

Biological Psychology

[Revised Edition]

BIOLOGICAL PSYCHOLOGY [REVISED EDITION]

August 2024

MICHAEL HOVE AND STEVEN A. MARTINEZ

ROTEL (Remixing Open Textbooks with an Equity
Lens) Project
Fitchburg, Massachusetts



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CONTENTS

Front Matter	1
<i>Acknowledgements</i>	2
<i>About the authors</i>	2
<i>License and Citation</i>	3
<i>Cover Art</i>	3
Land Acknowledgement Statement for the ROTEL Grant	5

Chapter 1: Introduction to Biological Psychology

1.1: Introduction	9
1.2: The Field of Biological Psychology	13
1.3: The Scientific Approach to Understand Brain and Behavior	17
1.4: Applications of Biological Psychology	22
1.5: Research with Animals	27
1.6: Diversity in Biological Psychology	29
1.7: Overview of the Book	31
1.8: Brain and Behavior Beyond this Book	35

1.9: References	37
<i>Parts of this chapter were adapted from:</i>	37
<i>References</i>	37

Chapter 2: The Brain and Nervous System

2.1: Introduction	43
2.2: Visualizing and Navigating the Human Brain	44
2.3: The Nervous System	47
2.4: The Peripheral Nervous System	50
<i>The Autonomic Nervous System</i>	51
<i>The Somatic Nervous System</i>	53
2.5: The Central Nervous System	59

2.6: The Brain	63
<i>Cerebral Cortex</i>	64
<i>Frontal Lobe</i>	69
<i>Temporal Lobe</i>	72
<i>Parietal Lobe</i>	74
<i>Occipital Lobe</i>	77
<i>Insula</i>	78
<i>Limbic System</i>	79
<i>Basal Ganglia</i>	82
<i>Thalamus</i>	83
<i>Hypothalamus</i>	86
<i>Cerebellum</i>	87
<i>Brainstem</i>	88
2.7: Non-Neuronal Structures in the Central Nervous System	92
<i>Ventricular System and Cerebrospinal Fluid</i>	92
<i>Vasculature</i>	94
2.8: Conclusion	97
2.9: Discussion Questions and Resources	98
2.10: References	100
<i>Parts of this chapter were adapted from:</i>	100
<i>The Brain and Nervous System References</i>	100

Chapter 3: Neurons

3.1: Introduction	105
3.2: The Structure of the Neuron	109
<i>Basic Nomenclature</i>	109
3.3: Types of Cells in the Brain	112
3.4: Communication Within and Between Neurons	116
<i>Resting Membrane Potential</i>	116
<i>Action Potential</i>	120
<i>The Change in Membrane Potential During an Action Potential</i>	124
3.5: Discussion Questions and Resources	128
3.6: References	132
<i>This chapter was adapted from:</i>	132
<i>References</i>	132

Chapter 4: Research Methods in Biological Psychology

4.1: Introduction	137
4.2: Historical Methods – Studies of Brain Damage in Humans	138
4.3: Invasive Physiological Research Methods	143
4.4: Tools of Cognitive Neuroscience – EEG and MEG	148

4.5: Tools of Cognitive Neuroscience – Brain imaging, PET and MRI	152
<i>Magnetic Resonance Imaging</i>	153
4.6: Techniques that Modulate Brain Activity	160
4.7: References	164
<i>Parts of this chapter were adapted from:</i>	164
<i>References</i>	164

Chapter 5: Psychopharmacology

5.1: Introduction	169
5.2: Pharmacokinetics: What Is It and Why Is It Important?	175
<i>Drug Administration</i>	175
<i>Drug Metabolism</i>	177
5.3: Recent Issues Related to Psychotropic Drugs and Metabolism	179
<i>Grapefruit Juice and Metabolism</i>	179
<i>Individualized Therapy, Metabolic Differences, and Potential Prescribing Approaches for the Future</i>	180
5.4: Other Controversial Issues	183
<i>Juveniles and Psychopharmacology</i>	183
<i>The Elderly and Psychopharmacology</i>	185

5.5: How Drugs Affect Neurotransmitters	188
<i>Alcohol</i>	188
<i>Caffeine</i>	189
<i>Cannabis</i>	191
<i>Opiates (Heroin, Morphine, Etc.)</i>	192
5.6: Discussion Questions and Resources	195
5.7: References	198
<i>Adapted from</i>	198
<i>References</i>	198

Chapter 6: Hormones, Sex, and Gender

6.1: Introduction to Hormones and Behavior	203
6.2: Sexual Differentiation	214
<i>Chromosomal Sex</i>	214
<i>Gonadal Differentiation</i>	215
<i>Hormones During Development</i>	215
6.3: Sex Differences in Psychology and the Brain	220
<i>Sex Differences in Psychology</i>	221
<i>Sex Differences in the Brain</i>	222
<i>Size and Distribution of Sex Differences</i>	223
<i>Brains and Hormones</i>	227

6.4: Hormones and Behavior: Aggression and Parental Behaviors	230
<i>Aggressive Behaviors</i>	230
<i>Parental Behaviors and Bonding</i>	233
6.5: Sex, Gender, and Sexual Orientation	238
<i>Sex, Gender, and Sexual Orientation: Three Different Aspects of You</i>	238
<i>Variations in Gender</i>	240
<i>Sexual Orientation</i>	244
<i>Development and Origins of Sexual Orientation</i>	246
<i>In Closing: Gender and Sexual Orientation</i>	249
6.6: Discussion Questions and Resources	252
6.7: References	255
<i>Parts of this chapter were adapted from:</i>	255
<i>References</i>	256

Chapter 7: Development of the Brain and Nervous System

7.1: Introduction	267
7.2: Embryonic Stage	268
<i>Neural Tube</i>	268
<i>Primary Vesicles</i>	270
<i>Secondary Vesicles</i>	271

7.3: Stages of Neuronal Development	273
<i>Neuron Growth</i>	275
<i>Neuronal Migration</i>	276
<i>Aggregation</i>	277
<i>Neuron Death</i>	277
<i>Adult Neurogenesis</i>	278
7.4: Neuroplasticity	280
7.5: Sensitive and Critical Periods of Development	284
<i>Sensitive Periods of Development</i>	284
<i>Critical Periods of Development</i>	286
<i>Adolescence as a sensitive period of development</i>	288
7.6: Trade-off between Plasticity and Efficiency	290
7.7: Characterizing Brain Development from Infancy through Young Adulthood	293
7.8: Conclusion	295
7.9: Discussion Questions and Resources	296
7.10: References	298
<i>Parts of this chapter were adapted from:</i>	298
<i>References</i>	298

Chapter 8: Learning and Memory

8.1: Introduction	307
-------------------	-----

8.2: Types of Memory	310
<i>Declarative Memory (Explicit)</i>	311
<i>Nondeclarative Memory (Implicit)</i>	312
<i>Working Memory</i>	314
8.3: Brain Structures in Memory	317
<i>Memory Consolidation and Relational Memory—Medial Temporal Lobes including the Hippocampus</i>	317
<i>Patient HM</i>	320
<i>Hippocampal Function</i>	322
<i>Declarative Memory—Cortex</i>	325
<i>Working Memory—Prefrontal Cortex</i>	326
<i>Habit or Procedural Memory—Striatum</i>	327
<i>Emotional Memories—Amygdala</i>	329
<i>Interim Summary</i>	331
8.4: Special Types of Neurons	334
<i>Place Cells</i>	334
<i>Grid Cells</i>	335
8.5: Stages of Memory	338
<i>Memory Encoding</i>	338
<i>Memory Consolidation</i>	339
<i>Memory Retrieval</i>	340
8.6: Memory Reconsolidation—New Views and Applications	343
<i>Memory Reactivation</i>	343
<i>Targeted Memory Reactivation</i>	345

8.7: Memory-Related Disorders	347
<i>Korsakoff's Syndrome</i>	348
8.8: Memory Enhancement Techniques	350
8.9: Discussion Questions and Resources	353
8.10: References	357
<i>Attributions</i>	357
<i>References</i>	357

Chapter 9: Genetics and Epigenetics in Psychology

9.1: Introduction	365
<i>DIG DEEPER</i>	368
<i>LINK TO LEARNING</i>	369
9.2: Fundamental Genetics and Genetic Variation	371
<i>DIG DEEPER</i>	374
9.3: The Nature-Nurture Question and Behavior Genetics	376
<i>Nature-Nurture and Twin Studies</i>	376
<i>What Have We Learned About Nature-Nurture?</i>	383

9.4: Epigenetics	389
<i>What Is the Epigenome, and What Does It Do?</i>	389
<i>How Does Epigenetics Work?</i>	390
<i>Can the Epigenome Change?</i>	392
<i>Epigenetics and Physical Health</i>	394
<i>Epigenetics in Psychology</i>	397
9.5: References	404
<i>Parts of this chapter were adapted from:</i>	404
<i>References</i>	404

Chapter 10: Emotion and Affective Neuroscience

10.1: Affective Neuroscience: What is it?	413
10.2: Basic Emotions	417
<i>Desire: The neural systems of reward-seeking</i>	417
<i>“Liking”: The neural circuits of pleasure and enjoyment</i>	419
<i>Fear: The neural system of freezing and fleeing</i>	420
<i>Rage: The circuits of anger and attack</i>	421
<i>Love: The neural systems of care and attachment</i>	423
<i>Grief: The neural networks of loneliness and panic</i>	424
10.3: Plasticity: Experiences Can Alter the Brain	426
10.4: Brain Structures have Multiple Functions	428
10.5: Conclusion	429
10.6: Discussion Questions and Resources	430

10.7: References	432
<i>This chapter was adapted from:</i>	432
<i>References</i>	432

Chapter 11: Brain Damage, Neurodegeneration, and Neurological Diseases

11.1: Introduction	439
11.2: Stroke	441
11.3: Brain Tumors	446
11.4: Traumatic Brain Injury	450
<i>How TBI Affects the Brain</i>	450
<i>Diagnosing and Treating TBIs</i>	454
<i>Chronic Traumatic Encephalopathy (CTE)</i>	455
<i>Causes of TBI</i>	457
<i>Traumatic Brain Injury from Intimate Partner Violence – By Prof. Eve Valera</i>	458
11.5: Neurological and Neurodegenerative Disorders	464
11.6: Alzheimer's Disease	465
11.7: Parkinson's Disease	471
11.8: Multiple Sclerosis	476
11.9: References	481
<i>Parts of this chapter were adapted from:</i>	481
<i>References</i>	482

Chapter 12: Biopsychology of Psychological Disorders

12.1: Biopsychology of Psychological Disorders Overview	489
<i>What are Psychological Disorders?</i>	490
<i>The American Psychiatric Association (APA) Definition of a Psychological Disorder</i>	490
<i>Understanding the Classification Systems of Psychological Disorders</i>	492
12.2: Schizophrenia	494
<i>Neural Mechanisms Underlying Schizophrenia</i>	495
<i>Treatments of Schizophrenia</i>	499
12.3: Mood Disorders: Depression and Bipolar Disorder	501
<i>Neural Mechanisms Underlying Depression</i>	502
<i>Treatments for Depressive Disorders</i>	504
<i>Neural Mechanisms Underlying Bipolar Disorders</i>	509
<i>Treatment of Bipolar Disorder</i>	511
12.4: Anxiety	512
<i>Neural Mechanisms Underlying Anxiety Disorders</i>	514
<i>Treatments of Anxiety Disorders</i>	515
12.5: Obsessive-Compulsive and Related Disorders	517
<i>Neural and Genetic Mechanisms Underlying Obsessive-Compulsive and Related Disorders</i>	521
<i>Treatments of OCD</i>	524

12.6: Post-Traumatic Stress Disorder	526
<i>Neural Mechanisms Underlying Post-Traumatic Stress Disorder</i>	526
<i>PTSD Treatments</i>	528
12.7: Conclusion	531
12.8: Discussion Questions and Resources	533
12.9: References	535
<i>Parts of this chapter were adapted from:</i>	535
<i>References for Psychological Disorders</i>	536
 Grant Information	 551
Vocabulary	552
Version History	596

FRONT MATTER

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Creating this free Open Education Resource was motivated by seeing students struggle to pay for textbooks. Many of our students would delay buying materials until their paycheck arrived, others would try to succeed in the class without the materials, and others would have to choose between buying food and classroom materials. We hope that this OER will lessen students' financial strain and help make class more accessible and inclusive.

We have been careful to be accurate and up to date in this textbook, but like any book, errors and outdated information can sometimes occur. With a web-based book, we can periodically update the book. If you have a suggestion for a correction, a comment, or general feedback, please email: BiologicalPsychology_OpenText@gmail.com. We will monitor that email and make minor edits to the book. If you are a teacher and use the book, we'd love to hear from you. Please let us know what aspects of the book you find useful or appealing, and what aspects you find less so (critical feedback is helpful for improving future editions). We also plan to compile teaching resources such as slides and assignments that can accompany the book.

We first released Biological Psychology in February 2024, and released an updated version in August 2024. The updated version added a new chapter on Learning and Memory (Ch 8); revamped the Hormones chapter (Ch 6) to include sections on endocrine disruptors and the biopsych of gender, sex, and sexual orientation; additional info on treatments of Psychological Disorders (Ch 12); and stylistic improvements throughout.

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spare time, he enjoys hiking, playing music and ice hockey, and hanging with his family. When his 4- and 6-year-old boys had a hard time sleeping, reading a few paragraphs from this book would put them right to sleep. Hopefully it's not so sleep inducing for you.

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Cover Art

“The Kiss” by Jeroen Blommaert (CC BY-SA 4.0) was in the [2021 Brain Art Competition](#). Here is Dr. Blommaert’s caption for the entry: “Cancer complicates about 1 in 1000 pregnancies. Luckily, we recently found that

treatment during pregnancy doesn't need to impair the neurodevelopment of the child (Blommaert et al. 2020), adding to the growing evidence that cancer treatment during pregnancy is possible.”

LAND ACKNOWLEDGEMENT STATEMENT FOR THE ROTEL GRANT

As part of ROTEL Grant's mission to support the creation, management, and dissemination of culturally-relevant textbooks, we must acknowledge Indigenous Peoples as the traditional stewards of the land, and the enduring relationship that exists between them and their traditional territories. We acknowledge that the boundaries that created Massachusetts were arbitrary and a product of the settlers. We honor the land on which the Higher Education Institutions of the Commonwealth of Massachusetts are sited as the traditional territory of tribal nations. We acknowledge the painful history of genocide and forced removal from their territory, and other atrocities connected with colonization. We honor and respect the many diverse indigenous people connected to this land on which we gather, and our acknowledgement is one action we can take to correct the stories and practices that erase Indigenous People's history and culture.

Identified tribes and/or nations of Massachusetts

Historical nations:

- Mahican
- Mashpee
- Massachuset
- Nauset
- Nipmuc
- Pennacook
- Pocomtuc
- Stockbridge

6 | LAND ACKNOWLEDGEMENT STATEMENT FOR THE ROTEL GRANT

- Wampanoag

Present day nations and tribes:

- [Mashpee Wampanoag Tribe](#)
- [Wampanoag Tribe of Gay Head Aquinnah](#)
- [Herring Pond Wampanoag Tribe](#)
- [Assawompsett-Nemasket Band of Wampanoags](#)
- [Pocasset Wampanoag of the Pokanoket Nation](#)
- [Pacasset Wampanoag Tribe](#)
- [Seaconke Wampanoag Tribe](#)
- [Chappaquiddick Tribe of the Wampanoag Indian Nation](#)
- [Nipmuc Nation](#) (Bands include the Hassanamisco, Natick)
- [Nipmuck Tribal Council of Chaubunagungamaug](#)
- [Massachusetts Tribe at Ponkapoag](#)

In the event that we have an incorrect link or are missing an existing band/nation, please let us know so that we may correct our error.

Suggested readings

[Massachusetts Center for Native American Awareness](#)

[A guide to Indigenous land acknowledgment](#)

[‘We are all on Native Land: A conversation about Land Acknowledgements’](#) YouTube video

[Native-Land.ca | Our home on native land](#) (mapping of native lands)

[Beyond territorial acknowledgments – âpihtawikosisân](#)

[Your Territorial Acknowledgment Is Not Enough](#)

CHAPTER 1: INTRODUCTION TO BIOLOGICAL PSYCHOLOGY

Learning Objectives

- Learn how the field of biological psychology is defined and identify some of the major branches in the field
- Understand the scientific method that is used to study the brain and behavior
- Know experimental and research terms, such as hypothesis, theory, independent variable, dependent variable, random assignment, replication
- Differentiate basic and applied research
- Learn about the payoffs of biological psychology, such as healing the brain and guiding artificial intelligence
- Understand and think about how and why research in biopsychology is performed on animals and the ethical principles that guides animal research
- Recognize the value of diversity in the field of biological psychology
- Get an overview of the contents of book

1.1: INTRODUCTION

As you start reading, take a couple of deep breaths. Breathing typically happens automatically and without your awareness, but you can easily control your body to take a deep breath. Now point your attention to your expanding chest, the feeling of air flowing past your lips, and the sound of your deep breath. After a few mindful breaths, you might feel more relaxed or “in your body.” After a few months of regularly attending to your breath (as is done in many meditation practices), you might notice improved attentional control, emotion regulation, and self-awareness, and actually change the physical structure of your brain (Tang et al., 2015).

This is all kind of strange and leads to questions such as:

- How can some bodily functions be maintained automatically without awareness, but can also be controlled under your volition?
- Why are we typically unaware of sensations that are constant, but we can direct our attention to consciously perceive them?
- Why do we even have subjective experience? Or from an evolutionary perspective, did having subjective experience help humans survive and pass on their genes?
- Who, what, and where is the “self” who experienced this? (There are no little characters pulling levers in your head like in the Disney movie *Inside Out*.)
- How can awareness of a few deep breaths change your emotional state?
- How can regularly performing an activity change the structure of your brain?

The answers to all these questions relate to the brain. Experience, awareness, the feeling of self, and in fact all of our thoughts, perceptions,

movements, and emotions, emerge from the patterns of electrochemical signals zipping along the 86 billion neurons in your brain. The human brain is the most complex object that we know of in the universe. Each neuron is as complex as a major city and connects with thousands of other neurons, resulting in 300 million neuronal connections in a single cubic millimeter of brain (that's the size of the tip of a ballpoint pen!) (Eagleman & Downar, 2016; Lichtman, n.d.). Scaling that up, the entire brain—about 1200 cubic centimeters and weighing around 3 pounds—contains about 60 trillion synaptic connections and essentially infinite possible patterns of activation. These patterns of brain activation make you, you.¹

We are still learning about the brain and many mysteries remain, but scientists know an astounding amount about how the brain works. In recent decades, researchers have gained major insights into the brain's molecular and chemical processes, neuronal communication, and the functions of specific brain areas and networks. We've advanced our understanding of how drugs and hormones affect brain function, how genes and environment shape brain and behavior, as well as how the brain develops and can deteriorate with damage, disease, or psychological disorders. We'll explore these topics and more in this book on Biological Psychology.

1. The nature of the self and what makes you “you” is a deep and nuanced scientific, philosophical, and even spiritual question. Understanding the nature of the “true self” is a primary goal of many spiritual traditions (Singer, 2007). For an excellent scientific treatment of the nature of the self, including the brain, bodily, social, and environmental underpinnings of selfhood, see the book “Who You Are: The Science of Connectedness” by Michael Spivey (2020).

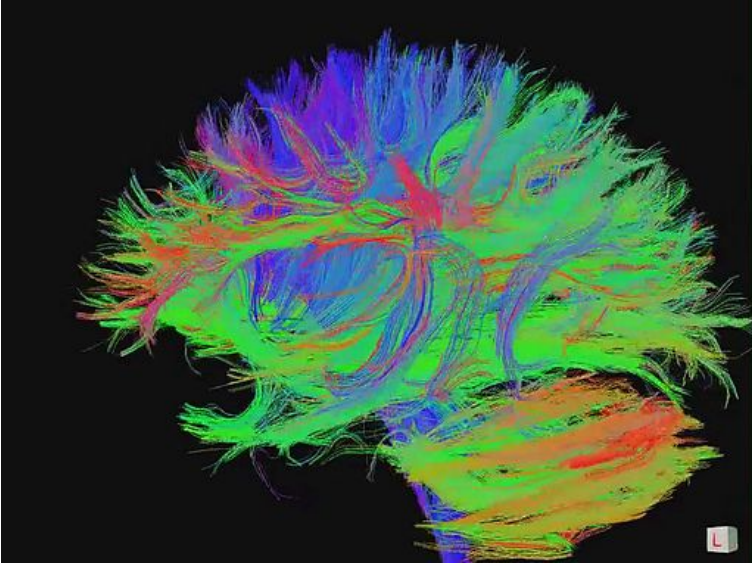


Figure 1a. Why we are the way we are: networks of axonal nerve fibers in the brain as measured by Magnetic Resonance Imaging (MRI), specifically diffusion tensor imaging.

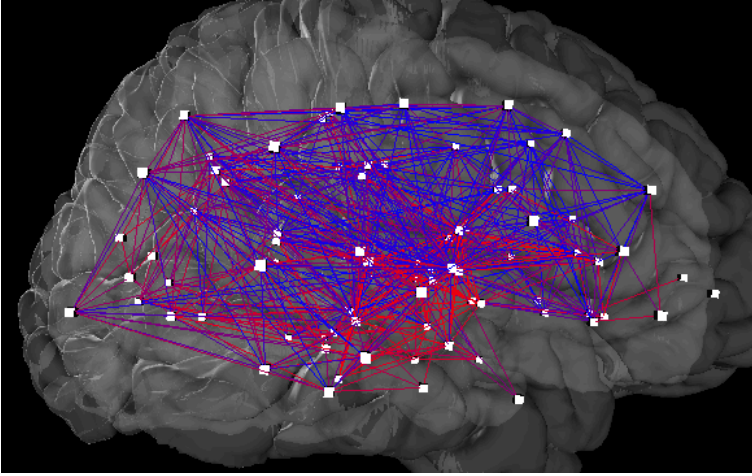


Figure 1b. A graphical depiction of the vast interconnectedness of large-scale brain regions. Nodes (i.e. major hubs in the brain) are depicted as white squares and interconnections between nodes are depicted in red-blue lines overlaid on a grayscale image of the brain.

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1.2: THE FIELD OF BIOLOGICAL PSYCHOLOGY

What is Biological Psychology? Biological psychology is the scientific study that links brain and behavior. Biological psychology, or biopsychology or biopsych for short, is related to neighboring disciplines including psycho-biology and behavioral neuroscience (Pinel & Barnes, 2017). The distinction is subtle, but we use the term biological psychology here because it emphasizes the centrality of psychology (i.e., the science of mental processes and behavior). Our goal is to understand the biological bases of psychology, rather than psychological aspects of biology or neuroscience. Thus, biological psychology investigates how biological factors like the brain, nervous system, hormones, and genes influence our cognition, emotions, motivations, memories, and actions. Biological psychology is not only a scientific discipline, but also a viewpoint that emphasizes that brain mechanisms underlie all of our thoughts and actions and that these brain mechanisms have evolved over eons from our ancient ancestors who survived and reproduced (Kalat, 2019).

The History of Biological Psychology. Thinkers have long mused about the nature of human behavior and experience, but the scientific discipline of biological psychology has roots in physiology, philosophy, and the early psychologists who adopted **empiricism** in the 19th century (Garrett, 2015). Wilhem Wundt, considered the founder of experimental psychology, started the first psychology laboratory in the 1870s in Leipzig, Germany, where his research emphasized systematic observation to understand consciousness and mental processes. In *The Principles of Psychology* (1890), William James argued that the scientific study of psychology should be grounded in an understanding of biology (Walinga, 2019). Although we can't pin down the exact start of the field of biological

psychology, the publication of Donald Hebb's groundbreaking book *The Organization of Behavior* in 1949 marked a defining moment. Hebb proposed the first brain-based account of how psychological phenomena like perception, thought, and memory could emerge from brain activity, and thereby challenged the prevailing view that psychological phenomena were too complex to originate from brain processes (Pinel & Barnes, 2017).

Divisions of Biological Psychology. Nowadays, biological psychology is a broad and diverse field that consists of many different approaches to studying links between the brain and behavior. Here are some major branches of biological psychology:

- **Psychopharmacology** examines how drugs and other substances affect the brain and behavior, as well as how they can be used to treat psychological disorders.
- **Neuropsychology** investigates the relationship between brain function and behavior, focusing on how brain damage or dysfunction can impact cognitive and psychological functioning especially in human patients.
- **Psychophysiology** studies of the relation between physical functions of organisms (physiology) and psychological processes. Common physiological measures include electroencephalogram (EEG), heart rate, and pupil dilation.
- **Psychoneuroimmunology** examines the relationships between the nervous system, immune system and hormones, and behavior. Psychoneuroimmunologists often study the impact of stress and stress hormones on illness susceptibility and recovery.
- **Evolutionary psychology** explores how evolutionary processes, like natural selection, have adaptively shaped human traits and behaviors.
- **Behavioral genetics** analyzes how genetic factors contribute to individual differences in behavior, cognition, personality, etc. and how genetic factors interact with environmental influences.
- **Cognitive neuroscience** studies the neural basis of human cognitive processes, including perception, attention, memory, language, and

decision-making. It often uses tools like functional brain imaging.

- **Comparative psychology** examines the behavior and mental processes of nonhuman animals to gain insights into the evolutionary and environmental factors that shape animal and human behavior and mental processes.

Biological psychology can be parsed into even more subfields, the subfields overlap, and researchers often work in more than one area. But this list shows the breadth of approaches used to study links between the brain and behavior.

Biological psychology is highly interdisciplinary and researchers may have trained in psychology, neuroscience, biology, computer science, medicine, philosophy, or engineering. Each discipline contributes a different approach to understanding the brain and its functions, but also poses new questions and problems that require collaboration and integration. Understanding and integrating knowledge from various subfields can be challenging for both students and researchers, but that integration provides a richer understanding of the brain and leads to breakthroughs that propel scientific progress.

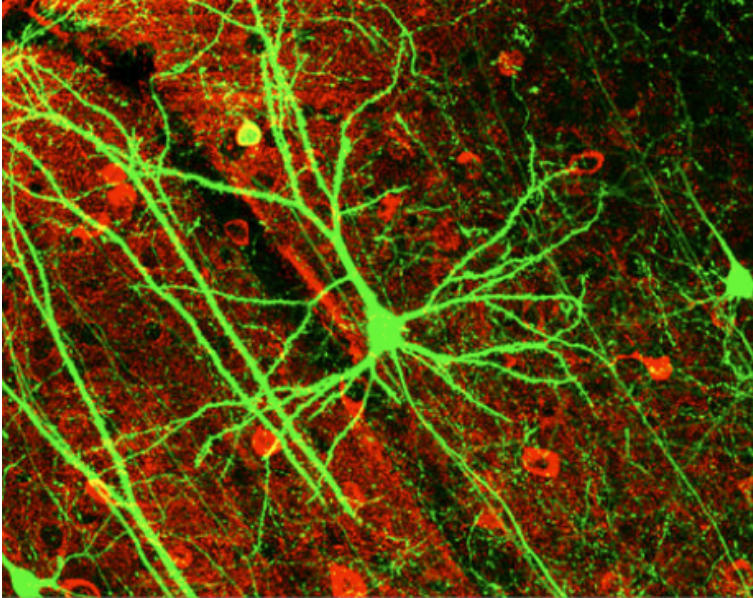


Figure 2. Pyramidal neurons in the mouse cerebral cortex expressing green fluorescent protein. The red staining indicates GABAergic interneurons.

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1.3: THE SCIENTIFIC APPROACH TO UNDERSTAND BRAIN AND BEHAVIOR

Biological psychology uses many techniques to observe, measure, and manipulate the brain, but researchers across all fields use the same underlying approach—science and the scientific method. The scientific method is a systematic way of gathering and testing evidence based on observation and experimentation.

The scientific process usually starts with an observation or question that one wants to understand. A researcher proposes a tentative explanation, called a **hypothesis**, to explain the phenomenon. A valid hypothesis must be testable. It should also be **falsifiable**, meaning that experimental results can disprove it. Importantly, science does not claim to “prove” anything because scientific understandings are always subject to modification with further information. This step—openness to disproving ideas—distinguishes science from non-science. The presence of the supernatural, for instance, is neither testable nor falsifiable. A hypothesis should also fit into the context of a scientific **theory**, a broad explanation for some aspect of the natural world that is consistently supported by evidence over time. A theory is the best understanding we have of that part of the natural world.

The researcher then tests the validity of the hypothesis by making observations or carrying out an experiment. An experiment will have one or more variables and one or more controls. A variable is any part of the experiment that can vary or change during the experiment; an **independent variable** is manipulated by the researcher, and a **dependent variable** is the outcome variable that is measured. The control group contains every feature of the experimental group except the manipulation

from the researcher's hypothesis. Therefore, if results from the experimental group differ from the control group, that difference must be due to the hypothesized manipulation, rather than some outside factor.

For example, if a researcher hypothesizes that a certain drug decreases appetite, they could perform an experiment with the independent (manipulated) variable "drug or no-drug," and the dependent (measured) variable "amount of food eaten." The researcher would randomly assign some participants to the experimental group who gets the drug, and other participants to the control group who gets a placebo pill that looks like the drug. Through **random assignment** and a proper control condition, only the drug would differ between the experimental and control groups. If the experimental (drug) group eats less than the control (placebo) group, then one could conclude that the hypothesis is supported. Conversely, the research could lead to rejecting the hypothesis if not supported by the experimental data.

After analyzing their data, researchers communicate their results and conclusions in publications or presentations so that others can critique, replicate, or build on the results. In addition to publishing a report, researchers now regularly publish their datasets, so that others can re-analyze the data to ensure quality and maybe find something new without having to collect new data. Study results inform future studies and help refine hypotheses (see Figure 3). Experimental outcomes can prompt shifts in approach or spark new research questions. Many times, science does not operate in a linear fashion. Instead, scientists continually draw inferences and make generalizations, finding patterns as their research proceeds.

Science and the scientific method are the best way to understand and study the brain because they provide us with rigorous, objective, and verifiable knowledge that can help us improve our health, education, and well-being.

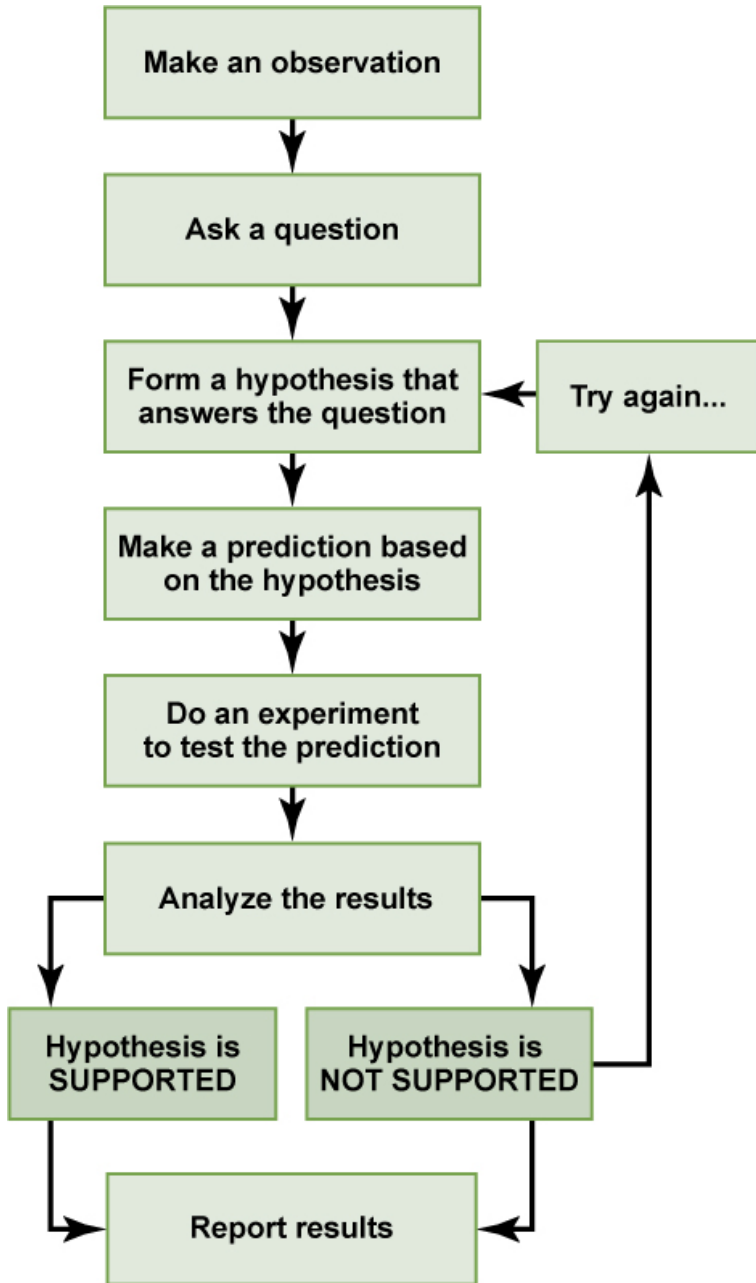


Figure 3. The scientific method consists of a series of well-defined steps. If a hypothesis is not supported by experimental data, one can propose a new hypothesis. The scientific method is an ongoing, iterative process, wherein the results from one study will inform and guide the process for a future hypothesis or study.

Basic and Applied Research. Across the various subfields of biological psychology, research can be categorized as basic or applied. **Basic research**, also known as pure research, is driven by scientific curiosity or an interest in understanding the mechanisms of brain function and brain-behavior relationships. It seeks to answer fundamental questions about how the brain works and explores the biological basis of behavior, emotions, and cognitive processes, by examining genetics, neurotransmission, brain circuitry, and other physiological processes. On the other hand, **applied research** in biological psychology takes findings from basic research and uses them to solve real-world issues. Examples of applied research include developing therapeutic interventions for mental disorders, devising strategies to optimize learning and memory, or creating neurofeedback methods for stress reduction. While the two types of research may seem distinct, they are interdependent. Basic research lays the groundwork for the applications that emerge from applied research, and applied research often raises new questions that drive basic research. In public and political debates, people sometimes argue for cutting funding of basic science because they contend it has no practical value. However basic science works in synergy with applied science—together they are both essential to the development of biological psychology and science more broadly.

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1.4: APPLICATIONS OF BIOLOGICAL PSYCHOLOGY

Biological psychology and related neuroscience fields are highly active areas of research. Billions of dollars are invested annually and tens of thousands of researchers study the brain and behavior. The vast endeavor to understand the brain will help unravel the mysteries of human nature and our human experience. Brain research also has impactful applications—it helps to heal brain damage and psychological disorders and guides the development of artificial intelligence and brain-compatible social policies (Eagleman & Downar, 2016).

Healing the brain. Brain damage and psychological disorders affect tens of millions of people each year. Basic brain science enhances patient care and treatment. Research on cellular and molecular mechanisms in the brain can lead to new drugs, ways to regrow neurons, and increased neural plasticity. Researchers have developed groundbreaking new technology like transcranial magnetic stimulation that stimulates the brain with magnetic pulses and can treat depression, or deep brain stimulation that uses brain implants to treat diseases like Parkinson's. Brain-computer interfaces pick up brain signals, analyze them, and translate them into commands for devices like wheelchairs or robotic arms. These can help people regain movement who have neuromuscular disorders including amyotrophic lateral sclerosis (ALS), spinal cord injury, or stroke (Figure 4).

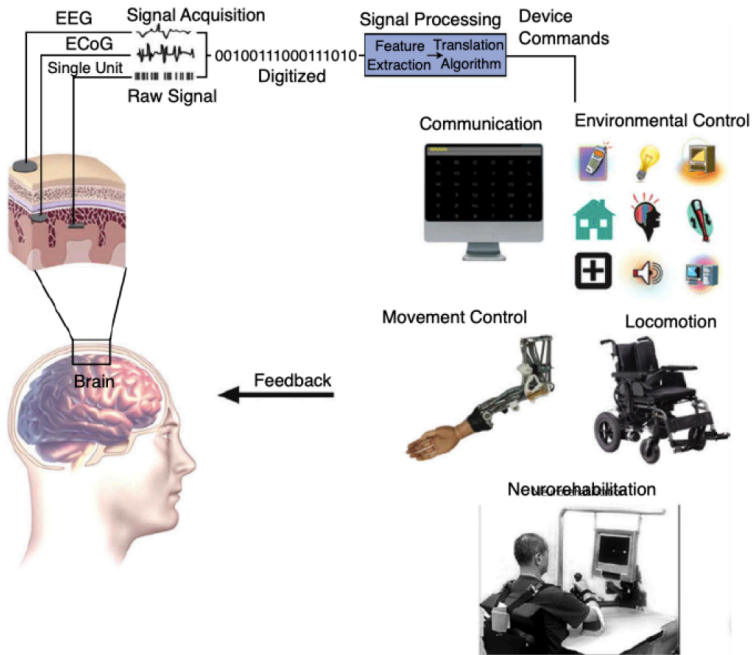


Figure 4. Components of a typical Brain-Computer Interface system that picks up brain signals, analyzes them, and translates them into commands to an external output device like a wheelchair or robotic arm.

Guiding Artificial Intelligence. Neuroscience is intertwined with artificial intelligence (AI). Understanding biological brains is important for building artificial brains and neuroscience has inspired the design of AI systems (Hassabis et al., 2017). Like neurons in the human brain, artificial neural networks have many interconnected units that work in parallel. Neuroscience provided early guidance for AI-system architecture (e.g., units organized in many layers) and algorithms (e.g., a “backpropagation algorithm” that adjusts the connections between units across multiple layers to enable learning). Another example of neuroscience-inspired AI is in attention—until recently artificial neural networks processed an entire image or video frame with equal priority given to all pixels. Conversely, humans focus on one small aspect at a time and strategically shift our

“spotlight of attention.” By incorporating a biologically-inspired approach with prioritized focus, AI-image processing improved performance and efficiency (Hassabis et al., 2017).

AI has recently made dramatic advances thanks to breakthroughs in “deep learning” and “reinforcement learning” methods (wherein learning is optimized by reinforcing or rewarding when desired outcomes occur). By incorporating principles from neuroscience, AI researchers have improved the efficiency and accuracy of AI algorithms, resulting in significant advances in areas like computer vision, decision-making, and natural language processing. Popular AI tools for text generation (like ChatGPT, Claude, and LLaMa) and image creation (like Stable Diffusion and DALL-E) are built on principles derived from neuroscience. Finally, advances in AI that were inspired by neuroscience are now being applied back to neuroscience as tools to understand the brain. For example, AI and deep learning approaches can analyze neuroimaging data, build computational models to simulate and study the brain, and predict the trajectory of psychological disorders or diseases like Alzheimer’s (Kreigeskorte & Douglas, 2018; Colliot, 2023).



Figure 5. AI-generated image from DALL-E 3 using the prompt “Artificial Intelligence computer system inspired by neurons and brains.”

Brain-compatible social policies. As outlined by Eagleman and Downar (2016), brain science can also have payoffs in guiding brain-compatible social policies. For example, psychology and neuroscience research has implications for how to view and address drug addiction. Advances in psychopharmacology and neuroscience reveal that addiction is driven by brain processes. As a result, policies that attack only drug *supply* are typically unsuccessful—if one point of supply is busted, another will pop up soon because the demand remains. Instead, policies should focus on attacking the demand for drugs. Treatments rooted in disrupting the brain

circuits driving addiction will be more effective than an incarceration-focused approach.

Finally, a large portion of the prison population in the U.S. is mentally ill. The prevalence of serious mental illness in jail inmates is around 15% for men and 31% for women (Steadman et al., 2009). Jails and prisons have become mental health care facilities. For example, the Rikers Island prison is New York's largest mental institution (Ransom & Harris, 2023), and more mentally ill persons are in jails and prisons than are in hospitals (Torrey et al., 2010). Brain science demonstrates that psychological disorders are rooted in the brain, so one must ask whether policies that support and treat those with mental-health problems might keep them from committing crimes, and whether a treatment approach could be more humane and cost-effective (Eagleman & Downar, 2016).

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1.5: RESEARCH WITH ANIMALS

To understand the human brain and human psychology, ideally we would only study humans. But some research cannot be conducted with humans, so biopsych researchers also perform research with animals. Most psychological research using animals is now conducted with rats, mice, and birds, as the use of other animals such as non-human primates is declining (National Research Council, 2011; Thomas & Blackman, 1992). Like research with humans, all research plans with animals must be reviewed by ethics boards to ensure that they meet important ethical principles such as:

- Use animals in research *only if* there is a reasonable expectation that the research will provide some benefit such as increasing understanding of the structures and processes underlying behavior or benefiting the health and welfare of humans or other animals.
- Use a procedure that subjects animals to pain or stress *only if* an alternative procedure is not available and the research goals are justified by its prospective scientific, educational, or applied value.
- Make every effort to minimize discomfort, illness, and pain of the animals.

People naturally disagree about the practice of using animals in research. Although many people accept the value of such research (Plous, 1996), a minority of people, including some animal-rights activists, believe that it is ethically wrong to conduct research on animals because animals are living creatures just as humans are, so no harm should be done to them.

Most scientists, however, argue that such beliefs ignore the benefits that

can come from animal research (Stangor et al., 2019). For instance, drugs to prevent or treat polio, diabetes, smallpox, cancer, or Alzheimer's disease may first be tested on animals, and surgery that can save human lives may first be practiced on animals. Research on animals has also led to a better understanding of the physiological causes of depression, phobias, and stress, among other illnesses. Many scientists believe that because there are many possible benefits from animal research, such research should continue as long as the animals are treated humanely and ethical principles mentioned above are met. The animal-research debate is complex, not a simple yes-or-no issue. Animal-rights advocacy has improved lab-animal welfare and conditions.

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1.6: DIVERSITY IN BIOLOGICAL PSYCHOLOGY

While biological psychology is diverse in the approaches to study the brain, historically the people involved in the research have not been especially diverse. Most early research was done by men of European descent due to social and cultural factors, systemic barriers, and unconscious biases. The field has been getting more diverse in the last decades and many leading labs are headed by women and historically underrepresented minorities. Diversity both across and within labs contributes to better quality science. If everyone has the same background and viewpoint, innovation lags because novel ideas are generated less often and new ideas may be derided and viewed as dissenting. Unique perspectives advance science, and research shows that more diverse groups outperform less diverse groups in many settings (Page, 2008). Diversity in science can be increased with policies and programs that address bias, harassment, mentorship, work-life balance, and educational and training opportunities, so that all have equal opportunity to succeed (Greider et al., 2019; National Academies of Sciences, Engineers, and Medicine, 2023).

Another area lacking diversity in biological psychology is in the research subjects. The vast majority of research subjects in psychology studies (96% by one estimate) are from Western, Educated, Industrialized, Rich, and Democratic (“WEIRD”) societies. These WEIRD subjects represent a very narrow slice of humankind, and research findings from them don’t necessarily generalize to other populations or serve the goal of understanding *human* psychology (Henrich et al., 2008).

Likewise, most participants in mental health studies, such as those looking at genetic risk in psychiatric disorders, have been of European ancestry. It is unclear how those studies benefit people of differing

ethnicities who may have different mental health needs and respond differently to treatments (Gordon, 2018). Research on diverse populations is crucial considering the long-standing disparities in mental health care—individuals from racial and ethnic minority groups, those with lower socioeconomic status, and residents of rural areas, are more likely to receive lower-quality mental health care (Agency for Healthcare Research and Quality, 2016). Funding agencies, including the National Institute of Mental Health (NIMH), are increasingly paying attention to the importance of including people from diverse backgrounds when developing funding mechanisms and reviewing grant proposals, which ultimately shapes the direction of the science.

In sum, biological psychology benefits from researchers and participants with different backgrounds to enrich the quality and creativity of the science, and make the findings and field more relevant and applicable for all.

1.7: OVERVIEW OF THE BOOK

This book consists of 12 chapters. It starts by covering foundations of biological psychology (e.g., brain anatomy, neurons, research methods), continues to higher-level topics that link biology and psychology (how drugs and hormones affect the brain and behavior, brain development, memory, genetics and emotions), and concludes with how things can go wrong in the brain (brain damage, neurological diseases, and psychological disorders). Here is a brief overview of each chapter:

Chapter 2 introduces the anatomy and structure of “**The Brain and Nervous System.**” It describes the organization of the central and peripheral nervous systems and introduces major brain regions and terminology that will be used in later chapters.

Chapter 3 on “**Neurons**” provides an overview of the basic structure of neurons and their means of communication. The goal of this chapter is to learn the anatomical structure of neurons and understand how they communicate via electrochemical signals to process sensory information and produce complex behaviors.

Chapter 4 introduces the “**Research Methods in Biological Psychology.**” Biological Psychology is a wide-ranging field, so not surprisingly, it employs many research techniques. Early insights into the function of specific brain regions emerged from rare cases of focal brain damage. Today, researchers can observe brain activity using brain recording methods like EEG, fMRI, and PET. Researchers can also test theories by activating or deactivating neurons with, for example, strong magnets (transcranial magnetic stimulation) or genetic manipulation (e.g., optogenetics). Much of what we know about the brain comes from studies with laboratory animals that use invasive research methods like implanting electrodes into animals’ brains or modifying an animal’s genes.

Chapter 5 introduces “**Psychopharmacology,**” or the study of how

drugs affect behavior. Drugs that change the way you think or feel are called psychoactive or psychotropic drugs, and almost everyone has used such a drug (yes, caffeine and alcohol are psychoactive). Drugs can increase or decrease activity at a neuron's synapse by blocking or mimicking the naturally occurring neurotransmitters. This can alter brain activity, and in turn, subjective experience, mood, behavior, and mental and physical health. This chapter examines the use of drugs to treat psychiatric disorders, and concludes with animations of how drugs like alcohol, caffeine, and cannabis affect neurotransmitters and synaptic processing in the brain.

Chapter 6 “**Hormones, Sex & Gender**” introduces the intricate relationships between hormones, brain, behavior, sex, and gender. Hormones are chemical messengers released from endocrine glands that travel through the blood system to influence the nervous system and regulate behaviors such as aggression, mating, and parenting. The chapter discusses how hormones shape biological sex characteristics, examines evidence for sex differences in psychology and the brain, and concludes with the diverse and variable nature of sex, gender, and sexual orientation.

Chapter 7 “**Development of the Brain and Nervous System**” covers the stages of development from the neural tube in the embryo to fully formed brain structures in adulthood. We discuss early neural growth and migration, the key developmental process of programmed neuron death, and the recent discovery of adult neurogenesis (adults do generate new neurons). The chapter covers neuroplasticity (the brain's ability to change), how plasticity varies across the lifespan (e.g., in sensitive periods), and tradeoffs between brain plasticity and processing efficiency. Brain plasticity and development have ramifications for learning, maturation, treatment of disorders, and staving off age-related declines.

Chapter 8 on “**Learning & Memory**” explores fundamental types of memory, including working, declarative, and nondeclarative memory, and examines the crucial brain structures involved, such as the hippocampus. It highlights the seminal case of Patient HM. The chapter delves into memory processing stages and the importance of sleep in memory consolidation.

It introduces exciting new research on “targeted memory reactivation,” wherein sounds or smells can be used to strengthen memories during sleep. The chapter concludes with memory disorders and research-based tips for improving your memory.

Chapter 9 covers “**Genetics and Epigenetics in Psychology.**” Psychological researchers study genetics to understand the biological factors that contribute to certain behaviors. Genes (nature) and the environment (nurture) both influence brain structure and function, shaping our thoughts and behaviors. In this chapter, we review fundamental genetics and look at how behavioral geneticists study the relative contributions of genes and environment. We discuss gene-environment interactions, and the relatively new field of epigenetics, which studies how the environment and behaviors can cause changes in how our genes work.

Chapter 10 on “**Emotion and Affective Neuroscience**” provides a brief overview of the neuroscience of emotion. The chapter integrates findings from human and animal research to describe the brain networks and associated neurotransmitters involved in basic affective systems and emotions such as fear, anger, pleasure, and love (Harmon-Jones & Harmon-Jones, 2023).

Chapter 11 “**Brain Damage, Neurodegeneration, and Neurological Disease**” presents some ways that healthy brain function can be disrupted. Understanding brain dysfunction helps appreciate the delicate balance and fragility of a healthy brain, and is important for developing effective treatments for brain damage and neurodegeneration. In the Neurological Disease section, we cover Parkinson’s Disease, Alzheimer’s Disease, and Multiple Sclerosis. In the Brain Damage section, we cover Stroke, Brain Tumors, and Traumatic Brain Injury (TBI). TBI has many causes including the widely recognized risks from contact sports or car accidents; a less recognized but rampant cause of TBI is Domestic or Intimate Partner Violence (IPV). To introduce that topic, we turn to an expert researcher from Harvard Medical School, Prof. Eve Valera. Note that this content can be distressing, especially for those directly or indirectly affected by IPV. We

provide CDC (Center for Disease Control and Prevention) resources on addressing and preventing Intimate Partner Violence.

Chapter 12 covers the “**Biopsychology of Psychological Disorders.**” Psychological disorders can be linked to brain dysfunction and genetic factors. This chapter examines such biological underpinnings and the symptoms of several common psychological disorders including schizophrenia, depression, bipolar disorder, anxiety, obsessive-compulsive disorder, and post-traumatic stress disorder. We briefly present some common biologically-based treatments for these disorders.

1.8: BRAIN AND BEHAVIOR BEYOND THIS BOOK

This book covers a lot of material, but much more could be included in a course on biological psychology. Some textbooks contain 30 or more chapters. Your teacher may supplement this book with material on additional topics such as movement control, perception, language processing, or the neural correlates of consciousness. We've tried to be concise; hopefully these 12 chapters provide a foundation for understanding brain-behavior links and spark your interest to continue learning about the brain and behavior in other courses or on your own.

Brain science is an exciting and rapidly developing field with an astounding amount of new information—more than 35,000 papers are published each year in neuroscience journals and the number has been increasing each year (Eagleman & Downar, 2016; Yeung et al., 2017). With so much new information, even trained scientists struggle to keep up with new developments, and students looking to learn more or enter the field often don't know where to start.

In addition to coursework, motivated students can learn about areas of their interest in many ways. For example, **popular press books** by leading researchers provide accessible overviews of a research area. More advanced undergraduates may dive deeper and find inspiration in **academic books** that are aimed at researchers in the field; academic books can be challenging to read, but they can be transformative and expand scholarly horizons (one way to find titles of interesting academic books is by searching the websites of academic publishers like [MIT Press](#) or [Oxford University Press](#)). Another challenging, but rewarding way to learn about recent big-picture advances is to read **review journal articles** that consolidate research findings. Some top academic journals specialize in publishing review

articles such as: *Nature Reviews Neuroscience*, *Current Opinion in Psychology*, *Trends in Cognitive Science*, and *Trends in Neuroscience*. You can find articles by entering your keywords of interest and a journal name into a search engine like scholar.google.com; links to full-text articles are often available, and when the article is behind a paywall, you might be able to access it through your university library or another [method](#). Finally, you can learn a lot about the brain from **online resources**, such as neuroscience-related websites like the [Dana Foundation](#), videos of research talks (e.g., TED talks or seminar presentations such as those archived at the [World Wide Neuro](#) website), or from the many great podcasts related to the brain (e.g., [The Brain Science Podcast](#) or [Brain Inspired](#)).

May your journey into the brain be interesting, enjoyable, and rewarding.

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CHAPTER 2: THE BRAIN AND NERVOUS SYSTEM

The Brain and Nervous System Learning Objectives

- Learn about the central and peripheral nervous systems and their subdivisions including the sympathetic and parasympathetic nervous systems
- Know terms to describe locations in the brain such as anterior, posterior, inferior, superior, dorsal, ventral, medial, and lateral
- Know the coronal, sagittal, and horizontal anatomical planes used to visualize the brain in two dimensions
- Describe the basic functions of the brainstem, cerebellum, thalamus, hypothalamus, and cerebral hemispheres
- Understand the differences between gray matter and white matter
- Learn about the four lobes of the cerebral cortex: occipital, temporal, parietal, and frontal lobes.
- Learn about the roles of major subcortical structures including the basal ganglia, hippocampus, amygdala, thalamus, and hypothalamus
- Understand important non-neuronal structures, including the meninges that surround and protect the brain, the

ventricles that contain cerebrospinal fluid, and the vasculature that supplies blood throughout the brain

2.1: INTRODUCTION

This chapter focuses on the structures of the brain and nervous system. Understanding brain structures is crucial to psychology, as they underpin mental processes. This book explores the role of different brain regions in cognition, emotion, perception, and neurological and psychological disorders.

An introduction to biological psychology can be fascinating, but also challenging for new students due to the extensive vocabulary and new information about nervous system structures. We encourage you to not get bogged down in vocabulary. Instead, on a first reading, pay particular attention to the broader concepts. Then, once familiar with the topic, pass back through with attention to learning the vocabulary. With the help of the figures and some studying, you can master nervous system terminology.

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2.2: VISUALIZING AND NAVIGATING THE HUMAN BRAIN

Before diving into nervous system organization, we present some important anatomical terms for visualizing and navigating the brain. The brain is a three-dimensional (3-D) structure that can be visualized in two-dimensional (2-D) slices. There are three standard anatomical planes for visualizing the brain: 1) the coronal or frontal plane; 2) the sagittal plane; and 3) the horizontal or axial plane (Figure 1). The coronal or frontal plane is a vertical plane and splits the brain into front and back sections. The sagittal plane is a vertical plane which splits the brain into left and right sections. The horizontal or axial plane is a horizontal plane which splits the brain into upper and lower sections.

Sectional Planes

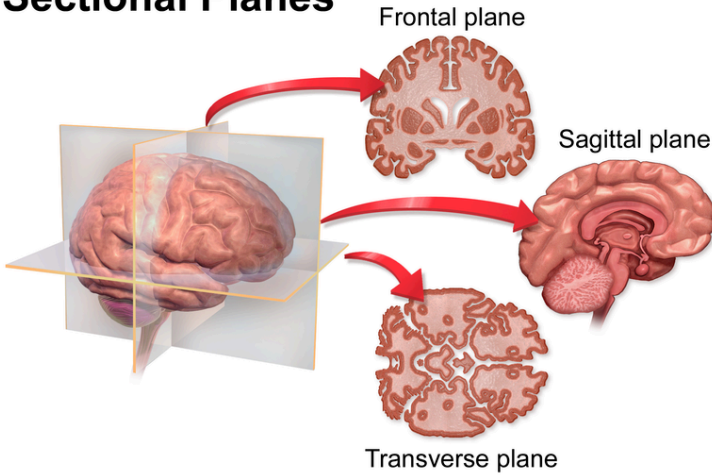


Figure 1: Slices of the human brain. Three possible 2-D cuts through the brain: a coronal or frontal slice (top image), a sagittal slice (middle), and a transverse, horizontal or axial slice (bottom).

Conventional terms describe locations and directions in the brain and are helpful for navigating around the brain.

- *Anterior* means toward the front of the brain; *Posterior* means toward the back of the brain.
- *Rostral* means toward the front or the “beak”; *Caudal* means toward the tail end.
- *Superior* means toward the top; *Inferior* means toward the bottom.
- *Dorsal* means toward the top or back (think dorsal fin); *Ventral* means toward the belly.
- *Medial* means toward the middle; *Lateral* toward the side.
- *Contralateral* means on the opposite (left/right) side; *Ipsilateral* means on the same side.

You’ll hear these terms a lot as you learn about the brain.

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2.3: THE NERVOUS SYSTEM

The [nervous system](#) can be thought of as the body's command center and communication network; it processes information, relays sensory input, and coordinates actions by transmitting signals to and from other body parts (Ahmad, 2023). The nervous system is divided into the **central nervous system** (CNS) and the **peripheral nervous system** (PNS) (**Figure 2**). The central nervous system consists of the brain and spinal cord. The peripheral nervous system consists of nerves outside the brain and spinal cord and forms the communication network between the CNS and other body parts. The PNS has several subdivisions that we explore in more detail in the following section.

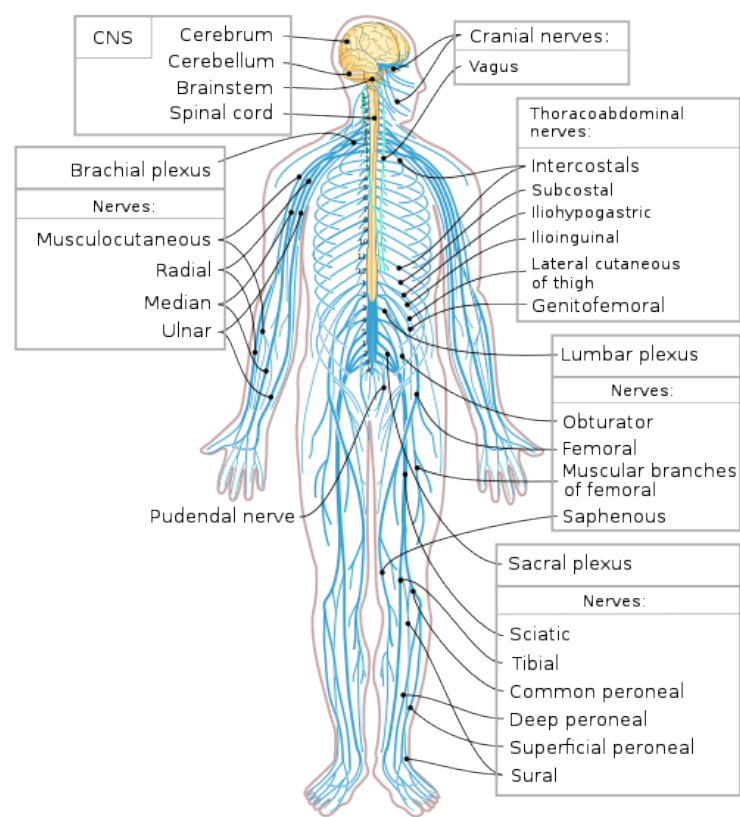


Figure 2. The human nervous system. The Central Nervous System (CNS), shown in yellow, is made up of the brain and spinal cord. The Peripheral Nervous System (PNS), shown in blue, is made up of nerves that connect the brain and spinal cord to the rest of the body.

Text Attributions

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2.4: THE PERIPHERAL NERVOUS SYSTEM

The **peripheral nervous system** (PNS) connects the central nervous system with the rest of the body. It serves as a communication relay between the CNS and muscles, organs, and glands. The peripheral nervous system includes nerves that are connected to the brain (cranial nerves) and the spinal cord (spinal nerves). Unlike the CNS, the PNS is not protected by the bone of the skull and spine. Nor does it have a barrier between itself and the blood (like the blood-brain barrier), leaving it exposed to toxins and mechanical injuries .

The PNS can be divided into the **autonomic nervous system**, which controls bodily functions without conscious control, and the **somatic nervous system**, which transmits sensory information from the skin, muscles, and sensory organs to the CNS and also sends motor commands from the CNS to the muscles (Figure 3).

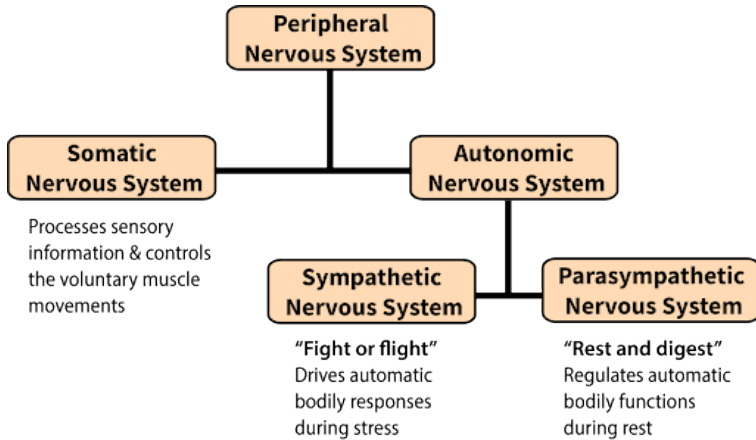


Figure 3: Components of the peripheral nervous system.

The Autonomic Nervous System

The autonomic nervous system serves as the relay between the CNS and the internal organs. It controls the lungs, the heart, smooth muscle, and exocrine and endocrine glands. The autonomic nervous system controls these organs largely without conscious control. It can continuously monitor the conditions of these different systems and implement changes as needed. There are two divisions of the autonomic nervous system that often have opposing effects: the **sympathetic nervous system** and the **parasympathetic nervous system**.

The Sympathetic Nervous System. The sympathetic nervous system is responsible for the “fight or flight” response that occurs when an animal encounters a dangerous situation. One way to remember this is to think of the surprise a person feels when encountering a snake (“snake” and “sympathetic” both begin with “s”). Examples of functions controlled by the sympathetic nervous system include an accelerated heart rate and inhibited digestion. These functions help prepare an organism’s body for

the physical strain required to escape a potentially dangerous situation or to fend off a predator.

The Parasympathetic Nervous System. While the sympathetic nervous system is activated in stressful situations, the parasympathetic nervous system allows an animal to “rest and digest.” One way to remember this is to think that during a restful situation like a picnic, the parasympathetic nervous system is in control (“picnic” and “parasympathetic” both start with “p”). The parasympathetic nervous system resets organ function after the sympathetic nervous system is activated (the common adrenaline dump you feel after a ‘fight-or-flight’ event). Thus the sympathetic and parasympathetic nervous systems work in a push–pull manner (**Figure 4**). Examples of functions controlled by the parasympathetic nervous system include slowing of heart rate, lowered blood pressure, and stimulation of digestion.

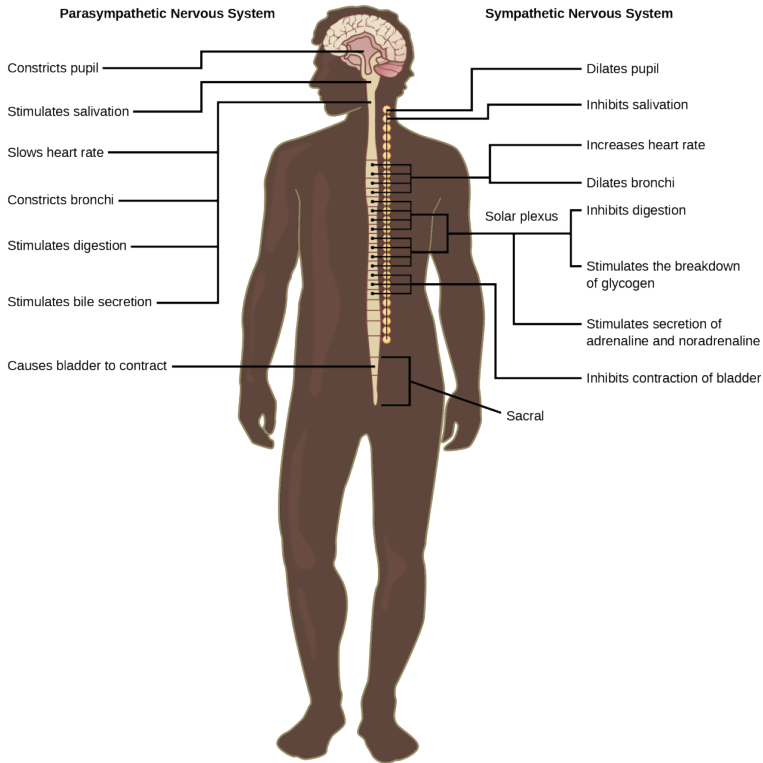


Figure 4. The sympathetic and parasympathetic nervous systems often have opposing effects on target organs.

The Somatic Nervous System

The somatic nervous system manages external interactions: sensing the environment via sensory neurons and sending commands to skeletal muscles via motor neurons. It often governs voluntary behaviors initiated by complex brain processes. For example, you hear your name, interpret the speech, and turn your head towards the sound.

The somatic nervous system is made up of cranial and spinal nerves and contains both sensory and motor neurons. Sensory neurons transmit

sensory information from the skin, skeletal muscle, and sensory organs to the CNS. Motor neurons transmit messages about desired movement from the CNS to skeletal muscles to make them contract. Without a somatic nervous system, an animal would be unable to process any information about its environment (what it sees, feels, hears, etc.) and could not control motor movements.

Cranial nerves. Humans have 12 cranial nerves; these nerves emerge from the skull (cranium), as opposed to the spinal nerves, which emerge from the vertebral column. Each cranial nerve is accorded a name, as shown in **Figure 5**. Some cranial nerves transmit only sensory information. For example, the olfactory nerve transmits information about smells from the nose to olfactory regions in the brain. Other cranial nerves transmit almost solely motor information. For example, the oculomotor nerve controls the opening and closing of the eyelid and some eye movements. Other cranial nerves contain a mix of sensory and motor fibers. For example, the glossopharyngeal nerve has a role in both taste (sensory) and swallowing (motor).

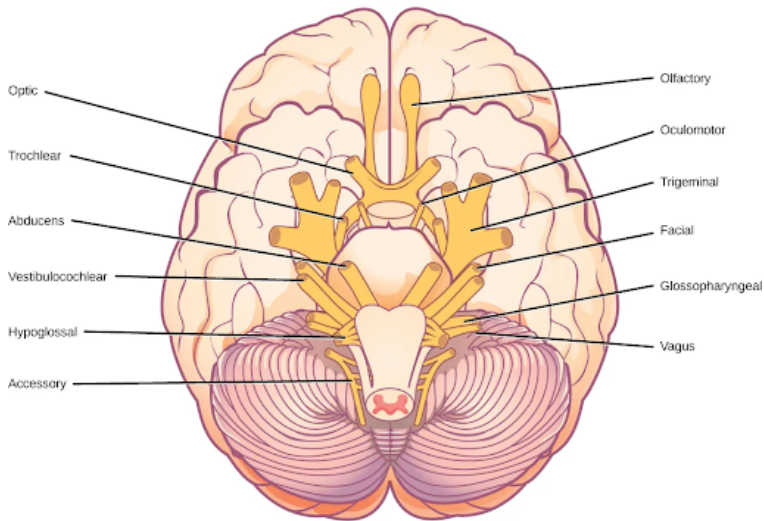


Figure 5. Inferior view (from below) of the human brain showing the 12 cranial nerves in orange. Cranial nerves receive sensory input and control motor output for the head and neck.

Spinal nerves. Spinal nerves transmit sensory and motor information between the spinal cord and the rest of the body. Each of the 31 spinal nerves in humans contains both sensory and motor axons. The sensory neuron cell bodies are grouped in structures called dorsal root ganglia (dorsal = toward back) (**Figure 6**). Each sensory neuron projects from a sensory receptor in skin, muscle, or sensory organs to a synapse with a neuron in the dorsal spinal cord. Motor neurons have cell bodies in the ventral gray matter of the spinal cord that project to muscle through the ventral root (ventral = toward belly). These neurons are usually stimulated by interneurons within the spinal cord but are sometimes directly stimulated by sensory neurons (as in a reflex arc). Each spinal nerve corresponds to different body regions—for example, spinal nerves that exit near the top of the spine correspond to the shoulders and arms, whereas spinal nerves that exit near the bottom of the spine correspond to legs and feet (**Figure 7**).

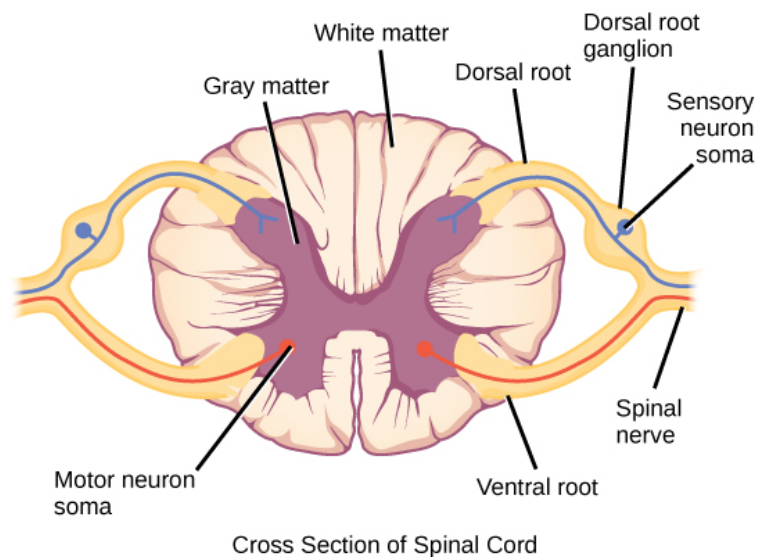


Figure 6. Spinal nerves contain both sensory and motor axons. The somas (cell bodies) of sensory neurons are located in dorsal root ganglia. The somas of motor neurons are found in the ventral portion of the gray matter of the spinal cord.

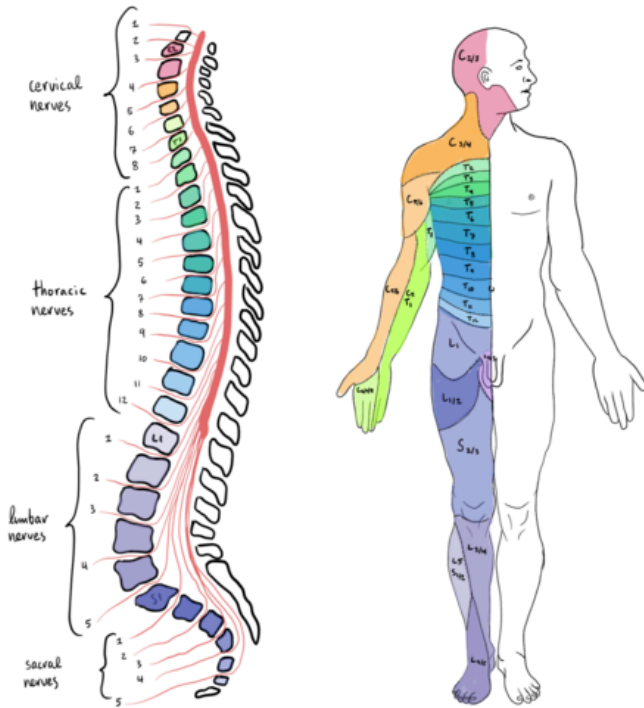


Figure 7. Spinal nerves exit the spinal cord through notches in the vertebrae. This figure illustrates the spinal cord segments in the vertebral column (cervical, thoracic, lumbar, sacral), and how each spinal nerve relates to different regions of the body.

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The Nervous System in General Biology (Boundless).

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Hall, C. N. (2023). 2 Exploring the brain: A tour of the structures of the nervous system. In *Introduction to Biological Psychology*. University of Sussex Library. Access for free at <https://openpress.sussex.ac.uk/introductiontobiologicalpsychology/chapter/exploring-the-brain-a-tour-of-the-structures-and-cells-of-the-nervous-system/> License: CC BY-NC 4.0 DEED

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2.5: THE CENTRAL NERVOUS SYSTEM

The **central nervous system** is made up of the brain and spinal cord. The brain and spinal cord are enclosed in three layers of protective coverings called meninges (from the Greek word for membrane) (**Figure 8**). The outermost layer is the dura mater (Latin for “hard mother”)—a thick layer that protects the brain and spinal cord and contains large blood vessels. The middle layer is the web-like arachnoid mater. The innermost layer is the pia mater (Latin for “soft mother”), which directly contacts and covers the brain and spinal cord like plastic wrap. The subarachnoid space between the arachnoid and pia mater is filled with cerebrospinal fluid (CSF), a fluid that helps cushion and protect the brain and spinal cord. We examine CSF more in the next section on The Brain.

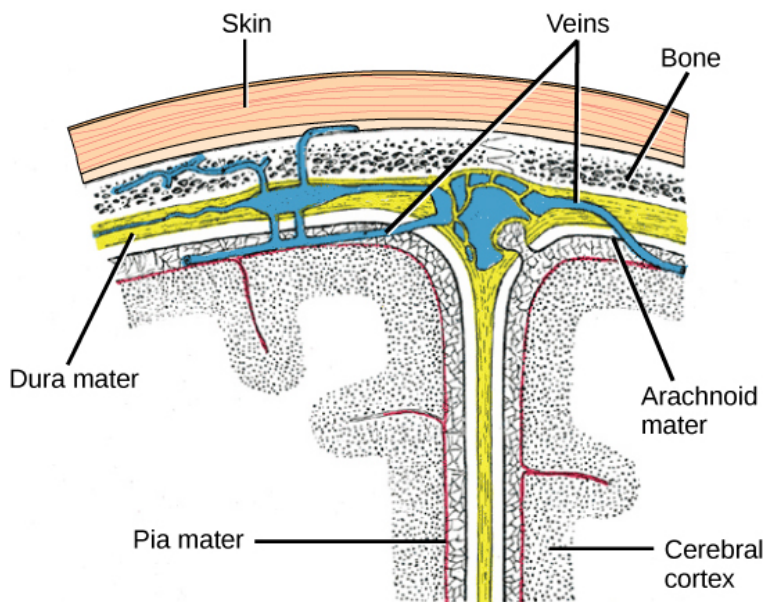


Figure 8. The cerebral cortex is covered by three layers of meninges: the dura, arachnoid, and pia maters (Credit: modification of work by Gray's Anatomy).

The Spinal Cord

The spinal cord is the major bundle of nervous tissues that extends from the brainstem down the backbone to the lumbar region of the spine. The spinal cord transmits information from the skin, muscles, and internal organs to the brain, and vice versa. Information that travels from the bodily periphery *toward* the brain (or deeper centrally within the brain) is called an **afferent** signal. Information that travels *away* from the brain, such as a motor command to a muscle, is called an **efferent** signal.

In addition to sending information to and from the brain, the spinal cord controls some simple reflexive movements like removing your hand from a hot object and the knee reflex. These reflexive movements are very fast because the sensory signal is processed and the motor command is

initiated directly in the spinal cord. Processing in the spinal cord avoids the time-consuming signal transmission to and from the brain, saving hundreds of milliseconds to protect our tissue from damage.

