Biological Psychology

BIOLOGICAL PSYCHOLOGY

MICHAEL J. HOVE AND STEVEN A. MARTINEZ

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

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We also plan to compile teaching resources such as slides and assignments that can accompany the book.

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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
- 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
- Massachusett 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

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 "in your body" or relaxed. After a few months of regularly attending to your breath (as is done in many meditation practices), you might notice increased 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, and 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]

---

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

We are still learning about the brain and many big mysteries remain, but scientists do know an astounding amount about how the brain works. In the past decades, researchers have made tremendous progress in understanding the molecular and chemical processes in the brain, how neurons communicate with each other, the function of different brain areas and networks, how drugs and hormones affect brain function, how genes and environment shape brain and behavior, how the brain develops and changes over time, and ways things can go wrong in the brain due to damage, disease, or psychological disorders. We'll explore these topics and more in this book on Biological Psychology.

environmental underpinnings of selfhood, see the book "Who You Are: The Science of Connectedness" by Michael Spivey (2020).

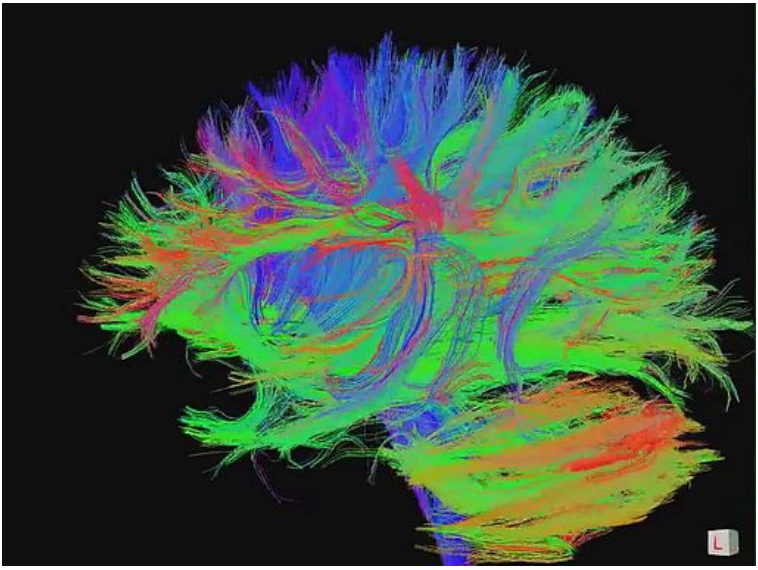

Figure 1a. Why we are the way we are: networks of axonal nerve fibers in the brain as measured by Magnetic Resonance Imaging (MRI), specifically diffusion tensor imaging.

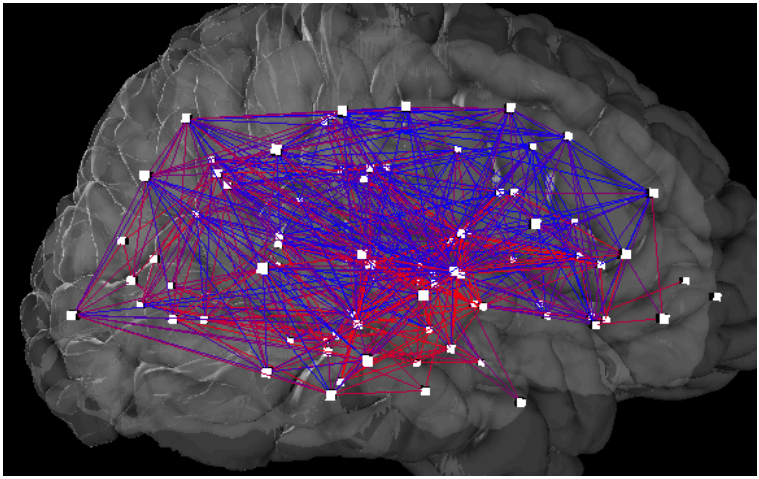

Figure 1b. A graphical depiction of the vast interconnectedness of large-scale brain regions. Nodes are depicted as white squares and interconnections between nodes (i.e., brain regions) are depicted in red-blue lines overlaid on a grayscale image of the brain.

Media Attributions

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- Interconnectedness of large-scale brain regions. © Wikipedia is licensed under a CC BY (Attribution) license

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, it is also a viewpoint that emphasizes that brain mechanisms underlie all of our thoughts and actions and that these brain mechanisms have evolved over an incredibly long time 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 processes 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 more subfields, the subfields overlap, and researchers often work in more than one of these areas. 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, engineering, etc. Each discipline contributes a different perspective and 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 brain structure and function and often leads to breakthroughs that propel scientific progress.

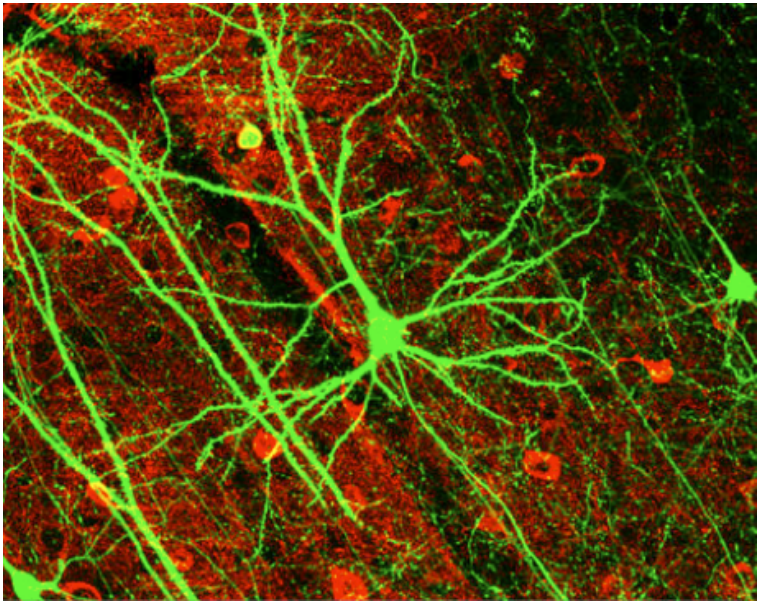

Figure 2. Pyramidal neurons in the mouse cerebral cortex expressing green fluorescent protein. The red staining indicates GABAergic interneurons.

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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–is what distinguishes sciences from non-sciences. The presence of the supernatural, for instance, is neither testable nor falsifiable. A hypothesis should also fit into

the context of a scientific **theory**, which is a broad explanation or group of explanations 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 it is not given 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. Results from one study inform future studies and guide refinement of the hypothesis (see Figure 3). Sometimes an experiment leads to conclusions that favor a change in approach or inspires entirely new scientific 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.

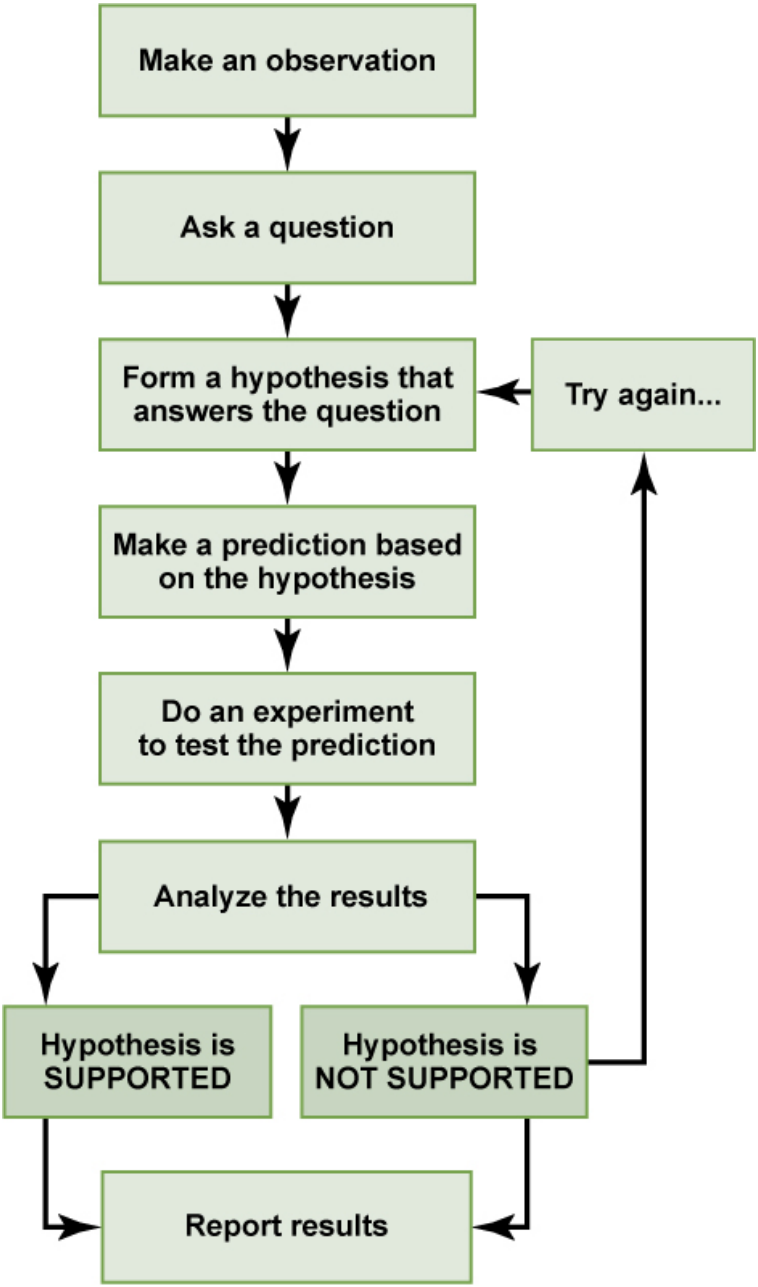
Make an observation
Ask a question
Form a hypothesis that answers the question
Try again...
Make a prediction based on the hypothesis
Do an experiment to test the prediction
Analyze the results
Hypothesis is SUPPORTED
Hypothesis is NOT SUPPORTED
Report results

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: PAYOFFS OF BIOLOGICAL PSYCHOLOGY

Biological psychology and related neuroscience fields are extremely active areas of research. Billions of dollars are invested annually and tens of thousands of researchers are studying the brain and behavior. The vast undertaking to understand the brain will help unravel the mysteries of human nature and our human experience. In addition, research on the brain 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. Treatment and care of afflicted patients benefits greatly from basic brain science. Research on cellular and molecular mechanisms of the brain can lead to the development of new drugs, and ways to regrow neurons and increase neural plasticity. Researchers have developed mind-boggling 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 that pick up brain signals, analyze them, and translate them into commands for an external device like a wheelchair or robotic arm can help people regain movement who have neuromuscular disorders including amyotrophic lateral sclerosis (ALS), spinal cord injury, or stroke (Figure 4).

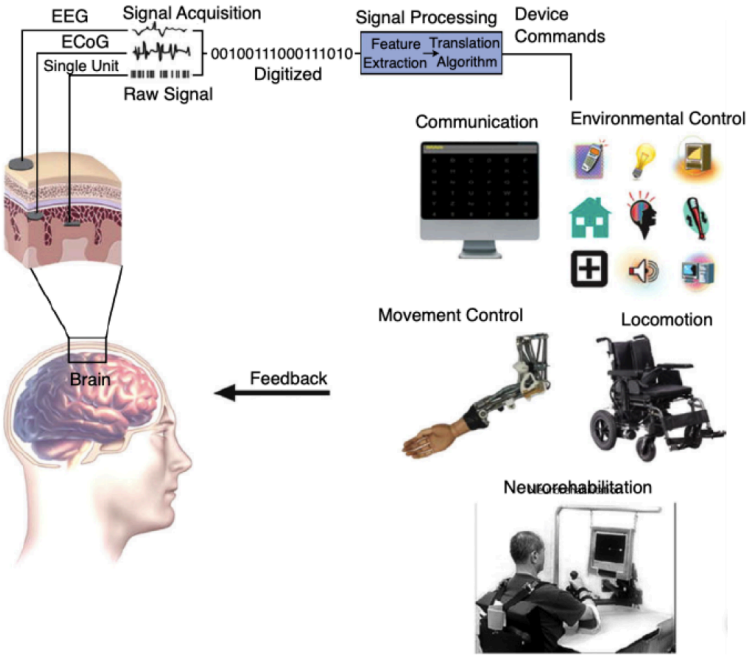

Figure 4. Components of a typical system for Brain-Computer Interface that picks up brain signals, analyzes them, and translates them into commands to an external output device like a wheelchair or robotic arm.

Guiding Artificial Intelligence. Neuroscience is closely 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). Similar to 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 very small aspect at a time and strategically shift our "spotlight of attention." By incorporating a biologically-inspired approach with prioritized focus, AI-image processing has 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 been able to improve the efficiency and accuracy of AI algorithms, resulting in significant advances in areas like computer vision, decision-making, and natural language processing. Those AI assistants you might have used, like

ChatGPT and LLaMa for text generation or Stable Diffusion and DALL-E for image generation, built on principles discovered in brain science. 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 can be used to analyze neuroimaging data, build computational models to simulate and study the brain, and identify 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. As brain science learns more about psychopharmacology and the brain mechanisms underlying addiction, it has become increasingly clear that addiction is

driven by biological processes in the brain. 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 that are rooted in interrupting the brain circuits that drive 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 clearly 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 researchers in biological psychology 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 it meets 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 active and ongoing, and need not be characterized as a simple dichotomy between "Yes, always" or "No, never." The efforts by animal-rights groups have led to better treatment and conditions for lab animals.

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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 of the early research was done by men of European descent due to social and cultural factors, systemic barriers, as well as 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; thus it is unclear how those studies will benefit people of differing ethnicities who might have different mental health needs and respond differently to treatments (Gordon, 2018). Research on diverse populations is especially important 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, the field of 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 11 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; 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 with 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 (like the left temporal lobe's role in speech perception) emerged from rare cases of focal brain damage. Today, researchers can observe brain activity using sophisticated brain recording and imaging 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, for example, blocking or mimicking the naturally occurring neurotransmitters. This can have a profound impact on brain activity, and in turn, subjective experience, mood, behavior, and mental and physical health. This chapter covers how pharmacokinetics (i.e., how a drug is processed by the body and brain) affects neural transmission and the use of drugs to treat psychiatric disorders. This chapter concludes with descriptions and

animations of how drugs like alcohol, caffeine, and cannabis affect neurotransmitters and synaptic processing in the brain.

Chapter 6 introduces "**Hormones & Behavior**" and the field of behavioral endocrinology (the scientific study of the interaction between hormones and behavior). 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 of individuals (Nelson, 2023). This chapter highlights differences between neural transmission and hormonal communication and introduces the powerful behavioral effects of several common hormones such as cortisol, estradiol, testosterone, and oxytocin.

Chapter 7 provides an overview of the **"Development of the Brain and Nervous System."** It covers the stages of development from the neural tube in embryo to fully formed brain structures in adulthood. We discuss early stages of neural growth and migration, the key developmental process of programmed neuron death, and the recent discovery of adult neurogenesis (adults do in fact 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. Understanding brain plasticity and development has ramifications for learning, maturation, treatments of developmental disorders, and staving off age-related declines.

Chapter 8 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 clearly influence the structure and function of the brain and therefore our thoughts and behaviors. In this chapter, we review fundamental genetics. Then we look at how behavioral geneticists study the relative contributions of genes and environment and try to tease apart the influences of nature and nurture. 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 9 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 10 "**Brain Damage, Neurodegeneration, and Neurological Disease**" presents some of the many 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 who've been directly or indirectly affected by IPV. We include some links to resources and guidance from the CDC (Center for Disease Control and Prevention) on ways to address and prevent Intimate Partner Violence.

Chapter 11 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. While this chapter doesn't focus on the full range of treatments of such disorders (that would be covered in a course on abnormal or clinical psychology), understanding the biological basis of psychological disorders does inform treatment approaches.

1.8: BRAIN AND BEHAVIOR BEYOND THIS BOOK

This book covers a lot of material, but much more material 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, memory encoding, language processing, the neural correlates of consciousness, etc. But hopefully, these 11 chapters provide a solid foundation for understanding links between brain and behavior and pique 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., 2107). With so much new information, even trained scientists struggle to keep up with new developments, and students looking to learn more or get into 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.

1.9: REFERENCES

Parts of this chapter were adapted from:

Clark, M. A., Douglas, M., & Choi, J. (2018). 1.1 The Science of Biology. In *Biology* (2nd ed.). OpenStax. Access for free at https://openstax.org/books/biology-2e/pages/1-1-the-science-of-biology

Spielman, R. M., Jenkins, W. J., & Lovett, M. D. (2020). 1.1 What Is Psychology? In *Psychology 2e.* OpenStax. Access for free at https://openstax.org/books/psychology-2e/pages/1-1-what-is-psychology

Stangor, C., Walinga, J. & Cummings, J. A. (2019). 3.1 Psychologists Use the Scientific Method to Guide Their Research. In *Introduction to Psychology*. University of Saskatchewan. https://openpress.usask.ca/introductiontopsychology/chapter/psychologists-use-the-scientific-method-to-guide-their-research/

References

Colliot, O. (Ed.). (2023). *Machine Learning for Brain*

Disorders. Springer. https://link.springer.com/book/10.1007/978-1-0716-3195-9

Eagleman, D., & Downar, J. (2016). *Brain and behavior: A cognitive neuroscience perspective.* Oxford University Press.

Garrett, B. (2015). *Brain and behavior: An introduction to biological psychology* (4th ed.). Sage Publications, Inc.

Gordon, J. (2018). Mental Health Research—Diversity Matters. https://www.nimh.nih.gov/about/director/messages/2018/mental-health-research-diversity-matters

Greider, C. W., Sheltzer, J. M., Cantalupo, N. C., Copeland, W. B., Dasgupta, N., Hopkins, N., ... & Wong, J. Y. (2019). Increasing gender diversity in the STEM research workforce. *Science, 366*(6466), 692-695.

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

Hassabis, D., Kumaran, D., Summerfield, C., & Botvinick, M. (2017). Neuroscience-inspired artificial intelligence. *Neuron*, *95*(2), 245-258.

Henrich, J., Heine, S. J., & Norenzayan, A. (2010). Most people are not WEIRD. *Nature, 466(*7302), 29-29.

Kriegeskorte, N., & Douglas, P. K. (2018). Cognitive computational neuroscience. *Nature Neuroscience, 21*(9), 1148-1160.

Lichtman, J., Pfister, H., & Reid, C. (n.d.). Connections in the Brain. Retrieved July 7, 2023.

https://www.rc.fas.harvard.edu/case-studies/connections-in-the-brain/

National Academies of Sciences, Engineering, and Medicine. 2023. *Advancing Antiracism, Diversity, Equity, and Inclusion in STEMM Organizations: Beyond Broadening Participation*. Washington, DC: The National Academies Press. Online Access: https://nap.nationalacademies.org/read/26803

National Research Council. (2011). *Chimpanzees in biomedical and behavioral research: Assessing the necessity*. The National Academies Press.

Nelson, R. J. (2023). Hormones & behavior. In R. Biswas-Diener & E. Diener (Eds), Noba textbook series: Psychology. Champaign, IL: DEF publishers. Retrieved from http://noba.to/c6gvwu9m

Page, S. (2008). *The difference: How the power of diversity creates better groups, firms, schools, and societies-new edition*. Princeton University Press.

Pinel, J. P., & Barnes, S. (2017). *Biopsychology* (11th ed.) Pearson.

Plous, S. (1996). Attitudes toward the use of animals in psychological research and education. *Psychological Science, 7,* 352–358.

Ransom, J. & Harris, A. J. (2023, December 23). *How Rikers Island Became New York's Largest Mental Institution*. New York Times. https://www.nytimes.com/2023/12/29/nyregion/nyc-rikers-homeless-mental-illness.html

Singer, M. (2007). *The untethered soul: The journey beyond yourself*. New Harbinger Publications.

Spivey, M. J. (2020). *Who you are: The science of connectedness*. MIT Press.

Steadman, H. J., Osher, F. C., Robbins, P. C., Case, B., & Samuels, S. (2009). Prevalence of serious mental illness among jail inmates. *Psychiatric Services, 60*(6), 761-765.

Tang, Y. Y., Hölzel, B. K., & Posner, M. I. (2015). The neuroscience of mindfulness meditation. *Nature Reviews Neuroscience*, *16*(4), 213-225.

Thomas, G., & Blackman, D. (1992). The future of animal studies in psychology. *American Psychologist, 47,* 1678.

Torrey, E. F., Kennard, A. D., Eslinger, D., Lamb, R., & Pavle, J. (2010). More mentally ill persons are in jails and prisons than hospitals: A survey of the states. Arlington, VA: Treatment Advocacy Center, 1-18.

Walinga, J. (2019). 2.1 Biological Psychology. In J. A. Cummings & L. Sanders (Eds). *Introduction to Psychology*. University of Saskatchewan Open Press. https://openpress.usask.ca/introductiontopsychology/chapter/biological-psychology-structuralism-and-functionalism/

Yeung, A. W. K., Goto, T. K., & Leung, W. K. (2017). The changing landscape of neuroscience research, 2006–2015: A bibliometric study. *Frontiers in Neuroscience, 11,* 120.

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

In this chapter we focus on the structures of the brain and nervous system. Understanding the biological structures of the nervous system is vital to understanding psychology, for the various brain structures play specific roles in psychological processes. Throughout this book, we refer to many brain structures and describe their role in emotion, cognition, perception, neurological diseases, and psychological disorders.

An introduction to the biological aspects of psychology can be very interesting, but also frustrating for new students of psychology. This is largely because there is so much new information and vocabulary associated with parts of the brain and nervous system. We encourage you not to get bogged down in difficult 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 the terminology of the nervous system.

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2.2: VISUALIZING AND NAVIGATING THE HUMAN BRAIN

Before diving into the organization of the nervous system and introducing brain structures, 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.

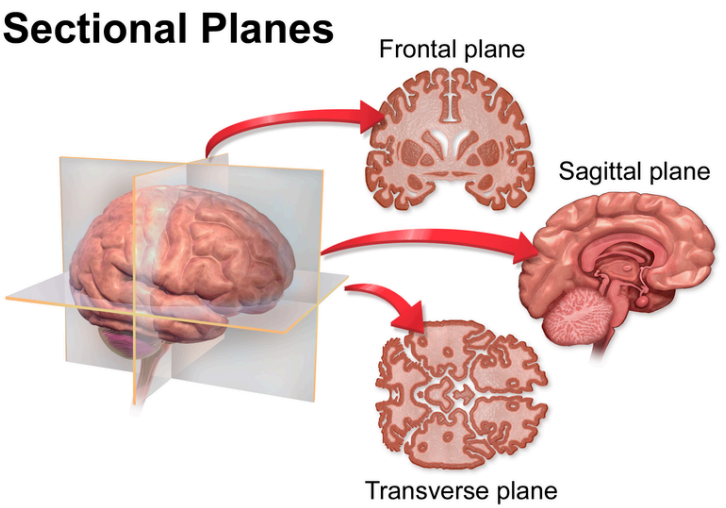

Figure 1: Slices of the human brain. Three possible 2-D cuts through the brain: a coronal or frontal slice (top image), a sagittal slice (middle), and a horizontal slice (bottom), which is also known as a transverse or axial slice.

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); and *ventral* means toward the belly. *Medial* means toward the middle; and *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.

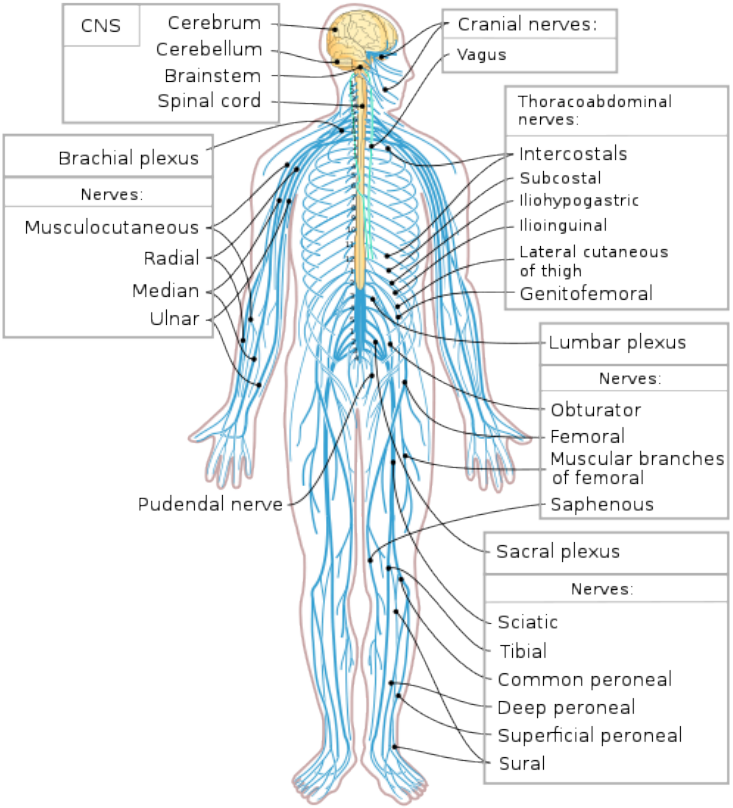

Figure 2. The human nervous system. The Central Nervous System (CNS), shown in yellow, is made up of the brain and spinal cord. The Peripheral Nervous System (PNS), shown in blue, is made up of nerves that connect the brain and spinal cord to the rest of the body.

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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).

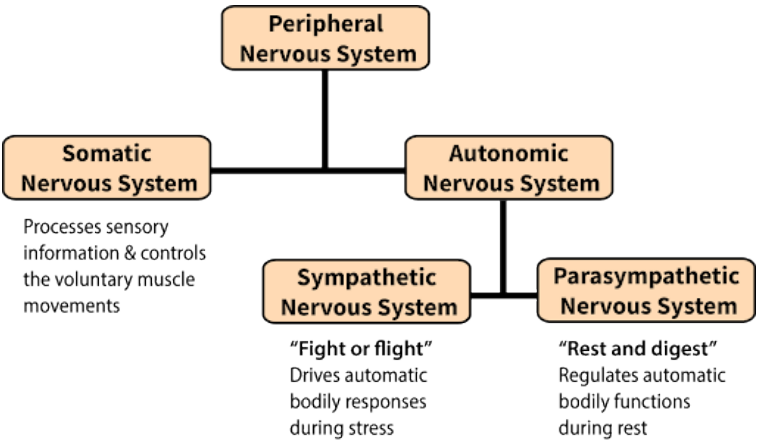

Figure 3: Components of the peripheral nervous system.

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.

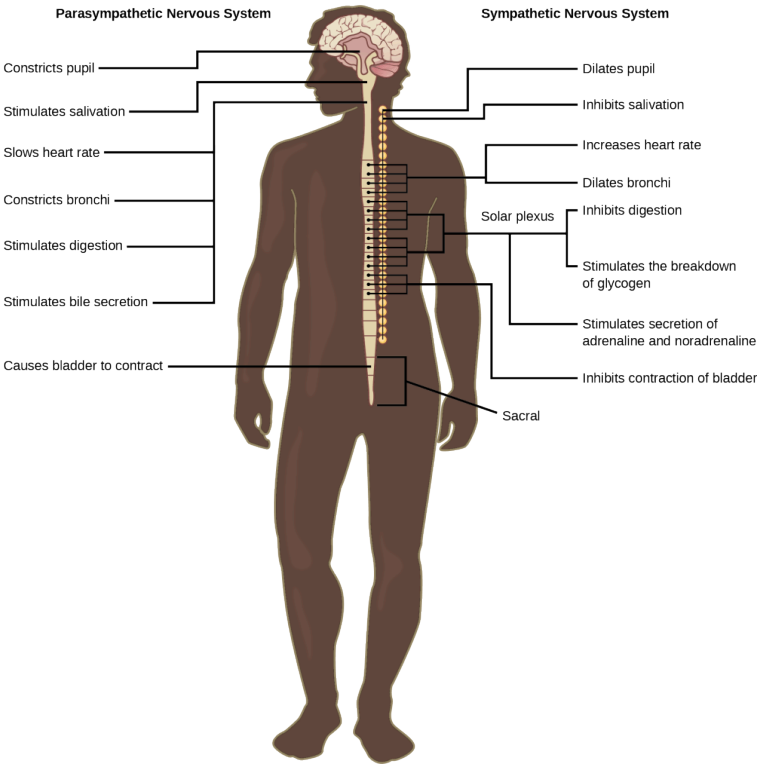

Figure 4. The sympathetic and parasympathetic nervous systems often have opposing effects on target organs.

The Somatic Nervous System

The somatic nervous system deals with interactions with the external environment, including sensing the outside world via sensory neurons and sending commands via motor neurons to skeletal muscles. Many behaviors associated with the somatic nervous system are voluntary and are initiated by complex

decision making processes in the brain. You hear a voice call your name, you 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).

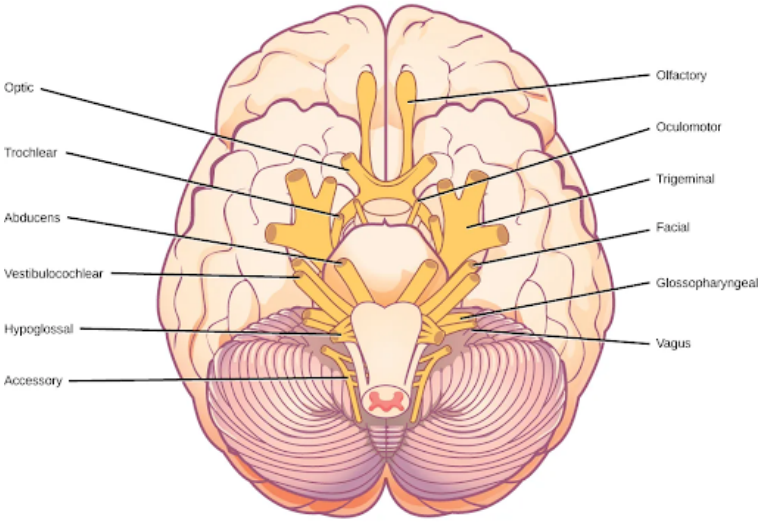

Figure 5. Inferior view (from below) of the human brain showing the cranial nerves in orange. The human brain contains 12 cranial nerves that receive sensory input and control motor output for the head and neck.

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 (**Figure 6**) (dorsal = toward back). 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 (see **Figure 7**).

