – Ibuprofen, naproxen, ketoprofen.
  - *Salicylates* – Aspirin, diflunisal, salsalate.
- Block cyclooxygenase
- *COX-2 Inhibitors* – *celecoxib* (Celebrex), *rofecoxib* (Vioxx) (removed from market because heart attack and stroke).

9.6 Opioid Systems at Work?

- Acupuncture
- The placebo effect activates the opioid system.
- For example, if I were to give you a pill, and said it was going to relieve your pain, but it was actually just a sugar pill, you would still feel relief from the pain. However, if I gave you a pill, such as Nalaxone (which is an opioid antagonist), you would not feel relief from the pain.

New Notes for 04/03/25

9.7 Carefully Plan Some Hypotheses

- *Conceptual Hypothesis* – A statement of the expected relationship between the IV and DV.
- *Statistical Hypothesis* – A statement of the expected relationship between the IV and DV in statistical terms.
- Consider the example "Does technology use disrupt sleep quality."
  - Conceptual:
    - Null: TU (tech users) do NOT have lower sleep quality than NTU (non-tech users).
    - Alternative: TU have lower sleep quality than NTU.
  - Statistical:
    - Null: $\mu_{TU} \geq \mu_{NTU}$
    - Alternative: $\mu_{TU} < \mu_{NTU}$
  - For the test that we would use to test this hypothesis, we would use a paired t-test.
- Consider another example "Does too little vitamin D lead to depressed mood?"
  - Conceptual:
    - Null: Adequate VD (vitamin D) participants do NOT have lower mood than inadequate IVD (inadequate vitamin D) participants.
    - Alternative: Adequate VD participants have lower mood than IVD participants.
  - Alternative:
    - Null: $\mu_{VD} \leq \mu_{IVD}$
    - Alternative: $\mu_{VD} > \mu_{IVD}$
- For our question, "Does nalaxone increase play?" we need to be careful how we operationalize play.
- For rats, they play by:
  - Boxing, chasing, dorsal contact, PINNING, and social proximity. But these are not sufficient enough.

9.7.1 Nonspecific Effects

- The IV produces changes in the DV by acting on a system not directly related to the system in question.

- For example, I sleep deprive people and they have less sex. Thus, does sleep deprivation interfere with sex OR maybe, sleep deprivation reduces motivation and that leads to sex declines along with lots of other things indirectly.
- **Could the effect we see on play be due to something else?**
  - Level of behavior
    - Spontaneous activity
    - Crossing
  - Motivation
    - Exploratory behavior
    - Rearing
  - Fear of emotionality
    - If no food is available, grooming

9.7.2 Results

- IRR
  - For play and nonspecific effect (crossing)
  - Descriptive (includes graph)
- Play
  - Descriptive (includes graph)
  - Inferential
- Nonspecific effect
  - Descriptive (includes graph)
  - Inferential
- Play and nonspecific effect separately
- How can I show the relationship between rater 1 and rater 2's ratings?
  - Graph?
    - Scatterplot
  - Statistic?
    - Perason's Correlation coefficient (r)
  - Jamovi Variables?
    - Rater1_pins, Rater2_pins, Rater1_ns, Rater2_ns

CHAPTER 10

LAB 3: SLEEP LAB

NEW NOTES FOR 04/10/25

10.1 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.

10.2 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 10.1: Summary of EEG Wave Characteristics

10.3 Two States of Consciousness

10.3.1 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

10.3.2 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

10.4 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 10.2: Chronotypes

Part II

Behavioral Neuroscience Practice Exams