The spinal cord also houses central pattern generators that control some simple rhythmic movements such as walking. Experiments with cats have shown that even after severing the spinal cord (thereby cutting off motor commands from the brain), cats can still produce relatively normal walking on a treadmill (Duysens & Van de Crommert, 1998).

The spinal cord is protected by the bony vertebrae in the backbone and cushioned by cerebrospinal fluid. However spinal cord injuries still can occur and are very serious. In the United States, around 10,000 spinal cord injuries occur each year. Because the spinal cord is the information superhighway connecting the brain with the body, damage to the spinal cord can lead to paralysis. The extent of the paralysis depends on the location of the injury along the spinal cord and whether the spinal cord was completely severed. For example, if the spinal cord is damaged at the level of the neck, it can cause paralysis from the neck down, whereas damage further down the spinal column may limit paralysis to the legs. Spinal cord injuries are notoriously difficult to treat because spinal nerves do not regenerate, although ongoing research suggests that stem-cell transplants may be able to act as a bridge to reconnect severed nerves.

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2.6: THE BRAIN

The brain is the most complex part of the human body, consisting of 86 billion neurons, each of which may connect with 1000s of other neurons. It is the center of higher-order processes like planning, memory, problem solving, and consciousness, and coordinates voluntary and involuntary movements and bodily functions. This section provides an introductory overview of the brain and some basic neuroanatomy.

The mammalian brain can be subdivided in many ways, resulting in some inconsistent and ambiguous naming conventions over the history of neuroanatomy (Swanson, 2000). One way to think about brain organization reflects brain development in the embryo. The human nervous system starts as a simple neural tube, and 3-4 weeks after conception, the tube expands into three primary vesicles—the forebrain, midbrain, and hindbrain. After a few more weeks, these primary vesicles give rise to secondary vesicles that eventually develop into the components of the adult nervous system (more detail on brain development in Chapter 7). As seen in **Figure 9**, the forebrain vesicle develops into a) the **cerebrum**, which includes the cerebral cortex (frontal, temporal, parietal, and occipital lobes) and underlying **subcortical** structures (e.g., the hippocampus, amygdala, and basal ganglia), and b) the **diencephalon**, which includes the thalamus and hypothalamus. The midbrain primary vesicle develops into part of the brainstem, including the superior and inferior colliculi. The hindbrain develops into the cerebellum and other brainstem regions including the pons and medulla oblongata. We introduce these brain structures in the section below.

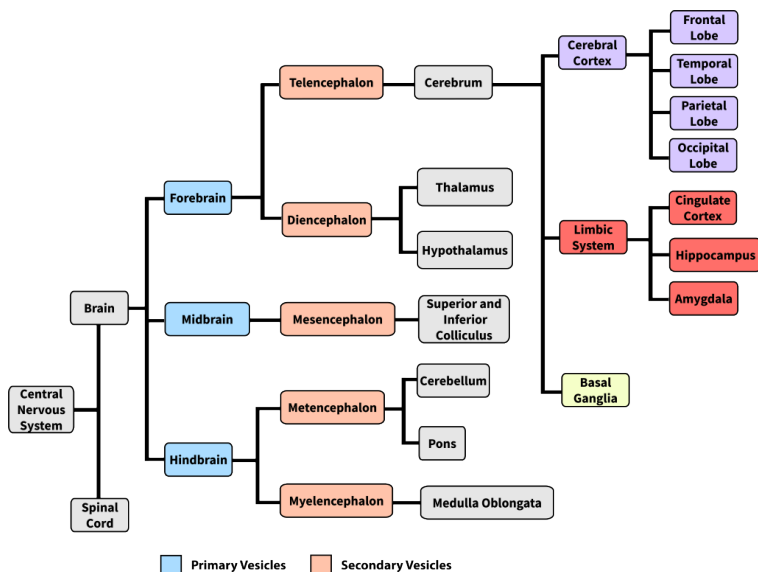


Figure 9: The central nervous system and its various major subdivisions.

Cerebral Cortex

The **cerebral cortex** is a thin sheet of neurons that makes up the outermost layer of the **cerebral hemispheres**. The term **cortex**, derived from the Latin for “bark,” refers to a thin sheet of neurons; in contrast, the term **nucleus** (plural: nuclei) in neuroanatomy refers to a cluster of neurons. The cerebral cortex is made up of **gray matter**, a type of tissue named for its color that consists largely of neuronal cell bodies and short-range connections. Conversely, **white matter** tissue consists largely of axons covered in myelin, a fatty white substance that insulates axons to speed the transmission of neural signals. White-matter fiber tracts underlie the gray matter of the cerebral cortex and send signals to more distant brain regions (**Figure 10**).

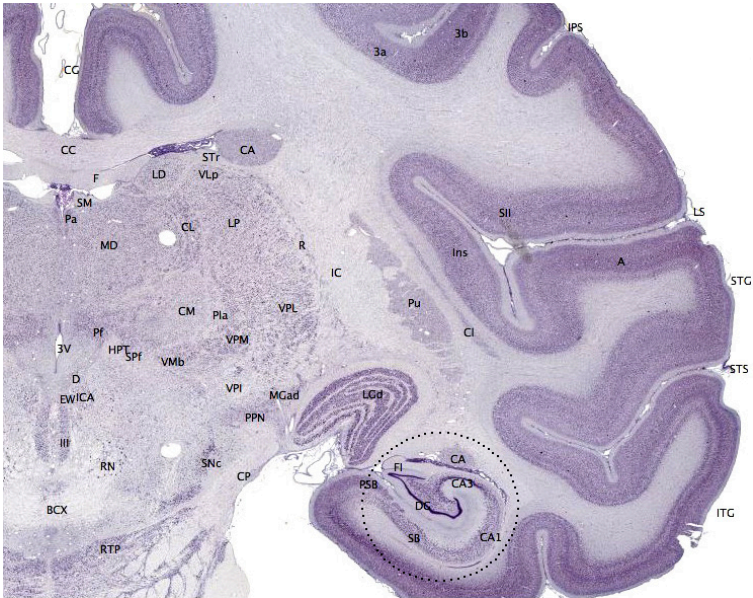


Figure 10. Coronal tissue slice from the brain of a macaque monkey. The gray matter of the cerebral cortex is the outer layer depicted in dark violet. The underlying white matter fiber tracts are shown in lighter color.

The cerebral cortex ‘bark’ is only 2–4 mm across, but most cortex consists of 6 layers. Each layer has characteristic cell types and connectivity—the innermost layers 5 and 6 send signals out of cortex, layer 4 receives input from the thalamus, layers 2 and 3 project to nearby regions within cortex, and layer 1 has very few cell bodies and mostly contains the tips of dendrites and axons (Hall, 2023).

The thin cortex has a surprisingly large surface area—the human cortex is about 1800 cm^2 , making the cortex in each hemisphere about the size of medium thin-crust pizza (minus the sauce, cheese, and toppings) (Van Essen et al., 2018) (**Figure 11**). This large surface area fits into the small volume of the cranium, because the human cortex is extensively folded (most other animals including small mammals have a smooth cortex).

Folding maximizes the surface-to-volume ratio, and improves packaging and communication efficiency (Shipp, 2007).

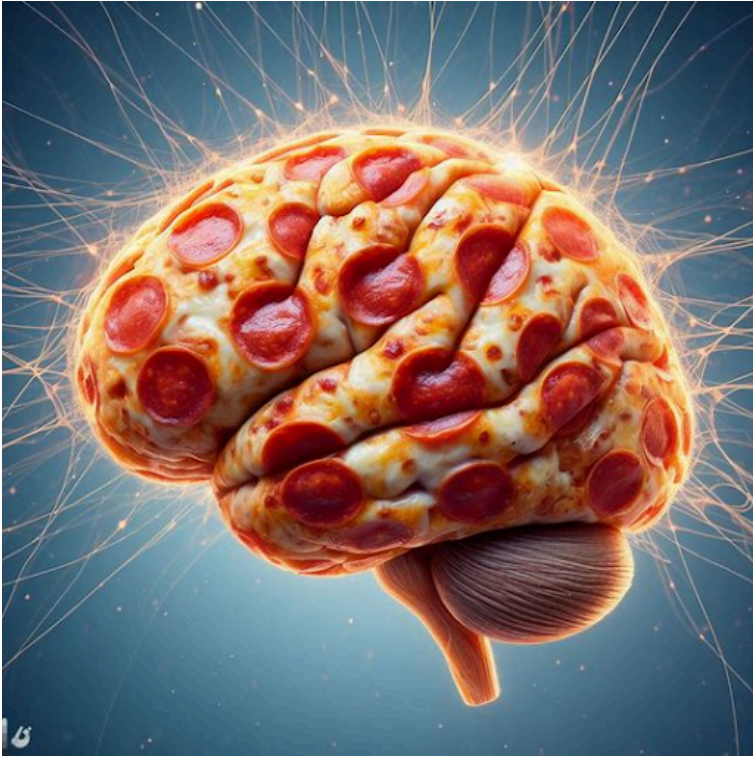


Figure 11. The thin outermost layer of each cerebral hemisphere, the cerebral cortex, is about the size of a medium thin-crust pizza—minus the sauce, cheese, and toppings.

The folding of the cortex also gives the brain its bumpy appearance. The bumps are called **gyri** (singular: **gyrus**) and the valleys between gyri are called **sulci** (singular: **sulcus**). Larger and deeper sulci are called **fissures**. Major gyri, sulci, and fissures are used as landmarks to separate the cortex into its major regions, including the frontal, temporal, parietal, and occipital lobes (**Figure 12**). The **central sulcus** marks the border between

the frontal and parietal lobes. The **lateral sulcus** (also called the Sylvian fissure), separates the temporal lobe from the frontal and parietal lobes. The occipital lobe has no obvious anatomical border on the outer surface of the brain. However, from the medial (inner) surface, an obvious landmark, the **parieto-occipital sulcus**, separates the parietal and occipital lobes.

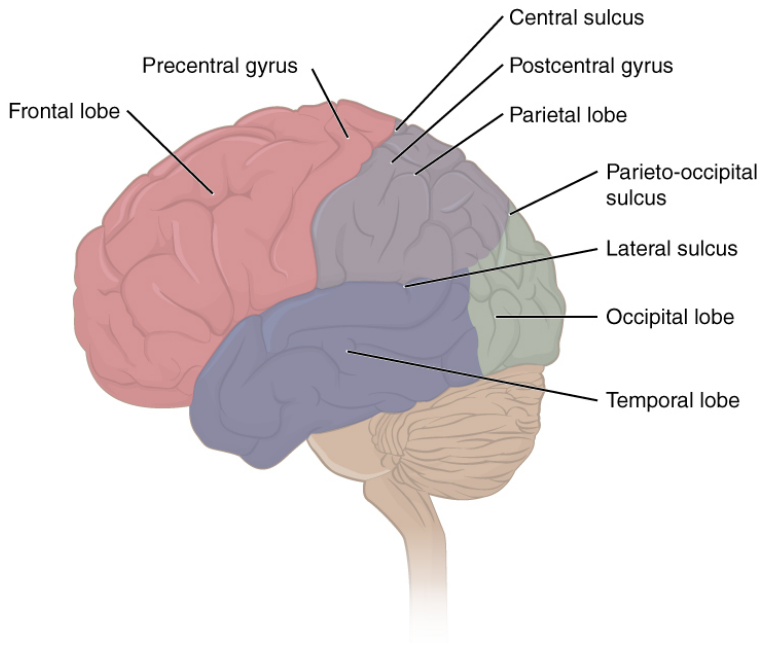


Figure 12: The lobes of the brain and the major sulci that mark the borders. The central sulcus separates the frontal and parietal lobes. The lateral sulcus marks the upper border of the temporal lobe. And the parieto-occipital sulcus (which is more clearly seen on the medial surface) separates the parietal and occipital lobes.

Another prominent landmark, the **longitudinal fissure**, runs down the brain's midline and separates the left and right cerebral hemispheres. The two cerebral hemispheres are connected to each other via the **corpus callosum**, a large white matter tract that passes information between

hemispheres. The left and right hemispheres are structurally symmetrical and often have overlapping and redundant functions, but there is some **lateralization** of function, where some brain functions are processed more in one hemisphere than the other. For example, touch signals and motor commands for each side of the body are processed in the contralateral (opposite) side of the brain, and language for most people is processed more in the left hemisphere.

Finally, smaller subregions of the cerebral cortex are associated with particular functions, a concept known as **localization of function**. In the early 1900s, a German neuroscientist named Korbinian Brodmann extensively studied the microscopic anatomy, or **cytoarchitecture**, of the cerebral cortex and divided the cortex into 52 separate regions based on the microscopic tissue structure. These “Brodmann areas” are still used today to describe anatomical regions within the cortex (**Figure 13**). Brodmann’s anatomical maps align well with the particular functions within the cortex. For example, Brodmann area 4 (as defined based on the microscopic tissue structure) aligns with the primary motor cortex that sends motor commands to the spinal cord.¹

1. This section contains material adapted from: Betts, J. G. et al. (2022). 13.2 The Central Nervous System. In *Anatomy and Physiology 2e*. OpenStax. Access for free at <https://openstax.org/books/anatomy-and-physiology-2e/pages/13-2-the-central-nervous-system> License: CC BY 4.0 DEED. – Hall, C. N. (2023). 2 Exploring the brain: A tour of the structures of the nervous system. In *Introduction to Biological Psychology*. University of Sussex Library. Access for free at <https://openpress.sussex.ac.uk/introductiontobiologicalpsychology/chapter/exploring-the-brain-a-tour-of-the-structures-and-cells-of-the-nervous-system/> License: CC BY-NC 4.0 DEED

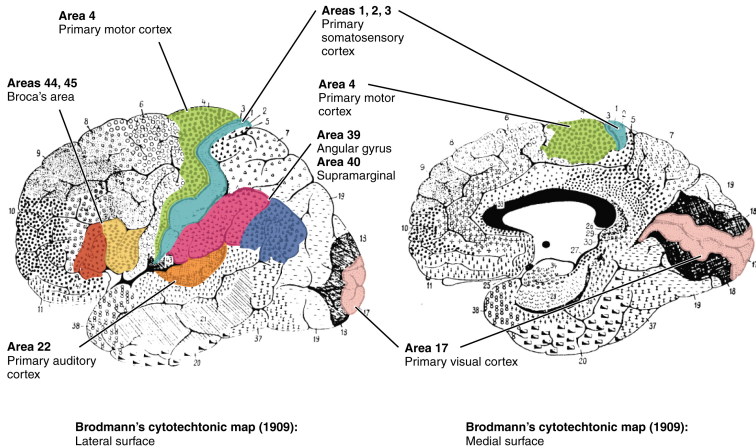


Figure 13. Brodmann's maps from 1909 that he built based on the cytoarchitecture or microscopic tissue structure and organization. Several important Brodmann areas are shown on the brain's lateral surface (left) and the medial surface (right).

Frontal Lobe

The **frontal lobe**, located in the front of the brain (where else?), is involved in planning and implementing movement, as well as higher-order cognitive processes such as attention, language, reasoning, problem solving, and abstract thought. The frontal lobe is made up of subregions that perform specialized functions. At the back of the frontal lobe is the precentral gyrus (the *gyrus* or bump directly *pre-* or anterior to the *central* sulcus); this region is the primary motor cortex, which contains neurons that send commands to the spinal cord to move skeletal muscles. Areas within the primary motor cortex map to different muscle groups in an ordered manner (**Figure 14**). Body parts that require especially fine motor control, like the fingers, lips, and tongue, occupy more “neural real estate” on the motor cortex than, say, the shoulder or trunk. Anterior to the primary

motor cortex are other areas associated with movement, including the premotor area (involved in movement planning) and the frontal eye fields (involved in eliciting eye movements and visual attention).

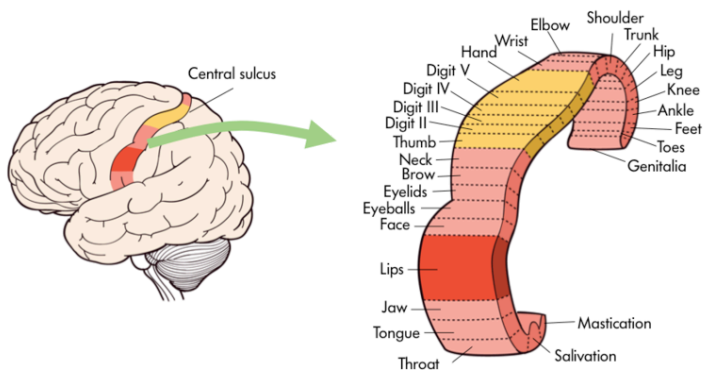


Figure 14. The primary motor cortex on the precentral gyrus is directly anterior to the central sulcus. It is organized so certain areas of the motor strip send signals to specific body parts like the tongue or fingers.

Anterior to the motor and premotor cortex is the prefrontal cortex (PFC), which is involved in many cognitive and executive functions (**Figure 15**). In the inferior prefrontal cortex (usually left lateralized) lies Broca's area (**Figure 16**), a region involved in language production. Broca's area is named after a French physician, Paul Broca, who in 1861, documented that damage here impaired speech production. Other major subregions of the prefrontal cortex include the dorsolateral PFC (dorsal=upper, lateral=outer) involved in working memory, planning, inhibiting responses, and cognitive flexibility, and the orbitofrontal cortex at the very front (by the orbits of the eye), which is involved in complex decision making, encoding value, emotion, sociality, and predicting the consequences of our actions (Rudebeck & Rich, 2018).

In general, more anterior regions in the brain and within the frontal lobe are roughly associated with 'higher' cognitive function, such as rule

learning at higher levels of abstraction. High-level abstract thought, executive function (such as maintaining goal-directed behavior), language, and navigating complex social contexts are crucial for what we consider “human” cognition. Indeed, the corresponding prefrontal regions are disproportionately large in humans and have expanded or reorganized in humans compared to other species, especially compared to species more distant on the evolutionary tree (Van Essen et al., 2018)

Humans with frontal lobe damage can have a variety of impairments depending on the location and extent of the damage. These impairments include changes in personality, cognition, learning, decision making, risk assessment, behavioral inhibition, and social function.²

2. This section contains material adapted from: Biswas-Diener, R. (2023). The brain and nervous system. In R. Biswas-Diener & E. Diener (Eds), Noba textbook series: Psychology. Champaign, IL: DEF publishers. Retrieved from <http://noba.to/4hzf8xv6> License: CC BY-NC-SA 4.0 DEED – Betts, J. G. et al. (2022). 13.2 The Central Nervous System. In Anatomy and Physiology 2e. OpenStax. Access for free at <https://openstax.org/books/anatomy-and-physiology-2e/pages/13-2-the-central-nervous-system> License: CC BY 4.0 DEED. – Clark, M.A., Douglas, M. & Choi, J. (2023). 35.3 The Central Nervous System. In Biology 2e. OpenStax. Access for free at <https://openstax.org/books/biology-2e/pages/35-3-the-central-nervous-system> License: CC BY 4.0 DEED.

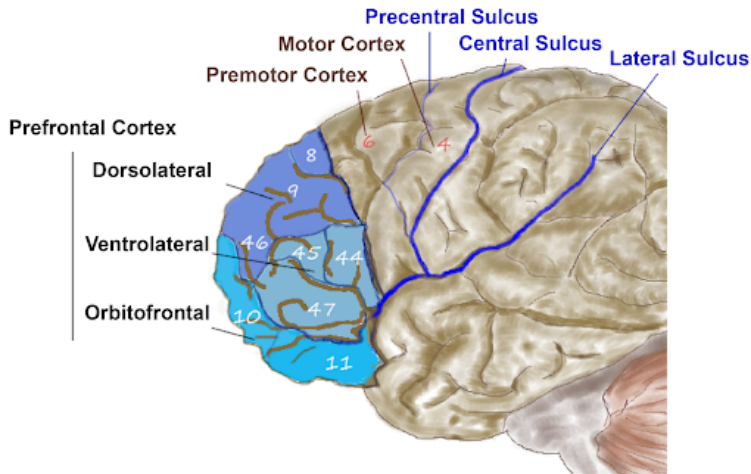


Figure 15. Prefrontal cortex in blue-ish colors. Subregions include: Broca's area marked by its Brodmann areas (BA) numbers 44 and 45; the dorsolateral prefrontal cortex [BA 9 and 46], and the orbitofrontal cortex [BA 10 and 11].

Temporal Lobe

The **temporal lobe** is located in the lateral portion of each hemisphere under the temples (hence “temporal”). It is involved in processing auditory information, understanding language, recognizing visual objects, and memory. The auditory cortex, which processes auditory information, is located in the superior temporal lobe. In the posterior part of the superior temporal lobe lies **Wernicke's area**, a region involved in language comprehension. Wernicke's area connects to the frontal Broca's area (involved in language production) through a white-matter fiber tract called the **arcuate fasciculus**, (Figure 16).

In addition to processing sound and language, the temporal lobe is critical for visual object recognition and memory. The ventral (bottom) surface of the temporal lobe receives visual signals from the visual cortex. It contains subregions specialized to perceive and recognize faces (the fusiform face area) and places and scenes (the parahippocampal place area). Damage to these regions, from a stroke for example, can impair specific abilities; inferior temporal lobe lesions may lead to prosopagnosia, the inability to recognize and identify faces (Kanwisher & Yovel, 2008). Finally, the medial temporal lobes are important for encoding long-term memory.³

3. This section contains material adapted from: Ahmad, A. (2024). The nervous system. In R. Biswas-Diener & E. Diener (Eds), Noba textbook series: Psychology. Retrieved from <http://noba.to/wnf72q34> License: CC BY NC SA 4.0 DEED. – Spielman, R. M., Jenkins, W. J., & Lovett, M. D. (2020). 3.4 The Brain and Spinal Cord. In Psychology 2e. OpenStax. Access for free at <https://openstax.org/books/psychology-2e/pages/3-4-the-brain-and-spinal-cord> License: CC BY 4.0 DEED.

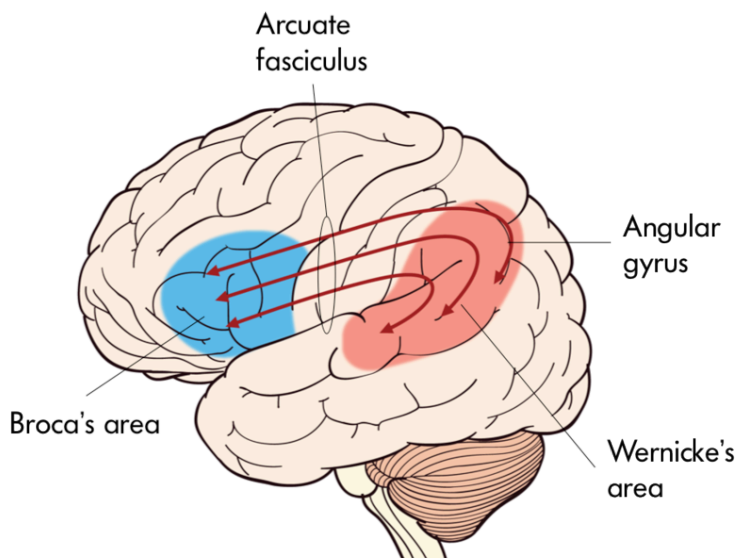


Figure 16. Broca's area in the left frontal gyrus; Wernicke's area in the superior temporal gyrus; and the arcuate fasciculus, a white matter tract that connects the caudal temporal cortex with the inferior frontal lobe.

Parietal Lobe

The **parietal lobe**, located above the temporal lobe and behind the frontal lobe, processes touch, bodily and spatial maps, and integrates senses. The postcentral gyrus (directly behind the central sulcus) houses the **primary somatosensory cortex (S1)**. This region processes the tactile senses, including touch, pressure, pain, itch, and vibration, as well as more general bodily senses of proprioception (body position) and kinesthesia (movement sense). The somatosensory cortex is organized topographically: adjacent skin areas are represented by adjacent cortical regions. Sensitive body parts have more nerve receptors on the skin and occupy larger cortical

areas than less sensitive parts. For example as seen in **Figure 17**, the highly sensitive fingers and lips occupy much more somatosensory cortex than the leg and trunk.

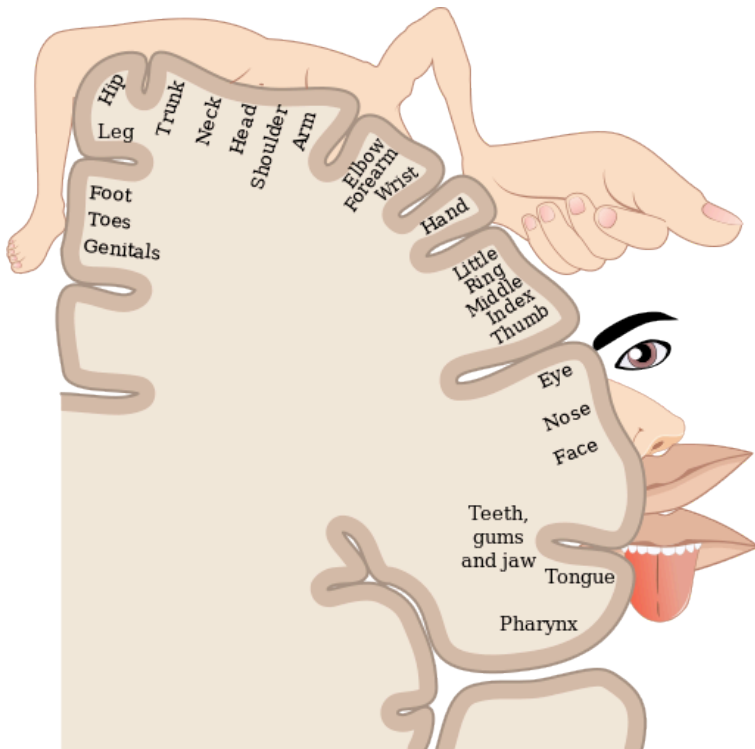


Figure 17. A coronal brain slice showing the somatosensory cortex and its topographic organization. More sensitive body parts, like the face and hands, are processed by larger regions of the somatosensory cortex, compared to less sensitive regions like the leg and trunk.

While the anterior parietal cortex processes body senses, the posterior parietal cortex is an “associative” region, meaning it is neither strictly sensory nor motor. Rather it integrates inputs from touch, proprioception, vision, audition, as well as from motor and prefrontal regions (Whitlock, 2017). This integration is crucial for making spatial maps that guide

attention and movement. In order to grasp an object, that object's location must be translated from its retinotopic coordinates (i.e., where it lands on the retina) into coordinates in space; this translation depends on the direction the eyes and head are pointed. Parietal maps of the locations of body parts and objects in space are critical for planning and executing movements to manipulate objects. These spatial maps output to frontal motor regions for planning body movement and to the frontal eye fields for directing eye movements and attention.

Damage to the posterior parietal lobe can impair visually guided reaching movements and spatial perception (Karnath, 1997). In light of its role in attention and awareness, damage here can also lead to a condition called **hemispatial neglect**, wherein a patient loses awareness of one side of space. For example, a stroke in the right posterior parietal lobe can lead to the inability to perceive the left visual field, causing the patient to act as if the left side of space doesn't exist (they might ignore food on the left side of their plate, or when asked to copy a picture, they might only draw the right half). Ultimately, the parietal lobe is critical for processing and integrating sensory information and transmitting this information to brain areas that control attention and movement.⁴

4. This section contains material adapted from: Betts, J. G. et al. (2022). 13.2 The Central Nervous System. In *Anatomy and Physiology 2e*. OpenStax. Access for free at <https://openstax.org/books/anatomy-and-physiology-2e/pages/13-2-the-central-nervous-system> License: CC BY 4.0 DEED. – Hall, C. N. (2023). 2.1: Exploring the brain: A tour of the structures of the nervous system. In *Introduction to Biological Psychology*. University of Sussex Library. Access for free at <https://openpress.sussex.ac.uk/introductiontobiologicalpsychology/chapter/exploring-the-brain-a-tour-of-the-structures-and-cells-of-the-nervous-system/> License: CC BY-NC 4.0 DEED – Spielman, R. M., Jenkins, W. J., & Lovett, M. D. (2020). 3.4 The Brain and Spinal Cord. In *Psychology 2e*. OpenStax. Access for free at <https://openstax.org/books/psychology-2e/pages/3-4-the-brain-and-spinal-cord> License: CC BY 4.0 DEED.

Occipital Lobe

The **occipital lobe**, located at the back of the brain, contains the visual cortex that processes visual information. Visual input from the eyes travels along the optic nerves to the **lateral geniculate nucleus (LGN)** in the thalamus, and continues to the visual cortex. Visual input enters the cortex at the most posterior portion of the occipital lobe—the primary visual cortex (V1). V1 (and other regions in the visual system) is organized retinotopically, meaning that adjacent regions of the retina (and visual field) are represented by adjacent parts of visual cortex. From V1, visual signals are sent to different brain regions (in the visual cortex and beyond) that specialize in processing different image features such as color, edges, orientation, texture, and movement. Visual regions are highly interconnected and recurrent, sending feedforward signals “up” the processing hierarchy, as well as feedback signals “back down” the processing chain (Van Essen et al., 1992). There are two main visual processing pathways—the lower ventral or “what” pathway proceeds to the inferior temporal lobe for object recognition, and the upper dorsal or “where” pathway proceeds to parietal regions for mapping object location, especially for eye or hand movements.⁵

5. This section contains material adapted from: Spielman, R. M., Jenkins, W. J., & Lovett, M. D. (2020). 3.4 The Brain and Spinal Cord. In *Psychology 2e*. OpenStax. Access for free at <https://openstax.org/books/psychology-2e/pages/3-4-the-brain-and-spinal-cord> License: CC BY 4.0 DEED.

Insula

The **insula** is part of the cerebral cortex tucked deep into the lateral sulcus. It lies underneath parts of the frontal, temporal, and parietal lobes (**Figure 18**). It is sometimes called the insular lobe, a fifth lobe of the cerebral cortex, but it remains less understood than the four cortical lobes visible on the brain's surface. The insula has been implicated in a dizzying array of functions, including sensory processing (e.g., taste and interoceptive processing of bodily states like hunger, pain, and arousal), representing emotions, motor control, self-awareness, empathy, risk prediction, cognitive functioning, consciousness, etc. (Gogolla, 2017). The insula's diverse functions and extensive connectivity to other brain regions highlight its role as a hub linking large-scale brain systems. The insula is thought to be involved in many psychological and neurological conditions including anxiety and depressive disorders, emotion dysregulation, autism spectrum disorders, and addiction. While the insula is considered one of the least understood cortical structures, a surge of recent research interest is making headway (Gogolla, 2017; Kortz & Lillehei, 2023).

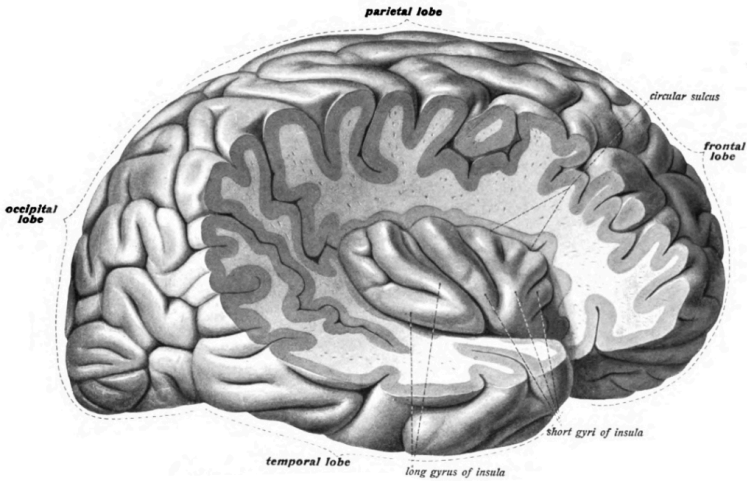


Figure 18. Anatomical illustration of the right insula from the 1908 edition of Sobotta's Anatomy Atlas. The insula is exposed here by removing portions of the overlying frontal, parietal, and temporal regions (these overlying areas are termed the "operculum").

Limbic System

The **limbic system** is a collection of highly specialized neural structures, both subcortical and cortical, that sit at the top of the brainstem (**Figure 19**). The limbic system was originally defined by Paul Broca (1880) as a series of structures near the border between the brainstem and the cerebral hemispheres ("limbus" is Latin for border). The limbic system is involved in many functions including memory, emotion, behavior, motivation, and olfaction. Given advances in neuroscience, the definition of which structures are included in the limbic system has gone through many iterations (Torricco & Abdijadid, 2019). Major components of the limbic system include the **hippocampus**, the **amygdala**, and the **cingulate cortex**.

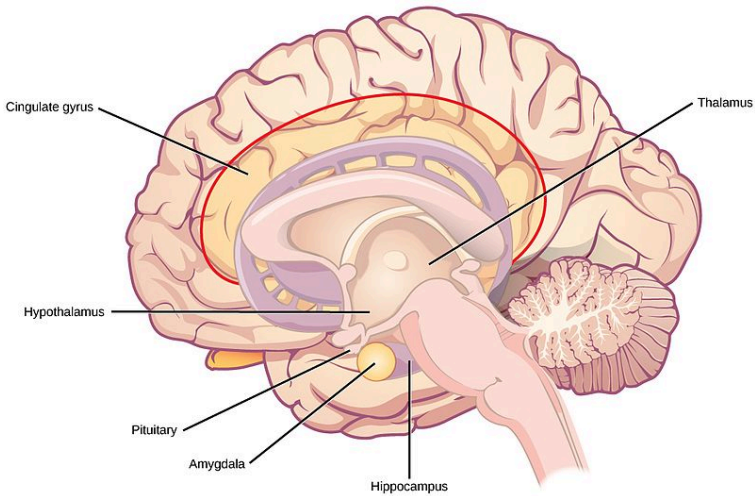


Figure 19: A midsagittal plane showing the interior of the brain and the locations of several limbic-system structures, including the hippocampus, amygdala, and cingulate cortex.

Hippocampus. The hippocampus is a seahorse-shaped structure involved in memory, learning, and spatial processing (**Figures 19 and 20**). The hippocampus is richly connected to many cortical and subcortical regions. During learning, the connection strengths of hippocampal neurons change, and those changes are important for particular aspects of memory, particularly the ability to remember more of an event or stimulus when exposed to only part of it (pattern completion), and to remember events or stimuli as distinct from each other (pattern separation). Damage to the hippocampus produces memory deficits. Hippocampus damage occurs early in Alzheimer’s disease, and extensive damage can lead to anterograde amnesia (the inability to form new memories). The hippocampus is also important for spatial navigation. As discovered in rats and mice, many neurons in the hippocampus respond as “place cells,” meaning that they fire bursts of action potentials when the animal passes through a specific place in its environment.

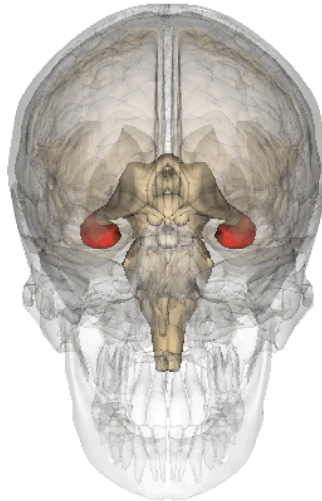


Figure 20. Location of the hippocampus in red.

Amygdala. The amygdala, named for its almond shape, lies next to the hippocampus beneath the cerebral cortex (**Figure 19**). It processes emotions, generating responses like fear, anxiety, and aggression, and facilitates emotional learning such as fear conditioning.

The amygdala receives input from sensory and prefrontal cortex, hippocampus, and brainstem, allowing it to integrate situational, contextual, memory, and bodily information. The amygdala sends output signals to regions throughout the brain, including the frontal lobes, hippocampus, basal ganglia, thalamus, and hypothalamus. This connectivity allows it to produce emotional responses appropriate to a given situation. For example, a punishment-associated stimulus can trigger

a fear response by altering hormone release via the hypothalamus, triggering freezing behaviors, and activating the sympathetic nervous system via the brainstem. Amygdala damage can lead to reduced emotional behavior (“flat affect”) and impaired learning about emotional or frightening stimuli.⁶

Basal Ganglia

The **basal ganglia (Figure 21)** are a group of subcortical nuclei (i.e., clusters of cell bodies that lie below the cerebral cortex) that are critical for regulating and selecting voluntary movement. In particular, the basal ganglia are traditionally defined as the **caudate nucleus**, **putamen**, and **globus pallidus**, but are known to rely on engagement with related nuclei, such as the **subthalamic nucleus** and **substantia nigra**, to initiate voluntary movement (Lanciego et al., 2012).

Information flows from widespread areas of the cerebral cortex, through the basal ganglia and thalamus, and back to the cerebral cortex.

These cortico-basal ganglia-thalamo-cortical loops are crucial for selecting motor actions, initiating and stopping behaviors, and aspects of motivated behavior, including action selection based on potential outcomes. The loops include excitatory and inhibitory pathways, the balance of which is important for initiating or inhibiting motor outputs. Disruptions to this circuitry can cause an imbalance between these excitatory and inhibitory effects, as is seen in a number of neurological

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conditions including Parkinson's disease and Huntington's disease, as well as schizophrenia, Tourette's syndrome, obsessive-compulsive disorder, and addiction.⁷

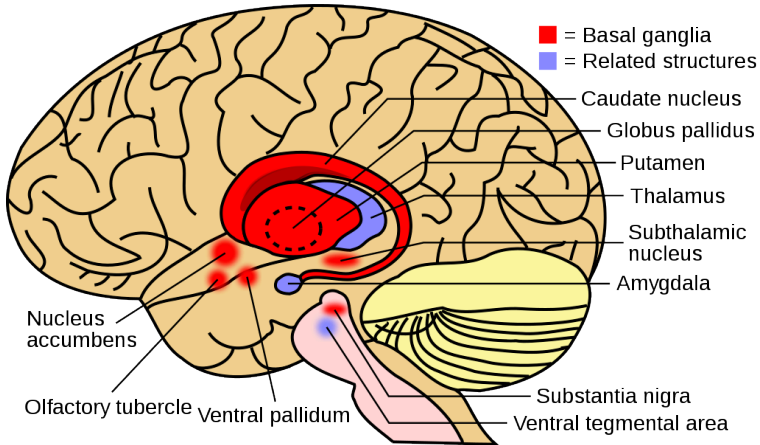


Figure 21: Basal Ganglia and related structures.

Thalamus

The **thalamus** is an information hub that relays information from and to widespread brain areas (**Figure 22A**). Nerve fibers project from the thalamus to the cerebral cortex in all directions, allowing it to act as an

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information hub. The thalamus is organized into specialized regions or nuclei that process specific modalities. All sensory systems, except smell, have a thalamic nucleus that receives sensory signals and sends them to their primary cortical areas. For example, the lateral geniculate nucleus of the thalamus receives visual information from the eye via the optic nerve and sends projections to primary visual cortex (**Figure 22B**); the medial geniculate nucleus receives auditory information from the ear via the inferior colliculus and projects to auditory cortex. Thalamic nuclei don't just relay information "upward" (to cortex), they also receive "descending" input from cortex, forming circuits termed thalamo-cortical loops.

Thalamocortical loops are not limited to sensory processing, but also play important roles in memory, attention, motor control, and decision making. These loops demonstrate that the 'input-computation-output' function of the nervous system is not simply in one direction. Instead, outputs from a given region often feed back to structures that provide inputs to that region, as well as sending outputs to 'upstream' brain areas. Finally, because of its role as informational/sensory hub, the thalamus plays a role in transitioning between sleep and wakefulness, as well as modulating alertness and attention (Portas et al., 1998).⁸

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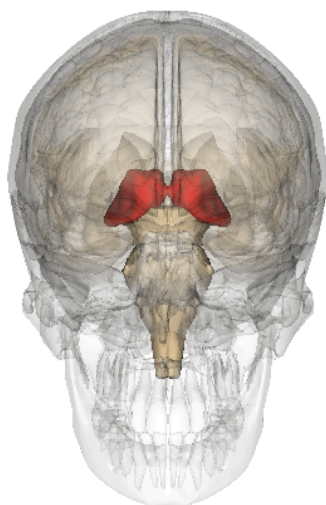


Figure 22A. Location of the thalamus in red.

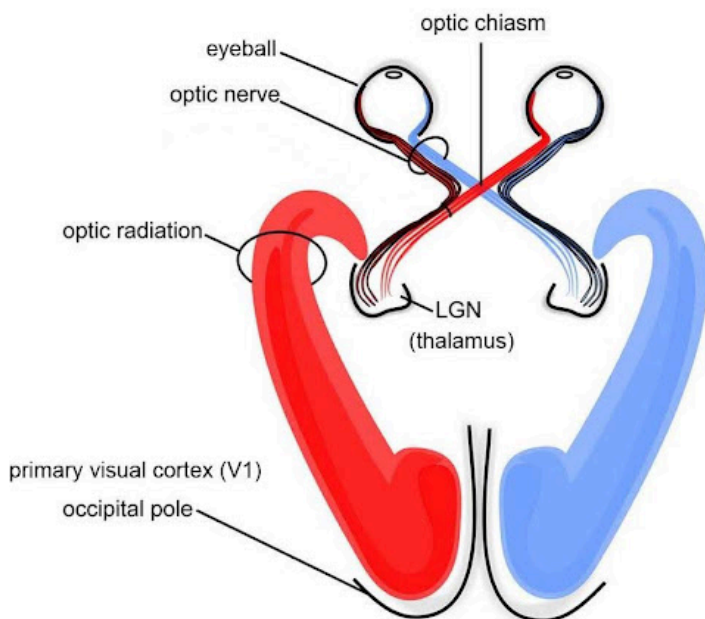


Figure 22B. Visual pathway from the eyes through the thalamus to the visual cortex. Visual information is sent from the retinas at the back of the eyeballs, along the optic nerve to the lateral geniculate nucleus (LGN) of the thalamus, then to the primary visual cortex. Blue color represents the path of information from the left visual field; red from the right visual field.

Hypothalamus

The **hypothalamus** is located below the thalamus (hence its name) and is primarily responsible for regulating endocrine hormones in conjunction with the **pituitary gland** that extends from the hypothalamus (**Figure 17**). Endocrine hormones are important for controlling mood, development, growth, and reproduction. Given its central location in the

brain, the hypothalamus connects to the brainstem, cerebral cortex, hippocampus, amygdala, and thalamus (Bear et al., 2018). As a result, the hypothalamus, both by trafficking sensory and motor information and secreting endocrine hormones across different brain regions, is well-positioned to regulate drives and motivations.

Cerebellum

The **cerebellum** (Latin for “little brain”) is the distinctive structure at the back of the brain (Beck & Tapia, 2023). In **Figure 23**, you can see the cerebellar white matter (*arbor vitae*) and the cerebellum’s tightly folded surface. The cerebellum is critical for coordinated movement and posture. It does not initiate motor commands, but contributes to movement precision, timing, and fine-tuning (based on sensory feedback), as well as motor learning. In addition to the cerebellum’s role in motor control, neuroimaging studies have implicated it in many cognitive functions, including language and attention. The cerebellum’s influence beyond movement aligns with its anatomy: it contains ~80% of the brain’s neurons (most of its neurons are tiny and densely packed granule cells, van Essen et al., 2018) and largely maps to cerebral brain networks involved in cognition (Buckner, 2013).⁹

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Figure 23. Image shows the location of the cerebellum at the bottom of the brain. Illustrated in white on the medial view are the cerebellar white matter tracts, the arbor vitae (their name stems from their branching, tree-like structure). On the lateral view, you can see the cerebellum's tightly folded surface.

Brainstem

The brainstem (or brain stem) is sometimes referred to as the “trunk” of the brain (Beck & Tapia, 2023). It contains many white matter tracts carrying information to and from the spinal cord, cranial nerves, and the rest of the brain. The brainstem is responsible for many neural functions that keep us alive, including regulating breathing, heart rate, and digestion. In keeping with its function, if a patient sustains severe damage to the brainstem they will often require life-support machines to keep them alive. The brainstem can be divided into multiple sections in descending order: midbrain, pons, and medulla oblongata (Figure 24). At the top of the brainstem is the midbrain, which houses dopamine-producing cells, regulates movement, and includes the superior and inferior colliculi, which process and relay visual and auditory information, respectively. Below the midbrain lies the pons which processes and relays sensory and motor information. By employing the cranial nerves, the pons serves as a bridge that connects the cerebral cortex with the medulla and exchanges information between the brain and the spinal cord. The lowest portion of the brainstem, the medulla oblongata, processes breathing, digestion, heart and blood vessel function,

swallowing, and sneezing. Collectively, these regions are involved in body regulation, the sleep–wake cycle, and sensory and motor function.¹⁰

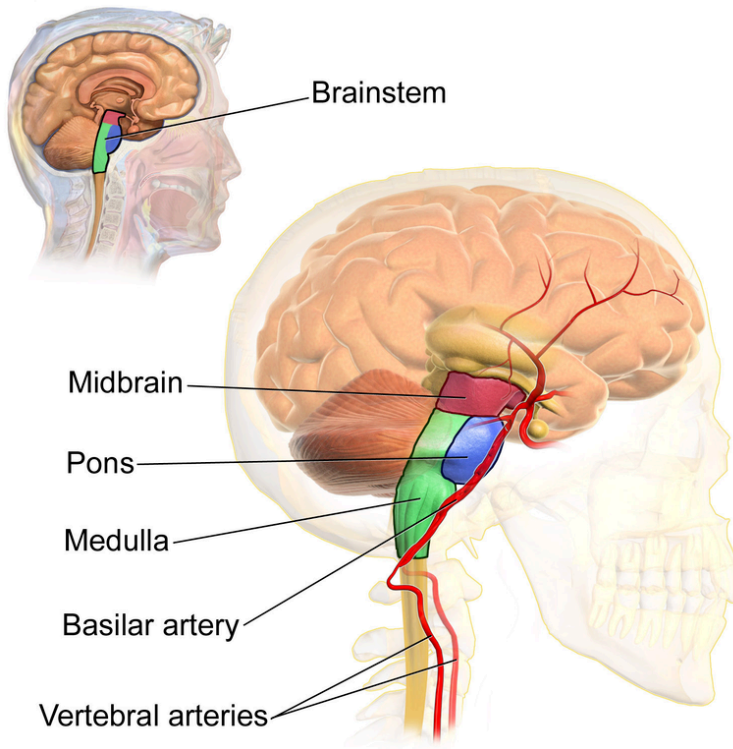


Figure 24. Brainstem and its component substructures, in descending order: the midbrain, pons, and medulla.

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2.7: NON-NEURONAL STRUCTURES IN THE CENTRAL NERVOUS SYSTEM

Ventricular System and Cerebrospinal Fluid

The **cerebral ventricular system** is a set of interconnected cavities known as cerebral ventricles that produce and transport **cerebrospinal fluid (CSF)** (Shenoy & Lui, 2022). This ventricular system consists of 4 main ventricles—2 lateral ventricles, the third ventricle, the fourth ventricle, and the cerebral aqueduct (**Figure 25**). CSF is produced in the ventricles by a tissue called choroid plexus. It drains through sinuses around the brain and through lymphatic vessels. CSF fills the subarachnoid space around the brain, so the brain is suspended in CSF. CSF thus acts as a shock absorber to cushion and protect the brain. Additionally, floating in CSF reduces the effective weight of the brain from around 1500 grams to around 50 grams (Wright et al., 2012). Without CSF, the brain's own weight would cut off blood supply and kill neurons especially in its lower regions. Finally, CSF circulates nutrients throughout the brain and helps clear waste products away from the brain.

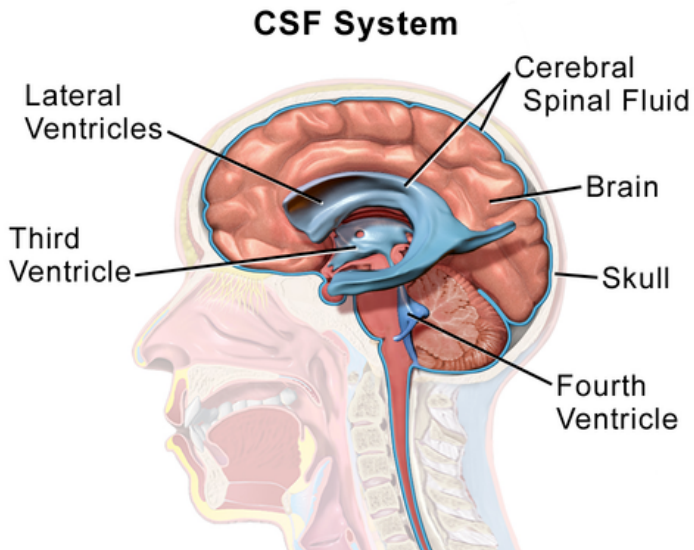


Figure 25: A) The cerebral ventricular system showing the 4 major ventricles.

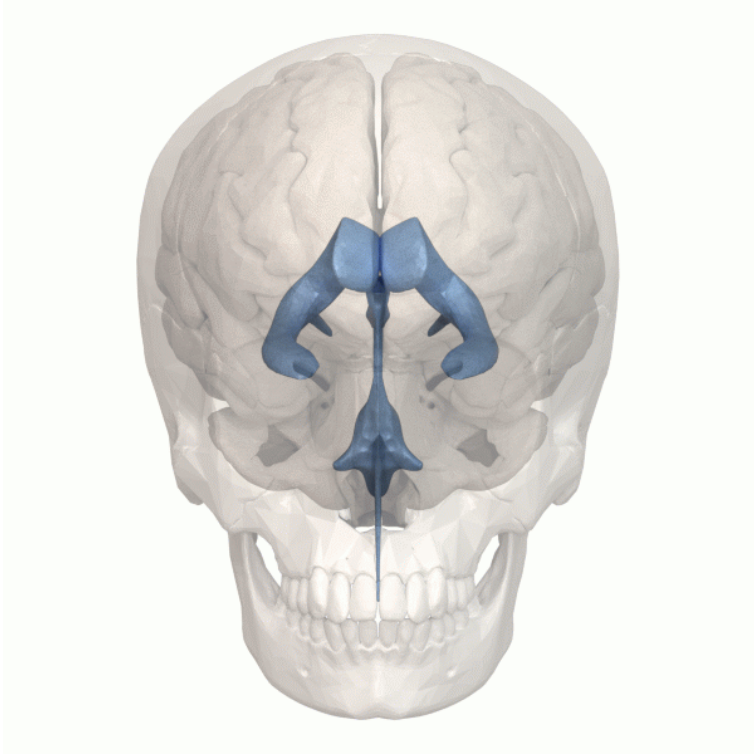


Figure 25: B) Rotating 3D rendering of the ventricles.

Vasculature

The brain is an energetically demanding organ. It is only 2% of the body's mass, but uses 20% of its energy when the body is resting (i.e., when muscles are not active). It relies on a constant supply of oxygen and glucose in the blood to sustain neurons—a disruption of blood flow to the brain leads to a loss of consciousness within 10 seconds. To deliver a constant flow of oxygenated blood, the brain has a complex and tightly regulated vasculature that directs blood to the most active brain regions. Four arteries feed the brain with oxygenated blood, forming a circle known as the circle

of Willis. Major arteries branch off the circle of Willis to supply different regions of the brain. Branches of these arteries form progressively smaller arteries and arterioles that pass through the subarachnoid space and enter the brain. Inside the brain, they branch further to form a dense capillary network (**Figure 26**). A mind-blowing 1 to 2 meters of capillaries exist in every cubic millimeter of brain tissue. These capillaries are less than 10 microns in diameter, so occupy only 2% of brain volume. In the cerebral cortex, a capillary is typically within 10-20 microns from a given neuron. This dense vascular network allows efficient oxygen and glucose delivery to active neurons.

The blood supply is finely adjusted according to the needs of each brain region. Active neurons produce molecules that dilate smooth muscle cells and pericytes on local arterioles and capillaries, increasing blood flow in active regions. Increased blood flow to active brain regions typically exceeds oxygen demand, resulting in elevated local blood oxygen levels. The BOLD (blood oxygen level dependent) signal can be detected using magnetic resonance imaging and serves as a proxy for neuronal activity in experiments on brain function (see Chapter 4—Research Methods).

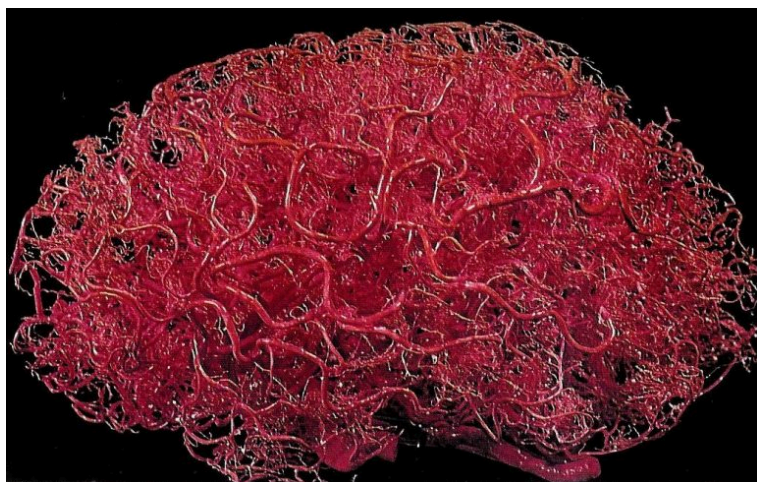


Figure 26. A cast of the brain's vasculature.

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2.8: CONCLUSION

Understanding the brain and nervous system has been a long journey of inquiry, spanning hundreds of years of meticulous studies in the fields of anatomy, neurology, neuroscience, philosophy, evolution, biology, cognitive sciences, and psychology (Ahmad, 2023). The journey continues with new discoveries about the brain emerging every day. A good foundational understanding of brain structure is critical for understanding brain function and the biological bases of psychology. Future research linking brain function to complex mental processes and behavior will help us better understand human psychology and ultimately improve well-being.

2.9: DISCUSSION QUESTIONS AND RESOURCES

Discussion Questions

1. In what ways does the segmentation of the brain into the brainstem, cerebellum, thalamus, hypothalamus, and cerebral hemispheres provide a natural division?
2. Compare and contrast the peripheral nervous system and central nervous system.
3. What are the similarities and differences between the somatic and autonomic nervous systems?
4. Describe the basic functions of the four cerebral lobes: occipital, temporal, parietal, and frontal.
5. What is the difference between gray and white matter?
6. Describe the basic functions of the major subcortical structures: basal ganglia, hippocampus, amygdala, thalamus, and hypothalamus

Outside Resources

Video: [Pt. 1 video on the anatomy of the nervous system](#)

Video: [Pt. 2 video on the anatomy of the nervous system](#)

Video: [To look at functions of the brain and neurons](#)

Web: Atlas of the Human Brain: interactive demos and brain sections

[The Human Brain · Atlas of the Human Brain](#)

Web: 3D interactive brain website and its associated free app: <https://www.brainfacts.org/3d-brain>

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CHAPTER 3: NEURONS

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This chapter provides an overview of the basic structure of neurons and their means of communication. Neurons receive information about the world around us from our sensory systems (vision, audition, olfaction, gustation, and somatosensation); in turn, they process that information and plan and execute appropriate responses, including attending to a stimulus, learning new information, speaking, eating, mating, and evaluating potential threats. This chapter aims to familiarize readers with the anatomy of neurons and explain how neurons use electrochemical signals to communicate, process sensory information, and generate complex behaviors. Understanding neurons is an essential foundation as you move forward in psychology.

Learning Objectives

- Differentiate the functional roles of the two main cell classes in the brain—neurons and glia.
- Describe how the forces of diffusion and electrostatic pressure work collectively to facilitate electrochemical communication.
- Define resting membrane potential, excitatory postsynaptic potentials, inhibitory postsynaptic potentials, and action potentials.
- Explain features of axonal and synaptic communication in neurons.

3.1: INTRODUCTION

Imagine trying to string words together into a meaningful sentence without knowing the meaning of each word or its function (i.e., Is it a verb, noun, or adjective?). Similarly, to appreciate how groups of cells work together in the brain, we must first understand how individual cells in the brain function. Much like words, brain cells, called *neurons*, have an underlying structure that provides the foundation for their functional purpose. Have you ever seen a neuron? Did you know that the basic structure of a neuron is the same whether it is from the brain of a rat or a human? How do the billions of neurons in our brain allow us to do all the things we enjoy, such as chatting with a friend, cheering on a sports team, or laughing?

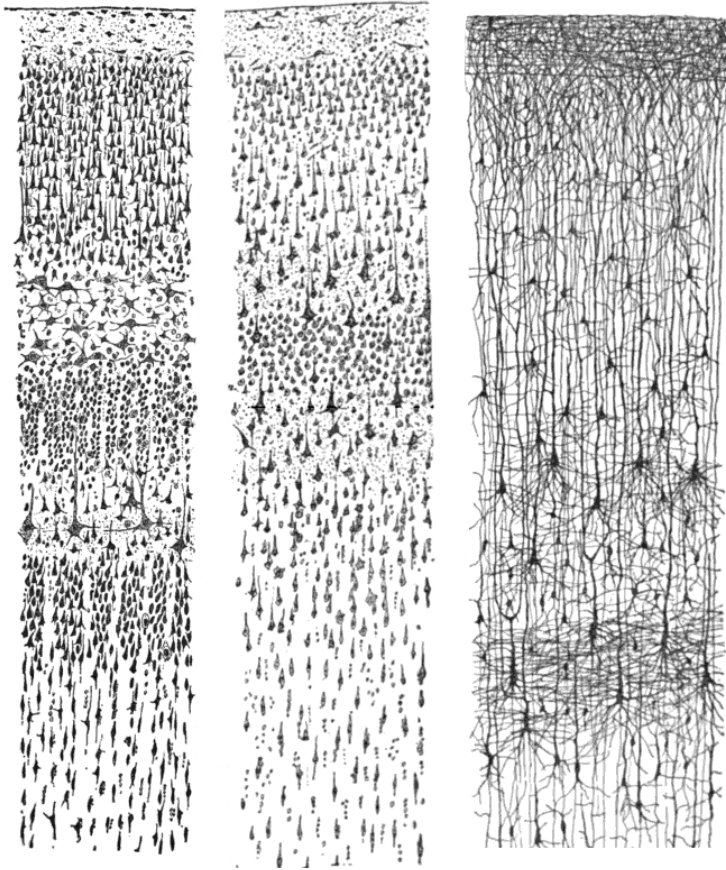


Figure 1. Three drawings by Santiago Ramón y Cajal, taken from “Comparative study of the sensory areas of the human cortex”, pages 314, 361, and 363. Left: Nissl-stained visual cortex of a human adult. Middle: Nissl-stained motor cortex of a human adult. Right: Golgi-stained cortex of a 11/2 month old infant.

Our journey into these questions begins more than 100 years ago with a scientist named Santiago Ramón y Cajal. Cajal (1911) boldly concluded that discrete individual neurons are the structural and functional units of the nervous system. He based his conclusion on the numerous drawings he made of Golgi-stained tissue, a stain named after the scientist who

discovered it, Camillo Golgi. Scientists use several types of stains to visualize cells. Each stain works in a unique way, which causes them to look different when viewed under a microscope. For example, a Nissl stain labels only the main part of the cell (i.e., the cell body; see left and middle panels of Figure 1). In contrast, a Golgi stain fills the cell body and all the processes that extend from it (right panel of Figure 1). Most notably, a Golgi stain only stains approximately 1–2% of neurons (Pasternak & Woolsey, 1975; Smit & Colon, 1969), permitting the observer to distinguish one cell from another. These qualities allowed Cajal to examine the full anatomical structure of individual neurons for the first time. This significantly enhanced the appreciation of the intricate networks their processes form. Based on his observation of Golgi-stained tissue, Cajal suggested neurons were distinct individual units rather than continuous structures. This opposed the dominant theory at the time proposed by Joseph von Gerlach, which stated that the nervous system was composed of a network of long continuous fibers, like telegraph wires (for review see Lopez-Munoz et al., 2006). Camillo Golgi himself had been an avid supporter of Gerlach's theory. Despite their scientific disagreement, Cajal and Camillo Golgi shared the Nobel Prize for Medicine in 1906 for their combined contribution to our understanding of neurons. This seminal work paved the way for our current understanding of the basic structure of the nervous system described in this chapter (for reviews see: De Carlos & Borrell, 2007; Grant, 2007).

This chapter first introduces some basic terminology and the anatomy of neurons in the section “The Structure of the Neuron.” The remainder of the chapter focuses on the electrochemical signals through which neurons communicate. While the electrochemical process might sound intimidating, it is broken down into manageable sections. The first subsection, “Resting Membrane Potential,” describes what occurs in a neuron at rest, when it is theoretically not receiving or sending signals. Building upon this, we examine the electrical conductance within a single neuron when it receives signals. Finally, the chapter concludes with a

description of the electrical conductance, which results in communication between neurons through a release of chemicals. At the end of the chapter, you should have a broad understanding of how neurons send and receive information by electrical and chemical signals.

A note of encouragement: This chapter introduces a vast amount of terminology that at times may feel overwhelming. Do not get discouraged or bogged down in the details. Utilize the book's glossary, which contains all terms in **bold typing**. On your first read of this chapter, try focusing on the broader concepts and functional aspects of the terms instead of trying to commit all the terminology to memory. I suggest reading this chapter at least twice, once before *and* once after the course lecture on this material. Repetition is the best way to gain clarity and commit to memory the challenging concepts and detailed vocabulary presented here.

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3.2: THE STRUCTURE OF THE NEURON

Basic Nomenclature

There are approximately 86 billion neurons in the human brain (Herculano-Houzel, 2009). Each neuron has three main components: dendrites, the soma, and the axon (see **Figure 2**). **Dendrites** are processes that extend outward from the **soma**, or cell body of a neuron, and typically branch several times. Dendrites receive information from thousands of other neurons and are the main source of input of the neuron. The **nucleus**, which is located within the soma, contains genetic information, directs protein synthesis, and supplies the energy and the resources the neuron needs to function. The main source of output of the neuron is the **axon**. The axon extends away from the soma and carries an important signal called an action potential to another neuron. The place at which the axon of one neuron approaches the dendrite of another neuron is a **synapse** (**Figures 2 and 3**). Typically, the axon of a neuron is covered with an insulating substance called a **myelin sheath** that allows the signal of one neuron to travel rapidly to another neuron.

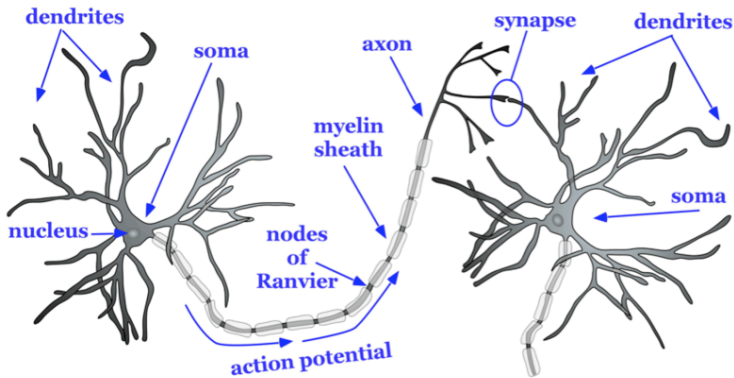


Figure 2. Basic structure of a neuron.

The axon splits many times so it can communicate, or synapse, with several other neurons (see **Figure 2**). At the end of the axon is a **terminal button**, which forms synapses with **spines**, or protrusions, on the dendrites of neurons. Synapses form between the *presynaptic* terminal button (neuron sending the signal) and the *postsynaptic* membrane (neuron receiving the signal; see **Figure 3**). Here we will focus specifically on synapses between the terminal button of an axon and a dendritic spine; however, synapses can also form between the terminal button of an axon and the soma or the axon of another neuron.

A tiny space called a **synaptic gap**, approximately 5 nm (nanometers), exists between the presynaptic terminal button and the postsynaptic dendritic spine. To give you a better idea of the size, the thickness of a dime is 1.35 mm (millimeters) or 1,350,000 nm. In the presynaptic terminal button, **synaptic vesicles** package together groups of chemicals called **neurotransmitters** (see **Figure 3**). Neurotransmitters are released from the presynaptic terminal button, travel across the synaptic gap, and activate ion channels on the postsynaptic spine by binding to *receptor sites*. We will discuss the role of receptors in more detail later in the chapter.

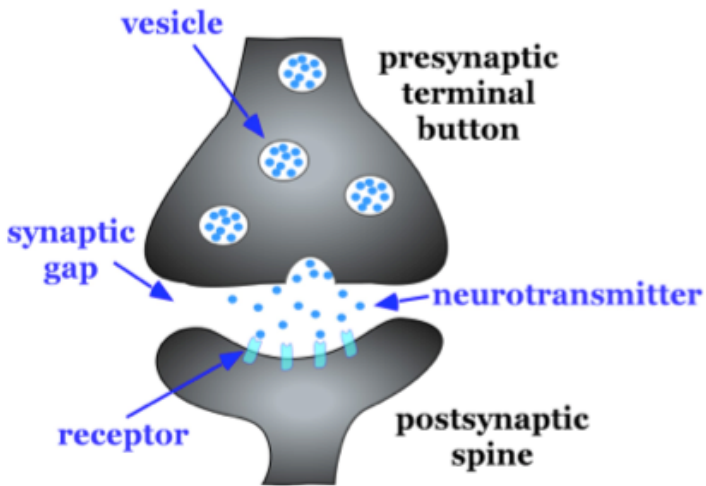


Figure 3. Characteristics of a synapse.

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- [synapse](#) © Noba is licensed under a [CC BY-NC-SA \(Attribution NonCommercial ShareAlike\)](#) license

3.3: TYPES OF CELLS IN THE BRAIN

Not all neurons are created equal. *Sensory* neurons help us receive information about the world around us. *Motor* neurons allow us to initiate movement and behavior, ultimately allowing us to interact with the world around us. *Interneurons* process sensory input from our environment into meaningful representations, plan behavioral responses, and connect to the motor neurons to execute these behavioral plans.

The main categories of neurons are defined by their specific structure. The structures support their unique functions. *Unipolar neurons* are structured in a way that is ideal for relaying information forward, so they have one neurite (axon) and no dendrites (**Figure 4**). They are involved in transmission of physiological information from the body's periphery such as communicating body temperature through the spinal cord up to the brain. *Bipolar neurons* are involved in sensory processing such as sensing light in the eye's retina. They have one axon and one dendrite which help acquire and pass sensory information to various regions in the brain. Finally, *multipolar neurons* are most common and communicate sensory and motor information in the brain. Multipolar neurons have one axon and many dendrites which allows them to communicate with other neurons. One of the most prominent neurons is a pyramidal neuron, which falls under the multipolar category. It gets its name from the triangular or pyramidal shape of its soma (for examples see, Furtak et al., 2007).

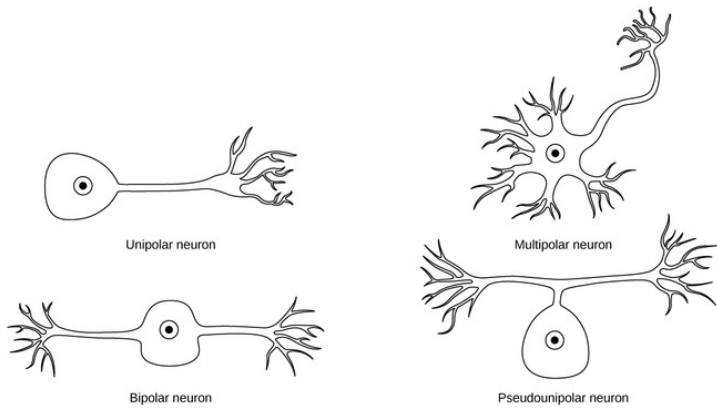


Figure 4. Types of Neurons: Neurons are broadly divided into a few main types based on the number and placement of axons: (1) unipolar, (2) bipolar, (3) multipolar, and (4) pseudounipolar.

In addition to neurons, non-neuronal cells in the nervous system called **glia** or *neuroglia* provide support and play essential roles in the functioning of neurons. Glial cells have several functions, just a few of which we will discuss here. One type of glial cell, called *oligodendroglia*, forms the myelin sheaths that insulate axons (Simons & Trotter, 2007; see Figures 5). In the central nervous system (CNS), oligodendroglia wrap their dendritic processes around the axons of neurons many times to form the myelin sheath. One cell will form the myelin sheath on several axons. In the peripheral nervous system (PNS), Schwann cells, another type of glial cell, form the myelin sheath for neurons. One cell will wrap around a singular axon in the PNS. Other types of glial cells, such as *microglia* and *astrocytes*, digest debris of dead neurons, carry nutritional support from blood vessels to neuron, and help to regulate the ionic composition of the extracellular fluid. Glial cells are essential for neuronal support, but unlike neurons, they do not conduct electrical signals or engage in cell-to-cell communication.

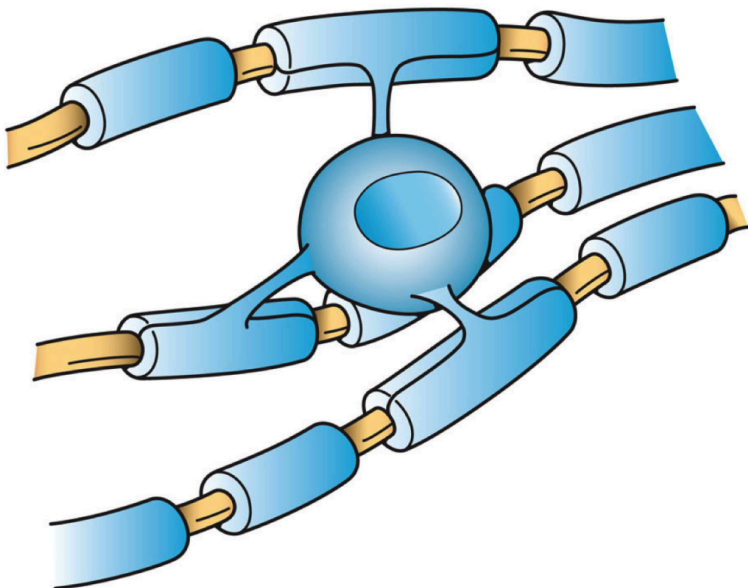


Figure 5. An oligodendrocyte myelinating several axons in the central nervous system.

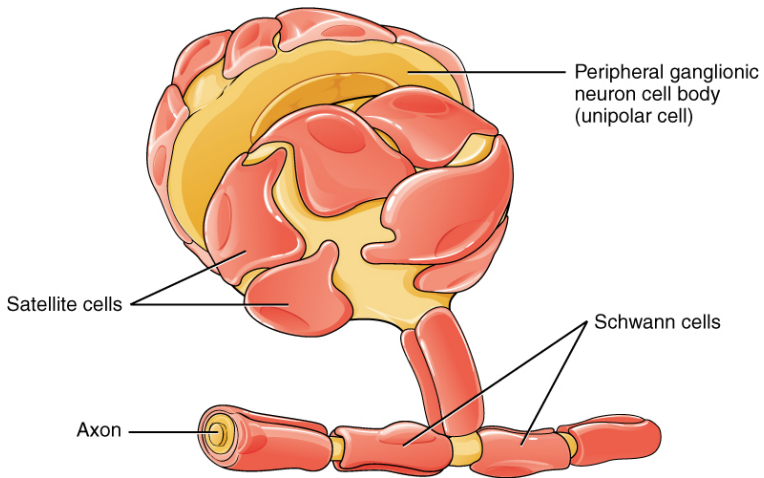


Figure 6. The peripheral nervous system (PNS) has myelinating Schwann cells.

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- [Glial Cells of the PNS](#) © [Wikimedia](#) is licensed under a [CC BY-SA \(Attribution ShareAlike\)](#) license

3.4: COMMUNICATION WITHIN AND BETWEEN NEURONS

Thus far, we have described the main characteristics of neurons, including how their processes come in close contact to form *synapses*. In this section, we consider the conduction of communication within a neuron and how this signal is transmitted to the next neuron. There are two stages of this electrochemical action in neurons. The first stage is the electrical conduction of dendritic input to the initiation of an action potential within a neuron. The second stage is a chemical transmission across the synaptic gap between the presynaptic neuron and the postsynaptic neuron of the synapse. To understand these processes, we first need to consider what occurs within a neuron at its steady state, called *resting membrane potential*.

Resting Membrane Potential

The intracellular (inside the cell) fluid and extracellular (outside the cell) fluid of neurons is composed of a combination of ions (electrically charged molecules; Figure 7). Cations are positively charged ions, and anions are negatively charged ions. The composition of intracellular and extracellular fluid is similar to salt water, containing sodium (Na^+), potassium (K^+), chloride (Cl^-), and anions (A^-).

The **cell membrane**, which is composed of a lipid bilayer of fat molecules, separates the cell from the surrounding extracellular fluid. Proteins span the membrane, forming **ion channels** that allow particular ions to pass between the intracellular and extracellular fluid (**Figure 7**).

These ions are in different concentrations inside the cell relative to outside the cell, and the ions have different electrical charges. Due to this difference in concentration and charge, two forces act to maintain a steady state when the cell is at rest: diffusion and electrostatic pressure. **Diffusion** is the force on molecules to move from areas of high concentration to areas of low concentration. **Electrostatic pressure** is the repulsive force between similarly charged ions and the attractive force between oppositely charged ions. Remember the saying “opposites attract”?