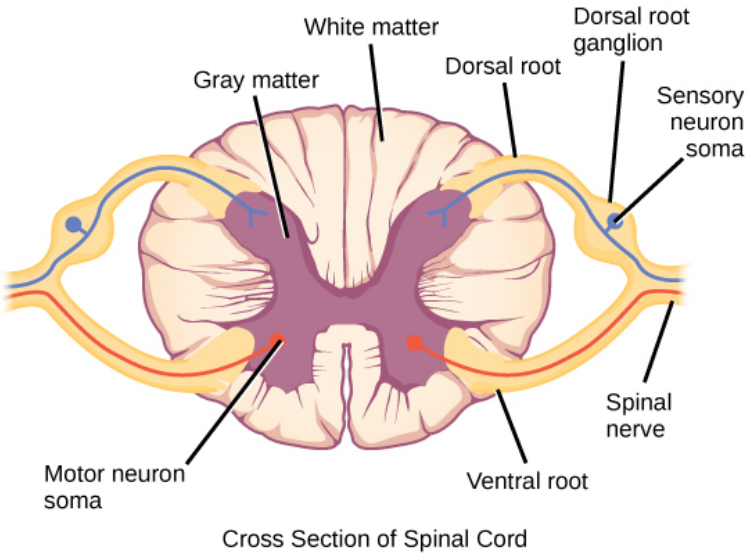

Figure 6. Spinal nerves contain both sensory and motor axons. The somas (cell bodies) of sensory neurons are located in dorsal root ganglia. The somas of motor neurons are found in the ventral portion of the gray matter of the spinal cord.

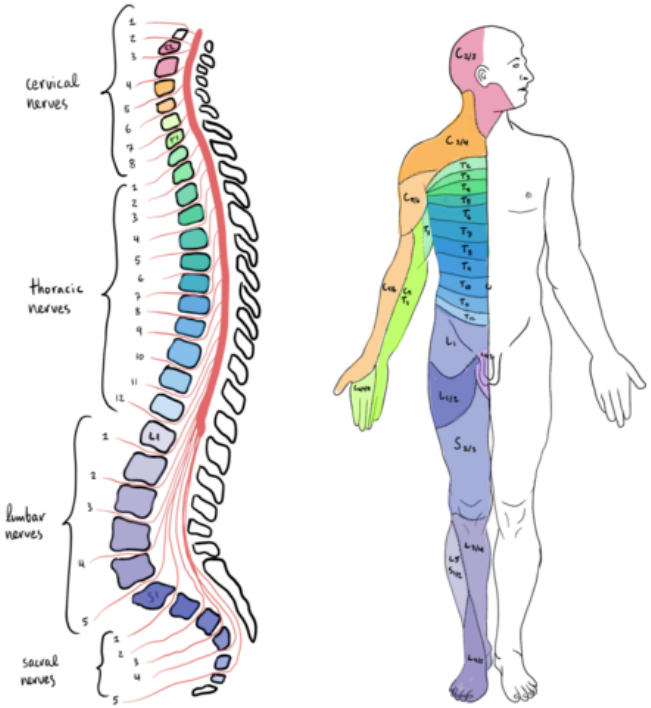

Figure 7. Spinal nerves exit the spinal cord through notches in the vertebrae. This figure illustrates the spinal cord segments in the vertebral column (cervical, thoracic, lumbar, sacral), and how each spinal nerve relates to different regions of the body.

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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 space between the arachnoid and pia maters, the subarachnoid space, is filled with cerebrospinal fluid (CSF), a fluid that helps cushion and protect the brain and spinal cord. We discuss cerebrospinal fluid in more detail in the next section on The Brain.

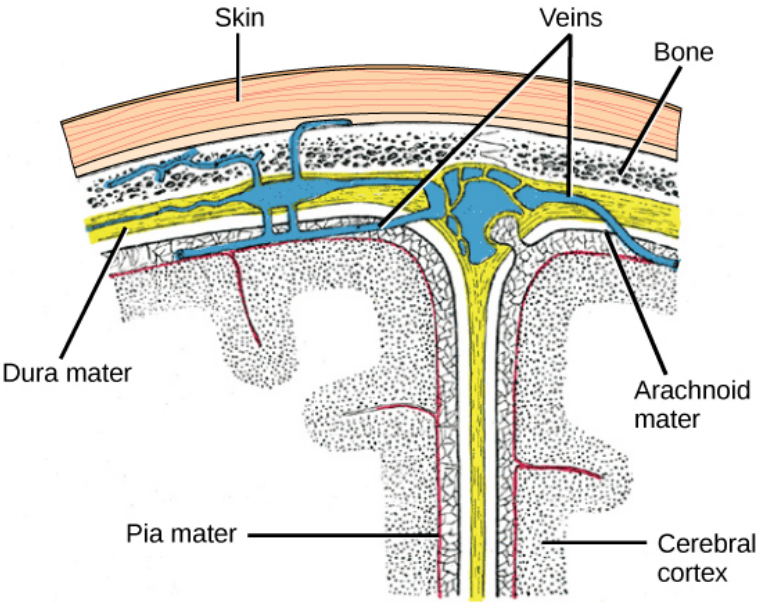

Figure 8. The cerebral cortex is covered by three layers of meninges: the dura, arachnoid, and pia maters (Credit: modification of work by Gray's Anatomy).

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, saves hundreds of milliseconds, and helps 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.

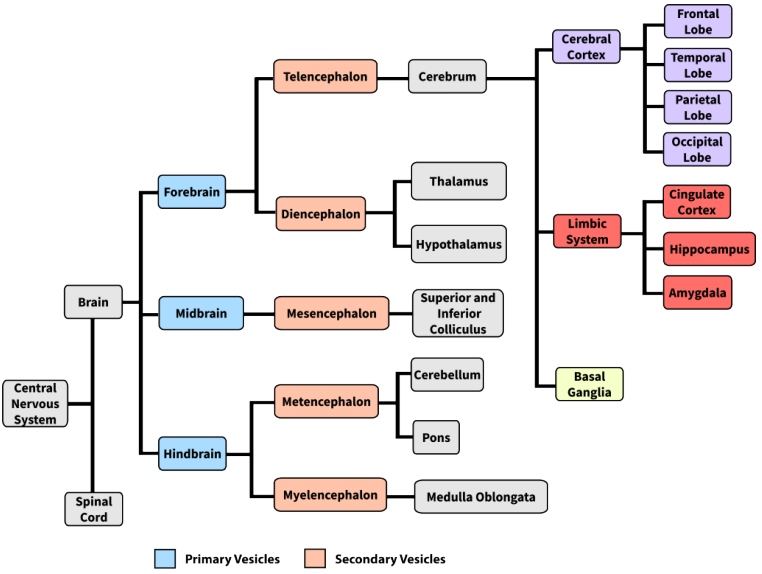

Figure 9: The central nervous system and its various major subdivisions.

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**).

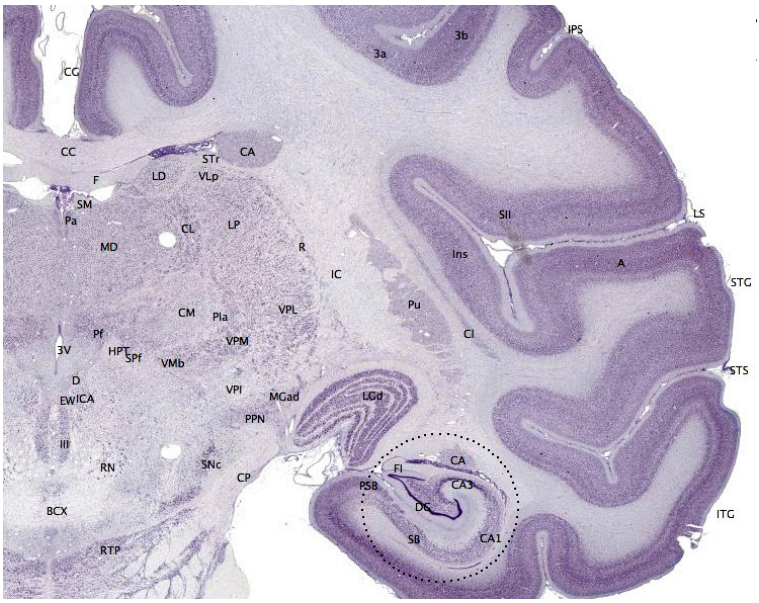

Figure 10. Coronal tissue slice from the brain of a macaque monkey. The gray matter of the cerebral cortex is the outer layer depicted in dark violet. The underlying white matter fiber tracts are shown in lighter color.

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 cm2, 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 smooth cortex). Folding maximizes the surface-to-volume ratio, and improves packaging and communication efficiency (Shipp, 2007).

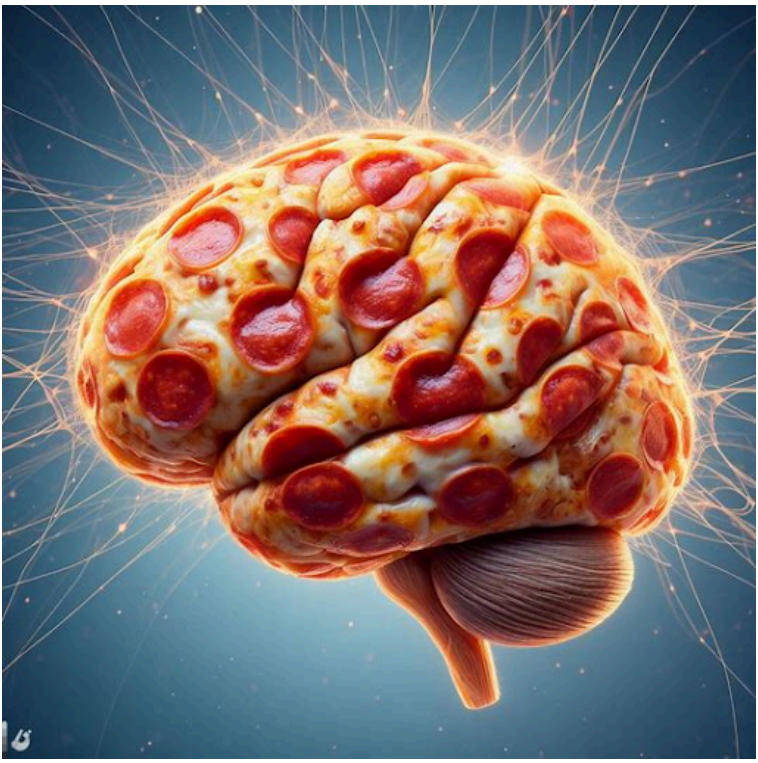

Figure 11. The thin outermost layer of each cerebral hemisphere, the cerebral cortex, is about the size of a medium thin-crust pizza–minus the sauce, cheese, and toppings.

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.

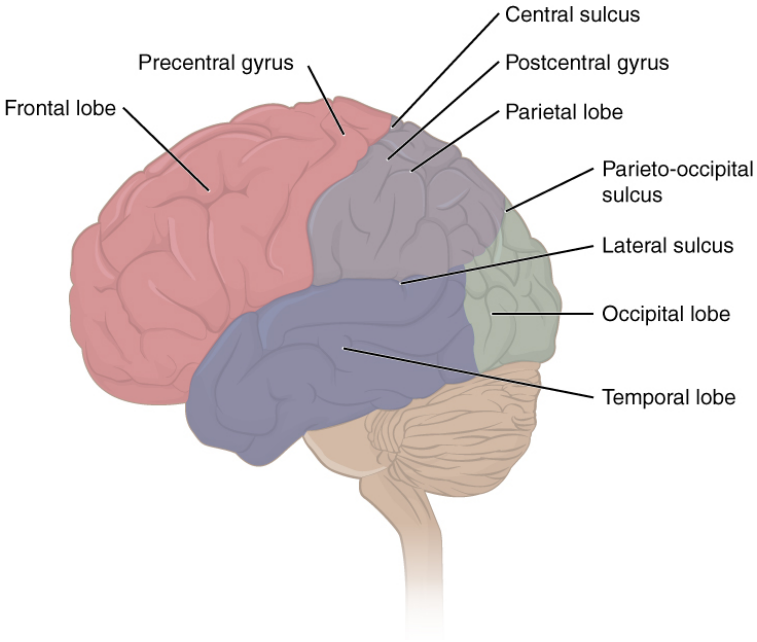

Figure 12: The lobes of the brain and the major sulci that mark the borders. The central sulcus separates the frontal and parietal lobes. The lateral sulcus marks the upper border of the temporal lobe. And the parieto-occipital sulcus (which is more clearly seen on the medial surface) separates the parietal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

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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/

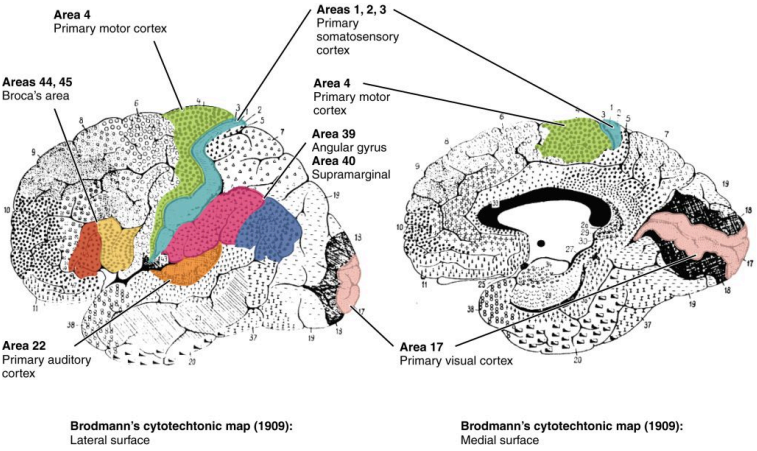

Figure 13. Brodmann's maps from 1909 that he built based on the cytoarchitecture or microscopic tissue structure and organization. Several important Brodmann areas are shown on the brain's lateral surface (left) and the medial surface (right).

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).

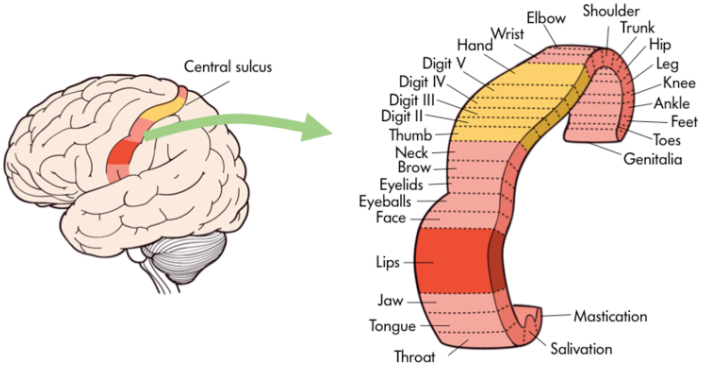

Figure 14. The primary motor cortex on the precentral gyrus is directly anterior to the central sulcus. It is organized so certain areas of the motor strip send signals to specific body parts like the tongue or fingers.

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]

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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.

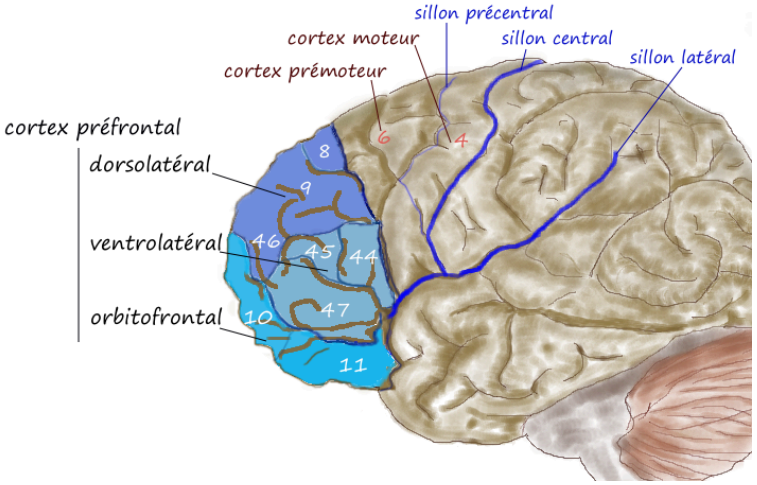

Figure 15. Prefrontal cortex in blue-ish colors. Subregions include: Broca's area marked by its Brodmann areas (BA) numbers 44 and 45; the dorsolateral prefrontal cortex [BA 9 and 46], and the orbitofrontal cortex [BA 10 and 11].

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, the main area responsible for processing 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 the **arcuate fasciculus**, a white-matter fiber tract **(Figure 16)**.

In addition to processing sound and language, the temporal lobe is also critical for visual object recognition and memory. The ventral (bottom) surface of the temporal lobe receives visual signals from the visual cortex and contains subregions that are highly 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 very specific abilities; lesions to the inferior temporal lobe 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]

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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.

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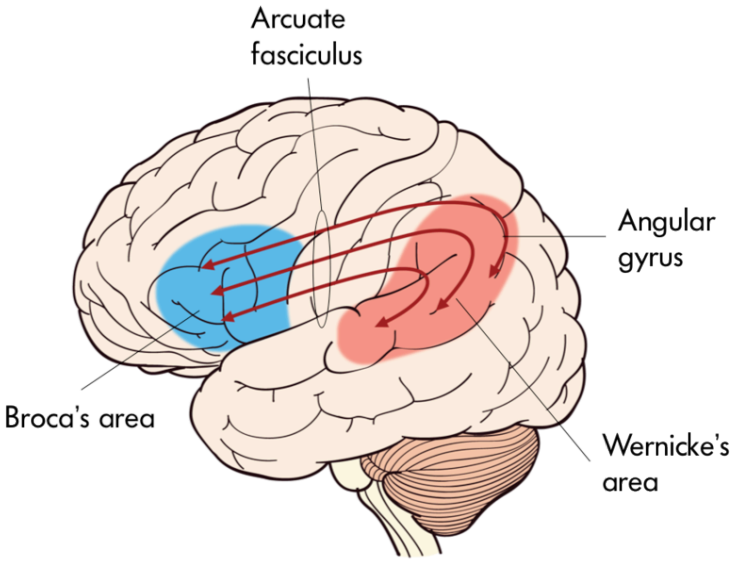

Figure 16. Broca's area in the left frontal gyrus; Wernicke's area in the superior temporal gyrus; and the arcuate fasciculus, a white matter tract that connects the caudal temporal cortex with the inferior frontal lobe.

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, meaning that adjacent parts of the skin are represented by adjacent areas of the somatosensory cortex. HIghly sensitive body parts have more nerve receptors on the skin and occupy larger regions of the cortex than less sensitive areas. For example as seen in **Figure 17**, the highly sensitive fingers and lips occupy much more somatosensory cortex than the leg and trunk.

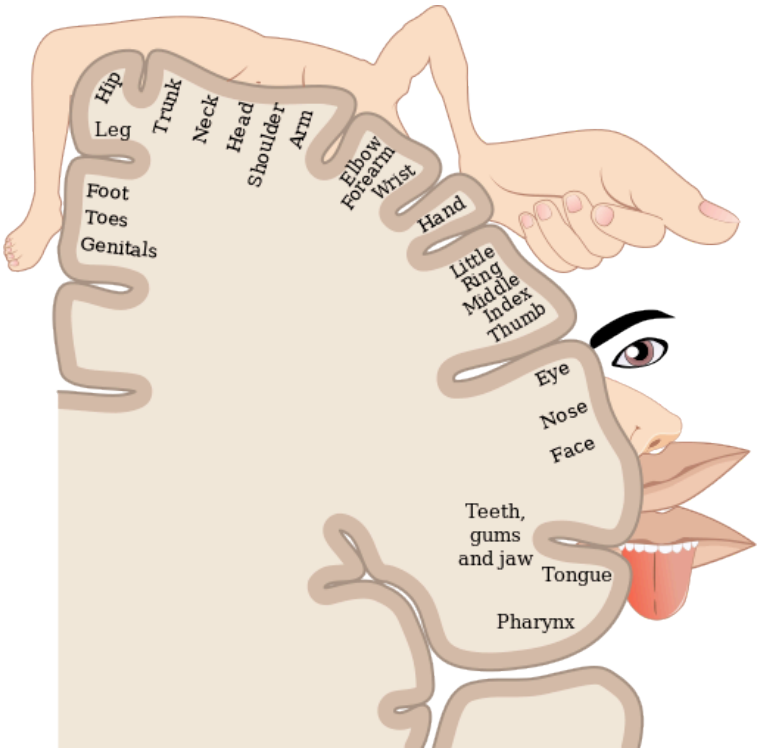

Figure 17. A coronal brain slice showing the somatosensory cortex and its topographic organization. More sensitive body parts, like the face and hands, are processed by larger regions of the somatosensory cortex, compared to less sensitive regions like the leg and trunk.

While the anterior parietal cortex processes body senses, the posterior parietal cortex is an "associative" region, meaning that it is neither strictly sensory nor motor. Rather it combines inputs from touch, proprioception, vision, and audition, as well as from motor and prefrontal regions (Whitlock, 2017). This integrative aspect makes it important for making spatial

maps to 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-

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 on to the visual cortex. Visual input enters the cortex at 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

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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]

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 involvement

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.

in so many functions and its heavy structural connectivity to other brain regions indicates its importance as a hub that links 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 of the brain and many open questions remain, a surge of recent research interest is making headway (Gogolla, 2017; Kortz & Lillehei, 2023).

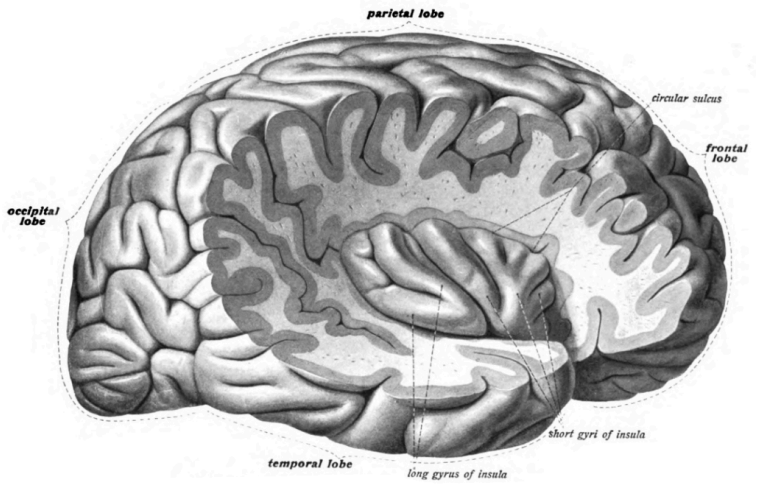

Figure 18. Anatomical illustration of the right insula from the 1908 edition of Sobotta's Anatomy Atlas. The insula is exposed here by removing portions of the overlying frontal, parietal, and temporal regions (these overlying areas are termed the "operculum").

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 (Torrico & Abdijadid, 2019). Major components of the limbic system include the **hippocampus**, the **amygdala**, and the **cingulate cortex**.

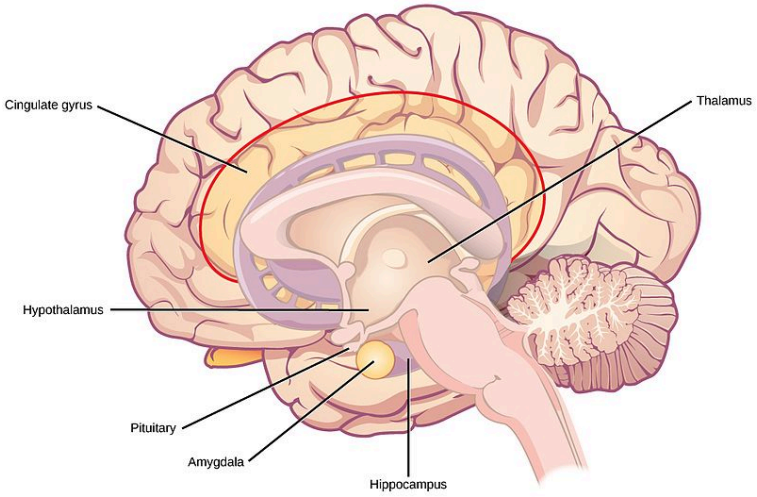

Figure 19: A midsagittal plane showing the interior of the brain and the locations of several limbic-system structures, including the hippocampus, amygdala, and cingulate cortex.

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 thought to be 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.

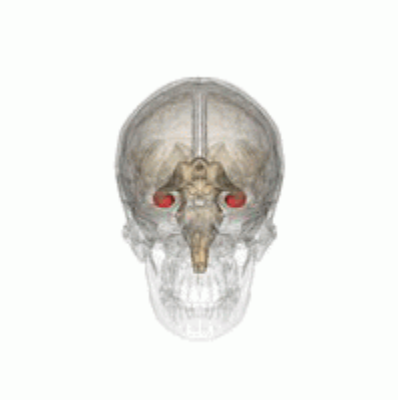

Figure 20. Location of the hippocampus in red.

Amygdala. The amygdala, named for its almond shape, sits adjacent to the hippocampus beneath the cerebral cortex (**Figure 19**). It is important for processing of emotions, including generating emotional responses (e.g., fear, anxiety, aggression) and emotional learning (e.g., fear conditioning).

The amygdala receives inputs from wide regions of sensory and prefrontal cortex, the hippocampus, and visceral information from the brainstem, enabling it to integrate

information about the situation, the bodily state, memory, and contextual information. The amygdala sends output signals to many 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, when a stimulus appears that is associated with punishment, a fear response can be produced by altering hormone release via the hypothalamus, triggering freezing behaviors, and activating the sympathetic nervous system via the brainstem. People with amygdala damage can display reduced emotional behavior or "flat affect", and show reduced learning about emotional or frightening stimuli or situations.[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

6. This section contains material adapted from: 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

cortex) that are especially 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,** in order 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 important for selecting motor actions, starting and stopping behaviors, and for aspects of motivated behavior (e.g., selecting actions based on whether they are likely to result in something good or bad happening to the individual). 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 conditions including Parkinson's disease and Huntington's disease, as well as schizophrenia, Tourette's syndrome, obsessive-compulsive disorder, and addiction.[7]

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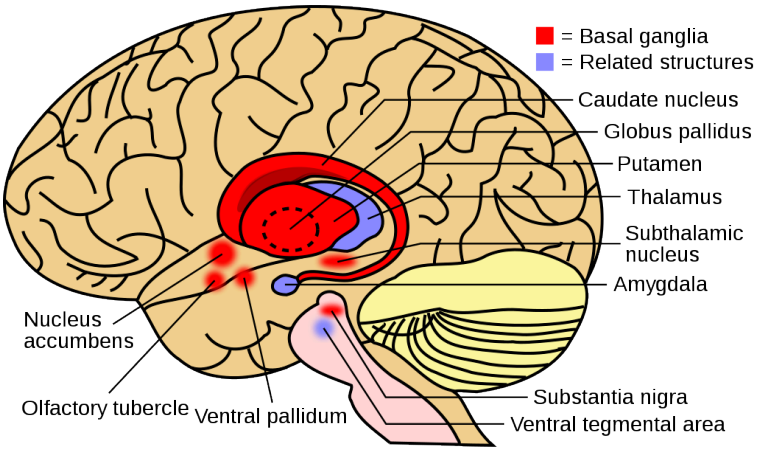

Figure 21: Basal Ganglia and related structures.

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 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 on to their corresponding 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. Rather than simply relaying information in one direction, however, a key feature of thalamic processing is that nuclei also receive descending information from the cortex, forming circuits termed thalamocortical 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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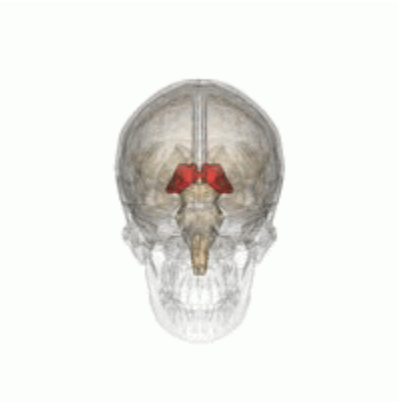

Figure 22A. Location of the thalamus in red.

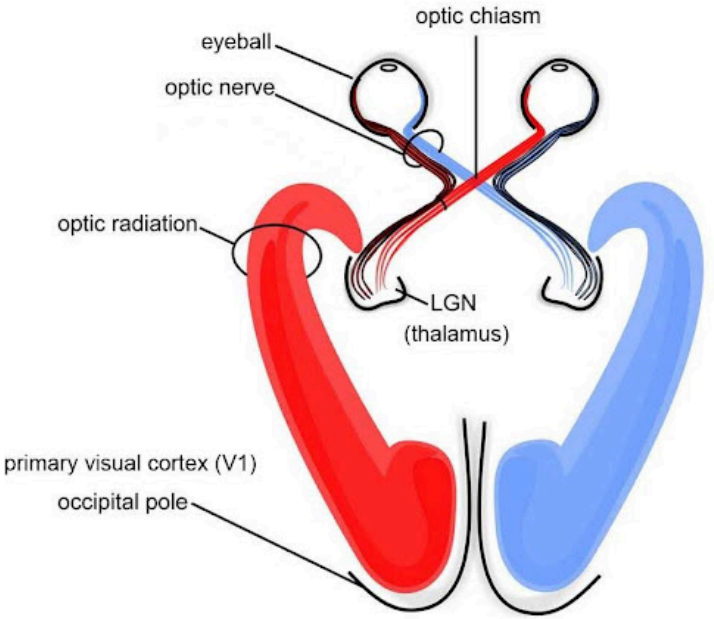

Figure 22B. Visual pathway from the eyes through the thalamus to the visual cortex. Visual information is sent from the retinas at the back of the eyeballs, along the optic nerve to the lateral geniculate nucleus (LGN) of the thalamus, then to the primary visual cortex. Blue color represents the path 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 known to be important for controlling mood, development, growth, and reproduction. Given its central location in the brain, the hypothalamus has connections 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 long established role in motor control, neuroimaging studies have implicated it in many cognitive functions, including language and attention. It is perhaps not surprising that the cerebellum's influence extends beyond movement, given that 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 the majority of the cerebellum maps to cerebral brain networks involved in cognition (Buckner, 2013).[9]

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 of the neural functions that keep us alive, including regulating breathing, heart rate, and

9. This section contains material adapted from: Beck, D. & Tapia, E. (2024). The brain. In R. Biswas-Diener & E. Diener (Eds), Noba textbook series: Psychology. Access for free at http://noba.to/jx7268sd License: CC BY-NC-SA 4.0 DEED

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 is able to serve as a bridge that connects the cerebral cortex with the medulla and exchange information back and forth 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]

10. This section contains material adapted from: Beck, D. & Tapia, E. (2024). The brain. In R. Biswas-Diener & E. Diener (Eds), Noba textbook series: Psychology. Access for free at http://noba.to/jx7268sd License: CC BY-NC-SA 4.0 DEED

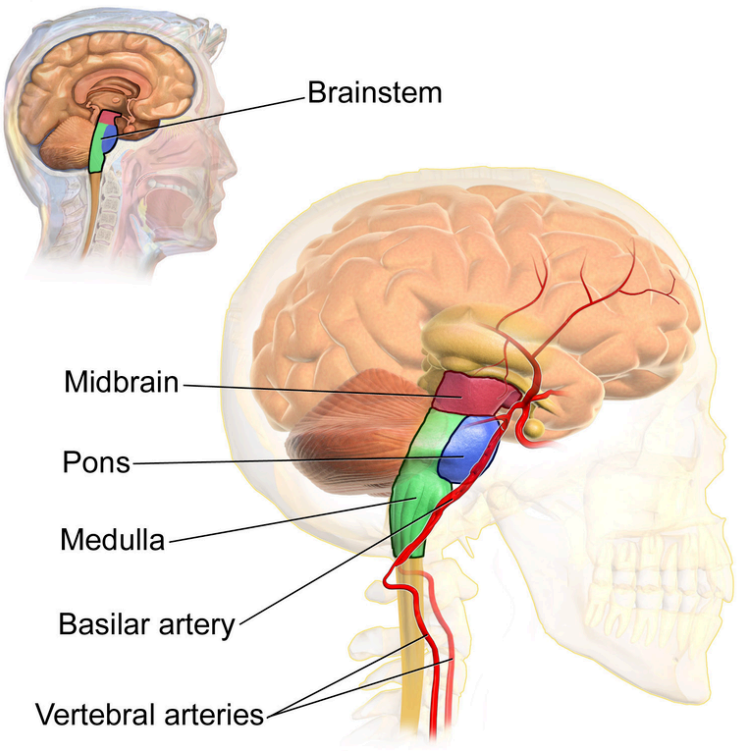

Figure 24. Brainstem and its component substructures, in descending order: the midbrain, pons, and medulla.