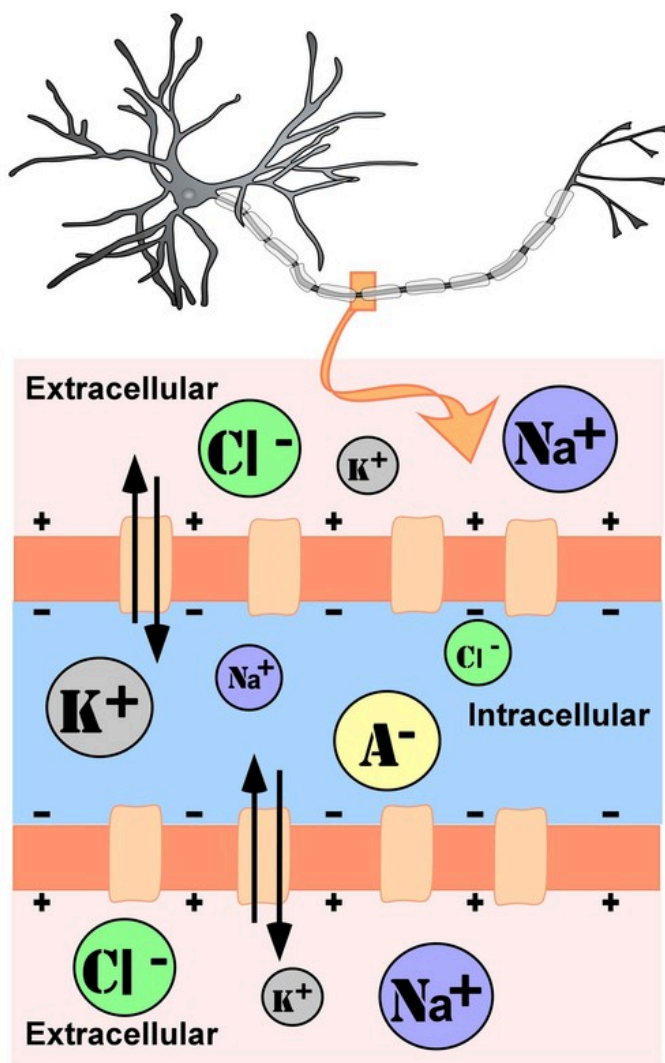


Figure 7. Representation of ion concentrations inside (intracellular) and outside (extracellular) a neuron in the unmyelinated segment of the axon.

There is a membrane potential at which the force of diffusion is equal and opposite to the force of electrostatic pressure. This voltage, called the

equilibrium potential, is the voltage at which no ions flow. Since several ions can permeate the cell's membrane, the baseline electrical charge inside the cell compared with outside the cell, referred to as **resting membrane potential**, is based on the collective drive of force on several ions. Relative to the extracellular fluid, the membrane potential of a neuron at rest is negatively charged at approximately -70 millivolts (mV). These voltages are tiny compared to those of batteries and electrical outlets, which are measured in volts, not millivolts, and range from 1.5 to 240 volts.

Let us see how these two forces, diffusion and electrostatic pressure, act on the four groups of ions mentioned above.

1. **Anions (A^-):** Anions are highly concentrated inside the cell and contribute to the negative charge of the resting membrane potential. Diffusion and electrostatic pressure are not forces that determine A^- concentration because Anions are impermeable to the cell membrane. There are no ion channels that allow for A^- to move between the intracellular and extracellular fluid.
2. **Potassium (K^+):** The cell membrane is permeable to potassium at rest, but potassium remains in high concentrations inside the cell. Diffusion pushes K^+ outside the cell because it is in high concentration inside the cell. However, electrostatic pressure pushes K^+ inside the cell because the positive charge of K^+ is attracted to the negative charge inside the cell. In combination, these forces oppose one another with respect to K^+ .
3. **Chloride (Cl^-):** The cell membrane is also very permeable to chloride at rest, but chloride remains in high concentration outside the cell. Diffusion pushes Cl^- inside the cell because it is in high concentration outside the cell. However, electrostatic pressure pushes Cl^- outside the cell because the negative charge of Cl^- is attracted to the positive charge outside the cell. These forces on Cl^- oppose one another.
4. **Sodium (Na^+):** The cell membrane is not very permeable to sodium at rest. Diffusion pushes Na^+ inside the cell because it is in high

concentration outside the cell. Electrostatic pressure also pushes Na^+ inside the cell because the positive charge of Na^+ is attracted to the negative charge inside the cell. Both of these forces push Na^+ inside the cell; however, Na^+ cannot permeate the cell membrane and remains in high concentration outside the cell. The small amounts of Na^+ inside the cell are removed by a **sodium-potassium pump**, which uses the neuron's energy (adenosine triphosphate, ATP) to pump 3 Na^+ ions out of the cell in exchange for bringing 2 K^+ ions inside the cell.

Action Potential

Now that we have considered what occurs in a neuron at rest, let us consider what changes occur to the resting membrane potential when a neuron receives input from the presynaptic terminal button of another neuron. Our understanding of the electrical signals or potentials within a neuron results from the seminal work of Hodgkin and Huxley that began in the 1930s at a well-known marine biology lab in Woods Hole, MA. Their work, for which they won the Nobel Prize in Medicine in 1963, resulted in the general model of electrochemical transduction described here (Hodgkin & Huxley, 1952). Hodgkin and Huxley studied a very large axon in the squid, a common species for that region of the United States. The squid's axon is roughly 100 times larger than axons in the mammalian brain, making it much easier to work with. Activation of the giant axon, whose large size allows for rapid electrical signal transmission, triggers a swift withdrawal response that enables the squid to escape from predators.

While studying this species, Hodgkin and Huxley noticed that if they applied an electrical stimulus to the axon, a large, transient electrical current conducted down the axon. This transient electrical current is known as an **action potential** (Figure 8). An action potential is an all-or-nothing response that occurs when there is a change in the charge or potential of the cell from its resting membrane potential (-70 mV) in a more positive

direction, which is a *depolarization* (**Figure 8**). An all-or-nothing response parallels the binary code used in computers, where only two possibilities exist: 0 or 1. There are no intermediate values; 0.5, for example, doesn't exist in binary code. Similarly, an action potential either occurs or doesn't occur, with no partial activation. This all-or-nothing principle applies to both binary code and action potentials: they are either triggered fully or not at all.

There is a specific membrane potential that the neuron must reach to initiate an action potential. This membrane potential, called the **threshold of excitation**, is typically around -50 mV. If the threshold of excitation is reached, then an action potential is triggered.

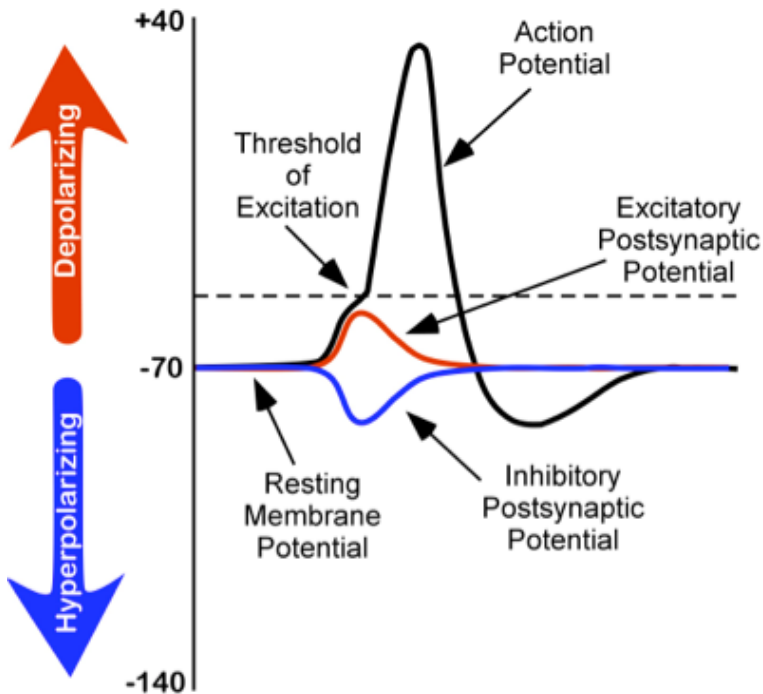


Figure 8. Changes in membrane potentials of neurons.

How is an action potential initiated? At any one time, each neuron may receive hundreds of inputs from the cells that synapse with it. These inputs can cause several types of fluctuations in the neuron's membrane potentials (**Figure 8**):

1. **Excitatory postsynaptic potentials (EPSPs)**: a *depolarizing* current that causes the membrane potential to become more positive and closer to the threshold of excitation
2. **Inhibitory postsynaptic potentials (IPSPs)**: a *hyperpolarizing* current that causes the membrane potential to become more negative and further away from the threshold of excitation

These postsynaptic potentials, EPSPs and IPSPs, *summate* or add together in time and space. The (inhibitory) IPSPs make the membrane potential more negative, but how much so depends on their strength. The (excitatory) EPSPs make the membrane potential more positive; again, how much more positive depends on their strength. If you have two small EPSPs at the same time and same synapse, then the result will be a large EPSP. If you have a small EPSP and a small IPSP at the same time and same synapse, then they will cancel each other out. Unlike the action potential, which is an all-or-nothing response, IPSPs and EPSPs are smaller and *graded* potentials, varying in strength. The change in voltage during an action potential is approximately 100 mV. In comparison, EPSPs and IPSPs are changes in voltage between 0.1 to 40 mV. They can be different strengths, or gradients, and they are measured by how far the membrane potentials diverge from the resting membrane potential.

The concept of summation can be confusing. As a child, I used to play a game with a very large parachute where you would try to knock balls out of the center of the parachute. This game illustrates the properties of summation. In this game, a group of children next to one another would work together to produce waves in the parachute in order to cause a wave large enough to knock the ball out of the parachute. The children would initiate the waves at the same time and in the same direction. The additive

result was a larger wave in the parachute, and the balls would bounce out of the parachute. However, if the waves they initiated occurred in the opposite direction or with the wrong timing, the waves would cancel each other out, and the balls would remain in the center of the parachute. EPSPs or IPSPs in a neuron work in the same fashion; they either add or cancel each other out. If you have two EPSPs, then they sum together and become a larger depolarization. Similarly, if two IPSPs come into the cell at the same time, they will sum and become a larger hyperpolarization in membrane potential. However, if two inputs were opposing one another, moving the potential in opposite directions, such as an EPSP and an IPSP, their sum would cancel each other out.

At any moment, each cell is receiving mixed messages, both EPSPs and IPSPs. If the summation of EPSPs is strong enough to depolarize the membrane potential to reach the threshold of excitation, then it initiates an action potential. The action potential then travels down the axon, away from the soma, until it reaches the ends of the axon (the terminal button). In the terminal button, the action potential triggers the release of neurotransmitters from the presynaptic terminal button into the synaptic gap. These neurotransmitters, in turn, cause EPSPs and IPSPs in the postsynaptic dendritic spines of the next cell (Figure 9). The neurotransmitter released from the presynaptic terminal button binds with **ionotropic receptors** in a lock-and-key fashion on the postsynaptic dendritic spine. Ionotropic receptors are receptors on ion channels that open, allowing some ions to enter or exit the cell, depending upon the presence of a particular neurotransmitter. The type of neurotransmitter and the permeability of the ion channel it activates will determine if an EPSP or IPSP occurs in the dendrite of the postsynaptic cell. These EPSPs and IPSPs summate as described above and the entire process occurs again in another cell.

The Change in Membrane Potential During an Action Potential

We discussed previously which ions are involved in maintaining the resting membrane potential. Not surprisingly, some of these same ions are involved in the action potential. When the cell becomes depolarized (more positively charged) and reaches the threshold of excitation, this opens a voltage-dependent Na^+ channel. A voltage-dependent ion channel is a channel that opens, allowing some ions to enter or exit the cell, depending upon when the cell reaches a particular membrane potential. When the cell is at resting membrane potential, these voltage-dependent Na^+ channels are closed. As we learned earlier, both diffusion and electrostatic pressure are pushing Na^+ inside the cells. However, Na^+ cannot permeate the membrane when the cell is at rest. Now that these channels are open, Na^+ rushes inside the cell, causing the cell to become very positively charged relative to the outside of the cell. This is responsible for the rising or depolarizing phase of the action potential (Figure 8). The inside of the cell becomes very positively charged, +40mV. At this point, the Na^+ channels close and become *refractory*. This means the Na^+ channels cannot reopen again until the cell returns to the resting membrane potential. Thus, a new action potential cannot occur during the refractory period. The refractory period also ensures the action potential can only move in one direction down the axon, away from the soma. As the cell becomes more depolarized, a second type of voltage-dependent channel opens; this channel is permeable to K^+ . With the cell depolarized (very positive relative to the outside of the cell) and the high concentration of K^+ within the cell, the forces of both diffusion and electrostatic pressure drive K^+ outside of the cell. The movement of K^+ out of the cell causes the cell potential to return to the resting membrane potential, the falling or hyperpolarizing phase of the action potential (Figure 8). A short hyperpolarization occurs partially due to the gradual closing of the K^+ channels. With the Na^+ closed, electrostatic pressure continues to push K^+ out of the cell. In addition, the

sodium-potassium pump is pushing Na^+ out of the cell. The cell returns to the resting membrane potential, and the excess extracellular K^+ diffuses away. This exchange of Na^+ and K^+ ions happens very rapidly, in less than 1 millisecond. The action potential occurs in a wave-like motion down the axon until it reaches the terminal button. Only the ion channels in close proximity to the action potential are affected.

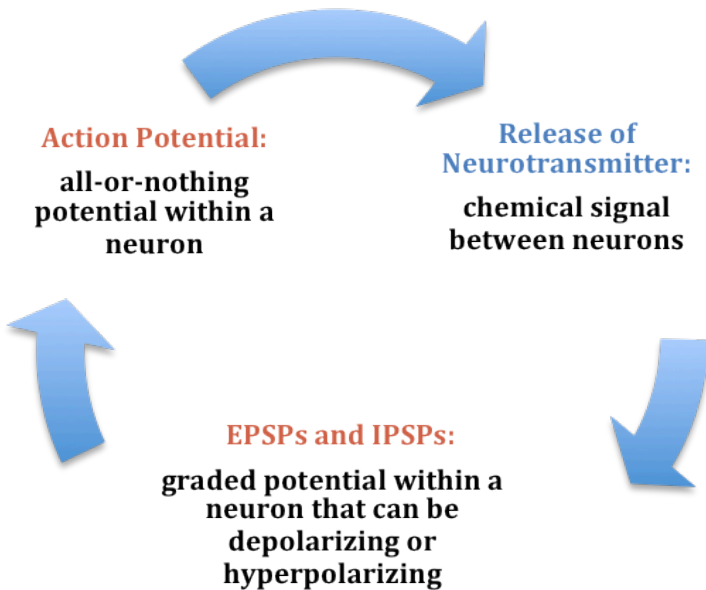


Figure 9. Summary of the electrochemical communication within and between neurons.

Earlier you learned that axons are often covered in myelin. Let us consider how myelin speeds up the process of the action potential. There are gaps in the myelin sheaths called *nodes of Ranvier*. The myelin insulates the axon and does not allow any fluid between the myelin and cell membrane. Under the myelin, when the Na^+ and K^+ channels open, no ions flow between the intracellular and extracellular fluid. This saves the cell from having

to expend the energy necessary to rectify or regain the resting membrane potential. (Remember, the pumps need ATP to run.) Under the myelin, the action potential degrades some, but still has a large enough potential to trigger a new action potential at the next node of Ranvier. Thus, the action potential jumps from node to node (Figure 10); this process is known as *saltatory conduction* (*Saltus* means “jump” in Latin).

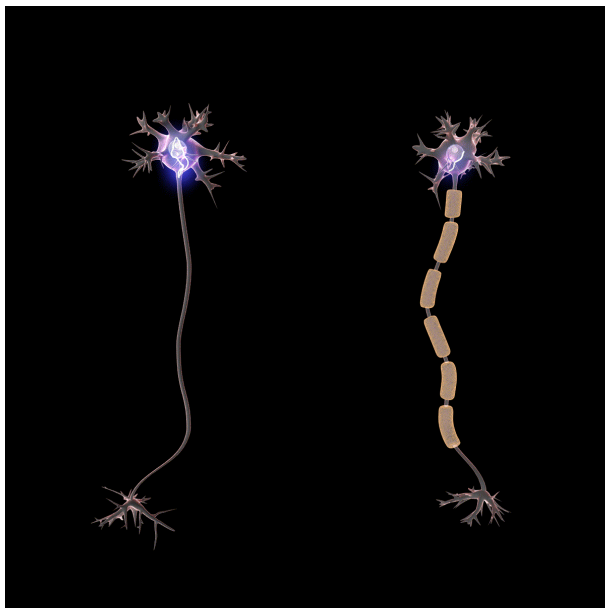


Figure 10.
Action
potential
propagation
in
myelinated
neurons
(right) is
faster than
in
unmyelinated
neurons
(left)
because of
saltatory
conduction.

In the presynaptic terminal button, the action potential triggers the release of neurotransmitters. Neurotransmitters cross the synaptic gap and open subtypes of receptors in a lock-and-key fashion (see Figure 9). Depending on the type of neurotransmitter, an EPSP or IPSP occurs in the dendrite of the postsynaptic cell. Neurotransmitters that open Na^+ or calcium (Ca^+) channels cause an EPSP; an example is the NMDA receptors, which are activated by glutamate (the main excitatory neurotransmitter in the brain). In contrast, neurotransmitters that open Cl^- or K^+ channels cause an IPSP; an example is gamma-aminobutyric acid (GABA) receptors, which are

activated by GABA, the main inhibitory neurotransmitter in the brain. Once the EPSPs and IPSPs occur in the postsynaptic site, the process of communication within and between neurons cycles on (Figure 9). A neurotransmitter that does not bind to receptors is broken down and inactivated by enzymes or glial cells, or it is taken back into the presynaptic terminal button in a process called *reuptake*, which will be discussed further in the chapter on psychopharmacology.

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3.5: DISCUSSION QUESTIONS AND RESOURCES

Discussion Questions

1. What structures of a neuron are the main input and output of that neuron?
2. What does the statement mean that communication within and between cells is an electrochemical process?
3. How does myelin increase speed and efficiency of the action potential?
4. How does diffusion and electrostatic pressure contribute to the resting membrane potential and the action potential?
5. Describe the cycle of communication within and between neurons.

Outside Resources

Video Series: Neurobiology/Biopsychology – Tutorial

animations of action potentials, resting membrane potentials, and synaptic transmission.

<http://www.sumanasinc.com/webcontent/animations/neurobiology.html>

Video: An animation and an explanation of an action potential

https://youtu.be/OZG8M_IdA1M

Video: What's so special about the human brain? Suzana Herculano-Houzel

https://www.youtube.com/watch?v=_7_XH1CBzGw&ab_channel=TED

Video: An animation of neurotransmitter actions at the synapse

<http://www.youtube.com/watch?v=90cj4NX87Yk>

Video: An interactive animation that allows students to observe the results of manipulations to excitatory and inhibitory post-synaptic potentials. Also includes animations and explanations of transmission and neural circuits.

<https://apps.childrenshospital.org/clinical/animation/neuron/>

Video: Another animation of an action potential

<http://www.youtube.com/watch?v=-SHBnExxub8&list=PL968773A54EF13D21>

Video: Another animation of neurotransmitter actions at the synapse

<http://www.youtube.com/watch?v=LT3VKAr4roo&list=PL968773A54EF13D21>

Video: Domino Action Potential: This hands-on activity helps students grasp the complex process of the action potential, as well as become familiar with the characteristics of transmission (e.g., all-or-none response, refractory period).

<https://www.youtube.com/watch?v=xzvZ11EutBY>

Video: For perspective on techniques in neuroscience to look inside the brain

<https://www.youtube.com/watch?v=s4smjT1qwZU>

Video: The Behaving Brain is the third program in the DISCOVERING PSYCHOLOGY series. This program looks at the structure and composition of the human brain: how neurons function, how information is collected and transmitted, and how chemical reactions relate to thought and behavior.

<http://www.learner.org/series/discoveringpsychology/03/e03expand.html>

Video: You can grow new brain cells. Here's how. -Can we, as adults, grow new neurons? Neuroscientist Sandrine Thuret says that we can, and she offers research and practical advice on how we can help our brains better perform neurogenesis—improving mood, increasing memory formation and preventing the decline associated with aging along the way.

https://www.youtube.com/watch?v=B_tjKYvEzil

Web: For more information on the Nobel Prize shared by Ramón y Cajal and Golgi

http://www.nobelprize.org/nobel_prizes/medicine/laureates/1906/

3.6: REFERENCES

This chapter was adapted from:

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CHAPTER 4: RESEARCH METHODS IN BIOLOGICAL PSYCHOLOGY

Learning Objectives

- Review how cases of brain damage provided early insight into the localization of brain function
- Examine invasive research methods used in animals, such as brain lesions, implanted recording devices, and genetic manipulations
- Understand advantages and disadvantages of various cognitive neuroscience methods used in humans such as EEG, TMS, PET, and MRI
- Examine how brain stimulation can provide causal evidence for how brain function drives thought and behavior

4.1: INTRODUCTION

Biological psychology is a broad and diverse field that consists of many different approaches including neuroscience, neuropsychology, cognitive neuroscience, behavioral genetics, and psychopharmacology. With so many different approaches, it is not surprising that the research methods used in biological psychology are also broad and diverse. Techniques range from low-level approaches like recording the activity of a single neuron and dissecting animal brains to high-level cognitive testing and brain imaging in humans. We've learned about brain function from case studies of brain damage and from technical marvels such as high-resolution brain imaging and optogenetics (in which cells in animal brains are genetically manipulated so they can be controlled by specific wavelengths of light while the animal is awake!).

Each different technique in biological psychology has strengths and limitations and can be used to answer distinct types of questions. When establishing the specific function of a particular brain area, the strongest evidence comes from **converging evidence**, whereby multiple studies using different methods report similar or converging findings (Beck & Tapia, 2023). In this chapter, we cover some of the major research methods in biopsychology and how the methods converge to help us understand how the three-pound human brain gives rise to our thoughts, actions, perceptions, feelings, and emotions.

4.2: HISTORICAL METHODS – STUDIES OF BRAIN DAMAGE IN HUMANS

Early insights into brain-behavior links emerged from cases of brain damage. Prominent examples from the 19th century include Phineas Gage and the patients of physicians like Paul Broca and Carl Wernicke.

In the mid-1800s, the railroad worker Phineas Gage was responsible for setting explosive charges to blast through rock for railroad tracks. Using a 1-meter long tamping iron, he would tamp down the charges, but on one September afternoon, a spark set off the explosive prematurely. The tamping iron shot through the air like a rocket, entering the side of Gage's face, passing behind his left eye, exiting the top of his head, and landing 80 feet away (see Figure 1). Amazingly, he survived the accident and even was able to talk and walk away from it. Although he lost a portion of his left frontal lobe, he lived for another 12 years without apparent impairment in speech, motor abilities, memory, or intelligence (Damasio et al., 1994). However, what's fascinating about this incident from a biopsych perspective is that Gage's personality changed drastically as a result of the accident (Infantolino & Miller, 2023). Before the accident, Gage had been responsible and socially well-adapted, but afterward, he became irreverent, vulgar, impulsive, did not follow social conventions, and had difficulty executing plans.

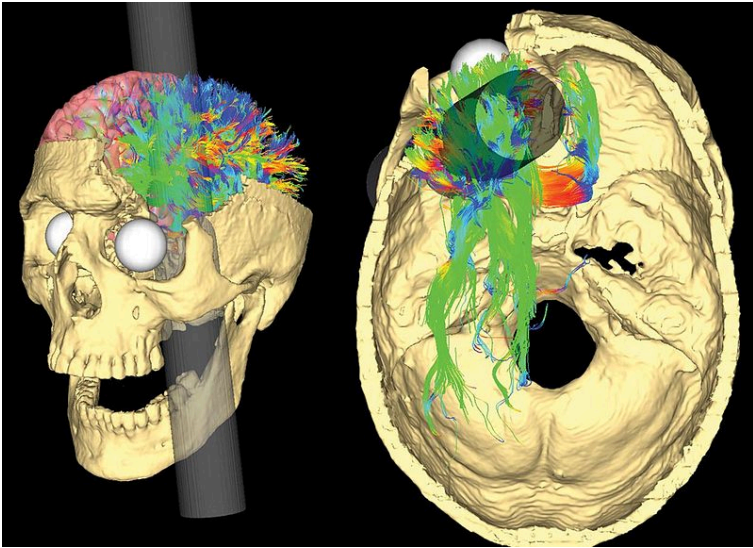


Figure 1: A computerized tomography (CT) image reconstruction of the path of the tamping rod that entered Phineas Gage's mouth and blasted through his skull and left frontal lobe. The bright colors represent White Matter fiber pathways likely intersected by the rod (Van Horn et al. 2012).

In another example from the 1800s, the French physician Paul Broca found that some patients who were unable to produce speech had brain damage to their left inferior frontal cortex. One of Broca's patients, nicknamed "Tan," could only produce the single syllable "tan" repeatedly. After Tan's death, Broca discovered a major lesion on Tan's left frontal lobe (see **Figure 2**). Another patient of Broca's was also severely aphasic (i.e., couldn't produce fluent speech) and had brain damage to the same portion of his left frontal lobe. This led Broca to surmise that speech production was localized to this region of the left inferior frontal lobe.

Around the same time, the German physician Carl Wernicke discovered that damage to a different brain region—the left superior temporal lobe—was associated with impaired speech *comprehension*. So together, this "double dissociation" showed that brain damage to specific locations is linked to specific types of behavioral impairments (Figure 3). (Here is a

memory gem for distinguishing Broca's and Wernicke's brain areas: use the first three letters of each word: BROca's area = speech PROduction = FRONtal; and WERnicke's area = speech PERception).



Figure 2. The brain of Broca's patient, "Tan," preserved in a jar in a museum in Paris. The arrow points to the damaged left inferior frontal lobe (associated with impaired speech production).

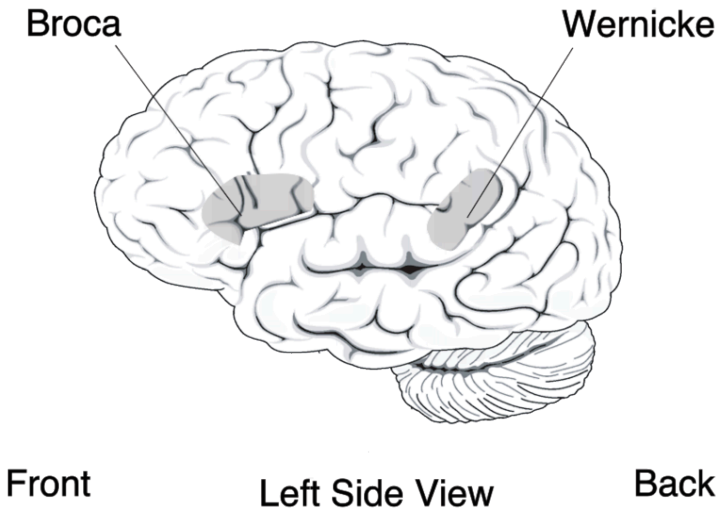


Figure 3. BROCa's area for Speech PROduction is located in the left FRONtal lobe. WERNicke's area for Speech PERception is located in the left temporal lobe.

These and countless other examples show that brain damage can lead to behavioral and cognitive impairments. Such cases demonstrate **localization of function**—that certain brain regions perform specific functions (like the previous examples of impulse control, speech production, and perception). However, studies with human brain damage are a limited tool for understanding the brain. For example, when a patient suffers brain damage from force, trauma, a tumor, stroke, or a neurosyphilitic lesion (like Broca's patient Tan), that brain damage is a) unique to that patient making it difficult to extrapolate or generalize to others' brains, and b) rarely confined to just one brain area thus making it difficult to isolate the roles of specific brain structures. Creating controlled and localized damage to human brains in laboratory experiments is not possible, so researchers have resorted to creating carefully controlled brain damage or lesions in laboratory animals, such as mice and rats.

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4.3: INVASIVE PHYSIOLOGICAL RESEARCH METHODS

Invasive techniques, such as lesioning brain regions or implanting recording electrodes in the brain, are commonly used in biopsych research with non-human animals. For the experimental procedure, the animal undergoes surgery using a **stereotaxic unit** that allows precise positioning in the brain (see **Figure 4**). The stereotaxic unit has two main parts: a head holder to immobilize the head, and an electrode holder, which holds the device to be inserted. After the animal is anesthetized, its head is immobilized in the head holder. To locate target positions in the brain, researchers use a stereotaxic atlas (like a road atlas, but showing locations of brain regions instead of roads and cities). Then the researcher drills a small hole and performs the surgery. In some studies, researchers will lesion or remove a part of the brain; this is called ablation. The surgeon may use a surgical knife, a current-passing electrode, or an aspirating (suction) pipette. After the target region is carefully removed or inactivated, the animal's behavior is tested to determine the function of the lesioned structure. For example, researchers may remove (sub)components of the amygdala or hypothalamus and test how behavior changes. Studies will often include a control condition, in which control animals receive a *sham lesion*, wherein they undergo a similar surgical procedure but don't receive a lesion. This control condition allows researchers to more confidently interpret that the change in behavior stems from the lesioned brain area, rather than the handling, anesthesia, or other ancillary procedures. In other words, the direct manipulation of the brain, coupled with the control condition, allows researchers to make causal claims (something that cannot be done with correlational research methods). After the animal's death,

its brain is often cut into thin slices and stained to highlight neuronal structures. These slices are then examined microscopically to verify the extent and precise location of the lesions.

As an alternative to *permanent* lesions, researchers can lesion brain regions *temporarily*. This can be achieved by cooling the target brain tissue or injecting it with an anesthetic. Additionally, electrical stimulation from implanted electrodes can temporarily inactivate or activate targeted brain regions.



Figure 4. A stereotaxic device used to perform surgeries on rodents. This unit would immobilize an anesthetized rat and allow precise placement of electrodes in the brain.



Figure 5. A lab rat with a brain implant that was used to record neuronal activity while the rat performed a particular task (vibration discrimination in this case). In this picture, a scientist feeds the rat apple juice through a pipette.

In addition to manipulating brain function by damaging or stimulating brain regions, researchers learn about brain function by implanting recording devices directly in animal brains to ‘listen in’ on brain activity. The animal undergoes a stereotaxic surgery wherein a recording device or electrode is inserted into a target area then fixed into position on the skull (see **Figure 5**). Different types of invasive electrophysiological recording include: *intracellular* unit recording, wherein a microelectrode is inserted *into* a single neuron to measure its electrical activity; *extracellular* recordings that pick up the firing of one nearby neuron (single unit recording) or several adjacent neurons (multiunit recording); and invasive electroencephalography (EEG), wherein a large electrode picks up the electrical brain activity of a large swath of nearby neurons. These electrodes detect neural activity as the animal performs tasks, providing insight into the relationship between neural activity and behavior.

Directly recording from within *human* brains for research is rare, as

invasively opening the skull cannot be ethically justified for research purposes alone. However, some patients who are already undergoing surgery for medical procedures, such as treatments for Parkinson's disease or epilepsy, might have electrodes placed directly on or in their brains. They occasionally participate in research. Such intracranial (meaning *within the skull*) electroencephalography (iEEG) or Electrocorticography (ECoG) is a valuable research tool because these direct recordings offer exceptionally clear and precise signals from the brain. However, these patients are rare, and the placement of electrodes is determined by the neurosurgeon and medical needs rather than the research question.

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4.4: TOOLS OF COGNITIVE NEUROSCIENCE – EEG AND MEG

Advances in technology have led to increasingly sophisticated brain recording techniques. Just as X-rays allow us to peer inside the body, neuroimaging techniques enable us to view the working brain (Raichle, 1994). Biopsychology employs various noninvasive methods to study human brain function, each with its own advantages and disadvantages. It's crucial to recognize that each technique offers a unique perspective on brain activity. Understanding these methods is essential, as our comprehension of the brain is closely tied to available technologies. As new techniques develop, we can anticipate an even deeper understanding of brain function (Biswas-Diener, 2023).

Electroencephalography (EEG) measures the electrical activity of the brain and has been used for a century (e.g., Berger, 1929). When large populations of neurons are active, they create a small electrical voltage that passes through the skull and scalp. Electrodes on the participant's head pick up the voltages, which are amplified and recorded. Researchers can record the voltages from brain activity as the participant performs a task.

The electrical signals generated in the brain become distorted as they travel through brain tissue, skin, and bone. As a result, researchers can only approximate the original source of these signals within the brain. This uncertainty is especially pronounced for signals originating deep within the brain (even with advanced tools such as structural brain scans, high-density electrode coverage from a cap with 256 electrodes, and sophisticated analysis algorithms for localization). Thus, EEG's ***spatial* resolution**—its ability to pinpoint *where* activity occurs in the brain—is relatively low. Conversely, EEG's ***temporal* resolution** is excellent and indicates *when*

something happens in the brain with millisecond precision. EEG's superior temporal resolution makes it ideal for examining the brain's rapid response to a stimulus event, or the event-related potentials (ERP). In a typical ERP experiment, researchers might play a visual or auditory event like a word, and measure the corresponding voltage changes that unfold in the brain over the next few hundred milliseconds. The amplitude, timing, and topography (position) of the EEG signal capture the underlying neural/mental processes.

The high temporal resolution and continuous recording of EEG allows it to capture different frequency brain waves, such as theta waves (oscillating at 4-7 Hertz (Hz), i.e., cycles per second), alpha waves (at 8-13 Hz), and beta waves (at 14-30 Hz). Brain oscillations, reflecting the combined activity of millions of neurons, capture attentional and conscious states. These oscillations play a crucial role in information encoding and attention modulation in the brain (da Silva, 2013). In addition to research applications, EEG plays a crucial role in clinical diagnosis, particularly in identifying epilepsy, seizures, and sleep disorders.



Figure 6. Participant wearing an EEG cap that uses electrodes to pick up voltages on the scalp.



Figure 7. An EEG readout of voltages at 16 electrode sites. Each row is one electrode; the voltage of each electrode is mapped on the vertical axis; and time is mapped on the horizontal axis with each vertical line marking 1 second. This particular EEG readout shows the characteristic 3 Hz spike and wave discharges in a child with epilepsy (notice the 3 peaks occurring every second).

Magnetoencephalography (MEG) is similar to EEG, but instead of electrical signals, MEG picks up the weak *magnetic* fields generated by the flow of electrical charge associated with neural activity. Because the magnetic fields generated by brain activity are so small, special rooms are needed that shield out magnetic fields in the environment so that the MEG sensors pick up magnetic fields from neural activity without environmental contamination. Similar to EEG, MEG also has excellent (millisecond)

temporal resolution. The spatial resolution of MEG is far better than EEG because magnetic fields pass relatively unchanged through hard and soft tissue, so are not distorted by skull and scalp. Despite MEG's excellent spatial *and* temporal resolution, it is less widely used than EEG because its much more expensive and complex to operate.

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4.5: TOOLS OF COGNITIVE NEUROSCIENCE – BRAIN IMAGING, PET AND MRI

Many imaging technologies can capture detailed inner images of the brain. In the 1970s, the development of computerized tomography (CT) scans allowed non-invasive imaging of the living brain using X-rays. CT scans are rarely used today for research purposes due to radiation exposure and relatively low image resolution.

Positron Emission Tomography (PET) scans are a powerful way to image brain *activation* (as opposed to brain structure). The PET scanner detects a radioactive substance that is injected into the bloodstream of the participant just before or while they perform a task (e.g., adding numbers). Because active neuron populations require metabolites, more blood flows into active regions bringing with it more radioactive substances. PET scanners detect the injected radioactive substance in specific brain regions, allowing researchers to infer that those areas were active during the task. PET scans are not common in biopsych research because they require the ability to work with radioactive materials and expose subjects to low-levels of radiation. However, PET is a powerful tool that provides the unique capability of identifying the distribution of particular molecules, like neurotransmitters or receptors, in the brain.

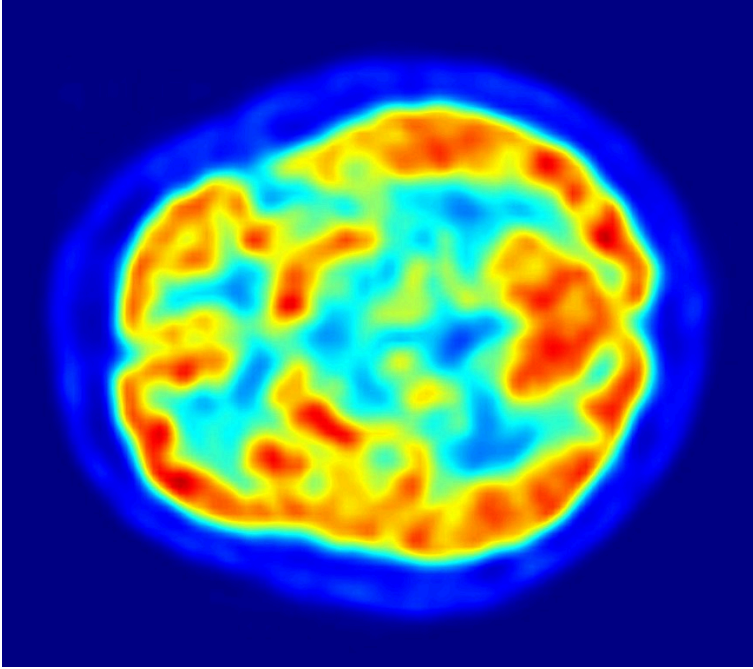


Figure 8. This is a transaxial slice of the brain taken with positron emission tomography (PET). Red areas show more accumulated tracer substance and blue areas show where little to no tracer has accumulated.

Magnetic Resonance Imaging

The most commonly used brain-imaging modality today is Magnetic Resonance Imaging (MRI). An MRI machine can produce different types of scans: high-resolution images of brain structure (*structural* MRI or sMRI) and brain function (*functional* MRI or fMRI). MRI scanners may be expensive, noisy, and claustrophobic to some, but they are harmless and painless and are powerful and prevalent tools for illuminating brain structure and function.

MR scanners use a strong magnetic field that is 60,000 times stronger than the Earth's magnetic field. As a person lies very still in the scanner,

the magnetic field forces protons in their body to align. Pulsations of low-energy radio frequencies cause the protons to change their spin. As the radiofrequency is turned off, these protons return to their aligned state and give off energy that is detected by MRI sensors. The timing and amount of energy released as protons realign with the magnetic field vary based on tissue type. This variation allows clear differentiation between the brain's white matter, gray matter, cerebrospinal fluid, bone, blood, and other tissues.



Figure 9. MRI scanner with subject laying down in the scanner bore.

Structural magnetic resonance imaging (sMRI) creates detailed images of brain structure with millimeter resolution. The high-resolution 3D

images might show the brain's gray matter and white matter in *voxels* (i.e. like 3D pixels) that are 1mm x 1mm x 1mm cubes. Researchers may use these images to compare the size of brain structures across different groups (for example, are areas associated with pleasure smaller in individuals with depression, or are areas controlling finger movements larger in string musicians compared to vocalists or trombonists?). These structural images can also enhance the spatial accuracy of functional magnetic resonance imaging (fMRI) measurements.

Diffusion Tensor Imaging (DTI) is a variant of structural Magnetic Resonance Imaging that focuses on myelinated axon pathways in the brain. DTI imaging is highly sensitive to the movement of water molecules in the brain. Because water moves differently along myelinated axons in the brain, DTI can map out the large white matter tracts, that, like superhighways, connect distant brain regions (e.g., the *corpus callosum*, a white matter fiber tract that connects right and left cerebral hemispheres, or the *arcuate fasciculus*, a bundle of axons that connects Broca's area and Wernicke's area, see **Figure 10**). DTI can be used to examine white matter integrity in diseases such as Multiple Sclerosis or to observe brain plasticity after learning a new skill like juggling.

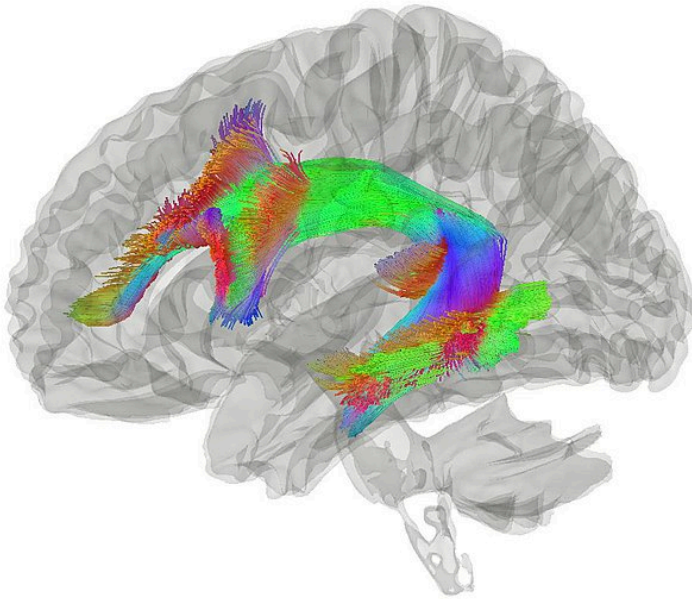


Figure 10. DTI image showing the white matter tracts, including the arcuate fasciculus, a bundle of axons that connects Broca's area and Wernicke's area.

Functional MRI (fMRI) uses the same MR scanners, but instead of capturing a high-resolution snapshot of brain structure, it measures brain “function” or activation while a subject performs some task. As a brain region becomes more active, it uses oxygen and causes an inflow of oxygenated blood to that region over the following few seconds. fMRI measures the change in the concentration of oxygenated hemoglobin, which is known as the blood-oxygen-level-dependent (BOLD) signal. From the BOLD signal, researchers infer neuronal activation in that brain region (note that fMRI does not *directly* measure the neuronal activity). Because cerebral blood flow is coupled with neural activation, researchers can map brain activation while people in the scanner perform tasks like reading,

speaking, viewing images of faces or places, recalling memories, etc. In this way, fMRI provides evidence of localization of function and which areas are active during specific tasks. fMRI has high ***spatial resolution*** and the activation maps in a typical fMRI study consist of cubic voxels that are a few mm on each side. However, the ***temporal resolution*** of fMRI is quite poor and it typically takes a snapshot of brain activation averaged over a 2- or 3-second window.

In addition to measuring BOLD responses while subjects perform some task, fMRI can measure subjects' brain activation over many minutes while they perform no task (so-called “resting state scans” wherein they might lay in the brain scanner for 10 minutes while instructed “don’t do anything in particular”). Such recordings have shown surprisingly correlated spontaneous fluctuations of brain regions that can be far apart from each other in the brain. Regions with highly correlated activation work together in the same large-scale distributed network. The brain has several large-scale networks including sensorimotor, attention, control, default mode, and limbic networks.

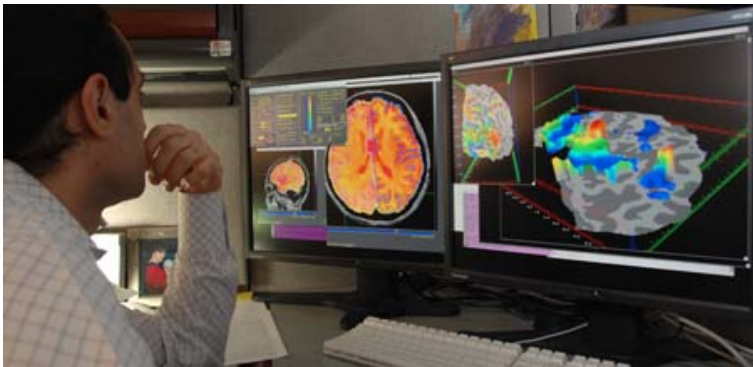


Figure 11. Researcher checking MRI images. On the monitor on the right, activations are overlaid on brain structure; typically “hotter” colors (reds and oranges) denote *more* brain activation than a baseline, and “cooler” colors (blues and greens) denote *less* brain activation than baseline.

While fMRI is popular and powerful and people find the pretty images convincing, they are correlational and don't fully explain the causal role of specific brain regions in determining mental processes. This is an important example of why it is essential to rely upon converging evidence—as an example, correlational fMRI data coupled with causal experimental data from lab animals. Also to address some of the limits of correlational research, researchers are developing techniques that can directly modulate brain activity.

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4.6: TECHNIQUES THAT MODULATE BRAIN ACTIVITY

Neuroimaging studies focus on correlations between brain activity and behavior and can't establish a causal role of a brain region in determining behavior. To establish a causal rather than correlational relationship, we need to alter brain function and observe resulting changes in behavior. Lesions are one way to modify brain structure and can reveal a causal relationship (e.g., when losing a brain region leads to loss of function, that brain area is necessary or involved in the function). However, invasive lesions can only be introduced in animals, which differ from humans in key ways. Lesions in human brains can only be studied in patient populations; that is, after a patient experiences brain damage from a stroke or other injury. New technologies allow researchers to temporarily and non-invasively modify human brain function.

Transcranial magnetic stimulation (TMS) is a form of brain stimulation that uses magnets to alter brain activity. Researchers place a magnetic coil over the scalp and apply a magnetic current that stimulates the neurons below the magnetic coil (**Figure 12**). Depending on the type and rate of magnetic pulses, TMS can temporarily “turn off” or “turn on” the brain area under the coil. In research domains, researchers might temporarily “turn off” or “turn on” parts of the frontal lobe and look at subsequent feelings of craving or emotion processing. TMS is also used in clinical settings and has effectively treated some individuals with depression (Perera et al., 2016).

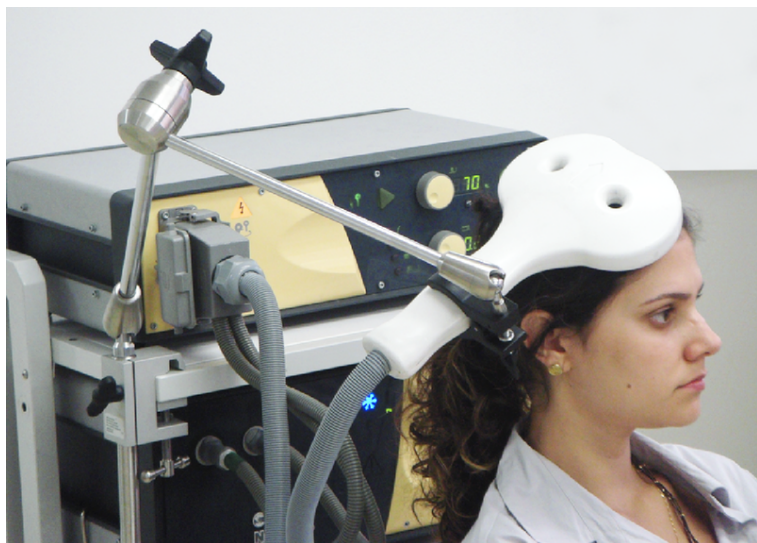


Figure 12. A transcranial magnetic stimulation (TMS) coil placed over a person's scalp.

Transcranial direct current stimulation (tDCS) is similar to TMS except that it uses electrical current directly (rather than inducing it with magnetic pulses) via small electrodes on the skull (Beck & Tapia, 2023). A brain area is stimulated by a low current (equivalent to an AA battery) for an extended time. When combined with cognitive training, tDCS has been shown to improve many cognitive functions such as mathematical ability, memory, attention, and coordination (e.g., Brasil-Neto, 2012; Feng et al., 2013; Kuo & Nitsche, 2012).

Gene Knockout is a genetic technique used in animals, wherein researchers remove or inactivate a specific gene. This allows researchers to study the function of that gene in a living organism and its effects on the phenotype. Gene knockout is considered a “loss-of-function mutation” (what function is lost after knocking out a specific gene?). Gene knockouts are used in many organisms including fruit flies, zebrafish, and mice. Studies using “knockout mice” have been extremely valuable in understanding the role of genes in brain development, neurological disease,

cancer, immune disorders, and even the genes involved in bad breath (Pol et al., 2018). **Gene Knock-in** is a related technique, but instead of removing a gene, knock-in inserts a gene. Gene knock-in is considered a “gain-of-function mutation” (what function is gained after inserting this gene?).

Brainbow is another innovative transgenic technique (transgenic means transferring genes from one organism to another) that inserts genetic material to label individual neurons with distinct colors and produces detailed neural maps. In Brainbow, green fluorescent protein, a protein found in jellyfish and corals that exhibits bright green fluorescence, is genetically modified to produce different colors. These various fluorescent proteins are then inserted into individual neurons in different ratios, flagging each neuron with a unique color (see **Figure 13**). Brainbow has enabled the *simultaneous* mapping of hundreds of neurons and allows scientists to trace the intricate connections between neurons. Thus, Brainbow has been groundbreaking for the field of neural connectomics, which studies the organization of neural networks. This technique provides striking images of neurons and highlights biopsych research at the molecular and cellular level.

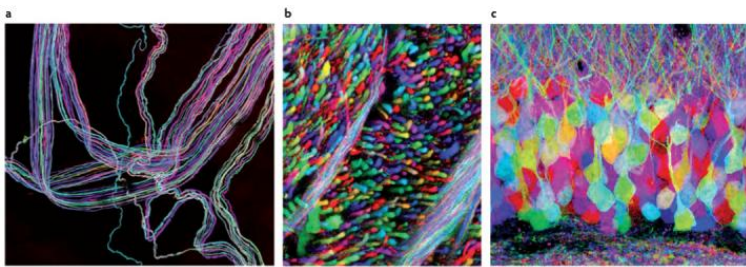


Figure 13. Three brainbows of mouse neurons from Lichtman et al. (2008). a) a motor nerve innervating ear muscle. b) An axon tract in the brainstem. c) The hippocampal dentate gyrus.

Optogenetics is an especially exciting technique for manipulating brain activity in non-human animals (Deisseroth, 2011). Optogenetics uses light

to control specific populations of neurons in living animals. For the neurons to be sensitive to light, researchers genetically insert light-sensitive proteins (taken from algae) into a specific type of neuron. After inserting tiny optical fibers into the animal's brain, researchers can turn on the light to excite or inhibit these specific cells. Scientists have used the ability to control the activity of specific neuronal populations to investigate their role in learning, memory, decision-making, addiction, movement, and many other areas of active research.

In sum, the various research techniques used in biological psychology each have their strengths and weaknesses in terms of spatial resolution, temporal resolution, ease-of-use, invasiveness, cost, precision, etc. Using the different tools in a complementary manner provides converging evidence for understanding how the brain works.

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CHAPTER 5: PSYCHOPHARMACOLOGY

This chapter was adapted from:

Barron, S. (2023). Psychopharmacology. In R. Biswas-Diener & E. Diener (Eds), *Noba textbook series: Psychology*. Champaign, IL: DEF publishers. Retrieved from <http://noba.to/umx6f2t8> License: CC BY-NC-SA 4.0 DEED

Psychopharmacology is the study of how drugs affect behavior. If a drug changes your perception or the way you feel or think, the drug exerts effects on your brain and nervous system. We call drugs that change the way you think or feel psychoactive or psychotropic drugs, and almost everyone has used a psychoactive drug at some point (yes, caffeine and alcohol count). Understanding some basics about psychopharmacology can help us better understand a wide range of things that interest psychologists and others. For example, the pharmacological treatment of certain neurodegenerative diseases, such as Parkinson's disease, tells us something about the disease itself. The pharmacological treatments used to treat psychiatric conditions such as schizophrenia or depression have undergone amazing development since the 1950s, and the drugs used to treat these disorders tell us something about what is happening in the brains of individuals with these conditions. Finally, understanding something about the actions of drugs of abuse and their routes of administration can help us understand why some

psychoactive drugs are so addictive. In this chapter, we provide an overview of some of these topics and discuss some current controversial areas in psychopharmacology. The chapter concludes with some examples and animations of how drugs like alcohol, opiates, cannabis, and caffeine work at the level of neurotransmitters and synapses.

Learning Objectives

- How do the majority of psychoactive drugs work in the brain?
- How does the route of administration affect how rewarding a drug might be?
- Why is grapefruit dangerous to consume with many psychotropic medications?
- Why might individualized drug doses based on genetic screening be helpful for treating conditions like depression?
- Why is there controversy regarding pharmacotherapy for children, adolescents, and the elderly?

5.1: INTRODUCTION

Psychopharmacology, the scientific study of how drugs affect the brain and behavior, is a relatively new science. However, people have been taking drugs to change how they feel and think since early human history (e.g., consuming fermented fruit, early forms of beer, coca leaves as stimulants, and mind-altering mushrooms in rituals). The term *psychopharmacology* tells us that this field bridges brain, behavior, and pharmacology, encompassing a broad range of topics.

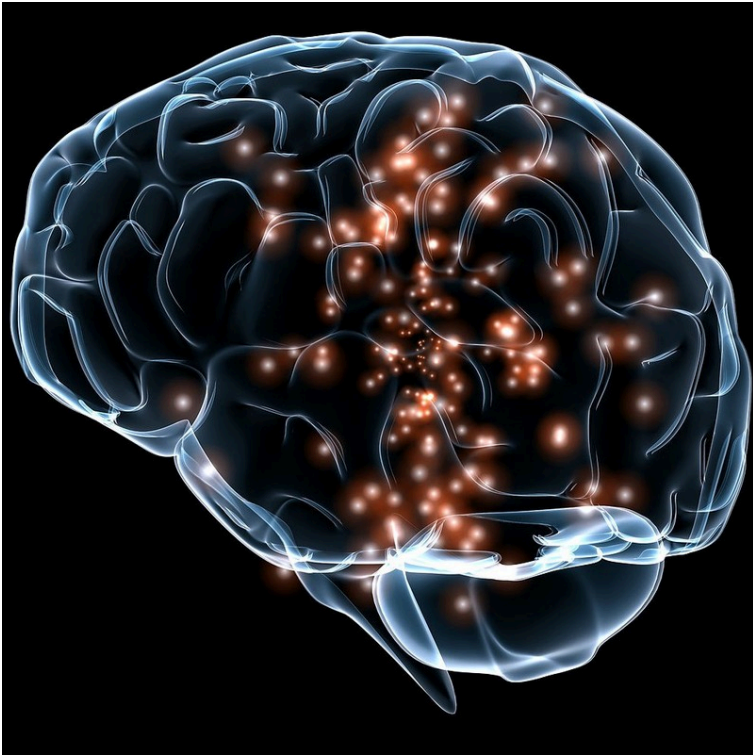


Figure 1. Drugs that alter our feelings and behavior do so by modulating neurotransmission in the brain.

Virtually any drug that changes the way you feel does so by altering how neurons communicate with each other. Neurons communicate with each other by releasing a chemical (**neurotransmitter**) across a tiny space between two neurons (the **synapse**). When the neurotransmitter crosses the synapse, it binds to a postsynaptic receptor on the receiving neuron, and the message may then be transmitted onward. Neurotransmission is far more complicated than this—we reviewed neurotransmission in a previous chapter, and links at the end of this chapter can provide useful additional information—but the first step is understanding that virtually all

psychoactive drugs modulate how neurons communicate with each other.

Several neurotransmitters play crucial roles in psychopharmacological treatments and drugs of abuse (examples in **Table 1**). The neurons that release these neurotransmitters, for the most part, are localized within specific circuits of the brain that mediate these behaviors. Psychoactive drugs can either increase activity at the synapse (these are called **agonists**) or reduce activity at the synapse (**antagonists**). Different drugs do this by various mechanisms, and examples of agonists and antagonists are presented in **Table 2**. Each example includes the drug's trade name from the drug company and its generic name in parentheses.

Table 1. How neurotransmitters affect behaviors or diseases

Neurotransmitter	Abbreviation	Behaviors of Diseases Related to These Neurotransmitter
Acetylcholine	ACh	Learning and memory; Alzheimer's disease' muscle movement in the peripheral nervous system
Dopamine	DA	Reward circuits; Motor circuits involved in Parkinson's disease; Schizophrenia
Norepinephrine	NE	Arousal; Depression
Serotonin	5HT	Depression; Aggression; Schizophrenia
Glutamate	GLU	Learning; Major excitatory neurotransmitter in the brain
GABA	GABA	Anxiety disorders; Epilepsy; Major inhibitory neurotransmitter in the brain
Endogenous Opioids	Endorphins, Enkephalins	Pain; Analgesia; Reward

A link at the end of this chapter shows various steps involved in neurotransmission and some ways drugs can alter them.

Table 2 provides examples of drugs and their primary mechanism of action, but it is important to realize that drugs also affect other neurotransmitters. This contributes to a drug's side effects. Current drugs lack precise targeting to specific brain regions or individual

neurotransmitter systems. In many cases, individuals are sometimes prescribed one **psychotropic drug** but then may also have to take additional drugs to reduce the side effects caused by the initial drug. Some side effects can be so severe that individuals stop taking their medication.

Table 2. Examples of drugs, their primary mechanism of action, use, and whether agonists (increase activity at the synapse) or antagonists (reduce activity at the synapse).

Drug	Mechanism	Use	Agonist/ Antagonist
L-dopa	Increase Synthesis of DA	Parkinson's disease	Agonist for DA
Adderall (mixed salts amphetamine)	Increase Synthesis of DA, NE	ADHD	Agonist for DA, NE
Ritalin (methylphenidate)	Blocks removal of DA, NE and lesser (5HT) from synapse	ADHD	Agonist for DA, NE mostly
Aricept (donepezil)	Blocks removal of ACh from synapse	Alzheimer's disease	Agonist for ACh
Prozac (fluoxetine)	Blocks removal of 5HT from synapse	Depression, obsessive- compulsive disorder	Agonist 5HT
Seroquel (quetiapine)	Blocks DA and 5HT receptors	Schizophrenia, bipolar disorder	Antagonist for DA, 5HT
Revia (naltrexone)	Blocks opioid post-synaptic receptors	Alcoholism, opioid addiction	Antagonist (for opioids)

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5.2: PHARMACOKINETICS: WHAT IS IT AND WHY IS IT IMPORTANT?

Pharmacokinetics refers to how the body handles a drug that we take. As mentioned earlier, psychoactive drugs exert their effects on behavior by altering neuronal communication in the brain, and the majority of drugs reach the brain by traveling in the blood. The acronym ADME is often used in pharmacology and stands for Absorption (how the drug gets into the blood), Distribution (how the drug gets to the organ of interest – in this chapter, that is the brain), Metabolism (how the drug is broken down so it no longer exerts its psychoactive effects), and Excretion (how the drug leaves the body). Let's examine these processes for psychoactive drugs.

Drug Administration

Drugs can be administered through various routes, each affecting the speed at which they reach the brain. The most common route of administration is oral administration, which is relatively slow and often the most variable route. Drugs enter the stomach and then get absorbed by the blood supply and capillaries that line the small intestine. The absorption rate can be affected by many factors, including the quantity and the type of food in the stomach (e.g., fats vs. proteins). This is why the medicine labels for some drugs (like antibiotics) may specifically state foods that you should or should NOT consume within an hour of taking the drug because they can affect the absorption rate. Two of the most rapid routes of administration include inhalation (i.e., smoking or gaseous anesthesia) and intravenous (IV) in which the drug is injected directly into the vein and hence the blood

supply. Both of these routes of administration can get the drug to the brain in less than 10 seconds. IV administration also has the distinction of being the most dangerous because if an adverse reaction occurs, there is little time to administer an antidote, as in the case of an IV heroin overdose.



Figure 2. A drug delivered by IV reaches the brain more quickly than if the drug is taken orally. While rapid delivery has advantages, there are also risks involved with IV administration.

Why might how quickly a drug gets to the brain be important? If a drug activates the reward circuits in the brain AND it reaches the brain very quickly, the drug has a high risk for abuse and addiction. Psychostimulants like amphetamine or cocaine are examples of drugs that have a high risk

for abuse because they are agonists at dopamine (DA) neurons involved in reward AND because these drugs exist in forms that can be either smoked or injected intravenously. Some argue that cigarette smoking is one of the most difficult addictions to overcome; this might partially stem from the rapid nicotine delivery to the brain (indirectly activating dopaminergic neurons), but the full story is more complicated. For drugs that reach the brain very quickly, not only is the drug very addictive, but so are the cues associated with the drug (see Rohsenow et al., 1990). For a crack user, this could be the pipe that they use to smoke the drug. For a cigarette smoker, however, the cue could be something as normal as finishing dinner or waking up in the morning (if that's when the smoker typically has a cigarette). For both the crack user and the cigarette smoker, the cues associated with the drug may cause craving and lead to relapse. This is one of the reasons individuals who enroll in drug treatment programs, especially out-of-town programs, are at significant risk of relapse if they later find themselves in proximity to old haunts, friends, etc. But this is much *more* difficult for a cigarette smoker. How can someone avoid common smoking cues like eating or avoid waking up in the morning, etc.? These examples help you begin to understand how important the route of administration can be for psychoactive drugs.

Drug Metabolism

Metabolism involves the breakdown of psychoactive drugs, and this occurs primarily in the liver. The liver produces **enzymes** (proteins that speed up a chemical reaction), and these enzymes help catalyze a chemical reaction that breaks down psychoactive drugs. Enzymes exist in “families,” and many psychoactive drugs are broken down by the same family of enzymes, the cytochrome P450 superfamily. There is not a unique enzyme for each drug; rather, certain enzymes can break down a wide variety of drugs. Tolerance to the effects of many drugs can occur with repeated exposure; that is, the drug produces less effect over time, so more of the drug is needed

to get the same effect. This is particularly true for sedative drugs like alcohol or opiate-based painkillers. *Metabolic tolerance* is one kind of tolerance, and it takes place in the liver. Some drugs (like alcohol) cause **enzyme induction**—an increase in the enzymes produced by the liver. For example, chronic drinking results in alcohol being broken down more quickly, so an alcoholic needs to drink more to get the same effect—of course, until so much alcohol is consumed that it damages the liver (alcohol can cause fatty liver or cirrhosis).

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5.3: RECENT ISSUES RELATED TO PSYCHOTROPIC DRUGS AND METABOLISM

Grapefruit Juice and Metabolism

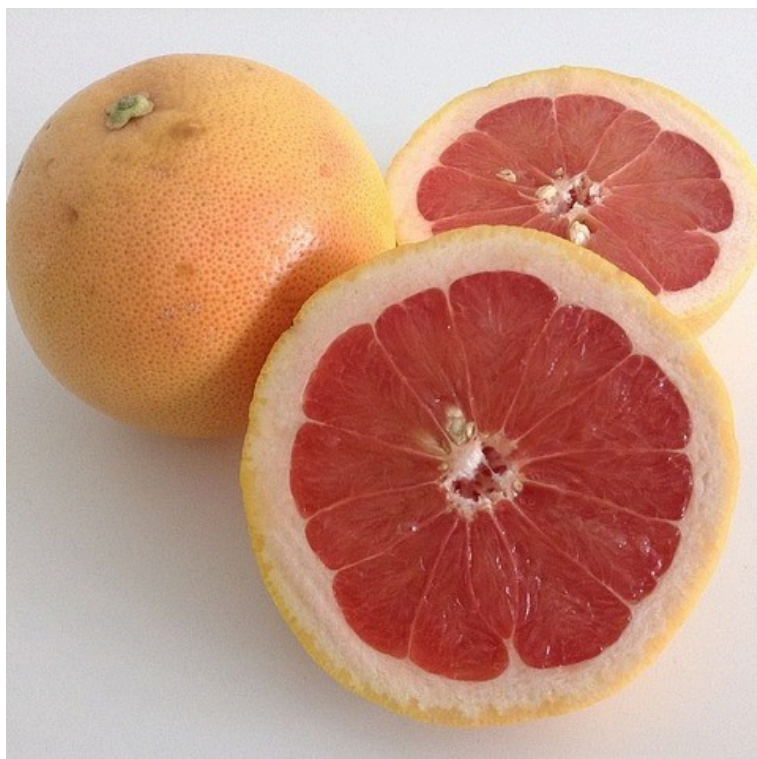


Figure 3. Grapefruit can interfere with enzymes in the liver that help the body to process certain drugs.

Certain types of food in the stomach can alter the rate of drug absorption, and other foods can alter the rate of drug metabolism. The most well-known is grapefruit juice. Grapefruit juice suppresses cytochrome P450 enzymes in the liver, and these liver enzymes normally break down a large variety of drugs (including some psychotropic drugs). If the enzymes are suppressed, drug levels can build up to potentially toxic levels. In this case, the effects can persist long after consuming grapefruit juice. As of 2013, at least 85 drugs have been shown to interact adversely with grapefruit juice (Bailey et al., 2013). Some psychotropic drugs that likely interact with grapefruit juice include carbamazepine (Tegretol), prescribed for bipolar disorder; diazepam (Valium), used to treat anxiety, alcohol withdrawal, and muscle spasms; and fluvoxamine (Luvox), used to treat obsessive-compulsive disorder and depression. A link at the end of this chapter gives the latest list of drugs reported to have this unusual interaction.

Individualized Therapy, Metabolic Differences, and Potential Prescribing Approaches for the Future

Mental illnesses contribute to more disability in Western countries than all other illnesses, including cancer and heart disease. Globally, depression and anxiety disorders are among the highest causes of health burden, and the mental health system in most countries is under-resourced (Santomauro et al., 2021). The numbers of people affected by mental health issues are astonishing, with estimates that 25% of adults experience a mental health issue in any given year, and this affects not only the individual but also their friends and family. One in 17 adults experience a serious mental illness (Kessler et al., 2005). Newer antidepressants are probably the most frequently prescribed drugs for treating mental health issues, although there is no “magic bullet” for treating depression or other conditions.

Pharmacotherapy with psychological therapy may be the most beneficial treatment approach for many psychiatric conditions, but many questions remain unanswered. For example, why does one antidepressant help one individual yet has no effect on another? Antidepressants can take 4 to 6 weeks to start improving depressive symptoms, and we don't understand why. Many individuals do not respond to the first prescribed antidepressant and may need to try various medications before finding an effective treatment. Some individuals show no improvement with any antidepressants (Ioannidis, 2008). As our understanding of individual differences improves, we can more quickly and effectively assist those in distress.

Recent interest has focused on personalized treatment approaches. Genetic variations in cytochrome P450 enzymes affect drug-metabolism rates. The general population falls into the following 4 categories: 1) ***ultra-extensive metabolizers*** break down certain drugs (like some antidepressants) very, very quickly, 2) ***extensive metabolizers*** are also able to break down drugs fairly quickly, 3) ***intermediate metabolizers*** break down drugs more slowly than the two above groups, and finally 4) ***poor metabolizers*** break down drugs much more slowly than the other groups. Now consider someone receiving a prescription for an antidepressant—what would be the consequences if they were an ultra-extensive metabolizer or a poor metabolizer? The ultra-extensive metabolizer would be told it will probably take 4 to 6 weeks for the antidepressants to begin working (this is true), but they metabolize the medication so quickly that it will never be effective for them. In contrast, the poor metabolizer given the same dose of that antidepressant may build up such high levels in their blood (because they are not breaking down the drug), that they will have a wide range of side effects—also not a positive outcome. What if instead, prior to prescribing an antidepressant, the doctor could take a blood sample and determine which type of metabolizer a patient actually was? They could make an informed decision about the best dose to prescribe. New genetic tests are available to individualize treatment. A blood sample can determine (at least for some drugs) which

category an individual fits into, but we need data to determine if this actually is effective for treating depression or other mental illnesses (Zhou, 2009). While currently costly and often not covered by insurance, such genetic testing may become crucial in psychopharmacology's future. This research, along with studies on cell membranes, neuronal DNA, and receptor-site alterations, aims to explain the delayed onset of antidepressant effects.

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5.4: OTHER CONTROVERSIAL ISSUES

Juveniles and Psychopharmacology

A recent Centers for Disease Control (CDC) report suggested that as many as 1 in 5 children between the ages of 5 and 17 may have some mental disorder (e.g., ADHD, autism, anxiety, depression) (CDC, 2013). The incidence of bipolar disorder in children and adolescents has also increased 40 times recently (Moreno et al., 2007), and it is now estimated that 1 in 36 children have been diagnosed with an autism spectrum disorder (CDC, 2023). Why has there been such an increase in these numbers? This important question has no single answer. Some believe that greater public awareness has increased teacher and parent referrals. Some attribute the rise to changes in diagnostic criteria. Still others suggest environmental factors, prenatally or postnatally, have contributed to this upsurge.



Figure 4. There are concerns about both the safety and efficacy of drugs like Prozac for children and teens.

This question raises further controversy regarding the treatment of young individuals. Many psychotropic drugs used for treating psychiatric disorders have been tested in adults, but few have been tested for safety or efficacy with children or adolescents. The most well-established psychotropics prescribed for children and adolescents are the psychostimulant drugs for treating attention deficit hyperactivity disorder (ADHD), and there are clinical data on these drugs' effectiveness. However, we know far less about the safety and efficacy in young populations of the drugs typically prescribed for treating anxiety, depression, or other psychiatric disorders. The young brain continues to mature until well after

age 20, so some scientists are concerned that drugs that alter neuronal activity in the developing brain could have significant consequences. Clinical trials in minors are needed to test the safety and effectiveness of these drugs, raising ethical concerns about consent, participation, and compensation.

The Elderly and Psychopharmacology

Elderly populations are often excluded from psychotropic drug safety and efficacy trials. Currently, little high-quality evidence is available to guide prescribing for older adults—clinical trials often exclude people with multiple comorbidities (other diseases, conditions, etc.), which are typical for elderly populations (see Hilmer & Gnjdickt, 2008; Pollock et al., 2008). This is a serious issue because the elderly consume a disproportionate number of the prescription meds prescribed. The term **polypharmacy** refers to the use of multiple drugs, which is very common in elderly populations in the United States. Demographic projections suggest that by 2030, individuals aged 65 or older will constitute approximately 20% of the U.S. population, potentially accounting for 40% of prescribed medication consumption. Table 3 illustrates why standard clinical trials poorly capture the reality of elderly populations.

Table 3. Characteristics of clinical trial subjects vs. actual patients (Schwartz & Abernethy, 2008)
* OTC = Over the counter

Clinical Trial Subjects	Aged Patients Who Receive Drug Therapies
One drug	Drug of interest and medications
Single dose	Chronic administration
No disease	Multiple diseases
No alcohol, tobacco, OTC* drugs, nutraceuticals	OTC* drugs, nutraceuticals, alcohol, tobacco, and other
20-40 years (vs 60-75 years)	65-100+ years
Caucasians	Caucasians and minorities
Selection bias	All corners/socioeconomic basis

Drug metabolism often slows considerably for elderly populations, so less of a drug can produce the same effect (or all too often, too much of a drug can result in a variety of side effects). One of the greatest risk factors for elderly populations is falling and breaking bones, which can happen if the elderly person gets dizzy from too much of a drug. Psychotropic medications can also reduce bone density, thus worsening the consequences of falls (Brown & Mezuk, 2012). Despite growing awareness, geriatric pharmacotherapy presents complex medical and ethical challenges.

This chapter provided an introduction to some of the important areas in the field of psychopharmacology. Understanding psychopharmacology is crucial for understanding behavior, and has significant societal implications.

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5.5: HOW DRUGS AFFECT NEUROTRANSMITTERS

The chapter concludes with some examples and animations of how drugs like alcohol, caffeine, cannabis, and opiates work at the level of neurotransmitters and synapses (The Brain from Top to Bottom, n.d.). These examples are adapted from the website The Brain from Top to Bottom. (<https://thebrain.mcgill.ca/>). Animations and descriptions of other drugs, including nicotine, amphetamines, ecstasy, and benzodiazepine, can be found there.

Alcohol

Alcohol passes directly from the digestive tract into the blood vessels. In minutes, the blood transports the alcohol to all parts of the body, including the brain.

Alcohol affects the brain's neurons in several ways. It alters their membranes as well as their ion channels, enzymes, and receptors. Alcohol also binds directly to the receptors for acetylcholine, serotonin, GABA, and the NMDA receptors for glutamate.

Watch the animation to learn about how a GABA synapse functions without alcohol and with alcohol. GABA's effect is to reduce neural activity by allowing chloride ions to enter the post-synaptic neuron. These ions have a negative electrical charge, which helps to make the neuron less

excitable. This physiological effect is amplified when alcohol binds to the GABA receptor, probably because it enables the ion channel to stay open longer and thus let more Cl⁻ ions into the cell.

The neuron's activity would thus be further diminished, thus explaining the sedative effect of alcohol. This effect is accentuated because alcohol also reduces glutamate's excitatory effect on NMDA receptors.

However, chronic consumption of alcohol gradually makes the NMDA receptors hypersensitive to glutamate while desensitizing the GABAergic receptors. It is this sort of adaptation that would cause the state of excitation characteristic of alcohol withdrawal.

Alcohol also helps to increase the release of dopamine by a process that is still poorly understood but that appears to involve curtailing the activity of the enzyme that breaks down dopamine.



One or more interactive elements has been excluded from this version of the text. You can view them online here:

<https://rotel.pressbooks.pub/biologicalpsychology/?p=170#video-170-1>

Alcohol Animation illustrating GABA synapse function without and with alcohol (click bottom right of video player to make full screen). Source:

https://thebrain.mcgill.ca/flash/i/i_03/i_03_m/i_03_m_par/i_03_m_par_alcool.html#drogue

Caffeine

The stimulant effect of coffee comes largely from the way it acts on the adenosine receptors in the neural membrane. Adenosine is a

neuromodulator that has specific receptors. When adenosine binds to its receptors, neural activity slows down, and you feel sleepy. Adenosine thus facilitates sleep and dilates the blood vessels, probably to ensure good oxygenation during sleep.

Caffeine acts as an adenosine-receptor antagonist. This means that caffeine binds to these same receptors, leaving fewer receptors available for adenosine and its natural “braking” effect; therefore neural activity speeds up (see animation).

The activation of numerous neural circuits by caffeine also causes the pituitary gland to secrete hormones that cause the adrenal glands to produce more adrenaline. Adrenaline is the “fight or flight” hormone, so it increases your attention level and gives your entire system an extra burst of energy. This is exactly the effect that many coffee drinkers are looking for.

In general, you get some stimulating effect from every cup of coffee, and any tolerance you build up is minimal. On the other hand, caffeine can create a physical dependency. The symptoms of withdrawal from caffeine begin within one or two days after you stop consuming it. They consist mainly of headaches, nausea, and sleepiness and affect about one out of every two individuals.

Lastly, like most drugs, caffeine increases the production of dopamine in the brain’s pleasure circuits, thus helping to maintain the dependency on this drug, which is consumed daily by 90% of all adults in the U.S.



One or more interactive elements has been excluded from this version of the text. You can view them online here:

<https://rotel.pressbooks.pub/biologicalpsychology/?p=170#video-170-2>

Caffeine Animation showing the effects of caffeine on a GABA synapse (click bottom right of video player to make full screen). Caffeine binds to

receptors, leaving fewer available for adenosine and its natural braking effect, and consequently accelerating neural activity. Source:

https://thebrain.mcgill.ca/flash/i/i_03/i_03_m/i_03_m_par/i_03_m_par_cafeine.html#drogues

Cannabis

The sensations of slight euphoria, relaxation, and amplified auditory and visual perceptions produced by marijuana are due almost entirely to its effect on the cannabinoid receptors in the brain. These receptors are present almost everywhere in the brain, and an endogenous molecule that binds to them naturally has been identified: anandamide (Devane et al., 1992). This mechanism parallels opiates, which bind directly to the receptors for endorphins, the body's natural morphines.

Anandamide is involved in regulating mood, memory, appetite, pain, cognition, and emotions. When cannabis is introduced into the body, its active ingredient, Delta-9-tetrahydrocannabinol (THC), can therefore interfere with all of these functions.

THC begins this process by binding to the CB1 receptors for anandamide. These receptors then modify the activity of several intracellular enzymes, including cAMP, whose activity they reduce. Less cAMP means less protein kinase A. The reduced activity of this enzyme affects the potassium and calcium channels so as to reduce the amount of neurotransmitters released. The general excitability of the brain's neural networks is thus reduced as well.

However, in the reward circuit, just as in the case of other drugs, more dopamine is released. As with opiates, this paradoxical increase is explained by the fact that the dopaminergic neurons in this circuit do not have CB1 receptors but are normally inhibited by GABAergic neurons that do have them. Cannabis removes this inhibition by the GABA neurons and hence activates the dopamine neurons.

In chronic consumers of cannabis, the loss of CB1 receptors in the

brain's arteries reduces the flow of blood, and hence of glucose and oxygen, to the brain. The main results are attention deficits, memory loss, and impaired learning ability.



One or more interactive elements has been excluded from this version of the text. You can view them online here:

<https://rotel.pressbooks.pub/biologicalpsychology/?p=170#video-170-3>

Cannabis animation. Video illustrating the effects of cannabis on GABA and dopamine neurons (click bottom right of video player to make full screen). Source: https://thebrain.mcgill.ca/flash/i/i_03/i_03_m/i_03_m_par/i_03_m_par_cannabis.html#drogues

Opiates (Heroin, Morphine, Etc.)

The human body naturally produces its own opiate-like substances and uses them as neurotransmitters. These substances include endorphins, enkephalins, and dynorphins, often collectively known as endogenous opioids. Endogenous opioids are produced within the body and modulate our reactions to painful stimuli. They also regulate vital functions such as hunger and thirst and are involved in mood control, immune response, and other processes.

The reason that opiates such as heroin and morphine affect us so powerfully is that these exogenous substances (originating from outside the body) bind to the same receptors as our endogenous opioids. There are three kinds of receptors widely distributed throughout the brain: mu, delta, and kappa receptors.

These receptors, through second messengers, influence the likelihood

that ion channels will open, which in certain cases reduces the excitability of neurons. This reduced excitability is the likely source of the euphoric effect of opiates and appears to be mediated by the mu and delta receptors.

This euphoric effect also appears to involve another mechanism in which the GABA-inhibitory interneurons of the ventral tegmental area come into play. By attaching to their mu receptors, exogenous opioids reduce the amount of GABA released (see animation). Normally, GABA reduces the amount of dopamine released in the nucleus accumbens. By inhibiting this inhibitor, the opiates ultimately increase the amount of dopamine produced and the amount of pleasure felt.

Chronic consumption of opiates inhibits the production of cAMP, but this inhibition is offset in the long run by other cAMP production mechanisms. When no opiates are available, this increased cAMP production capacity comes to the fore and results in neural hyperactivity and the sensation of craving the drug.



One or more interactive elements has been excluded from this version of the text. You can view them online here:

<https://rotel.pressbooks.pub/biologicalpsychology/?p=170#video-170-4>

Opiates animation showing the effects of exogenous opioids on GABA and dopaminergic neurons (click bottom right of video player to make full screen). Source: https://thebrain.mcgill.ca/flash/i/i_03/i_03_m/i_03_m_par/i_03_m_par_heroine.html#drogues

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This section contains material adapted from:

The Brain from Top to Bottom website <https://thebrain.mcgill.ca/>

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5.6: DISCUSSION QUESTIONS AND RESOURCES

Discussion Questions

1. What are some of the issues surrounding prescribing medications for children and adolescents? How might this be improved?
2. What are some of the factors that can affect relapse to an addictive drug?
3. How might prescribing medications for depression be improved in the future to increase the likelihood that a drug would work and minimize side effects?

Outside Resources

Video: Neurotransmission

<http://www.youtube.com/watch?v=FR4S1BqdFG4>

Web: Description of how some drugs work and the brain areas involved – 1

<http://www.drugabuse.gov/news-events/nida-notes/2007/10/impacts-drugs-neurotransmission>

Web: Description of how some drugs work and the brain areas involved-2

<http://learn.genetics.utah.edu/content/addiction/mouse/>

Web: Information about how neurons communicate and the reward pathways

<http://learn.genetics.utah.edu/content/addiction/rewardbehavior/>

Web: National Institute of Alcohol Abuse and Alcoholism

<http://www.niaaa.nih.gov/>

Web: National Institute of Drug Abuse

<http://www.drugabuse.gov/>

Web: National Institute of Mental Health

<http://www.nimh.nih.gov/index.shtml>

Web: Report of the Working Group on Psychotropic Medications for Children and Adolescents: Psychopharmacological, Psychosocial, and Combined Interventions for Childhood Disorders: Evidence Base, Contextual Factors, and Future Directions (2008)

<http://www.apa.org/pi/families/resources/child-medications.pdf>

Web: Ways drugs can alter neurotransmission

https://thebrain.mcgill.ca/flash/i/i_03/i_03_m/i_03_m_par/i_03_m_par.html

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CHAPTER 6: HORMONES, SEX, AND GENDER

This chapter explores the intricate relationships between hormones, brain, behavior, sex, and gender. It introduces the field of behavioral endocrinology, examining how hormones influence behavior and conversely how behavior can affect hormone levels. The chapter delves into sexual differentiation, explaining how hormones shape biological sex characteristics and brain organization. It examines evidence for sex differences in psychology and the brain, and discusses complexities in studying sex differences. The chapter concludes by examining the diverse and variable nature of sex, gender, and sexual orientation, and their biological and environmental influences.

Learning Objectives

- Explain the basic terminology and principles of hormones and hormone-behavior interactions, including organizational and activational effects.
- Describe the process of sexual differentiation and the role of hormones.
- Analyze the evidence for and limitations of sex differences

in brain structure and function.

- Discuss the role of hormones in aggression and parental behavior.
- Define and differentiate sex, gender, and sexual orientation, and examine their complexities and variations.
- Evaluate some biological and environmental factors contributing to gender identity and sexual orientation.

6.1: INTRODUCTION TO HORMONES AND BEHAVIOR

This section explores the relationship between hormones and behavior. Hormones can influence various behaviors. For example, sex-hormone concentrations in the blood increase during puberty and decrease with age, particularly after 50, mirroring trends in sexual behavior. Overuse of anabolic steroid hormones is associated with aggression. While many hormones affect a range of behaviors, and many behaviors influence hormone levels, this chapter focuses on a few illustrative examples.

To understand the hormone-behavior relationship, it is important to describe hormones. **Hormones** are organic chemical messengers produced and released by specialized **endocrine glands**. Major hormone-producing structures include the pituitary, pineal, thyroid, and adrenal glands, the hypothalamus, and the gonads (male testes and female ovaries). Hormones are released from these glands into the blood, where they may travel to act on target structures at some distance from their origin. Hormones are chemical messengers similar in function to **neurotransmitters**, however, hormones can operate over a greater distance and longer time than neurotransmitters (**Focus Topic 1**).

Major classes of hormones are steroid hormones and protein or peptide hormones. Steroid hormones are generally synthesized from cholesterol in the gonads and adrenal glands. Examples include **testosterone** (a common type of androgen), estradiol (a common type of estrogen), **progesterone** (a common type of progestogen), and cortisol (a common type of glucocorticoid) (see Table 1, A-B). Protein hormones and peptide hormones are chains of amino acids; prominent examples include **oxytocin**, vasopressin, **prolactin**, and leptin.

Focus Topic 1: Neural Transmission versus Hormonal Communication

Although neural and hormonal communication both rely on chemical signals that are similarly released and received by cells, several prominent differences exist. One major difference is where the messages can travel. Hormonal messages can reach far more destinations—they travel via the circulatory system, so can reach any cell that receives blood and cover distances up to meters. Neural messages are much more limited in where they can travel—action potentials can only travel along existing neural pathways connected by synapses, and neurotransmitters travel the short distance across the synapse (~20 nanometers).

In addition to “synaptic transmission” (across the synapse), another type of signaling in the brain is **neuromodulation**. In neuromodulation, chemical substances are released into the extracellular space and affect many neurons, rather than just a single postsynaptic neuron (Marder, 2012). Common neuromodulators include some neurotransmitters (e.g., dopamine, serotonin, and acetylcholine) and neurohormones made in the brain, such as oxytocin and vasopressin. When released from a cell, they can alter the firing properties and synaptic connectivity of tens of thousands of neurons.

The timing and strength of neural and hormonal messages also differ. Action potentials are all-or-none events with a rapid onset and offset, occurring in milliseconds. When neuromodulators are released, their effects are more graded and can linger for hundreds of milliseconds to several minutes. Hormonal messages may unfold over seconds or hours. Therefore, neural

messages often mediate rapid changes in the body like movement, whereas hormonal messages are involved in longer-term processes such as growth, development, reproduction, and metabolism. Lastly, there is often more voluntary control of neural signals than hormonal ones. For example, moving limbs on command is easy for most, but it's virtually impossible to will a change in thyroid-hormone levels.

Table 1-A: Prominent Hormones That Influence Behavior

Steroid Hormones	
Cortisol	Increases carbohydrate metabolism; mediates stress responses
Estradiol	Uterine and other female tissue development; regulates sexual motivation and performance in females and males
Testosterone	Promotes sperm production and male secondary sexual characteristics; promotes sexual motivation and behavior, sometimes by being converted to estradiol

Table 1-B: Prominent Hormones That Influence Behavior

Peptides and Protein Hormones	
Oxytocin	Stimulates milk letdown and uterine contractions during birth; Promotes social bonding
Prolactin	Many actions relating to reproduction, water balance, and behavior associated with parental care
Thyroxine	Increases oxidation rates in tissue and affects neural development
Vasopressin	Increases water reabsorption in the kidney and affects learning, memory, social behavior

Hormones coordinate the physiology and behavior of individuals by regulating, integrating, and controlling bodily functions. Over evolutionary time, hormones have often been co-opted by the nervous system to influence behavior to ensure reproductive success. For example, the same hormones, testosterone and estradiol, that cause gamete (egg or sperm) maturation also promote mating behavior. This dual hormonal function ensures that mating behavior occurs when animals have mature gametes available for fertilization. Another example of endocrine regulation of physiology and behavior is provided by pregnancy. Estrogens and progesterone concentrations are elevated during pregnancy, and these hormones are often involved in mediating **maternal behavior** in the mothers.

Not all cells are influenced by every hormone. Rather, a hormone can directly influence only cells with **receptors** specific for that hormone. Cells with these specific receptors are called **target cells** for the hormone. After a hormone binds to its target cell, a series of cellular events activates enzymatic pathways or turns on or off genes that regulate protein synthesis. The newly synthesized proteins may activate or deactivate other genes, causing another cascade of cellular events. Importantly, sufficient numbers

of hormone receptors must be available for a hormone to produce any effects. For example, testosterone is important for male sexual behavior. If men have too little testosterone, then sexual motivation may be low, and it can be restored by testosterone treatment. However, if men have normal or elevated levels of testosterone yet display low sexual drive, then it might be caused by a lack of receptors, so treatment with additional hormones will not be effective.

To illustrate how hormones can affect behavior, let's consider singing in zebra finches (Goodson et al., 2005). Only male zebra finches sing, and they sing to attract mates. If adult male finches have their testes removed (i.e., are castrated), then the birds reduce singing. But castrated finches regain singing behavior if their testes are reimplanted or if they are treated with either testosterone or estradiol. While androgens and estrogens are often considered 'male' and 'female' hormones respectively, testosterone, an androgen, is commonly converted to estradiol, an estrogen (Figure 1). Thus, many male-like behaviors are associated with the actions of estrogens!

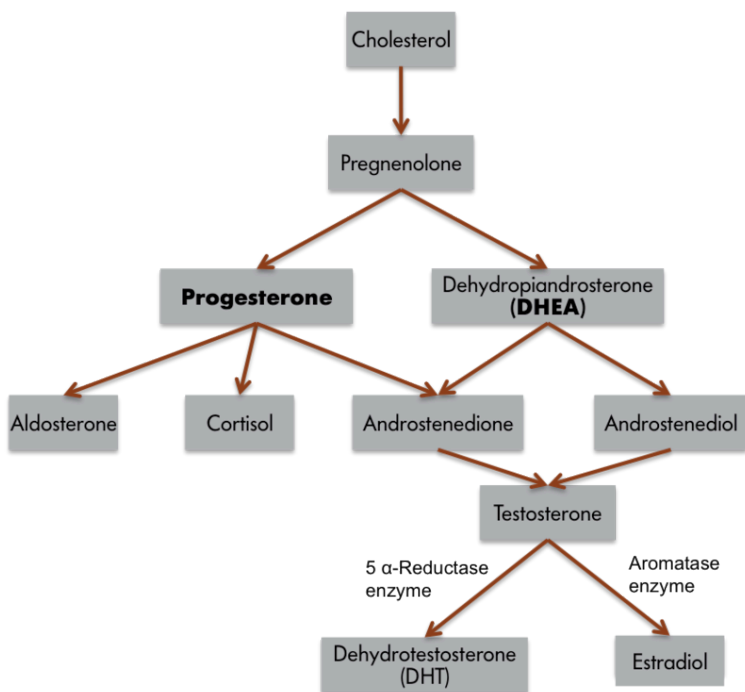


Figure 1: Biochemical Pathway for Steroid Hormone Synthesis: It is important to note that testosterone (an androgen) can be converted to another androgen, DHT, or an estrogen, estradiol. Too much or too little converting enzyme can influence the brain and behavior.

The birdsong example demonstrates how hormones can affect behavior, but the reciprocal relation also occurs—behavior can affect hormone levels. For example, seeing a territorial intruder may elevate a male bird's testosterone concentrations and thereby stimulate singing or fighting behavior. Similarly, male mice or rhesus monkeys that lose a fight decrease circulating testosterone concentrations for days or even weeks afterward. Comparable results occur in humans. Testosterone concentrations in humans are affected after physical combat, and even after simulated battles. For example, testosterone concentrations were elevated in winners and reduced in losers of regional chess tournaments.



Figure 2. The expectation of events can influence one's hormonal activity. How do you think hormonal activity is affected if you anticipate going on a date with a romantic interest?

People's hormone concentrations can also be affected by a contest even when they are not directly involved. Researchers measured testosterone levels of male soccer fans. Brazilian and Italian fans provided saliva samples before and after watching the 1994 World Cup final. Brazil won on a last-minute penalty kick. Their fans were elated and Italian fans were dejected. Results showed that, compared to pre-game baseline values, 11 of 12 Brazilian fans had increased testosterone, and 9 of 9 Italian fans had decreased testosterone (Dabbs & Dabbs, 2000).

Hormones can be affected by anticipation of behavior. Testosterone levels are known to influence sexual motivation and behavior in women, and one study compared testosterone levels in women for three activities: sexual intercourse, cuddling, and exercise (van Anders et al., 2007). Women provided a saliva sample from pre-activity, post-activity, and the next morning. Analyses revealed that the women's testosterone was elevated before intercourse as compared to other times, showing an anticipatory relationship between testosterone and sexual behavior. Testosterone levels were also higher post-intercourse compared to exercise, suggesting that sexual behavior may also influence hormone concentrations in women.

In sum, this section explores the bidirectional relationship between hormones and behavior, highlighting how hormones like testosterone and estradiol can influence behaviors such as singing in birds and sexual motivation in humans. While hormones can affect behavior, behaviors and even the anticipation of events can also impact hormone levels, as seen in studies involving competition and sexual activities. The field of neuroendocrinology, which studies the interface between the endocrine and nervous systems, is likely to yield significant insights into the hormone-behavior relationship.

Focus Topic 2: Bisphenol A (BPA) and Endocrine Disruption

You may have heard about the effects of bisphenol A (BPA), a chemical used in many plastic food-storage containers, drinking cups, aluminum cans, and other products. Research suggests BPA is an endocrine disruptor, meaning that it interferes with

the endocrine system. BPA mimics estrogens, and is particularly disruptive during prenatal and postnatal development.

The U.S. Food and Drug Administration (FDA) acknowledges concerns about BPA's potential effects on the brain, behavior, and prostate gland in fetuses, infants, and young children. In response, many US companies have removed BPA from baby products, and both Canada and the European Union have banned its use in these items. You'll now often see reusable water bottles boast "BPA free."

Studies in animals and humans have linked BPA exposure to various health issues, including developmental delays, altered thyroid signaling, sexual dysfunction, changes in brain structure and function, and increased cancer risks. However, some experts caution that more research is needed. In the meantime, the FDA recommends that consumers limit their exposure to BPA. In addition to purchasing foods in BPA-free packaging, consumers should avoid storing foods or liquids in containers with the recycling code 3 or 7. Foods and liquids should not be microwaved in any form of plastic: use paper, glass, or ceramics instead.

In addition to BPA, hundreds of other chemicals are considered endocrine disruptors with possible health risks to humans and other animals (NIEHS, n.d.). Well-studied chemicals that could disrupt your endocrine system (e.g., Atrazine, Dioxins, Phthalates, PFAS, PCBs, and Triclosan) are found in many everyday products, including some cosmetics, toys, packaging, non-stick pans, textile coatings, flame retardants, carpet, and pesticides. These chemicals end up in the environment and contact may occur through air, diet, skin, and water. Even in low levels, endocrine disruptors can interfere with normal hormone

function. Exposure is linked to health problems affecting the immune system, puberty (e.g., premature onset in girls and breast development in boys), reproduction (e.g., sexual dysfunction and reduced fertility), nervous system and psychological functioning (e.g., increased neurotoxicity, ADHD risk, memory issues), and cancer risk. Endocrine-disrupting chemicals cannot be completely avoided or removed; however, you can make informed choices to reduce exposure and risk of potential health effects.

Text Attributions

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6.2: SEXUAL DIFFERENTIATION

Sexual differentiation is the process by which a person develops into either a male or a female. For this chapter, the content will be based on a male/female binary to introduce the basic concepts of reproductive development. However, it is important to recognize that in real life, chromosomal sex, physical sex, and gender exist on a continuum and cannot always be simplified into a two-structure system.

During development, the body and the brain undergo A) feminization and de-masculinization or B) masculinization and de-feminization. In most cases, the differentiated brain will lead to behaviors that correspond appropriately to the differentiated gonads.

Chromosomal Sex

In humans, DNA is organized into 46 chromosomes—23 from the mother and 23 from the father. Twenty-two pairs are autosomal chromosomes, containing the same genes but potentially different alleles from each parent. The last pair are the sex chromosomes, X or Y, which determine biological sex (Figure 3). During fertilization, an egg (always one X chromosome) fuses with a sperm (one X or Y chromosome). An XX combination results in a female fetus, while XY results in a male fetus.

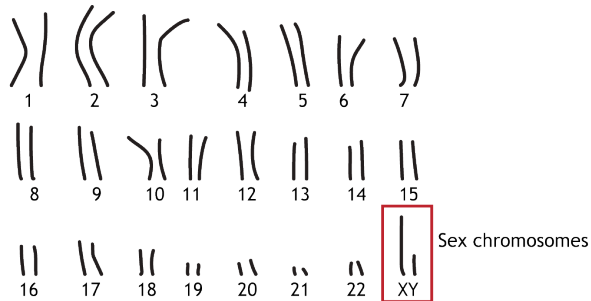


Figure 3. Humans have 23 pairs of chromosomes, making 46 total. 22 pairs are called autosomal and have similar structure from each parent. The final pair are the sex chromosomes that determine if the individual is a male or female. Sex chromosomes are named either X or Y.

Gonadal Differentiation

Six weeks after fertilization, fetuses have primordial gonads that could develop into testes or ovaries, as well as Wolffian ducts and Müllerian ducts that could develop into male or female reproductive organs, respectively. Proteins and hormones released over the following weeks lead to differentiation into male or female anatomy. In males, the sex-determining region (SRY) gene on the Y chromosome is activated, producing testis-determining factor, which results in the gonads becoming testes and testosterone secretion. In females, when the SRY gene and secreted hormones are absent, the gonads differentiate into the ovaries.

Hormones During Development

In addition to differentiating the reproductive organs, the presence or absence of gonadal hormones during development also differentiates the rest of the body, including the brain. Testosterone causes the brain, body, and behavior to be masculinized and defeminized (Figure 4). The inactive ovaries do not release hormones; this causes the brain, body, and behavior

to be feminized and demasculinized. Extensive research has established these principles in non-human animals. While hypothesized to extend to human brain and behavior, the evidence in humans is less conclusive.

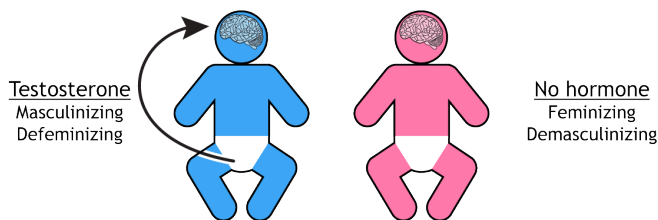


Figure 4. Testosterone presence during development masculinizes and defeminizes the body's physical traits. Based on animal studies, researchers hypothesize that testosterone may similarly affect brain structure and behavior patterns. Conversely, no hormone exposure during development feminizes and demasculinizes physical traits. Animal research suggests that no hormone exposure also feminizes brain and behavior, though more research is needed to confirm these effects in humans.

Critical Period. Secreted testosterone's effects on the brain must take place during a specific time in development, called a critical period. This early role of testosterone is called an **organizational effect** and results in a permanent change in organizing the nervous system and therefore behavior. Organizational effects of hormones lead to major, generally irreversible, aspects of cell and tissue differentiation. Organizational effects occur during critical periods like prenatal development and puberty (Figure 5). During puberty, higher levels of androgens in males lead to masculinizing organization, while ovarian hormone exposure has organizational effects in females (Schulz et al., 2009). In cases of pre-puberty castration, sexual maturation does not occur unless hormone replacement is provided.

In adulthood, the same hormones activate responses like inducing reproductive behavior or ovulation, but these influences, called **activational effects**, are reversible and short-lived. Removing the activating hormone stops the behavior, but reintroducing the hormone

later restarts the response. This occurs because the brain was previously organized to produce these behaviors in the presence of hormones.

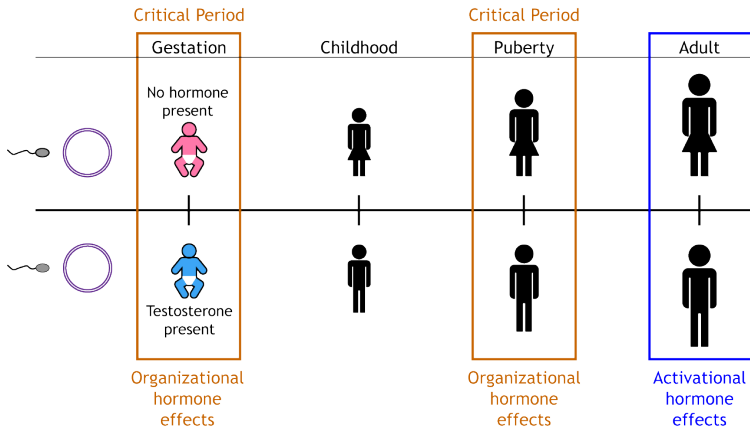


Figure 5. Hormones can have long-lasting, organizational effects when present during critical periods such as during the prenatal period or puberty. This phenomenon is well-established in the differentiation of human reproductive anatomy. For brain development and behavior, most evidence comes from non-human animal studies. During critical periods, hormones will alter the structure of the nervous system, setting up cells and circuits needed to display sex-typical behaviors later in life. Those sex-typical behaviors are then activated in adulthood by gonadal hormones.

The role of activational hormones can be demonstrated by adult castration in male rats. Healthy males with intact testes will show sexual behavior when placed with a female rat. Castration, the removal of the testes, will cause males to stop showing sexual behavior because the activating hormone, testosterone, is no longer present. However, if the castrated males receive testosterone replacement, they will resume showing sexual behavior. The sexual behavior brain circuit was organized during development by exposure to gonadal hormones, and in adulthood that circuit can be activated by testosterone. The adult behavior can only be seen when the activating hormone is present (Figure 6).

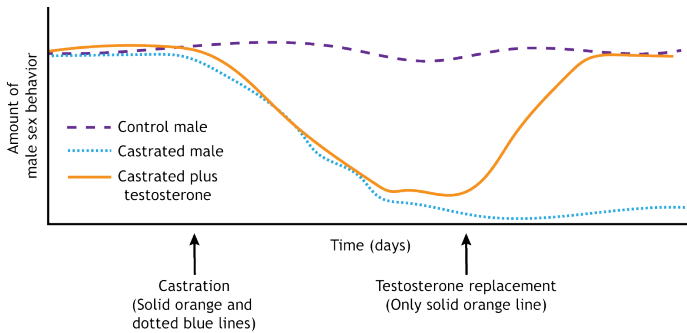


Figure 6. Removing testosterone by castrating an adult male rat will decrease the amount of sexual behavior displayed because the hormone can no longer activate sexual behaviors (solid orange and dotted blue lines). However, if the castrated animal is treated with testosterone, sexual behavior returns (solid orange line).

Key Takeaways

- During development, the body and the brain undergo either A) feminization and de-masculinization or B) masculinization and de-feminization.
- The sex chromosomes, X and Y, make up one pair of the 23 total pairs of chromosomes in humans. Females are genetically XX and males are genetically XY.
- The SRY gene on the Y chromosome is responsible for the development of the male reproductive system.
- In the absence of hormones, the female reproductive system develops.

- Organizational, long-lasting hormone effects take place during critical periods in development.
- Activational, short-lasting hormone effects “activate” the circuits organized by hormones in development.

Text Attributions

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6.3: SEX DIFFERENCES IN PSYCHOLOGY AND THE BRAIN

The process of sexual differentiation is relatively well understood for reproductive body parts and behaviors. They are sexually dimorphic, meaning they come in two distinct types—male or female.¹ Conversely, non-reproductive behaviors and body structures, including the brain, vary much more within and across sexes. Structures may differ between males and females on average, but their distributions greatly overlap, and they do not have a distinct male or female form (i.e., are not sexually dimorphic). Thus, sex differences in the brain and behavior are less clear, less well understood, and subject to greater debate.

The uncertainty and contention on sex differences stem from various factors. First, most early animal studies on brain and behavior included only male animals, making it impossible to study sex differences. This only recently changed and now funding agencies generally require that studies include both males and females and address how biological variables such as sex are factored into the research design (Clayton & Collins, 2014; Pinel & Barnes, 2021). Second, sex differences in human psychology can be politically and emotionally charged—given the historical misuse of biological data to justify sexist ideas, some fear that recognizing sex differences could lead to more sexist or discriminatory policies; conversely

1. As noted throughout the chapter, biological sex cannot always be simplified into a strict two-structure dichotomy; it exists along a continuum, and intersex conditions occur more frequently than many realize.

ignoring biological sex differences due to concerns about sexism may harm health outcomes by hindering the development of optimized sex-specific treatments.

Finally, human studies on sex differences are methodologically challenging; when differences are observed, effects are often small and their causes (biological and/or experiential) remain unclear. For example, a sex difference in the size of a brain region could stem from biological differences linked to the sex chromosomes, exposure to hormones, experiences of developing in a gendered society, and/or interactions among such factors (e.g., hormones or gendered experience could trigger epigenetic modifications, leading to gene expression or silencing that results in sex differences in the brain; Nugent & McCarthy, 2011). Ethical and practical constraints prevent experimental manipulation of variables in humans, while animal models may not generalize to the complexities of human sex differences.

Sex Differences in Psychology

Despite the scientific challenges, understanding sex differences could provide insights into behaviors, cognitive functions, and psychiatric disorders that manifest differently in males and females. The prevalence of several psychiatric conditions differs between males and females. Conditions more common in males include autism spectrum disorder, ADHD, schizophrenia, specific language impairment, and dyslexia. Conditions more common in females include Alzheimer's disease, anxiety disorders, anorexia nervosa, and depression (Ritchie et al., 2018; Ruigrok et al., 2014).

Sex differences have also been established in cognitive abilities, emotion, personality, and behavior. For example, on average, males perform better on some spatial tasks, such as rotating 3D objects. Males also show higher rates of aggression (Archer, 2004) and risk-taking (Cross et al., 2011). On average, females perform better on some memory tasks such as

remembering object identities and faces. Girls outperform boys on some verbal tasks including reading and writing (Miller & Halpern, 2014). Females also score higher on average for tests of empathy, self-reported interest in people versus things, and the personality trait agreeableness (Christov-Moore et al., 2014; Ritchie et al., 2018).

It's crucial to note that these differences represent average tendencies, and there is substantial overlap in performance for males and females on all these measures. In sum, several psychological phenomena differ between males and females and these differences likely arise from many biological and environmental factors. Investigating sex differences in the brain may provide insight into these psychological patterns, enhancing our understanding of cognition and behavior.

Sex Differences in the Brain

Research has identified several differences between male and female brains. Males have larger brains on average than females; with 9-13% greater volume in total brain, white matter, grey matter, and cerebrospinal fluid (Ruigrok et al., 2014). These overall size differences might be unsurprising, as males also have bigger bodies, hearts, lungs, feet, etc. Despite smaller brains, females have greater cortical thickness throughout most of the brain (Ritchie et al., 2018). Differences in volume occur in some brain regions.

An MRI study of over 5000 English adults found males had larger volumes in many subcortical regions, including the amygdala (involved in emotion and threat detection), hippocampus (involved in memory and spatial processing), and the nucleus accumbens (involved in reward processing). These sex differences persisted when controlling for height, but were less pronounced when controlling for total brain volume (Ritchie et al., 2018).

Recent debates challenge the extent of sex differences in the brain. Eliot et al. (2021) argue that when properly controlling for brain volume, sex-related differences in specific regions become limited and weak, and

conclude that the brain is not sexually dimorphic (i.e., it does not come in a distinct male and female form). Most researchers would reject the extreme binary concept of ‘sexually dimorphic’ brains. However, a meta-analysis that considered the methodological quality of studies found “highly reproducible sex differences in regional brain anatomy” beyond overall brain size. These sex differences are in the mean value of largely overlapping distributions, and they show small-to-moderate effect sizes (DeCasien et al., 2022).

The causal factors (biology versus experience) shaping sex differences in the brain continues to be a crucial area of scientific inquiry. Sex differences in the brain were most apparent in “mature” age participants (ages 18-59) (Ruigrok et al., 2014); and in the large English study, participants averaged 62 years of age (Ritchie et al., 2018). This raises the question of whether observed sex differences primarily result from long-term exposure to gendered societal experiences rather than innate biological factors such as hormones or genes.

However, some sex differences exist at birth, before gendered experience. Newborn males have 6% larger brains and more neocortical neurons than females, even when controlling for birth weight. Region-specific differences are also present: males have a larger medial temporal cortex (involved in sensory processing), while females have greater grey matter volume in the temporal-parietal junction (involved in social cognition) (Gilmore et al., 2018). These differences that developed before birth may relate to brain function later in life.

For an interesting overview, see the debate between Profs. Gina Rippon and Simon Baron-Cohen on sex differences and whether the brain is gendered. [Video link](#). [Podcast link](#).

Size and Distribution of Sex Differences

Although reliable sex differences exist in human brains and psychological

phenomena, the effect sizes are typically small to moderate and there is more variation within each sex than between sexes. Figure 7 (adapted from Maney, 2016) illustrates this concept by plotting male and female distributions for three traits.

Figure 7a shows external genitalia size, a sexually dimorphic trait with distinct male and female ranges (data from Wallen & Lloyd, 2008, Maney 2016). In this sample, all measurements from the females fall in one range, and all males fall in a separate range. So based on this trait, females and males could be accurately categorized (with only rare exceptions).

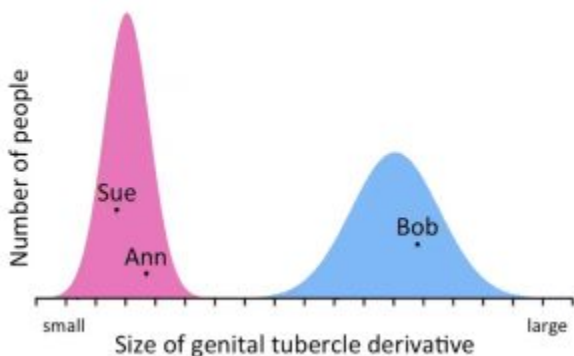


Figure 7a. The distributions of the size of the external genitalia—the “genital tubercle derivative” (i.e., the clitoris or penis) in a sample of human females (in pink) and males (in blue).

As shown in Figure 7b, height differs between males and females on average, but the distributions overlap considerably, and many females are taller than many males. If you only know someone’s height, you cannot accurately categorize them as male or female.

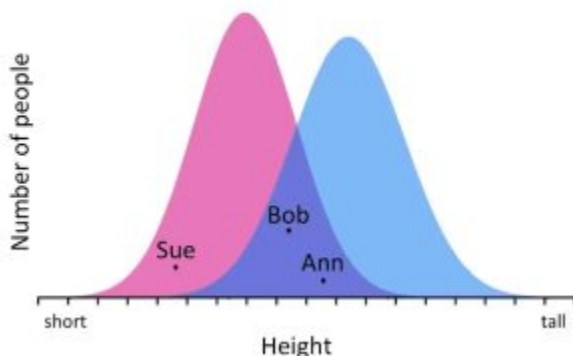


Figure 7b. The distributions of height in a sample of females and males. Overlap of distributions is shown in purple.

Figure 7c plots connectivity between brain regions, a small but reliable sex difference in the brain (data from Tunç et al., 2016). If you only knew someone's brain connectivity, you would correctly guess their sex about 51% of the time (Maney, 2016). This is only slightly above chance but reflects a reliable sex difference. Small differences can be important, but should be interpreted cautiously.

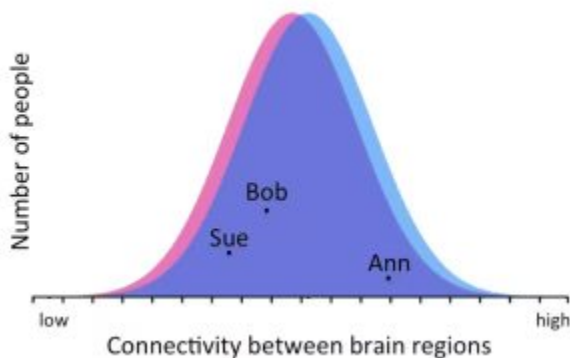


Figure 7c. The distribution of measurements of brain connectivity in a sample of females and males.

Given the considerable overlap in distributions of brain regions that show sex differences, human brains cannot be categorized into two distinct classes: “male brain” or “female brain.” Very few brains feature all male-associated regions or all female-associated regions. Human brains exist along a spectrum of traits associated with sex. Joel and colleagues (2015) thus proposed the concept of the “mosaic brain”, wherein “most brains are comprised of unique ‘mosaics’ of features, some more common in females compared with males, some more common in males compared with females, and some common in both females and males.”

While humans cannot look at a brain and accurately categorize it as male or female, recent artificial intelligence approaches can. Machine learning algorithms simultaneously using many features of the brain “mosaic”, can successfully identify whether a brain is from a male or female with over 90% accuracy (Ryali et al., 2024).

Brains and Hormones

Many causal factors can shape sex differences in the brain, including genetic encoding on the sex chromosomes, experience, and hormones (DeCasien et al., 2022; Ruigrok et al., 2014). We conclude this section with two examples of hormonal influences on sex differences in brain and behavior.

In rats, a region of the hypothalamus, the sexually dimorphic nucleus of the Preoptic Area (SDN-POA), is (as its name indicates) sexually dimorphic—it is 2.6 times larger in males than females. It is involved in reproduction. Lesioning it completely disrupts a male rat's ability to engage in sexual behavior. Experiments demonstrate that exposure to gonadal steroid hormones during early development have an “organizing” effect on this brain structure. Exposure to testosterone (which is converted to estradiol) or estradiol causes masculinization of the brain. Figure 8 shows the SDN-POA (dark cell bodies) in a male (left), a female (center), and a female treated with testosterone as a newborn (right). The SDN-POA of the untreated male is substantially larger than the untreated female, but is equal in size to the testosterone-treated female. This illustrates how early gonadal hormone exposure dramatically affects brain structure.

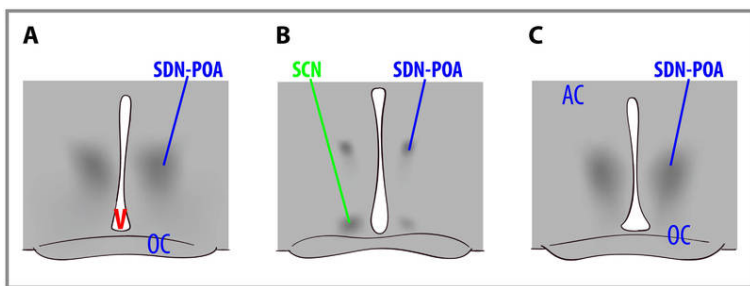


Figure 8. The sexually dimorphic nuclei of the preoptic area (SDN-POA) shown as dark cell bodies in an untreated male rat (left), an untreated female rat (center), and a female rat treated with testosterone as a newborn (right). Note that the SDN-POA of the male are substantially larger than those of the untreated female, but are equal in size to those of the testosterone-treated female. Exposure to testosterone (which is converted to estradiol) or estradiol causes masculinization of the brain. OC = optic chiasm; SCN = suprachiasmatic nucleus; V = third ventricle.

In humans, researchers cannot experimentally manipulate hormone levels that a newborn or fetus is exposed to. However, if the fluid in the amniotic sac around the fetus is measured for medical reasons, researchers can also measure the prenatal testosterone levels. Such data show that male fetuses are exposed to more testosterone on average than female fetuses. Interestingly, longitudinal studies have shown that prenatal hormone levels relate to behavior and brain structure many years later. For example, girls with higher levels of *prenatal* testosterone performed better on a test of mental rotation at age 7 (Grimshaw et al., 1995), and boys with higher levels of *prenatal* testosterone performed worse on a test of empathy at age 6-8 (Chapman et al., 2006).

Fetal testosterone levels also correlated with the volume of brain regions in a group of 8-11 year olds in a way that was congruent with sex differences observed in those regions (Lombardo et al., 2012). For example, some regions that were generally bigger in males, were also associated with higher levels of prenatal testosterone (and vice versa). While only correlational (and not causal like the rat experiment), these results suggest that prenatal

hormone exposure could play some role in organizing brain structure and sex differences in brain and behavior.

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6.4: HORMONES AND BEHAVIOR: AGGRESSION AND PARENTAL BEHAVIORS

Many different hormones can affect a wide range of behaviors. This section gives a brief overview of two illustrative examples: the effects of hormones on aggression and in parental behaviors and bonding.

Aggressive Behaviors

Aggressive behavior can arise whenever individuals' interests are in conflict (Nelson, 2006). Conflicts most often arise over limited resources such as territory, food, or mates. A social interaction decides which animal gains access to the contested resource. Sometimes that interaction involves physical aggression, but in many cases, a submissive posture from one animal or ritualized combat to establish dominance can resolve conflicts without physical harm.

Overwhelming evidence suggests that androgenic steroid hormones, particularly testosterone, mediate male aggressive behavior across many species. First, seasonal variations in blood concentrations of testosterone coincide with variations in aggression. For instance, aggressive behavior peaks for male deer in autumn when they are secreting high levels of testosterone. Second, aggressive behaviors increase during puberty when the testes become active, and blood concentrations of androgens rise. Juvenile deer do not participate in the fighting during the mating season. Third, male mammals are generally more aggressive than females. This is certainly true of deer—female deer rarely display aggressive behavior. Finally, castration typically reduces aggression in males, and subsequent

testosterone-replacement therapy restores aggression to pre-castration levels. Some exceptions to these general observations are outside the scope of this chapter.

In humans, males are generally more physically aggressive than females.¹ From early childhood, males consistently initiate more physical aggression than females, and many more men than women are convicted of violent crimes in North America. This sex difference in humans is widely recognized, but the underlying causes remain a subject of intense scientific debate. It is possible that males are more aggressive than females because: a) androgens promote aggressive behavior and males have higher androgen levels; b) brains of males are exposed to androgens prenatally causing brain “wiring” to organize in a way that increases aggression; and/or c) males are encouraged, and females are discouraged by family, peers, or others from acting aggressively. These hypotheses are not mutually exclusive, and are difficult to separate to account for sex differences in human aggression.

1. However, females exhibit more relational aggression (i.e., the purposeful harm to another through a social relationship; Bowie, 2007).



Figure 9. Researchers have electrically stimulated particular regions in people's brains, and these individuals have burst into aggressive, violent behavior, helping demonstrate that such responses are hardwired into us.

In humans, disentangling environmental and physiological influences on behavior is challenging. For instance, males and females differ in their rough-and-tumble play at a very young age, which might suggest an early physiological influence. However, parents usually play more roughly with male infants, which might suggest that sex differences in aggression are learned. Experimentally manipulating variables (e.g., by injecting testosterone) and tightly controlling the environment is not possible in human studies, so hormonal effects on sex-differentiated behavior is studied in non-human animal models.

Studies on mice reveal that sex differences in aggression result from both perinatal and adult androgen exposure. Male mice castrated early show low aggression even with adult testosterone treatment, while females given testosterone perinatally and in adulthood show male-like aggression. Thus,

in mice and many other species, androgens both “organize” the brain perinatally for aggression and “activate” aggressive behavior in adulthood. Finally, while we focus on testosterone here, other hormones including cortisol, corticosterone, and vasopressin are involved in aggression, and there is no one-to-one relationship between a hormone and behavior.

Parental Behaviors and Bonding

Parental behavior in mammals is crucial for offspring survival. In rats, who give birth to underdeveloped (altricial) young, mothers exhibit stereotyped behaviors like nest-building, nursing, and pup retrieval. Typically, adult rats avoid pups due to aversion to their smell and neophobia (the fear of new things), but daily exposure can sensitize them to behave maternally. However, for new mothers, immediate maternal behavior is necessary for survival, and is hormonally mediated. Around the time a mother gives birth, a rapid decline in progesterone, coupled with high estradiol, prolactin, and oxytocin levels overrides the fear response, enabling maternal behavior in the presence of newborns.

Rat maternal behavior involves brain activity of the hypothalamus’ medial preoptic area. This region can be inhibited by the amygdala and fear responses. Lesions in the amygdala or its input smell pathways can disinhibit (i.e., increase) maternal behavior. Hormones likely reduce amygdala activation, thus permitting maternal behavior. Studies show that giving female rats oxytocin increases maternal behavior and attachment to their pups (Kendrick, 2000).

One of the best studied examples of the biological basis of social bonding and attachment comes from prairie voles. Prairie voles are a North American rodent that display highly social behavior, have monogamous relationships after mating, and share parental duties such as resource collection and care for their young (Figure 10). Their close relative, the montane vole, on the other hand, is a non-social species that does not form pair bonds and only the female cares for the young. Comparing these

species has allowed researchers to identify several neurochemical signals implicated in bonding.



Figure 10. Prairie voles are monogamous rodents known for social behavior and shared parental care.

Oxytocin and vasopressin, similar neuropeptides, are crucial for pair bonding. In the social prairie voles, oxytocin and vasopressin are released by the hypothalamus in response to mating and act on limbic and reward systems. Female prairie voles have more oxytocin receptors in reward circuitry than asocial montane voles. After mating, oxytocin binds to these receptors to increase pair bonding and reinforce the rewarding association with a partner. Experiments show that giving oxytocin to female prairie voles increases bonding, while blocking oxytocin receptors decreases bonding. In male prairie voles, similar effects occur with vasopressin. Male prairie voles release vasopressin after mating; they have more vasopressin receptors in reward circuitry compared to montane voles; and giving vasopressin increases bonding, while blocking it decreases bonding. Notably, when males of a promiscuous species are genetically modified to

have more vasopressin receptors, those males display increased pair bonding and parental behavior (Rigney et al., 2022). This underscores the causal role of hormones in social bonding.

Human bonding and parental behaviors (most often studied in mothers) are also shaped by hormones. Oxytocin, vasopressin, and the reward system play crucial roles in human bonding. **fMRI** studies show increased activation in reward-related brain regions when subjects view pictures of their children or partners, compared to friends. These regions express oxytocin and vasopressin receptors, and the hormones are released during bond-forming activities like breastfeeding and intercourse. In addition to oxytocin and vasopressin, cortisol levels positively correlate with mothers' affectionate and vocal behaviors towards infants, especially in mothers with positive prenatal attitudes. Cortisol likely enhances maternal care indirectly by increasing the mother's arousal and responsiveness to infant cues. High-cortisol mothers are more attracted to and better at identifying their infants' odors and cues (Fleming et al., 1997).

In sum, hormones play a crucial role in shaping parental behaviors and bonding in both mothers and fathers across various species, influencing brain activity and behavioral responses that are essential for offspring care and survival.



Figure 11. Although cortisol may not directly increase maternal behaviors, the next time your mom gives you a hug, you know one hormone to thank.

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6.5: SEX, GENDER, AND SEXUAL ORIENTATION

Sex, Gender, and Sexual Orientation: Three Different Aspects of You

Applying for a credit card or filling out a job application requires your name, address, and birth date. Applications also usually ask for your sex or gender. The terms “sex” and “gender” are commonly used interchangeably, but they have distinct meanings.

Sex refers to a set of biological attributes including reproductive/sexual anatomy, genetics, and hormones. Sex is usually categorized as male or female, although variations occur in the biological attributes that comprise sex. By contrast, the term **gender** describes psychological (**gender identity**) and sociological (**gender role**) representations of biological sex. Ideas about gender vary over time and across cultures. At an early age, we begin learning cultural norms for what is considered masculine and feminine. For example, children may associate long hair or dresses with femininity. As adults, we often conform to these norms by behaving in gender-specific ways (Marshall, 1989; Money et al., 1955; Weinraub et al., 1984).

Sex and gender are important aspects of a person’s identity. However, they do not inform us about a person’s sexual orientation (Rule & Ambady, 2008). **Sexual orientation** refers to a person’s sexual attraction to others.

The international scientific and medical communities (e.g., World Health Organization, World Medical Association, World Psychiatric

Association, Association for Psychological Science) view variations of sex, gender, and sexual orientation as normal. Furthermore, variations of sex, gender, and sexual orientation occur naturally throughout the animal kingdom. More than 500 animal species display homosexual or bisexual behavior (Sommer & Vasey, 2006; Figure 12). Hermaphroditism—having both functional testes and ovaries and being able to produce both female and male gametes (i.e., viable eggs and sperm)—is a normal mode of reproduction in a wide range of animals (but is virtually nonexistent in humans). **Intersex** is characterized as having sexual characteristics that do not fall neatly into male and female categories (e.g., absence or combination of male and female reproductive organs, sex hormones, or sex chromosomes). Intersex occurs in both animals and humans (Hrabovszky & Hutson, 2002). In humans, estimates of the prevalence of intersex individuals vary widely: from 0.018% to 1.7% of the population depending on how it is defined (Blackless et al., 2000; Sax, 2002). Many conditions have been considered intersex, such as Androgen Insensitivity Syndrome and Turner’s Syndrome (Lee et al., 2006). The term “syndrome” can be misleading, as they otherwise lead relatively normal intellectual, personal, and social lives. In any case, intersex individuals demonstrate the diverse variations of biological sex.



Figure 12. A male Mallard duck couple—one of hundreds of species displaying homosexual or bisexual behavior.

Variations in Gender

Just as biological sex varies more widely than is commonly thought, so too does gender. Cisgender individuals' gender identities correspond with their birth sexes, whereas transgender individuals' gender identities do not correspond with their birth sexes. Because gender is so deeply ingrained culturally, rates of transgender individuals vary widely around the world (see Table 2). Some cultures formally recognize the presence of people who do not conform to an expectation that gender identity match biological sex (Figure 13).

Nation	Transgender people per 100,000
Sweden	.17
Poland	.26
Ireland	1.4
Japan	1.4
India	167
Thailand	333
United States	476
Malaysia	1,333

Table 2: Nations vary in the number of transgender people in their populations (De Gascun et al., 2006; Dulko & Imielinska, 2004; Landen et al., 1996; Okabe et al., 2008; Conron et al., 2012; Winter, 2009). Note that these sources are a few decades old, but they illustrate major variation across cultures.





Figure 13: First photo: Hjira dancer in Nepal; Second photo: Kathoey performers at a cabaret in Pattaya, Thailand.

Transgender rates and subtypes differ significantly between cultures and over time. **Transgender women** (TGW; whose birth sex was male and are sometimes called male-to-female or MTF individuals) were more common than **transgender men** (TGM; whose birth sex was female and are sometimes called female-to-male or FTM individuals) in 16 of 18 countries surveyed, and the TGW to TGM ratio was 3 to 1 (Meier & Labuski, 2013). However, this ratio is changing; in the U.S., the number of individuals seeking hormone therapy for TGW and TGM transitions is becoming more similar (Leinung & Joseph, 2020). This change could reflect greater acceptance, destigmatization, and decreasing barriers to care for TGM individuals.

Sex Hormones in Transgender Treatment. Feminizing or masculinizing hormone therapy is the administration of exogenous endocrine agents to induce changes in physical appearance. Transgender women are prescribed estrogen and anti-androgen medication. Transgender men are prescribed testosterone. Hormone therapy is inexpensive relative to surgery, and highly effective in the development of some secondary sex characteristics, such as facial and body hair in

transgender men (i.e., female-to-male individuals) or breast development in transgender women (i.e., male-to-female individuals). Thus, hormone therapy is often the first (and sometimes only) medical gender-affirmation intervention accessed by transgender individuals looking to develop masculine or feminine characteristics consistent with their gender identity. In some cases, hormone therapy may be required before surgical interventions can be conducted. Emerging scientific research on gender-affirming hormone therapy has shown that sex hormone applications influence mood, behavior, and cognition, as well as brain structure and function in the adult human brain (Kranz et al., 2020; Nguyen et al., 2018; Nguyen et al., 2019). For example, gender-affirming hormone therapy tends to reduce symptoms of anxiety and depression and lower social distress (Nguyen et al., 2018). Transgender men undergoing testosterone therapy showed brain changes, including increased total brain and hypothalamic volumes and altered white-matter microstructure, aligning more closely with cisgender male patterns (Nguyen et al., 2019).

Societal Understanding of Gender Variations. Our understanding of gender identity continues to evolve, and young people today have more opportunity to explore and openly express gender than previous generations. The transgender community has gained visibility in American society—an estimated 0.6% of adults in the USA identified as transgender in 2016 (Meerwijk & Sevelius, 2017), and that population growth is driven by younger generations. A 2017 survey revealed that 1.8% of high school students identified as transgender and another 1.6% were questioning their gender (Johns et al., 2019; Scheim et al., 2022). Recent studies indicate that most Millennials (birth years 1981-1996) regard gender as a continuum instead of a strict male/female binary. As young people lead the changing views on gender, other changes are emerging in a range of spheres, from public bathroom policies to retail organizations. For example, some retailers are changing traditional gender-based marketing of products, such as removing “pink and blue” clothing and toy aisles. Despite these changes, those outside of traditional gender norms face difficult challenges. Even

people who vary slightly from traditional norms can be the target of discrimination and even violence.

Sexual Orientation

A person's **sexual orientation** is their sexual and emotional attraction to a particular sex or gender, including a continuing pattern of romantic or sexual attraction to persons of a given sex or gender. According to the American Psychological Association (APA) (2016), sexual orientation also refers to a person's sense of identity based on those attractions, related behaviors, and membership in a community of others who share those attractions. Although a person's intimate behavior may have **sexual fluidity**—changing due to circumstances (Diamond, 2008)—sexual orientations are relatively stable over one's lifespan, and are influenced by genetics and other biological factors (Frankowski, 2004).





Figure 14: First photo: “Victory!” — This lesbian couple has been waiting 31 years to be able to marry (Sacramento, CA). Second photo: Two men holding hands, Gay Pride Project (Baltimore, MD).

A Continuum of Sexual Orientation. Sexual orientation is as diverse as gender identity. Instead of thinking of sexual orientation as being two categories—homosexual and heterosexual—sexuality researcher Alfred Kinsey argued that it’s a continuum (Kinsey, Pomeroy, & Martin, 1948). He measured sexual orientation on a continuum, using a 7-point Likert scale called the Heterosexual-Homosexual Rating Scale, in which 0 is exclusively **heterosexual**, 3 is **bisexual** with equal attractions to the same and opposite sexes, and 6 is exclusively **homosexual** (Figure 14). Later researchers using this method have found 18% to 39% of Europeans and Americans identify as somewhere between heterosexual and homosexual (Lucas et al., 2017; YouGov.com, 2015). These percentages drop dramatically (0.5% to 1.9%) when researchers force individuals to respond using only two categories (Copen, Chandra, & Febo-Vazquez, 2016; Gates, 2011).

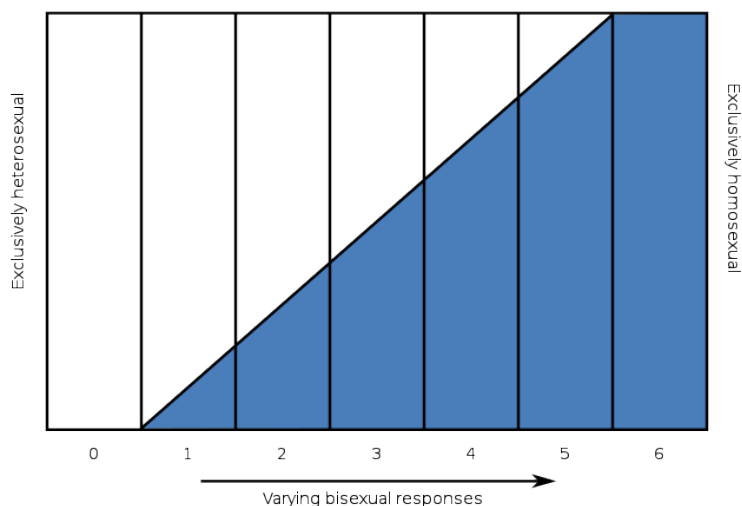


Figure 15: The Kinsey scale, a tool that enables an individual to select a response on a scale between heterosexual and homosexual. 0= exclusively heterosexual, 1= predominantly heterosexual, only incidentally homosexual, 2= predominantly heterosexual, more than incidentally homosexual, 3= equally heterosexual and homosexual, 4= predominantly homosexual, more than incidentally heterosexual, 5= predominantly homosexual, only incidentally heterosexual, and 6= exclusively homosexual. More blue on the horizontal axis corresponds to a higher score on the Kinsey scale.

Development and Origins of Sexual Orientation

Individuals are usually, but not always, aware of their sexual orientation between middle childhood and early adolescence, and sexual activity is not necessary for this recognition. There is no scientific consensus regarding the root cause(s) of sexual orientation, but it is not a conscious “choice” for either heterosexual or non-heterosexual individuals. Research has examined

many possible biological, developmental, social, and cultural influences on sexual orientation. Social factors (such as having homosexual parents, recruitment by homosexual adults, and experiencing disordered parenting) are generally not scientifically supported (Bailey et al., 2016). Nonsocial causes (such as genetics, prenatal hormone exposure, fraternal-birth order) have much more supporting evidence.

Genetics. One method of measuring the genetic roots of sexual orientation is concordance rates, which is the probability that a pair of individuals has the same sexual orientation. If both twins have the same sexual orientation, they are “concordant” for this trait. Concordance rates are compared between people who share the same genetics (**monozygotic twins**), some of the same genetics (**dizygotic twins** and siblings, 50%), and non-related people (randomly selected from the population). Concordance for sexual orientation is highest for monozygotic twins; and concordance rates for dizygotic twins, siblings, and randomly selected pairs are not significantly different (Bailey et al. 2016; Kendler et al., 2000). Since concordance rates (i.e. having the same sexual orientation) are higher for monozygotic twins, this indicates that “nature” (genetics) influences sexual orientation. However, monozygotic twins do not always have the same sexual orientation, so “nurture” (the environment and individual experiences) also plays a role in determining sexual orientation. Nonetheless, because sexual orientation is a debated issue, an appreciation of the genetic aspects of attraction is an important piece of this dialogue.

Prenatal Hormone Exposure. Adult hormone levels do not relate to sexual orientation. On average, gay and heterosexual men have similar levels of hormones, and lesbian and heterosexual women have similar levels of hormones. Sexual orientation is not affected by adult treatment with androgens or estrogens or adult gonadectomy (surgical removal of testes or ovaries resulting in loss of gonadal production of sex steroids) (Balthazart, 2011). However, hormone levels during early sensitive periods of brain development do impact sexual development and sexual orientation. In animal studies, experimentally manipulating prenatal exposure to sex hormones, including testosterone, impacts sexual physiology and behavior,

such as mounting and same-sex partner preference (Balthazart, 2011). In humans, excess or deficient exposure to hormones during prenatal development has been linked to non-heterosexual orientation. Females exposed to abnormally high amounts of prenatal androgens due to congenital adrenal hyperplasia (CAH) are much more likely to identify as bisexual or lesbian (Cohen-Bendahan, van de Beek, & Berenbaum, 2005).

Fraternal-Birth-Order Effect. The “fraternal-birth-order effect” refers to the consistent cross-cultural finding that homosexual males tend to have more older brothers than heterosexual males (Bailey et al., 2016). “The effect is almost certainly causal, with each additional older brother causing an increase in the chance of a man being homosexual. ... Assuming that a man without any older brothers has a 2% chance of being homosexual, a man with one older brother has a 2.6% chance; with two, three, and four older brothers, the chances are 3.5%, 4.6%, and 6.0%, respectively” (Bailey et al., 2016, page 79). This effect only occurs for biological brothers (Figure 15), meaning that the number of sons gestated by the mother is the important factor, whether or not the man was raised with those brothers. One proposed mechanism for this is that the mother creates antibodies against proteins on her developing son’s Y chromosome (a possibility which increases with each pregnancy of a son) and that those antibodies may alter the functioning of subsequent sons’ Y chromosomes (Bailey et al., 2016; O’Hanlan et al., 2018).



Figure 16: The Marx Brothers in “I’ll Say She Is!”—caricatures by John Decker (1924). Every biological older brother increases the likelihood of a man being homosexual. Groucho (the brother with the mustache) was the fourth brother and called himself “straight but curved around the edges” (<http://everydayheterosexism.blogspot.com/2012/11/the-marx-brothers.html>).

In Closing: Gender and Sexual Orientation

Sex, gender, and sexual orientation are distinct aspects of human identity. Sex refers to the biological characteristics of anatomy, genetics, and hormones, while gender describes psychological (gender identity) and sociological (gender role) representations of biological sex. Sexual orientation describes the pattern of emotional, romantic, and sexual

attraction. All three of these concepts exist along continuums rather than binary categories. There is natural variation across individuals and cultures in how sex, gender, and sexual orientation manifest. Current scientific evidence indicates these traits have strong biological underpinnings, with factors like genetics, prenatal hormone exposure, and fraternal birth order influencing their development, often before birth (O'Hanlan et al., 2018). Though historically stigmatized, modern perspectives increasingly recognize gender and sexual diversity as normal variations. Moving forward, reducing discrimination and achieving greater equality and acceptance for people across the full spectrums of sex, gender, and sexual orientation remain important goals.

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6.6: DISCUSSION QUESTIONS AND RESOURCES

Discussion Questions

1. What are some of the problems associated with attempting to determine causation in a hormone–behavior interaction? What are some good ways to address these problems?
2. How do organizational and activational effects of hormones differ in their influence on behavior? Provide an example of each and discuss how these effects might interact over an individual's lifespan.
3. Discuss the challenges in studying sex differences in human brains. How do researchers attempt to address these challenges, and what are the limitations of current research methods?
4. Compare and contrast the biological and social factors that contribute to gender identity development. How might this understanding inform societal approaches to gender diversity?
5. Analyze the evidence for hormonal influences on aggressive behavior. How does this research contribute to our understanding of sex differences in aggression, and what are the potential implications for society?

6. Evaluate the concept of the “mosaic brain” in relation to sex differences. How does this idea challenge traditional binary views of male and female brains, and what are its implications for our understanding of gender and behavior?
7. Imagine that you discovered that the brains of architects were different from those of non-architects—specifically, that the “drawstraighten nuclei” of the right temporal lobe were enlarged in architects as compared with non-architects. Would you argue that architects were destined to be architects because of their brain organization or that experience as an architect changed their brains? How would you resolve this issue?

Outside Resources

Book: Adkins-Regan, E. (2005). *Hormones and animal social behavior*. Princeton, NJ: Princeton University Press.

Book: Nelson, R. J. (2011). *An introduction to behavioral endocrinology* (4th ed.). Sunderland, MA: Sinauer Associates.

Book: Pfaff, D. W. (2009). *Hormones, brain, and behavior* (2nd ed.). New York: Academic Press.

Video: “Is the Brain Gendered?: The Debate” Interesting debate between Profs. Gina Rippon and Simon Baron-Cohen on sex differences and whether the brain is gendered.

<https://www.youtube.com/watch?v=kxfaE-gWZ9I&t=2492s>

Video: Endocrinology Video (Playlist) – This YouTube playlist contains many helpful videos on the biology of hormones, including reproduction and behavior. This would be a helpful resource for students struggling with hormone synthesis, reproduction, regulation of biological functions, and signaling pathways.

<https://www.youtube.com/playlist?list=PLqTetbgey0aemiTfD8QkMsSUq8hQzv-vA>

Video: Paul Zak: Trust, morality – and oxytocin- This Ted talk explores the roles of oxytocin in the body. Paul Zak discusses biological functions of oxytocin, such as lactation, as well as potential behavioral functions, such as empathy.

<https://www.youtube.com/watch?v=rFAdlU2ETjU>

Video: The Teenage Brain Explained- This is a great video explaining the roles of hormones during puberty.

<https://www.youtube.com/watch?v=hiduiTq1ei8>

Web: Society for Behavioral Neuroendocrinology – This website contains resources on current news and research in the field of neuroendocrinology.

<http://sbn.org/home.aspx>

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CHAPTER 7: DEVELOPMENT OF THE BRAIN AND NERVOUS SYSTEM

Learning Objectives

- Describe the different stages of neuronal development
- Relate the embryonic stage of nervous system development to the adult structures of the central nervous system
- Understand sensitive and critical periods of development
- Relate the trade-off between neuroplasticity and neural efficiency to brain development

7.1: INTRODUCTION

The **nervous system** develops in an intricately coordinated process from the early embryonic stages through childhood, adolescence, and adulthood. During early developmental stages, the brain develops the ability to dynamically transfer information across billions of interconnected neurons, and to coordinate and control mental and bodily functions, including perception, cognition, and movement.

In this chapter, we cover the stages of development of the human brain and nervous system. We examine prenatal and postnatal development from embryo through old age. We also cover different stages of neuronal development, including neuron growth, migration, and death, as well as adult neurogenesis. Lastly, we examine **neuroplasticity**—the brain’s ability to reorganize in response to experiences—and how neuroplasticity is strongest during sensitive and critical periods of development. Learning how the nervous system changes across the lifespan provides a more complete understanding of the brain.

7.2: EMBRYONIC STAGE

The **embryo** is initially formed through fertilization, which occurs when a sperm cell and an egg cell unite into a single cell. This fertilized egg cell, or **zygote**, starts dividing through the process of mitosis to generate the cells that make up an entire organism. Sixteen days after fertilization, embryonic cells form three layers that develop into different body tissues (Betts et al., 2022). The **endoderm**, or inner tissue, is responsible for generating the lining tissues of various spaces within the body, such as the mucosae of the digestive and respiratory systems. The **mesoderm**, or middle tissue, gives rise to most of the muscle and connective tissues. Finally the **ectoderm**, or outer tissue, develops into the body's outer layer of skin, hair, nails, as well as the nervous system. It is probably easy to see that the outer tissue of the embryo becomes the outer covering of the body, but how is it responsible for the nervous system?¹

Neural Tube

Two weeks into embryonic development, the human nervous system begins to form. As the embryo develops, a portion of the ectoderm differentiates into the precursor for the tissue of the nervous system (Betts

1. This section contains material adapted from: Betts et al., (2022). 13.1 The Embryologic Perspective. In *Anatomy and Physiology* 2e. OpenStax. Access for free at <https://openstax.org/books/psychology-2e/pages/15-4-anxiety-disorders> License: CC BY 4.0 DEED.

et al., 2022). Cells in this region form a neural plate that begins to fold inward to form a **neural groove** that is lined on each side by a neural fold. These two **neural folds** eventually fuse together to form the **neural tube** (Figure 1) and set up the development of the brain and spinal cord. Cells from the neural folds then separate from the ectoderm to form a cluster of cells referred to as the **neural crest**, which runs lateral to the neural tube. These neural crest cells migrate away from the nascent **central nervous system** (CNS) that will form along the neural groove and develop into several parts of the **peripheral nervous system** (PNS) including the enteric nervous system that governs the function of the gastrointestinal tract.

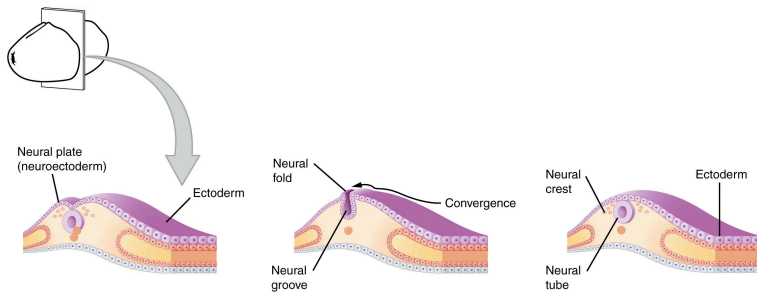


Figure 1: During the embryonic stage of development, the neuroectoderm folds inward to form the neural groove. As the two sides of the neural groove fuse together, they form the neural tube. The anterior end of the neural tube will develop into the brain, and the posterior portion will develop into the spinal cord.

During the third week of embryonic development, the anterior end of the neural tube begins developing into the brain, and the posterior portion begins developing into the spinal cord. This basic arrangement of tissue in

the nervous system gives rise to more complex structures by the fourth week of development.²

Primary Vesicles

As the anterior end of the neural tube starts to develop into the brain, it generates three **primary vesicles**: the forebrain (**prosencephalon**), the midbrain (**mesencephalon**), and the hindbrain (**rhombencephalon**) (Betts et al., 2022). The forebrain is the upper-most vesicle, the midbrain is the next vesicle, and the hindbrain is the lowest vesicle. One way to think about brain organization uses these three divisions—forebrain, midbrain, and hindbrain (Figure 2).³

2. This section contains material adapted from: Betts et al., (2022). 13.1 The Embryologic Perspective. In *Anatomy and Physiology* 2e. OpenStax. Access for free at <https://openstax.org/books/psychology-2e/pages/15-4-anxiety-disorders> License: CC BY 4.0 DEED.

3. This section contains material adapted from: Betts et al., (2022). 13.1 The Embryologic Perspective. In *Anatomy and Physiology* 2e. OpenStax. Access for free at <https://openstax.org/books/psychology-2e/pages/15-4-anxiety-disorders> License: CC BY 4.0 DEED.

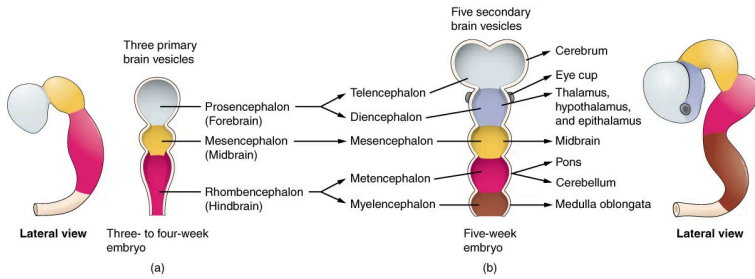


Figure 2: During the embryonic stage of development, the neural tube evolves into three primary vesicles. These three primary vesicles then give rise to five secondary vesicles.

Secondary Vesicles

By week 5, the three primary vesicles differentiate further into five **secondary vesicles** (Betts et al., 2022) (Figure 2). The **forebrain** enlarges into two new vesicles called the **telencephalon** and the **diencephalon**. The telencephalon will become the cerebrum—the largest part of the adult brain which contains the lobes of the cerebral cortex, hippocampus, and basal ganglia. The diencephalon will give rise to several structures including the thalamus (the central relay hub for sensory signals) and hypothalamus (involved in homeostasis and regulating functions including hunger, sleep, and mood).

A third secondary vesicle, the mesencephalon or **midbrain**, is composed of the **tectum**, the **cerebral aqueduct**, the **tegmentum**, and the **cerebral peduncles**. The midbrain is an established region of the brain at the primary vesicle stage and does not further differentiate into finer divisions. The rest of the brain develops around the midbrain, which is involved in many functions including head and eye movements, motivation, and reward.

The **hindbrain** develops into the final secondary vesicles, the

metencephalon and **myelencephalon**. The metencephalon gives rise to the **pons** and **cerebellum**. The cerebellum accounts for about 10 percent of the mass of the brain and is an important structure for coordinated movement, posture, and cognition. The cerebellum connects to the rest of the brain via the pons, because the pons and cerebellum develop out of the same vesicle. Finally, the myelencephalon gives rise to the adult structure known as the **medulla oblongata** (involved in breathing, digestion, heart rate, blood pressure, etc.). The structures that arise from the midbrain and hindbrain, except for the cerebellum, are collectively considered the **brain stem**, which specifically includes the midbrain, pons, and medulla.

We first learned about the above structures in Chapter 2: The Brain and Nervous System. To understand the outcome of fetal brain development, it may help to return to Chapter 2 to review details of these structures in the adult brain.⁴

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7.3: STAGES OF NEURONAL DEVELOPMENT

The brain is made up of **neurons** and **glial cells**. Neurons, also called nerve cells, are electrically excitable cells that transmit signals called action potentials to other neurons and are considered the fundamental units of the brain and nervous system (Ludwig et al., 2022). Neurons communicate information about sensations and movement, and process information within the brain. Glial cells, or neuroglia or simply glia, are the other type of cells found in the nervous system. Glial cells are considered support cells and help neurons complete their function for communication. We discuss six main types of glial cells—four in the CNS and two in the PNS. Figure 3 depicts different glial cells and Table 1 defines their common functions.

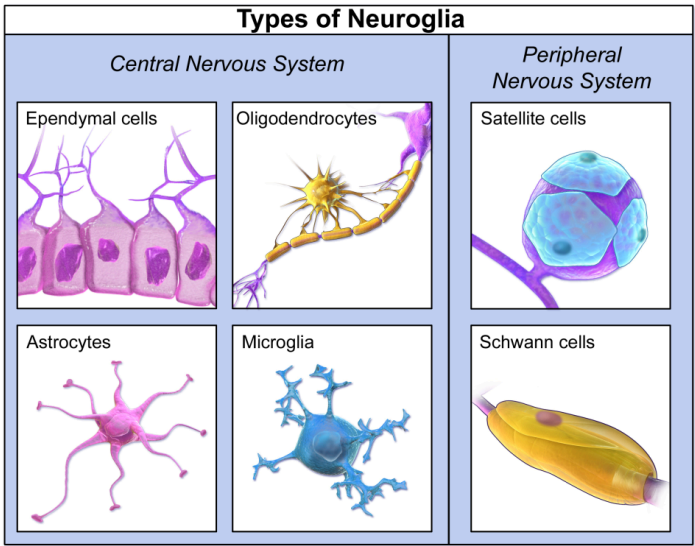


Figure 3: Visualizing the different glial cell types.

Glial Cell Types By Location and Function

Table 1: Different types of glial cells and their basic functions [Table adapted from: Anatomy and Physiology 2e: 12.2 Nervous Tissue] CC BY 4.0.