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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 is made up 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, being suspended 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 the lower sections of the brain. Finally, CSF circulates nutrients throughout the brain and helps clear waste products away from the brain.

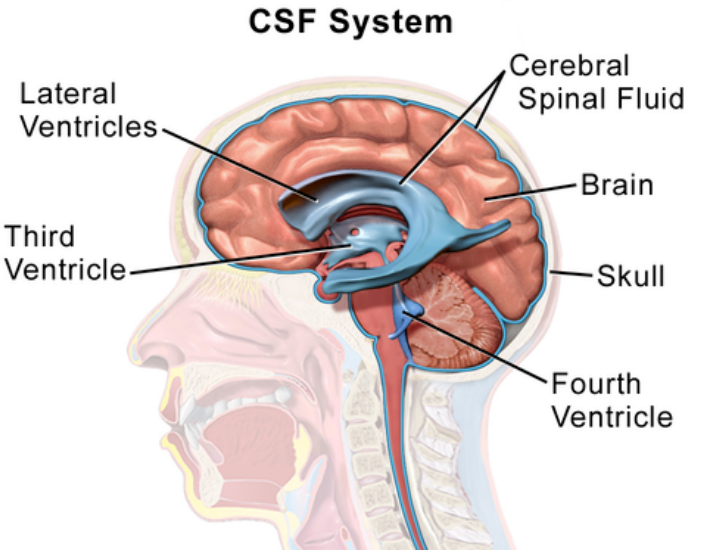

Figure 25: A) The cerebral ventricular system showing the 4 major ventricles.

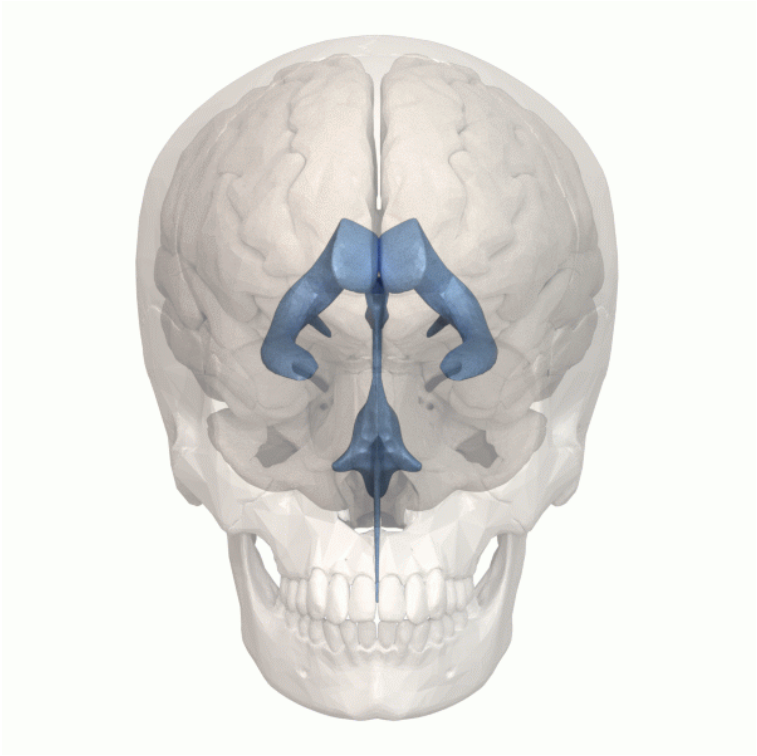

Figure 25: B) Rotating 3D rendering of the ventricles.

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—the circle of Willis. Several large arteries branch off the circle of Willis to perfuse different regions of the brain. Branches of these major arteries form smaller and smaller arteries and arterioles that pass through the subarachnoid space before diving into the brain, and branch yet 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, though, so they only take up about 2% of the brain volume. This means that, in cerebral cortex, each neuron is only around 10-20 microns from its nearest capillary. This dense vascular network can therefore supply oxygen and glucose very close 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 to these regions of increased activity. In fact this increase in blood flow usually supplies more oxygen than is needed, so that blood oxygen levels increase in active brain regions. This increase in blood oxygen gives rise to the BOLD (blood oxygen level dependent) signal that can be detected using magnetic resonance imaging and is often used as a surrogate for neuronal activity in experiments

studying the function of different brain regions (see Chapter 4–Research Methods).

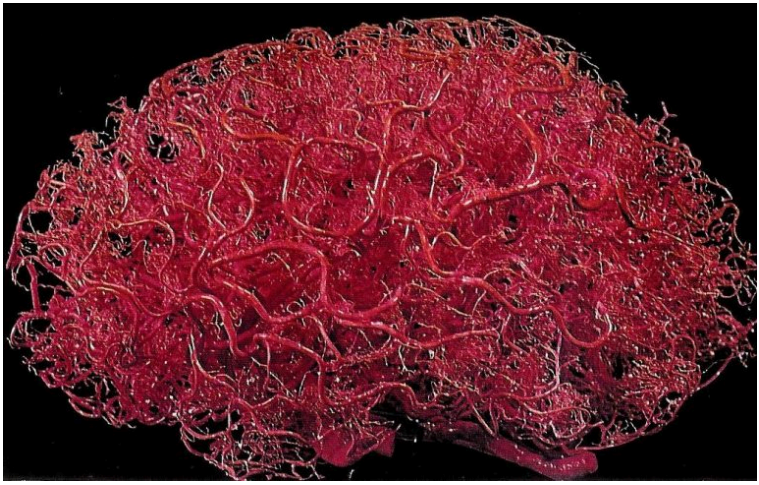

Figure 26. A cast of the brain's vasculature.

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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.

2.10: 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

2.9: REFERENCES

Parts of this chapter were adapted from:

Ahmad, A. (2023). The nervous system. In R. Biswas-Diener & E. Diener (Eds), *Noba textbook series: Psychology.* Champaign, IL: DEF publishers. http://noba.to/wnf72q34

Beck, D. & Tapia, E. (2023). The Brain. In R. Biswas-Diener & E. Diener (Eds), *Noba textbook series: Psychology.* Champaign, IL: DEF publishers. http://noba.to/jx7268sd

Betts, J. G. et al. (2022). *Anatomy and Physiology 2e.* OpenStax. https://openstax.org/details/books/anatomy-and-physiology-2e

Biswas-Diener, R. (2023). The brain and nervous system. In R. Biswas-Diener & E. Diener (Eds), *Noba textbook series: Psychology.* Champaign, IL: DEF publishers. http://noba.to/4hzf8xv6

Clark, M.A., Douglas, M. & Choi, J. (2023). *Biology 2e.* OpenStax. https://openstax.org/books/biology-2e

Hall, C. N. (2023). *Introduction to Biological Psychology.* University of Sussex Library. *https://openpress.sussex.ac.uk/introductiontobiologicalpsychology/*

The Nervous System. (2023, October 31). In General Biology. Boundless (now LumenLearning). https://bio.libretexts.org/@go/page/13875

Spielman, R. M., Jenkins, W. J., & Lovett, M. D. (2020). *Psychology 2e.* OpenStax. Access for free at https://openstax.org/books/psychology-2e/pages/1-1-what-is-psychology

The Brain and Nervous System References

American Association for the Advancement of Science (AAAS). (1880). Dr. Paul Broca. *Science*, 1(8), 93. http://www.jstor.org/stable/2900242

Bear, M. H., Reddy, V., & Bollu, P. C. (2018). Neuroanatomy, hypothalamus. In: *StatPearls.* StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK525993/

Buckner, R. L. (2013). The cerebellum and cognitive function: 25 years of insight from anatomy and neuroimaging. *Neuron, 80*(3), 807-815.

Duysens, J., & Van de Crommert, H. W. (1998). Neural control of locomotion: The central pattern generator from cats to humans. *Gait & Posture, 7*(2), 131-141.

Gogolla, N. (2017). The insular cortex. *Current Biology, 27*(12), R580-R586.

Hall, C. N. (2023). *Introduction to Biological Psychology.*

University of Sussex Library. https://openpress.sussex.ac.uk/introductiontobiologicalpsychology/

Kanwisher, N. & Yovel, G. (2006). The fusiform face area: a cortical region specialized for the perception of faces. *Philosophical Transactions of the Royal Society B: Biological Sciences, 361(*1476), 2109-2128.

Karnath, H. O. (1997). Spatial orientation and the representation of space with parietal lobe lesions. *Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences*, *352*(1360), 1411-1419.

Kortz, M.W., & Lillehei, K. O. (2023). Insular Cortex. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing.

Lanciego, J. L., Luquin, N., & Obeso, J. A. (2012). Functional neuroanatomy of the basal ganglia. *Cold Spring Harbor Perspectives in Medicine, 2*(12), a009621.

Portas, C. M., Rees, G., Howseman, A. M., Josephs, O., Turner, R., & Frith, C. D. (1998). A specific role for the thalamus in mediating the interaction of attention and arousal in humans. *Journal of Neuroscience*, *18*(21), 8979-8989.

Rudebeck, P. H., & Rich, E. L. (2018). Orbitofrontal cortex. *Current Biology, 28*(18), R1083-R1088.

Shenoy, S. S., & Lui, F. (2022). Neuroanatomy, ventricular system. In StatPearls [Internet]. StatPearls publishing.

Shipp, S. (2007). Structure and function of the cerebral cortex. *Current Biology, 17*(12), R443-R449.

Swanson, L. (2000). What is the brain? *Trends in Neurosciences, 23,* 519–527.

Torrico, T. J., & Abdijadid, S. (2019). Neuroanatomy, limbic system.

Van Essen, D. C., Anderson, C. H., & Felleman, D. J. (1992). Information processing in the primate visual system: An integrated systems perspective. *Science, 255*(5043), 419–423.

Van Essen, D. C., Donahue, C. J., & Glasser, M. F. (2018). Development and evolution of cerebral and cerebellar cortex. *Brain Behavior and Evolution, 91*(3), 158-169.

Whitlock, J. R. (2017). Posterior parietal cortex. *Current Biology, 27*(14), R691-R695.

Wright, B. L., Lai, J. T., & Sinclair, A. J. (2012). Cerebrospinal fluid and lumbar puncture: A practical review. *Journal of Neurology, 259,* 1530-1545.

CHAPTER 3: NEURONS

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This chapter relating to the biological basis of behavior provides an overview of the basic structure of neurons and their means of communication. Neurons, cells in the central nervous system, 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. The goal of this chapter is to become familiar with the anatomical

structure of neurons and to understand how neurons communicate by electrochemical signals to process sensory information and produce complex behaviors. A basic knowledge of the structure and function of neurons is a necessary foundation as you move forward in the field of 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, a noun, or an adjective?). In a similar fashion, to appreciate how groups of cells work together in a meaningful way 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 our favorite sports team, or laughing?

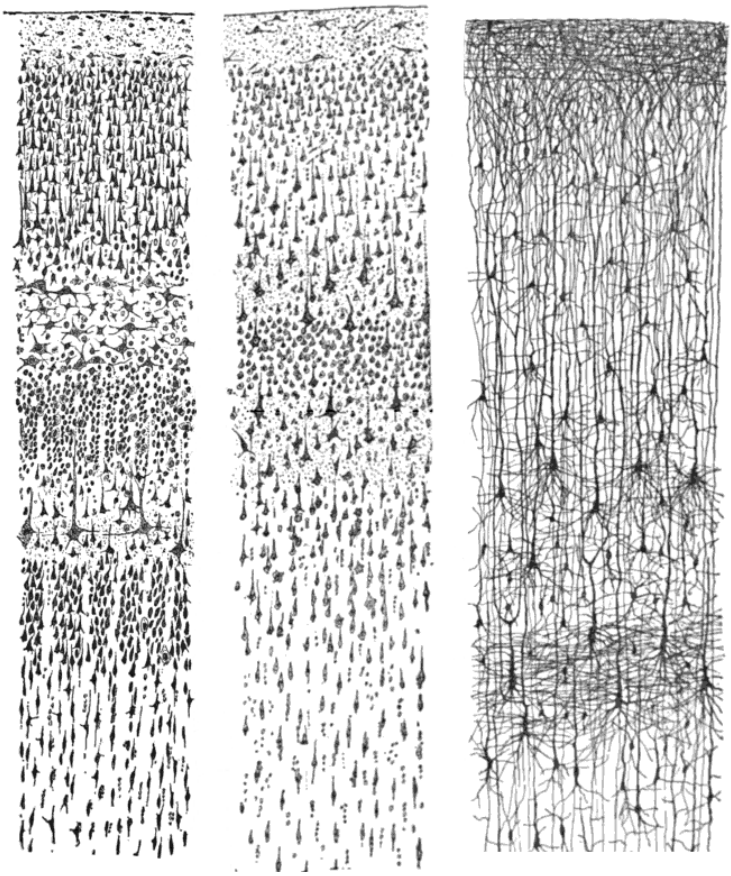

Figure 1. Three drawings by Santiago Ramón y Cajal, taken from "Comparative study of the sensory areas of the human cortex", pages 314, 361, and 363. Left: Nissl-stained visual cortex of a human adult. Middle: Nissl-stained motor cortex of a human adult. Right: Golgi-stained cortex of a 1 1/2 month old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

Our journey in answering 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 very common 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 (see right panel of Figure 1). A more notable characteristic of a Golgi stain is that it 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 was opposed to 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 called "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 that occurs 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 prior to *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.

Media Attributions

- Cajal cortex drawings © Santiago Ramón via wikimedia is licensed under a Public Domain license

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 2–3). 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.

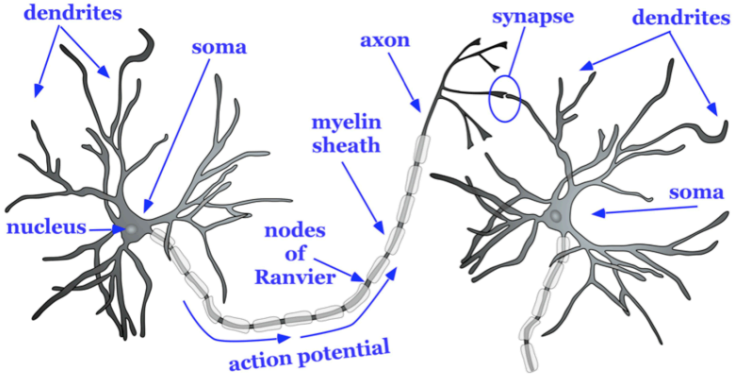

Figure 2. Basic structure of a neuron.

The axon splits many times so that 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, which is the 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 very small 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, there are **synaptic vesicles** that 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.

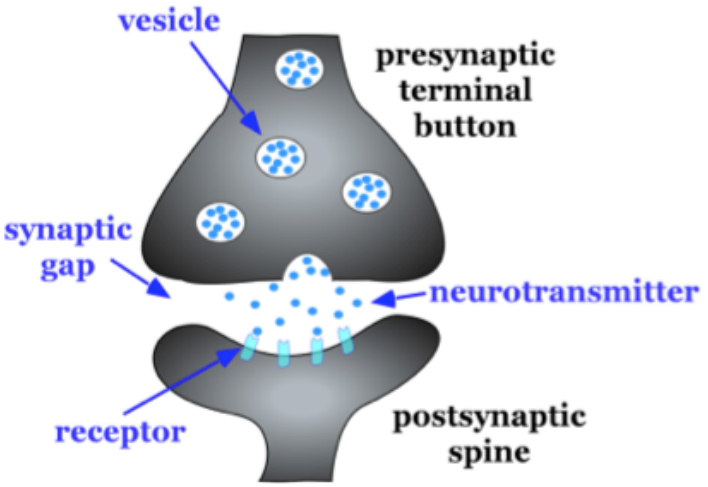

Figure 3. Characteristics of a synapse.

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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 perception such as perception of light in the retina of the eye. They have one axon and one dendrite which help acquire and pass sensory information to various centers in the brain. Finally, *multipolar neurons* are the most common and they 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).

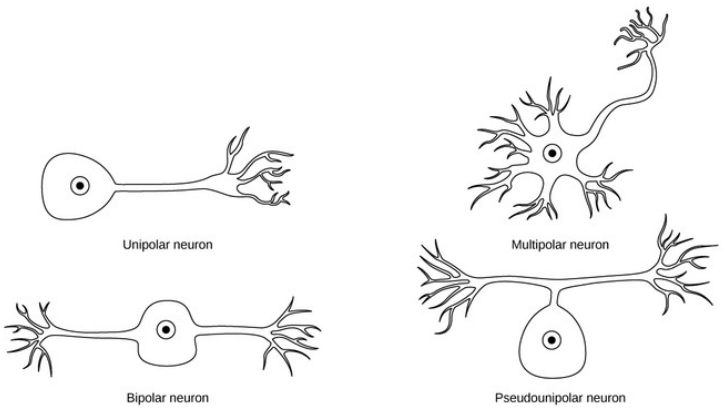

Figure 4. Types of Neurons: Neurons are broadly divided into a few main types based on the number and placement of axons: (1) unipolar, (2) bipolar, (3) multipolar, and (4) pseudounipolar.

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 the neurons, and help to regulate the ionic composition of the extracellular fluid. While glial cells play a vital role in neuronal support, they do not carry electrical signals or participate in the communication between cells as neurons do.

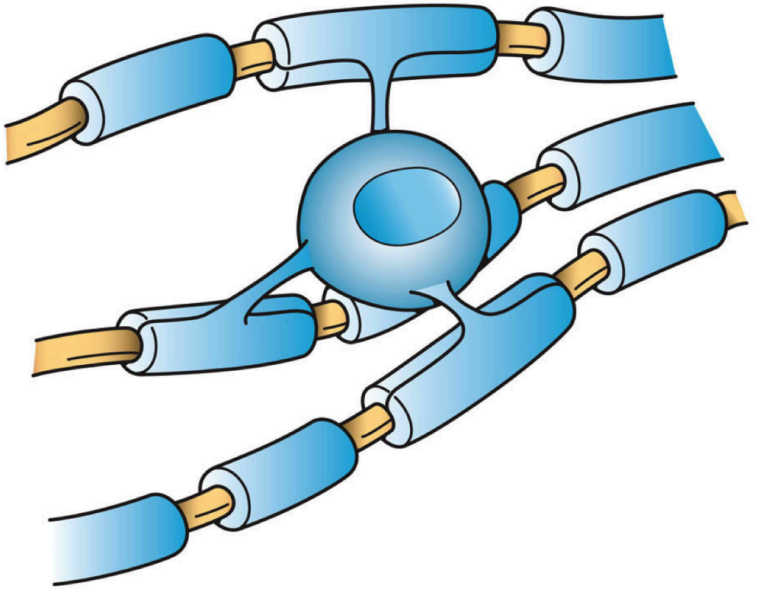

Figure 5. An oligodendrocyte myelinating several axons in the central nervous system.

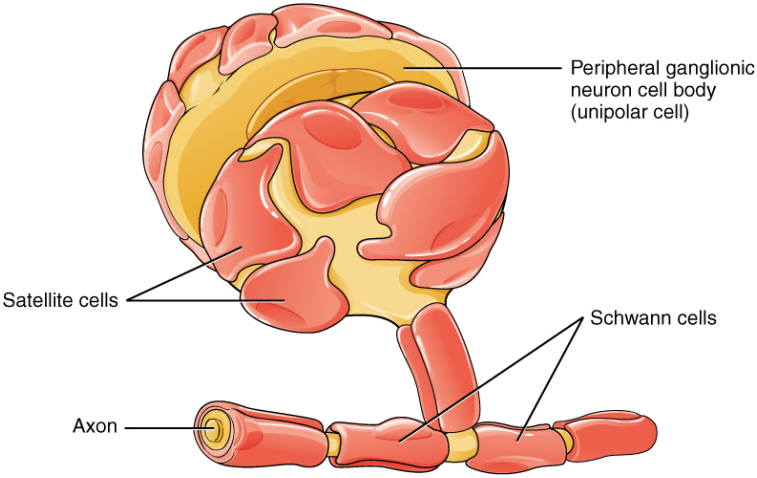

Figure 6. The peripheral nervous system (PNS) has myelinating Schwann cells.

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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 with one another 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 when it is at a 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. There are proteins that 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 force on two ions with similar charge to repel each other and the force of two ions with opposite charge to attract one another. Remember the saying "opposites attract"?

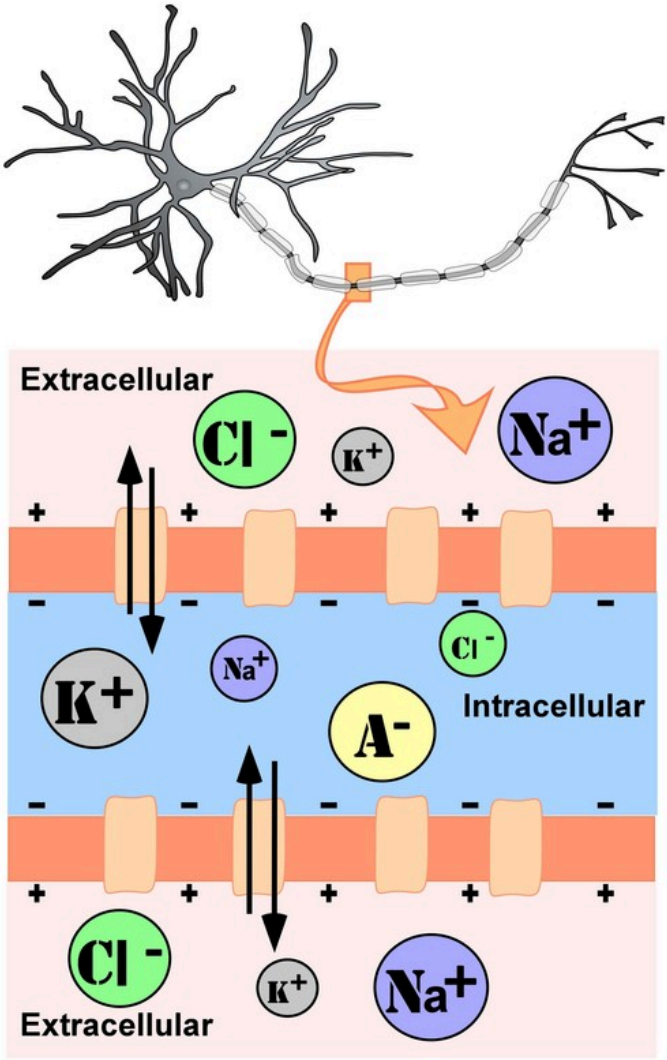

Figure 7. Representation of ion concentrations inside (intracellular) and outside (extracellular) a neuron in the unmyelinated segment of the axon.

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 there are several ions that 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 are very small voltages compared with the voltages of batteries and electrical outlets that 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 very 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 that occur 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 giant axon of the squid is roughly 100 times larger than that of axons in the mammalian brain, making it much easier to see and work with. Activation of the giant axon is responsible for a withdrawal response the squid uses when escaping from a predator. The large axon size is no mistake in nature's design; it allows for very rapid transmission of an electrical signal, enabling the squid a swift escape from its 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**). What is meant by an all-or-nothing response? This all-or-nothing concept parallels the binary code used in computers, where there are only two possibilities, 0 or 1. There is no halfway or in-between these possible values; for example, 0.5 does not exist in binary code. There are only two possibilities, either the value of 0 or the value of 1. The action potential is the same in this respect. There is no halfway; it occurs, or it does not occur. 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.

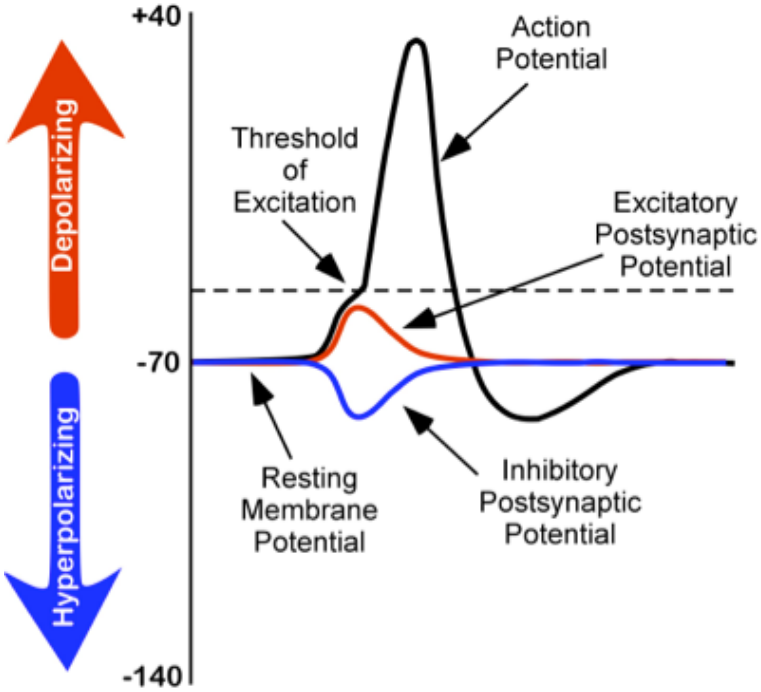

Figure 8. Changes in membrane potentials of neurons.

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.

I know the concept of summation can be confusing. As a child, I used to play a game in elementary school 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 rather well. In this game, a group of children next to one another would work in unison 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 as the properties of the waves in the parachute; 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 in the same fashion 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 causes a voltage-dependent Na+ channel to open. 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 after 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 very positive relative to the outside of the cell (depolarized) and the high concentration of K+ within the cell, both the force of diffusion and the force of electrostatic pressure drive K+ outside of the cell. The movement of K+ out of the cell causes the cell potential to return back 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 very close proximity to the action potential are affected.

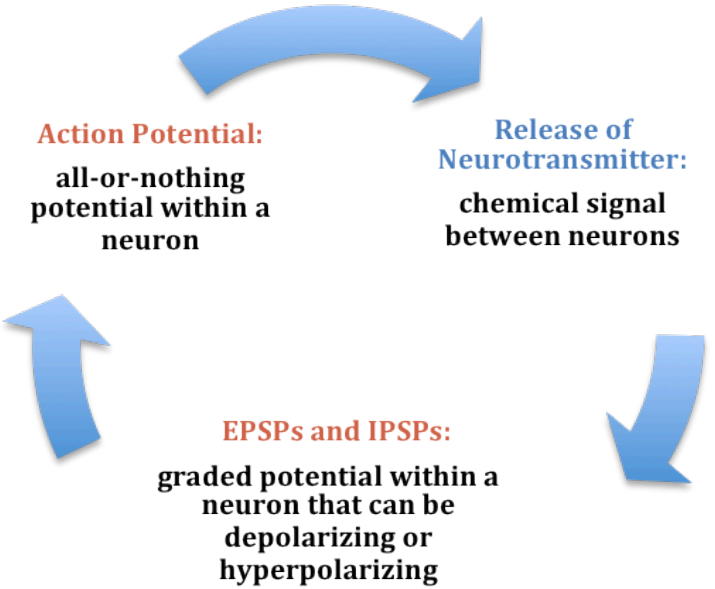

Figure 9. Summary of the electrochemical communication within and between neurons.

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 to exist 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).

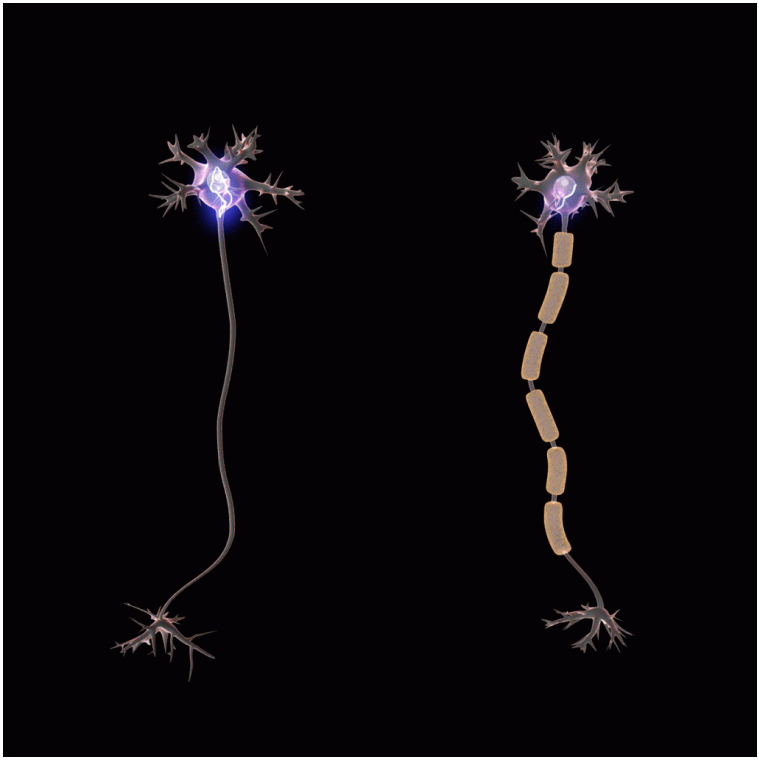

Figure 10. Action potential propagation in myelinated neurons (right) is faster than in unmyelinated neurons (left) because of saltatory conduction.