CNS Glia	PNS Glia	Function
Astrocyte	Satellite cell	Support
Oligodendrocyte	Schwann cell	Insulation, myelination
Microglia	–	Maintenance of neural networks
Ependymal cell	–	Creating cerebrospinal fluid

Neuron Growth

Neuronal development includes several stages. Once the neural tube has closed, the first stage of neuron growth, known as **neural proliferation**, begins to occur in the ventricular zone of the neural tube. **Neurogenesis**, the process of generating new neurons, begins approximately four weeks after conception during embryonic development. This critical phase is marked by a significant proliferation of cells within the neural tube, the precursor structure to the central nervous system. Most neurons in the human telencephalon (i.e., cortex, hippocampus, basal ganglia, etc.) are generated before birth. Extensive neurogenesis does occur after birth in other brain regions like the cerebellum. But all in all, the bulk of neurogenesis (i.e., the 86 billion neurons) in the CNS occurs between the fourth week post-conception to 18 months after birth—during this early developmental period, approximately 4.6 million neurons are generated every hour (Silbereis et al., 2016)!

During neural proliferation, the cells being formed are **neural stem cells**. There are two basic types of stem cells, pluripotent and totipotent cells. Pluripotent cells can give rise to all cell types that make up the body, whereas multipotent cells are more limited than pluripotent cells. Because pluripotent stem cells can develop into any cell type in the human body, scientists are examining how they can be used in regenerative cell-based treatments for various conditions, including diabetes, spinal cord injuries, and heart disease. In CNS development, neural stem cells are special pluripotent cells that produce only radial glial cells. These radial glial cells then differentiate into neurons and glial cells, forming the central nervous system. This process of neural proliferation generates billions of cells, ultimately developing into the complex structure of the CNS.

Neuronal Migration

Newly formed neurons may remain where they are and continue to divide, or migrate to other parts of the nervous system. Neuronal migration refers to the journey of neurons from their original location to a new target location. For neurons of the central nervous system, neural migration remains within the neural tube; whereas for neurons of the peripheral nervous system, neural migration may occur across different neural regions (Purves et al., 2001). During the migration period, neurons remain immature and lack fundamental neuronal characteristics such as **axons** and **dendrites**. Ultimately, neuronal migration is supported by sophisticated molecular and cellular signaling that results in pulling and pushing the immature neuron to its target location.

In general, migration tends to follow an inside-out pattern, where neurons travel from the inside of the neural tube outwards toward their target location. This migration can be classified into two modes: 1) **radial migration**, and 2) **tangential migration**. Radial migration, long seen as the primary mode of neuronal movement in the cortex, occurs when neurons are guided by radial glial cells to migrate toward the surface of the brain following the radial pattern of the neural tube and ultimately establish the layered organization of the neocortex (Marin et al., 2003; Wong, 2002). The second mode of neuronal movement, tangential migration, occurs when neurons move to the surface of the central nervous system (or orthogonal to the direction of radial migration). Of note, these two migration methods are not mutually exclusive, as some neurons may alternate from radial to tangential movement along the course of their migration to their target location (Marin et al., 2010).

Neuronal migration occurs through two main mechanisms. Somal translocation involves an extension reaching out from the immature neuron's soma to lead it to its target; this is used in both radial and tangential migration. Glial-mediated migration, specific to radial

migration, involves immature neurons “climbing” along extended glial cells to reach their target locations.

Upon reaching their target locations, immature neurons develop distinct neuronal structures like dendrites and axons, which enable communication with other neurons. This neuronal communication leads to the formation of functional neural circuits.

Aggregation

After migrating, neurons must align and integrate with other neurons to create neural circuits. This is called **aggregation**. Aggregation is supported by two key mechanisms. **Cell-adhesion molecules** on cell surfaces recognize and bind to molecules on other cells, enabling cell-to-cell interactions and tissue stabilization (Jaffe et al., 1990; Takeichi, 1988). Additionally, **gap junctions** form communication channels between adjacent cells, allowing exchange of ions and metabolites such as glucose, which promotes biochemical coupling between the two cells (Mese et al., 2007). These mechanisms facilitate neuronal interactions and integration, ultimately giving rise to the neural circuitry of the human nervous system.

Neuron Death

Neuronal cell death, which refers to the elimination of neurons in the nervous system, occurs extensively during development and actually supports brain development. Neuron death is typically categorized as either apoptosis or necrosis. **Apoptosis** refers to active, programmed cell death to maintain appropriate development, whereas **necrosis** refers to passive, accidental cell death resulting from environmental perturbations, such as trauma, toxins, or oxygen depletion (Khalid & Azimpouran, 2023). Apoptosis occurs after neuronal proliferation, selectively eliminating excess and immature neurons to enable proper neuronal connectivity and

maturation of functional networks (Hollville et al., 2019). Unlike apoptosis, necrosis is characterized by swelling and rupturing of the cell membrane, as well as leakage of the cellular contents (Rock & Kono, 2008). Necrosis leaves behind disruptive cellular debris, whereas apoptosis efficiently dismantles and “cleans up” the dead neuron, minimizing disruption to surrounding brain tissue. One example of necrosis occurs after a stroke, where disruption of blood flow may lead to accidental cell death. Excessive necrosis is detrimental and is associated with pathologies such as Alzheimer’s and Parkinson’s diseases (Boka et al., 1994; Goel et al., 2022; Tuo et al., 2022). Much work remains to understand and regulate cell death to preserve brain function.

Adult Neurogenesis

Until about 25 years ago, the prevailing view was that new neurons could not be generated in the human brain after birth. However, a landmark study showed that regions of the adult brain, such as the hippocampus, can generate new neurons throughout adulthood (Eriksson et al., 1997). Generating new neurons in the adult brain is referred to as **adult neurogenesis**. However, adult neurogenesis does not appear to take place in all parts of the brain. Neurogenesis has been most consistently observed in two regions: 1) the subventricular zone of the lateral ventricles and; 2) the subgranular zone in the dentate gyrus of the hippocampus (Ribeiro & Xapelli 2021). Additionally, many neurons generated during adulthood do not survive and cannot integrate into existing neural circuits. While multiple studies have demonstrated evidence of adult neurogenesis, the topic remains fairly controversial. Some studies suggest that 700 new neurons are generated in the adult hippocampus every day, while other studies suggest that adult hippocampal neurogenesis is undetectable or may not exist at all (Sorrel et al., 2018; Spalding et al., 2013). Nonetheless, given the potential clinical implications of new neurons and their possible role in

preserving cognitive function, future research will continue exploring the mechanisms that support adult neurogenesis.

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7.4: NEUROPLASTICITY

Anytime you learn something new, the structure of your brain physically changes. The brain's ability to reorganize or “rewire” its connections in response to intrinsic or extrinsic experiences is called neuroplasticity.

Learning depends on the plasticity of the circuits in the brain and the ability to make lasting changes in synaptic transmission (Clark et al., 2018; “The Brain from Top to Bottom”, n.d.). The brain can thus store information in networks of modified synapses, the arrangement of which constitutes the information. By activating these synaptic networks, the brain is able to retrieve the stored information.

Our understanding of the rules that govern the networking of neurons goes back to the groundbreaking work by Donald Hebb over 70 years ago. Hebb proposed that if two neurons are active at the same time, the synapses between them are strengthened—this is captured in the famous phrase “Neurons that fire together, wire together.” Inspired by this hypothesis, researchers discovered long-term potentiation (LTP) in the early 1970s, providing the first supporting mechanism.

Long-term potentiation (LTP) is a persistent strengthening of a synaptic connection (Clark et al., 2018). LTP is based on the Hebbian principle: cells that fire together wire together. While not fully understood, one key mechanism of synaptic strengthening involves postsynaptic glutamate receptors called NMDA receptors (Figure 4). These receptors, normally blocked by magnesium ions, open when rapid successive presynaptic inputs depolarize the postsynaptic neuron. This allows calcium (Ca^{2+}) ions to enter the cell, triggering a signaling cascade that causes AMPA receptors to migrate from within the postsynaptic cell and insert into the postsynaptic membrane. These newly available AMPA receptors allow positive ions to enter the cell. So the next time glutamate is released from the presynaptic neuron, it will have a larger excitatory effect (EPSP)

because glutamate binding to AMPA receptors will allow more positive ions into the cell. In sum, after being activated simultaneously, the increased presence of AMPA receptors strengthens the synapse and makes the postsynaptic neuron more likely to fire in response to presynaptic neurotransmitter release. Some drugs of abuse co-opt the LTP pathway, and this synaptic strengthening can lead to addiction.

In addition to LTP *strengthening* synaptic connections, neuroplasticity also requires *weakening* some connections. One well-studied process underlying the weakening of synaptic connections is **Long-Term Depression (LTD)**. Long-term depression is essentially the reverse of LTP. Similar to long-term potentiation, long-term depression also involves AMPA receptors. In this situation, calcium that enters through NMDA receptors initiates a different signaling cascade, which results in the removal of AMPA receptors from the postsynaptic membrane (**Figure 4**). Fewer AMPA receptors in the membrane make the postsynaptic neuron less responsive to glutamate released from the presynaptic neuron. While it may seem counterintuitive, LTD may be just as important as LTP for learning and memory. The weakening and pruning of unused synapses allows for unimportant connections to be lost and makes the synapses that have undergone LTP much stronger by comparison.

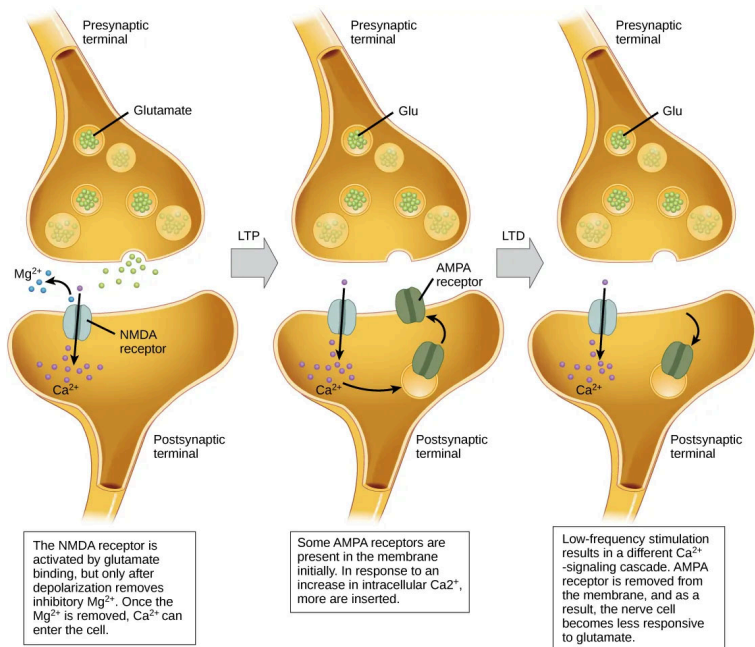


Figure 4. Calcium entry through postsynaptic NMDA receptors can initiate two different forms of synaptic plasticity: long-term potentiation (LTP) and long-term depression (LTD). LTP arises when a single synapse is repeatedly stimulated. This stimulation causes a calcium- and CaMKII-dependent cellular cascade, which results in the insertion of more AMPA receptors into the postsynaptic membrane. The next time glutamate is released from the presynaptic cell, it will bind to both NMDA and the newly inserted AMPA receptors, thus depolarizing the membrane more efficiently. LTD occurs when few glutamate molecules bind to NMDA receptors at a synapse (due to a low firing rate of the presynaptic neuron). The calcium that does flow through NMDA receptors initiates a different calcineurin and protein phosphatase 1-dependent cascade, which results in the endocytosis of AMPA receptors. This makes the postsynaptic neuron less responsive to glutamate released from the presynaptic neuron.

Even today, Hebb's rule, as it is often known, remains one of the primary factors for predicting which synapses will be strengthened in a network of neurons. More recent research has uncovered other characteristics of the networking of groups of neurons. For example, the LTP that leads

to synaptic strengthening is very specific to neurons that are activated simultaneously, and only to such neurons.

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Duboc, B. (2002). *The Brain From Top To Bottom: Memory and the Brain: Plasticity in Neural Networks*. Access for free at <https://thebrain.mcgill.ca/> License: CC (Copyleft).

7.5: SENSITIVE AND CRITICAL PERIODS OF DEVELOPMENT

Life experiences impact brain development and subsequent behavior. Sensitive and critical periods are developmental periods that are especially pertinent in shaping neural and behavioral outcomes. **Sensitive periods** refer to developmental time windows during which experiences have an especially strong impact on brain organization. While similar experiences can still affect the brain outside of these sensitive periods, the consequences for brain reorganization will not be as strong. **Critical periods** refer to the limited time windows during which experiences, or lack thereof, have lasting effects on brain function and behavior (Knudsen, 2004). Disruptions during critical periods due to atypical experiences or adversity may lead to irreversible changes to brain structure. Sensitive and critical periods both involve heightened neuroplasticity. Sensitive periods offer broad windows for experience to shape neural circuitry, while critical periods are a subset that can result in irreversible changes to the brain (Knudsen, 2004).

Sensitive Periods of Development

The brain is especially malleable and adaptive to environmental inputs during childhood. Early life experiences profoundly impact how brain networks organize and develop. For example, language acquisition occurs during early childhood. Research shows a close relationship between the age of exposure to a language and proficiency in that language—peak proficiency is far more likely for those exposed to that language in early childhood (Newport et al., 2001). This is especially pertinent for learning

a second language. A seminal study examined second language acquisition in native Chinese or Korean speakers who moved to the United States and learned English at different ages (Johnson & Newport, 1989). Results indicated that children who began learning the second language (English) before age 7 were able to reach proficiency akin to native English speakers; children arriving between age 7 and puberty were less proficient; and after puberty, an individual's second language proficiency is likely to remain low (Figure 5). These findings support a brain-maturation account, such that the ability to learn languages gradually declines and ultimately flattens as the brain matures. Importantly, this is not to say that learning a second language is impossible after brain maturation; but lower neuroplasticity after this sensitive period contributes to slower second language learning. The ability to learn second languages throughout life, albeit more slowly with age, demonstrates that second language acquisition reflects a sensitive rather than critical developmental period. In summary, children may be better equipped to learn a second language during this sensitive period due to the heightened neuroplasticity.

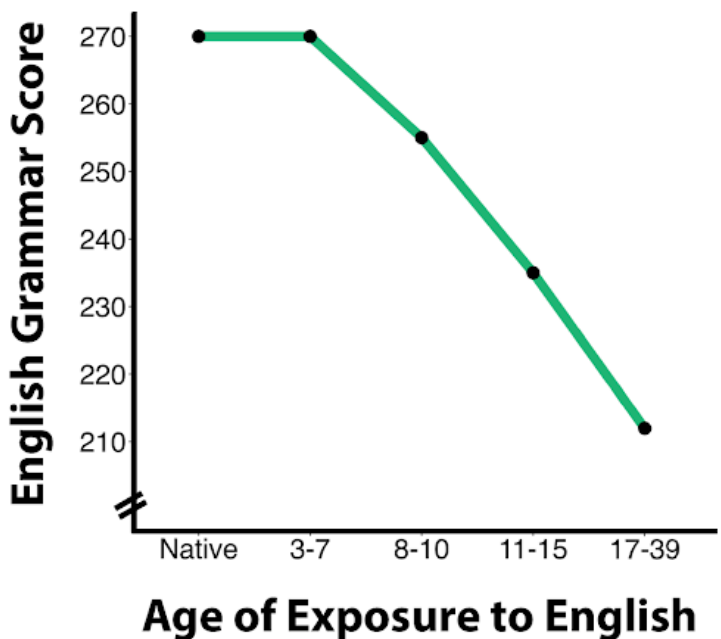


Figure 5: The relationship between age of learning a second language and total correct responses on an assessment of grammar for a second language [Image adapted from: Johnson, J. S., & Newport, E. L. (1989). Critical period effects in second language learning: The influence of maturational state on the acquisition of English as a second language. *Cognitive Psychology*, 21(1), 60-99.]

Critical Periods of Development

Early childhood also features critical periods when environmental input irreversibly shapes brain function and structure. Critical periods can be exemplified in sensory development and first language learning. Past experiments with animals have shown that sensory deprivation during infancy (e.g., an animal is deprived of sight or sound) can have lasting and irreversible consequences on their brain development (Hubel & Wiesel, 1970). For instance, animal studies show that depriving one eye of visual

input during a critical period permanently impairs vision by reducing cortical neuron responses to that eye (Gordon & Stryker, 1996). In response to such visual deprivation, the brain reorganizes and prioritizes visual input from the non-deprived eye.

The brain's adaptive nature can also be seen in individuals who are born blind or deaf and as a result may rely on other sensory systems. For example, in humans, the occipital cortex is typically involved in visual perception. In individuals with early blindness (who become blind during the first few years of life), the occipital cortex shifts from processing visual input to other sensory-related information, such as tactile and auditory sensations (Voss, 2013). This adaptive process is known as **cross-modal plasticity**. Recent research indicates that cross-modal plasticity can persist after sensory function (e.g., vision) is restored, suggesting brain reorganization during critical periods may persist throughout adulthood (Mowad et al., 2020).

Critical periods of development occur for first language acquisition. In the early 1970s, the tragic story of Genie, an adolescent girl who for most of her childhood experienced severe isolation and neglect, caught the world by storm. When discovered, Genie was unable to communicate verbally with language. Researchers studied Genie's linguistic development over many years and concluded that, despite initial progress in speech and grammar, her language proficiency remained severely impaired (Curtiss, 1974). A more recent study found that children, who lacked language input during the first year of life due to isolation or hearing difficulties, later had severe language-syntax impairments (Friedmann & Rusou, 2015). In sum, the absence of key environmental inputs, especially during critical periods in early childhood, may be particularly detrimental to subsequent brain development.

Adolescence as a sensitive period of development

Adolescence, the phase between childhood and adulthood (often considered ages 10-24), is marked by significant brain and behavioral changes. As a result of the ubiquitous social, cognitive, and emotional changes during adolescence, this stage of development is now widely considered a sensitive period of development.

How does brain development during adolescence shape behavior? Substantial neuroimaging research has shown that the frontal lobes, which include regions of the brain involved in executive function, such as the prefrontal cortex, are late-developing and undergo significant maturation that continues well into adolescence (Fuster et al., 2002; Casey et al., 1997; Giedd, 2004). Parallel to these brain development findings, prior work indicates that adolescence is marked by increased sensation-seeking and risk-taking behaviors (Spear, 2000). Neuroscientists have suggested that adolescent risk-taking may result from underdeveloped self-regulation, heightened sensation-seeking, and an immature executive function system unable to control reward-seeking impulses (Steinberg et al., 2004).

While the propensity for adolescents to take risks is often viewed negatively, it plays a role in adolescent development. Exploration and experimentation during this period are essential for forming personal identity, developing decision-making skills, and fostering independence. By navigating new experiences and challenges, teenagers learn to assess risks, understand consequences, and gradually develop the autonomy needed for adulthood. Some degree of risk-taking behavior in adolescence can contribute positively to cognitive, social, and emotional growth.

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7.6: TRADE-OFF BETWEEN PLASTICITY AND EFFICIENCY

Neuroplasticity varies across brain networks, with each developing on its own timeline (Dow-Edwards et al., 2019). The neural circuitry for basic sensory processes reaches peak plasticity in infancy and stabilizes by early childhood (thereby eliminating the need to relearn basic perception). In contrast, regions governing higher-order executive functions like self-regulation develop later and are highly plastic during adolescence. This developmental pattern illustrates the balance between neuroplasticity for development and stable and efficient processing in mature brains. A trade-off exists: high neuroplasticity and flexibility in a brain network corresponds to low stability and efficiency, and vice versa.

Neural efficiency refers to the brain's ability to meet task demands with minimal energy expenditure. It also encompasses the ease of communication between different brain regions. The efficiency of information flow across the brain accelerates in adolescence as axons gain myelin insulation, improving electrical transmission speed and reducing energy consumption (Spear, 2013).

Another factor underlying differences in neural efficiency is the formation of synapses. Early research revealed two general phases in synapse development: first a rapid overproduction of synapses, followed by programmed elimination of non-functional synapses to reach adult levels (Huttenlocher, 1979; Huttenlocher & Dabholkar, 1997; Shonkoff & Phillips, 2000). This synapse-formation pattern emerges at different timescales for different brain networks—synapse formation related to sensory processes peaks first, followed by language-related processes, and finally higher-order cognitive functions (Figure 6).

Relevant to neural efficiency, excess synapses during adolescence in

frontal lobe regions may render information processing less efficient in those brain regions (Blakemore, 2012). In other words, during adolescence, the brain may require many synapses to carry out cognitive processes. However, as these neuronal connections and functional networks become refined during development, the brain may require fewer synapses to carry out the same cognitive processes. In this way, the brain could shift toward prioritizing the most efficient synapses, which may ultimately lead to more efficient cognitive processing.

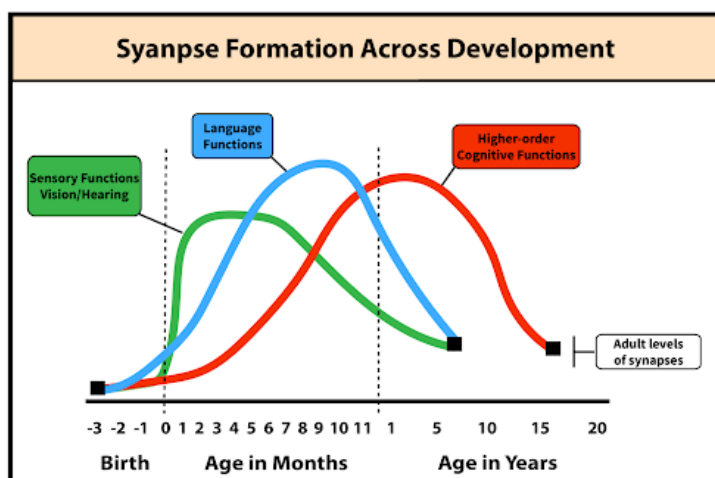


Figure 6. The number of new synapses related to sensory function, language skills, and higher-order cognition across development. Synapse formation peaks early for sensory-related functioning (in the first months of life), followed by language skills (late in the first year), and finally higher-order cognitive functions (during early childhood). Green = auditory and visual cortex; Blue = Broca's area; Red = prefrontal cortex. Image adapted from: The Developing Brain: <https://www.ncbi.nlm.nih.gov/books/NBK225562/figure/mmm00006/>

The tradeoff between neuroplasticity and stable efficient processing can be illustrated by recent research. In one study, a drug (valproate) reopened a critical period for a sensory task. When given this drug, adults could better

learn to identify the names of musical pitches (termed “absolute pitch”), a skill that typically can only be acquired early in life (Gervain et al., 2013). This discovery holds exciting potential for increasing adult plasticity to learn new skills and rewire undesired established neural pathways (e.g., for treating addiction or psychiatric disorders). However, caution is needed when tampering with plasticity in the brain. For example, critical periods have evolved for a reason, and reopening critical periods might destabilize long-established neural circuits for efficiently processing things like how to see the world or understand language.

Finally, psychedelic drugs have shown potential to treat addiction and some psychological disorders. A recent study suggests that psychedelic drugs can reopen critical periods and increase neuroplasticity in mice (Nardou et al., 2023). Additionally, psychedelics may induce cellular and molecular adaptations related to neuroplasticity and these may support the clinical effects of psychedelics in humans (de Vos et al., 2021; Calder & Hassler, 2023). While more work on psychedelics and neuroplasticity is needed, the possibility of inducing neuroplasticity could lead to rich learning and brain restructuring, but it also underscores the importance of working with a trained professional when the brain is in a more malleable state in order to not destabilize desired neural circuits.

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7.7: CHARACTERIZING BRAIN DEVELOPMENT FROM INFANCY THROUGH YOUNG ADULTHOOD

Adversity, especially early in childhood, has long-lasting consequences on brain development and behavioral outcomes. For instance, research has shown that experiencing poverty during early childhood is associated with lower academic performance, educational attainment, and adult earnings (Duncan et al., 1998, 2010). Relatedly, children whose families have higher family income tend to be associated with higher language, memory, social-emotional processing, and self-regulation skills (Noble et al., 2005, 2007). In terms of the brain, higher family income correlates with expanded surface area in brain regions governing language and executive function (Noble et al., 2015). While poverty clearly correlates with negative brain and behavioral outcomes, much remains unknown about how these effects on neural development emerge over time.

The [Baby's First Years](#) project is conducting the first randomized control trial of poverty reduction in early childhood, examining its impact on brain development (Noble et al., 2021). In the study, 1,000 diverse low-income mothers in four metropolitan areas in the United States were randomly assigned to receive a large (\$333) or nominal (\$20) monthly cash gift. By measuring infants' electrical brain activity one year into the poverty-reduction intervention, the researchers showed that infants whose mothers were randomized at the time of birth to receive a large monthly cash gift showed greater electrical brain activity in regions associated with better language, cognitive, and social-emotional outcomes in later childhood.

Scientists are continuing to explore how adversity affects brain organization and its potential impact on behavior.

Given the extensive social, emotional, and cognitive changes during adolescence, the [Adolescent Brain Cognitive Development \(ABCD\) study](#) was launched as the largest long-term study of brain development and child health in the United States. Twenty-one U.S. research sites are tracking over 11,000 children's biological and behavioral development over a decade from age nine through early adulthood (Luciana et al., 2018). The ABCD study assesses brain structure and function, cognition, physical and mental health, social and emotional function, and culture and environment, offering insights into adolescent brain development and its behavioral impacts. The ABCD study's extensive data explores key topics, such as links between family environment, children's behavior problems, and brain structure (Gong et al., 2021), effects of cannabis use on psychopathology (Paul et al., 2021), and links between screen time, academic performance, and mental health (Paulich et al., 2021).

These ongoing large-scale studies promise to provide insights into how environmental factors shape brain development and behavior, potentially informing future interventions and policies to support healthy child and adolescent development.

7.8: CONCLUSION

This chapter aimed to provide an overview of the development of the human nervous system and the brain. The different stages of nervous system and brain development are key for understanding how brain functions and behaviors emerge across the lifespan. Also, recognizing how neural networks emerge, as well as the extent of their malleability across the lifespan, is important for creating interventions to preserve cognitive function. Coordinated efforts to characterize brain development are underway and will advance our understanding of how individual differences in brain function and behavior may emerge across the lifespan.

7.9: DISCUSSION QUESTIONS AND RESOURCES

Discussion Questions

1. Describe neural stages of development from neuron growth to neuron death.
2. In what ways does the embryonic stage of development set the stage for the development of adult structures of the nervous system?
3. Compare and contrast sensitive and critical periods of development.
4. In what ways does the trade-off between neuroplasticity and neural efficiency shape brain function and behavior?

Outside Resources

Video: [Neural Stem Cells](#)

Video: Joan Stiles Lecture: [The Developing Brain](#)

Video: 2 minute walk-through on [Early Neural Development](#)

Web: [Build Your Network](#) – An interactive module demonstrating how neurons transfer information

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CHAPTER 8: LEARNING AND MEMORY

Learning Objectives

- Differentiate between the main types of memory, including working, declarative (explicit), and nondeclarative (implicit) memory.
- Describe the roles of key brain structures involved in memory, including the hippocampus, prefrontal cortex, and striatum.
- Explain the significance of the case of Patient HM in advancing our understanding of memory systems.
- Compare and contrast the functions of place cells and grid cells in spatial memory and navigation.
- Outline the stages of memory processing, including encoding, consolidation, and retrieval.
- Discuss the concept of memory reconsolidation and its implications for understanding the malleability of memory.
- Evaluate the role of memory reactivation during sleep in memory consolidation.
- Analyze the potential applications and limitations of targeted memory reactivation (TMR).
- Identify common memory-related disorders, such as Korsakoff's syndrome, and their underlying

neurobiological factors.

8.1: INTRODUCTION

Think back to your favorite birthday party. Where was it? Who was there? What did you do? Did you eat cake? Our ability to perform this task depends on creating, storing, and recalling memories. According to neuroscience, memory formation results from subtle changes among synapses distributed across several brain areas. Our capacity to learn new facts, recall recent events, or perform motor skills results from learning-induced neural plasticity.

The previous chapter covered neuroplasticity and how synaptic connections change with experience. This chapter explores how those changes translate into learning and memory. We'll examine different types of memory, stages of processing (encoding, consolidation, storage, retrieval), and the brain regions and specialized neurons involved. We review some recent trends in research on memory reconsolidation that can help stabilize memories or even help dampen maladaptive memories as in post-traumatic stress disorder (PTSD). The chapter concludes with a discussion of memory-related disorders.

Memory is the capacity to encode, store, and retrieve information (Squire, 2009). Memory is a broad concept that includes many distinct types of memory, stages of processing, and neural systems. Before we dig into the biological psychology of memory, we introduce some terminology and ways to categorize memory.

Scientists characterize memory in many ways. Scientists talk about types of memory (e.g., semantic, episodic, procedural) that differ in the type of information that is stored (see next section). Memory can also be categorized in terms of the time-frame that information remains available. An influential model proposes three stages of memory: sensory memory, short-term memory, and long-term memory (Atkinson & Shiffrin, 1968; Figure 1). **Sensory memory** acts as a buffer for information received

through the senses; the duration is very short (milliseconds or seconds). To illustrate, close your eyes; you briefly “see” a detailed image of what you were looking at; that is a visual sensory memory. **Short-term memory** (STM) and working memory last seconds to minutes and have limited capacity—typically 7 ± 2 separate items (Miller, 1956). Short-term memory and working memory hold information temporarily and either discard it or move it to long-term memory. You can think of it like the content on your computer screen: that information is saved to long-term memory (hard drive) or discarded (delete the document or close the web page). According to the three-stage model, information moves from STM (working memory) into the third stage of memory, **long-term memory** (LTM). Long-term memory has very large capacity and these memories can last days, years, or decades. When studying for an exam, you are trying to consolidate or solidify that information in long-term memory.

Memory **consolidation** (i.e., making a temporary memory more stable and long-lasting) is supported by structural and functional changes to the neurons. In addition to consolidation, memory involves different processes, including encoding, storage, and retrieval. **Encoding** involves the input of information into the memory system. **Storage** is the retention of the encoded information. **Retrieval** involves recovering stored information from memory back into awareness.

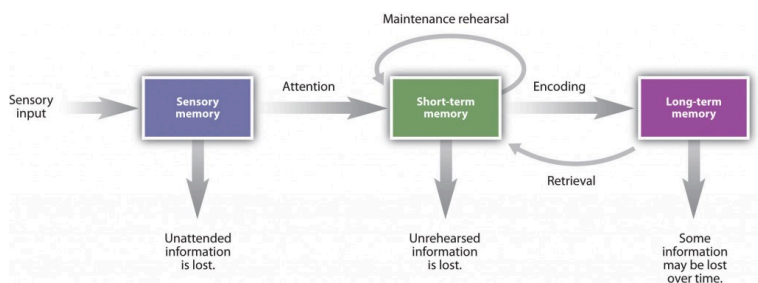


Figure 1. Memory Duration. Memory can be characterized in terms of stages — the length of time that information remains available to us.

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8.2: TYPES OF MEMORY

Memory can be arranged in several broad categories based on the type of information stored (Figure 2). Two main types of long-term memory are declarative (explicit) and nondeclarative (implicit). Declarative memory involves consciously accessible information that you can “explicitly” declare and describe. **Declarative memory** can be divided into semantic memory (for facts) and episodic memory (for events). In contrast, **nondeclarative memory** (implicit) cannot be explicitly described or consciously accessed. It encompasses various forms of learning that alter behavior without requiring awareness, such as learning a new skill, conditioning, priming, and perceptual learning.

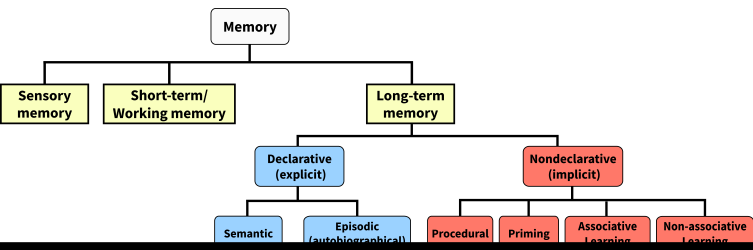


Figure 2. Different types of memory. Sensory memory, short-term memory, declarative memory, and nondeclarative memory are distinct. Sensory memory acts as a brief buffer for incoming sensory information. Working memory involves temporarily holding and manipulating a small amount of information. Declarative memories, also called explicit memories, are memories of information that can be stated explicitly. Declarative memories can be further subdivided into semantic memory (for facts), and episodic memory (for autobiographical events). Nondeclarative memories or implicit memories encompass memories learned and accessed without conscious awareness, including procedural memories (“knowing how”), priming, non-associative learning, and associative learning.

Declarative Memory (Explicit)

Declarative memories, also called explicit memories, are the pieces of information that can be consciously stated. Declarative memory can be subdivided into semantic memory and episodic memory. **Semantic memories** include memories for general knowledge about the world (e.g., concepts, facts), whereas **episodic memories** include memories of past personal experiences and events.

Semantic memories. Semantic memories reflect memories for general knowledge, facts, concepts, and information not directly linked to past personal experiences. Some examples of semantic memories include: 1. “Jupiter is the largest planet in our solar system.” 2. “Rosalind Franklin discovered the double helix structure of a DNA molecule.” 3. “The actor Keanu Reeves played the protagonist of the movie *The Matrix*.”

Episodic memories. An episodic memory, sometimes called an autobiographical memory, is the recollection of a moment in a person’s life. It can be thought of as “mental time travel” or re-experiencing past personal events. The following are examples of episodic memories: “When I got home, I put my wallet and phone on the table.” “I ordered pizza last night.” “In 2019, I saw my favorite musicians perform live.”

One important class of episodic memories are emotional memories, largely because emotional memories are often remembered more strongly than neutral memories (LaBar & Phelps, 1998; Kensinger, 2009; Sharot et al., 2004). For example, people tend to strongly remember emotionally-charged events, including positive events such as a high school graduation, or negative events such as throwing up in front of everyone at a wedding. It may feel intuitive that emotional events are better remembered than neutral events, but how do emotions enhance our memory? Researchers have begun characterizing neurobiological systems in the brain that may explain how emotions contribute to the stabilization of memories (see sections on memory encoding and memory consolidation).

Nondeclarative Memory (Implicit)

The other main category of long-term memory is nondeclarative or implicit memory. Unlike declarative (explicit) memory, implicit memory is acquired and used unconsciously. It affects thoughts and behaviors and results from experience-based neural plasticity. Different types of implicit memory include procedural memory, priming, non-associative learning, and associative learning.

Procedural memories. **Procedural memories** are unconscious and involve “knowing how” to perform actions. Unlike explicit memories, these cannot be consciously accessed or verbally described. They encompass skills and sequences of motor actions that, with practice, become automatic. Examples include riding a bicycle or an experienced musician playing scales. Procedural memory is sometimes colloquially called “muscle memory”, even though the muscles do not store any actual memory!

Priming. **Priming** occurs when exposure to a stimulus implicitly shapes the response to a subsequent stimulus, without conscious or intentional learning. There are different types of priming, including perceptual priming and semantic priming. Perceptual priming occurs when perceptual properties (e.g., shape, sound, appearance) of a stimulus inform the response to a subsequent stimulus. For example, after seeing the word “WATER”, individuals are more likely to complete the fragment “W_ _ _ R” with “WATER”, rather than an alternative word like “WIDER”. Semantic priming occurs when exposure to a stimulus activates associations with related concepts in memory, thereby making related stimuli more accessible. Semantic priming is captured in word association tasks. For example, after discussing “apples”, individuals are more likely to mention related concepts like “fruit” or “red”, rather than unrelated concepts.

Non-Associative Learning. **Non-associative learning**, a form of implicit memory, does not require learned associations and instead involves a change in behavior in response to repeated exposure to a single type

of stimulus. Non-associative memories emerge from habituation and sensitization. In **habituation**, responses decrease after repeated stimulus presentation as the individual learns that the stimulus lacks meaning. For example, if someone pokes you in the back, you will initially jump in surprise. However, if someone repeatedly pokes you in the back over and over again, you will habituate—your response will decrease and you realize that the stimulus is meaningless. In **sensitization**, repeated exposure to a stimulus can result in increased sensitivity, or stronger responsiveness to the stimulus. For example, a person who moves to a new city may initially show little responsiveness to the sound of car horns. However, with repeated exposure to the sound of car horns, the person may become sensitized to the noise and exhibit a stronger response (e.g., startle).

Associative Learning. **Associative learning**, another form of implicit memory, involves learning associations between unrelated items and results in associative memories. One way we create associative memories is through traditional Pavlovian conditioning. For example, recall the classic experiment conducted by Ivan Pavlov in the late 1800s (Figure 3). Normally, the presentation of dog food, an unconditioned stimulus (US), causes a dog to salivate naturally, an unconditioned response (UR). Dogs are not particularly interested in the sound of a bell: this neutral stimulus will produce a minor response, such as a head turn and attentional shift toward the sound source, but not much more. However, when this stimulus is paired repeatedly with the presentation of food, dogs quickly learn to associate that the bell signals food. After multiple pairings, upon hearing the bell (a conditioned stimulus, CS), the dogs begin to salivate (a conditioned response, CR), independent of any food. Associative learning can also be measured with instrumental conditioning where a rodent, for example, learns to associate a response with a meaningful stimulus. For example, a rodent will learn to press a lever to access food.

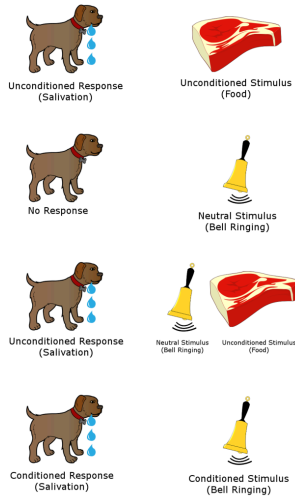


Figure 3. Associative Learning. Initially, in the presence of an unconditioned stimulus (food) the dog will salivate; however in the presence of a neutral stimulus (a ringing bell), the dog will not salivate. During conditioning, the unconditioned stimulus is paired with the bell, causing the dog to salivate. Following conditioning, the dog will salivate from only the presence of the bell.

Working Memory

Compared to long-term memory, working memory has limited duration and capacity. Related to short-term memory, working memory has been described as the use of attention to manage short-term memory, or as the system that temporarily holds and manipulates information in short-term memory (Cowan, 2008). Working memory is necessary for complex cognitive tasks such as learning, reasoning, having a conversation or argument, and doing mental arithmetic.

Short-term memory is often tested using a forward digit-span task, where participants immediately repeat a list of numbers they hear. Working

memory, which involves holding and manipulating information, is often tested with a backward digit-span task. In this test, participants hear a series of numbers and must repeat them *in reverse order*. Digit-span tests begin with short sequences and progressively increase in length until the participant can no longer correctly repeat or reverse the sequence. Performance on the backward digit-span correlates with fluid intelligence, reflecting its demand on cognitive resources (Cowan, 2008).

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8.3: BRAIN STRUCTURES IN MEMORY

Given the various types of memory and underlying processes, it's perhaps unsurprising that memory engages many brain regions. In this section, we present an overview of some brain structures involved in memory and their functions. We focus largely on the hippocampus, as it plays such an important and long-established role in memory. We also cover several other brain regions critical for different aspects of memory.

Memory Consolidation and Relational Memory—Medial Temporal Lobes including the Hippocampus

The main structures of the medial temporal lobes include the hippocampus, the entorhinal cortex, the perirhinal cortex, and parahippocampal cortex. Together, these structures are important in both consolidation and storage of declarative memories.

The hippocampus derives its name from the Greek word for “seahorse,” reflecting its resemblance to the sea creature (Figure 4). It is located along the ventral and medial surface of the brain (Figure 5). The hippocampus is a critical structure in the limbic system, an evolutionarily ancient brain network involved in several functions, including emotions and memory.



Figure 4. The hippocampus (left), a crucial brain structure for memory formation, derives its name from the Greek word for “seahorse” due to its resemblance to the marine creature (right).

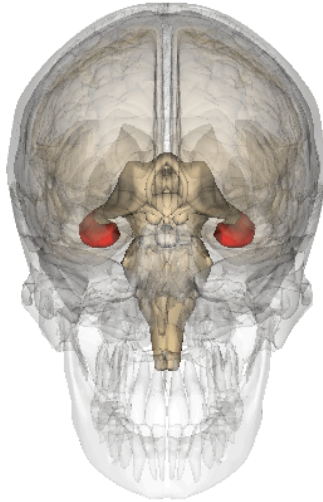


Figure 5. The hippocampi are located deep in the medial temporal lobes.

The hippocampus is involved in memory consolidation, binding information to spatial or temporal contexts (i.e., relational binding), and creating mental maps of our world. When we enter a new building for the first time and we search for a new classroom, the hippocampus facilitates spatial memory by binding distinct items (e.g., lockers) to the current spatial context (e.g., first floor). Further, the hippocampus supports temporal memory by binding these events to a timeline (e.g., Monday morning). Once these memories become stabilized or consolidated, retrieving the spatial context (e.g., first floor) or temporal context (e.g., Monday morning) can help cue our memory for where the classroom is located.

Patient HM

The most influential case study in the neuroscience of memory is the story of Patient HM, whose real name was Henry Molaison (1926-2008). HM grew up in a small Connecticut town. In his childhood, HM began having severe seizures, possibly the result of a head injury. In his teenage years, he started having tonic-clonic seizures, the most severe form of seizures that produces a loss of consciousness and convulsions. In his early adulthood, he was having a tonic-clonic seizure monthly and several minor seizures daily, preventing him from working a normal job or living a normal life, despite taking a cocktail of anti-epileptic medications.

Neurosurgeon William Scoville proposed a “frankly experimental operation” to treat HM. It was known that most epilepsy originates in patches of neurons of the medial temporal lobe, and HM’s epilepsy was typical in this respect. Scoville suggested to surgically remove the medial temporal lobe. In 1953, Scoville removed about 8 cm (~3 inches) of the medial temporal lobe bilaterally, including part of the amygdala, and notably most of the hippocampus. The surgery succeeded at its primary goal: HM’s seizures were less frequent and less severe. However, HM was left with an unusual and life-altering side effect: He was unable to create new declarative memories, a memory deficit called **anterograde amnesia**. “Antero” means going forward, so anterograde is an inability to form new memories going forward from (i.e., after) an event. In contrast, **retrograde amnesia** affects the ability to retrieve old memories; “retro” means backward, so retrograde affects memories backward from (i.e. before) an event. After the surgery, HM could not remember what he had eaten for lunch just minutes after finishing the last bite. It was as if he was permanently living in the present.

However, despite his pervasive memory deficits, HM did not display any deficits in intelligence. His language and speech were unaffected, and word recall was excellent, as he loved completing crossword puzzles and often did so successfully late in life with few spelling errors. He was also capable of

recalling things from his early childhood, such as geography facts he had learned in elementary school.

HM's medial temporal lobe surgery disrupted some types of memories (e.g., memory for facts and new events) while others remained intact (e.g., motor skills). This inspired neuropsychiatrists to try to define different forms of memory. Much of the research was led by [Dr. Brenda Milner](#), who conducted groundbreaking tests on HM to determine which memory types relied on the intact medial temporal lobe and which functioned without it.

Several tests concluded that HM had lost his ability to create new semantic memories. In one such study, HM was asked if a word was made up or real. For words with old origins, such as “shepherd” or “butcher,” he performed as well as the control group. For words that were made up, such as “phlage” or “thweise,” he also performed as well as the controls. However, when shown words that were added to the dictionary after his 1953 surgery, such as “granola” or “jacuzzi,” he performed near chance, as if he never learned the meaning of these new words.

HM was also unable to create episodic (autobiographical) memories. When asked to recall one of his adult birthday celebrations, he couldn't give any significant details. Interestingly, HM's memories of his childhood were still intact. While HM displayed some retrograde amnesia (memory loss from before the surgery), it was much more evident for events shortly before the surgery. Thus, HM's retrograde amnesia was temporally graded, meaning that recent memories were more affected than older memories. Many of his memories for the two years before his surgery were completely lost, but memories from his youth and teenage years were intact.

From this observation, researchers concluded that the medial temporal lobe functions as a temporary storage site for memories, but after some years, those memories get relocated to other brain areas outside of the medial temporal lobe. Current scientific evidence supports this idea that over years, memory storage relies less on the hippocampus and more on distributed cortical networks (discussed below).

While HM lost the ability to create new declarative memories, he

maintained a different class of memory—implicit memory, including procedural memory. The original test of procedural memory conducted by Dr. Brenda Milner was called the mirror tracing task. In this test, participants attempt to trace the outline of a star, but only based on seeing the mirrored reflection of their hand. This mirror tracing task is difficult, but over days of practice, people learn to complete it faster and more accurately. Over training, HM learned to finish the task ten times faster than initially. He retained these improved skills for up to a year, even without regular practice. Surprisingly, each day Milner examined HM, she would need to reintroduce herself and re-explain the task, since he had forgotten her and the task. HM couldn't form declarative memories about the experiment or people involved, but retained his ability to acquire procedural memories and motor skills for the task.

Based on the deficits seen in Patient HM and other experimental manipulations of the hippocampus, Dr. Milner and other scientists concluded that the hippocampus is strongly implicated in declarative memories and spatial navigation. Since some of HM's memory functions, such as procedural and working memory, were still intact, these functions were identified as largely independent of hippocampus function.

Hippocampal Function

The profound insights gained from studying patient HM significantly advanced our understanding of memory, establishing separate subtypes of memory and the crucial role of the hippocampus in declarative memory formation. Studying the hippocampus in animals such as rodents has established its pivotal role in other aspects of memory, including spatial memory, navigation, and binding together information.

Hippocampus: Item-Spatial Context. One spatial test often used in rodents is the Morris water maze (Figure 6). In this test, a shallow pool is filled with an opaque liquid, making it difficult to see through. Hidden somewhere in this pool is a clear plexiglass platform, and surrounding the

pool are different items (i.e., navigational cues) that can be seen from the surface of the water. The water is deep enough that when a rodent is put into the Morris water maze, they must swim to stay afloat. The rodents swim around aimlessly until they find the platform. Researchers record the time it takes to find the platform. Over additional trials, the animals learn that the platform is located near certain navigational cues. In future trials, they spend more time near those items and find the platform more quickly. When their hippocampus is surgically inactivated or removed, rodents perform poorly in the Morris water maze.

So the hippocampus plays an important role in navigation and spatial learning. More specifically, researchers have proposed that the hippocampus binds the navigational cue items to the spatial contexts of the pool. This hippocampal “relational binding” is thought to support the development of a stable memory representation of the water maze, and allows successful navigation.

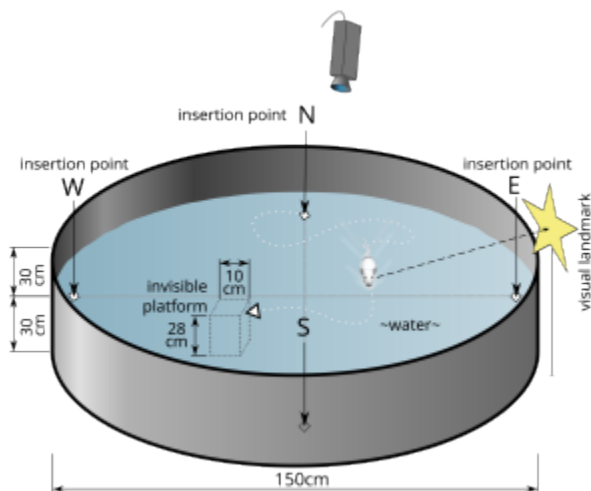


Figure 6. The Morris water maze tests rodents' spatial memory. In an opaque-filled pool with a hidden platform, rodents swim to find escape. Visual cues surround the pool. A camera tracks the rodent's path, and researchers record the time taken to find the platform. Over multiple trials, rodents learn to use the navigational cues, reducing their search time to find the platform.

Hippocampus: Item-Temporal Context. Similar to how items can be bound to a spatial context in memory, items can also be bound to a temporal- or time-context in memory. Temporal context in memory refers to how memories are shaped by the timing and sequence of events. For example, if someone asks “what did you do last weekend?”, it’s likely that retrieving the temporal context (e.g., Saturday) will help cue your memory for events. The landmark temporal context model describes how retrieving the temporal context of an event helps memory retrieval (Howard & Kahana, 2002). Here, the temporal context is represented as a timeline of when events were experienced. The temporal context model includes principles of contiguity and recency (Howard & Kahana, 2002). The contiguity effect refers to the finding that items that occur closer together in time become associated. For example, when recalling a list of words,

recalling one word can trigger or cue memory of temporally adjacent words (Solway et al., 2012). The recency effect shows that memory is stronger for recent items. As time passes or more intervening items appear, memory typically weakens. For instance, in a word list, you're more likely to remember the last few words than earlier words. The temporal context model explains this observation by proposing that the temporal context for recently encountered items is more similar to the current temporal context, which makes the more recently encountered items more readily accessible in memory (Howard & Kahana, 2002).

Hippocampus: Item-Context Binding. Although early perspectives of the hippocampus in memory focused on its role in encoding spatial maps or temporal sequences, some newer memory models propose that the hippocampus may instead serve a more general computational role by binding relations associated with an item (Davachi, 2006; Eichenbaum et al., 2007). A memorable item or event consists of multiple elements and is associated with various contexts, including spatial, temporal, and other associated details. In a relational binding framework, the hippocampus binds together item and contextual information from other regions of the brain. Successful memory retrieval relies on retrieving the context associated with the item (Yonelinas et al., 2019). Recent fMRI studies in humans and neurophysiological studies in rodents and monkeys show that hippocampal subregions and other subregions of the medial temporal lobes (e.g., perirhinal and parahippocampal cortex) make distinct contributions to encoding and binding items, contexts, recollection, familiarity, etc. (see Davachi, 2006; Eichenbaum et al., 2007 for details). In sum, the hippocampus binds items with their associated contexts, and this item-context binding function is essential for forming, storing, and recalling complex memories of information and experiences.

Declarative Memory—Cortex

In addition to the hippocampus, several other brain regions are involved in

processing memory, and early studies established the role of the cortex. In the 1950's, the scientist Karl Lashley was interested in finding a location in the brain where memories were stored. His experiments searched for the location within the cortex of what he called an “**engram**” or memory trace. He trained rats to run in a complex maze to reach a food reward. After the animals learned to run the maze successfully, Lashley would lesion different areas of the rat cortex and then test the rats in the maze again. He found that regardless of where the cortex was lesioned, the lesions impaired their ability to run the maze and remember the food's location. Instead of finding a specific cortical area where the memories were stored, Lashley discovered that the size of the lesion corresponded to the amount of memory deficit in the animal. This demonstrated that the memory trace (engram) was widely spread across the cortex.

Lashley's work from the 1950's nicely predicted some current understanding of how memory features are encoded in several primary and associative cortical regions. Various features of an experience are encoded in widespread cortical areas. According to a standard consolidation model of memory (see below), information across these distributed cortical regions is coordinated or integrated by the hippocampus. As the memory is consolidated (strengthened) over time, the connections between cortical regions strengthen and these memories become more independent of the hippocampus (Frankland & Bontempi, 2005).

Working Memory—Prefrontal Cortex

The prefrontal cortex is involved in higher-order cognitive processing, decision making, and personality (Figure 7). In the context of memory, neural circuits in the prefrontal cortex are important for short-term and working memory (the memory system involved in temporarily storing and manipulating information for cognitive tasks).

Both animal and human studies have demonstrated the prefrontal

cortex's crucial role in working memory. In a delayed-response task, a monkey observes food placement in a randomly selected compartment, which is then concealed. After a delay, the monkey must locate the food. This task depends on prefrontal cortex activity; monkeys with prefrontal lesions perform worse than those with intact prefrontal cortices.

Human patients with injuries to their prefrontal cortex after stroke, tumors, or aneurysm, performed worse on a variety of working memory tasks such as the backward digit span test. Additionally, people with frontotemporal dementia, a neurodegenerative disorder characterized by a degradation of the frontal lobe, often have difficulty with working memory.

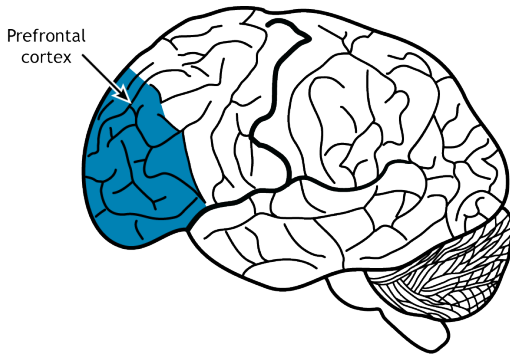


Figure 7. Prefrontal Cortex. The prefrontal cortex, shown in blue in an external view of the brain, is located in the anterior portion of the frontal lobe.

Habit or Procedural Memory—Striatum

The striatum (Figure 8), made up of the caudate nucleus and putamen, is important for habit or procedural memory and reward in learning. A T-maze is used to test procedural learning (Figure 9). In this task, a rodent is placed at the bottom of the T in the maze. The animal is trained to turn either left (with one tone) or right (with a different tone) once they reach

the cross of the T. If the animal completes the task successfully, they are rewarded with a treat. The ability of the animal to learn this task depends on activity within the striatum. Animals with striatal lesions have impaired performance on the T-maze, but not on tasks that rely on other types of memory.

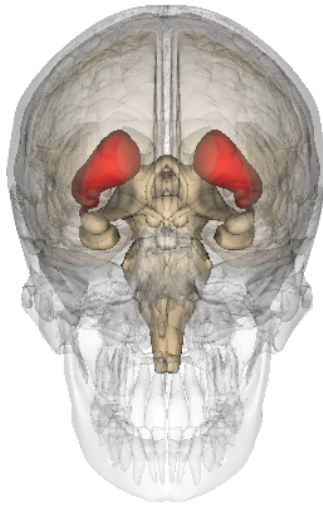


Figure 8. Location of the striatum (in red), which is involved in procedural memory.



Figure 9. A T maze is used to test procedural memory and reward in learning. In this task, a rodent is placed at the area of the maze that corresponds to the bottom of the T. The animal is trained to turn either left or right. If the animal completes the task successfully, they are rewarded with a treat.

Emotional Memories—Amygdala

The amygdala plays a well-known role in processing emotions like fear and aggression, and is also involved in forming and storing memories, especially of emotionally arousing experiences. For example, Josselyn (2010) demonstrated the amygdala's role in storing fear memories in a study with rats. The researchers conditioned rats to fear a tone by pairing it with foot shocks. After conditioning, the rats would freeze upon hearing the tone, indicating they remembered the tone-shock association. When researchers induced cell death in the rats' lateral amygdala, this fear memory faded. Conditioning and implicit memory are also impaired in humans with amygdala damage (Bechara et al., 1995).

In addition to fear conditioning and implicit learning, the amygdala is also involved in encoding and storing emotional events. Emotional experiences form strong memories, with the amygdala playing a crucial

role. The basolateral amygdala (BLA) is particularly important, as stress hormones and neurotransmitters, especially noradrenaline, in this region enhance the consolidation of emotional memories. Noradrenaline is released in response to emotional or stressful events. In experiments with rodents, noradrenaline injections into the BLA, but not adjacent parts of the amygdala, enhanced consolidation of emotional memories. This enhancement occurred by stimulating cAMP-dependent cell signaling and increasing neuroplasticity (Roozendaal et al., 2009). Noradrenaline plays a crucial role in synaptic plasticity in the amygdala and interconnected regions, including the hippocampus and neocortex. These mechanisms typically help form strong emotional memories, but under traumatic or chronic stress conditions, they can contribute to anxiety and the retention of traumatic memories, as seen in PTSD.

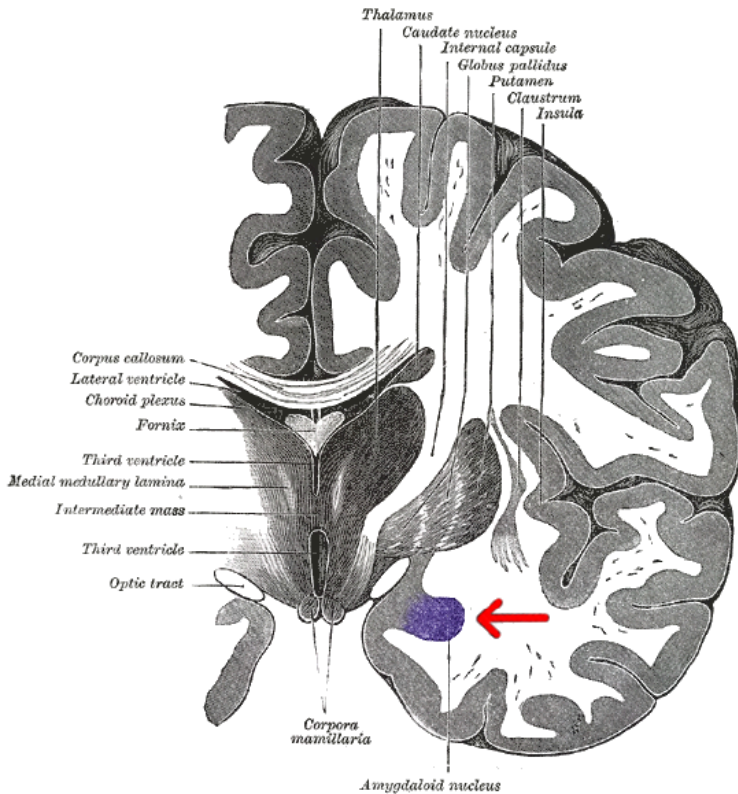


Figure 10. Illustration of a coronal slice of the human brain from Gray's Anatomy of the Human Body (1918), showing the amygdala in purple pointed to by the arrow. The amygdala is important for processing emotional memories.

Interim Summary

This section highlights several brain structures involved in memory. We focus largely on the hippocampus for its well-established role in declarative memory. We cover other brain regions involved in memory, including distributed cortical networks that store long-term memories, prefrontal cortex that processes working memory, the striatum for procedural

memory, and the amygdala for emotional memories. This list of brain structures involved in memory is certainly not exhaustive. For example, the cerebellum is involved in procedural memory; the orbitofrontal cortex plays a role in positive emotional memories; and sensory cortices are important for storing aspects of memories processed in those areas. A single memory could be stored in several brain areas, much like a mosaic.

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8.4: SPECIAL TYPES OF NEURONS

A memory is distributed across several different parts of the brain. However, a few special types of neurons mainly in the medial temporal lobe contribute to highly specific types of memories.

Place Cells

Place cells are a special population of pyramidal cells of the hippocampus (Figure 11). These neurons increase their firing rates when the animal occupies a specific location in its environment. Figure 11 illustrates this phenomenon, showing a rat navigating a maze while its hippocampal place cells are recorded. The colored dots represent the rat's position on the maze when each place cell fires, with each color corresponding to a unique cell. This visualization demonstrates that individual place cells consistently fire when the rat occupies a particular spatial location. The place cells, when firing at the right times, help the animal create a spatial map of their surroundings.

Interestingly, these spatial maps are consolidated during sleep. When the rat sleeps after learning to run a particular maze during the day, their place cells fire in a sequence consistent with the spatial layout of the maze (even though they are not moving to these locations while asleep). This suggests that they are “replaying” their experience during sleep to learn and consolidate the spatial memory (Klinzing et al., 2019; see section on memory reactivation during sleep).

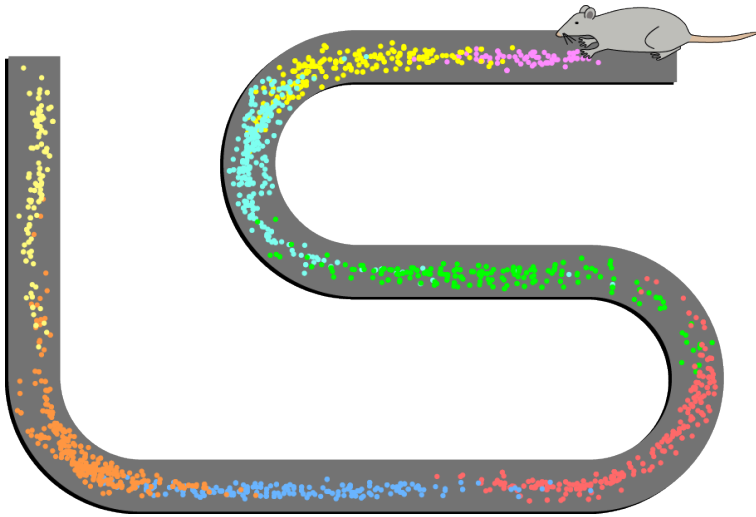


Figure 11. Place Cells. Place cells, a special population of neurons in the hippocampus, fire action potentials when an animal is in a specific location and are important in navigational memory. Here a rat is placed in a maze and place cells in its hippocampus are recorded. Where each place cell fires is indicated on the maze with colored dots. Dots of the same color indicate firing of the same place cell.

Grid Cells

Grid cells are located in the entorhinal cortex, the main input structure to the hippocampus. Closely related to the place cells, grid cells increase their firing periodically when an animal is at an intersection of a “grid” in a wide-open, previously-explored environment. The grid itself is roughly hexagonal and spans the whole environment an animal is in (Figure 12). The overlap of multiple grids gives the animal an idea of the surroundings. The scientific description of place cells and grid cells earned three scientists, Edvard Moser, May-Britt Moser, and John O’Keefe, a Nobel Prize in Physiology or Medicine in 2014.

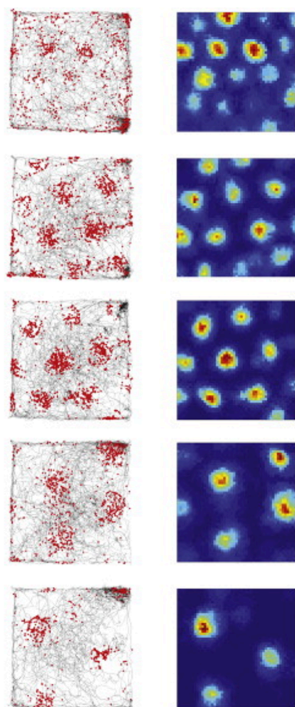


Figure 12. Grid cells are a special population of neurons located in the entorhinal cortex, which serves as the main input structure to the hippocampus. Similar to place cells, grid cells fire when an animal is at an intersection of a “grid” in a wide-open, previously-explored environment. These images on the left show the movement of a rat through a square environment depicted by a black line. The red dots indicate locations within the environment where a specific entorhinal grid cell fired. The images on the right show a spatial autocorrelogram that corresponds to the neuronal activity of the grid cell from the figures on the left.

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8.5: STAGES OF MEMORY

This section gives a brief overview of memory processing stages, including encoding, consolidation, and retrieval.

Memory Encoding

Encoding refers to the process of converting incoming information into a mental representation that the brain can retain. In real life, you are presented with countless stimuli simultaneously. Imagine walking down a busy street, and the number of different sights, smells, and sounds you experience. Storing memories is an energetically costly process, and we are limited in the fact that all of our sensory inputs cannot possibly get encoded. Instead, our memory systems have evolved to adaptively encode the most salient information, such as environmental cues associated with threatening or rewarding experiences.

Decades of research have established that emotional memories are more strongly and vividly remembered than neutral memories, which may be partially driven by the preferential encoding of emotional events. The neurobiological mechanisms that prioritize emotional events include arousal from stress hormones (e.g., noradrenaline), fight-or-flight-related neurotransmitters (e.g., norepinephrine), and increased recruitment of the amygdala. These may drive the enhanced encoding of the most salient features of emotional events (Clewett & Murty, 2019; Mather & Sutherland, 2011).

Memory Consolidation

Memory consolidation refers to the process where short-term memories are transformed into long-term memories. While many theories have addressed how memories are stabilized over time, systems consolidation theory has emerged as the dominant perspective. Systems consolidation theory suggests that memories are stabilized as a result of interactions between the hippocampus and different regions of the neocortex (Alvarez & Squire, 1994; McClelland et al., 1995; Cowan et al., 2021). More specifically, the hippocampus is initially crucial for storing and retrieving memories; but over time, these memories become less dependent on the hippocampus and shift to being stored in the neocortex (Figure 13). Systems consolidation aligns with Patient HM's memory capacity. Recall HM's temporally graded retrograde amnesia, where he lost memories from the two years before his surgery, but maintained memories from his more distant past. The memories from shortly before the surgery still depended on the hippocampus, so were lost when his hippocampi were removed. Conversely, his childhood memories had fully transferred to the neocortex and no longer involved the hippocampus, so they were maintained after removing the hippocampus.

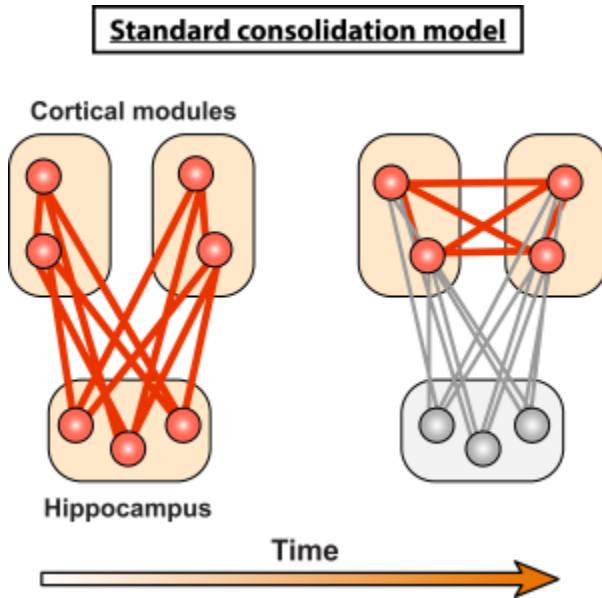


Figure 13. Standard consolidation model. New memories are encoded across areas of cortex that represent the memory's features (e.g., sights, sounds, associations of the item and context); the hippocampus integrates and binds together that information. Over time, the hippocampal-cortical connections weaken and cortico-cortical connections strengthen until the memory is transferred to cortex (independent of the hippocampus) for long-term storage (consolidation). [Image adapted from Frankland & Bontempi, 2005]

Memory Retrieval

The process of accessing and recalling information previously encoded and stored in memory is known as retrieval. Memory retrieval is crucial for allowing people to use past information, knowledge, and skills in everyday life and to integrate learning of new information. Although memory retrieval is typically thought of as the conscious retrieval of stored facts and life events (i.e., declarative memories), retrieval also happens with

procedural memories, as when you recall or perform a skilled action. Memory retrieval can be differentiated from memory encoding using a cued word-recall test. Imagine being given a list of 50 words to memorize, where the words belong to a few different conceptual categories (such as cinnamon, pepper, and curry, which fall under the category ‘food flavors’). In a free-recall test, where you’re asked to write down as many words as possible from memory, you might remember about 30% of the words. However, in a cued-recall test, where you’re cued with categories (like ‘food flavors’), you’d likely perform much better, possibly recalling 75% of the words. Higher scores in cued-recall show how retrieving information is helped by cues that activate contexts and associations between items encoded in memory.

State- and context-dependent memory. State-dependent memory refers to the phenomenon where memory retrieval is most effective when a person is in the same state of consciousness as when the memory was formed. This applies to states induced by psychoactive substances like alcohol, as well as moods or other internal conditions. Context-dependent memory is related but instead of internal conditions, it involves external environments—memory retrieval is most effective when the person is in the same external environment as when the memory was formed. For example, in state-dependent memory, information studied while caffeinated is best retrieved in a similar state of caffeination. Whereas in context-dependent memory, information studied in one room is best retrieved in that same room. Biologically, memories are encoded through changes in synaptic strength and stored as spatiotemporal patterns of activity across neuronal networks. Being in the same state or context activates part of the neuronal pattern associated with the memory, facilitating full activation of the memory trace for retrieval.

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8.6: MEMORY RECONSOLIDATION—NEW VIEWS AND APPLICATIONS

Early perspectives of memory believed that memory storage was a singular and linear process, such that each time we remembered a prior experience, the original memory trace was retrieved (Alberini & LeDoux, 2013). However, recent work suggests that memories are susceptible to change, and as a result, memories can be distorted each time they are retrieved. In other words, it's possible that each time we recall a memory of a past event, it might change a little. Our memories are not fixed recordings of an event, but rather, dynamic reconstructions that evolve. This process is known as **memory reconsolidation**. Below, we briefly discuss current perspectives on reconsolidation and how researchers leverage reconsolidation to selectively update memories.

Memory Reactivation

Although it's well-established that memories become consolidated or stabilized over time, scientists are actively investigating the neural mechanisms underlying memory consolidation. Neuronal firing patterns present during encoding are repeatedly reactivated during 'offline' periods of post-encoding rest (e.g., sleep, awake rest) (McClelland et al., 1995; Alvarez and Squire, 1994; Tambini & Davachi, 2019). Indeed, landmark animal research revealed that place cells within the hippocampus that were active during recent exploration were preferentially reactivated during subsequent sleep (Pavlidis & Winson, 1989; Wilson & McNaughton, 1994). Place-cell activation patterns observed during exploration and

subsequent sleep were absent in pre-exploration sleep. Thus, the neuronal reactivation after exploration represented a replay of waking experiences. Critically, memory reactivation during sleep is linked with improved memory the next day.

Although early rodent research focused on reactivating spatial memories, recent human research has demonstrated memory reactivation of nonspatial, episodic experiences (Tambini & Davachi, 2019). In an fMRI study, participants learned pairs of items that consisted of an object and a picture of a scene. Researchers analyzed brain activation in the medial temporal lobe while participants encoded the pairs and while they rested after encoding. Participants were later tested if they remembered the object that was paired with a scene. Results showed that brain activation during encoding and rest was highly similar for remembered pairs; whereas brain activation during encoding and rest was dissimilar for forgotten pairs (Staresina et al., 2013). These results show that memory reactivation occurred during the post-encoding rest period, and was linked to subsequent memory performance.

Researchers have begun examining when memory reactivation most likely occurs. Reactivation of neuronal sequences are most pronounced during a brain state that can be measured with EEG, called high-frequency oscillatory events or sharp wave ripples (SWRs) (Skaggs & McNaughton, 1996). Although SWRs can occur during periods of awake rest, they primarily occur during slow-wave-sleep, also known as non-rapid-eye-movement (NREM) sleep, which is thought to be the most restorative stage of sleep. Several studies have shown that disturbances to SWRs can impair learning and later memory (Tambini & Davachi, 2019). These memory impairments likely stem from disrupted memory reactivation. In sum, given the mounting evidence connecting reactivation to later memory performance, researchers increasingly view neural reactivation as a key mechanism underlying memory consolidation in humans.

Targeted Memory Reactivation

Targeted memory reactivation (TMR) is a noninvasive technique to selectively strengthen or weaken memories during sleep or awake rest (Oudiette & Paller, 2013). In TMR studies, sensory cues (e.g., sounds or scents) are paired with items (e.g., words or pictures) during a learning session. During subsequent sleep, the same sensory cues are presented to trigger the reactivation of the associated memory and thereby strengthen the memory for specific items (Hoffman et al., 2024) (Figure 14). Indeed, several TMR sleep studies have reported enhanced memory for items that were cued during sleep compared to items that were not cued (Rasch et al., 2007; Rudoy et al., 2009). Critically, this memory benefit is attributed to the memory reactivation processes described in the section above. A recent meta-analysis reviewed 90 TMR studies and found general support for TMR-related memory benefits and that the effects of TMR are most pronounced during non-rapid-eye-movement stages of sleep, and particularly slow-wave-sleep (Hu et al., 2020).

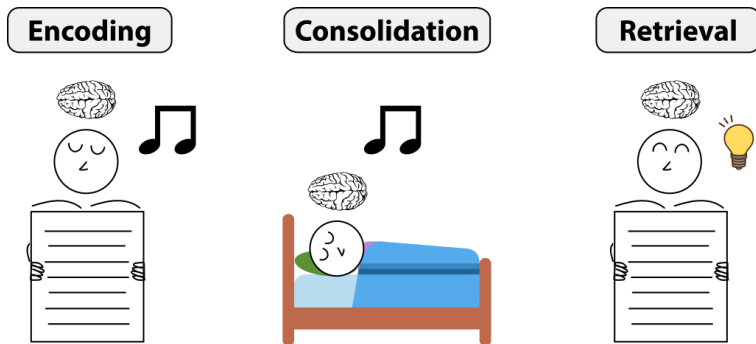


Figure 14. Targeted Memory Reactivation (TMR) involves pairing sensory cues (e.g., sounds) with items to be remembered (e.g., words) during a learning session (encoding). During subsequent sleep, the sensory cues are presented to trigger the reactivation of the associated memory (consolidation). After waking up, retrieval for memory that was targeted and reactivated is stronger (without presenting the sensory cue). [Image adapted from: Carbone & Diekelmann, 2024]

TMR has been shown to be effective across different types of memory, including declarative and procedural memory. Given the compelling experimental findings, researchers have begun examining applications of TMR to improve people's lives. For example, recent TMR studies on vocabulary and grammatical learning have found TMR-related memory benefits (Batterink et al., 2017). Thus, using cues to reactivate memories during sleep could support language acquisition in educational contexts. Moreover, given the relationship between TMR and procedural memory, TMR could be leveraged to support motor skill development (Cousins et al., 2014). This might be applied to improve athletic or musical performance, or to clinical disorders related to motor impairments. Finally, TMR is not only applied to strengthen memories, but several studies have explored using TMR to weaken specific memories (Simon et al., 2018; Schectman et al., 2020). Thus, TMR has been proposed to be a psychotherapeutic instrument for weakening memories related to traumatic events, which is especially relevant for anxiety or post-traumatic stress disorder (PTSD). However, the relationship between TMR and emotional memories remains mixed—one study showed that TMR-related memory benefits appeared for neutral, but not emotional memories (Groch et al., 2016), whereas another study showed that TMR was indeed effective for dampening emotional memories (Lehmann et al., 2016). Targeted memory reactivity (TMR) is an exciting and rapidly evolving area of research with potentially impactful applications.

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8.7: MEMORY-RELATED DISORDERS

Memory is fundamental to our daily functioning and sense of self, yet it can be fallible and fragile. Memory disorders represent a diverse group of conditions that disrupt our ability to encode, store, or retrieve information. Memory disorders can range from mild forgetfulness to severe impairments that profoundly affect an individual's quality of life.

Memory impairments are prevalent across many clinical conditions, including amnesia, traumatic brain injury, and neurodegenerative conditions such as Alzheimer's disease. Cases of amnesia, such as Patient HM after surgical removal of his hippocampi, are among the earliest documentations of brain-related memory dysfunction. Traumatic brain injuries and concussions have also been shown to be related to memory impairment, particularly short-term memory loss (McDowell et al., 1997; Malojcic et al., 2008; Covassin & Elbin, 2010). Neurodegenerative conditions, such as Alzheimer's disease, can also be characterized by short-term and long-term memory degradation (covered in more detail in Chapter 11). Researchers have been working intensely to understand how disruptions to neural, genetic, and vascular systems may give rise to different types of memory dysfunction (Morely & Farr, 2014; El Haj et al., 2016; Religa et al., 2013). As our population ages and the prevalence of memory disorders such as dementia and Alzheimer's increases, understanding these disorders will be increasingly relevant to society.

Another memory-related condition that may affect younger adults and is interesting to students is Korsakoff's syndrome. This section concludes with an examination of Korsakoff's syndrome, exploring its effects and neurobiological underpinnings.

Korsakoff's Syndrome

Korsakoff's syndrome is a disorder resulting from a severe deficiency of thiamine. Thiamine (vitamin B-1) is essential for metabolic processes, such as producing energy from glucose. Dietary thiamine is found in whole grains, legumes such as beans and peas, and some meats and fish. Healthy people with a well-balanced diet get sufficient thiamine, however, gastrointestinal illnesses can cause an inability to absorb thiamine properly. The body's ability to absorb thiamine is also disrupted by chronic alcohol misuse. Alcohol misuse, in addition to its toxic effects on brain cells, can cause Korsakoff's syndrome. While chronic alcohol consumption is the primary cause of Korsakoff's syndrome, malnutrition, eating disorders, and genetic factors can also increase susceptibility to the condition.

People with Korsakoff's syndrome experience several kinds of cognitive and memory impairments. They can have both retrograde and anterograde amnesia, as well as severely impaired short-term memory. The patients may confabulate or make up information they can't remember. People who confabulate do not consciously recognize that their statements are untrue, and are not intentionally trying to deceive others, which is why it is sometimes called "honest lying." Generally, confabulation only happens as a person is trying to recall recent autobiographical memories; their semantic and procedural memories are less susceptible to confabulation. Scientists propose that individuals with retrograde amnesia confabulate to fill memory gaps.

Korsakoff's syndrome leads to decreased glucose metabolism in the brain, reducing its primary fuel source, and causes destruction of both neurons and glial cells. As a result of this cell loss, there is often shrinkage of the cortex, thalamus, cerebellum, and hippocampus. Korsakoff's syndrome can be treated by giving thiamine supplements and eliminating alcohol consumption. If treated within days after the onset of brain damage, people generally recover completely. However, one of the major challenges is

making a proper diagnosis, since the symptoms of Korsakoff's syndrome present similarly to other disorders.

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8.8: MEMORY ENHANCEMENT TECHNIQUES

Recent findings in biopsychology and neuroscience have enhanced our understanding of memory and can be applied to improve memory performance. This is especially relevant for students, who must learn and recall vast amounts of information. The chapter concludes with some scientifically-based strategies for improving memory.

Spacing effect

The spacing effect, also known as distributed practice, shows that information is retained better when learning is spread over time rather than condensed into one session. This may be due to increased opportunities for memory reactivation and consolidation during rest or sleep (Cowan et al., 2024). Whether studying for an exam, practicing a sport, or learning a new skill, consistent daily sessions are more effective than cramming the same amount of time into a single session.

Elaborative rehearsal

Deeply processing information enhances long-term memory retention. Elaborative rehearsal is an effective memory technique that involves connecting new information to existing knowledge or experiences (Bartsch et al., 2018). This process can include forming meaningful associations through analogies, creating vivid mental images, or drawing parallels. Such techniques help integrate new information into existing memory stores. Students can apply elaborative rehearsal by connecting new information to previously learned material or relevant life experiences.

Retrieval practice

Retrieval practice, also known as the testing effect, involves actively recalling information rather than passively reviewing it. This technique

enhances long-term retention by reactivating neural pathways associated with learned information each time it is recalled. To prepare for an exam, many students just re-read material, which is less effective for recall when it counts. Instead, active recall strategies like using flashcards, creating practice questions, or peer quizzing prove more beneficial than passively re-reading materials.

Get enough sleep

While sleeping, your brain is at work organizing and consolidating information in long-term memory. During sleep, particularly during slow-wave sleep, neural patterns associated with recent learning are reactivated. This strengthens or consolidates the memory, and enables the transfer of information from the hippocampus to more long-term storage in the cortex. Despite the tendency for college students to sacrifice sleep due to busy schedules, optimizing sleep quality can enhance sleep-dependent memory consolidation.

Physical exercise

Physical exercise, particularly aerobic activity, is associated with enhanced hippocampal function and improved memory. Regular aerobic exercise has been linked with increased hippocampal volume, brain-derived neurotrophic factor (BDNF), and hippocampal neurogenesis (Erickson et al., 2011; Ma et al., 2017), which are associated with memory formation and retention. Aerobic exercise has been linked to improved episodic, spatial, and procedural memory (Roig et al., 2013). Taking exercise breaks can enhance learning and memory.

Minimizing interference

Divided attention and distractions can interfere with memory encoding and retrieval (Fernandes & Moscovitch, 2000). To reduce interference and enhance memory, study in a distraction-free environment, avoiding television, phones, and social media alerts. One effective technique for focused work is the “Pomodoro Technique,” named after a tomato-shaped kitchen timer. This method involves focusing on a single task for 25-minute intervals (no internet, TV, social media, etc.), followed by a short 3-5 minute break. Repeat this cycle as needed.

Mnemonic devices

Mnemonic devices can enhance memory by organizing information and creating meaningful associations between items in ways that support memory encoding and retrieval. For example, chunking is a common mnemonic technique wherein individuals group items into meaningful units (e.g., remembering a phone number as 222-875-4344 rather than individual numbers). The method of loci, or memory palace, is a mnemonic technique that engages spatial memory systems in the brain. In this method, individuals assign items they want to remember to imagined spatial locations to improve memory. By strategically organizing information and establishing relationships between items, individuals can optimize their memory performance.

Emotional encoding

Emotional experiences form strong memories, due to several factors including amygdala-hippocampal activation, stress hormones, and neuromodulators. Students can hack this emotion-memory link by framing new information with an emotionally charged narrative. For example, when learning something for class, like the neural underpinnings of memory consolidation, making that information more emotional (a scary or sexy hippocampus?) could strengthen that memory.

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8.g: DISCUSSION QUESTIONS AND RESOURCES

Key Takeaways

- Memory can be broadly categorized into sensory memory, short-term and working memory, and long-term memory, which includes declarative (explicit) and nondeclarative (implicit) types. Declarative memory can be divided into semantic and episodic memory; Implicit memory includes procedural memory, priming, and associative learning.
- The hippocampus plays a crucial role in the formation of new declarative memories and spatial navigation, as demonstrated by the case of Patient HM and research with rodents.
- The prefrontal cortex is essential for working memory, while the striatum is important for procedural memory.
- Specialized neurons like place cells in the hippocampus and grid cells in the entorhinal cortex contribute to spatial memory and navigation.
- Memory processing involves multiple stages: encoding, consolidation, and retrieval, each supported by different neural mechanisms.
- Memory consolidation involves the gradual transfer of information from the hippocampus to distributed cortical

- networks, as explained by systems consolidation theory.
- Memory reactivation during sleep, particularly during slow-wave sleep, plays a significant role in memory consolidation.
 - Targeted memory reactivation (TMR) is a technique that can potentially enhance or weaken specific memories during sleep, with potential applications in education and therapy.
 - Current views of memory reconsolidation suggest that memories are not fixed but can be modified each time they are retrieved, challenging earlier views of memories as static and fixed.
 - Memory disorders, such as Alzheimers's disease and Korsakoff's syndrome, illustrate the complex relationships between brain function, nutrition, and behavior, and highlight the fragility of our memory systems.
 - You can apply biopsych research findings to improve your memory and study habits.

Discussion Questions

1. How does the case of Patient HM illustrate the distinction between different types of memory? What insights did his condition provide about the role of the hippocampus in memory formation?

2. Compare and contrast declarative and nondeclarative memory. How might these different memory systems interact in everyday life?
3. Discuss the potential implications of memory reconsolidation for understanding the malleability of memories. How might this concept impact our understanding of eyewitness testimony or therapy for trauma-related disorders?
4. How do place cells and grid cells contribute to spatial memory and navigation? Can you think of any real-world applications or technologies that might leverage our understanding of these specialized neurons?
5. Evaluate the potential benefits and ethical considerations of using targeted memory reactivation (TMR) in educational or clinical settings. What are some potential risks or limitations of this technique?
6. How does the process of memory consolidation during sleep contribute to learning? Discuss how this knowledge might inform study strategies or sleep habits for optimal learning.
7. Compare the roles of the hippocampus, prefrontal cortex, and striatum in different aspects of memory. How do these structures work together to support various memory functions?
8. Discuss the relationship between emotion and memory encoding. How might this relationship explain why some memories are more vivid or easily recalled than others?
9. Consider the various memory-related disorders discussed in the chapter. How might advances in our understanding of memory systems and neurobiology contribute to potential treatments or interventions for these conditions?

10. Reflect on the memory-enhancement techniques mentioned at the end of the chapter. Which ones do you use when studying and which ones should you try to use? How are they related to what we know about the biopsychology of memory?

Outside resources

Book: Patient H.M.: A Story of Memory, Madness, and Family Secrets (2017) by Luke Dittrich. Account of the life of Patient H.M. written by his grandson, Luke Dittrich. [Link](#).

Podcast: Brain Inspired 133 (2022) – Ken Paller: Lucid Dreaming, Memory, and Sleep. Dr. Paller discusses his recent research on memory, sleep, and targeted memory reactivation. [Link](#).

Movie: Memento (2000) by Christopher Nolan. Quest for revenge by a guy whose head injury leaves him unable to form new memories. [Trailer](#).

Movie: Eternal Sunshine of a Spotless Mind (2004) by Michel Gondry/Charlie Kaufman. After a bad breakup with his girlfriend, Joel (Jim Carrey) decides to erase his memories of her. [Trailer](#).

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CHAPTER 9: GENETICS AND EPIGENETICS IN PSYCHOLOGY

Psychological researchers study genetics to better understand the biological factors that contribute to behavior. Genes and the environment shape the nervous system's structure and function, ultimately influencing our thoughts, behaviors, and unique personal traits. In this chapter, we first review fundamental genetics. Then we look at how behavioral geneticists study the relative contributions of genes and environment to tease apart nature and nurture. We discuss gene-environment interactions and introduce the relatively new field of epigenetics, which studies how the environment and behaviors can change how our genes work.

Learning Objectives

- Explain the basic principles of the theory of evolution by natural selection
- Describe the differences between genotype and phenotype
- Discuss how gene-environment interactions are critical for the expression of physical and psychological characteristics

- Understand why nature–nurture questions are difficult to study empirically.
- Know the major research designs that can be used to study nature–nurture questions.
- Understand what epigenetics is and how epigenetic mechanisms can alter gene expression and impact physical and mental health

9.1: INTRODUCTION

In this chapter, we'll explore questions such as: Why do two people infected by the same disease have different outcomes: one surviving and one succumbing to the ailment? How are genetic diseases passed through family lines? Are there genetic components to psychological disorders such as depression or schizophrenia?

To explore these questions, let's start with a specific genetic disorder, sickle-cell anemia, and how it might manifest in two affected sisters (Spielman et al., 2020). Sickle-cell anemia is a genetic condition in which red blood cells, which are normally round, take on a crescent-like shape (Figure 1). The changed shape of these cells affects how they function: sickle-shaped cells can clog blood vessels and block blood flow, leading to high fever, severe pain, swelling, and tissue damage.

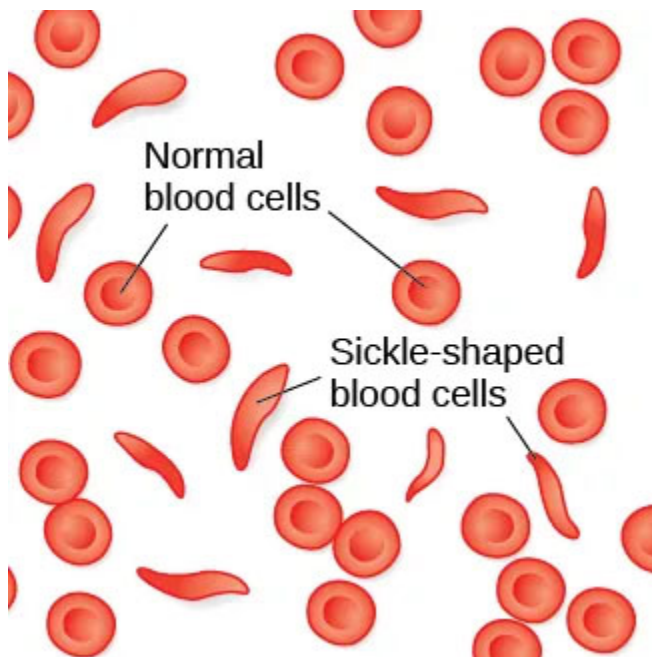


Figure 1. Normal blood cells travel freely through the blood vessels, while sickle-shaped cells form blockages preventing blood flow.

Many people with sickle-cell anemia—and the particular genetic mutation that causes it—die at an early age. While the notion of “survival of the fittest” may suggest that people with this disorder have a low survival rate and, therefore, the disorder will become less common, this is not the case. Despite the negative evolutionary effects associated with this genetic mutation, the sickle-cell gene remains relatively common among people of African descent. Why is this? The explanation is illustrated with the following scenario.

Imagine two young women—Luwi and Sena—sisters in rural Zambia, Africa. Luwi carries the gene for sickle-cell anemia; Sena does not carry the gene. Sickle-cell carriers have one copy of the sickle-cell gene but do not have full-blown sickle-cell anemia. They experience symptoms only if

they are severely dehydrated or are deprived of oxygen (as in mountain climbing). Carriers are thought to be immune from malaria (an often deadly disease that is widespread in tropical climates) because changes in their blood chemistry and immune functioning prevent the malaria parasite from having its effects (Gong et al., 2013). However, full-blown sickle-cell anemia, with two copies of the sickle-cell gene, does not provide immunity to malaria.

While walking home from school, both sisters are bitten by mosquitoes carrying the malaria parasite. Luwi is protected against malaria because she carries the sickle-cell mutation. Sena, on the other hand, develops malaria and dies just two weeks later. Luwi survives and eventually has children, to whom she may pass on the sickle-cell mutation.

Malaria is rare in the United States, so the sickle-cell gene benefits nobody: the gene manifests primarily in minor health problems for carriers with one copy or a severe full-blown disease with no health benefits for carriers with two copies. However, the situation is quite different in other parts of the world. In parts of Africa where malaria is prevalent, having the sickle-cell mutation does provide health benefits for carriers (protection from malaria).

The story of malaria fits with Charles Darwin's theory of evolution by natural selection (Figure 2). In simple terms, the theory states that organisms that are better suited to their environment will survive and reproduce, while those that are poorly suited to their environment will die off. In our example, we can see that, as a carrier, Luwi's mutation is highly adaptive in her African homeland; however, if she resided in the United States (where malaria is rare), her mutation could prove costly—with a high probability of the disease in her descendants and minor health problems of her own.

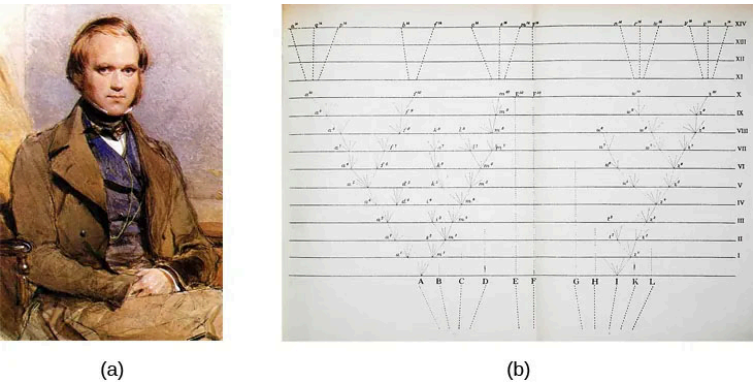


Figure 2. (a) In 1859, Charles Darwin proposed his theory of evolution by natural selection in his book *On the Origin of Species*. (b) The book contains just one illustration: this diagram that shows how species evolve over time through natural selection.

DIG DEEPER

Two Perspectives on Genetics and Behavior

The interaction of genes and the environment is studied in the fields of evolutionary psychology and behavioral genetics. In both fields, it is understood that genes code for particular traits and contribute to patterns of cognition and behavior. How can we tell these fields apart?

Evolutionary psychology focuses on how universal patterns of behavior and cognitive processes have evolved over time. Therefore, variations in cognition and behavior would make

individuals more or less successful in reproducing and passing those genes on to their offspring. Evolutionary psychologists study a variety of psychological phenomena that may have evolved as adaptations, including fear response, food preferences, mate selection, and cooperative behaviors (Confer et al., 2010).

While evolutionary psychologists focus on universal patterns that evolved over millions of years, behavioral geneticists study how individual differences arise, in the present, through the interaction of genes and the environment. When studying human behavior, behavioral geneticists often employ twin and adoption studies to research questions of interest (discussed later in this chapter). Both approaches provide some insight into the relative importance of genes and environment for the expression of a given trait.

LINK TO LEARNING

Watch this [interview with evolutionary psychologist David Buss](#) to learn more about how a psychologist approaches evolution and how this approach fits within the social sciences.

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9.2: FUNDAMENTAL GENETICS AND GENETIC VARIATION

Genetic variation, the genetic difference between individuals, contributes to a species' adaptation to its environment (Spielman et al., 2020). In humans, genetic variation begins with an egg, about 100 million sperm, and fertilization. Roughly once per month, active ovaries release an egg from follicles. During the egg's journey from the ovary through the fallopian tubes to the uterus, a sperm may fertilize the egg.

The egg and the sperm each contain 23 chromosomes. **Chromosomes** are long strings of **deoxyribonucleic acid (DNA)**. DNA is a helix-shaped molecule made up of nucleotide base pairs. In each chromosome, sequences of DNA make up **genes** that control or partially control a number of visible characteristics, known as traits, such as eye color, hair color, and so on. A single gene may have multiple possible variations or **alleles**. So, a given gene may code for the trait of hair color, and the different alleles of that gene affect which hair color an individual has.

When a sperm and egg fuse, each of their 23 chromosomes combine to create a zygote with 46 chromosomes (23 pairs). Therefore, each parent contributes half the genetic information carried by the offspring; the resulting physical characteristics of the offspring (called the phenotype) are determined by the interaction of genetic material supplied by the sperm and egg (called the genotype). A person's **genotype** is the genetic makeup of that individual. **Phenotype**, on the other hand, refers to the individual's inherited physical characteristics, which are a combination of genetic and environmental influences (Figure 3).

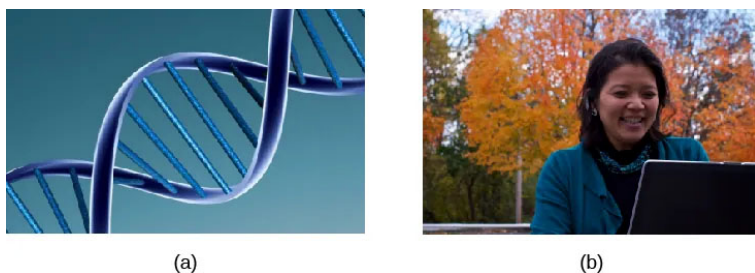
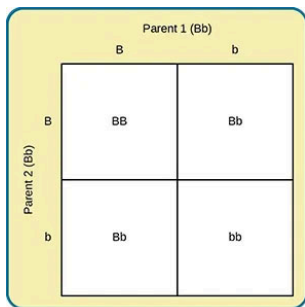


Figure 3. (a) Genotype refers to the genetic makeup of an individual based on the inherited genetic material (DNA). (b) Phenotype describes an individual's observable characteristics, such as hair color, skin color, height, and build. (credit a: modification of work by Caroline Davis; credit b: modification of work by Cory Zanker)

Most traits are controlled by multiple genes, but some, like cleft chin, are influenced by a single gene from each parent. Let's call the gene for cleft chin "B" and for smooth chin "b." Cleft chin is dominant, meaning having the **dominant allele** from one (Bb) or both (BB) parents results in a cleft chin. Individuals with two copies of the same allele are **homozygous**, while those with different alleles are **heterozygous**. Smooth chin is a recessive trait, requiring two **recessive alleles** (bb) to appear.

When a person with a cleft chin mates with someone with a smooth chin, the offspring's chin type depends on the parents' alleles. If the cleft-chinned parent is homozygous (BB), offspring will always have a cleft chin. If the cleft-chinned parent is heterozygous (Bb), the offspring will have a 50% chance of cleft chin (Bb) and 50% chance of smooth chin (bb) because the smooth-chinned parent (bb) will always contribute the recessive allele (bb) (Figure 4).



(a)



(b)

Figure 4. (a) A Punnett square is a tool used to predict how genes will interact in the production of offspring. The capital B represents the dominant allele, and the lowercase b represents the recessive allele. In the example of the cleft chin, where B is the cleft chin (dominant allele), wherever a pair contains the dominant allele, B, you can expect a cleft chin phenotype. You can expect a smooth chin phenotype only when there are two copies of the recessive allele, bb. (b) A cleft chin, shown here, is an inherited trait.

In sickle cell anemia, heterozygous carriers (like Luwi from the example) can develop blood resistance to malaria infection while those who are homozygous (like Sena) have a potentially lethal blood disorder. Sickle-cell anemia is just one of many genetic disorders caused by the pairing of two recessive genes. For example, phenylketonuria (PKU) is a condition in which individuals lack an enzyme that normally converts harmful amino acids into harmless byproducts. If someone with this condition goes untreated, they will experience significant deficits in cognitive function, seizures, and an increased risk of various psychiatric disorders. Because PKU is a recessive trait, each parent must have at least one copy of the recessive allele in order to produce a child with the condition.

So far, we have discussed traits that involve just one gene, but few human characteristics are controlled by a single gene. Most traits are **polygenic**: influenced by more than one gene. Examples of polygenic traits include height, skin color, weight, intelligence, schizophrenia, cancer, heart disease, and diabetes.

Harmful genes, like those causing PKU, often arise from **mutations**—sudden, permanent changes in genes. While many mutations are harmful or lethal, some can be beneficial, giving individuals advantages over others. This genetic variability is crucial for evolution, as it provides variability in traits that allow for adaptability to environmental changes. If a population consisted of identical individuals, then any dramatic environmental changes would affect everyone the same, and there would be no variation in selection. Instead, diversity in genes and associated traits allows some individuals to better survive and reproduce, passing their genes to future generations. This process underlies the theory of evolution, where those best adapted to their environments are more likely to reproduce and transmit their genes.

DIG DEEPER

Human Diversity

This chapter focuses on biology. Other areas of psychology, such as social psychology, study issues of race, prejudice, and discrimination. When we focus strictly on biology, race becomes a weak construct. After the human genome was completely sequenced at the turn of the 21st century, many scientists began to argue that race was not a useful variable in genetic research and that its continued use represents a potential source of confusion and harm. The racial categories that some believed to be helpful in studying genetic diversity in humans are largely irrelevant. A person's skin tone, eye color, and hair texture are functions of their genetic makeup,

but there is actually more genetic variation within a given racial category than there is between racial categories. In some cases, focus on race has led to difficulties with misdiagnoses and/or underdiagnoses of diseases ranging from sickle cell anemia to cystic fibrosis. Some argue that we need to distinguish between ancestry and race and then focus on ancestry. This approach would facilitate a greater understanding of human genetic diversity (Yudell et al., 2016).

Text Attributions

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9.3: THE NATURE-NURTURE QUESTION AND BEHAVIOR GENETICS

Nature-Nurture and Twin Studies

People have a deep intuition about what has been called the “nature–nurture question” (Turkheimer, 2023). Some aspects of our behavior feel as though they originate in our genetic makeup, while others feel like the result of our upbringing or our hard work. The scientific field of behavioral genetics attempts to study these differences empirically, either by examining similarities among family members with different degrees of genetic relatedness or, more recently, by studying differences in the DNA of people with different behavioral traits. The scientific methods that have been developed are ingenious but often inconclusive. Many of the difficulties encountered in the empirical science of behavioral genetics turn out to be conceptual, and our intuitions about nature and nurture get more complicated the harder we think about them. In the end, it is an oversimplification to ask how “genetic” some particular behavior is. Genes and environments always combine to produce behavior, and the real science is in the discovery of how they combine for a given behavior.

It may seem obvious that we are born with certain characteristics while others are acquired, yet in the history of psychology, the “nature–nurture debate” has caused much controversy and offense: We are so concerned with nature–nurture because our very sense of moral character seems to depend on it. While we may admire the athletic skills of a great basketball player, we think of his height as simply a gift, a payoff in the “genetic lottery.” For the same reason, no one blames a short person for his height

or someone's congenital disability on poor decisions. To state the obvious, it's "not their fault." But we do praise the concert violinist (and perhaps her parents and teachers as well) for her dedication, just as we condemn cheaters, slackers, and bullies for their bad behavior.

The problem is that most human characteristics aren't usually as clear-cut as height or instrument mastery, affirming our nature–nurture expectations strongly one way or the other. In fact, even the great violinist might have some inborn qualities—pitch perception talent or long, nimble fingers—that support and reward her hard work. And the basketball player might have eaten a diet while growing up that promoted his genetic tendency to be tall. When we think about our own qualities, they seem under our control in some respects yet beyond our control in others. Often, the traits that don't seem to have an obvious cause are the ones that concern us the most and are far more personally significant. What about how much we drink or worry? What about our honesty, or religiosity, or sexual orientation? They all come from that uncertain zone, neither fixed by nature nor totally under our control.



Figure 5. Researchers have learned a lot about the nature-nurture dynamic by working with animals. But of course, many techniques used to study animals cannot be applied to people. Separating these two influences in human subjects is a greater research challenge.

One major problem with answering nature-nurture questions about people is how to set up an experiment. In nonhuman animals, relatively straightforward experiments can tackle nature–nurture questions. Say, for example, you are interested in aggressiveness in dogs. You want to test for the more important determinant of aggression: being born to aggressive dogs or being raised by them. You could mate two aggressive dogs—angry Chihuahuas—together, and mate two nonaggressive dogs—happy beagles—together, then switch half the puppies from each litter between the different sets of parents to raise. You would then have puppies born to aggressive parents (the Chihuahuas) but raised by nonaggressive parents (the Beagles), and vice versa. The big questions are: Would the Chihuahua parents raise aggressive beagle puppies? Would the beagle parents raise nonaggressive Chihuahua puppies? Would the puppies’ nature win out, regardless of who raised them? Or... would the result be a combination of

nature and nurture? Much of the most significant nature–nurture research has been done in this way (Scott & Fuller, 1998), and animal breeders have been doing it successfully for thousands of years. In fact, it is fairly easy to breed animals for behavioral traits.

With people, however, we can't assign babies to parents at random, or select parents with certain behavioral characteristics to mate, merely in the interest of science (though history does include horrific examples of such practices in misguided attempts at “eugenics,” the shaping of human characteristics through intentional breeding). In typical human families, children's biological parents raise them, so it is difficult to know whether children act like their parents due to genetic (nature) or environmental (nurture) reasons. Nevertheless, despite our restrictions on setting up human-based experiments, we see real-world examples of nature-nurture at work in the human sphere—though they only provide partial answers to our many questions.

The science of how genes and environments work together to influence behavior is called **behavioral genetics**. The easiest opportunity we have to observe this is the **adoption study**. When children are put up for adoption, the parents who give birth to them are no longer the parents who raise them. This setup isn't quite the same as the experiments with dogs (children aren't assigned to random adoptive parents to suit the particular interests of a scientist), but adoption still tells us some interesting things. For instance, if the biological child of tall parents were adopted into a family of short people, do you suppose the child's growth would be affected? What about the biological child of a Spanish-speaking family adopted at birth into an English-speaking family? What language would you expect the child to speak? And what might these outcomes tell you about the difference between height and language in terms of nature-nurture?



Figure 6. Studies focused on twins have led to important insights about the biological origins of many personality characteristics.

Another option for observing nature-nurture in humans involves **twin studies**. There are two types of twins: monozygotic (MZ) and dizygotic (DZ). Monozygotic twins, also called “identical” twins, result from a single zygote (fertilized egg) and have the same DNA. They are essentially clones. Dizygotic twins, also known as “fraternal” twins, develop from two zygotes and share 50% of their DNA. Fraternal twins are ordinary siblings who

happen to have been born at the same time. To analyze nature–nurture using twins, we compare the similarity of MZ and DZ pairs. Sticking with the features of height and spoken language, let’s look at how nature and nurture apply: Identical twins, unsurprisingly, are almost perfectly similar in height. The heights of fraternal twins, however, are like any other sibling pairs: more similar to each other than to people from other families, but hardly identical. This contrast between twin types gives us a clue about the role genetics plays in determining height. Now consider spoken language. If one identical twin speaks Spanish at home, the co-twin with whom she is raised almost certainly does too. But the same would be true for a pair of fraternal twins raised together. In terms of spoken language, fraternal twins are just as similar as identical twins, so it appears that the genetic match of identical twins doesn’t make much difference.

Twin and adoption studies are two instances of a much broader class of methods for observing nature–nurture called **quantitative genetics**, the scientific discipline in which similarities among individuals are analyzed based on how biologically related they are. We can do these studies with siblings and half-siblings, cousins, and twins who have been separated at birth and raised separately (Bouchard et al., 1990; such twins are very rare and play a small role in the science of nature–nurture), or with entire extended families (see Plomin et al., 2012, for a complete introduction to research methods relevant to nature–nurture).

For better or for worse, contentions about nature–nurture have intensified because quantitative genetics produces a number called a **heritability coefficient**, varying from 0 to 1, that is meant to provide a single measure of genetics’ influence on a trait. In a general way, a heritability coefficient measures how strongly differences among individuals are related to differences in their genes. But beware. Heritability coefficients, although simple to compute, are deceptively difficult to interpret. Nevertheless, numbers that provide simple answers to complicated questions tend to have a strong influence on the human imagination, and a great deal of time has been spent discussing whether

the heritability of intelligence or personality or depression is equal to one number or another.

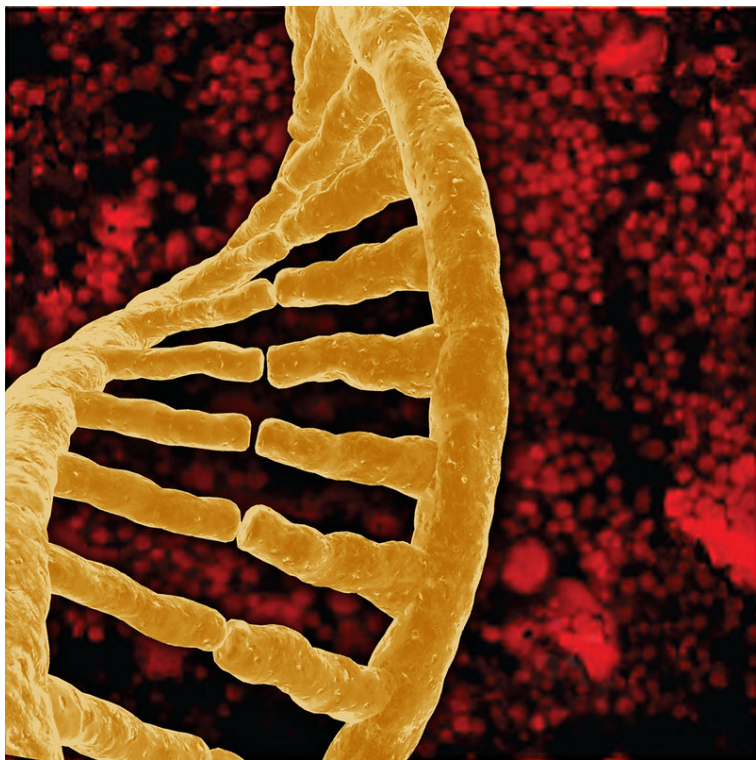


Figure 7. Quantitative genetics uses statistical methods to study the effects that both heredity and environment have on test subjects. These methods have provided us with the heritability coefficient which measures how strongly differences among individuals for a trait are related to differences among their genes.

One reason nature–nurture continues to fascinate us is that we live in an era of great scientific discovery in genetics. DNA was discovered by Watson and Crick in the 1950s; the human genome—about 3 billion base pairs long—was completely sequenced at the turn of the 21st century, and we are now on the verge of being able to obtain the specific DNA

sequence of anyone at a relatively low cost (the cost of sequencing a human genome has fallen from around \$10 million in 2007 to below \$500 today; Collins, 2024; National Human Genome Research Institute, 2021). Every day, it seems, new discoveries are made, and new possibilities are proposed. No one knows what this new genetic knowledge will mean for the study of nature–nurture, but as we will see in the next section, answers to nature–nurture questions have turned out to be far more difficult and mysterious than anyone imagined.

What Have We Learned About Nature–Nurture?

It would be satisfying to be able to say that nature–nurture studies have given us conclusive and complete evidence about where traits come from, with some traits clearly resulting from genetics and others almost entirely from environmental factors such as childrearing practices and personal will, but that is not the case. Instead, everything has turned out to have some footing in genetics. The more genetically related people are, the more similar they are—for everything: height, weight, intelligence, personality, mental illness, etc. Sure, it seems like common sense that some traits have a genetic bias. For example, adopted children resemble their biological parents even if they have never met them, and identical twins are more similar to each other than are fraternal twins. However, while certain psychological traits, such as personality or mental illness (e.g., schizophrenia), seem reasonably influenced by genetics, it turns out that the same is true for political attitudes, how much television people watch (Plomin et al., 1990), and whether or not they get divorced (McGue & Lykken, 1992). The message is clear: You can't leave genes out of the equation. But keep in mind, no behavioral traits are completely inherited, so you can't leave the environment out altogether, either.



Figure 8. Research over the last half-century has revealed how central genetics are to behavior. The more genetically related people are, the more similar they are, not just physically but also in terms of personality and behavior.

Trying to untangle nature-nurture influences on human behavior can be messy, and common-sense notions can get in the way of good science. Behavioral genetics has taught us a crucial lesson: with biologically related subjects, we can't assume behavior stems solely from nurture, even when environmental influence seems clear. For example, data showing better reading scores in children whose mothers read to them frequently might suggest that parental reading is key to academic success. But the study as described is inconclusive because both genetic and environmental factors could affect the parenting practices and the abilities of their children.

An issue with the heritability coefficient is that it divides traits' determinants into two portions—genes and environment—which are then calculated together for the total variability. This is a little like asking how much of the experience of a symphony comes from the horns and how much from the strings; the ways instruments or genes integrate is more complex than that.

The heritability coefficient does not capture the complexity of the nature-nurture relationship. Genetics affect traits under some environmental circumstances but not others—a phenomenon called gene-environment interaction, or $G \times E$. In one well-known example, Caspi et al. (2002) found that among maltreated children, those who carried a particular allele of the MAOA gene showed a predisposition to violence and antisocial behavior, while those with other alleles did not. However, in children who had not been maltreated, the gene had no effect. In another example of gene-environment interaction, adoptees whose biological mothers had schizophrenia and who had been raised in a disturbed family environment were much more likely to develop schizophrenia than were any of the other groups in the study (Tienari et al., 2004):

- Of adoptees whose biological mothers had schizophrenia (high genetic risk) and who were raised in disturbed family environments, 36.8% were likely to develop schizophrenia.
- Of adoptees whose biological mothers had schizophrenia (high genetic risk) and who were raised in healthy family environments, 5.8% were likely to develop schizophrenia.
- Of adoptees with a low genetic risk (whose mothers did not have schizophrenia) and who were raised in disturbed family environments, 5.3% were likely to develop schizophrenia.
- Of adoptees with a low genetic risk (whose mothers did not have schizophrenia) and who were raised in healthy family environments, 4.8% were likely to develop schizophrenia.

The study shows that adoptees with high genetic risk were most likely to

develop schizophrenia if they were raised in disturbed home environments. This research suggests genetic vulnerability and environmental stress both contribute to developing schizophrenia and that genes (or environment) alone do not tell the full tale (Spielman et al., 2020). Making matters even more complicated are recent studies of what is known as epigenetics (covered in the next section), a process in which genes can be turned “on” or “off” in response to environmental events, and those epigenetic changes transmitted to children.



Figure 9. The answer to the nature–nurture question has not turned out to be as straightforward as we would like. The many questions we can ask about the relationships among genes, environments, and human traits may have many different answers, and the answer to one tells us little about the answers to the others.

Nature–nurture questions often focus on trait malleability and whether we “have a choice” about it. These are complex issues, as illustrated by phenylketonuria—a genetic disorder caused by a single gene that could

result in intellectual disability and death, but is manageable through diet, and height—firmly rooted genetics, but affected by environmental factors as shown by the height increases in some Asian and European populations over the last 100 years due to changes in diet and reduced poverty.

With the Human Genome Project and DNA sequencing, it was believed that we would easily be able to link specific genes with specific behaviors. That has not happened. A few rare genes have been found to have significant effects, such as the single genes that cause Huntington's disease or early-onset dementia in some Alzheimer's cases. Most genetic influences on behavior are distributed across many genes, each with tiny effects, making them difficult to catalog. Similarly, environmental effects are typically hard to pinpoint. Extreme environmental hardship is catastrophic for behavioral outcomes, but fortunately, such extreme cases are very rare. Within the normal range of environments, events responsible for differences (e.g., why some children in a suburban third-grade classroom perform better than others) are much more difficult to pinpoint.

Nature-nurture problems resist simple solutions. With nature-nurture, what seems straightforward and possible to index with a single number becomes more complicated the closer we look. Questions about gene-environment interactions in human traits (e.g., sensitivity to environmental change, parental versus cultural influence, genetic variability in a population, whether traits involve single or multiple genes, etc.) may have different answers, with limited implications for the others. We should continue studying nature-nurture relationships without oversimplifying their complexity.

Text Attributions

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9.4: EPIGENETICS

What Is the Epigenome, and What Does It Do?

Your genes play an important role in your health, but so do your environment and behaviors, such as exercise and diet (NHGRI, 2020). Epigenetics is the study of how your behaviors and environment can cause changes that affect the way your genes work. Epigenetic changes do not change your DNA sequence, but they can change how your body reads a DNA sequence. Since your environment and behaviors can result in epigenetic changes, it is easy to see the connection between your behaviors and environment, your genes, and your physical and mental health.

The **epigenome** is a multitude of chemical compounds that can tell the genome what to do. As discussed above, the genome is the DNA that holds instructions for building the proteins that carry out a variety of functions in a cell. The epigenome consists of chemical compounds and proteins that can attach to DNA and direct such actions as turning genes “on” or “off”. The epigenome can control **gene expression** or the production of proteins in particular cells. When epigenomic compounds attach to DNA and modify its function, they are said to have “marked” the genome. These marks do not change the sequence of the DNA; rather, they change the way cells use the DNA’s instructions.

A human being has trillions of cells, specialized for different functions in muscles, bones, and the brain, and each of these cells carries essentially the same genome in its nucleus. The differences among cells are determined by how and when different sets of genes are turned on or off in various kinds of cells. Specialized cells in the eye turn on genes that make proteins that can detect light, while specialized cells in red blood cells make proteins that

carry oxygen from the air to the rest of the body. The epigenome controls many of these changes to the genome. The modifications occur as a natural process of development and tissue differentiation, can be heritable, and can be altered in response to environmental exposures or disease¹.

How Does Epigenetics Work?

Epigenetic changes affect gene expression in different ways. Two of the most well-studied types of epigenetic changes are **DNA methylation** and **histone modification** (Figure 10).

DNA Methylation. DNA methylation works by adding a chemical group to DNA. Typically, this group is added to specific places on the DNA, where it blocks the proteins that attach to DNA to “read” the gene. This turns genes “off.” The chemical group can be removed through a process called demethylation, which turns genes “on.”

Histone modification. DNA wraps around proteins called histones, which form spool-like structures that enable DNA’s very long molecules to be wound up neatly into chromosomes inside the cell nucleus. When histones are tightly packed together, the DNA is tightly coiled and bunched together, so proteins that ‘read’ the gene cannot access the DNA, and the gene is turned “off.” When histones are loosely packed, more DNA is exposed or not wrapped around a histone and can be accessed by proteins that ‘read’ the gene, so the gene is turned “on.” Chemical groups can be

1. This section contains material adapted from: Epigenomics Fact Sheet from the National Institutes of Health’s (NIH) National Human Genome Research Institute. <https://www.genome.gov/about-genomics/fact-sheets/Epigenomics-Fact-Sheet> Public Domain

added to or removed from histones to make the histones more tightly or loosely packed, turning genes “off” or “on.”²

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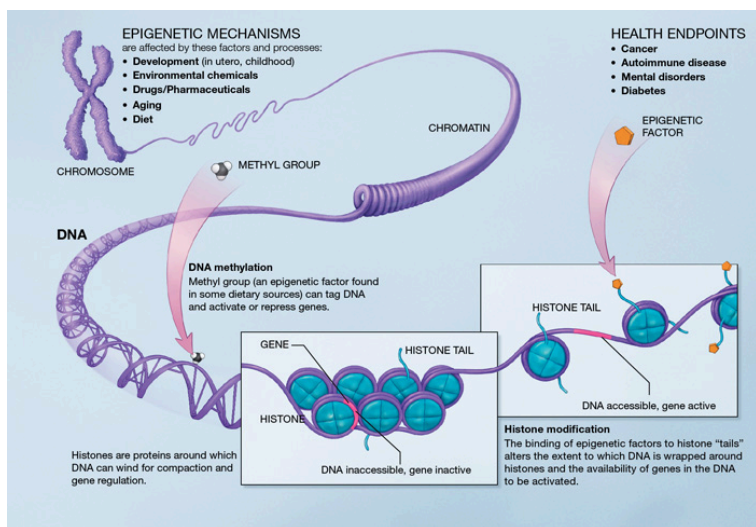


Figure 10. A Scientific Illustration of How Epigenetic Mechanisms Can Affect Health. Epigenetic mechanisms are affected by several factors and processes, including development in utero and in childhood, environmental chemicals, drugs and pharmaceuticals, aging, and diet. DNA methylation occurs when methyl groups, an epigenetic factor found in some dietary sources, tag DNA to activate or repress genes. Histones are proteins around which DNA can wind for compaction and gene regulation. Histone modification occurs when epigenetic factors bind to histone "tails" altering how DNA wraps around histones and the availability of genes in the DNA to be activated. These processes can influence people's health, possibly resulting in cancer, autoimmune disease, mental disorders, diabetes, or other illnesses.

Can the Epigenome Change?

Although all cells in the body contain essentially the same genome, the DNA marked by chemical tags on the DNA and histones gets rearranged when cells become specialized. The epigenome can also change throughout a person's lifetime. Lifestyle and environmental factors (such as smoking, diet, and infectious disease) can expose a person to pressures that prompt

chemical responses. These responses, in turn, often lead to changes in the epigenome, some of which can be damaging. However, the ability of the epigenome to adjust to the pressures of life appears to be required for normal human health. Your epigenetics change as you age, both as part of normal development and aging and in response to your behaviors and environment (CDC, 2022).



Figure 11. “Identical” twins are the perfect example of epigenetics. Although they share exactly the same DNA, their unique experiences in life will cause some genes (and not others) to express themselves. This is why, over time, identical twins come to look and behave differently.

Epigenetics and Development. Epigenetic changes begin before you are born. All your cells have the same genes but look and act differently. As you grow and develop, epigenetics helps determine which function a cell will have, for example, whether it will become a heart cell, skin cell, or nerve cell. Epigenetics allows nerve cells to turn “on” genes that produce proteins

important for its job, while turning “off” genes important for other cell types, such as a heart cells.

Epigenetics and Reversibility. Not all epigenetic changes are permanent. Some epigenetic changes can be added or removed in response to changes in behavior or environment.

EXAMPLE: SMOKERS VS. NON-SMOKERS VS. FORMER SMOKERS. Smoking can result in epigenetic changes. For example, at certain parts of the AHRR gene (related to tumors, Zudaire et al. 2008), smokers tend to have less DNA methylation than non-smokers. The difference is greater for heavy smokers and long-term smokers. After quitting smoking, former smokers can begin to have increased DNA methylation at this gene. Eventually, they can reach levels similar to those of non-smokers. In some cases, this can happen in under a year, but the length of time depends on how long and how much someone smoked before quitting (McCartney et al. 2018)³.

Epigenetics and Physical Health

Epigenetic changes can affect your health in different ways (CDC, 2022).

Infections. Germs can change your epigenetics to weaken your immune system. This helps the germ survive.

EXAMPLE: MYCOBACTERIUM TUBERCULOSIS. Mycobacterium tuberculosis causes tuberculosis. Infections with these germs can cause changes to histones in some of your immune cells that result in turning “off” the IL-12B gene. Turning “off” the IL-12B gene

3. This section contains material adapted from: Centers for Disease Control and Prevention (CDC) (2022) What is Epigenetics? <https://www.cdc.gov/genomics/disease/epigenetics.htm>
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weakens your immune system and improves the survival of *Mycobacterium tuberculosis* (Chandran et al., 2015).

Cancer. Certain genetic mutations make you more likely to develop cancer. Likewise, some epigenetic changes increase your cancer risk. For example, having a mutation in the BRCA1 gene that prevents it from working properly makes you more likely to get breast and other cancers. Similarly, increased DNA methylation that results in decreased BRCA1 gene expression raises your risk for breast and other cancers (Tang et al. 2016).

Nutrition During Pregnancy and Beyond. A pregnant woman's environment and behavior during pregnancy, such as whether she eats healthy food, can change the baby's epigenetics. Some of these changes can remain for decades and might make the child more likely to get certain diseases.

EXAMPLE: DUTCH HUNGER WINTER FAMINE (1944-1945). People whose mothers were pregnant with them during the famine were more likely to develop certain diseases such as heart disease, type 2 diabetes, and schizophrenia (Rosenboom, 2019). Around 60 years after the famine, researchers looked at methylation levels in people whose mothers were pregnant with them during the famine. These people had increased methylation at some genes and decreased methylation at other genes compared with their siblings who were not exposed to famine before their birth (Heijmans et al. 2008). These differences in methylation could help explain why prenatal exposure to famine can be associated with an increased likelihood of certain diseases and structural brain abnormalities later in life (Hulshoff et al., 2000; Pidsley et al., 2012; Rosenboom, 2019).



Figure 12. Whether or not your parents knew the science behind it, telling you to eat your veggies as a kid really does make you healthier and stronger—at least your DNA, that is.

The old adage “you are what you eat” might be true on more than just a physical level. The food you choose (and even what your parents and grandparents chose) is reflected in your personal development and risk for disease in adulthood (Wells, 2003). Nutrients can reverse or change DNA methylation and histone modifications, thereby modifying the expression of critical genes associated with physiological and pathological processes, including embryonic development, aging, and cancer formation. Nutrients can influence the epigenome via DNA methylation or histone modifications. Data suggest that early-life nutrition has the potential to influence epigenetic programming in the brain not only during early development but also in adult life. In this regard, nutritional epigenetics

has been viewed as an attractive tool to prevent pediatric developmental diseases and cancer, as well as to delay aging-associated processes⁴.

Epigenetics in Psychology

Mental health and cognition can be affected by environmental factors during childhood and adolescence via changes in gene expression. Thus, examining genetic–epigenetic–environment interactions may help determine the nature of gene misregulation in psychological disorders (Weaver, 2023).

Early childhood experience, parental investment, and programming of stress responses in the offspring

Early childhood experiences and parenting impact an individual's development. For example, the degree of positive attachment in the parent–infant bond and parental investment (including the nutrients provided by the parent) also program the development of the stress responses in the brain via epigenetic markers, which then affect the organization and function of neural circuits and molecular pathways involved in memory, attention, and emotion.

The most comprehensive study of parental investment and epigenetic inheritance is on the maternally transmitted responses to stress in rats. In

4. This section contains material adapted from: Centers for Disease Control and Prevention (CDC) (2022) What is Epigenetics? <https://www.cdc.gov/genomics/disease/epigenetics.htm>
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rat pups, maternal nurturing (licking and grooming) during the first week of life is associated with long-term programming of stress responsiveness, emotionality, cognitive performance, and reproductive behavior (Caldji et al., 1998; Liu et al., 1997). In adulthood, the offspring that received more maternal licking and grooming during the first week of life showed increased expression of the glucocorticoid receptor in the hippocampus (a brain structure associated with stress responsivity, learning, and memory) and a lower hormonal response to stress (Francis et al., 1999; Liu et al., 1997). Moreover, rat pups that received little maternal licking and grooming showed decreased histone acetylation and increased DNA methylation of the glucocorticoid receptor gene (Weaver et al., 2004). This led to reduced expression of this gene, fewer glucocorticoid receptors in the brain, and higher hormonal response to stress throughout their life. The effects of maternal care on an offspring's stress-hormone responses and behavior can be eliminated with pharmacological treatments targeting histone modification and DNA methylation (Weaver et al., 2004; Weaver et al., 2005). This research shows that histone modification and DNA methylation of the glucocorticoid-receptor gene leads to the long-term physiological and behavioral outcomes of poor maternal care, and suggests a possible molecular target for treating the effects of childhood maltreatment in humans.



Figure 13. Parental care during one's childhood has important and consequential effects on the development of an individual, effects that persist even into adulthood.

Several studies have attempted to determine to what extent the findings from model animals are transferable to humans. A study examining newborn humans showed that methylation of the glucocorticoid receptor gene promoter may be an early epigenetic marker of maternal mood and risk of increased hormonal responses to stress in infants (Oberlander et al., 2008). These findings are consistent with epigenetics, glucocorticoid gene expression, and hormonal responses in rat offspring of low-grooming mothers discussed above. Examination of brain tissue from suicide victims found that the human glucocorticoid receptor gene promoter is also more methylated in the brains of individuals who had experienced maltreatment during childhood (McGowan et al., 2009). These findings suggest that DNA methylation mediates the effects of early environment in both rodents and humans and points to the possibility of new therapeutic approaches stemming from translational epigenetic research.

Epigenetic regulation of learning and memory

Epigenetic mechanisms influence genomic activities in the brain to produce long-term changes in synaptic signaling, organization, and structure, which in turn support learning and memory (Day & Sweatt, 2011).

Neuronal activity in the hippocampus of mice is associated with changes in DNA methylation (Guo et al., 2011), and disruption to DNA methylation machinery causes learning and memory impairments (Feng et al., 2010). Pharmacological inhibition of DNA methylation can impair memory (Day & Sweatt, 2011). These findings highlight the role of DNA methylation in mediating synaptic plasticity and cognitive functions, both of which are often impaired in psychological disorders.

Changes in histone modifications can also influence long-term memory formation by altering the expression of genes relevant to learning and memory (Guan et al., 2002; Schaefer et al., 2009).

In humans, genetic defects in genes encoding the DNA methylation and histone modification machinery exhibit profound effects on cognitive function and mental health (Jiang et al., 2004). The two best-characterized examples are Rett syndrome (Amir et al., 1999) and Rubinstein-Taybi syndrome (Alarcon et al., 2004), which are profound intellectual disability disorders.

Together, these studies demonstrate that misregulation of epigenetic modifications and their regulatory enzymes can cause prominent deficits in neuronal plasticity and cognitive function. Knowledge from these studies may provide greater insight into other mental disorders such as depression and suicidal behaviors.

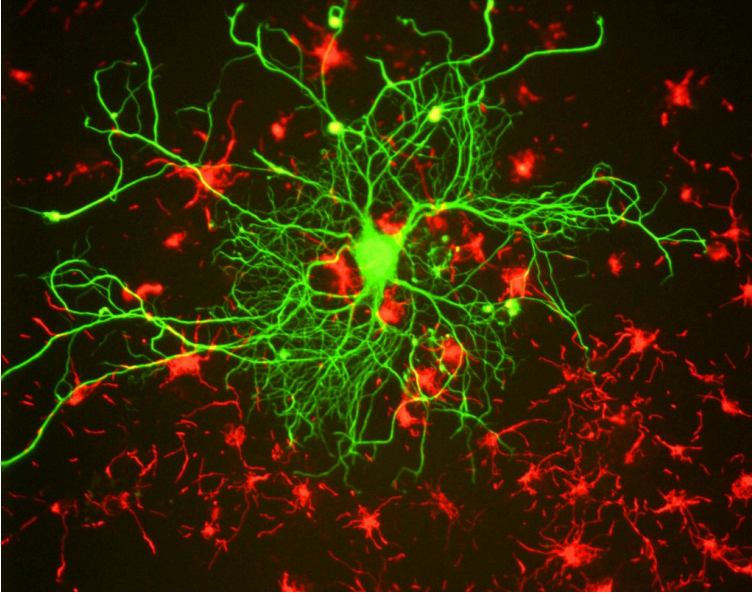


Figure 14. Neural plasticity is the change of neural pathways and synapses which allows for our ability to learn new things and remember them.

Epigenetic mechanisms in psychological disorders

Epigenome-wide studies have identified several dozen sites with DNA-methylation alterations in genes involved in brain development and neurotransmitter pathways that were associated with mental illness (Mill et al., 2008). These disorders are complex and typically start at a young age and cause lifelong disability. Often, limited benefits from treatment make these diseases some of the most burdensome disorders for individuals, families, and society. Efforts to identify the primary causes of complex psychiatric disorders may benefit from studying links between the environment and changes within the individual cells.

Epigenetic events that regulate gene expression have been associated with

depression-related behavior and action of antidepressant medications; increasing evidence is emerging for similar mechanisms in post-mortem brains of depressed individuals. In mice, social avoidance resulted in decreased expression of hippocampal genes important in mediating depressive responses (Tsankova et al., 2006). Consistent with these findings, levels of histone markers were downregulated in human post-mortem brain samples from individuals with a history of clinical depression (Covington et al., 2009).

Administration of antidepressants increased histone markers of increased gene expression and reversed the gene repression induced by defeat stress (Lee et al., 2006). These results provide support for the use of histone deacetylase inhibitors against depression, and they have been found to exert antidepressant effects by modifying distinct cellular targets (Cassel et al., 2006).

Aberrant gene expression resulting from altered epigenetic regulation is also associated with the pathophysiology of suicide (McGowan et al., 2008; Poulter et al., 2008). Thus, it is tempting to speculate that there is an epigenetically determined reduced capacity for gene expression, which is required for learning and memory, in the brains of suicide victims.

Finally, environmental factors such as air and water pollution interact with the genome. For example, living close to a freeway while in utero is associated with higher rates of autism in childhood, and the negative effects of pollution are likely mediated by epigenetic effects (Tordjman et al., 2014). With such clear links between environment, genes, and epigenetics, effective public policy that regulates environmental factors and mitigates pollution is crucial for protecting public health and reducing the prevalence of mental and physical disorders⁵.

5. This section contains material adapted from: Weaver, I. (2023). Epigenetics in psychology. In R. Biswas-Diener & E. Diener (Eds.), *Noba textbook series: Psychology*. Champaign, IL: DEF publishers. Retrieved from <http://noba.to/37p5cb8v> License: CC BY-NC-SA 4.0

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CHAPTER 10: EMOTION AND AFFECTIVE NEUROSCIENCE

By Eddie Harmon-Jones and Cindy Harmon-Jones

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Harmon-Jones, E. & Harmon-Jones, C. (2023). Affective neuroscience. In R. Biswas-Diener & E. Diener (Eds), Noba textbook series: Psychology. Champaign, IL: DEF publishers. Retrieved from <http://noba.to/qnv3erb9> License: CC BY-NC-SA 4.0 DEED

This chapter provides a brief overview of the neuroscience of emotion. It integrates findings from human and animal research and describes the brain networks and associated neurotransmitters involved in basic affective systems.

Learning Objectives

- Define affective neuroscience.
- Describe neuroscience techniques used to study emotions in humans and animals.
- Name five emotional systems and their associated neural structures and neurotransmitters.
- Give examples of exogenous chemicals (e.g., drugs) that influence affective systems and discuss their effects.
- Discuss multiple affective functions of the amygdala and the nucleus accumbens.
- Name several specific human emotions and discuss their relationship to the affective systems of nonhuman animals.

10.1: AFFECTIVE NEUROSCIENCE: WHAT IS IT?

Affect, in psychology, refers to the experience of emotions, moods, and feelings, so **affective neuroscience** examines how the brain creates emotional responses. Emotions are psychological phenomena that involve changes to the body (e.g., facial expression), changes in autonomic nervous system activity, feeling states (subjective responses), and urges to act in specific ways (motivations; Izard, 2010). Affective neuroscience aims to understand how matter (brain structures and chemicals) creates one of the most fascinating aspects of the mind—emotions. Affective neuroscience uses unbiased, observable measures that provide credible evidence to other scientists and laypersons on the importance of emotions. It also leads to biologically based treatments for affective disorders, such as depression and bipolar disorder.



Figure 1. Although we experience emotions all the time, they are very difficult to describe and study. Fortunately, technological advances and the tools of neuroscience are making this easier.

The human brain and its emotional processes are complex and flexible. In order to study emotions in humans, human neuroscience must rely primarily on noninvasive techniques such as electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) and on studies of individuals with brain lesions caused by accident or disease. Invasive neuroscience techniques, such as electrode implantation, lesioning, and hormone administration, are more powerful experimental tools but can only readily be used in nonhuman animals. While nonhuman animals possess simpler nervous systems and arguably more basic emotional responses than humans, affective circuits found in other species, particularly social mammals such as rats, dogs, and monkeys, function similarly to human affective networks. Thus, animal research serves as a valuable model for understanding affective processes in humans.

In humans, emotions and their associated neural systems have additional layers of complexity and flexibility. Compared to animals, humans experience a vast variety of nuanced and sometimes conflicting emotions. Humans also respond to these emotions in complex ways, such that conscious goals, values, and other cognitions influence behavior in addition to emotional responses. However, in this chapter, we focus on the similarities between organisms rather than the differences. We often use the term “organism” to refer to the individual who is experiencing an emotion or showing evidence of particular neural activations. An organism could be a rat, a monkey, or a human.

Across species, emotional responses are organized around the organism’s survival and reproductive needs. Emotions influence perception, cognition, and behavior to help organisms survive and thrive (Farb et al., 2013). Networks of structures in the brain respond to different needs, with some overlap between different emotions. Specific emotions are not located in a single structure of the brain. Instead, emotional responses involve networks of activation, with many parts of the brain activated during any emotional process. In fact, the brain circuits involved in emotional reactions include nearly the entire brain (Berridge & Kringelbach, 2013). Brain circuits located deep within the brain below the cerebral cortex are primarily

responsible for generating basic emotions (Berridge & Kringelbach, 2013; Panksepp & Biven, 2012). In the past, research attention was focused on specific brain structures that will be reviewed here, but future research may find that additional areas of the brain are also important in these processes.

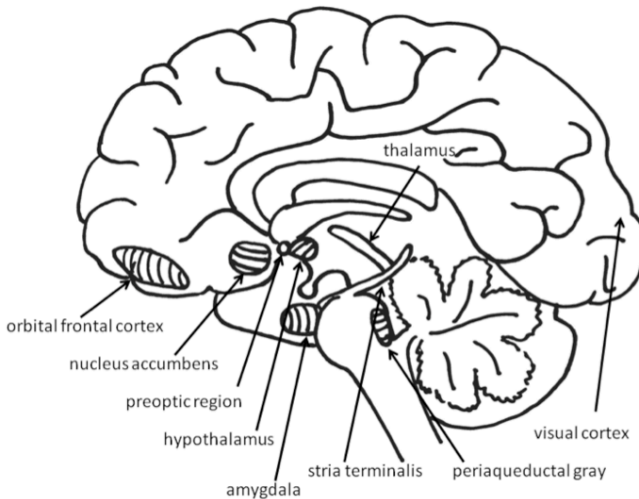


Figure 2: Some of the many structures involved in emotion processing in the brain.

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10.2: BASIC EMOTIONS

Desire: The neural systems of reward-seeking

One of the most important affective neuronal systems relates to feelings of desire or the appetite for rewards. Researchers refer to these appetitive processes using terms such as “wanting” (Berridge & Kringelbach, 2008), “seeking” (Panksepp & Biven, 2012), or “behavioral activation sensitivity” (Gray, 1987). When the appetitive system is aroused, the organism shows enthusiasm, interest, and curiosity. These neural circuits motivate the animal to move through its environment in search of rewards such as appetizing foods, attractive sex partners, and other pleasurable stimuli. When the appetitive system is underaroused, the organism appears depressed and helpless.

Much evidence for the structures involved in this system comes from animal research using direct brain stimulation. When an electrode is implanted in the lateral hypothalamus or in cortical or mesencephalic regions to which the **hypothalamus** is connected, animals will press a lever to deliver electrical stimulation, suggesting that they find the stimulation pleasurable. Other regions in the desire system also include the amygdala, nucleus accumbens, and **frontal cortex** (Panksepp & Biven, 2012). The neurotransmitter dopamine, produced in the mesolimbic and mesocortical dopamine circuits, activates these regions. It creates a sense of excitement, meaningfulness, and anticipation. These structures are also sensitive to drugs such as cocaine and amphetamines, chemicals that have similar effects to dopamine (Panksepp & Biven, 2012).



Figure 3. Just looking at an image of appealing food should increase the activity in your left frontal cortex. Yum!

Research in both humans and nonhuman animals shows that the left frontal cortex (compared to the right frontal cortex) is more active during appetitive emotions such as desire and interest. Early researchers noted that persons who suffered damage to the left frontal cortex developed depression, whereas those with damage to the right frontal cortex developed mania (Goldstein, 1939). The relationship between left frontal activation and approach-related emotions has been confirmed in healthy individuals using EEG and fMRI (Berkman & Lieberman, 2010). For example, increased left frontal activation occurs in 2- to 3-day-old infants when sucrose is placed on their tongues (Fox & Davidson, 1986), and in

hungry adults as they view pictures of desirable desserts (Gable & Harmon-Jones, 2008). In addition, greater left frontal activity in appetitive situations has been found to relate to dopamine (Wacker et al., 2013).

“Liking”: The neural circuits of pleasure and enjoyment

Surprisingly, the amount of desire an individual feels toward a reward need not correspond to how much they like that reward. The neural structures responsible for enjoying rewards differ from those involved in desiring rewards. “Liking” (e.g., enjoyment of a sweet liquid) can be measured in babies and nonhuman animals by measuring licking speed, tongue protrusions, and happy facial expressions, whereas “wanting” (desire) is shown by the willingness to work hard to obtain a reward (Berridge & Kringelbach, 2008). Liking has been distinguished from wanting in research on topics such as drug abuse. For example, drug addicts often desire drugs even when they know that the ones available will not provide pleasure (Stewart et al., 1984).

Research on liking has focused on a small area within the **nucleus accumbens** and on the posterior half of the ventral pallidum. These brain regions are sensitive to opioids and endocannabinoids. Stimulation of other regions of the reward system increases wanting but does not increase liking and, in some cases, even decreases liking. The research on the distinction between desire and enjoyment contributes to the understanding of human addiction, particularly why individuals often continue to frantically pursue rewards such as cocaine, opiates, gambling, or sex, even when they no longer experience pleasure from obtaining these rewards due to habituation.

The experience of pleasure also involves the **orbitofrontal cortex**. Neurons in this region fire when monkeys taste or merely see pictures of desirable foods. In humans, this region is activated by pleasant stimuli,

including money, pleasant smells, and attractive faces (Gottfried et al., 2002; O'Doherty et al., 2001; 2002; 2003).

Fear: The neural system of freezing and fleeing



Figure 4. Because fear is so important for our survival (i.e., fear informs us when something threatens us), our brains are able to “recognize” frightening stimuli before we are even consciously aware of them.

Fear is an unpleasant emotion that motivates avoidance of potentially harmful situations. Slight stimulation of fear-related brain areas causes

animals to freeze, whereas intense stimulation causes them to flee. The fear circuit extends from the central amygdala to the **periaqueductal gray** in the midbrain. These structures are sensitive to glutamate, corticotrophin-releasing factor, adreno-cortico-trophic hormone, and several different neuropeptides. Benzodiazepines and other tranquilizers inhibit activation in these areas (Panksepp & Biven, 2012).

The role of the amygdala in fear responses has been extensively studied. Perhaps because fear is so important to survival, two pathways send signals to the **amygdala** from the sensory organs. When an individual sees a snake, for example, the sensory information travels from the eye to the **thalamus** and then to the **visual cortex**. The visual cortex sends the information on to the amygdala, provoking a fear response. However, the thalamus also quickly sends the information straight to the amygdala so that the organism can react before consciously perceiving the snake (LeDoux et al., 1990). The pathway from the thalamus to the amygdala is fast but less accurate than the slower pathway from the visual cortex. Damage to the amygdala or areas of the ventral hippocampus interferes with fear conditioning in both humans and nonhuman animals (LeDoux, 1996).

Rage: The circuits of anger and attack

Anger or rage is an arousing, unpleasant emotion that motivates organisms to approach and attack (Harmon-Jones et al., 2013). Anger can be evoked through goal frustration, physical pain, or physical restraint. In territorial animals, anger is provoked by a stranger entering the organism's home territory (Blanchard & Blanchard, 2003). The neural networks for anger and fear are near one another but separate (Panksepp & Biven, 2012). They extend from the medial amygdala, through specific parts of the hypothalamus, and into the periaqueductal gray of the midbrain. The anger circuits are linked to the appetitive circuits, such that lack of an anticipated reward can provoke rage. In addition, when humans are

angered, they show increased left frontal cortical activation, supporting the idea that anger is an approach-related emotion (Harmon-Jones et al., 2013). The neurotransmitters involved in rage are not yet well understood, but the neurotransmitter and neuromodulator Substance P (also involved in pain and stress) may play an important role (Panksepp & Biven, 2012). Other neurochemicals that may be involved in anger include testosterone (Peterson & Harmon-Jones, 2012) and arginine-vasopressin (Heinrichs et al., 2009). Several chemicals inhibit the rage system, including opioids and high doses of antipsychotics, such as chlorpromazine (Panksepp & Biven, 2012).

Love: The neural systems of care and attachment



Figure 5. Just as scientists today distinguish between types of love like “romantic” and “parental,” so did the ancient Greeks, who used the terms “eros” and “storge.”

For social animals such as humans, attachment to other members of the same species produces the positive emotions of attachment: love, warm feelings, and affection. The emotions that motivate nurturing behavior (e.g., maternal care) are distinguishable from those that motivate staying close to an attachment figure in order to receive care and protection (e.g., infant attachment). Important regions for maternal nurturing include the

dorsal **preoptic area** (Numan & Insel, 2003) and the bed nucleus of the **stria terminalis** (Panksepp, 1998). These regions overlap with the areas involved in sexual desire and are sensitive to some of the same neurotransmitters, including oxytocin, arginine-vasopressin, and **endogenous** opioids (endorphins and enkephalins).

Grief: The neural networks of loneliness and panic

The neural networks involved in infant attachment are also sensitive to separation. These regions produce the painful emotions of grief, panic, and loneliness. When infant humans or other infant mammals are separated from their mothers, they produce distress vocalizations or crying. The attachment circuits are those that cause organisms to produce distress vocalizations when electrically stimulated.

The attachment system begins in the midbrain periaqueductal gray, very close to the area that produces physical pain responses, suggesting that it may have originated from the pain circuits (Panksepp, 1998). Separation distress can also be evoked by stimulating the dorsomedial thalamus, ventral septum, dorsal preoptic region, and areas in the bed nucleus of stria terminalis (near sexual and maternal circuits; Panksepp et al., 1988).

These regions are sensitive to endogenous opiates, oxytocin, and prolactin. All of these neurotransmitters prevent separation distress. Opiate drugs such as morphine and heroin, as well as nicotine, artificially produce feelings of pleasure and gratification similar to those normally produced during positive social interactions. This may explain why these drugs are addictive. Panic attacks appear to be an intense form of separation distress triggered by the attachment system, and panic can be relieved by opiates. Testosterone also reduces separation distress, perhaps by reducing attachment needs. Consistent with this, panic attacks are more common in women than in men.

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10.3: PLASTICITY: EXPERIENCES CAN ALTER THE BRAIN

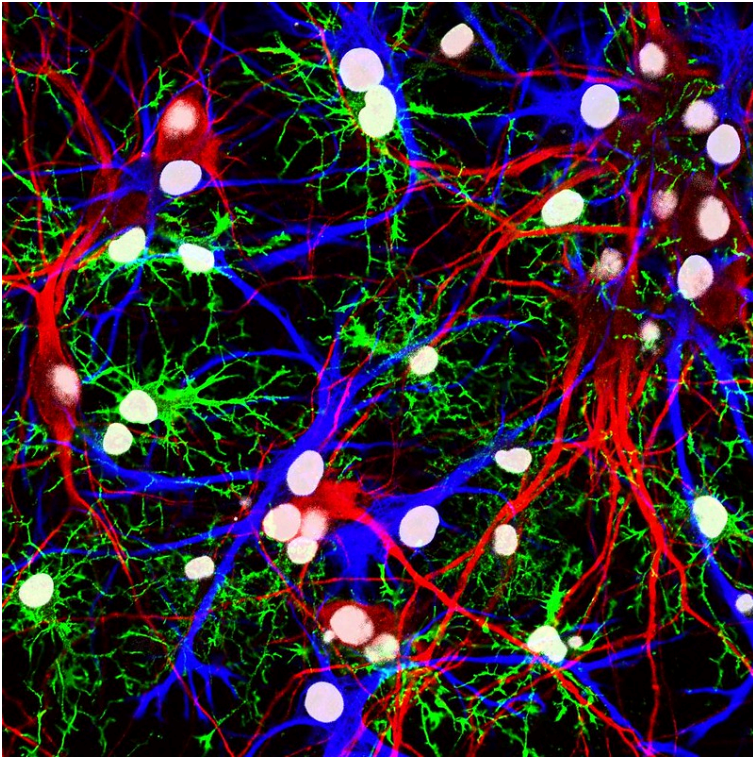


Figure 6. Neural plasticity can be summed up in the phrase: “Neurons that fire together, wire together.” Or in other words, when certain emotions are paired with certain contexts, we learn to associate the two together.

The responses of specific neural regions may be modified by experience. For

example, the front shell of the nucleus accumbens is generally involved in appetitive behaviors, such as eating, and the back shell is generally involved in fearful defensive behaviors (Reynolds & Berridge, 2001, 2002). Research using human neuroimaging has also revealed this front–back distinction in the functions of the nucleus accumbens (Seymour et al., 2007). However, when rats are exposed to stressful environments, their fear-generating regions expand toward the front, filling almost 90% of the nucleus accumbens shell. On the other hand, when rats are exposed to preferred home environments, their fear-generating regions shrink, and the appetitive regions expand toward the back, filling approximately 90% of the shell (Reynolds & Berridge, 2008).

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10.4: BRAIN STRUCTURES HAVE MULTIPLE FUNCTIONS

Although much affective neuroscience research has emphasized whole structures, such as the amygdala and nucleus accumbens, it is important to note that many of these structures are more accurately referred to as complexes. They include distinct groups of nuclei that perform different tasks. At present, human neuroimaging techniques such as fMRI are unable to examine the activity of individual nuclei in the way that invasive animal neuroscience can. For instance, the amygdala of the nonhuman primate can be divided into 13 nuclei and cortical areas (Freese & Amaral, 2009). These regions of the amygdala perform different functions. The central nucleus sends outputs involving brain stem areas that result in innate emotional expressions and associated physiological responses. The basal nucleus is connected with striatal areas that are involved with actions such as running toward safety. Furthermore, it is not possible to make one-to-one maps of emotions onto brain regions. For example, extensive research has examined the involvement of the amygdala in fear, but research has also shown that the amygdala is active during uncertainty (Whalen, 1998) as well as positive emotions (Anderson et al., 2003; Schulkin, 1990).

10.5: CONCLUSION

Research in affective neuroscience has contributed to knowledge regarding emotional, motivational, and behavioral processes. The study of the basic emotional systems of nonhuman animals provides information about the organization and development of more complex human emotions. Although much still remains to be discovered, current findings in affective neuroscience have already influenced our understanding of drug use and abuse, psychological disorders such as panic disorder, and complex human emotions such as desire and enjoyment, grief, and love.

10.6: DISCUSSION QUESTIONS AND RESOURCES

Discussion Questions

1. The neural circuits of “liking” are different from the circuits of “wanting.” How might this relate to the problems people encounter when they diet, fight addictions, or try to change other habits?
2. The structures and neurotransmitters that produce pleasure during social contact also produce panic and grief when organisms are deprived of social contact. How does this contribute to an understanding of love?
3. Research shows that stressful environments increase the area of the nucleus accumbens that is sensitive to fear, whereas preferred environments increase the area that is sensitive to rewards. How might these changes be adaptive?