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_ldA1M

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_tjKYvEziI

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:

Furtak, S. (2021). Neurons. In R. Biswas-Diener & E. Diener (Eds), Noba textbook series: Psychology. Champaign, IL: DEF publishers. Retrieved from http://noba.to/s678why4 License: CC BY-NC-SA 4.0 DEED

References

De Carlos, J. A., & Borrell, J. (2007). A historical reflection of the contributions of Cajal and Golgi to the foundations of neuroscience. *Brain Res Rev*, 55(1), 8-16. doi: 10.1016/j.brainresrev.2007.03.010

Furtak, S. C., Moyer, J. R., Jr., & Brown, T. H. (2007). Morphology and ontogeny of rat perirhinal cortical neurons. *J Comp Neurol*, 505(5), 493-510. doi: 10.1002/cne.21516

Grant, G. (2007). How the 1906 Nobel Prize in Physiology or Medicine was shared between Golgi and Cajal. *Brain*

Res Rev, 55(2), 490-498. doi: 10.1016/j.brainresrev.2006.11.004

Herculano-Houzel, S. (2009). The human brain in numbers: a linearly scaled-up primate brain. *Frontiers in Human Neuroscience, 31.*

Hodgkin, A. L., & Huxley, A. F. (1952). A quantitative description of membrane current and its application to conduction and excitation in nerves. *J Physiol*, 117(4), 500-544.

Lopez-Munoz, F., Boya, J., & Alamo, C. (2006). Neuron theory, the cornerstone of neuroscience, on the centenary of the Nobel Prize award to Santiago Ramon y Cajal. *Brain Res Bull*, 70 (4-6), 391-405. doi: 10.1016/j.brainresbull.2006.07.010

Pasternak, J. F., & Woolsey, T. A. (1975). On the "selectivity" of the Golgi-Cox method. *J Comp Neurol*, 160(3), 307-312. doi: 10.1002/cne.901600304

Ramón y Cajal, S. (1911). Histology of the nervous system of man and vertebrates. New York, NY: Oxford University Press.

Simons, M., & Trotter, J. (2007). Wrapping it up: the cell biology of myelination. *Curr Opin Neurobiol*, 17(5), 533-540. doi: 10.1016/j.conb.2007.08.003

Smit, G. J., & Colon, E. J. (1969). Quantitative analysis of the cerebral cortex. I. Aselectivity of the Golgi-Cox staining technique. *Brain Res*, 13(3), 485-510.

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 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 by using 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 the field of 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

Some early influential examples showing links between brain and behavior come 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 placing 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). Prior to 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.

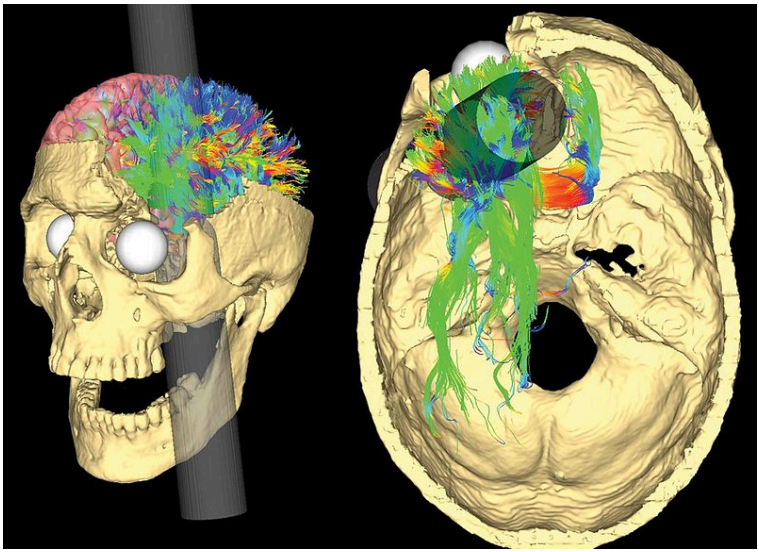

Figure 1: A computerized tomography (CT) image reconstruction of the path of the tamping rod that entered Phineas Gage's mouth and blasted through his skull and left frontal lobe. The bright colors represent White Matter fiber pathways that were likely intersected by the rod (Van Horn et al. 2012).

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 was referred to as "Tan" because his speech production was limited to the single repetition of the syllable "Tan." After Tan's death, Broca discovered a major lesion on the surface of 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 can be associated with 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).

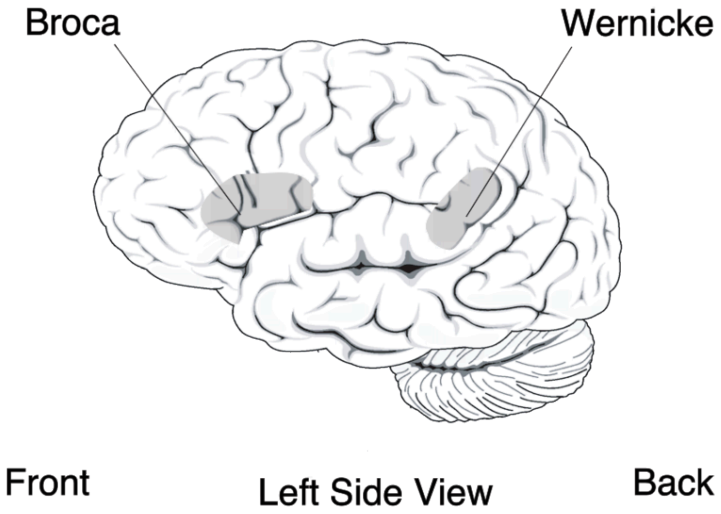

Figure 3. Broca's area for Speech Production is located in the left frontal lobe. Wernicke's area for Speech Perception is located in the left temporal lobe.

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 clearly 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 biological psychology 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 exact 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 behavior of the animal 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 other correlational research methods). After the animal's death, its brain is often cut into thin slices, prepared with a staining procedure to allow a clear view of some part of the neuronal structure, then examined with a microscope to verify the extent and precise location of the lesions.

As an alternative to *permanent* lesions through ablation, researchers can *temporarily* lesion brain regions, for example, by cooling down or injecting an anesthetic into the target brain tissue. Additionally, electrical stimulation from implanted electrodes can be used to 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.

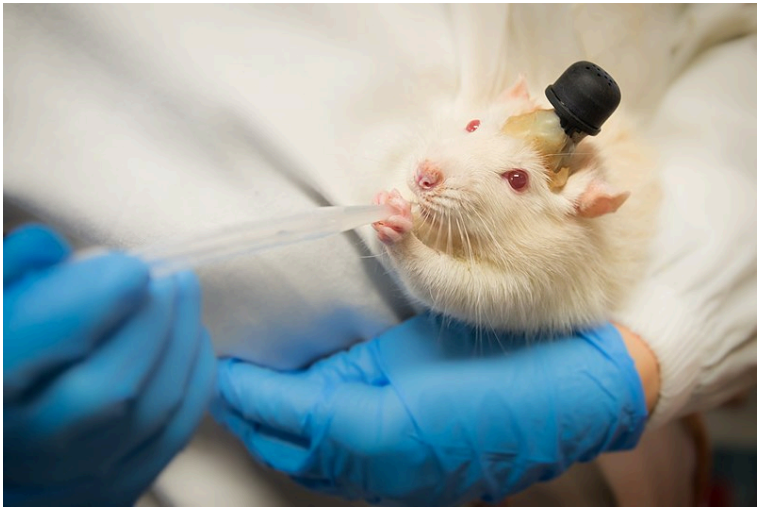

Figure 5. A lab rat with a brain implant that was used to record neuronal activity while the rat performed a particular task (vibration discrimination in this case). In this picture, a scientist feeds the rat apple juice through a pipette.

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: *intra*cellular unit recording, wherein a microelectrode is inserted *into* a single neuron to measure its electrical activity; *extra*cellular 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 can pick up neural activity while the animal is performing some task and provide insight into links between neural activity and behavior.

Directly recording from within *human* brains for research is uncommon because it's not justifiable to invasively cut open the skull solely for research. However, some patients who are already undergoing surgery for medical procedures, such as treatments of 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 especially 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.

Media Attributions

4.4: TOOLS OF COGNITIVE NEUROSCIENCE – EEG AND MEG

Advances in technology have led to ever more sophisticated brain recording techniques. Just as X-ray technology allows us to peer inside the body, neuroimaging techniques allow us to view the working brain (Raichle,1994). Many noninvasive techniques for studying human brain function are used in the field of biopsychology and each technique has advantages and disadvantages. It is important to recognize that each method allows us to "see'" brain activity through a different lens. As a result, it is important to understand how each technique works. It is fascinating to think about how our understanding of the brain is intimately related to the available technologies. As new technologies and techniques are developed, we will be able to develop 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 placed 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.

Because the small voltages are distorted as they pass through brain tissue, skin, and bone, researchers only have a rough idea where in the brain a signal was generated. This uncertainty is especially the case for signals coming from deep within the brain (even if the researchers have the person's structural brain scan, high-density electrode coverage from a cap with 256 electrodes, and sophisticated localization analysis algorithms). Thus, EEG's ***spatial* resolution** of *where* something occurs in the brain is rather low. Conversely, EEG's ***temporal* resolution** is excellent and indicates *when* something happens in the brain to the millisecond. With the excellent temporal resolution, EEG is well suited for examining the brain's 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, then 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 reflect the summed activity of millions of neurons. They capture attentional or conscious states and play a role in how specific information is encoded and how attention is modulated in the brain (da Silva, 2013). In addition to the research uses noted above, EEG is also particularly important in clinical diagnosis, specifically with respect to diagnosing epilepsy as well as seizure and sleep disorders.

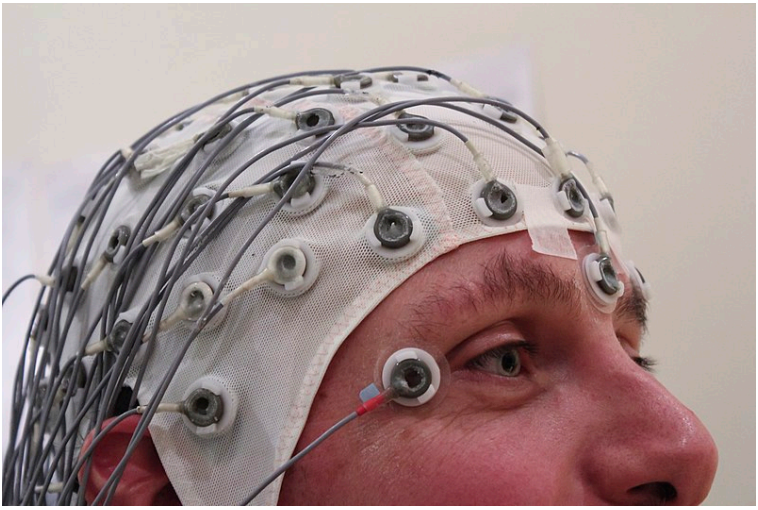

Figure 6. Participant wearing an EEG cap that uses electrodes to pick up voltages on the scalp.

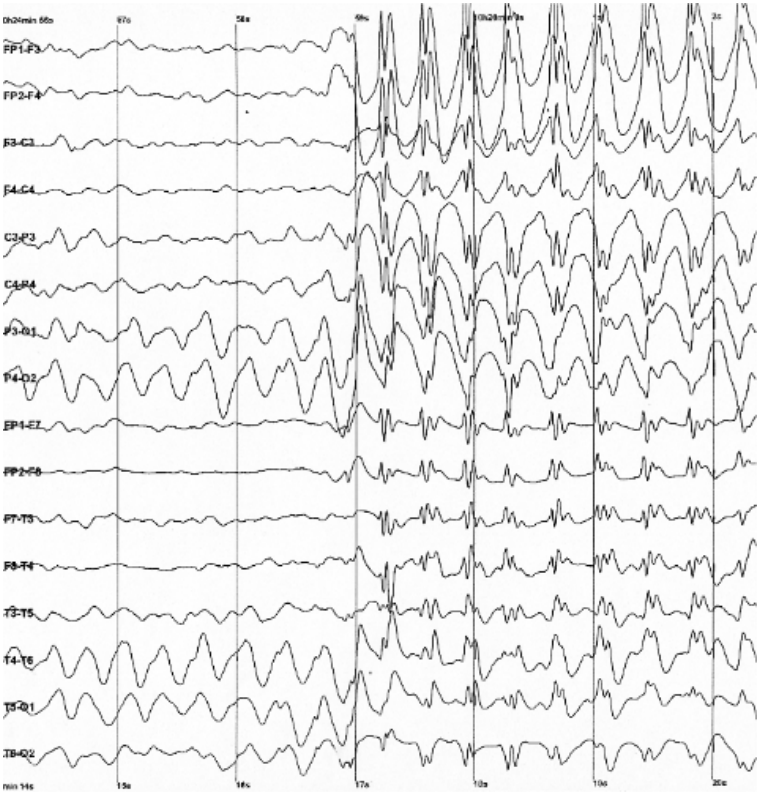

Figure 7. An EEG readout of voltages at 16 electrode sites. Each row is one electrode; the voltage of each electrode is mapped on the vertical axis; and time is mapped on the horizontal axis with each vertical line marking 1 second. This particular EEG readout is showing characteristic 3 Hz spike and 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 that of EEG because magnetic fields are able to pass relatively unchanged through hard and soft tissue and therefore are not distorted by skull and scalp. In spite of MEG's excellent spatial *and* temporal resolution, it is used much less widely than EEG because the MEG apparatus is much more expensive and unwieldy than that for EEG.

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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 purely research purposes due to the 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.

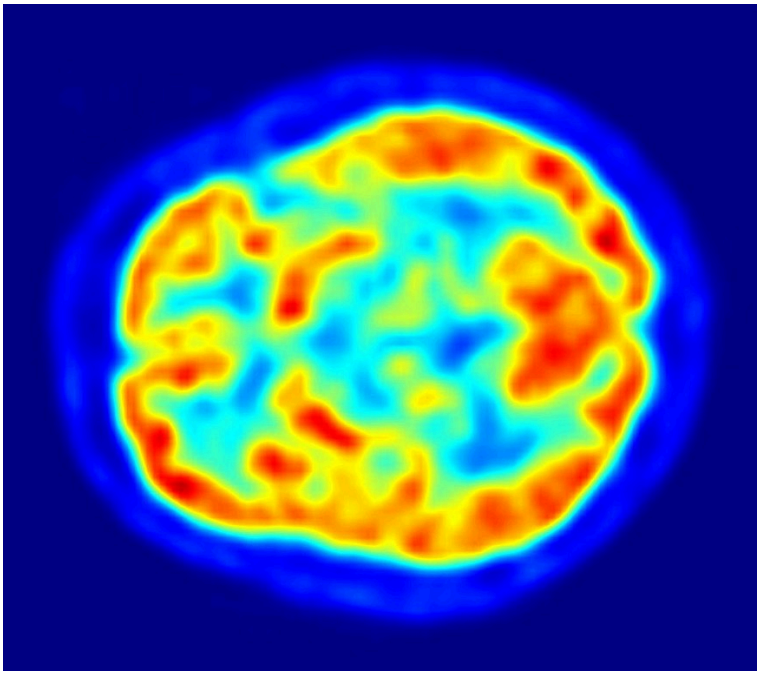

Figure 8. This is a transaxial slice of the brain taken with positron emission tomography (PET). Red areas show more accumulated tracer substance and blue areas show where little to no tracer has accumulated.

Magnetic Resonance Imaging

The most commonly used brain-imaging modality today is Magnetic Resonance Imaging (MRI). Different types of scans from the same MRI machine can give 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 around 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 the protons realign with the magnetic field differs based on the type of tissue, and can clearly depict differences between the brain's white matter, gray matter, cerebrospinal fluid, bone, blood, blood vessels, etc.

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 the image to compare the size of structures in different groups of people (for example, Are areas associated with pleasure smaller in individuals with depression or are areas for controlling fingers larger in string musicians than vocalists or trombonists?). These structural images can also be used to increase the accuracy of locations as measured with functional magnetic resonance imaging (fMRI).

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 look at white matter integrity in diseases such as Multiple Sclerosis or the brain plasticity after learning a new skill like juggling.

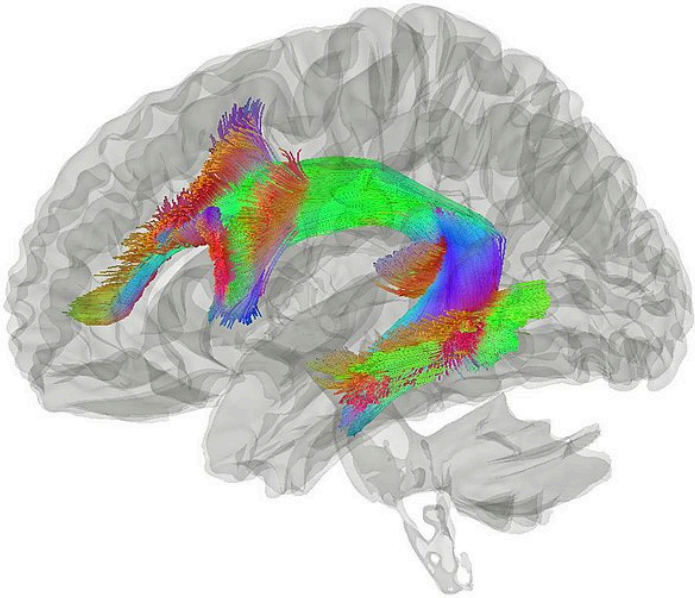

Figure 10. DTI image showing the white matter tracts, including the arcuate fasciculus, a bundle of axons that connects Broca's area and Wernicke's area.

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. In order to establish a causal rather than correlational relationship, we need to alter brain function and observe subsequent change in behavior. Lesions are one way to alter the brain and can reveal a casual 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 have been developed that allow researchers to temporarily and non-invasively alter brain function in humans.

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 be used to 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 or medical settings, and has been shown to be an effective treatment for some people with depression (Perera et al., 2016).

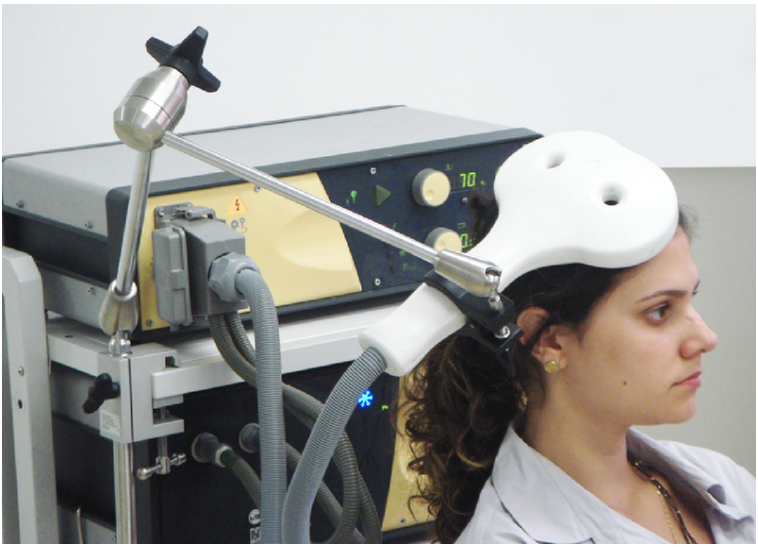

Figure 12. A transcranial magnetic stimulation (TMS) coil positioned over a person's scalp.

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 period of time. When used in combination with cognitive training, tDCS has been shown to improve performance of 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 specific 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 with "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 mutated to produce different colors; these different color fluorescent proteins are inserted into individual neurons in different ratios to flag 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 how neural networks are organized. The brainbow technique provides beautiful images of neurons and highlights biopsych research at the molecular and cellular level.

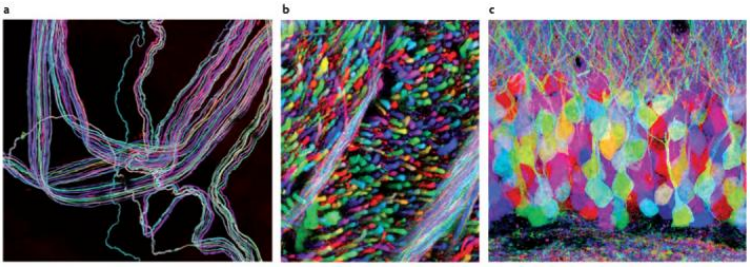

Figure 13. Three brainbows of mouse neurons from Lichtman et al. (2008). a) a motor nerve innervating ear muscle. b) An axon tract in the brainstem. c) The hippocampal dentate gyrus.

Optogenetics is an especially exciting technique to change 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 a genetically defined set of neurons to understand their contribution to learning, memory, decision making, addiction, movement, and many other active research areas.

In sum, the various research techniques used in biological psychology each have their own 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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4.7: REFERENCES

Parts of this chapter were adapted from:

Beck, D. & Tapia, E. (2023). The brain. In R. Biswas-Diener & E. Diener (Eds), Noba textbook series: Psychology. Champaign, IL: DEF publishers. Retrieved from http://noba.to/jx7268sd

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

References

Beck, D. & Tapia, E. (2023). The brain. In R. Biswas-Diener & E. Diener (Eds), Noba textbook series: Psychology. Champaign, IL: DEF publishers. Retrieved from http://noba.to/jx7268sd

Berger, H. (1929). Über das Elektrenkephalogramm des Menschen. *Archiv für Psychiatrie und Nervenkrankheiten, 87(1)*, 527-570.

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

Brasil-Neto, J. P. (2012). Learning, memory, and transcranial direct current stimulation. *Frontiers in Psychiatry*, 3(80). doi: 10.3389/fpsyt.2012.00080.

da Silva, F. L. (2013). EEG and MEG: Relevance to neuroscience. *Neuron, 80(5)*, 1112-1128.

Damasio, H., Grabowski, T., Frank, R., Galaburda, A. M., & Damasio, A. R. (1994). The return of Phineas Gage: clues about the brain from the skull of a famous patient. *Science, 264(5162),* 1102-1105.

Deisseroth, K. (2011). Optogenetics. *Nature Methods, 8(1)*, 26-29.

Feng, W. W., Bowden, M. G., & Kautz, S. (2013). Review of transcranial direct current stimulation in poststroke recovery. *Topics in Stroke Rehabilitation*, 20, 68–77.

Kuo, M. F., & Nitsche, M. A. (2012). Effects of transcranial electrical stimulation on cognition. *Clinical EEG and Neuroscience*, 43, 192–199.

Lichtman, J. W., Livet, J., & Sanes, J. R. (2008). A technicolor approach to the connectome. *Nature Reviews Neuroscience, 9*(6), 417-422.

Infantolino, Z. & Miller, G. A. (2023). Psychophysiological methods in neuroscience. In R. Biswas-Diener & E. Diener

(Eds), Noba textbook series: Psychology. Champaign, IL: DEF publishers. Retrieved from http://noba.to/a6wys72f

Perera, T., George, M. S., Grammer, G., Janicak, P. G., Pascual-Leone, A., & Wirecki, T. S. (2016). The clinical TMS society consensus review and treatment recommendations for TMS therapy for major depressive disorder. *Brain Stimulation, 9(3)*, 336-346.

Pol, A., Renkema, G. H., Tangerman, A., Winkel, E. G., Engelke, U. F., de Brouwer, A. P., ... & Wevers, R. A. (2018). Mutations in SELENBP1, encoding a novel human methanethiol oxidase, cause extraoral halitosis. *Nature Genetics, 50*(1), 120-129.

Raichle, M. E. (1994). Images of the mind: Studies with modern imaging techniques. *Annual Review of Psychology, 45(1)*, 333-356.

Van Horn, J. D., Irimia, A., Torgerson, C. M., Chambers, M. C., Kikinis, R., & Toga, A. W. (2012). Mapping connectivity damage in the case of Phineas Gage. *PloS One*, *7*(5), e37454.

CHAPTER 5: PSYCHOPHARMACOLOGY

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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 the field of 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 study of how drugs affect the brain and behavior, is a relatively new science, although people have probably been taking drugs to change how they feel from early in human history (consider the eating of fermented fruit, ancient beer recipes, and chewing on the leaves of the cocaine plant for stimulant properties as examples). The word *psychopharmacology* itself tells us that this is a field that bridges our understanding of behavior (and brain) and pharmacology, and the range of topics included within this field is extremely broad.

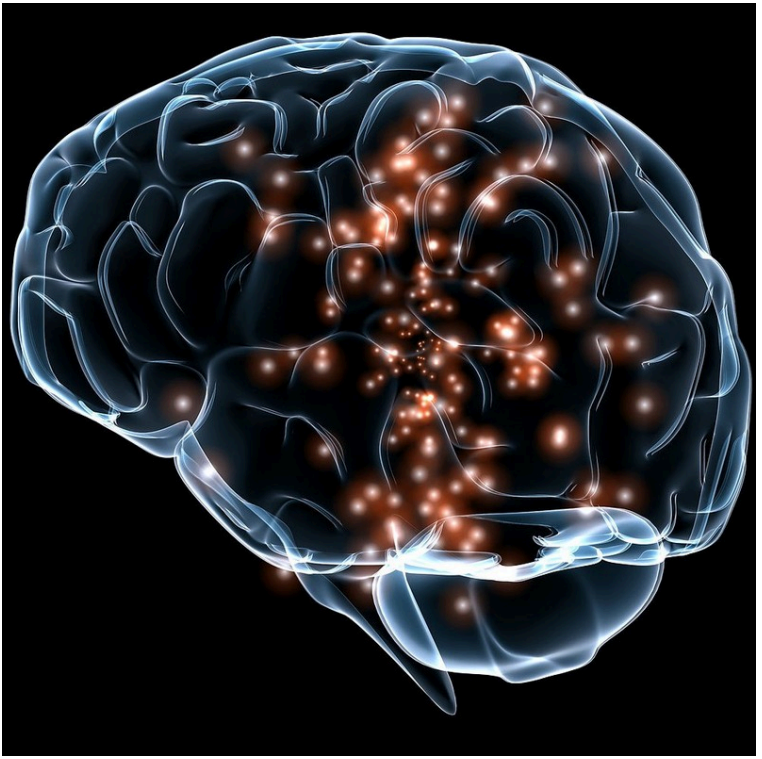

Figure 1. Drugs that alter our feelings and behavior do so by affecting the communication between neurons in the brain.

Virtually any drug that changes the way you feel does this by altering how neurons communicate with each other. Neurons (86 billion in your nervous system) 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 (protein) on the receiving neuron, and the message may then be transmitted onward. Obviously,

neurotransmission is far more complicated than this—we reviewed neurotransmission in a previous chapter, and links at the end of this chapter can provide some useful additional background information—but the first step is understanding that virtually all **psychoactive drugs** interfere with or alter how neurons communicate with each other.

There are many neurotransmitters. Some of the most important in terms of psychopharmacological treatment and drugs of abuse are outlined 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 different mechanisms, and some examples of agonists and antagonists are presented in **Table 2**. For each example, the drug's trade name, which is the name of the drug provided by the drug company, and generic name (in parentheses) are provided.

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	SHT	Depression; Aggression; Schizophrenia
Glutamate	GLU	Learning; Major excitatory neurotransmitter in the brain
GABA	GABA	Anxiety disorders; Epilepsy; Major inhibitory neurotransmitter in the brain
Endogenous Opiods	Endorphins, Enkephalins	Pain; Analgesia; Reward

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

Table 2 provides examples of drugs and their primary mechanism of action, but it is very important to realize that drugs also have effects on other neurotransmitters. This contributes to the kinds of side effects that are observed when someone takes a particular drug. The reality is that no drugs currently available work exactly where we would like them to be in the brain or only on a specific neurotransmitter. 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. Sometimes individuals stop taking medication because the side effects can be so profound.

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 opiod post-synaptic receptors	Alcoholism, opiod addiction	Antagonist (for opioids)

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

While this section may sound more like pharmacology, it is important to realize how important pharmacokinetics can be when considering psychoactive drugs. **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). We will talk about a couple of these to show their importance for psychoactive drugs.

Drug Administration

There are many ways to take drugs, and these routes of drug administration have a significant impact on how quickly that drug reaches the brain. The most common route of administration is oral administration, which is relatively slow and perhaps surprisingly often the most variable and complex route of administration. Drugs enter the stomach and then get absorbed by the blood supply and capillaries that line the small intestine. The rate of absorption can be affected by a variety of 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 rate of absorption. 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 there is an adverse drug reaction, there is very little time to administer any antidote, as in the case of an IV heroin overdose.

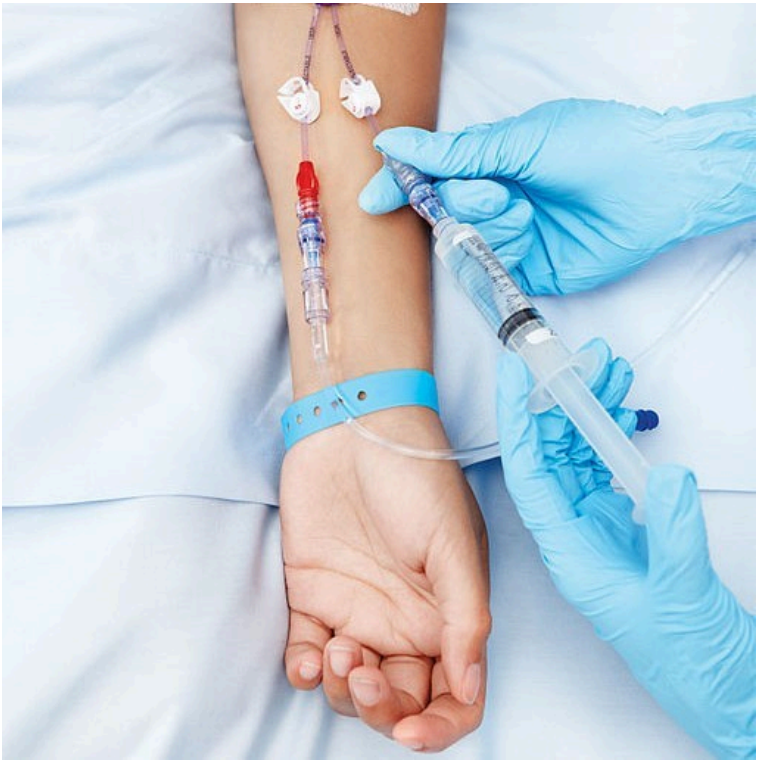

Figure 2. A drug delivered by IV reaches the brain more quickly than if the drug is taken orally. While rapid delivery has advantages, there are also risks involved with IV administration.

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 hardest addictions to quit, and although part of the reason for this may be that smoking gets the nicotine into the brain very quickly (and indirectly acts on DA neurons), it is a more complicated story. 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, it could be something as normal as finishing dinner or waking up in the morning (if that is when the smoker usually has a cigarette). For both the crack user and the cigarette smoker, the cues associated with the drug may actually cause craving that is alleviated by (you guessed it)—lighting a cigarette or using crack (i.e., 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 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 of an 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 also 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 of the psychotropic drugs). If the enzymes are suppressed, drug levels can build up to potentially toxic levels. In this case, the effects can persist for extended periods of time after the consumption of 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 are likely to 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 experiences 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 have no effect on another? Antidepressants can take 4 to 6 weeks to start improving depressive symptoms, and we don't really understand why. Many people do not respond to the first antidepressant prescribed and may have to try different drugs before finding something that works for them. Other people just do not improve with antidepressants (Ioannidis, 2008). As we better understand why individuals differ, the easier and more rapidly we will be able to help people in distress.

One area that has received interest recently has to do with an individualized treatment approach. We now know that there are genetic differences in some of the cytochrome P450 enzymes and their ability to break down drugs. The general population falls into the following 4 categories: 1) ***ultra-extensive metabolizers*** break down certain drugs (like some

of the current 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 either of the two above groups and finally 4) ***poor metabolizers*** break down drugs much more slowly than all of the other groups. Now consider someone receiving a prescription for an antidepressant—what would the consequences be if they were either an ultra-extensive metabolizer or a poor metabolizer? The ultra-extensive metabolizer would be given antidepressants and told it will probably take 4 to 6 weeks 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 daily dose of the same antidepressant may build up such high levels in their blood (because they are not breaking the drug down), that they will have a wide range of side effects and feel really badly – 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 then make a more informed decision about the best dose to prescribe. New genetic tests are now available to better individualize treatment in this way. 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). Currently, this genetic test is expensive and not many health-insurance plans cover this

screen, but this may be an important component in the future of psychopharmacology. Again, this is just one area of research to explain the length of time that it takes for antidepressants to kick in. Other research is investigating additional processes such as changes in the cell membrane and neuron DNA as well as changes at receptor sites.

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5.4: OTHER CONTROVERSIAL ISSUES

Juveniles and Psychopharmacology

A recent Centers for Disease Control (CDC) report has suggested that as many as 1 in 5 children between the ages of 5 and 17 may have some type of 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? There is no single answer to this important question. Some believe that greater public awareness has contributed to increased teacher and parent referrals. Others argue that the increase stems from changes in criteria currently used for diagnosing. Still others suggest environmental factors, either 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.

We do not have an answer, but the question brings up an additional controversy related to how we should treat this population of children and adolescents. 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 used for treating attention deficit hyperactivity disorder (ADHD), and there are clinical data on how effective these drugs are. 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. There is an obvious need for clinical trials in children and adolescents to test the safety and effectiveness of many of these drugs, which also brings up a variety of ethical questions about who decides what children and adolescents will participate in these clinical trials, who can give consent, who receives reimbursements, etc.

The Elderly and Psychopharmacology

Another population that has not typically been included in clinical trials to determine the safety or effectiveness of psychotropic drugs is the elderly. Currently, there is very little high quality evidence to guide prescribing for older people—clinical trials often exclude people with multiple comorbidities (other diseases, conditions, etc.), which are typical for elderly populations (see Hilmer & Gnjidict, 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. As our population ages, some estimate that the proportion of people 65 or older will reach 20% of the U.S. population by 2030, with this group consuming 40% of the prescribed medications. As shown in Table 3 (from Schwartz & Abernethy, 2008), it is quite clear why the typical clinical trial that looks at the safety and effectiveness of psychotropic drugs can be problematic if we try to interpret these results for an elderly population.

*** OTC = Over the counter**

Table 3. Characteristics if clinical trial subjects vs. actual patients. (Reprinted by permission from Schwartz & Abernethy, 2008.)

Clinical Trial Subjects	Aged Patients Who Receive Drug Therapies
One drug	Drug of interest and medications
Single does	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
Caucaisians	Caucasians and minorities
Selection bias	All corners/ socioeconomic basis

Metabolism of drugs is often slowed 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. There is also evidence that psychotropic medications can reduce bone density (thus worsening the consequences of falls) (Brown &

Mezuk, 2012). Although we are gaining awareness of some of the issuefacing pharmacotherapy in older populations, this is a very complex area with many medical and ethical questions.

This chapter provided an introduction to some of the important areas in the field of psychopharmacology. It should be apparent that this chapter just touched on a number of topics included in this field. It should also be apparent that understanding more about psychopharmacology is important to anyone interested in understanding behavior and that our understanding of issues in this field has important implications for society.

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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=329#video-329-1

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 it binds to these same receptors but without reducing neural activity. Fewer receptors are thus available to the natural "braking" action of adenosine, and neural activity therefore 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. Adrenalin 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 you drink, 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.

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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). We are thus dealing with the same kind of mechanism as in the case of opiates that 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. The 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:
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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=329#video-329-4

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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

5.7: REFERENCES

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

"The Brain from Top to Bottom" (n.d.). Retrieved on June 1, 2023 from https://thebrain.mcgill.ca/

References

Bailey D. G., Dresser G., & Arnold J. M. (2013). Grapefruit-medication interactions: forbidden fruit or avoidable consequences? *Canadian Medical Association Journal, 185*, 309–316.

Brown, M. J., & Mezuk, B. (2012). Brains, bones, and aging: psychotropic medications and bone health among older adults. *Current Osteoporosis Reports, 10*, 303–311.

Centers for Disease Control and Prevention (CDC) (2011) Prevalence of autism spectrum disorders – autism and developmental disabilities monitoring network, 14 sites,

United States, 2008. *Morbidity and Mortality Weekly Report 61*(SS03) 1–19.

Centers for Disease Control and Prevention (CDC) (2013) Mental health surveillance among children – United States, 2005—2011. *Morbidity and Mortality Weekly Report 62* Suppl, 1-35.

Centers for Disease Control and Prevention (CDC) (2023). Data & Statistics on Autism Spectrum Disorder. https://www.cdc.gov/ncbddd/autism/data.html

Devane, W. A., Hanuš, L., Breuer, A., Pertwee, R. G., Stevenson, L. A., Griffin, G., ... & Mechoulam, R. (1992). Isolation and structure of a brain constituent that binds to the cannabinoid receptor. *Science, 258*(5090), 1946-1949.

Hilmer, N., & Gnjidict, D. (2008). The effects of polypharmacy in older adults. *Clinical Pharmacology & Therapeutics, 85*, 86–88.

Ioannidis, J. P. A. (2008). Effectiveness of antidepressants: an evidence myth constructed from a thousand randomized trials? *Philosophy, Ethics, and Humanities in Medicine, 3*,14.

Kessler, R. C., Chiu, W. T., Demler, O., & Walters, E. E. (2005). Prevalence, severity, and comorbidity of twelve-month DSM-IV disorders in the National Comorbidity Survey Replication (NCS-R). *Archives of General Psychiatry, 62*, 617–627.

Moreno, C., Laje, G., Blanco, C., Jiang, H., Schmidt, A. B., & Olfson, M., (2007). National trends in the outpatient

diagnosis and treatment of bipolar disorder in youth. *Archives of General Psychiatry, 64*(9), 1032–1039.

Pollock, B. G., Forsyth, C. E., & Bies, R. R. (2008). The critical role of clinical pharmacology in geriatric psychopharmacology. *Clinical Pharmacology & Therapeutics, 85*, 89–93.

Rohsenow, D. J., Niaura, R. S., Childress, A. R., Abrams, D. B., & Monti, P. M. (1990). Cue reactivity in addictive behaviors: Theoretical and treatment implications. *International Journal of Addiction, 25*, 957–993.

Santomauro, D. F., Herrera, A. M. M., Shadid, J., Zheng, P., Ashbaugh, C., Pigott, D. M., ... & Ferrari, A. J. (2021). Global prevalence and burden of depressive and anxiety disorders in 204 countries and territories in 2020 due to the COVID-19 pandemic. *The Lancet, 398*(10312), 1700-1712.

Schwartz, J. B., & Abernethy, D. R. (2008). Aging and medications: Past, present, future. *Clinical Pharmacology & Therapeutics, 85*, 3–10.

"The Brain from Top to Bottom" (n.d.). Retrieved on June 1, 2023 from https://thebrain.mcgill.ca/

World Health Organization (2004). *Promoting mental health: concepts, emerging evidence, practice* (Summary Report). Geneva, Switzerland: Author. Retrieved from http://www.who.int/mental_health/evidence/en/promoting_mhh.pdf;

Zhou, S. F. (2009). Polymorphism of human cytochrome

P450 2D6 and its clinical significance: Part II. *Clinical Pharmacokinetics, 48*, 761–804.

CHAPTER 6: HORMONES AND BEHAVIOR

Chapter adapted from: Nelson, R. J. (2023). Hormones & behavior. In R. Biswas-Diener & E. Diener (Eds), *Noba textbook series: Psychology.* Champaign, IL: DEF publishers. Retrieved from http://noba.to/c6gvwu9m

The goal of this chapter is to introduce you to the topic of hormones and behavior. This field of study is also called behavioral endocrinology, which is the scientific study of the interaction between hormones and behavior. This interaction is bidirectional: hormones can influence behavior, and behavior can sometimes influence hormone concentrations. Hormones are chemical messengers released from endocrine glands, and they travel through the blood system to influence the nervous system to regulate behaviors such as aggression, mating, and parenting of individuals.

Learning Objectives

- Define the basic terminology and basic principles of hormone–behavior interactions.
- Explain the role of hormones in behavioral sex differentiation.
- Explain the role of hormones in aggressive behavior.
- Explain the role of hormones in parental behavior.
- Provide examples of some common hormone–behavior interactions.

6.1: INTRODUCTION

This chapter describes the relationship between hormones and behavior. Many readers are likely already familiar with the general idea that hormones can affect behavior. Students are generally familiar with the idea that sex-hormone concentrations increase in the blood during puberty and decrease as we age, especially after about 50 years of age. Sexual behavior shows a similar pattern. Most people also know about the relationship between aggression and anabolic steroid hormones, and they know that administration of artificial steroid hormones sometimes results in uncontrollable, violent behavior called "roid rage." Many different hormones can influence several types of behavior, but for the purpose of this chapter, we will restrict our discussion to just a few examples of hormones and behaviors. Behavioral endocrinologists are interested in how the general physiological effects of hormones alter the development and expression of behavior and how behavior may influence the effects of hormones.

To understand the hormone-behavior relationship, it is important to describe hormones. **Hormones** are organic chemical messengers produced and released by specialized glands called **endocrine glands**. 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 similar in function to **neurotransmitters**, the chemicals used by the nervous system in coordinating animals' activities. However, hormones can operate over a greater distance and over a much longer time than neurotransmitters (**Focus Topic 1**). Examples of hormones that influence behavior include steroid hormones such as **testosterone** (a common type of androgen), estradiol (a common type of estrogens), **progesterone** (a common type of progestogen), and cortisol (a common type of glucocorticoid) (see **Table 1, A-B**). Several types of protein or peptide (small protein) hormones also influence behavior, including **oxytocin**, vasopressin, **prolactin**, and leptin.

Focus Topic 1: Neural Transmission versus Hormonal Communication

Although neural and hormonal communication both rely on chemical signals, several prominent differences exist. Communication in the nervous system is analogous to traveling on a train. You can use the train in your travel plans as long as tracks exist between your proposed origin and destination. Likewise, neural messages can travel only to

destinations along existing nerve tracts. Hormonal communication, on the other hand, is like traveling in a car. You can drive to many more destinations than train travel allows because there are many more roads than railroad tracks. Similarly, hormonal messages can travel anywhere in the body via the circulatory system; any cell receiving blood is potentially able to receive a hormonal message.

Neural and hormonal communication differ in other ways as well. To illustrate them, consider the differences between digital and analog technologies. Neural messages are digital, all-or-none events that have rapid onset and offset: neural signals can take place in milliseconds. Accordingly, the nervous system mediates changes in the body that are relatively rapid. For example, the nervous system regulates immediate food intake and directs body movement. In contrast, hormonal messages are analog, graded events that may take seconds, minutes, or even hours to occur. Hormones can mediate long-term processes, such as growth, development, reproduction, and metabolism.

Hormonal and neural messages are both chemical in nature, and they are released and received by cells in

a similar manner; however, there are important differences. Neurotransmitters, the chemical messengers used by neurons, travel a distance of only 20–30 nanometers (10-9 m)—to the membrane of the postsynaptic neuron, where they bind with receptors. Hormones enter the circulatory system and may travel from 1 millimeter to more than 2 meters before arriving at a target cell, where they bind with specific receptors.

Another distinction between neural and hormonal communication is the degree of voluntary control that can be exerted over their functioning. In general, there is more voluntary control of neural than of hormonal signals. It is virtually impossible to will a change in your thyroid hormone levels, for example, whereas moving your limbs on command is easy.

Although these are significant differences, the division between the nervous system and the endocrine system is becoming more blurred as we learn more about how the nervous system regulates hormonal communication. A better understanding of the interface between the endocrine system and the nervous system, called neuroendocrinology, is likely

to yield important advances in the future study of the interaction between hormones and behavior.

Table 1-A: Prominent Hormones That Influence Behavior

Steroid Hormones	
Cortisol	Increases carbohydrate metabolism; mediates stress respones
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, typically 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 and memory

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 physiological and behavioral function 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 each and every hormone. Rather, any given hormone can directly influence only cells that have specific hormone **receptors** for that particular hormone. Cells that have these specific receptors are called **target cells** for the hormone. The interaction of a hormone with its receptor begins a series of cellular events that eventually lead to the activation of enzymatic pathways or, alternatively, turn on or turn off gene activation that regulates protein synthesis. The newly synthesized proteins may activate or deactivate other genes, causing yet another cascade of cellular events. Importantly, sufficient numbers of appropriate hormone receptors must be available for a specific 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 even 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.

How might hormones affect behavior? In terms of behavior, one can think of humans and other animals as composed of three interacting components: (1) input systems (sensory systems), (2) integrators (the central nervous system), and (3) output systems or effectors (e.g., muscles). Hormones do not *cause* behavioral changes. Rather, hormones influence

these three systems so that specific stimuli are more likely to elicit certain responses in the appropriate behavioral or social context. In other words, hormones change the probability that a particular behavior will be emitted in the appropriate situation (Nelson, 2011). This is a critical distinction that can affect how we think of hormone-behavior relationships.

We can apply this three-component behavioral scheme to a simple behavior, singing in zebra finches. Only male zebra finches sing, and they sing to attract mates or ward off potential competitors from their territories. If the testes of adult male finches are removed, then the birds reduce singing, but castrated finches resume singing if the testes are reimplanted or if they are treated with either testosterone or estradiol. Although people often consider androgens to be "male" hormones and estrogens to be "female" hormones, testosterone is commonly converted to estradiol (**Figure 1**). Thus, many male-like behaviors are associated with the actions of estrogens! Indeed, all estrogens must first be converted from androgens because of the typical biochemical synthesis process. If the converting enzyme is low or missing, then it is possible for females to produce excessive androgens and subsequently develop associated male traits. Again, singing behavior is most frequent when blood testosterone or estrogen concentrations are high.

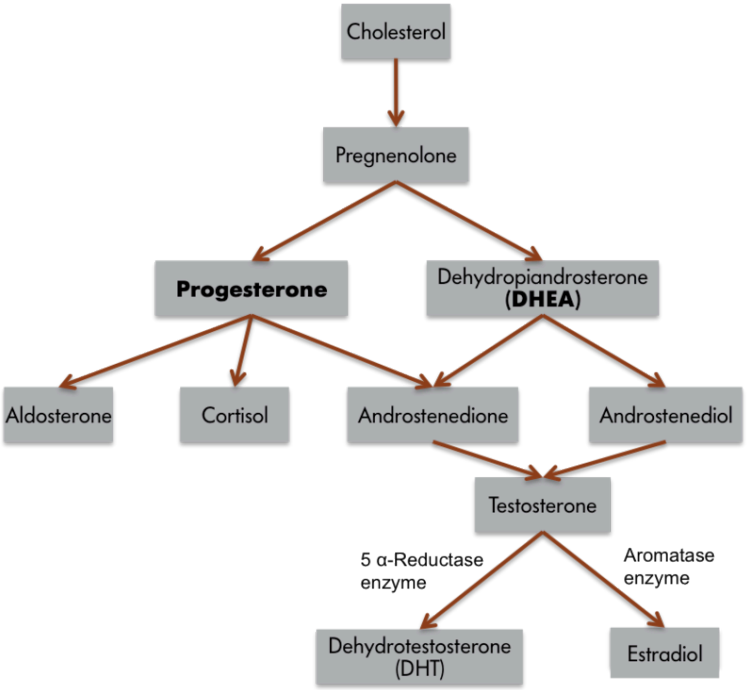

Figure 1: Biochemical Pathway for Steroid Hormone Synthesis: It is important to note that testosterone (an androgen) can be converted to another androgen, DHT, or an estrogen, estradiol. Too much or too little of the converting enzymes can influence the brain and behavior.

Estrogens are somehow involved in singing, but how might the three-component framework help us formulate hypotheses to explore the role of estrogen in this behavior? Estrogens could affect birdsong by influencing the sensory capabilities, central processing system, or effector organs of a bird. By examining input systems, we could determine whether estrogens alter the birds' sensory capabilities, making the environmental cues that

normally elicit singing (like females or competitors) more salient. Estrogens also could influence the central nervous system, for example, by altering neuronal architecture or the speed of neural processing. Finally, the effector organs, like the muscles in a songbird's vocal apparatus, could be affected by the presence of estrogens. We do not understand completely how estrogens, derived from testosterone, influence birdsong, but in most cases, hormones can be considered to affect behavior by influencing one, two, or all three of these components, and this three-part framework can aid in the design of hypotheses and experiments to explore these issues.

How might behaviors affect hormones? The birdsong example demonstrates how hormones can affect behavior, but as noted, the reciprocal relation also occurs—behavior can affect hormone concentrations. For example, the sight of a territorial intruder may elevate testosterone concentrations in resident male birds and thereby stimulate singing or fighting behavior. Similarly, male mice or rhesus monkeys that lose a fight decrease circulating testosterone concentrations for several days or even weeks afterward. Comparable results have also been reported in humans. Testosterone concentrations are affected not only in humans involved in physical combat but also in those involved in 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 do not have to be directly involved in a contest to have their hormones affected by the outcome of the contest. Male fans of the Brazilian and Italian soccer teams were recruited to provide saliva samples to be assayed for testosterone before and after the final game of the World Cup soccer match in 1994. Brazil and Italy were tied, but Brazil won on a penalty kick at

the last moment. The Brazilian fans were elated, and the Italian fans were crestfallen. When the samples were assayed, 11 of 12 Brazilian fans who were sampled had increased testosterone concentrations, and 9 of 9 Italian fans had decreased testosterone concentrations, compared with pre-game baseline values (Dabbs, 2000).

In some cases, hormones can be affected by anticipation of behavior. For example, testosterone concentrations also influence sexual motivation and behavior in women. In one study, the interaction between sexual intercourse and testosterone was compared with other activities (cuddling or exercise) in women (van Anders et al., 2007). On three separate occasions, women provided a saliva sample from pre-activity, post-activity, and the next morning, analyses showed that the women's testosterone was elevated prior to intercourse as compared to other times. Thus, an anticipatory relationship exists between sexual behavior and testosterone. Testosterone values were higher post-intercourse compared to exercise, suggesting that engaging in sexual behavior may also influence hormone concentrations in women.

Media Attributions

6.2: SEX DIFFERENCES

The discussion below focuses on how sex-specific hormonal differences may lead to differences in brain development and behavior. Although we focus mainly on sex-related differences, it's important to recognize that gender-related differences can also impact brain development and behavior.[1] (For a more comprehensive review of sex versus gender, see Lips, 2020.)

Hens and roosters are different. Cows and bulls are different. Human males and females are different. Humans, like many animals, are sexually dimorphic (*di*, "two"; *morph*, "type") in the size and shape of their bodies, their physiology, and for our purposes, their behavior (cf. Fausto-Sterling, 2000). The behavior of males and females differs in many ways. Young females generally excel in verbal tasks relative to young males, who are nearly twice as likely as females to suffer from dyslexia (reading difficulties) and stuttering. Young males

1. According to the World Health Organization, sex refers to "the different biological and physiological characteristics of females, males and intersex persons, such as chromosomes, hormones and reproductive organs." Gender refers to "the characteristics of women, men, girls and boys that are socially constructed. This includes norms, behaviors and roles associated with being a woman, man, girl or boy. Gender varies from society to society and can change over time."

generally perform better at visuospatial tasks. More than 90% of all anorexia nervosa cases involve young females. Young males are twice as likely to suffer from schizophrenia. Young males are much more physically aggressive and generally engage in more rough-and-tumble play (Berenbaum et al., 2008). Many sex differences, such as the difference in aggressiveness, persist throughout adulthood. For example, many more males than females are serving prison sentences for violent behavior. The hormonal differences between males and females may account for adult sex differences that develop during puberty, but what accounts for behavioral sex differences among children *prior* to puberty and activation of their gonads? While societal and cultural factors play a role (discussed below), hormones are a major determinant of sex differences. Hormonal secretions from the developing gonads determine whether the individual develops in a male or female manner. The mammalian embryonic testes produce androgens, as well as peptide hormones, that steer the development of the body, central nervous system, and subsequent behavior in a male direction. The embryonic ovaries of mammals are virtually quiescent and do not secrete high concentrations of hormones. In the presence of ovaries or in the complete absence of any gonads, morphological, neural, and later, behavioral development follows a female pathway.

Figure 3. Sex differences in appearance are often more pronounced in nonhuman animals than in humans. Male birds particularly, for example, roosters, tend to have physical features that differ from the females and also differ significantly in size.

Gonadal steroid hormones have organizational (or programming) effects on the brain and behavior (Phoenix et al., 1959). The organizing effects of steroid hormones are relatively constrained to the early stages of development. An asymmetry exists in the effects of testes and ovaries on the organization of behavior in mammals. Hormone exposure early in life has organizational effects on subsequent rodent behavior; early steroid hormone treatment causes relatively irreversible and permanent **masculinization** of rodent behavior (mating and aggressiveness). These early hormone effects can be contrasted with the reversible behavioral

influences of steroid hormones provided in adulthood, which are called activational effects. The activational effects of hormones on adult behavior are temporary and may wane soon after the hormone is metabolized. Thus, typical male behavior requires exposure to androgens during gestation (in humans) or immediately after birth (in rodents) to somewhat masculinize the brain and also requires androgens during or after puberty to activate these neural circuits. Typical female behavior requires a lack of exposure to androgens early in life, which leads to **feminization** of the brain and also requires estrogens to activate these neural circuits in adulthood. But this simple dichotomy, which works well with animals with very distinct sexual dimorphism in behavior, has many caveats when applied to people.

If you walk through any major toy store, you will likely observe some aisles filled with pink-packaged toys and adjacent aisles without any pink packages. Remarkably, you will also see a strong self-segregation of girls and boys in these aisles. Toy manufacturers are often accused of making toys that are gender biased, but it seems more likely that boys and girls enjoy playing with specific types and colors of toys. Indeed, toy manufacturers would immediately increase their sales if they could sell toys to both sexes. Boys *generally* prefer toys such as trucks and balls, and girls *generally* prefer toys such as dolls. Although it is doubtful that there are genes that encode preferences for toy cars and trucks on the Y chromosome, it is possible that hormones might shape the development of a

child's brain to prefer certain types of toys or styles of play behavior. It is reasonable to believe that children learn which types of toys and which styles of play are appropriate to their gender. How can we separate the contribution of physiological mechanisms from learning in order to understand sex differences in human behaviors?

To untangle the contributions of physiological mechanisms from learning in sex-specific behaviors, animal models are often used. Unlike in humans, where sex differences are usually only a matter of degree (often slight), in some animals, members of only one sex may display a particular behavior. As noted, often only male songbirds sing. Studies of such strongly sex-biased behaviors are particularly valuable for understanding the interaction among behavior, hormones, and the nervous system.

A study of vervet monkeys calls into question the primacy of learning in the establishment of toy preferences (Alexander & Hines, 2002). Female vervet monkeys preferred girl-typical toys, such as dolls or cooking pots, whereas male vervet monkeys preferred boy-typical toys, such as cars or balls. There were no sex differences in preference for gender-neutral toys, such as picture books or stuffed animals. Presumably, monkeys have no prior concept of "boy" or "girl" toys. Young rhesus monkeys also show similar toy preferences.

Figure 4. If you think back to the toys and clothing you played with and wore in your youth, do you think they were more a result of your hormonal activity or the choices that society and your parents made for you?

What, then, underlies the sex difference in toy preference? It is possible that certain attributes of toys (or objects) appeal to either boys or girls. Toys that appeal to boys or male monkeys, in this case, a ball or toy car, are objects that can be moved actively through space and can be incorporated into active, rough-and-tumble play. The appeal of toys that girls or female

vervet monkeys prefer appears to be based on color. Pink and red (the colors of the doll and pot) may provoke attention in infants.

Society may reinforce such stereotypical responses to gender-typical toys. The sex differences in toy preferences emerge by 12 or 24 months of age and seem fixed by 36 months of age, but are sex differences in toy preference present during the first year of life? It is difficult to ask preverbal infants what they prefer, but in studies where the investigators examined the amount of time that babies looked at different toys, eye-tracking data indicate that infants as young as 3 months showed sex differences in toy preferences: girls preferred dolls, whereas boys preferred trucks. Another result that suggests, but does not prove, that hormones are involved in toy preferences is the observation that girls diagnosed with congenital adrenal hyperplasia (CAH), whose adrenal glands produce varying amounts of androgens early in life, played with masculine toys more often than girls without CAH. Further, a dose-response relationship between the extent of the disorder (i.e., degree of fetal androgen exposure) and the degree of masculinization of play behavior was observed. Are the sex differences in toy preferences or play activity, for example, the inevitable consequences of the differential endocrine environments of boys and girls, or are these differences imposed by cultural practices and beliefs? Are these differences the result of receiving gender-specific toys from an early age, or are these differences some combination of endocrine and

cultural factors? Again, these are difficult questions to unravel in people.

Even when behavioral sex differences appear early in development, there seems to be some question regarding the influence of societal expectations. One example is the pattern of human play behavior during which males are more physical; this pattern is seen in a number of other species, including nonhuman primates, rats, and dogs. Is the difference in the frequency of rough-and-tumble play between boys and girls due to biological factors associated with being male or female, or is it due to cultural expectations and learning? If there is a combination of biological and cultural influences mediating the frequency of rough-and-tumble play, then what proportion of the variation between the sexes is due to biological factors, and what proportion is due to social influences? Importantly, is it appropriate to talk about "normal" sex differences when these traits virtually always arrange themselves along a continuum rather than in discrete categories?

Sex differences are common in humans and in nonhuman animals. Because males and females differ in the ratio of androgenic and estrogenic steroid hormone concentrations, behavioral endocrinologists have been particularly interested in the extent to which behavioral sex differences are mediated by hormones. The process of becoming female or male is called **sexual differentiation**. The primary step in sexual differentiation occurs at fertilization. In mammals, the ovum

(which always contains an X chromosome) can be fertilized by a sperm bearing either a Y or an X chromosome; this process is called **sex determination**. The **chromosomal sex** of homogametic mammals (XX) is female; the chromosomal sex of heterogametic mammals (XY) is male. Chromosomal sex determines **gonadal sex**. Virtually all subsequent sexual differentiation is typically the result of differential exposure to gonadal steroid hormones. Thus, gonadal sex determines hormonal sex, which regulates morphological sex. Morphological differences in the central nervous system, as well as in some effector organs, such as muscles, lead to behavioral sex differences. The process of sexual differentiation is complicated, and the potential for errors is present. Perinatal exposure to androgens is the most common cause of anomalous sexual differentiation among females. The source of androgen may be internal (e.g., secreted by the adrenal glands) or external (e.g., exposure to environmental estrogens). Turner syndrome results when the second X chromosome is missing or damaged; these individuals possess dysgenic ovaries and are not exposed to steroid hormones until puberty. Interestingly, women with Turner syndrome often have impaired spatial memory.

Female mammals are considered the "neutral" or "default" sex, as additional physiological steps are required for male differentiation; more steps bring more possibilities for errors in differentiation. Some examples of male anomalous sexual differentiation include **5α-reductase** deficiency (in which XY

individuals are born with ambiguous genitalia because of a lack of dihydrotestosterone and are reared as females, but masculinization occurs during puberty) and androgen insensitivity syndrome or TFM (in which XY individuals lack receptors for androgens and develop as females). By studying individuals who do not neatly fall into the dichotic boxes of female or male and for whom the process of sexual differentiation is atypical, behavioral endocrinologists glean hints about the process of typical sexual differentiation.

We may ultimately want to know how hormones mediate sex differences in the human brain and behavior (to the extent to which these differences occur). To understand the mechanisms underlying sex differences in the brain and behavior, we return to the birdsong example. Birds provide the best evidence that behavioral sex differences are the result of hormonally induced structural changes in the brain (Goodson et al., 2005). In contrast to mammals, in which structural differences in neural tissues have not been directly linked to behavior, structural differences in avian brains have been directly linked to a sexual behavior—birdsong.

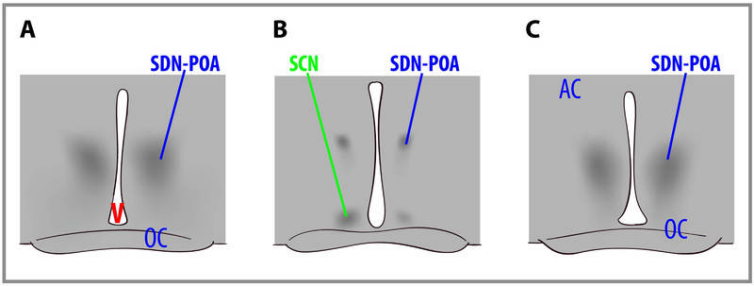

Figure 5: The sexually dimorphic nuclei of the preoptic area (SDN-POA). Gonadal steroid hormones have organizing effects on the brain and behavior. The organizing effects of steroid hormones are relatively constrained to the early stages of development. Exposure to testosterone (which is converted to estradiol) or estradiol causes masculinization of the brain. These are cross-sections through the brains of rats that show a male (left), a female (center), and a female treated with testosterone as a newborn (right). Note that the SDN-POA (the dark cell bodies) of the male are substantially larger than those of the untreated female but are equal in size to those of the testosterone-treated female. The extent to which these sex differences in brain structure account for sex differences in behavior remains unspecified in mammals. OC = optic chiasm; SCN = suprachiasmatic nucleus; V = third ventricle.