Outside Resources

Video: A 1-hour interview with Jaak Panksepp, the father of affective neuroscience

https://www.youtube.com/watch?v=u4lCY6-7hJo&ab_channel=SpektrumderWissenschaft

Video: A 15-minute interview with Kent Berridge on pleasure in the brain

https://www.youtube.com/watch?v=51rGE1Dglo0&ab_channel=YaleCourses

Video: A 5-minute interview with Joseph LeDoux on the amygdala and fear

https://www.youtube.com/watch?v=fDD5wvFMH6U&ab_channel=BigThink

Web: Brain anatomy interactive 3D model

<http://www.pbs.org/wnet/brain/3d/index.html>

10.7: REFERENCES

This chapter was adapted from:

Harmon-Jones, E. & Harmon-Jones, C. (2023). Affective neuroscience. In R. Biswas-Diener & E. Diener (Eds), Noba textbook series: Psychology. Champaign, IL: DEF publishers. Retrieved from <http://noba.to/qnv3erb9>

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CHAPTER 11: BRAIN DAMAGE, NEURODEGENERATION , AND NEUROLOGICAL DISEASES

Learning Objectives

- Describe the symptoms, causes, and treatments of several examples of brain damage, including tumor, stroke, and traumatic brain injury
- Understand the less recognized epidemic of traumatic brain injury caused by intimate partner violence.
- Describe the symptoms, causes, and treatments of several examples of neurological diseases, including Parkinson's Disease, Alzheimer's Disease, and Multiple Sclerosis.

11.1: INTRODUCTION

The complexity and capabilities of a well-functioning human brain are astonishing. The three-pound mass of molecules is organized in an intricate web of billions of neurons and support cells. These interconnected neural networks coordinate our most mundane functions and our most profound thoughts. The distributed patterns of brain activity enable us to perceive, learn, experience, create, communicate, empathize, and dream, propelling our species toward unending innovation and discovery. Yet, for all its capabilities and general resilience, the brain remains vulnerable.

The delicate balance in a well-functioning brain can be disrupted in many ways. Brain cells need oxygen and nutrients to survive—interrupted supply can be devastating. Neurons use neurotransmitters to communicate—too little or too much can stop communication or kill cells. Brain cells are fragile and easily damaged by force or invading agents. Proteins can build up and disrupt function. Brain cells can die and cause atrophy.

This chapter delves into the darker side of brain biology: brain damage and neurodegeneration. We will explore how things can go awry in this intricate organ and lead to serious alterations in behavior, cognition, and quality of life. Understanding these aspects is not only crucial for appreciating the brain's fragility but also for developing effective therapies for brain damage and neurodegeneration.

Brain damage can occur in many ways, including traumatic brain injury, tumor, stroke, encephalitis (inflammation of the brain often caused by infections), hydrocephalus (fluid buildup inside the skull that increases pressure), lack of oxygen, and meningitis (inflammation of the meninges, the protective membrane around the brain, usually caused by infection). In this section, we'll go into detail about three of the most common types of brain damage: brain tumor, stroke, and traumatic brain injury (TBI). With

TBI, we focus on an under-recognized epidemic—TBI that stems from intimate partner violence.

There are also many forms of neurological diseases and neurodegeneration. We conclude this chapter with sections on three common ones—Parkinson’s disease, Alzheimer’s disease, and Multiple Sclerosis.

11.2: STROKE

Overview. A stroke is a medical emergency involving an interruption of blood flow to the brain. The interrupted blood flow prevents brain tissue from getting oxygen and nutrients. In turn, neuronal function is impaired within seconds, and brain cells start to die within minutes. Stroke is the leading cause of long-term adult disability and was the fifth leading cause of death in the United States in 2021 (CDC, 2023a). Long-term effects of stroke depend on the extent and location of the brain damage and include paralysis, problems with cognition or memory, issues speaking or understanding speech, emotional disturbances, pain, and unusual bodily sensations (NINDS, 2023a).

Types of Strokes. Strokes can be classified into two major categories: ischemic (pronounced ‘ih-**skee**-muhk’) and hemorrhagic (pronounced “heh-mr-a-juhk”). Most strokes are ischemic. **Ischemic strokes** are caused by interruption of the blood supply to one or more regions of the brain. The interruption is most commonly caused by a blood clot or cellular debris that blocks a blood vessel in the brain (NINDS, 2023a). A clot might develop at the site of the blockage (“thrombosis”) or it might create a blockage after moving from another part of the body (“embolism.”) The third cause of ischemic stroke is “stenosis” in which an artery narrows, often due to plaques or fatty deposits on artery walls. The other major category of stroke, **hemorrhagic stroke**, happens when an artery in the brain leaks blood or ruptures (breaks open). The leaked blood puts too much pressure on brain cells and damages them.

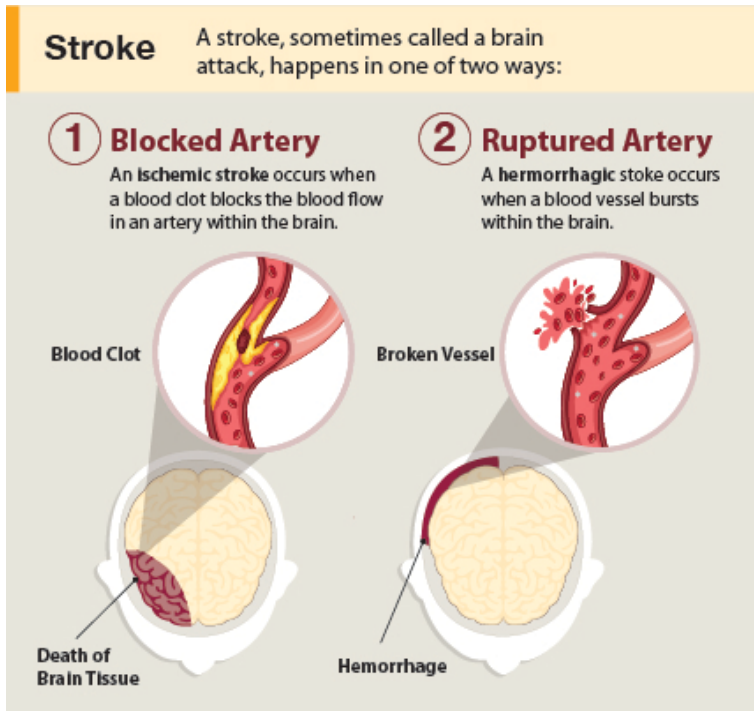


Figure 1. A stroke, sometimes called a brain attack, happens in one of two ways: 1) ischemic strokes occur when an artery is blocked, and 2) hemorrhagic stroke occurs when a blood vessel ruptures.

Cell death. After a stroke, some brain cells die because they stop getting the oxygen and nutrients needed to function. Other brain cells die because they are damaged by sudden bleeding in or around the brain. Some brain cells die quickly, but many linger in a compromised or weakened state for several hours. Stroke causes permanent brain damage over minutes to hours (NINDS, 2023a).

One specific cellular mechanism underlying ischemic-induced cell death is glutamate excitotoxicity. Glutamate is a major excitatory neurotransmitter important for memory and long-term potentiation (covered in Chapter 7). Glutamate is key for healthy brain function, but too much glutamate can kill neurons—this is known as glutamate

excitotoxicity. When a stroke blocks oxygen-rich blood supply to the brain, negatively charged ATP levels drop, making the interior of the neuron more positively charged. This leads to excess glutamate released into the synapse, which causes the postsynaptic neuron to fire excessively; calcium ions flood the postsynaptic cell, cytotoxic enzymes are activated, and it eventually dies. Critically, as a neuron dies, it releases its glutamate reserves, which restarts the process in nearby cells. This glutamate excitotoxicity repeats itself in a vicious cycle that spreads quickly and kills many neurons in minutes (Kuang, 2019; Mark, 2001).

Identifying stroke. With stroke, the sooner treatment begins, the better. Knowing the signs of stroke and calling 911 immediately can help save a relative, neighbor, or friend. A mnemonic for remembering the signs of strokes is FAST (standing for Facial droop, Arm weakness, Speech difficulty, Time to call emergency services, see Figure 2). With timely treatment, it is possible to save brain cells and greatly reduce the damage (NINDS, 2023a).



Figure 2. Acting F.A.S.T. is key to stroke survival. Face: Does one side of the face droop when smiling? Arms: Does one arm drift downward when both arms are raised? Speech: Is speech slurred or strange when repeating a simple phrase? Time: If you see any of these signs, call emergency services such as 9-1-1 immediately.

Treatments. At the emergency room, patients can receive drugs that dissolve a clot. These drugs will not work if the stroke occurred more than three hours before arriving at the hospital or was caused by a burst blood vessel (Clark et al., 2018). For those hemorrhagic strokes, surgeons may clip blood vessels to stop bleeding, drain excess fluid, or even temporarily remove part of the skull to relieve pressure from swelling.

Recovery from a stroke can take weeks, months, or even years. Some people fully recover, whereas others have lifelong disabilities. Treatment following a stroke can include blood pressure medication, healthy lifestyle changes to prevent future strokes, and physical and speech therapy.

Risk factors of stroke. Despite the possibility of death or long-term disability, there is some “good news”: About 4 in 5 strokes are preventable (CDC, 2023b). Risk factors can be categorized as modifiable and nonmodifiable. Nonmodifiable risk factors include age (older adults have a higher risk), sex (men have a higher risk), and race/ethnicity (stroke incidence among Black and Hispanic Americans is almost double that of White Americans, and Black and Hispanic Americans tend to have strokes at a younger age) (Boehme et al. 2017; NINDS, 2023a). The “good news” is that some risk factors are modifiable and can be controlled by lifestyle and behavior changes. High blood pressure is the most important risk factor and can be managed by eating a healthy diet (low fat, low cholesterol, low salt, whole grains, and veggies), exercising (2.5+ hours per week), not drinking too much alcohol, and not smoking (smokers are twice as likely to have a stroke) (CDC, 2023b).

Finally, air pollution, noise pollution, and even light pollution are linked to a higher risk of stroke, hypertension, and other cardiovascular diseases (Boehme, 2017; Van Kempen & Babisch, 2012). While these factors are modifiable, they are not controllable at the individual level, especially for poor people (who have fewer housing options and often can’t afford to move away from such environmental hazards) (Crea, 2021). Thus, some prevention measures are best viewed at the population level, and this underscores the connection between health and sensible public policy that mitigates risk factors.

Text Attributions

This section contains material adapted from:

National Institute of Neurological Disorders and Stroke (NINDS) (2023). Stroke. <https://www.ninds.nih.gov/health-information/disorders/stroke> Public domain.

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11.3: BRAIN TUMORS

A brain tumor is a mass of abnormal cells that form into a growth in the brain. Tumors occur when something goes wrong with genes that regulate cell growth, allowing cells to grow and divide out of control (NINDS, 2023c). Tumors can be noncancerous (benign) or cancerous (malignant).

Benign tumors don't spread to other body parts and often can be removed surgically. **Malignant tumors** can invade surrounding tissue; some malignant brain tumors can be removed entirely through surgery, whereas others have hard-to-define edges so are difficult to remove completely.

Tumors can also be categorized as primary tumors, which start within the brain, and secondary or metastatic tumors, which are caused by cancer cells that break away from a primary tumor somewhere else in the body and spread to the brain. Metastatic tumors are more common than primary tumors in the brain and occur more often in adults than in children.

Symptoms. Brain tumors cause many different symptoms, and they depend on tumor type, location, size, and rate of growth. In infants, the most obvious sign of a brain tumor is a rapidly widening head or bulging crown (see Figure 3 for an image of a bulging skull in an adult). In older children and adults, a tumor can cause headaches, seizures, balance problems, and personality changes. As with all brain damage and neurological disorders, the effects are location-specific. For example, a tumor in the frontal lobe might contribute to poor cognition or inappropriate social behavior; a tumor in the cerebellum might cause poor balance and movement control; a tumor in emotional regions might cause new bouts of inappropriate laughter or rage. A good friend of author MH reported no symptoms until his face and head swelled up after a flight; an emergency MRI revealed a tennis-ball sized meningioma (a tumor in the meninges surrounding the brain; see Figure 3 for a meningioma in another person). In retrospect, he noted possible coordination deficits, that

for example may have caused him to lose to his brother in golf. The tumor was surgically removed and he has resumed “trouncing” his brother in golf.



Figure 3. A meningioma, a benign tumor that developed in the meninges (thin membrane covering the brain), has caused a large hyperostosis (excessive bone growth of the skull).

Diagnosis and Treatment. Diagnosing a brain tumor usually involves a neurological exam with a doctor, lab tests of blood and urine, and diagnostic imaging with magnetic resonance imaging (MRI). MRI scans can provide high-resolution information about tumor cell density and a precise map of the tumor and neighboring structures (see **Figure 4** for an MRI scan of a tumor). Surgery is used to obtain tissue for diagnosis and to remove as much tumor as safely possible. Radiation therapy and chemotherapy are often used to kill cancer cells or stop them from spreading. Biological or immunotherapies are being developed to enhance the body’s immune response and to recognize and fight cancer cells. Outcomes for treatments differ greatly based on the tumor type, location, degree of spreading, etc. Malignant glioblastomas, an especially aggressive spreading cancer, usually have poor outcomes (median survival of 14 months; Delgado-Lopez, 2016); while benign meningiomas (non-

spreading tumors that develop in the meninges membrane covering the brain) have good outcomes because they haven't invaded the brain and can be removed surgically.

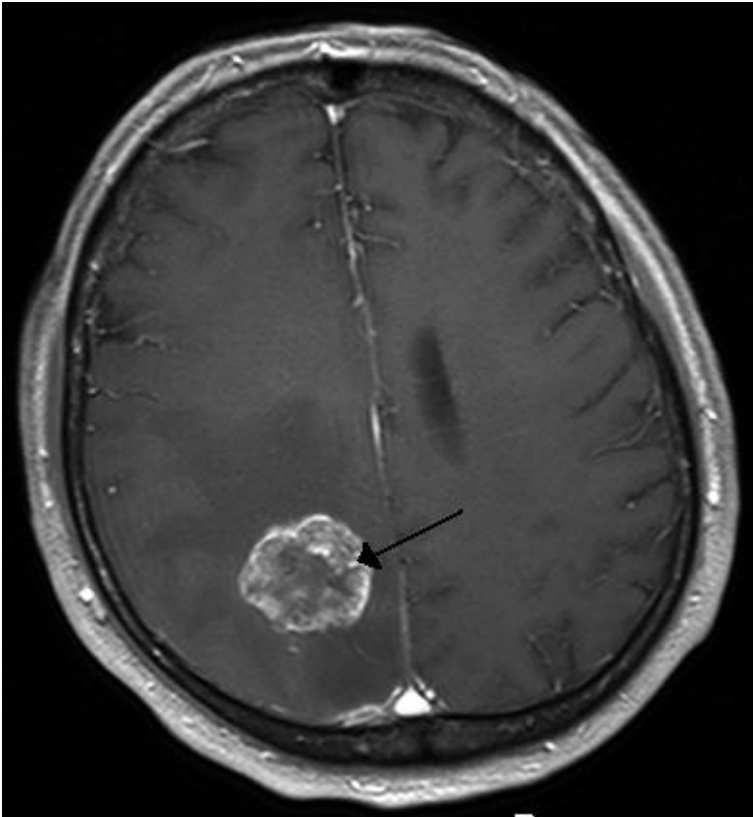


Figure 4. A metastatic tumor in the cerebral hemisphere from lung cancer, shown on magnetic resonance imaging.

Text Attributions

This section contains material adapted from:

National Institute of Neurological Disorders and Stroke (NINDS) (2023c). Brain and Spinal Cord Tumors.

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11.4: TRAUMATIC BRAIN INJURY

A traumatic brain injury (TBI) is an injury to the brain caused by an external force. TBIs can be caused by a forceful bump, blow, or jolt to the head or body (a “non-penetrating TBI”), or from an object that pierces the skull and enters the brain (a “penetrating TBI”). TBI is a major cause of death and disability: the United States had over 69,000 TBI-related deaths in 2021, and about 15% of all U.S. high-school students self-reported one or more sports or recreation-related concussions (a type of TBI) within the preceding 12 months (CDC, 2023c).

Some types of TBI can cause temporary or short-term problems with brain function, including problems with how the person thinks, understands, moves, communicates, sleeps, and acts. More serious TBI can lead to severe and permanent disability or death. TBI severity is categorized as mild, moderate, or severe. One common way to categorize severity uses a combination of three factors: 1) the Glasgow Coma scale (a test of eye, verbal, and motor responses); 2) duration of post-traumatic amnesia or memory loss (less than 1 day for mild TBI, more than 7 days for severe TBI); and 3) duration of Loss of Consciousness (0-30 minutes for mild TBI and more than 24 hours for severe TBI) (Departments of Defense and Veterans Affairs, 2008). Most TBIs are mild TBIs or concussions.

How TBI Affects the Brain

Primary effects on the brain include bleeding and tearing forces that injure nerve fibers and cause inflammation, metabolic changes, and brain swelling (NINDS, 2023d). Some examples include:

- Diffuse Axonal Injury, one of the most common types of brain injuries, refers to widespread damage to the myelinated white matter tracts. It usually results from rotational forces (twisting) or sudden forceful stopping that stretches or tears these axon bundles (see Figure 5). Diffuse Axonal Injury can disrupt and break down communication among neurons. It also leads to the release of brain chemicals that can cause further damage.

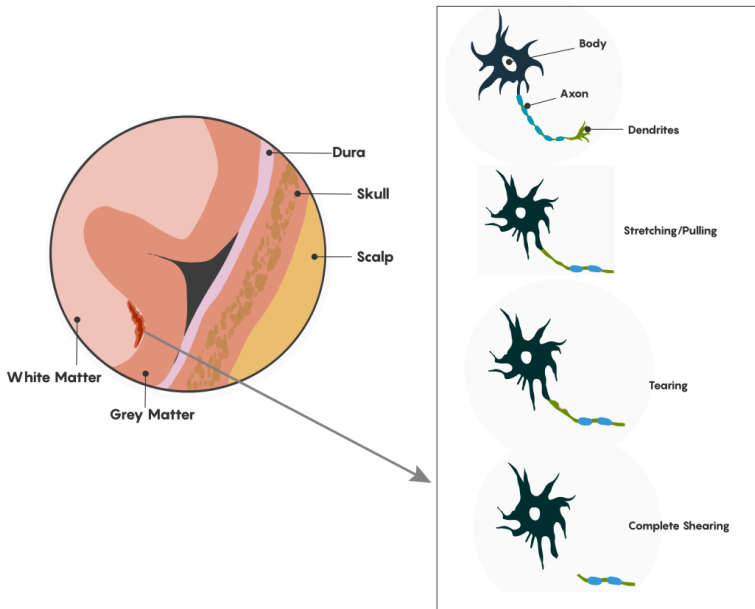


Figure 5. Diagram of diffuse axonal injury following TBI/concussion. Many types of damage can occur along the length of the axon, including stretching/pulling of axons which may affect myelination and localization of axonal channel proteins, and tearing and shearing, which will cause loss of axonal integrity.

- Concussion is a type of mild TBI that may be considered a temporary injury to the brain but could take several months to heal. A small minority of individuals report symptoms that persist for years or indefinitely. The individual can suddenly lose consciousness

or have a sudden altered state of consciousness. A second concussion closely following the first one causes further damage to the brain, and may result in a slower recovery or the so-called “second impact syndrome” that could lead to permanent damage or even death (which is why concussion-monitoring protocols and sitting out while injured is critical in sports).

- Hematomas are bleeding around the brain caused by a rupture of a blood vessel. In a hematoma, blood can collect in or around the meninges (the protective membranes surrounding the brain) or into the brain itself, damaging the surrounding tissue.
- Contusions are bruising or swelling of the brain that occurs when small blood vessels bleed into brain tissue. Contusions can occur directly under the impact site (a **coup** injury) or, more often, on the complete opposite side of the brain from the impact (a **contrecoup** injury). Coup and contrecoup injuries generally occur when the head abruptly decelerates, which causes the brain to hit one side of the skull and then bounce back and hit the other side (such as in a high-speed car crash or in shaken baby syndrome) (**Figure 6**).

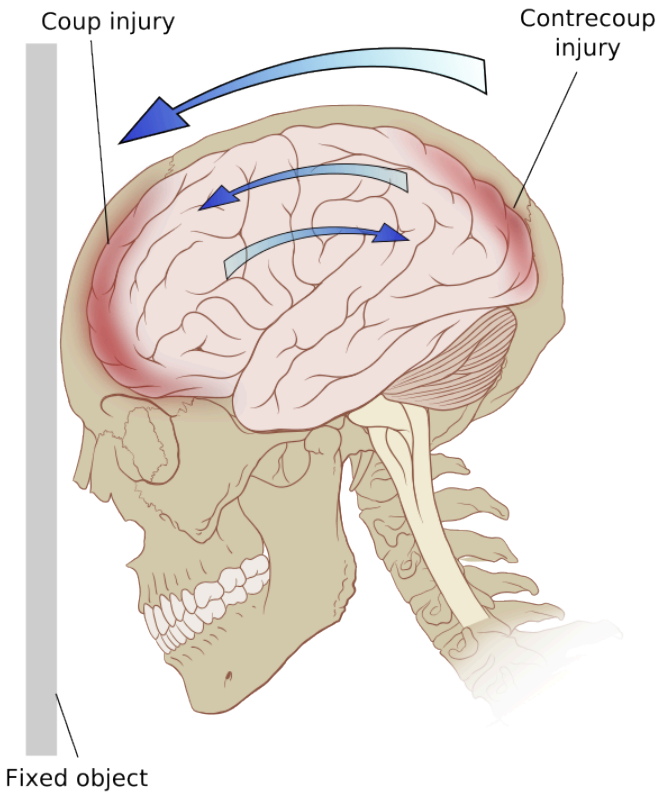


Figure 6. A diagram of the forces on the brain in a coup-contrecoup injury.

- The blood-brain barrier that protects the central nervous system from toxins and pathogens can break down from a TBI. Once the blood-brain barrier is disrupted, blood and other foreign substances can leak into the space around neurons and trigger a chain reaction that causes brain swelling. It can also trigger harmful inflammation or the release of neurotransmitters that can kill nerve cells when depleted or overexpressed.¹

Diagnosing and Treating TBIs

All TBIs require immediate assessment by a professional who has experience evaluating head injuries. A neurological exam will test motor, sensory, and speech skills, coordination and balance, cognitive and memory performance, and changes in mood or behavior. An exam might check for a normal pupil response to changes in light and assign a Glasgow Coma Score. In addition, diagnostic brain imaging with a CT or MRI scan can help evaluate the extent of the brain injuries and determine if surgery is needed.

Many factors—including the size, severity, and location of the brain injury—influence how a TBI is treated and how quickly a person might recover. Although brain injury often occurs at the moment of head impact, much damage in a severe TBI develops from secondary injuries that happen days or weeks after the initial trauma. For this reason, people who receive immediate medical attention at a certified trauma center tend to have the best health outcomes.

Some people with a mild TBI, such as concussion, may not require treatment other than rest and over-the-counter pain relievers. For more severe TBIs, immediate treatment focuses on preventing death, stabilizing vital organ function, ensuring proper breathing, and preventing further brain damage. Once the patient is stabilized, a rehabilitation program is employed to help recovery. This may include physical therapy, occupational therapy, speech-language therapy, cognitive or vestibular rehabilitation therapy, and psychological support for emotional well-being. Novel

1. This section contains material adapted from: National Institute of Neurological Disorders and Stroke (NINDS) (2023d). Traumatic Brain Injury (TBI). <https://www.ninds.nih.gov/health-information/disorders/traumatic-brain-injury-tbi> Public Domain.

therapies, such as neuroprotective agents and stem cell therapy, are under active research and hold promise for future treatment possibilities.²

Chronic Traumatic Encephalopathy (CTE)

A history of experiencing repeated head traumas has been associated with Chronic Traumatic Encephalopathy (CTE). CTE is a progressive neurological disorder associated with symptoms that may include problems thinking, understanding, and communicating; motor disorders (affecting movement); problems with impulse control and depression; and irritability. CTE occurs in those with extraordinary exposure to multiple blows to the head, and symptoms generally start to appear 8-10 years after repeated head injuries (NINDS, 2023d; McKee, 2009). CTE can only be diagnosed after death. After death, a person's brain is removed, and doctors check whether the person had CTE or another disease, such as Alzheimer's disease, or no disease at all (CDC, 2019). A brain with CTE is characterized by atrophy (shrinkage) of several brain areas, including the cerebral hemispheres, the medial temporal lobe, the thalamus, and the brain stem, as well as dilation of the ventricles (**Figure 7**) (McKee 2009). Microscopic examination of brain tissue reveals the pathological signature of CTE—phosphorylated tau protein (p-tau) that builds up in neurons, astrocytes, and cell processes around small blood vessels of the cortex, typically at the depth of cortical sulci (Asken, 2017; McKee, 2009) (**Figure 8**). The distribution of tau

2. This section contains material adapted from: National Institute of Neurological Disorders and Stroke (NINDS) (2023d). Traumatic Brain Injury (TBI). <https://www.ninds.nih.gov/health-information/disorders/traumatic-brain-injury-tbi> Public Domain.

protein in CTE differs from other tau-related disorders, such as Alzheimer's Disease. But in both tau pathologies, tau buildup and the neurofibrillary tangles formed from tau eventually disrupt brain cells' ability to communicate with other cells.

Researchers do not know how many people in the United States have CTE. Some evidence suggests rates around 30% for those with histories of repeated head injuries (Asken, 2017). Most studies on CTE have focused on a small group of people who experienced head or brain injuries over many years. People in this group had their brains donated for research, and according to reports from family members, they often had problems with thinking, emotions, or behavior while they were alive (CDC, 2019).³

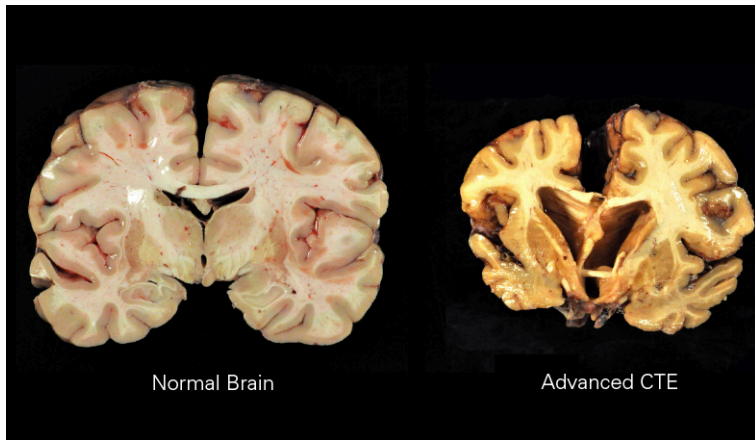


Figure 7. A normal brain (left) and one with advanced CTE (right).

3. This section contains material adapted from: National Institute of Neurological Disorders and Stroke (NINDS) (2023d). Traumatic Brain Injury (TBI). <https://www.ninds.nih.gov/health-information/disorders/traumatic-brain-injury-tbi> Public Domain.

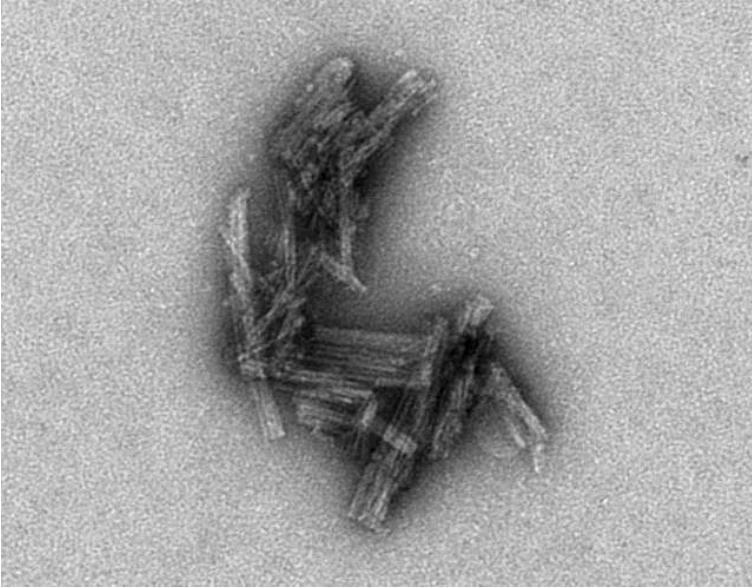


Figure 8. Electron micrograph of tau protein clusters that occur in Alzheimer's Disease and CTE.

Causes of TBI

Traumatic brain injury has many causes, including falls, vehicle accidents, gunshots, explosions, and blows to the head. Recently attention has surged on brain injury in sports, especially soccer (from repeatedly heading the ball; Lipton et al., 2013), combat sports (e.g., boxing, kickboxing, and mixed martial arts), and contact sports (e.g., ice hockey, professional wrestling, and American football). In National Football League (NFL) players, repeated blows to the head over a career are linked to Traumatic Brain Injury and CTE. These links have been clearly established since a landmark 2006 study by pathologist Bennet Omalu (famously depicted by Will Smith in the film “Concussion”). In a convenience sample of deceased

NFL football players who donated their brains for research, 110 of 111 had neuropathological evidence of CTE, suggesting that CTE may be related to playing football [note that participation in the brain-donation program was likely motivated by players' and their families' awareness of links between head trauma and CTE; this could bias the sample, and accordingly the authors caution that "estimates of prevalence cannot be concluded or implied from this sample" (Mez et al., 2017)]. In addition, the high-profile suicides of former NFL players Junior Seau, Dave Duerson, and Aaron Hernandez, who had signs of CTE in their brains, thrust the topic of brain injury into the national consciousness.

In spite of extensive attention on professional football, the overall case count of brain injuries in NFL players (~hundreds per year) is dwarfed by the number of brain injuries in other domains, such as the military (~thousands per year) or from intimate partner violence (~millions per year) (Hillstrom, 2022). In the next section, we turn to Dr. Eve Valera, a professor at Harvard Medical School and expert on brain injury in intimate partner violence, to discuss this less-recognized and under-studied epidemic.

Traumatic Brain Injury from Intimate Partner Violence – By Prof. Eve Valera

Harvard Medical School and Massachusetts General Hospital

Content Notice – This section describes some possible

effects on the brain from Intimate Partner Violence or Domestic Violence. The content may be distressing, especially for those who have been directly or indirectly affected by violence.

If you or someone you know has been affected, support resources are available, for example, through your university's counseling center or various health agencies. In the U.S., the National Domestic Violence Hotline is available 24/7; Text LOVEIS to 22522, call 1-800-799-7233, or visit <https://www.thehotline.org/get-help/>. In Canada, services can be found at: <https://www.canada.ca/en/public-health/services/health-promotion/stop-family-violence/services.html>

Intimate Partner Violence (IPV) is any violence perpetrated by a current or former partner, spouse, significant other, girlfriend, or boyfriend with whom one has had an intimate relationship. Though the term domestic violence is often used interchangeably with IPV, domestic violence is broader in scope and also includes child abuse, elder abuse, and abuse from a child to a parent. IPV does not need to occur within the home and can occur in the context of a relationship of any length.

Globally, approximately one in three women experience physical or sexual violence in their lifetime (García-Moreno et al., 2013). Women in peak reproductive age groups—18 to 24-year-olds, followed by 25 to 34-year-olds—experience the highest rates of IPV (Catalano, 2012). Furthermore, people from groups that are and have been marginalized, such as people from racial and ethnic minority groups or LGBTQ+ individuals, are at higher risk for more abuse and/or worse consequences (CDC, 2022).

IPV can take many forms, including physical, psychological, and sexual

abuse. When considering physical abuse, 80-90% of injuries are to the head, face, and neck, with women having their heads punched, slapped, kicked, and slammed against other objects. These behaviors can result in traumatic brain injuries (TBIs) in which external forces result in alterations in brain function. Although women sustain TBIs of all severities, the majority of TBIs are concussions, which are on the milder end of the TBI spectrum.

Though limited, data show that IPV-related brain injuries are associated with negative emotional, cognitive, and neural outcomes. For example, women with higher brain injury scores (based on number, recency, and severity of brain injuries) performed worse on tests of memory, learning, and cognitive flexibility than women with lower brain injury scores. Similarly, women with higher brain injury scores also tended to have higher levels of depression, worry, anxiety, general distress, and PTSD symptomatology (Valera & Berenbaum, 2003). Higher brain injury scores and more IPV-related brain injuries were also associated with measures of functional and structural connectivity within the brain analogous to those occurring in people who sustained brain injuries from accidents or sports (Valera & Kucyi, 2017; Valera et al., 2019).

Strangulation is another form of IPV and can be defined as “sustained impairment of air or blood flow through the neck as a result of external pressure” (Armstrong & Strack, 2016). This can lead to alterations (including losses) in consciousness. Strangulation-related alterations in consciousness (AIC) can result in a strangulation-related acquired brain injury. As such, when considering injuries to the brain from IPV, it is important to consider both TBIs and strangulation-related brain injuries or what can be considered “concussion+”. In a study on the effects of strangulation-related AICs, we found that women who sustained strangulation-related AICs performed more poorly on tests of working and long-term memory and had higher levels of depression and PTSD symptomatology (Valera et al., 2022). Furthermore, there’s also been an alarming rise in consensual “rough sex” among young adults, particularly

sexual strangulation or choking, which can damage the brain (Herbenick et al., 2023; Orenstein, 2024).⁴

Preventing intimate partner violence. Several factors may affect the prevalence and risk of intimate partner violence. To prevent intimate partner violence, we must understand and address the factors that put people at risk and protect them from violence. Promoting healthy, respectful, and nonviolent relationships and communities can help reduce the occurrence of IPV. For example, school curricula with courses on healthy relationships and communication are crucial. Such efforts are critical to prevent the harmful and long-lasting effects of IPV on individuals, families, and communities (CDC, 2022). See Figure 9 for ways to address and prevent intimate partner violence.⁵

4. Additional Reading: Orenstein, P. (2024, April 12). The Troubling Trend in Teenage Sex. New York Times. <https://www.nytimes.com/2024/04/12/opinion/choking-teen-sex-brain-damage.html>. Hillstrom, C. (2022, March 1). The Hidden Epidemic of Brain Injuries From Domestic Violence. New York Times. <https://www.nytimes.com/2022/03/01/magazine/brain-trauma-domestic-violence.html>

5. This section contains material adapted from: Center for Disease Control and Prevention (CDC) (2022). Fast Facts: Preventing Intimate Partner Violence <https://www.cdc.gov/violenceprevention/intimatepartnerviolence/fastfact.html> Public Domain



Figure 9: Ways to address and prevent intimate partner violence.

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11.5: NEUROLOGICAL AND NEURODEGENERATIVE DISORDERS

Neurodegenerative disorders are illnesses characterized by a loss of nervous system functioning that are usually caused by neuronal death (Clark et al., 2018). Although some of these diseases occur in children and young adults, most occur in older adults. These diseases generally worsen over time as more and more neurons die. The resulting impairments may be predominantly cognitive, as in Alzheimer's-type dementia, or predominantly motor, as in Parkinson's disease, or a combination of the two, as in Huntington's disease. The symptoms of a particular neurodegenerative disease are related to where in the nervous system the death of neurons occurs. For example, spinocerebellar ataxia is associated with neuronal death in the cerebellum, which causes problems with balance and walking. Neurodegenerative disorders include Huntington's disease, amyotrophic lateral sclerosis (ALS), Alzheimer's disease and other types of dementia disorders, multiple sclerosis (MS), and Parkinson's disease. Here, we discuss Alzheimer's, Parkinson's disease, and multiple sclerosis in more depth.

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11.6: ALZHEIMER'S DISEASE

Dementia describes a group of symptoms associated with a decline in memory, reasoning, or other cognitive skills. **Alzheimer's disease** is the most common cause of dementia in the elderly (Clark et al., 2018). In 2023, an estimated 6.7 million Americans are living with Alzheimer's disease, and costs for their care are estimated at \$345 billion. Roughly one in every eight people age 65 or older has the disease. Due to the aging of the baby-boomer generation, there are projected to be as many as 13 million Alzheimer's patients in the United States in the year 2050.

Symptoms of Alzheimer's disease include disruptive memory loss, confusion about time or place, difficulty planning or executing tasks, poor judgment, and personality changes. Problems smelling certain scents can also be indicative of Alzheimer's disease and may serve as an early warning sign. Many of these symptoms are also common in people who are aging normally, so it is the severity and longevity of symptoms that determine whether a person is suffering from Alzheimer's.

Alzheimer's disease was named for Alois Alzheimer, a German psychiatrist who published a report in 1911 about a woman with severe dementia symptoms. He examined the woman's brain following her death and reported the presence of abnormal clumps, which are now called amyloid plaques, along with tangled brain fibers called neurofibrillary tangles. Amyloid plaques, neurofibrillary tangles, and an overall shrinking of brain volume are hallmarks of degeneration in the brains of Alzheimer's patients. Loss of neurons in the hippocampus is especially severe in advanced Alzheimer's patients. **Figure 10** compares a normal brain to the brain of an Alzheimer's patient.

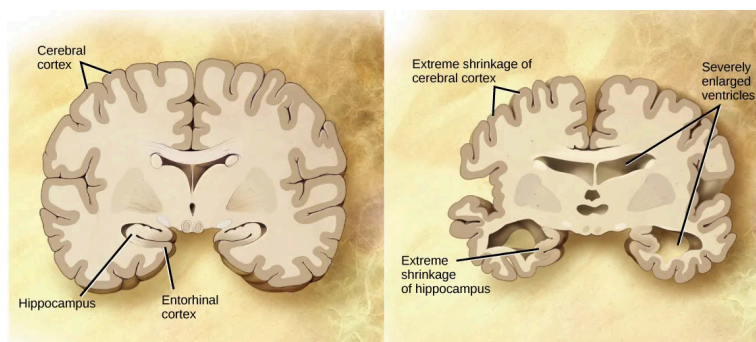


Figure 10. Compared to a normal brain (left), the brain of a patient with Alzheimer's disease (right) shows a dramatic neurodegeneration, particularly at the shrunken hippocampus and enlarged ventricles.

Amyloid plaques and neurofibrillary tangles are the two main biological markers associated with Alzheimer's (The Brain from Top to Bottom, n.d.). Both are buildups of protein that occur as part of the normal aging process, but in people with Alzheimer's-type dementias, the amounts of these proteins that build up are far greater.

Amyloid plaques. The beta-amyloid protein involved in Alzheimer's comes in several different molecular forms that collect between neurons (NIA, 2017). It is formed from the breakdown of a larger protein called amyloid-precursor protein. One form, beta-amyloid 42, is thought to be especially toxic. In the Alzheimer's brain, abnormal levels of this naturally occurring protein clump together to form plaques that collect between neurons and disrupt cell function. Research is ongoing to understand how and at what stage of the disease the various forms of beta-amyloid influence Alzheimer's disease symptoms.

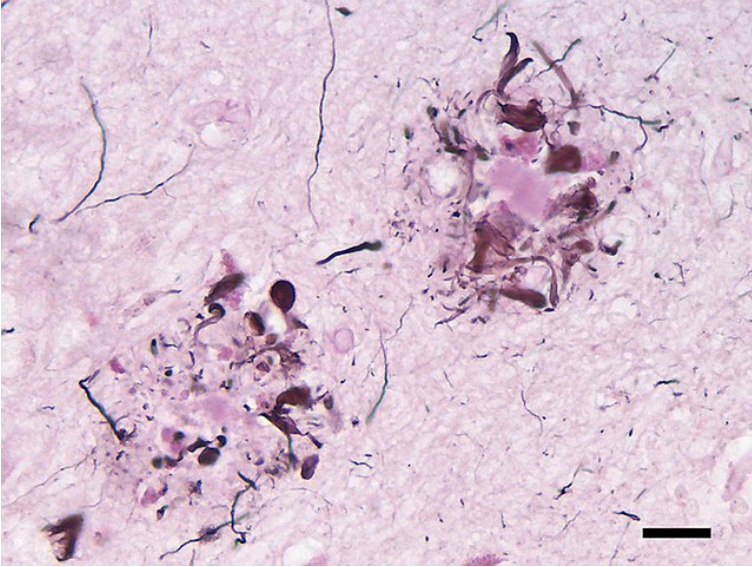


Figure 11. Two amyloid plaques from the brain of a patient with Alzheimer's disease. In this photomicrograph, neurites are darkly stained, and the elements stained pink include the plaque cores. The black bar is 20 microns (0.02mm) in length.

Neurofibrillary tangles. Neurofibrillary tangles are abnormal accumulations of a protein called tau that collect inside neurons. Healthy neurons, in part, are supported internally by structures called microtubules, which help guide nutrients and molecules from the cell body to the axon and dendrites. In healthy neurons, tau normally binds to and stabilizes microtubules. In Alzheimer's disease, however, abnormal chemical changes cause tau to detach from microtubules and stick to other tau molecules, forming threads that eventually join to form tangles inside neurons (Figure 12). These tangles block the neuron's transport system, harming synaptic communication between neurons.

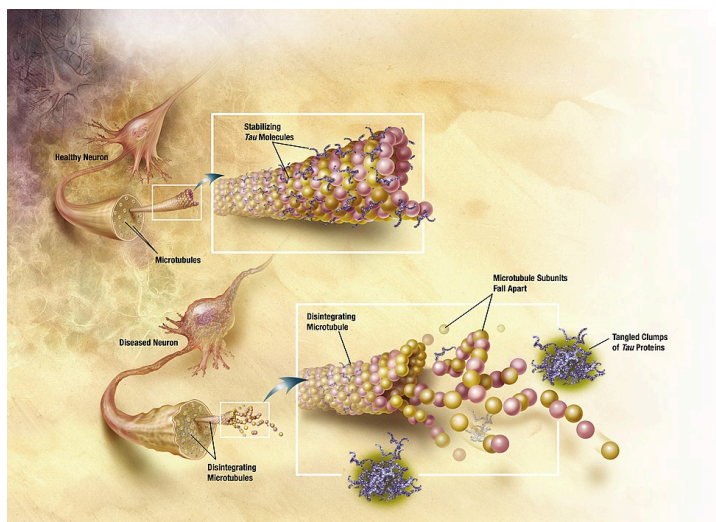


Figure 12. Diagram of how microtubules disintegrate with Alzheimer's disease. Source: National Institute on Aging.

Emerging evidence suggests that Alzheimer's-related brain changes may result from a complex interplay among abnormal tau and beta-amyloid proteins and several other factors. It appears that abnormal tau accumulates in specific brain regions involved in memory. Beta-amyloid clumps into plaques between neurons. As the level of beta-amyloid reaches a tipping point, there is a rapid spread of tau throughout the brain (NIA, 2017).

A rare form of early-onset Alzheimer's disease causes dementia beginning between the ages of 30 and 60; it is usually caused by mutations in one of three known genes (Clark et al., 2018). The more prevalent, late-onset form of the disease also has a genetic component; however research has not identified its genetic contributors as clearly as with the early-onset form of the disease. That said, one particular gene, apolipoprotein E (APOE), has a variant that increases a carrier's likelihood of getting the disease. One APOE-E4 allele doubles or triples the chance of getting a diagnosis of Alzheimer's disease. Having two copies increases the risk about

eight to twelvefold. Many other genes have been identified that might be involved in the pathology of late-onset Alzheimer's disease.

Unfortunately, there is no cure for Alzheimer's disease. Approved treatments focus on managing the symptoms of the disease. Because a decrease in the activity of cholinergic neurons (neurons that use the neurotransmitter acetylcholine) is common in Alzheimer's disease, several drugs used to treat the disease work by increasing acetylcholine neurotransmission, often by inhibiting the enzyme that breaks down acetylcholine in the synaptic cleft. Many treatments currently in development use humanized monoclonal antibodies from mouse models and aim to clear the bad proteins in human patients. While some clinical trials of compounds have shown clearing of the bad proteins on brain PET scans, serious side effects such as Amyloid-related imaging abnormalities (ARIA) have been detected in brain MRI, and the effects on cognition and daily functioning have been disappointing.

Other clinical interventions focus on behavioral therapies like psychotherapy, sensory therapy, and cognitive exercises. Since Alzheimer's disease appears to hijack the normal aging process, prevention research is prevalent. Smoking, obesity, and cardiovascular problems may be risk factors for the disease, so treatments for those may also help to prevent Alzheimer's disease. Studies show that engaging in mentally stimulating activities like puzzles, reading, playing music, and socializing in later life may reduce the risk of developing Alzheimer's disease.

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11.7: PARKINSON'S DISEASE

Like Alzheimer's disease, **Parkinson's disease** is a neurodegenerative disease. It was first characterized by James Parkinson in 1817. Each year, 50,000-60,000 people in the United States are diagnosed with the disease. Parkinson's disease causes the loss of dopamine neurons in the substantia nigra, a midbrain structure that regulates movement. Loss of these neurons causes many symptoms, including tremor (shaking of fingers or a limb), slowed movement, speech changes, balance, posture and gait problems, and rigid muscles. The combination of these symptoms often causes a characteristic slow, hunched, shuffling walk (**Figure 13**). Patients with Parkinson's disease can also exhibit cognitive and psychological symptoms, such as dementia or emotional problems (Clark et al., 2018).

Although some patients have a form of the disease known to be caused by a single mutation, for most patients the exact causes of Parkinson's disease remain unknown: the disease likely results from a combination of genetic and environmental factors (similar to Alzheimer's disease). Post-mortem analysis of brains from Parkinson's patients shows the presence of Lewy bodies—abnormal protein clumps—in dopaminergic neurons. The prevalence of these Lewy bodies often correlates with the severity of the disease.

There is no cure for Parkinson's disease, and treatment is focused on easing symptoms. One of the most commonly prescribed drugs for Parkinson's is L-DOPA, which is a chemical that is converted into dopamine by neurons in the brain. This conversion increases the overall level of dopamine neurotransmission and can help compensate for the loss of dopaminergic neurons in the substantia nigra. Other drugs work by inhibiting the enzyme that breaks down dopamine. L-DOPA can have side effects such as headache, dizziness, psychosis, delusions, and even an increased risk of pathological gambling. Additionally, the effectiveness of

L-DOPA typically declines after a few years and many symptoms become “dopa-resistant.”



Figure 13. Parkinson's patients often have a characteristic hunched posture and walk with slow, shuffling steps. People with Parkinson's also have an elevated fall risk.

Parkinson's disease can also be treated with non-pharmacological methods. For example, walking difficulties in Parkinson's have been effectively treated with music or metronome cues (Hove et al., 2012). Dancing is also an effective technique for treating motor, cognitive, and emotional symptoms of Parkinson's (Earhart, 2009).

An exciting and invasive tool for treating and relieving symptoms of Parkinson's disease is **Deep Brain Stimulation** (DBS). DBS requires neurosurgery and a medical device called a neurostimulator that sends electrical impulses through wire electrodes implanted in the brain (Figure 14). For movement disorders, electrodes target brain structures involved in motor control. Rigidity, tremor, and dopamine-induced dyskinesia (uncontrolled involuntary movement) in people with PD are treated with stimulation in basal-ganglia-system structures, including the subthalamic nucleus (STN) or the internal segment of the globus pallidus (GPi). DBS to part of the thalamus is used to treat symptoms in PD (NINDS, n.d.). PD is treated by applying high-frequency (> 100 Hz) stimulation to the target site. The patient can typically control the stimulation; turning on the current often results in an almost immediate decrease in symptoms such as tremor, and turning stimulation off leads to a quick return of symptoms. Many videos on the internet demonstrate the sudden and dramatic effects of DBS.

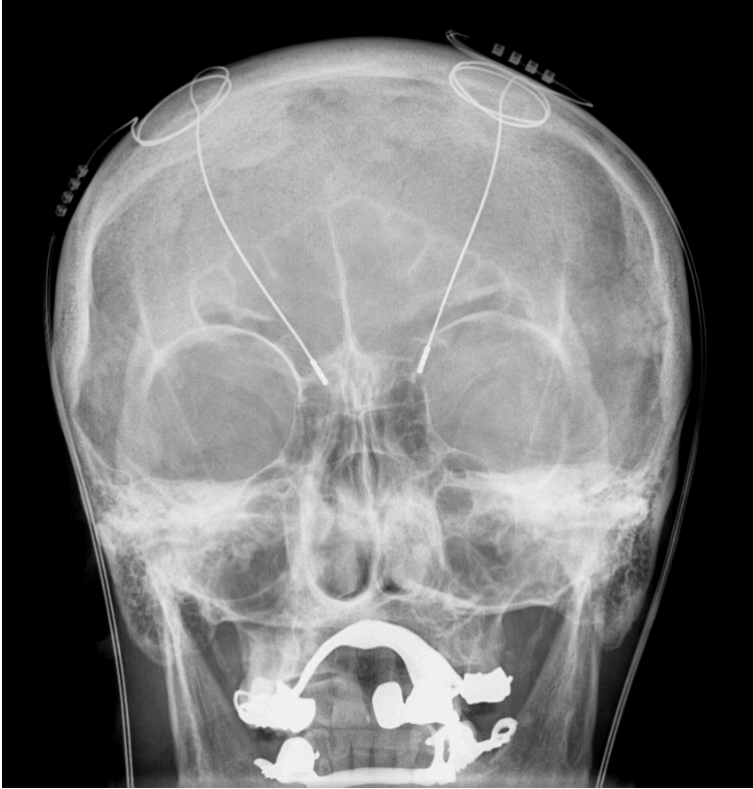


Figure 14. Deep Brain Stimulation probes shown in an X-ray of the skull.

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11.8: MULTIPLE SCLEROSIS

Multiple sclerosis (MS) is a disease of the central nervous system that involves **demyelination** and neurodegeneration. MS is the most common disabling neurological disease of young adults. Symptom onset generally occurs between the ages of 20 and 40 years. It affects about 2.5 million people worldwide. Symptoms of MS include muscle weakness (often in the hands and legs), tingling and burning sensations, numbness, chronic pain, coordination and balance problems, fatigue, vision problems, and difficulty with bladder control (**Figure 15**). People with MS also may feel depressed and have trouble thinking clearly (NINDS, 2023b).



Figure 15. Symptoms in Multiple Sclerosis include (clockwise from top right): white matter lesions, weakness and difficulties walking, spasms, Babinski sign (an abnormal toe reflex), incontinence, single-sided vision, blurred vision, double vision, tremor, and internuclear ophthalmoplegia (a gaze and eye movement abnormality).

MS involves the loss of **oligodendrocytes**, the glial cells that generate and maintain the myelin sheath in the central nervous system. As discussed in Chapter 2, myelin makes up the brain's "white matter" and insulates axons for efficient transmission of action potentials. The loss of oligodendrocytes leads to myelin thinning or loss, and as the disease progresses, the axons themselves deteriorate (as do cell bodies in gray matter). Without myelin, a neuron loses its ability to effectively conduct electrical signals. During the early stages of the disease, a repair mechanism known as **remyelination** occurs, but the oligodendrocytes are incapable of fully restoring the myelin sheath. With each subsequent attack, remyelination becomes increasingly ineffective, eventually leading to the formation of scar-like plaques around the damaged axons. These plaques are visible using magnetic resonance imaging (MRI) and can be as small as a pinhead or as large as a golf ball. They most commonly affect the white matter in the optic nerve, brain stem, basal ganglia, and spinal cord (Compston & Coles, 2008). The symptoms of MS depend on the location and extent of the plaques, as well as the severity of inflammatory reaction.

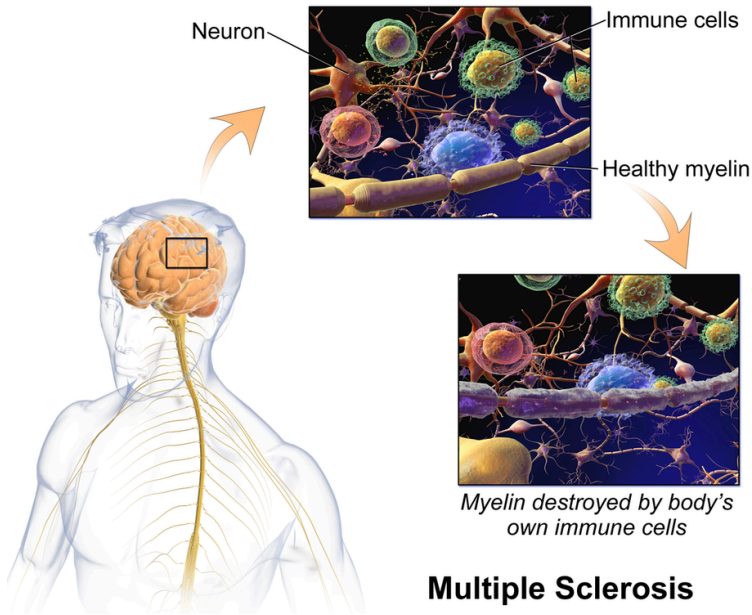


Figure 16. In MS, the immune system cells that normally protect us from viruses, bacteria, and unhealthy cells mistakenly attack myelin in the central nervous system.

MS is considered an autoimmune disorder, in which the body's immune system, which usually defends against viruses, bacteria, and unhealthy cells, attacks part of the body as if it were a foreign substance. In MS, immune cells mistakenly attack the body's own oligodendrocytes. Apart from demyelination, another characteristic sign of MS is inflammation. Inflammation is caused by immune-system T cells that enter the brain after disruptions in the blood–brain barrier, often following infection. Beyond demyelination and inflammation, MS involves additional damage to neurons, and it is generally agreed that MS is driven by the interplay between immune response and neurodegeneration (Faissner et al., 2019; Pinel & Barnes, 2017).

MS affects people differently. A small number of people with MS will have a mild course with little to no disability, whereas others will have a

progressive form that steadily worsens and increases disability over time. Most people with MS, however, have “relapsing-remitting MS” characterized by short periods of symptoms followed by long stretches of relative quiescence (inactivity). The disease is rarely fatal, and most people with MS have a normal life expectancy.

Epidemiology and risk factors. The exact causes of who gets MS are not fully known, but several environmental and genetic risk factors have been identified.

- Females are more frequently affected than males.
- Susceptibility may be inherited, and if one of your parents, siblings, or your twin had MS, you are at a higher risk. Dozens of genes are linked to vulnerability to MS, and most of these genes are associated with immune-system function.
- Certain infections are linked to MS, including Epstein-Barr, the virus that causes mononucleosis; note that only about 5% of the population has not been infected by Epstein-Barr, but they have a lower risk for developing MS.
- MS is more likely to develop in people with low levels of vitamin D (or who have very limited exposure to sunlight, which helps the skin produce vitamin D; Note: this is not a recommendation to sunbathe, due to significant skin-cancer risks). Researchers believe that vitamin D may help regulate the immune system in ways that reduce the risk of MS or autoimmunity in general.
- People from regions near the equator, where there is a great deal of bright sunlight, generally have a much lower risk of MS compared to people far from the equator, for example, in the U.S., Canada, and Europe.
- Finally, studies have found that people who smoke are more likely to develop MS and have a more aggressive disease course.

Treatments. Although MS has no cure, some conventional treatments can improve symptoms, reduce the number and severity of relapses, and delay

the disease's progression. The initial approved medications used to treat MS were modestly effective, though were poorly tolerated and had adverse side effects. Several medications with better safety and tolerability profiles have been introduced, improving the prognosis of MS (McGinley et al., 2021), especially for relapse-remitting MS, but treatment of the progressive forms of the disease remains unsatisfactory (Faissner et al., 2019). Many people with MS try some form of complementary health approach, including yoga, exercise, acupuncture, dietary supplements, and special diets (such as a diet low in saturated fats and high in polyunsaturated fatty acids, such as fish oils) (NCCIH, 2019).

Despite extensive ongoing research into treatments and causes of multiple sclerosis, one take-home message is clear: myelin is critical for a properly functioning nervous system, and damaged myelin leads to major issues in neural function and wellbeing (Eagleman & Downar, 2016).

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CHAPTER 12: BIOPSYCHOLOGY OF PSYCHOLOGICAL DISORDERS

Learning Objectives

- Understand the concept of psychological disorder
- Identify the formal criteria that must be met for thoughts, feelings, and behaviors to be considered symptomatic of a psychological disorder
- Describe the main symptoms of schizophrenia, mood disorders, anxiety, obsessive-compulsive disorder, and posttraumatic stress disorder
- Describe the biological factors underlying schizophrenia, mood disorders, anxiety, obsessive-compulsive disorder, and posttraumatic stress disorder

12.1: BIOPSYCHOLOGY OF PSYCHOLOGICAL DISORDERS OVERVIEW

Most psychological researchers and clinicians agree that mental health is best understood through a “biopsychosocial” perspective that considers how biological, psychological, and sociocultural factors contribute to **psychopathology**. This biopsychology textbook focuses on the biological underpinnings of psychological disorders, emphasizing brain function and genetics. While treatment approaches are introduced, more comprehensive coverage is found in clinical and abnormal psychology courses.

Psychological disorders emerge from complex interactions among biological, social, and environmental factors. The precise nature of these interactions in shaping disorders for individuals remains a challenging question. Interacting factors and varied symptom profiles (within and across individuals) complicate diagnosis. To promote consensus in diagnoses, researchers and clinicians have developed classification systems that traditionally focus on observable symptoms. Although biological factors influence psychological functioning (Wyatt & Midkiff, 2006), biological evidence was rarely used to inform diagnosis. Historically, technological limitations (e.g., in neuroimaging and genetic testing) hampered scientists from adequately examining the biological bases of psychological disorders. Now, given technological advances, scientists have begun exploring how biological factors, such as brain structure, brain function, brain chemistry, and genetics contribute to psychological disorders and may eventually inform diagnosis.

What are Psychological Disorders?

Perhaps the simplest approach to conceptualizing psychopathology is to label behaviors, thoughts, and inner experiences that are atypical, distressful, dysfunctional, and sometimes even dangerous, as signs of a psychological disorder. For example, if you ask a classmate for a date and you are rejected, you probably would feel a little dejected. Such feelings would be normal. If you felt extremely depressed—so much so that you lost interest in activities, had difficulty eating or sleeping, felt utterly worthless, or contemplated suicide—your feelings would be atypical, would deviate from the norm, and could signify the presence of a psychological disorder. However, just because something is atypical, does not necessarily mean it is disordered.¹

The American Psychiatric Association (APA) Definition of a Psychological Disorder

A formal definition developed by the American Psychiatric Association (APA, 2022) characterizes a psychological disorder as a condition that consists of the following:

- **Significant disturbances in thoughts, feelings, and behaviors.** A
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1. This section contains material adapted from: Spielman, R. M., Jenkins, W. J., & Lovett, M. D. (2020). 15.1 What Are Psychological Disorders?. In Psychology 2e. OpenStax. Access for free at <https://openstax.org/books/psychology-2e/pages/15-1-what-are-psychological-disorders>
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person must experience inner states (e.g., thoughts and/or feelings) and exhibit behaviors that are clearly disturbed—that is, unusual, but in a negative, self-defeating way. Often, such disturbances are troubling to those around the individual. For example, if an individual is uncontrollably preoccupied with germs and bathes for hours each day, their inner experiences and behaviors would be considered atypical and negative (disturbed) and would likely trouble family members.

- **The disturbances reflect some kind of biological, psychological, or developmental dysfunction.** Disturbed patterns of inner experiences and behaviors should reflect some flaw (dysfunction) in the internal biological, psychological, and developmental mechanisms that lead to normal, healthy psychological functioning. For example, the hallucinations observed in schizophrenia could be a sign of brain abnormalities.
 - **The disturbances lead to significant distress or disability in one's life.** A person's inner experiences and behaviors reflect a psychological disorder if they cause the person considerable distress, or greatly impair their ability to function as a normal individual. As an illustration, a person's fear of social situations might be so distressing that they avoid all social situations (e.g., preventing that person from being able to attend class or apply for a job).
 - **The disturbances do not reflect expected or culturally approved responses to certain events.** Disturbances in thoughts, feelings, and behaviors must be socially unacceptable responses to certain events that often happen in life. For example, it is perfectly natural (and expected) that a person would experience great sadness and might wish to be left alone following the death of a close family member. Because such reactions are culturally expected, they wouldn't signify a mental disorder.²
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Understanding the Classification Systems of Psychological Disorders

Studying psychological disorders begins with systematically discerning significant signs and symptoms. Identifying and labeling a set of symptoms is crucial for a proper diagnosis. This process enables professionals to use a common language and communicate about the disorder with the patient, colleagues, and the public. For these reasons, classification systems that systematically organize psychological disorders are necessary. The current main classification system is the **Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR)** published by the American Psychiatric Association (2022). Another classification system used for mental and behavioral disorders is the **International Classification of Diseases (ICD-11)** and is primarily used by the World Health Organization to support the global comparison of morbidity statistics. While the ICD-11 is also used in medical settings around the globe, the DSM-5 remains the main instrument for diagnosis. Despite its dominance in the field, using the DSM-5 for clinical diagnosis has some limitations. For example, individuals displaying very different symptoms may be diagnosed with the same psychological disorder, or conversely, individuals displaying very similar symptoms may be diagnosed with different disorders. Given this variation in symptom display and the DSM-5's focus on mapping symptoms onto psychological disorders, it makes sense that scientists are examining how biological factors may inform understanding and diagnosing psychological disorders.

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2. This section contains material adapted from: Spielman, R. M., Jenkins, W. J., & Lovett, M. D. (2020). 15.1 What Are Psychological Disorders?. In Psychology 2e. OpenStax. Access for free at <https://openstax.org/books/psychology-2e/pages/15-1-what-are-psychological-disorders>
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In the rest of this chapter, we give an overview of some common psychological disorders and their underlying biological factors. Overall, there are hundreds of psychological disorders (characterized by the DSM-5 in over 1000 pages). Here we cover a few that are interesting to students: schizophrenia, mood disorders including depression and bipolar disorder, anxiety, obsessive-compulsive disorder, and post-traumatic stress disorder.³

3. This section contains material adapted from: Spielman, R. M., Jenkins, W. J., & Lovett, M. D. (2020). 15.2 Diagnosing and Classifying Psychological Disorders. In Psychology 2e. OpenStax. Access for free at <https://openstax.org/books/psychology-2e/pages/15-2-diagnosing-and-classifying-psychological-disorders> License: CC BY 4.0 DEED.

12.2: SCHIZOPHRENIA

Schizophrenia is a psychological disorder that is characterized by major disturbances in thought, perception, emotion, and behavior. About 0.3-0.7% of the population experiences schizophrenia, and the disorder is usually first diagnosed during early adulthood (late teens to mid-20s). Many people with schizophrenia report significant difficulties in some day-to-day activities, such as holding a job, paying bills, caring for oneself, and maintaining relationships with others. Symptoms of schizophrenia fall into three categories: 1) positive symptoms (symptoms that are “added”), which include hallucinations and delusions; 2) negative symptoms (symptoms that are “subtracted” or taken away), which include flat affect and social withdrawal; and 3) disorganized symptoms, which include disorganized speech and behavior (APA, 2022).

A **hallucination** is a perceptual experience that occurs in the absence of external stimulation. Auditory hallucinations (e.g., hearing voices) are most common, occurring in roughly two-thirds of patients with schizophrenia (Andreasen, 1987).

Delusions are beliefs that are contrary to reality and are firmly held despite contradictory evidence. **Paranoid delusions** refer to the (false) belief that other people are plotting to harm them (e.g., that their mother is plotting with the FBI to poison their coffee). **Grandiose delusions** refer to beliefs that one holds special power, unique knowledge, or is extremely important (e.g., claiming to be Jesus Christ or be a great philosopher). **Somatic delusions** refer to the belief that something highly abnormal is happening to one’s body (e.g., that one’s kidneys are being eaten by cockroaches).

Negative symptoms refer to a reduction or absence of normal behaviors related to motivation, interest, or expression (Correll & Schooler, 2020). Negative symptoms of schizophrenia include withdrawal from

social relationships, reduced speaking, blunted emotion, and reduced experience of pleasure.

Disorganized thinking refers to disjointed and incoherent thought processes—usually detected by what a person says. The person might ramble, exhibit loose associations, jump from topic to topic, or talk so incomprehensibly that it seems they are randomly combining words.

Disorganized or abnormal motor behavior refers to unusual behaviors and movements: becoming unusually active, exhibiting silly child-like behaviors (giggling and self-absorbed smiling), engaging in repeated and purposeless movements, or displaying odd facial expressions and gestures. In some cases, the person exhibits **catatonic behaviors**, showing decreased reactivity to the environment or maintaining a rigid, bizarre postures for extended periods.¹

Neural Mechanisms Underlying Schizophrenia

Scientists have identified several neural and biological signatures of schizophrenia. A highly consistent abnormality in brain structure in schizophrenia is enlarged ventricles (the cerebrospinal fluid-filled spaces in the brain). The ventricles in individuals with schizophrenia average around 30% larger than in controls (**Figure 1**) (Horga et al., 2011). Individuals with schizophrenia typically have smaller hippocampi, amygdalae, and thalami (van Erp et al., 2016) and thinner cortex in frontal and temporal lobe regions (van Erp et al., 2018). Functional neuroimaging studies have

1. This section contains material adapted from: Spielman, R. M., Jenkins, W. J., & Lovett, M. D. (2020). 15.8 Schizophrenia. In *Psychology 2e*. OpenStax. Access for free at <https://openstax.org/books/psychology-2e/pages/15-8-schizophrenia> License: CC BY 4.0 DEED.

shown that patients with schizophrenia display hyperactivity in the hippocampus, a neural structure involved in learning and memory (Kraguljac et al., 2021). This hippocampal hyperactivity is thought to dysregulate the dopamine circuit, which may contribute to distorted interpretations of salience in individuals with schizophrenia. Dopamine dysregulation is one of the most prominent neural mechanisms underlying schizophrenia, and as a result, the most common schizophrenia medications target dopaminergic circuitry.

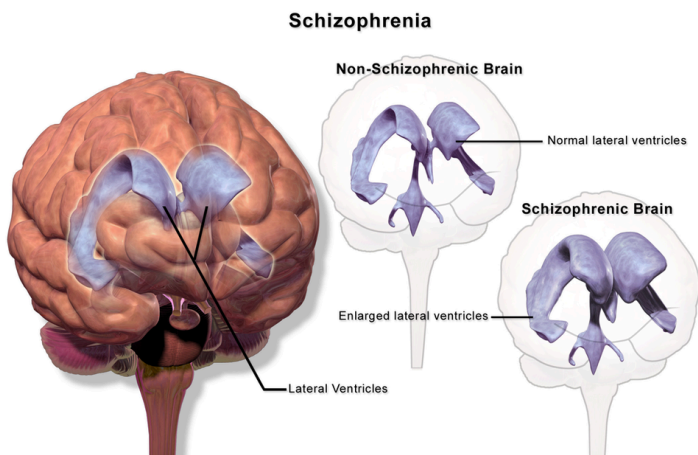


Figure 1. Image showing enlarged ventricles that are often observed in individuals with schizophrenia. Ventricles are cavities in the brain that are filled with cerebro-spinal fluid.

One early influential biological account of schizophrenia is the **“dopamine hypothesis of schizophrenia,”** which suggests that excessive **dopamine** activity is related to schizophrenia (Meltzer & Stahl, 1976). This account was inspired by work showing that drugs that decrease dopamine activity may reduce symptoms related to schizophrenia, and drugs that enhance dopamine activity may increase symptoms (Carlsson & Lindqvist, 1963).

Newer iterations of the dopamine hypothesis have proposed region-specific dopamine imbalances, with reduced dopaminergic activity in the frontal cortex linked to negative symptoms (e.g., social and emotional withdrawal) and hyperactive dopaminergic activity in the striatum associated with positive symptoms (e.g., delusions and hallucinations) (Davis et al., 1991; Pycock et al., 1980). Excess dopamine in the striatum (a subcortical structure involved in processing salience) might cause delusions and hallucinations by making neutral items seem overly important or “aberrantly salient” (Figure 2) (Kapur et al., 2003).

The dopamine hypothesis is an influential but by no means complete explanation for schizophrenia, as newer research has established the important role of other neurotransmitter systems including serotonin and glutamate (Stahl, 2018).

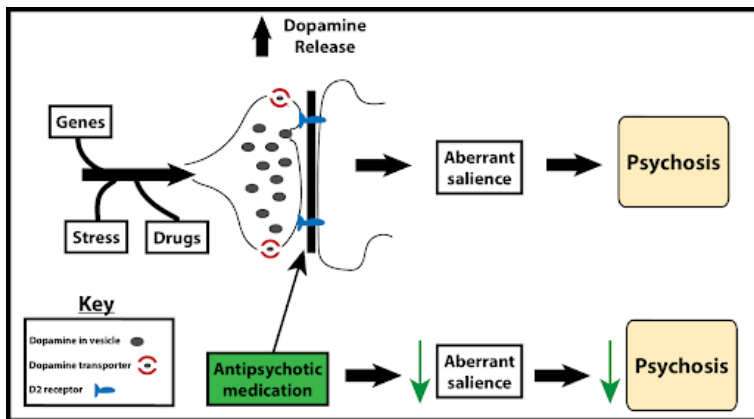


Figure 2. Visualizing striatal dopamine dysregulation's influence on psychosis: excessive dopamine in the striatum could lead to “aberrant salience” (i.e., ascribing too much importance to a stimulus), and ultimately, psychosis. Current antipsychotic medication acts downstream of the primary dopaminergic dysregulation. [Image: Adapted from Howes, O. D., & Kapur, S. (2009)].

Another influential account is the **neural diathesis-stress model of schizophrenia**, which proposes that schizophrenia may result from an

interaction between preexisting vulnerabilities (“diathesis” means vulnerability or predisposition) and stress caused by life experiences. As discussed in the Genetics Chapter, schizophrenia is highly heritable and has a strong genetic component. People with a close genetic relative with schizophrenia, like a parent, sibling, or twin, are more likely to develop schizophrenia. However, genetically predisposed individuals are far more likely to develop schizophrenia if they experience significant life stress—the stressful events can trigger or catalyze the development of the disorder.

Schizophrenia is highly comorbid with substance abuse disorder and some evidence suggests that the use of various substances (particularly marijuana) may increase an individual’s risk of developing schizophrenia if the genetic predisposition is also present (McCutcheon et al., 2020; Patel et al., 2020). Finally, psychedelics, like LSD and psilocybin, may also increase the risk of psychotic episodes (Simonsson et al., 2023). While psychedelics research shows promise for treating some psychiatric conditions, studies typically exclude individuals with or at risk for schizophrenia or psychotic disorders.

Stress worsens symptoms of schizophrenia and the diathesis (predisposition) is marked by a heightened stress response (Walker & Diforio, 1997). The hypothalamic-pituitary-adrenal gland (HPA) axis releases the hormone cortisol in response to stress. HPA-axis dysfunction, possibly linked to hippocampal abnormalities in schizophrenia, may amplify dopamine neurotransmission and stress sensitivity. Hippocampal, HPA axis, and dopamine dysfunction likely combine to heighten stress responses and schizophrenia vulnerability. To combat the effects of stress, researchers highlight resilience or protective factors, including social support, self-esteem, coping skills, and antipsychotic medication (Pruessner et al., 2017).

While we focus here on the diathesis-stress model for schizophrenia, diathesis-stress models (i.e., the important interaction between predisposition and stressful life events) also apply to other disorders such as depression and anxiety (Arnau-Soler et al., 2019).

Treatments of Schizophrenia

While schizophrenia symptoms are most effectively managed with a combination of psychopharmacological, psychological, and family interventions (where family members are taught about treatment and support options), rarely do these treatments restore a patient to premorbid levels of functioning (Kurtz, 2015). Despite recent advances in treating schizophrenia, it is still viewed as requiring lifelong treatment and care.

Psychopharmacological treatments. Among the first antipsychotic medications used for the treatment of schizophrenia was Thorazine, which is thought to primarily work by blocking postsynaptic D2 dopamine receptors (thereby decreasing dopamine activity in certain parts of the brain). Thorazine decreases positive symptoms, calms severely agitated patients, and allows for the organization of thoughts. Despite their effectiveness in managing psychotic symptoms, conventional antipsychotics such as Thorazine also produced significant side effects including muscle tremors, involuntary movements, and muscle rigidity.

Due to the side effects of conventional antipsychotic drugs, newer, arguably more effective second-generation or atypical antipsychotic drugs have been developed (e.g., clozapine, risperidone, aripiprazole). Atypical antipsychotics affect both dopamine and serotonin receptors, unlike conventional antipsychotics that target only dopamine receptors. This broader action makes atypical antipsychotics more effective in treating both positive and negative symptoms, leading to their use as the typical first-line treatment of schizophrenia (Barnes & Marder, 2011).

Over half of schizophrenic patients discontinue antipsychotic medications due to side effects and other factors like homelessness, substance use disorders, and lack of health insurance (Leucht et al., 2011). Therefore, it is important to incorporate psychological interventions, such as cognitive behavioral therapy (CBT) and family therapy, along with psychopharmacological treatment to both address medication adherence,

and provide additional support for managing symptoms (Bridely & Daffin, 2024).²

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2. This section contains material adapted from: Bridley, A., & Daffin, L. W., Jr., (2024). Fundamentals of Psychological Disorders. Washington State University. <https://opentext.wsu.edu/abnormal-psych/> License: CC BY-NC-SA 4.0

12.3: MOOD DISORDERS: DEPRESSION AND BIPOLAR DISORDER

Mood disorders are characterized by severe disturbances in mood and emotions—most often depression, but also mania and elation (Rothschild, 1999). All of us experience fluctuations in our moods and emotions, and often these fluctuations are caused by events in our lives. We become elated if our favorite sports team wins the big game and dejected if a romantic relationship ends or if we lose our job. At times, we feel fantastic or miserable for no clear reason. People with mood disorders also experience mood fluctuations, but their fluctuations are extreme, may last longer, distort their outlook on life, and impair their ability to function.

The DSM-5 includes two general categories of mood disorders: depressive disorders and bipolar disorders. **Depressive disorders** are a group of disorders in which depression is the main feature. Depression is a vague term that, in everyday language, refers to an intense and persistent sadness. People with depressive disorders often feel sad, discouraged, and hopeless. They may lose interest in activities once enjoyed, experience a decrease in drives such as hunger and sex, and/or doubt personal worth. Depressive disorders vary by degree, but this chapter highlights the most well-known: major depressive disorder (sometimes called unipolar depression).