Sex differences in human brain size have been reported for years. More recently, sex differences in specific brain structures have been discovered (**Figure 5**). Sex differences in a number of cognitive functions have also been reported. Females are generally more sensitive to auditory information, whereas males are more sensitive to visual information. Females are also typically more sensitive than males to taste and olfactory input. Women display less lateralization of cognitive functions than

men. On average, females generally excel in verbal, perceptual, and fine motor skills, whereas males outperform females on quantitative and visuospatial tasks, including map reading and direction finding. Although reliable sex differences can be documented, these differences in ability are slight. It is important to note that there is more variation *within* each sex than *between* the sexes for most cognitive abilities (**Figure 6**).

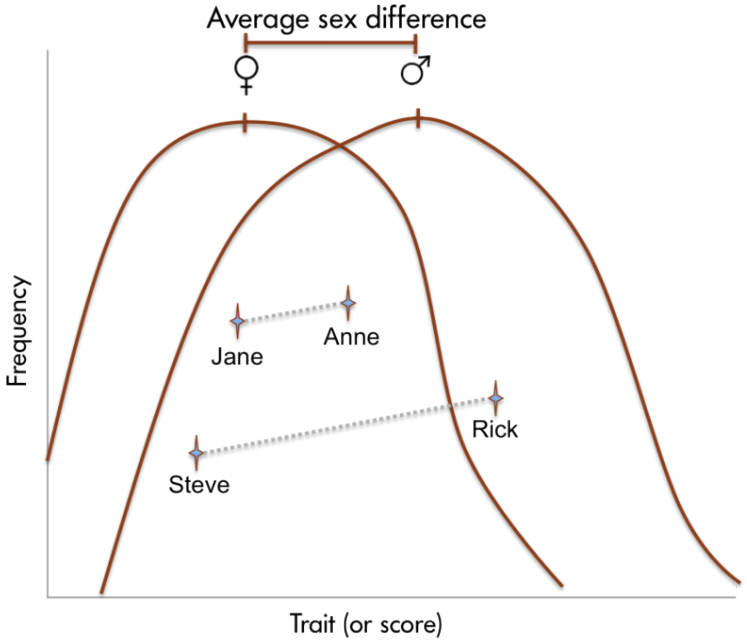

Figure 6: The average sex differences in human performance often reflect significant overlap between the sexes. There are often greater differences in performance between individuals of the same sex (for example, between Steve and Rick in the figure) than between individuals of the opposite sex (for example, between Steve and Jane in the figure).

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6.3: AGGRESSIVE BEHAVIORS

The possibility for **aggressive behavior** exists whenever the interests of two or more individuals are in conflict (Nelson, 2006). Conflicts are most likely to arise over limited resources such as territories, food, and mates. A social interaction decides which animal gains access to the contested resource. In many cases, a submissive posture or gesture on the part of one animal avoids the necessity of actual combat over a resource. Animals may also participate in threat displays or ritualized combat in which dominance is determined, but no physical damage is inflicted.

There is overwhelming circumstantial evidence that androgenic steroid hormones mediate aggressive behavior across many species. First, seasonal variations in blood plasma concentrations of testosterone coincide with seasonal 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 at the time of 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, in any given species, males are generally more aggressive than

females. This is certainly true of deer; relative to males, female deer rarely display aggressive behavior, and their rare aggressive acts are qualitatively different from the aggressive behavior of aggressive males. Finally, castration typically reduces aggression in males, and testosterone replacement therapy restores aggression to pre-castration levels. There are some interesting exceptions to these general observations that are outside the scope of this chapter.

As mentioned, males are generally more aggressive than females. Certainly, human males are much more aggressive than females although research in developmental psychology notes that females may engage in relational aggression (e.g., causing harm to social status or relationships) at higher rates than males. Many more men than women are convicted of violent crimes in North America. The sex differences in human aggressiveness appear very early. At every age throughout the school years, many more males than females initiate physical assaults. Almost everyone will acknowledge the existence of this sex difference, but assigning a cause to behavioral sex differences in humans always elicits much debate. It is possible that males are more aggressive than females because androgens promote aggressive behavior, and males have higher blood concentrations of androgens than females. It is possible that males and females differ in their aggressiveness because the brains of males are exposed to androgens prenatally, and the "wiring" of their brains is thus organized in a way that facilitates the expression of aggression. It is also possible that

males are encouraged, and females are discouraged by family, peers, or others from acting in an aggressive manner. These three hypotheses are not mutually exclusive, but it is extremely difficult to discriminate among them to account for sex differences in human aggressiveness.

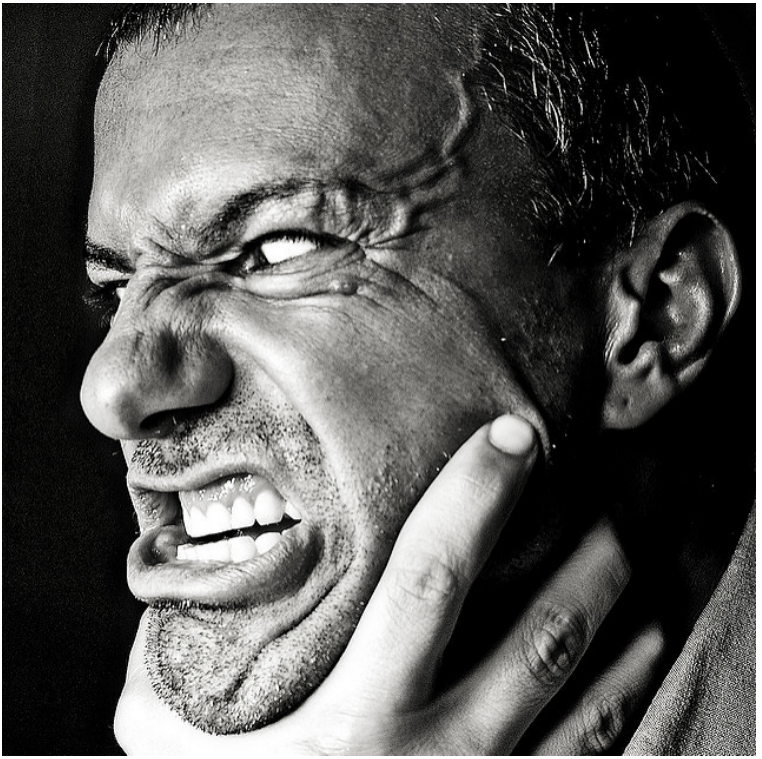

Figure 7. Researchers have electrically stimulated particular regions in people's brains, and these individuals have burst into aggressive, violent behavior, helping demonstrate that such responses are hardwired into us.

What kinds of studies would be necessary to assess these hypotheses? It is usually difficult to separate out the influences of environment and physiology on the development of behavior in humans. For example, males and females differ in their rough-and-tumble play at a very young age, which suggests an early physiological influence on aggression. However, parents interact with their male and female offspring differently; they usually play more roughly with male infants than with females, which suggests that the sex difference in aggressiveness is partially learned. This difference in parental interaction style is evident by the first week of life. Because of these complexities in the factors influencing human behavior, the study of hormonal effects on sex-differentiated behavior has been pursued in nonhuman animals, for which environmental influences can be held relatively constant. Animal models for which sexual differentiation occurs postnatally are often used so that this process can be easily manipulated experimentally.

Again, with the appropriate animal model, we can address the questions posed above: Is the sex difference in aggression due to higher adult blood concentrations of androgens in males or because male brains are organized differently by perinatal hormones? Or does the sex difference in aggression stem from an interaction of early and current blood androgen concentrations? If male mice are castrated prior to their sixth day of life, then treated with testosterone propionate in adulthood, they show low levels of aggression. Similarly,

females ovariectomized prior to their sixth day but given androgens in adulthood do not express male-like levels of aggression. Treatment of perinatally gonadectomized males or females with testosterone prior to their sixth day of life and also in adulthood results in a level of aggression similar to that observed in typical male mice. Thus, in mice, the increased aggressiveness in males is organized perinatally by androgens but also requires the presence of androgens after puberty in order to be fully expressed. In other words, aggression in male mice is both organized and activated by androgens. Testosterone exposure in adulthood without prior organization of the brain by steroid hormones does not evoke typical male levels of aggression. Aggressive behavior is both organized and activated by androgens in many species, including rats, hamsters, voles, dogs, and possibly some primate species.

Media Attributions

6.4: PARENTAL BEHAVIORS

Parental behavior can be considered to be any behavior that contributes directly to the survival of fertilized eggs or offspring that have left the body of the female. There are many patterns of mammalian parental care. The developmental status of the newborn is an important factor driving the type and quality of parental care in a species. **Maternal** care is much more common than **paternal** care. The vast majority of research on the hormonal correlates of mammalian parental behavior has been conducted on rats. Rats have altricial (underdeveloped) young, and mothers perform a cluster of stereotyped maternal behaviors, including nest building, crouching over the pups to allow nursing and provide warmth, pup retrieval, and increased aggression directed at intruders. If you expose nonpregnant female rats (or males) to pups, their most common reaction is to huddle far away from them. Rats avoid new things (neophobia). However, if you expose adult rats to pups every day, they soon begin to behave maternally. This process is called concaveation or sensitization and it appears to serve to reduce the adult rats' fear of pups.

A new mother needs to act maternally as soon as her offspring arrives—not in a week. The onset of maternal

behavior in rats is mediated by hormones. Several methods of study, such as hormone removal and replacement therapy, have been used to determine the hormonal correlates of rat maternal behavior. A fast decline of blood concentrations of progesterone in late pregnancy, in combination with high concentrations of estradiol and probably prolactin and oxytocin, induces female rats to behave maternally almost immediately in the presence of pups. This pattern of hormones at birth overrides the usual fear response of adult rats toward pups, and it permits the onset of maternal behavior. Thus, the so-called maternal "instinct" requires hormones to increase the approach tendency and lower the avoidance tendency; the quality and type of maternal behaviors, however, are mediated by both hormones and maternal modeling in rodents as well as humans.

Figure 8. Although cortisol may not directly increase maternal behaviors, the next time your mom gives you a hug, you know one hormone to thank.

A series of elegant experiments by Alison Fleming and her collaborators studied the endocrine correlates of the behavior of human mothers and maternal attitudes. Mothers self-reported on questionnaires approach behaviors, including affectionate behaviors (e.g., patting, cuddling, or kissing the baby) and vocal behaviors (e.g., talking, singing, or cooing to the baby). Basic caregiving activities, such as changing diapers

and burping the infants, were also recorded. In these self-report studies, no relationship between hormone concentrations and maternal responsiveness, as measured by questionnaires, was found. However, when actual behavior, rather than questionnaire responses, was compared with hormone concentrations, a different story emerged. Cortisol concentrations were positively associated with approach behaviors. In other words, women with high concentrations of cortisol, in samples obtained immediately before or after nursing, engaged in more physically affectionate behaviors and talked more often to their babies than mothers with low cortisol concentrations. Additional analyses revealed that the correlation was even greater for mothers that had reported positive maternal regard (feelings and attitudes) during gestation. Indeed, nearly half of the variation in maternal behavior among women could be accounted for by cortisol concentrations and positive maternal attitudes during pregnancy.

Presumably, cortisol does not induce maternal behaviors directly, but it may act indirectly on the quality of maternal care by evoking an increase in the mother's general level of arousal, thus increasing her responsiveness to infant-generated cues. New mothers with high cortisol concentrations were also more attracted to their infant's odors, were superior in identifying their infants, and generally found cues from infants highly appealing (Fleming et al., 1997).

The medial preoptic area is critical for the expression of rat

maternal behavior. The amygdala appears to tonically inhibit the expression of maternal behavior. Adult rats are fearful of pups, a response that is apparently mediated by chemosensory information. Lesions of the amygdala or afferent sensory pathways from the vomeronasal organ to the amygdala disinhibit the expression of maternal behavior. Hormones or sensitization likely act to disinhibit the amygdala, thus permitting the occurrence of maternal behavior. Although correlations have been established, direct evidence of brain structural changes in human mothers remains unspecified (Fleming & Gonzalez, 2009).

Considered together, there are many examples of hormones influencing behavior and of behavior feeding back to influence hormone secretion. More and more examples of hormone–behavior interactions have been discovered, including hormones in the mediation of food and fluid intake, social interactions, salt balance, learning and memory, stress coping, as well as psychopathology, including depression, anxiety disorders, eating disorders, postpartum depression, and seasonal depression. Additional research should reveal how these hormone–behavior interactions are mediated.

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6.5: 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 the best ways to address these problems?
2. Hormones cause changes in the rates of cellular processes or in cellular morphology. What are some ways that these hormonally induced cellular changes might theoretically produce profound changes in behavior?
3. List and describe some behavioral sex differences that you have noticed between female and male children. What causes

females and males to choose different toys? Do you think that the sex differences you have noted arise from biological causes or are learned? How would you go about establishing your opinions as fact?

4. Why is it inappropriate to refer to androgens as "male" hormones and estrogens as "female" hormones?
5. Imagine that you discovered that the brains of architects were different from those of non-architects—specifically, that the "drawstraightem 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: Beach, F. A. (1948). Hormones and behavior. New York: Paul Hoeber.

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.

Book: Pfaff, D. W., Phillips, I. M., & Rubin, R. T. (2005). Principles of hormone/behavior relations. New York: Academic Press.

Article: Beach, F. A. (1975). Behavioral endocrinology: An emerging discipline. American Scientist, 63: 178–187.

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

6.6: REFERENCES

Adapted from:

Nelson, R. J. (2023). Hormones & behavior. In R. Biswas-Diener & E. Diener (Eds), Noba textbook series: Psychology. Champaign, IL: DEF publishers. Retrieved from http://noba.to/c6gvwu9m License: CC BY-NC-SA 4.0 DEED

References

Alexander, G. M. & Hines, M. (2002). Sex differences in response to children's toys in nonhuman primates (Cercopithecus aethiops sabaeus). Evolution and Human Behavior, 23, 467–479.

Berenbaum, S. A., Martin, C. L., Hanish, L. D., Briggs, P. T., & Fabes, R. A. (2008). Sex differences in children's play. In J. B. Becker, K. J. Berkley, N. Geary, E. Hampson, J. Herman, & E. Young (Eds.), Sex differences in the brain: From genes to behavior. New York: Oxford University Press.

Dabbs, J. M. (2000). Heroes, rogues, and lovers: Testosterone and behavior. Columbus, OH: McGraw Hill.

Fausto-Sterling, A. (2000). The five sexes, revisited. Sciences, 40, 18-23.

Fleming, A. S., & Gonzalez, A. (2009). Neurobiology of human maternal care. In P. T. Ellison & P. B. Gray (Eds.), Endocrinology of social relationships (pp. 294–318). Cambridge, MA: Harvard University Press.

Fleming, A. S., Steiner, M., & Corter, C. (1997). Cortisol, hedonics, and maternal responsiveness in human mothers. Hormones and Behavior, 32, 85–98.

Goodson, J. L., Saldanha, C. J., Hahn, T. P., Soma, K. K. (2005). Recent advances in behavioral neuroendocrinology: Insights from studies on birds. Hormones and Behavior, 48, 461–73.

Kidd, K. A., Blanchfield, P. J., Mills, K. H., Palace, V. P., Evans, R. E. Lazorchak, J. M. & Flick, R. (2007). Collapse of a fish population following exposure to a synthetic estrogen. Proceedings of the National Academy of Sciences,104, 8897–8901.

Lips, H. M. (2020). Sex and gender: An introduction. Waveland Press.

Nelson, R. J. (Ed.) (2006). Biology of aggression. New York: Oxford University Press.

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

Phoenix, C. H., Goy, R. W., Gerall, A. A., & Young, W. C. (1959). Organizing action of prenatally administered testosterone propionate on the tissues mediating mating behavior in the female guinea pig. Endocrinology, 65: 369–382.

van Anders, S., Hamilton, L., Schmidt, N., & Watson, N. (2007). Associations between testosterone secretion and sexual activity in women. Hormones and Behavior, 51, 477–82.

World Health Organization (WHO) (n.d.) Gender and health. Retrieved December 5, 2023, from https://www.who.int/health-topics/gender

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 development of the **nervous system** is a complex and intricately coordinated process spanning multiple stages, from the early embryonic stages through childhood, adolescence, and adulthood. During early developmental stages, the brain becomes able to dynamically transfer information across billions of interconnected neurons, and coordinate and control mental and bodily functions, including perception, cognition, and movement.

In this chapter, we cover the stages of nervous system and brain development in humans. We examine prenatal and postnatal stages of development from embryo through old age. We will also cover different stages of neuronal development, including neuron growth, migration, and death, as well as adult neurogenesis. Lastly, we will examine **neuroplasticity**—the brain's ability to reorganize in response to intrinsic or extrinsic experiences—and how neuroplasticity is strongest during sensitive and critical periods of development. Learning how the nervous system develops and 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, the developing embryo's cells belong to one of three layers that form into the different tissues in the body (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]

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.

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 a specialized region of neuroectoderm, which is the precursor for the tissue of the nervous system (Betts 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.

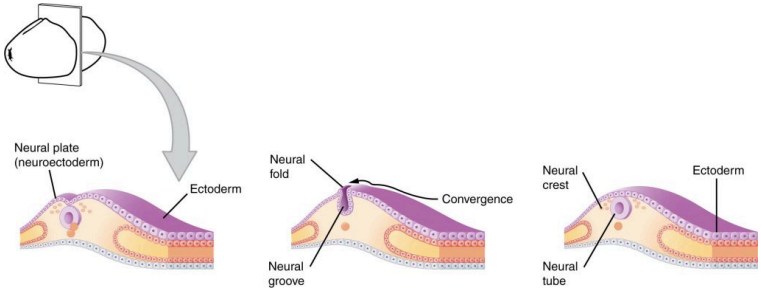

Figure 1: During the embryonic stage of development, the neuroectoderm folds inward to form the neural groove. As the two sides of the neural groove fuse together, they form the neural tube. The anterior end of the neural tube will develop into the brain, and the posterior portion will develop into the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

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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.

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 of thinking about how the brain is arranged is to use these three regions—forebrain, midbrain, and hindbrain (Figure 2).[3]

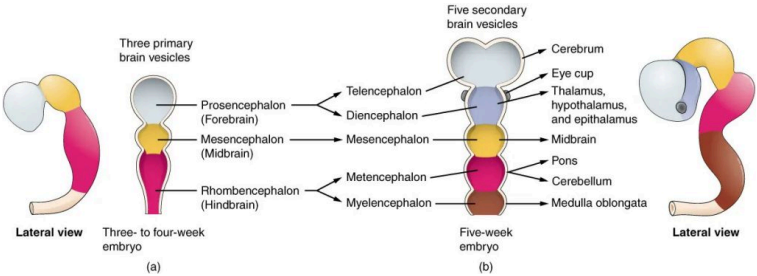

Figure 2: During the embryonic stage of development, the neural tube evolves into three primary vesicles. These three primary vesicles then give rise to five secondary vesicles.

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.

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, as well as 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. In order to understand the outcome of fetal brain development, it may be helpful 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

As discussed in previous chapters, 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 movements, 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 supporting cells, and help neurons complete their function for communication. We discuss six main types of glial cells. Four of them are found in the CNS and two are found in the PNS. Figure 3 provides a visualization of the different types of glial cells and Table 1 defines their common characteristics and functions.

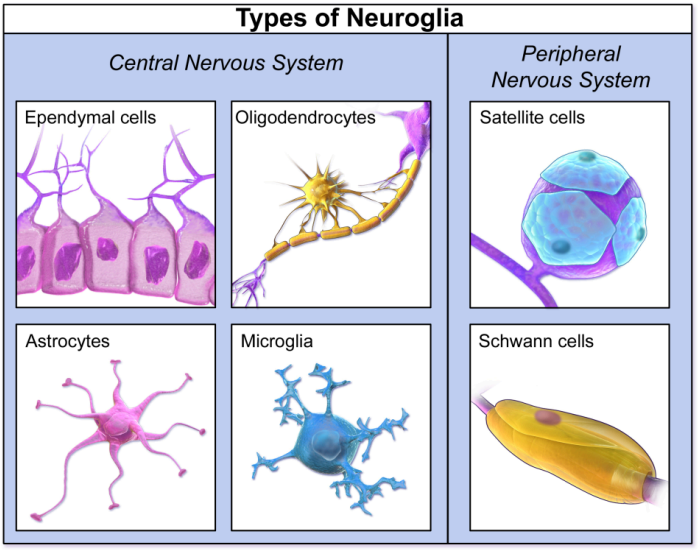

Figure 3: Visualizing the different glial cell types.

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	Satelite 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. Roughly four weeks into embryonic development, **neurogenesis** begins, such that cells of the neural tube begin to increase significantly in number (i.e., proliferate). The cells produced during neural proliferation will eventually develop into neurons that integrate into the neural circuitry that give rise to the central nervous system (brain and spinal cord). The vast majority of neurons in the human telencephalon (i.e., cortex, hippocampus, basal ganglia,

etc.) are generated before birth. Extensive neurogenesis does occur after birth in other regions of the brain (e.g., cerebellum). But all in all, the bulk of neurogenesis (i.e., the 86 billion neurons) in the CNS occurs between 4th week post-conception to 18 months after birth—this means that about 4.6 million neurons are generated every hour during this early developmental period (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 of the cell types that make up the body, whereas multipotent cells are more limited than pluripotent cells. Given that pluripotent stem cells can give rise to all cell types that make up the body, scientists have begun focusing on how pluripotent cells can be used in regenerative cell-based treatment strategies to counter a wide-range of diseases including diabetes, spinal cord injury, and heart disease. In regard to CNS development, neural stem cells are a special type of pluripotent cell, in that they only generate radial glial cells, which eventually give rise to the neurons and glial cells of the central nervous system. In summary, neural proliferation is the process by which billions of cells are generated, and certain cell types (i.e., neural stem cells), have the capability of differentiating into the neurons and glial cells that will develop into the central nervous system.

Neuronal Migration

Newly formed neurons may remain where they are and continue to divide, or may migrate to other parts of the nervous system. Neuronal migration refers to the process by which neurons travel from their original location to a new target location. For neurons of the central nervous system, neural migration remains within the confines of the neural tube, whereas for neurons of the peripheral nervous system, neural migration may take place across different neural regions (Purves et al., 2001). During the migration period, neurons remain immature, and still 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 appropriate target location.

In general, migration tends to follow an inside-out pattern, where neurons travel from the inside of the neural tube, also known as the ventricular zone, 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).

Additionally, the mechanisms of migration are interesting. One method, called somal translocation, involves an extension that reaches out from the soma of the immature neuron to lead it on its journey to its target location. Both radial and tangential migration can occur through somal translocation. A second method is called glial-mediated migration. This involves the immature neuron "hopping onto" an extended glial cell. This immature neuron "pulls" itself up the glial cell to its target location. Radial migration occurs according to glial-mediated migration.

After reaching their target location, the immature neurons begin acquiring distinct neuronal characteristics, such as dendrites and axons, which allow neurons to communicate with other neurons via **synapses**. Ultimately, the ability for neurons to communicate with one another leads to the establishment of functional neural circuits that make up the adult nervous system.

Aggregation

By the end of migration, neurons are aligned in such a manner that enables them to acquire specific functions, interact with other neurons, and eventually give rise to neural circuits that make up the human nervous system; a process known as **aggregation**. Aggregation is thought to be supported by **cell-adhesion molecules**, which are located on the surfaces of cells. Cell-adhesion molecules are able to recognize identical or different cell types and subsequently adhere to molecules on other cells (Jaffe et al., 1990; Takeichi, 1988). **Gap junctions** are also thought to support migration and aggregation processes. Gap junctions are clusters of communication channels between neighboring cells that link the cytoplasm of two cells and facilitate the exchange of ions and metabolites such as glucose, which subsequently promotes biochemical coupling between the two cells (Mese et al., 2007). Ultimately, through supportive mechanisms such as cell-adhesion molecules and gap junctions, neurons are able to interact and coalesce to give rise to the neural circuitry that makes up 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 is actually helpful for supporting 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). One example of apoptosis can be seen after neuronal proliferation, when excess neurons and immature neurons must be selectively eliminated in order to enable adequate neuronal connectivity and support the maturation of functional networks (Hollville et al., 2019). Unlike apoptosis, necrosis is characterized by swelling and rupturing of the cell membrane, as well as a leakage of the cellular contents (Rock & Kono, 2008). Additionally, apoptosis also involves a better "clean up process" of the dead neuron compared to necrosis which may leave disruptive remnants in the brain. One example of necrosis can be seen after a stroke, where disruption of blood flow may lead to accidental cell death. Understandably, excessive necrosis can have detrimental consequences and is known to be associated with pathologies such as Alzheimer's disease, Parkinson's disease, and stroke (Boka et al., 1994; Goel et al., 2022; Tuo et al., 2022). Accordingly, much work remains to better 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 research study showed that regions of the adult brain, such as the hippocampus, are able to generate new neurons throughout adulthood (Eriksson et al., 1997). The generation of 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, of the neurons that are generated during adulthood, many neurons do not survive and as a result, cannot integrate into existing neural circuits. While multiple studies have demonstrated evidence of adult neurogenesis, the topic remains fairly controversial in the field. 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 throughout adulthood, and their potential for possibly preserving cognitive function, future research will continue exploring the mechanisms that support neurogenesis especially in adulthood.

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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 be said to 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." This hypothesis inspired many researchers, and the first mechanism supporting it, long-term potentiation (LTP), was discovered a few decades later in the early 1970s.

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. There are various mechanisms, none fully understood, behind the synaptic strengthening seen with LTP. One known mechanism involves a type of postsynaptic glutamate receptor, called NMDA (N-Methyl-D-aspartate) receptors. These receptors are normally blocked by magnesium ions; however, when the postsynaptic neuron is depolarized by multiple presynaptic inputs in quick succession (either from one neuron or multiple neurons), the magnesium ions are forced out, allowing calcium (Ca2+) ions to pass into the postsynaptic cell. Next, Ca2+ ions entering the cell initiate a signaling cascade that causes a different type of glutamate receptor, called AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) receptors, to migrate from within the postsynaptic cell to the cell membrane and insert into the postsynaptic membrane. This is relevant to neuroplasticity, since activated 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) on the postsynaptic cell because the binding of glutamate to these newly available AMPA receptors will allow more positive ions into the cell. The insertion of additional AMPA receptors on the cell membrane strengthens the synapse and means that the postsynaptic neuron is 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 of 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)**. The decrease in AMPA receptors in the membrane makes the postsynaptic neuron less responsive to glutamate released from the presynaptic neuron. While it may seem counterintuitive, LTD may be just as important for learning and memory as LTP. The weakening and pruning of unused synapses allows for unimportant connections to be lost and makes the synapses that have undergone LTP that much stronger by comparison.

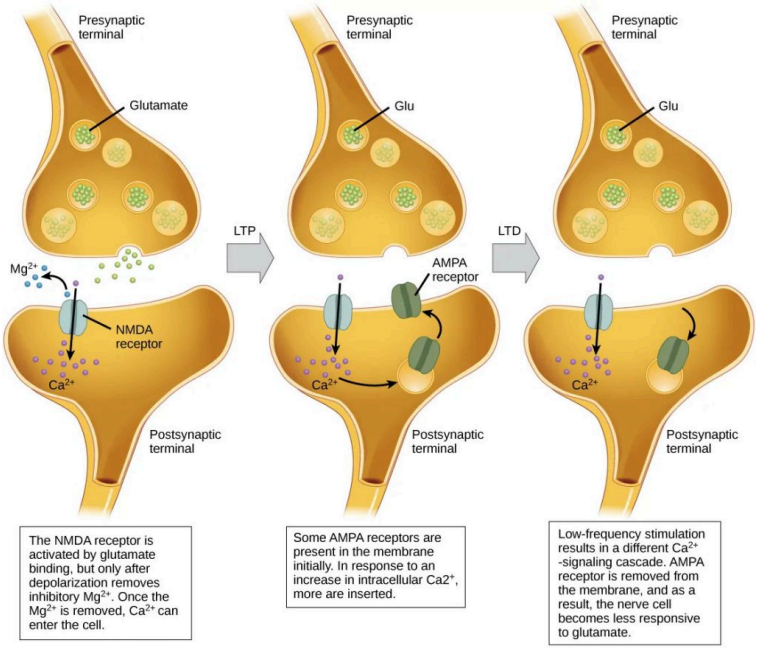

Figure 4. Calcium entry through postsynaptic NMDA receptors can initiate two different forms of synaptic plasticity: long-term potentiation (LTP) and long-term depression (LTD). LTP arises when a single synapse is repeatedly stimulated. This stimulation causes a calcium- and CaMKII-dependent cellular 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.

Text Attributions

This section contains material adapted from:

Clark, M. A., Douglas, M., & Choi, J. (2018). 35.2 How Neurons Communicate. In Biology 2e. OpenStax. Access for free at https://openstax.org/books/biology-2e/pages/35-2-how-neurons-communicate License: CC BY 4.0 DEED.

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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 the developmental time windows during which experiences have an especially strong impact on brain organization. Of note, 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). Indeed, disruptions during critical periods due to atypical experiences or adversity may lead to irreversible changes to brain structure. While sensitive and critical periods both share heightened neuroplasticity, sensitive periods are a broad time window during which experience may shape neural circuitry, whereas critical periods are a special class of sensitive periods that result in potentially irreversible changes in brain function (Knudsen, 2004).

Sensitive Periods of Development

Early childhood is a time that the brain is especially malleable and adaptive to environmental inputs. Early life experiences have a profound impact on how brain networks are organized 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 who were 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 language-learning ability 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 fact that second languages are still able to be learned throughout the lifespan, albeit at a slower rate, further exemplifies how age-related differences in second language learning reflect a sensitive, rather than critical, period in development. In summary, children may be better equipped to learn a second language during this sensitive period due to the heightened brain malleability.