The criteria for diagnosing major depressive disorder (MDD) are detailed in the DSM-5 (APA, 2022). Briefly, to meet criteria for major depressive disorder, an individual must experience symptoms regarded as severe, including either depressed mood or loss of interest in activities most of the day, almost every day for at least two weeks. The symptoms must impair functioning or cause significant distress.

Major depressive disorder is experienced each year by about 7% of the population in the United States (APA, 2022; Bridley & Daffin, 2024). Young adults (18 to 29 year-olds) report higher rates of MDD than any other age group. Rates of MDD in women are about twice as high as in men. The estimated lifetime prevalence of major depressive disorder in women is 21.3% compared to 12.7% in men (Nolen-Hoeksema, 2001; Bridley & Daffin, 2024).

Bipolar disorder and related disorders are a group of disorders in which mania is the defining feature. **Mania** is a state of extreme elation and agitation. When people experience mania, they may become extremely talkative, behave recklessly, or take on many tasks simultaneously.¹

Bipolar disorders are diagnosed based on the presence of manic or hypomanic episodes (APA, 2022; Bridley & Daffin, 2024). Bipolar I requires at least one manic episode, characterized by abnormal, persistent mood elevation or irritability lasting nearly all day, every day, for at least a week. Bipolar II is diagnosed when only less severe *hypomanic* episodes occur for at least 4 days. A manic episode might be preceded and/or followed by a major depressive episode. Bipolar I disorder afflicts 1.5% and bipolar II disorder afflicts 0.8% of the U.S. population.

Neural Mechanisms Underlying Depression

Brain Activity. Depression involves an overall reduction in brain activity, and some parts of the brain are more affected than others. In brain-imaging

1. This section contains material adapted from: Spielman, R. M., Jenkins, W. J., & Lovett, M. D. (2020). 15.7 Mood and Related Disorders. In Psychology 2e. OpenStax. Access for free at <https://openstax.org/books/psychology-2e/pages/15-7-mood-and-related-disorders> License: CC BY 4.0 DEED.

studies using PET scans, people with depression display abnormally low activity in the **prefrontal cortex**, a brain region involved in cognitive control, decision-making, planning, and emotion regulation.

Abnormal activity in the prefrontal cortex, especially in its lateral, orbitofrontal, and ventromedial regions, often correlates with the severity of the depression. The **lateral prefrontal cortex** is involved in cognitive control—directing attention, inhibition, and working memory to perform a task. The **orbitofrontal cortex** is involved in decision-making and reward valuation, crucial for delaying gratifications to obtain long-term benefits. The **ventromedial prefrontal cortex** is involved in several social and emotional processes such as regulating negative emotions and processing of self-relevant information. Disruption of these brain regions contributes to hallmark characteristics of mood disorders, including impaired concentration, poor decision-making, increased self-focus and negative affect.

Some research shows that *left* prefrontal activity is associated with positive feelings. The left prefrontal cortex is thought to inhibit negative emotions generated by limbic structures like the **amygdala**, which are overly active in people with depression. Patients who respond to antidepressants show reduced amygdala overactivity; whereas continuing amygdala overactivity despite treatment often predicts depression relapse.

Genetics. Genetics contributes to depressive disorders. Heritability for depressive disorders is about 40% and the risk of developing depression when a family member has had depression is 1.5-3 times higher than the general population (Fan et al., 2020; Kendler et al., 2009). Nevertheless, depressive disorders are still thought to arise from complex gene-environment interactions.²

2. This section contains material adapted from: Duboc, B. (2002). The Brain from Top to Bottom. Mental Disorders: Depression and Manic Depression: Parts of the Brain That Slow

Brain Chemistry. Mood disorders are associated with abnormal levels of certain neurotransmitters, particularly serotonin and norepinephrine (Thase, 2009). These neurotransmitters regulate bodily functions often disrupted in mood disorders, including appetite, sex drive, sleep, arousal, and mood. Low activity levels of serotonin and norepinephrine have long been documented as contributing factors to developing depressive disorders. This relationship was discovered accidentally in the 1950s when monoamine oxidase inhibitors (MAOIs) (which increase available serotonin and norepinephrine) were given to tuberculosis patients, and miraculously, their depressive moods also improved (Bridley & Daffin, 2024). While these neurotransmitters are involved in depression and can be targeted to reduce symptoms, the exact mechanisms are still under investigation.

Treatments for Depressive Disorders

Pharmacology. Major Depressive Disorder is among the most frequent and debilitating psychiatric disorders, so research on treatments is extensive. Antidepressants, such as selective serotonin reuptake inhibitors (SSRIs), are often the most common first-line attempt at treatment for MDD. As their name indicates, SSRIs block the reuptake of serotonin into the presynaptic cell. This action maintains higher levels of serotonin in the synapse, potentially reducing depressive symptoms (Figure 3). However, while serotonin levels can rise within an hour after taking an SSRI, it

typically takes several weeks for SSRIs to actually improve symptoms.³ Although their exact mechanism of action is unclear, SSRIs are commonly prescribed due to their effectiveness and relatively mild side effects. However, other drug classes, including tricyclics and MAOIs, can also be effective in treating depression.

3. This section contains material adapted from: Gershon, A. & Thompson, R. (2024). Mood disorders. In R. Biswas-Diener & E. Diener (Eds.), Noba textbook series: Psychology. Champaign, IL: DEF publishers. Retrieved from <http://noba.to/aqy9rsxe> License: CC BY-NC-SA 4.0 DEED

Synapse

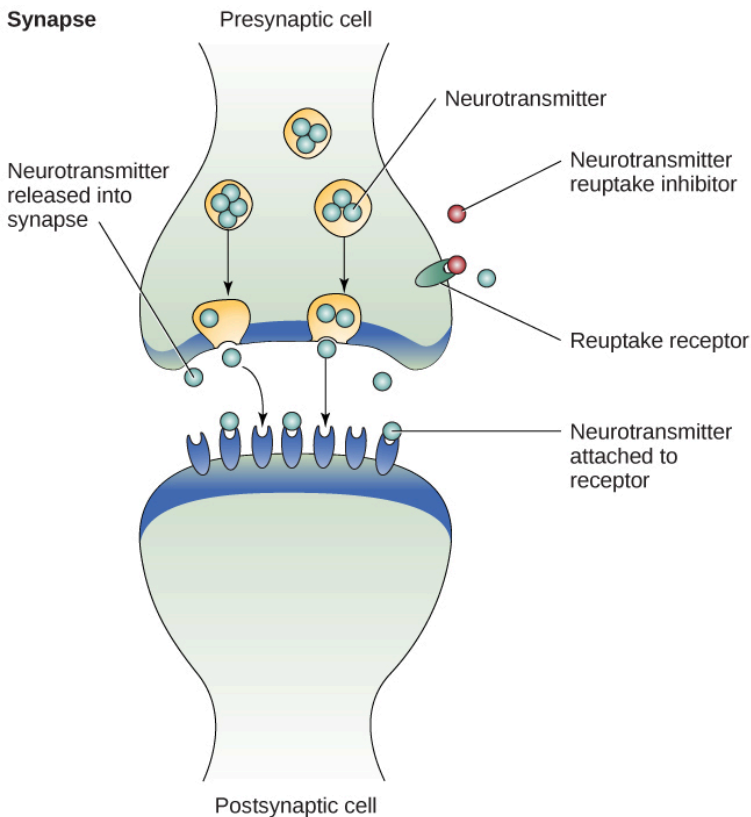


Figure 3. Many medications designed to treat mood disorders work by altering neurotransmitter activity in the neural synapse. Selective serotonin reuptake inhibitors (SSRIs), for example, inhibit the reuptake of serotonin back into the presynaptic cell, which preserves high levels of serotonin in the synapse.

Tricyclic antidepressants are like SSRIs in that they work by altering the number of neurotransmitters available for neurons. More specifically, they block the absorption or reuptake of serotonin and norepinephrine, thus increasing their availability for postsynaptic neurons.

Monoamine oxidase inhibitors (MAOIs) also work by increasing the available neurotransmitters. In basic terms, monoamine oxidase is released

in the brain to remove excess norepinephrine, serotonin, and dopamine. MAO *inhibitors* essentially block the monoamine oxidase from removing these neurotransmitters, thus resulting in an increase in these brain chemicals, which are all involved with depressive symptoms (Shulman, Herman & Walker, 2013).

Psychotherapy—Cognitive Behavior Therapy (CBT). While we focus more on biomedical-related approaches in this biopsychology book, psychotherapy approaches, such as CBT are common and effective treatments for MDD. Cognitive Behavioral Therapy (CBT) focuses on the interconnected cognitive triangle of cognitions (thoughts), behaviors, and emotions. CBT aims to improve mood by modifying maladaptive thoughts and behaviors through various cognitive and behavioral interventions. CBT generally follows four phases of treatment:

- Phase 1: Increasing pleasurable activities.
- Phase 2: Challenging automatic, negative thoughts that can maintain depressive symptoms.
- Phase 3: Identifying negative thoughts as they arise. This helps the patient see how their thoughts contribute to their disorder.
- Phase 4: Changing thoughts. The final stage involves challenging the negative thoughts and replacing them with positive thoughts.

Brain Stimulation. For some people with depression, medications and psychotherapy don't work. In cases of "treatment-resistant depression" (defined as at least two unsuccessful trials with antidepressant pharmacotherapy), several other treatment options can be effective.

Electroconvulsive therapy (ECT) involves electrically stimulating the brain of an anesthetized patient in a hospital setting. Electrodes placed on the head pass electrical currents through the brain to induce a seizure (Figure 4). ECT is very effective in treating depression—one meta-analysis showed major decreases in depression symptoms with remission rates around 50% (Dierckx et al., 2012) and ECT may be more effective than drug therapy (UK ECT Review Group, 2003). ECT's mechanisms of

action are not well understood, but ECT alters neurotransmitter levels (e.g., increased excitatory glutamate) and its effects could stem from disrupting and rewiring neural circuits (Ousdal et al., 2022). Electroconvulsive therapy does have some side effects, such as short-term memory impairments, but is generally safe and well-tolerated (Semkovska & McLoughlin, 2010). Finally, ECT is considered one of the safer treatment options for severely depressed pregnant women in terms of fetal impact (Pompili et al., 2014).



Figure 4. An illustration depicting electroconvulsive therapy, showing an anesthetized patient with electrodes attached to his head.

More invasive than ECT, **Deep Brain Stimulation (DBS)** uses electrodes implanted in the brain to disrupt limbic-cortical circuits and can effectively treat depression (Mayberg et al., 2005). Less invasively, **repetitive transcranial magnetic stimulation (rTMS)** uses repetitive pulses of magnetic stimulation over the scalp to depolarize underlying neurons in the prefrontal cortex. This modulates neural circuitry involved in emotion regulation and depressive symptoms, and has been shown to be a safe and effective way to treat depression in an outpatient setting (McClintock et al., 2017).

Psychedelic-assisted therapy. Another promising approach for treatment-resistant depression is psychedelic-assisted therapy, which combines psychotherapy with the use of psychedelic substances like LSD

or psilocybin. This method aims to induce altered states of consciousness to facilitate therapeutic breakthroughs. In treating depression, these substances may help patients gain new perspectives on their lives, break negative thought patterns, increase emotional responsiveness, and induce neuroplasticity. Sessions are conducted in controlled settings with a trained professional, and typically involve preparation, the psychedelic experience itself, and integration therapy afterward. Studies show promising results for treatment-resistant depression, with many patients showing significant and lasting improvements after a single psychedelic session (This contrasts with typical antidepressant treatments, which often involve years of continuous use). (Carhart-Harris et al., 2021; Goodwin et al., 2022; Nutt & Carhart-Harris, 2020; Voineskos et al., 2020).

In sum. Major depressive disorder has a variety of effective treatment options. Research has shown that psychopharmacological interventions are more effective in rapidly reducing symptoms, while psychotherapy, or combined pharmacological and therapy approach, is more effective in establishing long-term relief of symptoms. For cases of treatment-resistant depression, other treatment options, including brain stimulation and psychedelic-assisted therapy can be effective.⁴

Neural Mechanisms Underlying Bipolar Disorders

Research on the cause, course, and treatment of **bipolar disorders** (BD) have made major advances, but the mechanisms underlying episode onset and relapse remain poorly understood. BD has biological causes and is

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highly heritable (McGuffin et al., 2003). High heritability may suggest that BD is fundamentally a biological phenomenon. However, the course of BD varies greatly both within a person over time and across people (Johnson, 2005). For those with genetic vulnerability, psychosocial factors can trigger episodes (Johnson et al., 2008; Malkoff-Schwartz et al., 1998). Recent findings suggest bipolar disorders and schizophrenia have similar brain and genetic profiles, potentially aligning bipolar more closely with psychotic disorders than depression (Birur et al., 2017; Lichtenstein et al., 2009).

Biological explanations of bipolar disorder have centered on brain function. Many fMRI studies of BD focus on emotional processing, reflecting the view that BD is primarily an emotional disorder (APA, 2000). Findings show that regions of the brain involved in emotional processing are activated differently in people with BD relative to healthy controls (Altshuler et al., 2008; Hassel et al., 2008; Lennox et al., 2004). However, emotional brain-response studies in BD patients yield inconsistent results. The variability stems from testing participants in different illness phases (manic, depressed, inter-episode), small sample sizes, and lab stimuli that may not elicit a sufficiently strong brain response.

In terms of psychosocial factors in bipolar, research has focused on the environmental contributors. Environmental stressors, particularly severe stressors (e.g., loss of a significant relationship), can adversely impact the course of BD. Following a severe life stressor, people with BD have increased risk of relapse (Ellicott et al., 1990) and suffer more depressive symptoms (Johnson et al., 1999). Interestingly, positive life events can also adversely impact the course of BD. After attaining a desired goal, people with BD can suffer more manic symptoms (Johnson et al., 2008). Such findings suggest that people with BD may have a hypersensitivity to rewards.

Due to the close relationship between depression and bipolar disorder, researchers initially believed that bipolar disorder involved low levels of norepinephrine and serotonin. However, it is now believed that low levels

of serotonin and *high levels* of norepinephrine may explain mania episodes (Soreff & McInnes, 2014).

Treatment of Bipolar Disorder

Treatment for bipolar disorder is debated. One approach uses mood stabilizers like Lithium or Depakote. These mood stabilizers are less potent at treating depressive symptoms, so are sometimes combined with antidepressants if necessary. The alternative is using newer antidepressants early without mood stabilizers, but this lacks strong research support and risks triggering manic episodes in bipolar patients. Consequently, mood stabilizers, especially Lithium, remain the primary treatment for bipolar disorder (Bridley & Daffin, 2024). Lithium affects neuronal activity by decreasing excitatory (dopamine and glutamate) neurotransmission while increasing inhibitory (GABA) neurotransmission, along with other compensatory neurotransmitter changes to achieve homeostasis (Malhi et al., 2013).

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12.4: ANXIETY

What is **anxiety**? Most of us feel some anxiety almost every day of our lives. Maybe you have an important upcoming test, presentation, big game, or date. Anxiety can be defined as a negative mood state that is accompanied by bodily symptoms such as increased heart rate, muscle tension, a sense of unease, and apprehension about the future (APA, 2013; Barlow, 2002) (**Figure 5**).

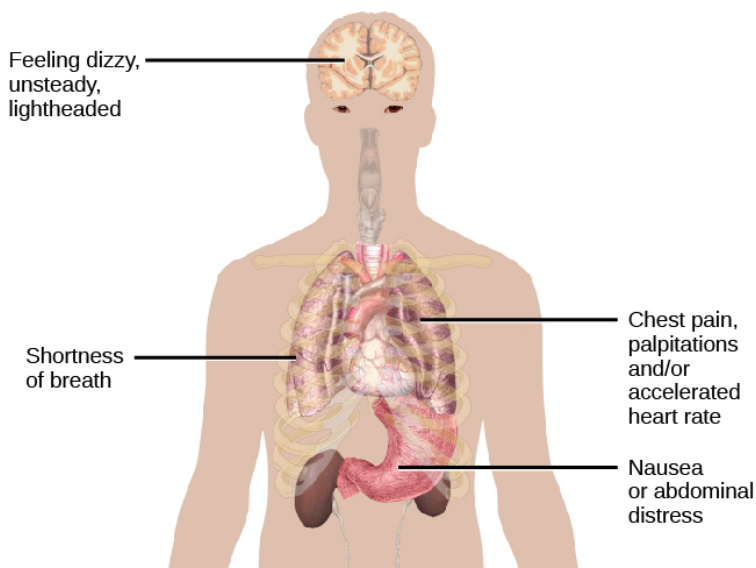


Figure 5. Common physical symptoms of anxiety are feeling dizzy, unsteady, and lightheaded; shortness of breath; chest pain, palpitations and/or accelerated heart rate; and nausea or abdominal distress. People may also experience sweating, trembling, feelings of faintness, or a fear of losing control, among other symptoms.

Anxiety disorders are characterized by excessive and persistent fear and anxiety, and by related disturbances in behavior (APA, 2013). While anxiety is universally experienced, anxiety disorders cause considerable distress. Anxiety disorders are common: approximately 25–30% of the U.S. population meets the criteria for at least one anxiety disorder during their lifetime (Kessler et al., 2005). Anxiety disorders affect more women than men; within a 12-month period, about 23% of women and 14% of men will experience an anxiety disorder (National Comorbidity Survey, 2007). Anxiety disorders are the most frequently occurring class of mental disorders and are often comorbid with each other and with other mental disorders (Kessler et al., 2009).¹

While all anxiety disorders are characterized by excessive fear, anxiety, or avoidance behavior, they differ from one another in the types of objects or situations that provoke these responses (Bridley & Daffin, 2024). Some common anxiety disorders are:

- Generalized anxiety disorder (GAD)—an underlying excessive worry related to a wide range of events or activities and an inability to control that worry.
- Specific phobia—fear or anxiety specific to an object or a situation (e.g., animals, heights, water, needles, airplanes, elevators).
- Agoraphobia—intense fear of public situations or places where escape seems difficult
- Social anxiety disorder—fear or anxiety related to social situations,

1. This section contains material adapted from: Barlow, D. H. & Ellard, K. K. (2024). Anxiety and related disorders. In R. Biswas-Diener & E. Diener (Eds.), Noba textbook series: Psychology. Champaign, IL: DEF publishers. Retrieved from <http://noba.to/xms3nq2c> License: CC BY-NC-SA 4.0 DEED – Spielman, R. M., Jenkins, W. J., & Lovett, M. D. (2020). 15.4 Anxiety Disorders. In Psychology 2e. OpenStax. Access for free at <https://openstax.org/books/psychology-2e/pages/15-4-anxiety-disorders> License: CC BY 4.0 DEED.

especially when evaluation by others is possible

- Panic disorder—series of unexpected panic attacks coupled with the fear of future panic attacks

Neural Mechanisms Underlying Anxiety Disorders

Anxiety disorders are associated with genetic factors and abnormalities in brain circuits that regulate and process emotion. Family and twin studies indicate that anxiety disorders have a moderate genetic heritability (~30-40%; making it less heritable than schizophrenia or bipolar disorder) (Hettema et al., 2001). Over 200 genes link to anxiety disorders, with distinct gene clusters for subtypes like generalized anxiety disorder, social anxiety disorder, and panic disorder. The identified genes are expressed in brain regions linked to anxiety and emotion processing, such as the basal ganglia, hippocampus, and amygdala (Karunakaran & Amemori, 2023).

The brain circuits underlying anxiety involve bottom-up signals from the amygdala that indicate the presence of potentially threatening stimuli, and top-down control mechanisms from the prefrontal cortex that signal the emotional salience of stimuli (Nuss, 2015). The amygdala is involved in triggering panic attacks through its **central nucleus**, which connects with brain structures (e.g. in the brainstem), that control autonomic functions such as respiration and heart rate. Animal studies have shown that electrically or pharmacologically stimulating the amygdala's central nucleus produces behaviors associated with panic (Herdade et al., 2006). People with an anxiety disorder show hyperactive amygdala response to stimuli (Etkin & Wager, 2007). These bottom-up signals from the amygdala might be over-indicating the presence of potentially threatening stimuli. "Top-down" control originating from prefrontal areas can inhibit the amygdala to regulate emotion. However, people with anxiety disorders show reduced prefrontal activation (Etkin, 2010), and they require more prefrontal activation to successfully reduce negative emotions (Nuss, 2015).

Treatments of Anxiety Disorders

Research examining the role of neurotransmitters in anxiety-related circuits has focused largely on GABA, the primary inhibitory neurotransmitter in the brain that reduces neuronal excitability. Insufficient GABAergic inhibition of neurons might drive the amygdala hyperactivity seen in anxiety disorders. Therefore GABA receptors are a primary target for anti-anxiety medication. In animal studies, injecting GABA agonists (activators) into the amygdala (thereby activating the inhibitory neurons) decreased measures of fear and anxiety (Sanders & Shekhar, 1995). GABA receptors are modulated by drugs called benzodiazepines, such as well-known brand names like Valium, Xanax, and Ativan. Benzodiazepines bind to the GABA_A receptors, which causes an influx of chloride (Cl^-) ions. The increase of negative chloride ions hyperpolarizes the neuron's membrane potential, thereby inhibiting it and making it less likely to fire. Through enhanced neuronal inhibition, benzodiazepines reduce amygdala reactivity to aversive stimuli and anxiety (Del-Ben et al., 2012).

Benzodiazepines were the primary anxiety treatment for decades. However, due to addiction risk and limited long-term efficacy, they're now recommended only for short-term use (2-4 weeks). While GABA is an important target for modulating anxiety response in the amygdala, other neurotransmitters such as serotonin, endocannabinoids, and oxytocin, are also important. Current treatment guidelines for anxiety disorders now recommend antidepressants, including serotonin reuptake inhibitors (SSRIs) or serotonin–noradrenaline reuptake inhibitors (SNRIs) (Nuss, 2015).

Cognitive behavioral therapy (CBT) is a well-established non-pharmacological treatment for anxiety disorders and can reduce amygdala hyperactivation (Straube et al., 2006). Finally, even placebos have been shown to decrease anxiety; when individuals thought they received an anti-anxiety drug, some showed a lower anxiety response to emotional pictures. Their placebo response was associated with decreased amygdala activation,

as well as increased activation in a modulatory system including the anterior cingulate and the prefrontal cortex (Petrovic et al., 2005). In sum, irrespective of the technique, reducing activity in the amygdala or increasing activity in emotion-regulating circuits can decrease anxiety. Ongoing research seeks to optimize how these networks can be targeted to manage anxiety.

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12.5:

OBSESSIVE-COMPULSIVE AND RELATED DISORDERS

Obsessive-compulsive and related disorders are a group of overlapping disorders that generally involve intrusive, unpleasant thoughts or repetitive behaviors. Many of us experience unwanted thoughts from time to time (e.g., craving double cheeseburgers when dieting), and many of us engage in repetitive behaviors on occasion (e.g., pacing when nervous). However, obsessive-compulsive and related disorders are characterized by intrusive thoughts and repetitive behaviors that are so intense they significantly disrupt daily life. Included in this category are obsessive-compulsive disorder (OCD), body dysmorphic disorder, and hoarding disorder.¹

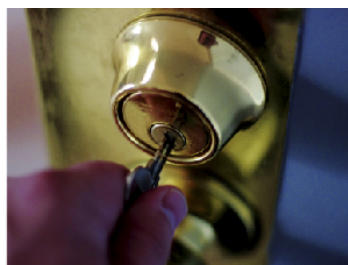
OCD involves time-consuming (>1 hour daily) obsessions, compulsions, or both, unrelated to substance use, a medical condition, or another mental disorder (APA, 2013). Obsessions are more severe than fleeting unwanted thoughts or routine worries. Obsessions are persistent, unintentional, and unwanted thoughts and urges that are highly intrusive, unpleasant, and distressing (APA, 2013). Common obsessions include concerns about germs and contamination, doubts (“Did I turn the water off?”), order and symmetry (“I need all the spoons in the tray to be arranged a certain way”), and aggressive or lustful urges. The individual typically

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recognizes that these thoughts and urges are irrational and attempts to suppress or ignore them, but finds it extremely difficult to do so. Obsessive symptoms can overlap, such as combined contamination and aggressive obsessions (Abramowitz & Siqueland, 2013).



(a)



(b)

Figure 6. (a) Repetitive hand washing and (b) checking (e.g., that a door is locked) are common compulsions among those with obsessive-compulsive disorder.

Compulsions are repetitive and ritualistic acts performed mainly to reduce distress caused by obsessions or prevent feared events (APA, 2013). Compulsions often include such behaviors as extensive hand washing, cleaning, checking (e.g., that a door is locked), and ordering (e.g., lining up all the pencils in a particular way), and they also include such mental acts as counting or reciting something to oneself (**Figure 6**). Compulsions in OCD aren't pleasurable or realistically connected to the source of distress or feared event. A cycle of obsessive thoughts, anxiety, compulsions, and temporary relief deeply affects individuals with OCD (**Figure 7**). Approximately 2.3% of the U.S. population will experience OCD in their lifetime (Ruscio et al., 2010) and, if left untreated, OCD tends to be a

chronic condition creating lifelong interpersonal and psychological problems (Norberg et al., 2008).²

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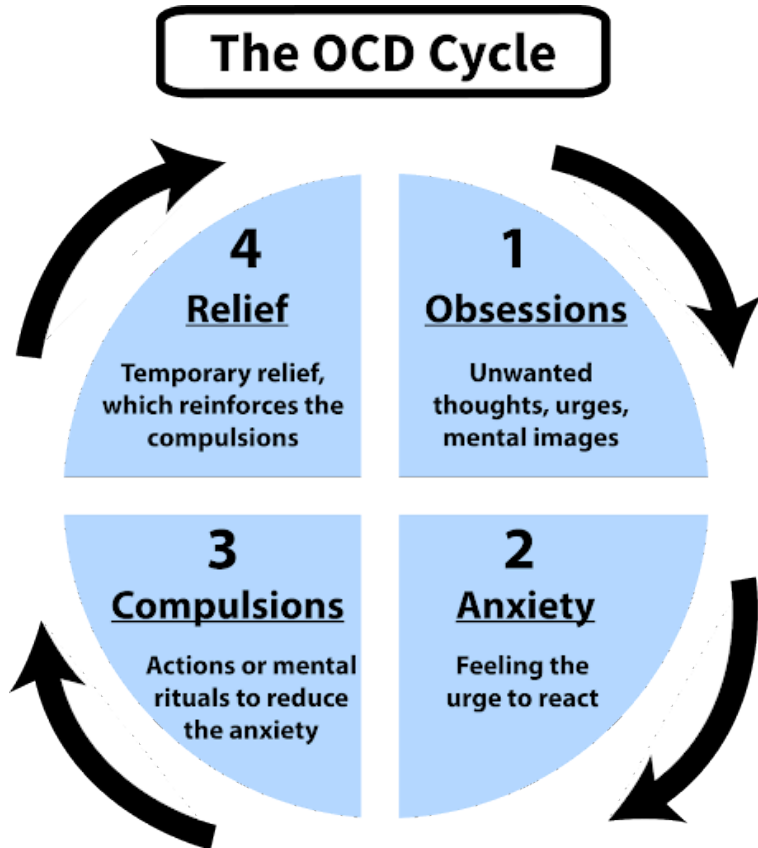


Figure 7. Visualizing the typical cycle of obsessive-compulsive disorder.
[Image adapted from: <https://psychcentral.com/ocd/ocd-cycle>].

Body Dysmorphic Disorder. Similar to OCD, **body dysmorphic disorder** involves an obsession with a *perceived* flaw in physical appearance that is nonexistent or barely noticeable to other people (APA, 2013). Individuals believe they are unattractive or deformed, and typically focus on skin, face, or hair. This preoccupation with imagined physical flaws leads to repetitive behaviors and thoughts like excessive mirror-checking, hiding the perceived flaw, comparing with others, and sometimes seeking cosmetic surgery (Phillips, 2005). About 2.4% of U.S. adults meet the criteria for

body dysmorphic disorder, with slightly higher rates in women than in men (APA, 2013).³

Hoarding Disorder. Once considered a symptom of OCD, hoarding is now recognized as a distinct disorder (Mataix-Cols et al., 2010). People with **hoarding disorder** compulsively keep possessions, regardless of value, cluttering living spaces to dysfunctional levels. Excessive clutter often prevents people from using their kitchen or sleeping in their bed. People with this disorder struggle to discard items, believing the items might be useful later or due to sentimental attachment (APA, 2013). A diagnosis of hoarding disorder requires that hoarding isn't caused by another medical condition or disorder (e.g., schizophrenia). (APA, 2013).⁴

Neural and Genetic Mechanisms Underlying Obsessive-Compulsive and Related Disorders

Genetics. The results of family and twin studies suggest that OCD has a moderate genetic component. The disorder is five times more frequent in first-degree relatives of people with OCD (Nestadt et al., 2000). Additionally, the concordance rate of OCD is 57% for identical twins and 22% for fraternal twins (Bolton et al., 2007). Studies have implicated about

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two dozen potential genes involved in OCD; these genes regulate the function of three neurotransmitters: serotonin, dopamine, and glutamate (Pauls, 2010).

Brain regions involved in OCD. A key brain region implicated in OCD is the orbitofrontal cortex (Kopell & Greenberg, 2008) (**Figure 8**). In individuals with OCD, the orbitofrontal cortex becomes hyperactive when exposed to triggering stimuli, such as images of unclean toilets or asymmetrically hung pictures (Simon et al., 2010). The orbitofrontal cortex is a region in the “OCD circuit” that, collectively, influences the perceived emotional value of stimuli and the selection of behavioral and cognitive responses (Graybiel & Rauch, 2000). As with the orbitofrontal cortex, other regions of the OCD circuit (e.g., dorsolateral prefrontal cortex, precuneus, and left superior temporal gyrus) show heightened activity during symptom provocation (Rotge et al., 2008). These findings suggest that abnormalities in these regions may contribute to OCD symptoms (Saxena et al., 2001). Consistent with this network explanation, people with OCD show substantially higher connectivity of the orbitofrontal cortex with other regions of the OCD circuit (Beucke et al., 2013).

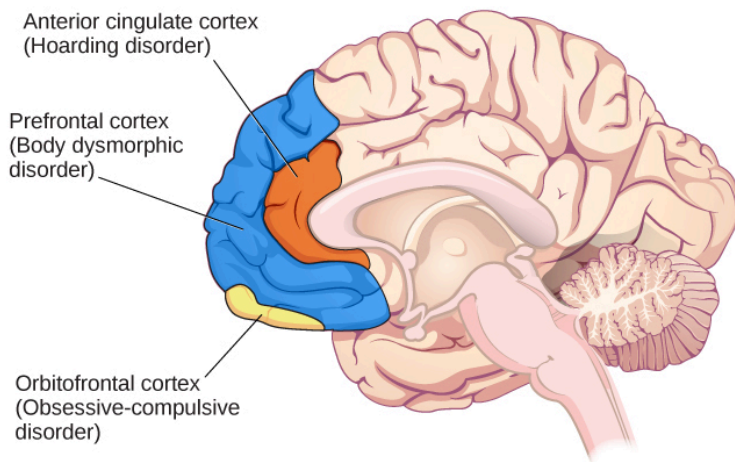


Figure 8. Different regions of the brain are associated with obsessive-compulsive disorder and related disorders. For example, the anterior cingulate cortex for hoarding disorder; the prefrontal cortex for body dysmorphic disorder; and the orbitofrontal cortex for obsessive-compulsive disorder.

Neuroimaging studies have also highlighted the role of the prefrontal cortex in OCD and body dysmorphic disorder. Individuals with body dysmorphic disorder often abnormally perceive body areas. An fMRI study showed that when people with body dysmorphia viewed faces, they had abnormal prefrontal cortex activity, which may be associated with the perceptual distortions seen in body dysmorphic disorder (Feusner et al., 2007).

These neuroimaging findings highlight the importance of brain dysfunction in OCD and body dysmorphic disorder. However, neuroimaging approaches are limited by their inability to explain differences in obsessions and compulsions, and correlations between brain abnormalities and OCD symptoms are not evidence of causality (Abramowitz & Siqueland, 2013).

Treatments of OCD

Several approaches are commonly used to treat OCD. One effective treatment is a form of Cognitive Behavioral Therapy called exposure and response prevention. In therapy sessions, individuals with OCD are gradually exposed to situations or objects designed to mildly provoke their obsessions in a safe environment. They are instructed to avoid their compulsive responses. Eventually, the high anxiety situations become less anxiety-provoking and more manageable. Exposure and response is also very effective with panic disorder (which is an anxiety disorder). Cognitive Behavioral Therapy is often used in conjunction with pharmacological treatments for OCD. Selective serotonin reuptake inhibitors (SSRIs) are used to treat OCD, but often at higher doses than are used to treat depression. Finally, OCD can be treated effectively with brain stimulation, including both non-invasive techniques like transcranial magnetic stimulation that uses magnetic pulses to stimulate the prefrontal cortex (Trevizol et al., 2016), and invasive techniques like deep brain stimulation that requires surgically implanting a device deep in the brain that can modulate activity in the OCD brain circuit (Alonso et al., 2015).⁵

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12.6: POST-TRAUMATIC STRESS DISORDER

Experiencing extremely stressful or traumatic events, such as combat, crimes, and natural disasters, increases the risk of developing psychological disorders such as **post-traumatic stress disorder (PTSD)**. A diagnosis of PTSD requires that the individual must be exposed to actual or threatened death, serious injury, or sexual violence. This strict diagnostic criterion differs from a common misperception that PTSD could stem from lesser stressors, like an upsetting but non-violent romantic breakup. PTSD symptoms include intrusive memories and flashbacks, avoidance of trauma-related stimuli, persistent negative emotions (e.g., fear, anger, guilt, shame), detachment, irritability, outbursts, and an exaggerated startle response (jumpiness). For PTSD to be diagnosed, these symptoms must occur for at least one month.

Roughly 6% of adults in the United States experience PTSD in their lifetime, with rates about twice as high in women than in men (Goldstein et al., 2016; Olf, 2017). Higher rates occur among people exposed to mass trauma and whose jobs involve duty-related trauma exposure (e.g., police officers, firefighters, and emergency medical personnel) (APA, 2013). Nearly 21% of residents of areas affected by Hurricane Katrina had PTSD one year following the hurricane (Kessler et al., 2008), and 12.6% of Manhattan residents were observed as having PTSD 2–3 years after the 9/11 terrorist attacks (DiGrande et al., 2008).

Neural Mechanisms Underlying

Post-Traumatic Stress Disorder

Both the hippocampus and amygdala are involved in emotional processing and are linked to PTSD (**Figure 9**). Individuals with PTSD show reduced volume of several parts of the **hippocampus**, which may result from decreased levels of neurogenesis and dendritic branching (the generation of new neurons and the generation of new dendrites in existing neurons, respectively) (Wang et al., 2010). After effective pharmacological treatment or cognitive-behavioral therapy for PTSD, hippocampus size increases (Bremner & Vermetten, 2004; Levy-Gigi et al., 2013).

Recent work highlights how threat reactivity, the hippocampus, and arousal-related **norepinephrine** (NE) release may interact to shape PTSD severity. Prior work highlights how threat reactivity (i.e., how someone responds to threat-related stressors) is heightened in PTSD. Research in both animals and humans indicates that norepinephrine, a hormone released in response to stress, is associated with abnormal threat reactivity in PTSD (Naegeli et al., 2018; Southwick et al. 1999). Critically, threat alters hippocampal functioning, and a reliable neural signature of PTSD is reduced hippocampal activity during states of threat (Eichenbaum, 2001; Hayes et al., 2011). To clarify how threat may disrupt hippocampal functioning, a recent review proposed that threat-induced arousal increases norepinephrine release, which redirects information processing away from the hippocampus to emotional memory structures like the amygdala (Clewett & Murty, 2019).

The [Advanced Understanding of Recovery after trauma \(AURORA\) study](#) is a multi-site study tracking brain and cognitive development in trauma patients for one year after an emergency department visit (McClean et al., 2020). This landmark effort will generate a comprehensive collection of brain, biospecimen, and behavioral measures to characterize trauma-related disorders, such as PTSD.

One AURORA study (Tanriverdi et al., 2022) examined the relationship between threat reactivity, hippocampus function,

norepinephrine systems, and PTSD symptoms. Participants with more severe PTSD symptoms showed weaker hippocampal responses to threat; that link was especially strong in those with greater fear-based startle responses (a marker of arousal-related norepinephrine release). This suggests excessive threat-induced arousal may divert processing from the hippocampus. These findings highlight the interplay between threat reactivity, arousal, and hippocampal function in how PTSD may or may not emerge after exposure to trauma. Finally, whether or not PTSD emerges after trauma is also influenced by genetics, as genes play an important role in the fear and stress circuitry (Banerjee et al., 2017).

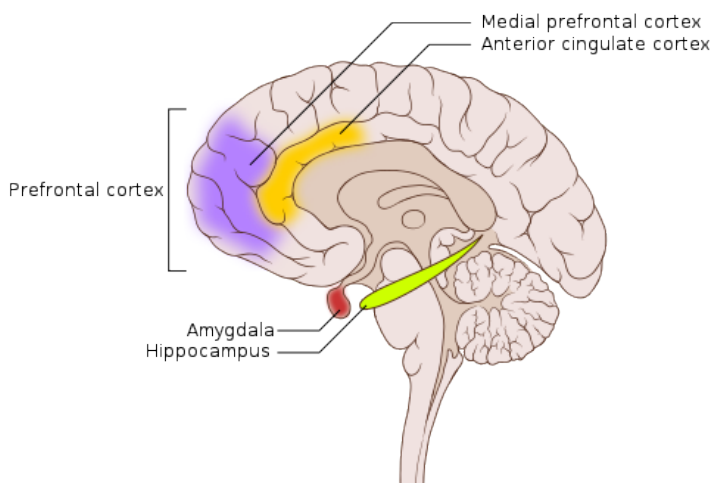


Figure 9. Brain regions typically associated with post-traumatic stress disorder include the prefrontal cortex, hippocampus, cingulate cortex, and amygdala.

PTSD Treatments

Several treatment approaches are available to alleviate the symptoms of

PTSD (Bridley & Daffin, 2024). Treatment usually starts with a psychotherapeutic intervention, such as:

- Psychological debriefing, wherein individuals who experienced a traumatic event discuss or process their thoughts within 72 hours of the event.
- Cognitive Behavioral Therapy (CBT) works by identifying and challenging the negative cognitions (thoughts) surrounding the traumatic event and replacing them with positive, more adaptive cognitions.
- Exposure Therapy involves a therapist exposing the individual to cues or situations associated with their traumatic memory, then having them use positive coping strategies such as relaxation techniques to reduce their feelings of distress. Exposure therapy, originally developed for anxiety disorders, has proven effective in treating PTSD by helping patients extinguish fears associated with traumatic events. The main types of exposure techniques are *imaginal* (mentally recreating the trauma), *in vivo* (using tangible reminders, such as videos or images), and *flooding* (immediate exposure to most distressing elements). While *imaginal* and *in vivo* exposures follow a gradual approach, *flooding* presents the most distressing memories upfront, potentially risking higher dropout rates. Some research indicates that combining exposure therapy with propranolol drug administration during memory retrieval can weaken the emotional aspects of traumatic memories (“reconsolidation interference” as discussed in the memory chapter) (Brunet et al., 2008; Beckers & Kindt, 2017).
- Eye Movement Desensitization and Reprocessing (EMDR) combines components of CBT and exposure therapy with lateral eye movements following a therapist’s finger movements. The eye movements are thought to accelerate information processing and the adaptive resolution of traumatic memories (Shapiro & Maxfield, 2002).

When psychotherapy does not produce relief from symptoms, psychopharmacology interventions are an effective second line of treatment and may include SSRIs, MAOIs, and tricyclic antidepressants.¹ Finally, recent research on psychedelic-assisted therapy, including treatments using MDMA (aka “ecstasy” or “molly”), psilocybin, and ketamine, has shown promise in effectively treating PTSD. In light of promising research, the U.S. Food and Drug Administration awarded MDMA “breakthrough therapy status” to fast-track studies on MDMA treatments of PTSD (Krediet et al., 2020; Mitchell et al., 2023).

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12.7: CONCLUSION

The biological perspective links psychological disorders to biological factors, such as genetics, chemical imbalances, and brain abnormalities (Spielman et al., 2020). Widespread evidence indicates that most psychological disorders have a genetic component. Researchers search for specific genes, genetic mutations, and epigenetic markers that contribute to mental disorders; these may be targeted in future genetic-based therapies (Davidson et al., 2022). Neuroimaging has revealed that abnormalities in brain structure and function are directly involved in many disorders. Progress in neuroimaging technology will continue to improve our understanding of psychological disorders. Advances in understanding neurotransmitters and hormones have yielded insights into their role in psychological disorders, and guide pharmacological treatment approaches.

Over the past decades, biological-based research has made incredible strides in understanding psychological disorders and informing treatment. However, biological markers are generally not reliable enough yet to be useful for clinicians in diagnosing disorders (Abi-Dargham et al., 2023).

In this chapter, we largely focused on pharmacological treatments, but many treatment approaches are effective. In addition to psychotherapy in its various forms, other effective treatment approaches include deep brain stimulation to treat depression, as well as yoga, music therapy, and exercise, as interventions to alleviate symptoms of anxiety. As biological, psychological, and sociocultural factors all contribute to psychopathology, it only makes sense that effective treatment approaches take various forms.

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12.8: DISCUSSION QUESTIONS AND RESOURCES

Discussion Questions

1. What are the formal criteria that indicate the existence of a psychological disorder?
2. What are the four components of the Version III dopamine hypothesis in schizophrenia?
3. How might symptoms of OCD be related to abnormal brain function?
4. How may PTSD symptoms relate to hippocampal functioning in PTSD?

Outside Resources

Video: 5-minute TED Talk: [The Psychology of PTSD](#)

Video: 2-minute Neuroscience: [Obsessive-Compulsive Disorder](#)

Video: 2 minute walk-through on [Early Neural Development](#)

Video: TED Talk: [Toward a new understanding of mental illness](#)

Video: [Five psychological disorders share some of the same genes](#)

12.9: REFERENCES

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For more information about the ROTEL Project, please visit our [project website](#).

VOCABULARY

5 α -reductase

An enzyme required to convert testosterone to 5 α -dihydrotestosterone.

action potential

A transient all-or-nothing electrical current that is conducted down the axon when the membrane potential reaches the threshold of excitation.

activational effects

Physiological and behavioral responses that are reversible and short-lived, occurring in adulthood

adoption study

A behavioral genetic research method that involves the comparison of adopted children to their adoptive and biological parents.

adult neurogenesis

The process in which new neurons are generated in the adult brain.

affect

An emotional process that includes moods, subjective feelings, and discrete emotions.

affective neuroscience

The study of how the brain and nervous system process emotions

Afferent

Signals that travel from the periphery *toward* the central nervous system and brain, or travel deeper centrally within the brain

aggregation

The stage of neuronal development after migration where different classes of neurons coalesce to form different nervous system structures.

aggressive behavior

A form of social interaction that includes threat, attack, and fighting.

agonists

A drug that increases or enhances a neurotransmitter's effect

allele

Specific version of a gene

amygdala

Almond-shaped neural structure that is primarily responsible for regulating emotional responses, especially fear.

amyloid plaques

A build-up of misfolded proteins in the brain that play a central role in Alzheimer's disease

antagonists

A drug that blocks a neurotransmitter's effect

anterograde amnesia

Inability to create new declarative memories

anxiety

Intense, excessive, and persistent worry and fear about everyday situations. Linked to heightened physical sensations, such as fast heart rate, rapid breathing, sweating, and fatigue

anxiety disorders

A group of disorders that are characterized by excessive and persistent feelings of intense worry, fear, and dread, as well as physical sensations like increased blood pressure and fast heart rate

Apoptosis

The process of programmed cell death to eliminate unwanted cells.

applied research

Research that can be directly applied to an existing problem

arcuate fasciculus

A fiber tract that connects Wernicke's and Broca's areas

associative learning

Association of a stimulus with a cue such as with classical Pavlovian conditioning or instrumental conditioning

autonomic nervous system

A part of the peripheral nervous system that connects to glands and smooth muscles. Consists of sympathetic and parasympathetic divisions.

axon

Part of the neuron that extends off the soma, splitting several times to connect with other neurons; main output of the neuron.

axons

A long threadlike part of a neuron that carries electrical impulses away from the cell body and to other neurons

basal ganglia

Subcortical structures of the cerebral hemispheres involved in voluntary movement.

basic research

Also known as pure or fundamental research, seeks to expand scientific knowledge and understand the mechanisms of brain function

behavioral genetics

The empirical science of how genes and environments combine to generate behavior.

benign tumors

Tumors that don't spread to other body parts

Bipolar disorder and related disorders

A type of obsessive-compulsive disorder. Characterized by persistent, intense focus and anxiety over perceived body defects and flaws in appearance

bipolar disorders

Characterized by extreme mood swings from depressive lows to manic highs

bisexual

Attraction to two sexes.

body dysmorphic disorder

A class of psychological disorders; characterized by mania as the defining feature

brain stem

Composed of the medulla oblongata, pons, and the midbrain. The part of the brain that connects the cerebrum to the spinal cord.

Brainbow

A genetic technique in which individual neurons can be labeled and mapped using fluorescent proteins.

catatonic behaviors

Subtype of disorganized or abnormal motor behavior; involves significant reductions in voluntary movement and reduced reactivity to environmental stimulation

caudate nucleus

A “C” shaped subcortical structure located near the thalamus that contributes to the formation of the basal ganglia. There is a caudate nucleus located in each cerebral hemisphere.

cell membrane

A bi-lipid layer of molecules that separates the cell from the surrounding extracellular fluid.

cell-adhesion molecules

A subset of cell surface molecules that are involved in the binding of cells with other cells.

central nervous system

The portion of the nervous system that includes the brain and spinal cord.

central nucleus

Spherical cell group located in the amygdala that is primarily responsible for the bodily reactions associated with fear

central sulcus

The major fissure that divides the frontal and the parietal lobes.

cerebellum

The distinctive structure at the back of the brain between the cerebrum and brainstem. Important for muscle control, such as balance and movement.

cerebral aqueduct

Narrow, 15mm, channel that connects the third ventricle with the fourth ventricle and facilitates the transport of cerebrospinal fluid (CSF).

cerebral cortex

The outermost layer of gray matter of the cerebral hemispheres.

cerebral hemispheres

The cerebral cortex, underlying white matter, and subcortical structures.

cerebral peduncles

Two bundles of nerve fibers that are located in the ventral midbrain and connect the cerebrum to the brain stem.

cerebral ventricular system

Interconnected cavities within the brain tissue that produce and secrete cerebrospinal fluid to protect the brain

cerebrospinal fluid

Cerebrospinal fluid is an ultrafiltrate of plasma that surrounds the brain and spinal cord.

cerebrum

Usually refers to the cerebral cortex and associated white matter, but in some texts includes the subcortical structures.

chapter

a section of a book.

chromosomal sex

The sex of an individual as determined by the sex chromosomes (typically XX or XY) received at the time of fertilization.

chromosomes

a long strand of genetic information

cingulate cortex

A medial cortical brain region that is a part of the limbic system and is involved in emotion, motivation, learning, and memory.

consolidation

Making a temporary memory more stable and long-lasting

converging evidence

Similar findings reported from multiple studies using different methods.

corpus callosum

Primary bundle of white matter tracts that connect the left and right cerebral hemispheres.

cortex

In neuroanatomy, cortex refers to a thin sheet of neurons

coup

A brain injury that occurs under the site of impact (coup) and on the side opposite the impact due to the brain moving inside the skull (contrecoup)

Coup and contrecoup

A brain injury that occurs under the site of impact (coup) and on the side opposite the impact due to the brain moving inside the skull (contrecoup)

cranial nerves

A set of 12 paired nerves that emerge directly from the brain and relay information between the brain and parts of the body; primarily to the head and neck regions.

critical periods

A special class of sensitive periods in which the effects of experience have lasting consequences on subsequent brain development. Absence of key experiences may lead to a disrupted course of brain development.

cross-modal plasticity

An adaptive process of the brain, such that loss of one sensory modality induces cortical reorganization that leads to enhanced sensory performance in other sensory modalities.

cytoarchitecture

The study of the cellular composition of the central nervous system's tissues, with a focus on the arrangement, structure, and function of cells.

Declarative memory

Memory that involves remembering events and facts. Also called explicit memory.

deep brain stimulation

implanting electrodes within areas of the brain. The electrodes produce electrical impulses that affect brain activity to treat certain medical conditions.

delusions

False beliefs that are contrary to external reality and are firmly held despite contrary evidence

demyelination

Damage or loss of the myelin sheath surrounding axons in the brain.

dendrite

Part of a neuron that extends away from the cell body and is the main input to the neuron.

dendrites

A branch-like structure of the neuron that extends from the cell body.

deoxyribonucleic acid (DNA)

Helix-shaped molecule made of nucleotide base pairs

dependent variable

The outcome variable that is measured by the researcher. The dependent variable depends on changes of the independent variable.

depressive disorders

A class of mood disorders; marked by a persistent feeling of sadness and loss of interest that causes significant impairments in daily life

Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR)

The current classification system used to diagnose psychological disorders by mental health professionals. Editions of the DSM are typically updated every 5-7 years

diencephalon

Neural structure located deep in the brain that includes the thalamus and hypothalamus. Connects the midbrain to the forebrain.

diffusion

The force on molecules to move from areas of high concentration to areas of low concentration.

Diffusion Tensor Imaging

A variant of Magnetic Resonance Imaging that can non-invasively reveal unique information of white matter microstructures and axonal pathways within the central nervous system.

disorganized or abnormal motor behavior

Prominent feature of Schizophrenia; characterized by extremely disjointed and atypical motor behavior that can cause problems in everyday life, ranging from childlike silliness to unpredictable agitation

disorganized thinking

Prominent feature of Schizophrenia; characterized by a pattern of incoherent and illogical thought processes

dizygotic twins

Twins conceived from two ova and two sperm.

DNA methylation

An epigenetic mechanism wherein a methyl group can tag DNA and activate or repress genes

dominant allele

Allele whose phenotype will be expressed in an individual that possesses that allele

dopamine

Neurotransmitter involved in learning, motivation, and reward. Implicated in schizophrenia

dopamine hypothesis of schizophrenia

An enduring account that suggests a dysregulated dopamine system contributes to symptomatology of schizophrenia; has undergone many iterations

ectoderm

Outermost of the three germ layers in a developing embryo.

efferent

Signals that travel away from the central nervous system or brain to the periphery, such as motor command

electroconvulsive therapy (ECT)

Psychiatric procedure that involves passing electrical currents through the brain to trigger a brief seizure. Effective in treating depression.

Electroencephalography

A neuroimaging technique that measures electrical brain activity via multiple electrodes on the scalp.

electrostatic pressure

The force on two ions with similar charge to repel each other; the force of two ions with opposite charge to attract to one another.

embryo

A growing organism in the initial stages of development after fertilization.

empiricism

A method for acquiring knowledge is one based on observation, including experimentation, rather than a method based only on forms of logical argument or previous authorities.

encoding

The process of initially learning new information

endocrine gland

A ductless gland from which hormones are released into the blood system in response to specific biological signals.

endoderm

Innermost of the three germ layers in a developing embryo.

endogenous

Originating from within an organism. For example, endogenous opioids such as endorphins are produced in the brain.

engram

memory trace, or a hypothetical construct that represents the physical changes in the brain that constitute memory.

enzyme induction

The process by which a drug can enhance the production of an enzyme

enzymes

A protein produced by a living organism that allows or helps a chemical reaction to occur

epidemiology

the branch of medicine that investigates the incidence, causes, and possible control of diseases

epigenome

The genome-wide distribution of epigenetic marks. These marks tell the genome what to do and where and when to do it.

episodic memories

Memory of an autobiographical event (e.g., personal experience)

excitatory postsynaptic potentials

A depolarizing postsynaptic current that causes the membrane potential to become more positive and move towards the threshold of excitation.

falsifiable

A theory or hypothesis is falsifiable (or refutable) if it can be logically contradicted by an empirical test.

feminization

The induction of female traits.

fissure

A deep or large sulcus or valley in the brain

fissures

forebrain

Also referred to as the prosencephalon. The forward most part of the brain. Consists of the telencephalon and diencephalon.

frontal cortex

The frontal cortex contains four main gyri.

frontal lobe

The front most (anterior) part of the cerebrum; anterior to the central sulcus and responsible for motor output and planning, language, judgment, and decision-making.

Functional MRI (fMRI)

Functional magnetic resonance imaging (fMRI): A neuroimaging technique that infers brain activation by measuring changes in oxygen levels in the blood.

gap junctions

A type of cell junction in which neighboring cells are connected through intercellular channels. Also facilitates the transfer of molecules directly from the cytoplasm of one cell to another cell.

gender

The psychological and sociological representations of one's biological sex.

gender identity

Personal depictions of masculinity and femininity.

gender role

Societal expectations of masculinity and femininity.

gene expression

Gene expression is the process by which the information encoded in a gene is used to direct the assembly of a protein molecule and ultimately affect the phenotype.

Gene Knock-in

A research technique that involves inserting a specific gene in an organism, which allows researchers to study the effect of that gene on the phenotype.

Gene Knockout

A research technique that involves removing or inactivating a specific gene in an organism (often a fruit fly, zebrafish, or mouse), which allows researchers to study the effect of that gene on the phenotype.

genes

A sequence of DNA that controls or partially controls physical characteristics

genotype

Genetic makeup of an individual

glia cells

Non-neuronal cells in the nervous system that play a wide range of supporting roles in the nervous system.

glial cells

Non-neuronal cells that support and insulate neurons. Important for supporting typical brain function and protecting neurons.

globus pallidus

A nucleus of the basal ganglia.

gonadal sex

The sex of an individual as determined by the possession of either ovaries or testes. Females have ovaries, whereas males have testes.

grandiose delusions

Characterized by intense irrational thoughts and fears centered on perceived victimization or belief that one is being persecuted

gray matter

Composes the bark or the cortex of the cerebrum and consists of the cell bodies of the neurons (see also white matter).

grid cells

Specialized cells in the entorhinal cortex that fire at consistent intervals as an animal moves through space. Important for establishing cognitive maps of different environments.

gyri

(plural) Folds between sulci in the cortex.

gyrus

(plural: gyri)

A fold between sulci in the cortex.

habituation

Decrease in response after repeated presentation of a stimulus

hallucination

Perceptual experience that emerges in the absence of external stimulation. Extends across different sensory sources (i.e., visual, auditory, tactile, etc.)

hemispatial neglect

Neuropsychological condition in which damage to the parietal lobe impairs attention and awareness of one side of space. Damage to the left hemisphere would lead to neglect of the right visual field.

hemorrhagic stroke

Strokes caused by a ruptured or leaking blood vessel

heritability coefficient

An easily misinterpreted statistical construct that purports to measure the role of genetics in the explanation of differences among individuals.

heterosexual

Opposite-sex attraction.

heterozygous

Consisting of two different alleles

hindbrain

Also referred to as the rhombencephalon. The lower portion of the brain stem. Consists of the metencephalon and myelencephalon.

hippocampus

(plural form, hippocampi)

A nucleus inside (medial) the temporal lobe implicated in learning and memory.

histone modification

An epigenetic mechanism in which a chemical group can be attached to a histone to alter the extent to which DNA is wrapped around histones and thereby alters the availability of genes in the DNA and gene expression

hoarding disorder

A type of obsessive-compulsive disorder. Characterized by persistent difficulty in parting with possessions due to a perceived need to save the items

homosexual

Same-sex attraction.

homozygous

Consisting of two identical alleles

hormones

An organic chemical messenger released from endocrine cells that travels through the blood to interact with target cells at some distance to cause a biological response.

hypothalamus

Part of the diencephalon. Regulates biological drives with pituitary gland.

hypothesis

a tentative explanation of some phenomenon that is used as a starting point for further investigation.

independent variable

A variable that is manipulated by the researcher. The independent variable is “independent” of other variables and is typically considered the cause.

inhibitory postsynaptic potentials

A hyperpolarizing postsynaptic current that causes the membrane potential to become more negative and move away from the threshold of excitation.

insula

Region in the cerebral cortex tucked deep into the lateral sulcus. The insula is involved in many functions and serves as a hub that links large-scale brain systems.

International Classification of Diseases (ICD-11)

A classification system for mental and behavioral disorders used primarily by the World Health Organization to support the global comparison of mortality and morbidity statistics.

intersex

Born with either an absence or some combination of male and female reproductive organs, sex hormones, or sex chromosomes.

ion channels

Proteins that span the cell membrane, forming channels that specific

ions can flow through between the intracellular and extracellular space.

ionotropic receptors

Ion channel that opens to allow ions to permeate the cell membrane under specific conditions, such as the presence of a neurotransmitter or a specific membrane potential.

Ischemic strokes

Strokes caused by interruption of blood supply

Korsakoff's syndrome

A condition of the central nervous system caused by severe deficiency of thiamine (vitamin B-1) that primarily affects the memory system.

lateral geniculate nucleus (LGN)

(or LGN) A nucleus in the thalamus that is innervated by the optic nerves and sends signals to the visual cortex in the occipital lobe.

lateral prefrontal cortex

Part of the prefrontal cortex that supports higher-order functions such as working memory, selective attention, and planning. It is implicated in mood disorders.

lateral sulcus

The major fissure that delineates the temporal lobe below the frontal and the parietal lobes.

lateralization

Refers to the idea that specific functions may reside primarily in one

hemisphere or the other (e.g., for the majority of individuals, the left hemisphere is most responsible for language).

limbic system

Involved in learning and emotion. Includes the subcortical structures of the amygdala and hippocampal formation as well as some cortical structures, such as the cingulate cortex. Responsible for aversion and gratification.

localization of function

Different brain functions are processed in or localized to specific brain areas

long-term depression (LTD)

A long lasting decrease in the strength of synaptic connection based on recent patterns of activity.

long-term memory

Memories that have become stabilized over an extended period of time (days, weeks, years).

long-term potentiation (LTP)

A persistent strengthening of synaptic connections based on recent patterns of activity. A mechanism underlying “neurons that fire together, wire together.”

longitudinal fissure

Deep groove that separates the two cerebral hemispheres of the brain.

Magnetoencephalography (MEG)

A brain science technique that measures brain activity by picking up the tiny magnetic fields generated by neural activity.

malignant tumors

Tumors that can spread and invade surrounding tissue

Mania

Prominent feature of bipolar disorder and related disorders; a state of abnormally and persistently excessive enthusiasm and irritable mood

masculinization

The induction of male traits.

maternal behavior

Parental behavior performed by the mother.

medulla oblongata

Extension of the spinal cord that forms the lowest part of the brain stem.

memory reconsolidation

The process in which reactivated memories become transiently sensitive to modifications

mesencephalon

One of the three primary vesicles. Also referred to as the midbrain.

mesoderm

Middle layer of the three germ layers in a developing embryo.

Metabolism

Breakdown of substances

metencephalon

The part of the hindbrain that develops into the cerebellum and pons.

midbrain

Also referred to as the mesencephalon. The top-most portion of the brain stem. Consists of the tectum, the cerebral aqueduct, the tegmentum, and the cerebral peduncles.

monozygotic twins

Twins conceived from a single ovum and a single sperm, therefore genetically identical.

Mood disorders

A class of psychological disorders marked by severe disturbances to emotions and mood

mutation

Sudden, permanent change in a gene

myelencephalon

The part of the hindbrain that develops into the medulla oblongata.

myelin sheath

Substance around the axon of a neuron that serves as insulation to allow the action potential to conduct rapidly toward the terminal buttons.

necrosis

A form of cell injury which results in premature, unprogrammed cell death due to environmental factors such as injury or disease.

negative symptoms

Refer to an absence or reduction of normal behaviors related to motivation and interest, such as social withdrawal, diminished affective response, lack of interest.

nervous system

Complex network of nerves and cells that transmit information between the brain and the rest of the body.

neural crest

A temporary cluster of cells that originate from the side of the neural tube proximal to the epidermal layer. Neural crest cells give rise to diverse cell types that can support many different systems.

neural diathesis-stress model of schizophrenia

Stress, through its effects on cortisol, acts upon a pre-existing vulnerability to trigger or worsen schizophrenia symptoms.

neural efficiency

The process in which the brain spends fewer energy resources to carry

out specific brain functions and subsequent behavior. Typically indicative of a matured functional brain network.

neural folds

Ridges of the ectoderm on the neural plate that form around the neural groove and fuse to form the neural tube.

neural groove

Formed when the neural plate folds inward and extends the entire length of the embryo.

neural proliferation

The mass production of cells. Most prominent during early embryonic development.

neural stem cells

Self-renewing cells that ultimately generate neurons or glial cells, which give rise to the entire nervous system.

neural tube

The hollow longitudinal tube formed by the infolding of the neural plate and subsequent fusion of the neural folds. Sets the basis for development of the brain and spinal cord.

Neurofibrillary tangles

abnormal accumulations of a protein called tau that collect inside neurons and is a key biological marker in Alzheimer's disease

neurogenesis

The process by which new neurons are formed in the brain.

neuromodulation

the process by which neurons use chemical signals (e.g., some neurotransmitters) to bias many neurons, resulting in changes to neuronal properties such as firing activity and synaptic connectivity.

Neuronal migration

The period when neurons migrate from their origin location to their target location. Neuronal Migration brings different classes of neurons together so that they can interact and give rise to various nervous system structures.

neurons

The fundamental units in the brain that transfer information from the brain to the rest of the body.

neuroplasticity

The ability of the brain to reorganize and adapt its activity in response to intrinsic or extrinsic experiences.

neurotransmitter

A chemical substance produced by a neuron that is used for communication between neurons

neurotransmitters

Chemical substance released by the presynaptic terminal button that acts on the postsynaptic cell.

Non-associative learning

Changes in behavior in response to repeated exposure to a stimulus

nondeclarative memory

Memory for information that does not require conscious learning. Includes procedural memory, priming, non-associative learning, and associative learning.

norepinephrine

A neurotransmitter and hormone. Plays an important role in arousal and the “fight-or-flight” response. It is housed primarily in the locus coeruleus.

nucleus

(plural: nuclei)

In neuroanatomy, nucleus or nuclei refers to a cluster of neurons.

Collection of nerve cells found in the brain which typically serve a specific function.

nucleus accumbens

A region of the basal forebrain located in front of the preoptic region.

Obsessive-compulsive and related disorders

A group of disorders that center on a cycle of intrusive thoughts, feelings of anxiety, repetitive behaviors, and short-term reliefs.

occipital lobe

The back most (posterior) part of the cerebrum; involved in vision.

oligodendrocytes

glial cells that generate and maintain the myelin sheath

Optogenetics

A biological technique to control the activity of neurons or other cell types with light.

orbitofrontal cortex

A region of the frontal lobes of the brain above the eye sockets.

organizational effect

Early, generally irreversible, effects of steroid hormones that occur during development

oxytocin

A peptide hormone secreted by the pituitary gland to trigger lactation, as well as social bonding.

paranoid delusions

Characterized by intense irrational thoughts and fears centered on perceived victimization or belief that one is being persecuted

parasympathetic nervous system

A division of the autonomic nervous system that is slower than its counterpart—that is, the sympathetic nervous system—and works in opposition to it. Generally engaged in “rest and digest” functions.

parental behavior

Behaviors performed in relation to one’s offspring that contributes directly to the survival of those offspring

parietal lobe

The part of the cerebrum between the frontal and occipital lobes; involved in bodily sensations, visual attention, and integrating the senses.

parieto-occipital sulcus

Deep sulcus that divides the parietal lobe from the occipital lobe.

paternal care

Parental behavior performed by the father or other male.

periaqueductal gray

The gray matter in the midbrain near the cerebral aqueduct.

peripheral nervous system

All of the nerve cells that connect the central nervous system to all the other parts of the body.

pharmacokinetics

The action of a drug through the body, including absorption, distribution, metabolism, and excretion

phenotype

The observable characteristics of an individual

pituitary gland

Small pea-sized gland that produces and secretes hormones as part of the endocrine system. Interacts with the hypothalamus to monitor the regulation of growth, development, and metabolism.

place cells

Specialized cells in the hippocampus that code specific locations in an environment. Important for establishing cognitive maps of different environments

polygenic

Multiple genes affecting a given trait

polypharmacy

The use of many medications

pons

Part of the hindbrain. A bridge that connects the cerebral cortex with the medulla, and reciprocally transfers information back and forth between the brain and the spinal cord.

Positron Emission Tomography (PET)

A neuroimaging technique that measures brain activity by detecting the presence of a radioactive substance in the brain that is initially injected into the bloodstream and then pulled in by active brain tissue.

post-traumatic stress disorder (PTSD)

A psychological disorder that develops in some individuals who have experienced a traumatic event. It is characterized by intense, vivid memories of the traumatic event or related events and intense emotional and physical reactions.

prefrontal cortex

Covers the front part of the frontal lobe of the cerebral cortex. Supports executive functions such as goal-directed behavior, cognitive

flexibility, habit formation. Implicated in many psychological disorders

preoptic area

A part of the anterior hypothalamus.

primary somatosensory cortex (S1)

Located on the postcentral gyrus of the parietal lobe; primarily responsible for processing sensory information from the body.

primary vesicles

The three primary vesicles include the prosencephalon (forebrain), mesencephalon (midbrain), and rhombencephalon (hindbrain).

priming

The presentation of one stimulus influences the response to a subsequent stimulus

procedural memories

Type of unconscious memory that allows for remembering procedures and performance of specific tasks

progesterone

A primary progestin that is involved in pregnancy and mating behaviors.

prolactin

A protein hormone that is highly conserved throughout the animal kingdom. It has many biological functions associated with reproduction and synergistic actions with steroid hormones.

prosencephalon

One of the three primary vesicles. Also referred to as the forebrain.

psychoactive drugs

A drug that changes mood or the way someone feels

psychopathology

The scientific study of mental illness or disorders.

psychotropic drug

A drug that changes mood or emotion, usually used when talking about drugs prescribed for various mental conditions (depression, anxiety, schizophrenia, etc.)

putamen

A subcortical structure that contributes to the formation of the basal ganglia. Involved in learning and motor control.

quantitative genetics

Scientific and mathematical methods for inferring genetic and environmental processes based on the degree of genetic and environmental similarity among organisms.

radial migration

The most common mode of neuronal migration in which neurons migrate in a radial pattern to ultimately establish the different layers of the cortex.

random assignment

A way of placing participants into different groups with randomization. Every member of the sample has an equal chance of being placed in a control group or an experimental group.

receptors

A chemical structure on the cell surface or inside of a cell that has an affinity for a specific chemical configuration of a hormone, neurotransmitter, or other compound.

recessive allele

Allele whose phenotype will be expressed only if an individual is homozygous for that allele

remyelination

Regenerative process by which the myelin sheath around a demyelinated axon is restored

Research Domain Criteria (RDoC)

A research framework for investigating mental disorders in terms of varying degrees of dysfunction in psychological and biological systems

resting membrane potential

The voltage inside the cell relative to the voltage outside the cell while the cell is at rest (approximately -70 mV).

Retrieval

The process of accessing stored memories

retrograde amnesia

Inability to retrieve memories from one's past

rhombencephalon

One of the three primary vesicles. Also referred to as the hindbrain.

Schizophrenia

Schizophrenia is a psychological disorder characterized by major disturbances in thought, perception, emotion, and behavior. Major symptoms include hallucinations, delusions, disorganized thinking, abnormal motor behavior, and negative symptoms.

secondary vesicles

The five secondary vesicles include the telencephalon, diencephalon, mesencephalon, metencephalon, and myelencephalon.

semantic memories

Memory of factual information

sensitive periods

Time limited period of development where intrinsic and extrinsic experiences have an especially strong impact on brain development.

sensitization

Increased responsivity after repeated exposure to the same stimulus

sensory memory

Short-term retention of incoming sensory information (e.g., sights, sounds, smells)

sex

A biological descriptor based on reproductive, hormonal, anatomical, and genetic characteristics. Typical sex categories include male, female, and intersex.

sex determination

The point at which an individual begins to develop as either a male or a female. In animals that have sex chromosomes, this occurs at fertilization. Females are XX and males are XY. All eggs bear X chromosomes, whereas sperm can either bear X or Y chromosomes. Thus, it is the males that determine the sex of the offspring.

sexual differentiation

The process by which individuals develop the characteristics associated with being male or female. Differential exposure to gonadal steroids during early development causes sexual differentiation of several structures including the brain.

sexual fluidity

Personal sexual attributes changing due to psychosocial circumstances.

sexual orientation

A person's sexual attraction to other people.

short-term memory

Temporary memory store that holds and processes information for a limited period of time

sodium-potassium pump

An ion channel that uses the neuron's energy (adenosine triphosphate, ATP) to pump three Na^+ ions outside the cell in exchange for bringing two K^+ ions inside the cell.

soma

Cell body of a neuron that contains the nucleus and genetic information and directs protein synthesis.

somatic delusion

Characterized by false beliefs that a person's internal or external bodily functions are abnormal

somatic nervous system

A part of the peripheral nervous system that uses cranial and spinal nerves in volitional actions.

spatial resolution

A term that refers to how small the elements of an image are; high spatial resolution means the device or technique can resolve very small elements; in neuroscience, it describes how small a structure in the brain can be imaged.

spinal nerves

Mixed nerves that carry sensory and motor information between the spinal cord and rest of the body.

spines

Protrusions on the dendrite of a neuron that form synapses with terminal buttons of the presynaptic axon.

stereotaxic unit

A surgical device that immobilizes an animal's head and allows precise positioning in an animal's brain using a three-dimensional coordinate system.

storage

Retention of encoded information

stria terminalis

A band of fibers that runs along the top surface of the thalamus.

structural magnetic resonance imaging

A neuroimaging technique that uses the magnetic resonance scanner to create high resolution images of brain structure. The images show brain anatomy, including location, size, and integrity of white and gray matter (but does not reveal brain function or neuronal activity).

subcortical

Structures that lie beneath the cerebral cortex, but above the brainstem.

substantia nigra

Involved in transferring chemical signals related to reward. Interacts with the basal ganglia to facilitate motor and reward processes.

subthalamic nucleus

A small lens-shaped nucleus located within the diencephalon. Interacts with the basal ganglia to facilitate motor regulation.

sulci

(plural) Grooves separating folds of the cortex.

sulcus

(plural: sulci)

A groove separating folds of the cortex.

sympathetic nervous system

A division of the autonomic nervous system, that is faster than its counterpart that is the parasympathetic nervous system and works in opposition to it. Generally engaged in “fight or flight” functions.

synapse

The tiny space separating neurons

synapses

Specialized junction through which neural signals are transmitted between neurons.

synaptic gap

Also known as the synaptic cleft; the small space between the presynaptic terminal button and the postsynaptic dendritic spine, axon, or soma.

synaptic vesicles

Groups of neurotransmitters packaged together and located within the terminal button.

tangential migration

Another mode of neuronal migration in which neurons migrate tangentially and may emerge as a result of interactions with axons, astrocytes, or independent of interactions with other cells. Does not rely on glial cells for migration.

target cells

A cell that has receptors for a specific chemical messenger (hormone or neurotransmitter).

tectum

The uppermost part of the midbrain.

tegmentum

The ventral portion of the midbrain.

telencephalon

Largest portion of the central nervous system and consists of the cerebrum and related structures.

temporal lobe

The part of the cerebrum in front of (anterior to) the occipital lobe and below the lateral fissure; involved in vision, auditory processing, memory, and integrating vision and audition.

temporal resolution

A term that refers to how small a unit of time can be measured; high temporal resolution means capable of resolving very small units of time; in neuroscience, it describes how precisely in time a process can be measured in the brain.

terminal button

The part of the end of the axon that forms synapses with postsynaptic dendrite, axon, or soma.

testosterone

The primary androgen secreted by the testes of most vertebrate animals, including men.

thalamus

A part of the diencephalon that works as a gateway for incoming and outgoing information.

theory

A broad explanation or group of explanations for some aspect of the natural world that is consistently supported by evidence over time

threshold of excitation

Specific membrane potential that the neuron must reach to initiate an action potential.

transcranial direct current stimulation (tDCS)

A neuroscience technique whereby a weak current is applied to the head that temporarily activates or inhibits ongoing neuronal activity.

transcranial magnetic stimulation (TMS)

A neuroscience technique whereby a brief magnetic pulse is applied to the head that temporarily activates or inhibits ongoing neuronal activity.

transgender man

A transgender person whose birth sex was female.

transgender woman

A transgender person whose birth sex was male.

twin studies

A behavior genetic research method that involves a comparison of the similarity of identical (monozygotic; MZ) and fraternal (dizygotic; DZ) twins.

ventromedial prefrontal cortex

Part of the prefrontal cortex that is involved in value computation, decision-making, and emotion regulation. Implicated in mood disorders

visual cortex

The part of the brain that processes visual information that is located in the back of the brain.

Wernicke's area

A language area in the temporal lobe where linguistic information is comprehended (Also see Broca's area).

white matter

Regions of the nervous system that represent the axons of the nerve cells; whitish in color because of myelination of the nerve cells.

zygote

A cell formed by the union of a female gamete (egg) with a male gamete (sperm).

VERSION HISTORY

Below is the version history for Biological Psychology.

Version	Publication Date	Changes
First Edition: link to first edition	February 5, 2024	—
Revised Edition: link to revised edition	August 30, 2024	This revised version added a new chapter on Learning and Memory (Ch 8); revised the Hormones chapter (Ch 6) to include information on endocrine disruptors and the biology of sex, and sexual orientation; added new research treatments of Psychological Disorders; and stylistic improvements throughout.