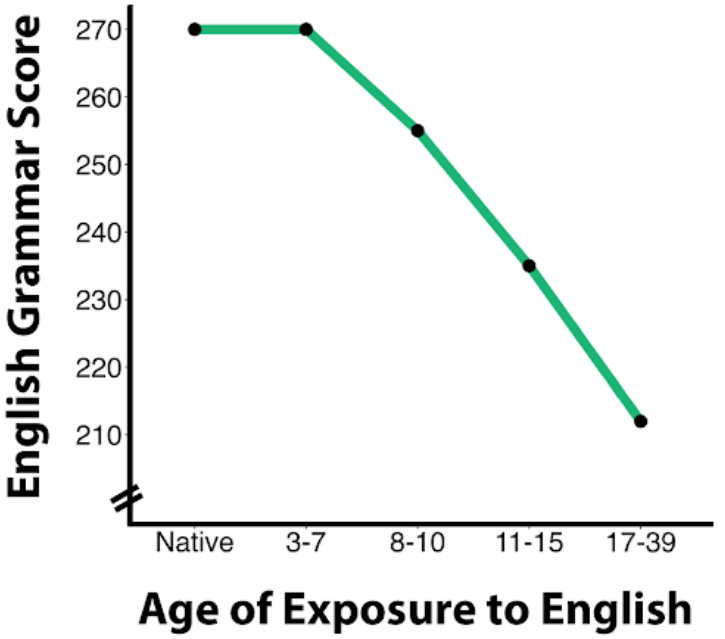

Figure 5: The relationship between age of learning a second language and total correct responses on an assessment of grammar for a second language [Image adapted from: Johnson, J. S., & Newport, E. L. (1989). Critical period effects in second language learning: The influence of maturational state on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

Critical Periods of Development

Critical periods of development, during which exposure to environmental input causes irreversible changes to brain

function and structure also occur during early childhood. 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, in research with animals, visual deprivation to one eye during a critical period causes lasting vision loss due to decreased cortical neuron spiking responses to the deprived eye (Gordon & Stryker, 1996). In response to visual deprivation to one eye during a critical period, 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 processing 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 may persist even after sensory functioning (i.e., vision) is restored, which may suggest that the manner in which the brain reorganizes itself during a critical period could persist throughout adulthood (Mowad et al., 2020).

Critical periods of development have also been discussed 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. Upon encountering Genie, it was determined that she was unable to verbally communicate through language. A research team began working with Genie to study her linguistic development and ultimately concluded that, while Genie showed initial progress in learning speech production and grammatical structure, her language proficiency remained atypical and severely impaired (Curtiss, 1974). A more recent study assessed children who did not receive the required language input during the first year of life, due to either isolation or hearing difficulties, and found that those children later showed 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 of life between childhood and adulthood, which is generally considered ages 10-24 years, 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 to be 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 also suggests that adolescence is marked by increased sensation-seeking and risk-taking behaviors (Spear, 2000). Neuroscientists have since suggested that the increase in risk-taking during adolescence may emerge as a result of delayed development of self-regulatory capabilities, which may arise as the product of an interaction between heightened sensation-seeking and an immature executive function system that is not yet able to modulate reward-seeking impulses (Steinberg et al., 2004).

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7.6: TRADE-OFF BETWEEN PLASTICITY AND EFFICIENCY

When considering neuroplasticity, it's important to recognize that different brain networks develop at different timescales (Dow-Edwards et al., 2019). For example, as mentioned earlier, brain regions involved in higher-order cognition, such as self-regulation, undergo a protracted, late development—neuroplasticity during adolescence is geared more toward refining those higher-order executive functions than basic sensory processes. The neural circuitry underlying basic sensory processes has peak plasticity during infancy and is firmly established by early childhood. It would be inefficient for the adolescent or adult brain to constantly re-learn how to process sensory information. This example highlights the trade-off between neuroplasticity and neural efficiency.

Neural efficiency refers to the process of the brain expending fewer energy resources to meet task demands. This efficiency can also be represented in how easily different brain regions are able to communicate with each other. Indeed, research has shown that the efficiency of information flow across the brain is accelerated during adolescence because

axons become more insulated with myelin, which improves the speed of electrical transmission and reduces the energy needed to carry out this process (Spear, 2013). However, neural efficiency emerges separately in different brain regions depending on developmental timescales. For example, sensory processing and its underlying circuitry develop rapidly during early childhood and become more efficient and less malleable by late childhood.

One important factor underlying differences in neural efficiency is the formation of synapses. Early research showed a pattern in synapse formation during brain development such that there is first a rapid overproduction of synapses, followed by a programmed elimination of non-functional synapses, which eventually brings the overall number of synapses down to 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, one hypothesis proposes that excess synapses during adolescence in frontal lobe regions, such as the prefrontal cortex, 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 throughout development, the brain may require fewer synapses to carry out the same cognitive processes. In this way, the brain is hypothesized to shift toward prioritizing the most efficient synapses, which may ultimately lead to more efficient cognitive processing.

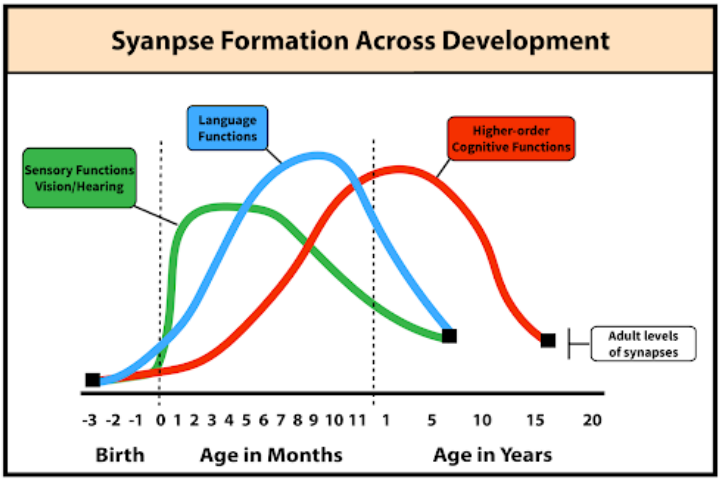

Figure 6. The number of new synapses related to sensory function, language skills, and higher-order cognition across development. Synapse formation related to sensory functioning is thought to peak first, followed by language skills, and lastly higher-order cognitive functions.

The tradeoff between neuroplasticity and stable efficient processing can be illustrated by recent research. In one study, a drug (valproate) was shown to reopen 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). While this finding has exciting ramifications for increasing plasticity in adults to learn new skills and rewire undesired established neural pathways (e.g., for treating addiction or psychiatric disorders), one must exercise caution 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 been recognized for their potential to treat addiction and psychological disorders. A recent study suggests that psychedelic drugs can reopen critical periods and increase plasticity in the brain 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 so as to not destabilize desired neural circuits.

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7.7: CHARACTERIZING BRAIN DEVELOPMENT FROM INFANCY THROUGH YOUNG ADULTHOOD

Exposure to adversity, especially early in childhood, is known to have long-lasting consequences on brain development and subsequent 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 shaping the brain, higher family income has been associated with expanded surface area in brain regions involved in language and executive functioning (Noble et al., 2015). Ultimately, while it's clear that poverty is closely associated with negative effects on the brain and behavior, much remains unknown about how these effects on neural development emerge over time. One landmark study, the

Baby's First Years project, is carrying out the first randomized control trial of poverty reduction in early childhood and assessing how poverty reduction influences children's brain development over time (Noble et al., 2021). As part of the study, 1,000 diverse low-income mothers in four metropolitan areas in the United States were randomly assigned to receive either 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. Ultimately, brain development during early childhood is responsive to their lived experiences, and as such, scientists are beginning to further explore how exposure to adversity may influence brain organization and how this may be associated with behavioral outcomes.

Given the extensive array of social, emotional, and cognitive changes that take place 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 research sites across the country are following over 11,000 children for ten years, beginning at age nine and continuing through adolescence into early adulthood and tracking their biological and behavioral development (Luciana et al., 2018). By conducting

assessments on brain structure and function, neurocognition, physical and mental health, social and emotional function, and culture and environment, the ABCD study will provide a comprehensive window into how this sensitive period of development unfolds in the brain and how that may lead to differences in behavior from childhood through young adulthood. The rich data from this massive ABCD study will provide key insights into understanding important 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).

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 already 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

7.10: REFERENCES

Parts of this chapter were adapted from:

Clark, M. A., Douglas, M., & Choi, J. (2018). 35.2 How Neurons Communicate. In Biology 2e. OpenStax. Access for free at https://openstax.org/books/biology-2e/pages/35-2-how-neurons-communicate

Betts, J. G., Young, K. A., Wise, J. A., Johnson, E., Poe, B., Kruse, D. H., Korol, O., Jonhson, J. E., Womble, M., & DeSaix, P. (2022). 13.1 The Embryologic Perspective. In Anatomy and Physiology 2e. OpenStax. Access for free at https://openstax.org/books/anatomy-and-physiology-2e/pages/13-1-the-embryologic-perspective

Duboc, B. (2002). The Brain from Top to Bottom (n.d.). Access for free at https://thebrain.mcgill.ca/

References

Blakemore, S.-J. (2012). Imaging brain development: The adolescent brain. NeuroImage, 61(2), 397–406. https://doi.org/10.1016/j.neuroimage.2011.11.080

Boka, G., Anglade, P., Wallach, D., Javoy-Agid, F., Agid, Y., & Hirsch, E. C. (1994). Immunocytochemical analysis of tumor necrosis factor and its receptors in Parkinson's disease. Neuroscience Letters, 172, 151–154. https://doi.org/10.1016/0304-3940(94)90684-X

Calder, A. E., & Hasler, G. (2023). Towards an understanding of psychedelic-induced neuroplasticity. Neuropsychopharmacology, 48(1), 104-112. https://doi.org/10.1038/s41386-022-01389-z

Casey, B. J., Trainor, R. J., Orendi, J. L., Schubert, A. B., Nystrom, L. E., Giedd, J. N., Castellanos, F. X., Haxby, J. V., Noll, D. C., Cohen, J. D., Forman, S. D., Dahl, R. E., & Rapoport, J. L. (1997). A Developmental Functional MRI Study of Prefrontal Activation during Performance of a Go-No-Go Task. Journal of Cognitive Neuroscience, 9(6), 835–847. https://doi.org/10.1162/jocn.1997.9.6.835

Curtiss, S., Fromkin, V., Krashen, S., Rigler, D., & Rigler, M. (1974). The Linguistic Development of Genie. Language, 50(3), 528–554. https://doi.org/10.2307/412222

De Vos, C. M., Mason, N. L., & Kuypers, K. P. (2021). Psychedelics and neuroplasticity: a systematic review unraveling the biological underpinnings of psychedelics. Frontiers in psychiatry, 12, 724606. https://doi.org/10.3389/fpsyt.2021.724606

Dow-Edwards, D., MacMaster, F. P., Peterson, B. S., Niesink, R., Andersen, S., & Braams, B. R. (2019). Experience during adolescence shapes brain development: From

synapses and networks to normal and pathological behavior. Neurotoxicology and Teratology, 76, 106834. https://doi.org/10.1016/j.ntt.2019.106834

Duncan, G. J., Yeung, W. J., Brooks-Gunn, J., & Smith, J. R. (1998). How Much Does Childhood Poverty Affect the Life Chances of Children? American Sociological Review, 63(3), 406–423. https://doi.org/10.2307/2657556

Duncan, G. J., Ziol-Guest, K. M., & Kalil, A. (2010). Early-Childhood Poverty and Adult Attainment, Behavior, and Health. Child Development, 81(1), 306–325. https://doi.org/10.1111/j.1467-8624.2009.01396.x

Eriksson, P. S., Perfilieva, E., Björk-Eriksson, T., Alborn, A.-M., Nordborg, C., Peterson, D. A., & Gage, F. H. (1998). Neurogenesis in the adult human hippocampus. Nature Medicine, 4(11), Article 11. https://doi.org/10.1038/3305

Friedmann, N., & Rusou, D. (2015). Critical period for first language: The crucial role of language input during the first year of life. Current Opinion in Neurobiology, 35, 27–34. https://doi.org/10.1016/j.conb.2015.06.003

Gervain, J., Vines, B., Chen, L., Seo, R., Hensch, T., Werker, J., & Young, A. (2013). Valproate reopens critical-period learning of absolute pitch. Frontiers in Systems Neuroscience, 7. https://www.frontiersin.org/articles/10.3389/fnsys.2013.00102

Giedd, J. N. (2004). Structural Magnetic Resonance Imaging of the Adolescent Brain. Annals of the New York Academy

of Sciences, 1021(1), 77–85. https://doi.org/10.1196/annals.1308.009

Goel, P., Chakrabarti, S., Goel, K., Bhutani, K., Chopra, T., & Bali, S. (2022). Neuronal cell death mechanisms in Alzheimer's disease: An insight. Frontiers in Molecular Neuroscience. https://doi.org/10.3389/fnmol.2022.937133

Gong, W., Rolls, E. T., Du, J., Feng, J., & Cheng, W. (2021). Brain structure is linked to the association between family environment and behavioral problems in children in the ABCD study. Nature Communications, 12(1), 3769.

Gordon, J. A., & Stryker, M. P. (1996). Experience-dependent plasticity of binocular responses in the primary visual cortex of the mouse. Journal of Neuroscience, 16(10), 3274-3286.

Hollville, E., Romero, S. E., & Deshmukh, M. (2019). Apoptotic Cell Death Regulation in Neurons. The FEBS Journal, 286(17), 3276–3298. https://doi.org/10.1111/febs.14970

Hubel, D. H., & Wiesel, T. N. (1970). The period of susceptibility to the physiological effects of unilateral eye closure in kittens. The Journal of Physiology, 206(2), 419–436.

Huttenlocher, P. R., & Dabholkar, A. S. (1997). Regional differences in synaptogenesis in human cerebral cortex. Journal of Comparative Neurology, 387(2), 167–178. https://doi.org/

10.1002/(SICI)1096-9861(19971020)387:2<167::AID-CNE1>3.0.CO;2-Z

Jaffe, S. H., Friedlander, D. R., Matsuzaki, F., Crossin, K. L., Cunningham, B. A., & Edelman, G. M. (1990). Differential effects of the cytoplasmic domains of cell adhesion molecules on cell aggregation and sorting-out. Proceedings of the National Academy of Sciences, 87(9), 3589–3593. https://doi.org/10.1073/pnas.87.9.3589

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.

Khalid, N., & Azimpouran, M. (2023). Necrosis. In StatPearls. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK557627/

Knudsen, E. I. (2004). Sensitive Periods in the Development of the Brain and Behavior. Journal of Cognitive Neuroscience, 16(8), 1412–1425. https://doi.org/10.1162/0898929042304796

Lorenzini, L., Baldassarro, V., Stanzani, A., & Giardino, L. (2021). Nerve Growth Factor: The First Molecule of the Neurotrophin Family. In Advances in experimental medicine and biology (Vol. 1331, pp. 3–10). https://doi.org/10.1007/978-3-030-74046-7_1

Luciana, M., Bjork, J. M., Nagel, B. J., Barch, D. M., Gonzalez, R., Nixon, S. J., & Banich, M. T. (2018). Adolescent neurocognitive development and impacts of substance use:

Overview of the adolescent brain cognitive development (ABCD) baseline neurocognition battery. Developmental Cognitive Neuroscience, 32, 67–79. https://doi.org/10.1016/j.dcn.2018.02.006

Ludwig, P. E., Reddy, V., & Varacallo, M. (2022). Neuroanatomy, Neurons. In StatPearls [Internet]. StatPearls Publishing.

Marín, O., & Rubenstein, J. L. R. (2003). Cell Migration in the Forebrain. Annual Review of Neuroscience, 26(1), 441–483. https://doi.org/10.1146/annurev.neuro.26.041002.131058

Marín, O., Valiente, M., Ge, X., & Tsai, L.-H. (2010). Guiding Neuronal Cell Migrations. Cold Spring Harbor Perspectives in Biology, 2(2), a001834. https://doi.org/10.1101/cshperspect.a001834

Meşe, G., Richard, G., & White, T. W. (2007). Gap Junctions: Basic Structure and Function. Journal of Investigative Dermatology, 127(11), 2516–2524. https://doi.org/10.1038/sj.jid.5700770

Nardou, R., Sawyer, E., Song, Y. J., Wilkinson, M., Padovan-Hernandez, Y., de Deus, J. L., Wright, N., Lama, C., Faltin, S., Goff, L. A., Stein-O'Brien, G. L., & Dölen, G. (2023). Psychedelics reopen the social reward learning critical period. Nature, 1–9. https://doi.org/10.1038/s41586-023-06204-3

Newport, E. L., Bavelier, D., & Neville, H. J. (n.d.). Critical

Thinking about Critical Periods: Perspectives on a Critical Period for Language Acquisition.

Noble, K. G., Houston, S. M., Brito, N. H., Bartsch, H., Kan, E., Kuperman, J. M., Akshoomoff, N., Amaral, D. G., Bloss, C. S., Libiger, O., Schork, N. J., Murray, S. S., Casey, B. J., Chang, L., Ernst, T. M., Frazier, J. A., Gruen, J. R., Kennedy, D. N., Van Zijl, P., ... Sowell, E. R. (2015). Family income, parental education and brain structure in children and adolescents. Nature Neuroscience, 18(5), Article 5. https://doi.org/10.1038/nn.3983

Noble, K. G., Magnuson, K., Gennetian, L. A., Duncan, G. J., Yoshikawa, H., Fox, N. A., & Halpern-Meekin, S. (2021). Baby's First Years: Design of a Randomized Controlled Trial of Poverty Reduction in the United States. Pediatrics, 148(4), e2020049702. https://doi.org/10.1542/peds.2020-049702

Noble, K. G., McCandliss, B. D., & Farah, M. J. (2007). Socioeconomic gradients predict individual differences in neurocognitive abilities. Developmental Science, 10(4), 464–480. https://doi.org/10.1111/j.1467-7687.2007.00600.x

Noble, K. G., Norman, M. F., & Farah, M. J. (2005). Neurocognitive correlates of socioeconomic status in kindergarten children. Developmental Science, 8(1), 74–87. https://doi.org/10.1111/j.1467-7687.2005.00394.x

Paul, S. E., Hatoum, A. S., Fine, J. D., Johnson, E. C., Hansen, I., Karcher, N. R., ... & Bogdan, R. (2021). Associations

between prenatal cannabis exposure and childhood outcomes: results from the ABCD study. JAMA Psychiatry, 78(1), 64-76.

Paulich, K. N., Ross, J. M., Lessem, J. M., & Hewitt, J. K. (2021). Screen time and early adolescent mental health, academic, and social outcomes in 9-and 10-year old children: Utilizing the Adolescent Brain Cognitive Development(ABCD) Study. PloS one, 16(9), e0256591.

Peter R., H. (1979). Synaptic density in human frontal cortex—Developmental changes and effects of aging. Brain Research, 163(2), 195–205. https://doi.org/10.1016/0006-8993(79)90349-4

Purves, D., Augustine, G. J., Fitzpatrick, D., Katz, L. C., LaMantia, A.-S., McNamara, J. O., & Williams, S. M. (2001). Neuronal Migration. In Neuroscience. 2nd edition. Sinauer Associates. https://www.ncbi.nlm.nih.gov/books/NBK10831/

Rock, K. L., & Kono, H. (2008). The inflammatory response to cell death. Annual Review of Pathology, 3, 99. https://doi.org/10.1146/annurev.pathmechdis.3.121806.151456

Shonkoff, J. P., Phillips, D. A., & National Research Council (U.S.) (Eds.). (2000). From neurons to neighborhoods: The science of early child development. National Academy Press.

Silbereis, J. C., Pochareddy, S., Zhu, Y., Li, M., & Sestan, N. (2016). The cellular and molecular landscapes of the

developing human central nervous system. Neuron, 89(2), 248-268.

Sorrells, S. F., Paredes, M. F., Cebrian-Silla, A., Sandoval, K., Qi, D., Kelley, K. W., James, D., Mayer, S., Chang, J., Auguste, K. I., Chang, E., Gutierrez Martin, A. J., Kriegstein, A. R., Mathern, G. W., Oldham, M. C., Huang, E. J., Garcia-Verdugo, J. M., Yang, Z., & Alvarez-Buylla, A. (2018). Human hippocampal neurogenesis drops sharply in children to undetectable levels in adults. Nature, 555(7696), 377–381. https://doi.org/10.1038/nature25975

Spalding, K. L., Bergmann, O., Alkass, K., Bernard, S., Salehpour, M., Huttner, H. B., Boström, E., Westerlund, I., Vial, C., Buchholz, B. A., Possnert, G., Mash, D. C., Druid, H., & Frisén, J. (2013). Dynamics of Hippocampal Neurogenesis in Adult Humans. Cell, 153(6), 1219–1227. https://doi.org/10.1016/j.cell.2013.05.002

Spear, L. P. (2000). The adolescent brain and age-related behavioral manifestations. Neuroscience & Biobehavioral Reviews, 24(4), 417–463. https://doi.org/10.1016/S0149-7634(00)00014-2

Spear, L. P. (2013). Adolescent Neurodevelopment. Journal of Adolescent Health, 52(2, Supplement 2), S7–S13. https://doi.org/10.1016/j.jadohealth.2012.05.006

Steinberg, L. (2004). Risk Taking in Adolescence: What Changes, and Why? Annals of the New York Academy of Sciences, 1021(1), 51–58. https://doi.org/10.1196/annals.1308.005

Takeichi, M. (1988). The cadherins: Cell-cell adhesion molecules controlling animal morphogenesis. Development, 102(4), 639–655. https://doi.org/10.1242/dev.102.4.639

Temple, S. (2001). The development of neural stem cells. Nature, 414(6859), Article 6859. https://doi.org/10.1038/35102174

THE BRAIN FROM TOP TO BOTTOM. (n.d.). Retrieved June 20, 2023, from https://thebrain.mcgill.ca/flash/i/i_07/i_07_cl/i_07_cl_tra/i_07_cl_tra.html

Tuo, Q., Zhang, S., & Lei, P. (2022). Mechanisms of neuronal cell death in ischemic stroke and their therapeutic implications. Medicinal Research Reviews, 42(1), 259–305. https://doi.org/10.1002/med.21817

Voss, P. (2013). Sensitive and critical periods in visual sensory deprivation. Frontiers in Psychology, 4. https://www.frontiersin.org/articles/10.3389/fpsyg.2013.00664

Wong, K., Wu, J. Y., & Rao, Y. (2002). Neuronal Migration. In Encyclopedia of Life Sciences. John Wiley & Sons, Ltd. https://doi.org/10.1038/npg.els.0000796

CHAPTER 8: GENETICS AND EPIGENETICS IN PSYCHOLOGY

Psychological researchers study genetics in order to better understand the biological factors that contribute to certain behaviors. Genes and the environment clearly influence the structure and function of the nervous system and therefore our thoughts, behaviors, and what makes us unique. In this chapter, we first review fundamental genetics. Then we look at how behavioral geneticists study the relative contributions of genes and environment and try to tease apart the influences of nature and nurture. We will 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.

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

8.1: 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 by focusing on 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.

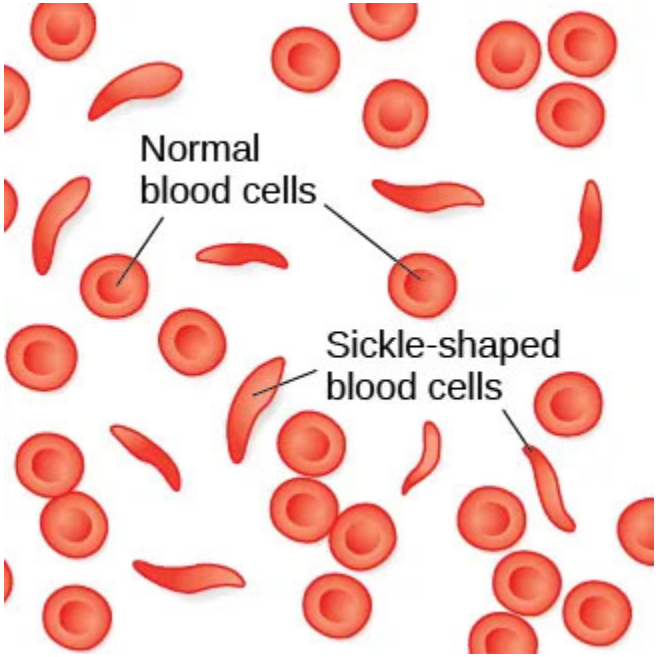


Figure 1. Normal blood cells travel freely through the blood vessels, while sickle-shaped cells form blockages preventing blood flow.

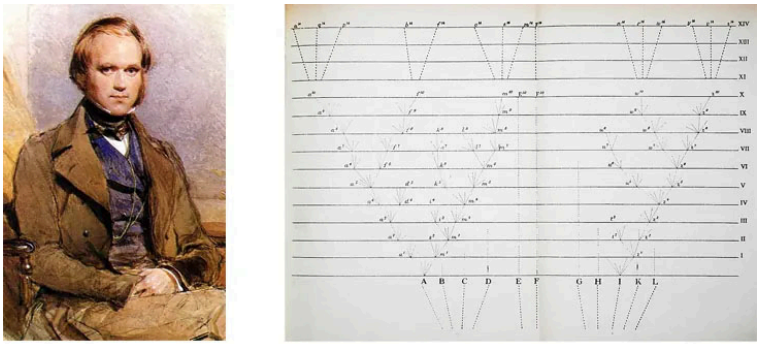
Many people with sickle-cell anemia—and the particular genetic mutation that causes it—die at an early age. While the notion of "survival of the fittest" may suggest that people with this disorder have a low survival rate and, therefore, the disorder will become less common, this is not the case. Despite 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.



(a) (b)

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.

Text Attributions

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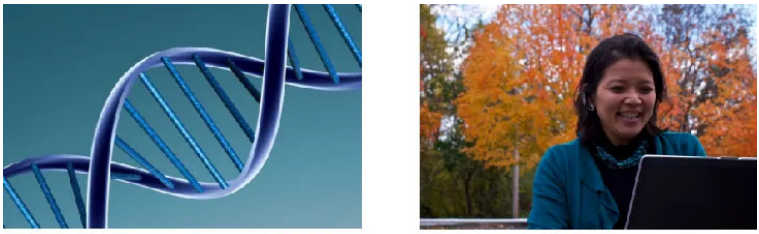
8.2: FUNDAMENTAL GENETICS AND GENETIC VARIATION

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. An **allele** is a specific version of a gene. 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).



(a) (b)

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)

The vast majority of traits are controlled by multiple genes, but some traits are controlled by one gene. A characteristic like cleft chin, for example, is influenced by a single gene from each parent. In this example, we will call the gene for cleft

chin "B" and the gene for smooth chin "b." Cleft chin is a dominant trait, which means that having the **dominant allele** either from one parent (Bb) or both parents (BB) will always result in the phenotype associated with the dominant allele. When someone has two copies of the same allele, they are said to be **homozygous** for that allele. When someone has a combination of alleles for a given gene, they are said to be **heterozygous**. For example, smooth chin is a recessive trait, which means that an individual will only display the smooth chin phenotype if they are homozygous for that **recessive allele** (bb).

Imagine that a person with a cleft chin mates with a person with a smooth chin. What type of chin will their offspring have? The answer to that depends on which alleles each parent carries. If the parent with a cleft is homozygous for cleft chin (BB), their offspring will always have cleft chin (because the offspring will get the dominant allele (B) from the cleft chin parent). It gets a little more complicated, however, if the parent with a cleft is heterozygous for this gene (Bb). Since the other person has a smooth chin—therefore homozygous for the recessive allele (bb)—we can expect the offspring to have a 50% chance of having a cleft chin (Bb) and a 50% chance of having a smooth chin (bb) (Figure 4).

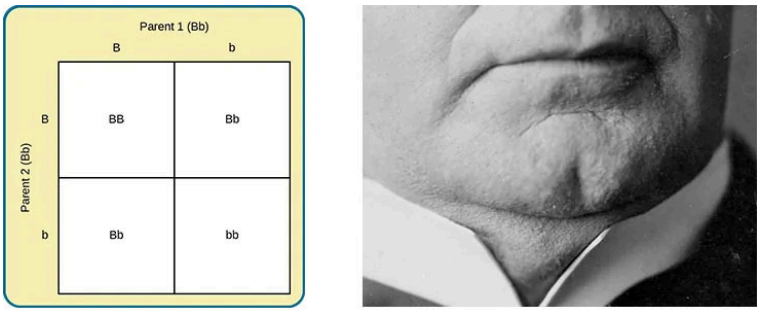


Figure 4. (a) A Punnett square is a tool used to predict how genes will interact in the production of offspring. The capital B represents the dominant allele, and the lowercase b represents the recessive allele. In the example of the cleft chin, where B is the cleft chin (dominant allele), wherever a 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.

Where do harmful genes that contribute to diseases like PKU come from? Gene mutations provide one source of harmful genes. A mutation is a sudden, permanent change in a gene. While many mutations can be harmful or lethal, once in a while, a mutation benefits an individual by giving that person an advantage over those who do not have the **mutation**. Recall that the theory of evolution asserts that individuals best adapted to their particular environments are more likely to reproduce and pass on their genes to future generations. In order for this process to occur, there must be competition—more technically, there must be variability in genes (and resultant traits) that allow for variation in adaptability to the environment. If a population consisted of identical individuals, then any dramatic changes in the environment would affect everyone in the same way, and there would be no variation in selection. In contrast, diversity in genes and associated traits allows some individuals to perform slightly better than others when faced with environmental change. This creates a distinct advantage for individuals best

suited for their environments in terms of successful reproduction and genetic transmission.

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).

Media Attributions

8.3: 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 own 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. And 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 own control.

Figure 5. Researchers have learned a great deal about the nature-nurture dynamic by working with animals. But of course, many of the 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 being 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 very 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 do 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 in order 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 take a 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 smaller role than is commonly believed 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.

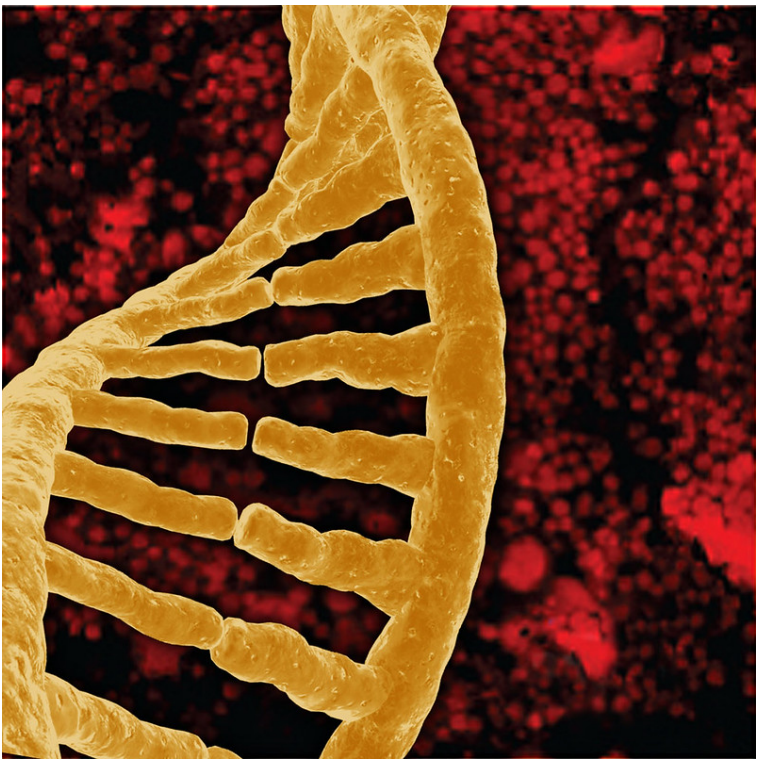


Figure 7. Quantitative genetics uses statistical methods to study the effects that both heredity and environment have on test subjects. These methods have provided us with the heritability coefficient which measures how strongly differences among individuals for a trait are related to differences among 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 well below $1000 today; 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 the various ways nature-nurture influences human behavior can be messy, and often common-sense notions can get in the way of good science. One very significant contribution of behavioral genetics that has changed psychology for good can be very helpful to keep in mind: When your subjects are biologically related, no matter how

clearly a situation may seem to point to environmental influence, it is never safe to interpret behavior as wholly the result of nurture without further evidence. For example, when presented with data showing that children whose mothers read to them often are likely to have better reading scores in third grade, it is tempting to conclude that reading to your kids is important to success in school; this may well be true, but the study as described is inconclusive because there are genetic as well as environmental pathways between the parenting practices of mothers and the abilities of their children. This is a case where "correlation does not imply causation." To establish that reading aloud causes success, a scientist can either study the problem in adoptive families (in which the genetic pathway is absent) or by conducting an experiment that randomly assigns children to oral reading conditions.

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.

As noted in the previous section, the heritability coefficient does not capture the complexity of the nature-nurture relationship. Instead, for many traits, genetic differences affect behavior under some environmental circumstances but not others—a phenomenon called gene-environment interaction,

or G x 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.

Some common questions about nature–nurture are: how susceptible is a trait to change, how malleable is it, and do we "have a choice" about it? These questions are much more complex than they may seem at first glance. For example, phenylketonuria is an inborn error of metabolism caused by a single gene; it prevents the body from metabolizing phenylalanine. Untreated, it causes intellectual disability and death. However, it can be treated effectively by a straightforward environmental intervention: avoiding foods

containing phenylalanine. Height seems like a trait firmly rooted in our nature and unchangeable, but the average height of many populations in Asia and Europe has increased significantly in the past 100 years, due to changes in diet and the alleviation of poverty.

With the Human Genome Project and DNA sequencing, it was believed that we would be easily able to link specific genes with specific behaviors. That has not happened. A few rare genes have been found to have significant (almost always negative) effects, such as the single gene that causes Huntington's disease or the Apolipoprotein gene that causes early-onset dementia in a small percentage of Alzheimer's cases. Aside from these rare genes of great effect, however, the genetic impact on behavior is broken up over many genes, each with very small effects. For most behavioral traits, the effects are so small and distributed across so many genes that we have not been able to catalog them in a meaningful way. In fact, the same is true of environmental effects. We know that extreme environmental hardship causes catastrophic effects for many behavioral outcomes, but fortunately, extreme environmental hardship is very rare. Within the normal range of environmental events, those responsible for differences (e.g., why some children in a suburban third-grade classroom perform better than others) are much more difficult to grasp.

Finding clear-cut solutions to nature–nurture problems is difficult. With nature-nurture, what at first seems straightforward and possible to index with a single number

becomes more and more complicated the closer we look. The many questions we can ask about the intersection among genes, environments, and human traits—how sensitive are traits to environmental change, are parents or culture more relevant; how sensitive are traits to differences in genes, and how much do the relevant genes vary in a particular population, does the trait involve a single gene or many genes, and is the trait more easily described in genetic or more complex behavioral terms?—may have different answers, and the answer to one tells us little about the answers to the others. Overall, we should continue studying and thinking about nature and nature or genes and the environment without being tempted to oversimplify these complex relationships.

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8.4: 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 is made up of chemical compounds and proteins that can attach to DNA and direct such actions as turning genes "on" or "off". For this reason, 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 disease[1].

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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

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 added to or removed from histones to make the histones more tightly or loosely packed, turning genes "off" or "on."

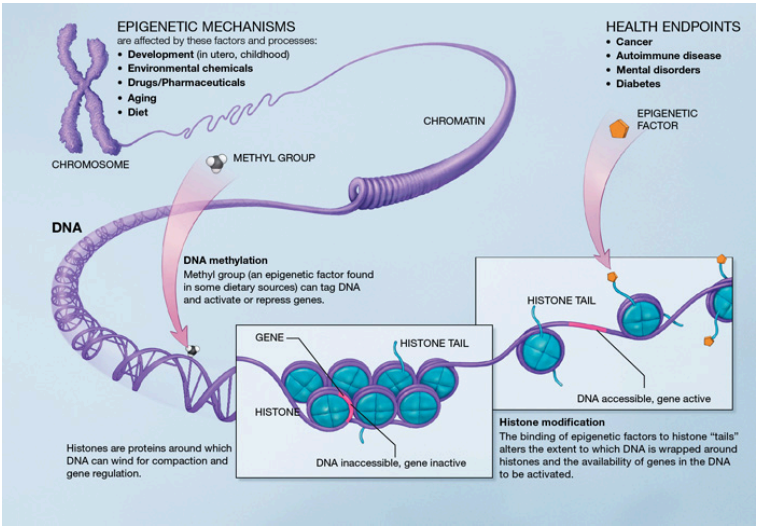

Figure 10. A Scientific Illustration of How Epigenetic Mechanisms Can Affect Health. Epigenetic mechanisms are affected by several factors and processes, including development in utero and in childhood, environmental chemicals, drugs and pharmaceuticals, aging, and diet. DNA methylation occurs when methyl 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.

2

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).

2. 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

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 the nerve cell to turn "on" genes to make proteins important for its job and turn "off" genes important for a heart cell's job.

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).

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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 Public Domain

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 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 (Hulsfhoff 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 own personal development and risk for disease in adult life (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 the development of cancer. It appears that 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 processes[4].

Epigenetics in Psychology

In addition to chronic physical conditions, mental health, and

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 Public Domain

cognition can be affected by environmental factors during early 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 variations in parental investment and epigenetic inheritance in mammals is of the maternally transmitted responses to stress in rats. In 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 during the first week of life showed decreased histone acetylation and increased DNA methylation of a neuron-specific promoter 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 in adulthood by pharmacological treatments that influence histone modification, DNA methylation, and expression of the glucocorticoid receptor gene (Weaver et al., 2004; Weaver et al., 2005). These experiments show that histone modification and DNA methylation of the glucocorticoid-receptor gene promoter leads to the long-term physiological and behavioral outcomes of poor maternal care. This points to a possible molecular target for treatments that may reverse the traces of childhood maltreatment.

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

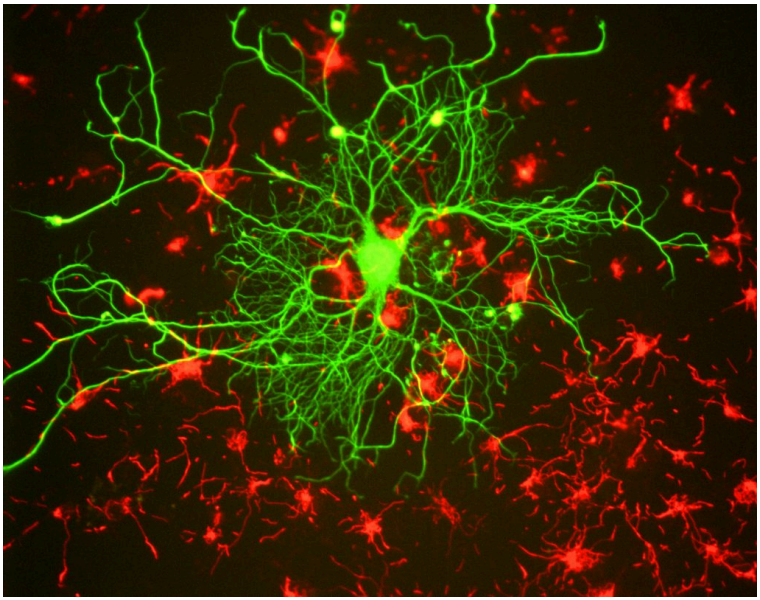

Figure 14. Neural plasticity is the change of neural pathways and synapses which allows for our ability to learn new things and remember them.

Epigenetic mechanisms 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 genes encoding the DNA methylation machinery causes learning and memory impairments (Feng et al., 2010). DNA methylation has also been implicated in maintaining long-term memories, as pharmacological inhibition of DNA methylation can impair memory (Day & Sweatt, 2011). These findings indicate the importance of DNA methylation in mediating synaptic plasticity and cognitive functions, both of which are disturbed in psychological illness.

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.

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, which had previously been 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 disorders[5].

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8.5: REFERENCES

Parts of this chapter were adapted from:

Spielman, R. M., Jenkins, W., & Lovett, M. (2020). Psychology 2e. OpenStax. Houston, Texas. https://openstax.org/books/psychology-2e/pages/3-1-human-genetics

Centers for Disease Control and Prevention (CDC) (2022) What is Epigenetics? https://www.cdc.gov/genomics/disease/epigenetics.htm

National Human Genome Research Institute (NHGRI) (2020). Epigenetics Fact Sheet. https://www.genome.gov/about-genomics/fact-sheets/Epigenomics-Fact-Sheet

Turkheimer, E. (2023). The nature-nurture question. In R. Biswas-Diener & E. Diener (Eds.), Noba textbook series: Psychology. Champaign, IL: DEF publishers. Retrieved from http://noba.to/tvz92edh

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

References

Alarcon, J. M., Malleret, G., Touzani, K., Vronskaya, S., Ishii, S., Kandel, E. R., & Barco, A. (2004). Chromatin acetylation, memory, and LTP are impaired in CBP+/- mice: a model for the cognitive deficit in Rubinstein-Taybi syndrome and its amelioration. Neuron, 42(6), 947–959.

Amir, R. E., Van den Veyver, I. B., Wan, M., Tran, C. Q., Francke, U., & Zoghbi, H. Y. (1999). Rett syndrome is caused by mutations in X-linked MECP2, encoding methyl-CpG-binding protein 2. Nature Genetics, 23(2), 185–188.

Bouchard, T. J., Lykken, D. T., McGue, M., & Segal, N. L. (1990). Sources of human psychological differences: The Minnesota study of twins reared apart. Science, 250(4978), 223–228.

Caldji, C., Tannenbaum, B., Sharma, S., Francis, D., Plotsky, P. M., & Meaney, M. J. (1998). Maternal care during infancy regulates the development of neural systems mediating the expression of fearfulness in the rat. Proceedings of the National Academy of Sciences U S A, 95(9), 5335–5340.

Caspi, A., McClay, J., Moffitt, T. E., Mill, J., Martin, J., Craig, I. W., Taylor, A. & Poulton, R. (2002). Role of genotype in the cycle of violence in maltreated children. Science, 297(5582), 851–854.

Cassel, S., Carouge, D., Gensburger, C., Anglard, P., Burgun, C., Dietrich, J. B., . . . Zwiller, J. (2006). Fluoxetine and cocaine induce the epigenetic factors MeCP2 and MBD1 in

adult rat brain. Molecular Pharmacology, 70(2), 487–492. doi: 10.1124/mol.106.022301

Chandran, A., Antony, C., Jose, L., Mundayoor, S., Natarajan, K., & Kumar, R. A. (2015). Mycobacterium tuberculosis infection induces HDAC1-mediated suppression of IL-12B gene expression in macrophages. Frontiers in Cellular and Infection Microbiology, 5, 90.

Confer, J. C., Easton, J. A., Fleischman, D. S., Goetz, C. D., Lewis, D. M. G, Perilloux, C., & Buss, D. M. (2010). Evolutionary psychology: Controversies, questions, prospects, and limitations. American Psychologist, 65, 110–126.

Covington, H. E., Maze, I., LaPlant, Q. C., Vialou, V. F., Ohnishi, Y. N., Berton, O., ... & Nestler, E. J. (2009). Antidepressant actions of histone deacetylase inhibitors. Journal of Neuroscience, 29(37), 11451-11460.

Day, J. J., & Sweatt, J. D. (2011). Epigenetic mechanisms in cognition. Neuron, 70(5), 813–829.

Feng, J., Zhou, Y., Campbell, S. L., Le, T., Li, E., Sweatt, J. D., . . . Fan, G. (2010). Dnmt1 and Dnmt3a maintain DNA methylation and regulate synaptic function in adult forebrain neurons. Nature Neuroscience, 13(4), 423–430. doi: 10.1038/nn.2514

Francis, D., Diorio, J., Liu, D., & Meaney, M. J. (1999). Nongenomic transmission across generations of maternal behavior and stress responses in the rat. Science, 286(5442), 1155–1158.

Gong, L., Parikh, S., Rosenthal, P. J., & Greenhouse, B. (2013). Biochemical and immunological mechanisms by which sickle cell trait protects against malaria. Malaria Journal. Advance online publication. doi:10.1186/1475-2875-12-317

Guan, Z., Giustetto, M., Lomvardas, S., Kim, J. H., Miniaci, M. C., Schwartz, J. H., . . . Kandel, E. R. (2002). Integration of long-term-memory-related synaptic plasticity involves bidirectional regulation of gene expression and chromatin structure. Cell, 111(4), 483–493.

Guo, J. U., Ma, D. K., Mo, H., Ball, M. P., Jang, M. H., Bonaguidi, M. A., . . . Song, H. (2011). Neuronal activity modifies the DNA methylation landscape in the adult brain. Nature Neuroscience, 14(10), 1345–1351.

Heijmans, B. T., Tobi, E. W., Stein, A. D., Putter, H., Blauw, G. J., Susser, E. S., ... & Lumey, L. H. (2008). Persistent epigenetic differences associated with prenatal exposure to famine in humans. Proceedings of the National Academy of Sciences, 105(44), 17046-17049.

Hulshoff Pol, H. E., Hoek, H. W., Susser, E., Brown, A. S., Dingemans, A., Schnack, H. G., ... & Kahn, R. S. (2000). Prenatal exposure to famine and brain morphology in schizophrenia. American Journal of Psychiatry, 157(7), 1170-1172.

Jiang, Y. H., Bressler, J., & Beaudet, A. L. (2004). Epigenetics and human disease. Annual Review of Genomics and Human Genetics, 5, 479–510.

Lee, M. G., Wynder, C., Schmidt, D. M., McCafferty, D. G., & Shiekhattar, R. (2006). Histone H3 lysine 4 demethylation is a target of nonselective antidepressive medications. Chemistry & Biology, 13(6), 563–567.

Liu, D., Diorio, J., Tannenbaum, B., Caldji, C., Francis, D., Freedman, A., . . . Meaney, M. J. (1997). Maternal care, hippocampal glucocorticoid receptors, and hypothalamic-pituitary-adrenal responses to stress. Science, 277(5332), 1659–1662.

McCartney, D. L., Stevenson, A. J., Hillary, R. F., Walker, R. M., Bermingham, M. L., Morris, S. W., ... & Marioni, R. E. (2018). Epigenetic signatures of starting and stopping smoking. EBioMedicine, 37, 214-220.

McGowan, P. O., Sasaki, A., Huang, T. C., Unterberger, A., Suderman, M., Ernst, C., . . . Szyf, M. (2008). Promoter-wide hypermethylation of the ribosomal RNA gene promoter in the suicide brain. PLoS ONE, 3(5), e2085. doi: 10.1371/journal.pone.0002085

McGue, M., & Lykken, D. T. (1992). Genetic influence on risk of divorce. Psychological Science, 3(6), 368–373.

Mill, J., Tang, T., Kaminsky, Z., Khare, T., Yazdanpanah, S., Bouchard, L., . . . Petronis, A. (2008). Epigenomic profiling reveals DNA-methylation changes associated with major psychosis. American Journal of Human Genetics, 82(3), 696–711.

National Human Genome Research Institute (2021). The cost of sequencing a human genome.

https://www.genome.gov/about-genomics/fact-sheets/Sequencing-Human-Genome-cost

Oberlander, T. F., Weinberg, J., Papsdorf, M., Grunau, R., Misri, S., & Devlin, A. M. (2008). Prenatal exposure to maternal depression, neonatal methylation of human glucocorticoid receptor gene (NR3C1) and infant cortisol stress responses. Epigenetics, 3(2), 97–106.

Pidsley, R., Dempster, E., Troakes, C., Al-Sarraj, S., & Mill, J. (2012). Epigenetic and genetic variation at the IGF2/H19 imprinting control region on 11p15. 5 is associated with cerebellum weight. Epigenetics, 7(2), 155-163.

Plomin, R., Corley, R., DeFries, J. C., & Fulker, D. W. (1990). Individual differences in television viewing in early childhood: Nature as well as nurture. Psychological Science, 1(6), 371–377.

Plomin, R., DeFries, J. C., Knopik, V. S., & Neiderhiser, J. M. (2012). Behavioral genetics. New York, NY: Worth Publishers.

Poulter, M. O., Du, L., Weaver, I. C., Palkovits, M., Faludi, G., Merali, Z., . . . Anisman, H. (2008). GABAA receptor promoter hypermethylation in suicide brain: implications for the involvement of epigenetic processes. Biological Psychiatry, 64(8), 645–652.

Roseboom, T. J. (2019). Epidemiological evidence for the developmental origins of health and disease: effects of prenatal undernutrition in humans. Journal of Endocrinology, 242(1), T135-T144.

Schaefer, A., Sampath, S. C., Intrator, A., Min, A., Gertler, T. S., Surmeier, D. J., . . . Greengard, P. (2009). Control of cognition and adaptive behavior by the GLP/G9a epigenetic suppressor complex. Neuron, 64(5), 678–691.

Scott, J. P., & Fuller, J. L. (1998). Genetics and the social behavior of the dog. Chicago, IL: University of Chicago Press.

Tang, Q., Cheng, J., Cao, X., Surowy, H., & Burwinkel, B. (2016). Blood-based DNA methylation as biomarker for breast cancer: a systematic review. Clinical Epigenetics, 8, 1-18.

Tienari, P., Wynne, L. C., Sorri, A., et al. (2004). Genotype–environment interaction in schizophrenia spectrum disorder: long-term follow-up study of Finnish adoptees. British Journal of Psychiatry, 184, 216–222.

Tordjman, S., Somogyi, E., Coulon, N., Kermarrec, S., Cohen, D., Bronsard, G., ... & Xavier, J. (2014). Gene × Environment interactions in autism spectrum disorders: Role of epigenetic mechanisms. Frontiers in Psychiatry, 5, 53.

Tsankova, N. M., Berton, O., Renthal, W., Kumar, A., Neve, R. L., & Nestler, E. J. (2006). Sustained hippocampal chromatin regulation in a mouse model of depression and antidepressant action. Nature Neuroscience. 9(4): 519–525.

Turkheimer, E. (2000). Three laws of behavior genetics and

what they mean. Current Directions in Psychological Science, 9(5), 160–164.

Weaver, I. C., Cervoni, N., Champagne, F. A., D'Alessio, A. C., Sharma, S., Seckl, J. R., . . . Meaney, M. J. (2004). Epigenetic programming by maternal behavior. Nature Neuroscience, 7(8), 847–854.

Weaver, I. C., Champagne, F. A., Brown, S. E., Dymov, S., Sharma, S., Meaney, M. J., & Szyf, M. (2005). Reversal of maternal programming of stress responses in adult offspring through methyl supplementation: altering epigenetic marking later in life. Journal of Neuroscience, 25(47), 11045–11054.

Wells, J. C. (2003). The thrifty phenotype hypothesis: thrifty offspring or thrifty mother? Journal of Theoretical Biology, 221(1), 143–161.

Yudell, M., Roberts, D., DeSalle, R., & Tishkoff, S. (2016). Taking race out of human genetics. Science, 351(6273), 564–565.

Zudaire, E., Cuesta, N., Murty, V., Woodson, K., Adams, L., Gonzalez, N., ... & Cuttitta, F. (2008). The aryl hydrocarbon receptor repressor is a putative tumor suppressor gene in multiple human cancers. The Journal of Clinical Investigation, 118(2), 640-650.

CHAPTER 9: EMOTION AND AFFECTIVE NEUROSCIENCE

By Eddie Harmon-Jones and Cindy Harmon-Jones

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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.

9.1: 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.

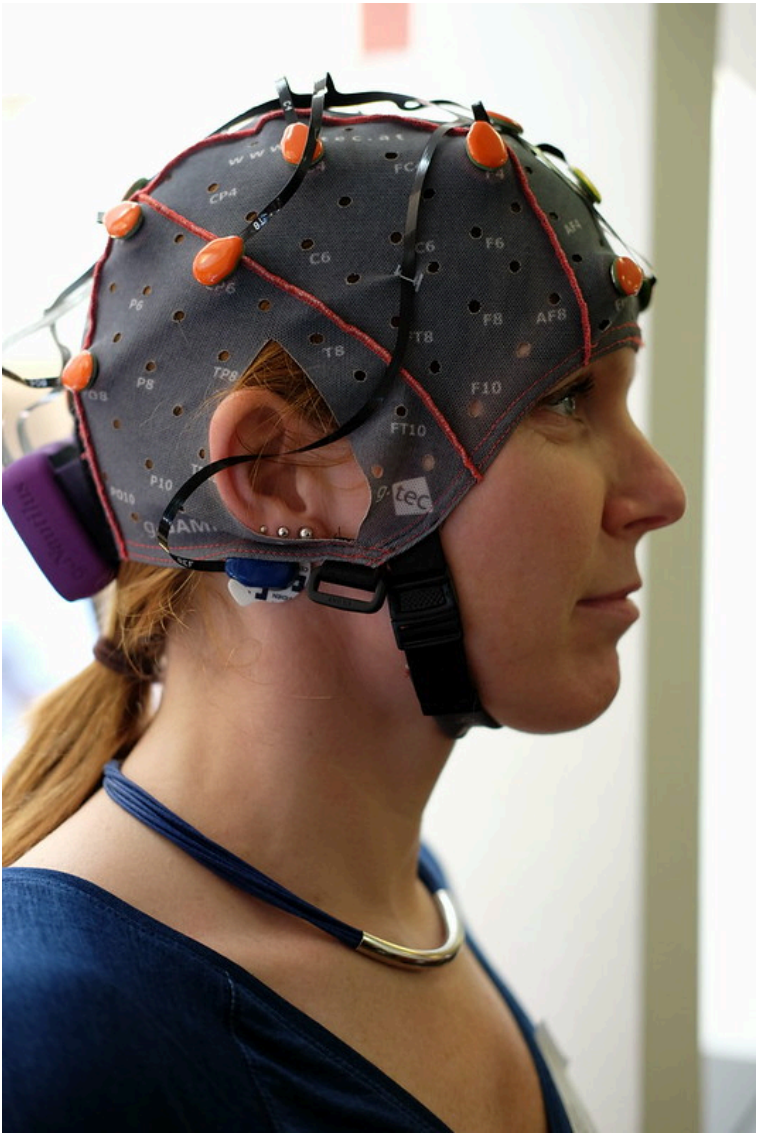

Figure 1. Although we experience emotions all the time, they are very difficult to describe and study. Fortunately, technological advances and the tools of neuroscience are making this easier.

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.

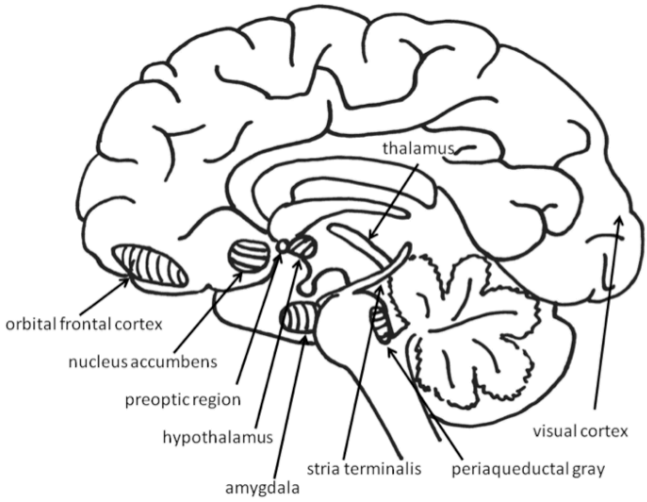

Figure 2: Some of the many structures involved in emotion processing in the brain.

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9.2: 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 he or she likes that reward. This is because the neural structures involved in the enjoyment of rewards are different from the structures involved in the desire for the 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 the fear-related areas in the brain 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-corticotrophic 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 effectively 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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9.3: PLASTICITY: EXPERIENCES CAN ALTER THE BRAIN

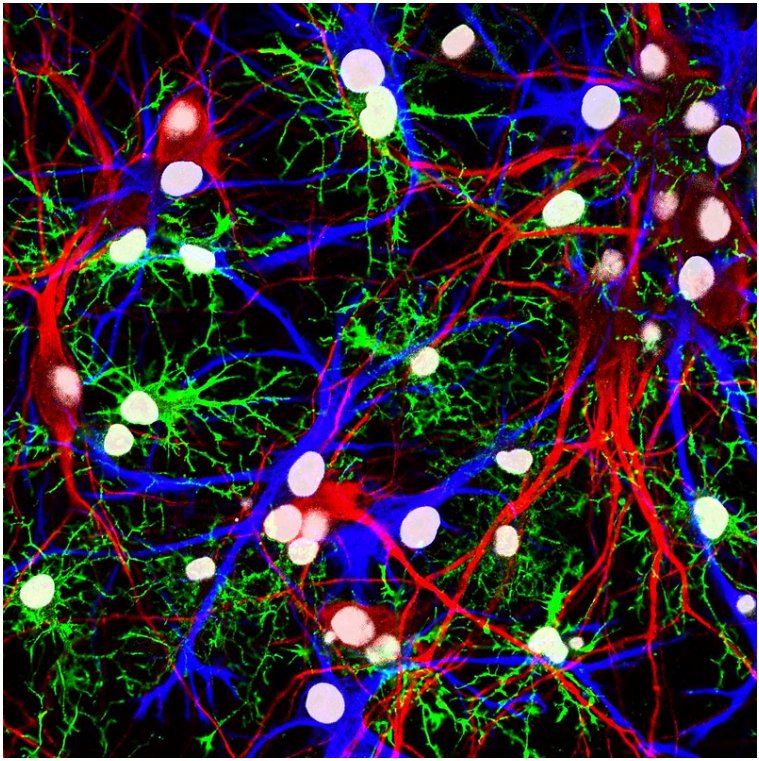

Figure 6. Neural plasticity can be summed up in the phrase: "Neurons that fire together, wire together." Or in other words, when certain emotions are paired with certain contexts, we learn to associate the two together.

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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9.4: 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).

9.5: 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.

9.6: 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=u4ICY6-7hJo&ab_channel=SpektrumderWissenschaft

Video: A 15-minute interview with Kent Berridge on pleasure in the brain

https://www.youtube.com/watch?v=51rGE1DgIo0&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

9.7: 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

References

Anderson, A. K., Christoff, K., Stappen, I., Panitz, D., Ghahremani, D. G., Glover, G., . . . Sobel, N. (2003). Dissociated neural representations of intensity and valence in human olfaction. Nature Neuroscience, 6, 196–202.

Berkman, E. T., & Lieberman, M. D. (2010). Approaching the bad and avoiding the good: Lateral prefrontal cortical asymmetry distinguishes between action and valence. Journal of Cognitive Neuroscience, 22(9), 1970–1979. doi: 10.1162/jocn.2009.21317

Berridge, K. C., & Kringelbach, M. L. (2013). Neuroscience of affect: brain mechanisms of pleasure and displeasure.

Current Opinion in Neurobiology, 23, 294–303. doi.org/10.1016/j.conb.2013.01.017

Berridge, K. C., & Kringelbach, M. L. (2008). Affective neuroscience of pleasure: Reward in humans and animals. Psychopharmacology, 199, 457–480. doi: 10.1007/s00213-008-1099-6

Blanchard, D. C., & Blanchard, R. J. (2003). What can animal aggression research tell us about human aggression? Hormones and Behavior, 44, 171–177.

Farb, N.A.S., Chapman, H. A., & Anderson, A. K. (2013). Emotions: Form follows function. Current Opinion in Neurobiology, 23, 393–398. http://dx.doi.org/10.1016/j.conb.2013.01.015

Fox, N. A., & Davidson, R. J. (1986). Taste-elicited changes in facial signs of emotion and the asymmetry of brain electrical activity in human newborns. Neuropsychologia, 24, 417–422.

Freese, J. L., & Amaral, D. G. (2009). Neuroanatomy of the primate amygdala. In P. J. Whalen & E. A. Phelps (Eds.), The human amygdala (pp. 3–42). New York, NY: Guilford Press.

Gable, P. A., & Harmon-Jones, E. (2008). Relative left frontal activation to appetitive stimuli: Considering the role of individual differences. Psychophysiology, 45, 275-278.

Goldstein, K. (1939). The organism: An holistic approach to biology, derived from pathological data in man. New York, NY: American Book.

Gottfried, J. A., O'Doherty, J., & Dolan, R. J. (2002). Appetitive and aversive olfactory learning in humans studied using event-related functional magnetic resonance imaging. Journal of Neuroscience, 22, 10829–10837.

Gray, J. A. (1987). The psychology of fear and stress (2nd ed.). Cambridge, England: Cambridge University Press.

Harmon-Jones, E., Harmon-Jones, C., & Price, T. F. (2013). What is approach motivation? Emotion Review, 5, 291–295. doi: 10.1177/1754073913477509

Heinrichs, M., von Dawans, B., & Domes, G. (2009). Oxytocin, vasopressin, and human social behavior. Frontiers in Neuroendocrinology, 30, 548–557.

Izard, C. E. (2010). The many meanings/aspects of emotion: Definitions, functions, activation, and regulation. Emotion Review, 2, 363–370. doi: 10.1177/1754073910374661

LeDoux, J. E. (1996). The emotional brain: The mysterious underpinnings of emotional life. New York, NY: Simon & Schuster.

LeDoux, J. E., Farb, C. F., Ruggiero, D. A. (1990). Topographic organization of neurons in the acoustic thalamus that project to the amygdala. Journal of Neuroscience, 10, 1043–1054.

Numan, M., & Insel, T. R. (2003). The neurobiology of parental behavior. New York, NY: SpringerVerlag.

O'Doherty J. P., Deichmann, R., Critchley, H. D., & Dolan, R. J. (2002). Neural responses during anticipation of a primary taste reward. Neuron, 33, 815–826.

O'Doherty, J., Kringelbach, M. L., Rolls, E. T., Hornak, J., & Andrews, C. (2001). Abstract reward and punishment representations in the human orbitofrontal cortex. Nature Neuroscience, 4, 95–102.

O'Doherty, J., Winston, J., Critchley, H., Perrett, D., Burt, D. M., & Dolan, R. J. (2003). Beauty in a smile: The role of medial orbitofrontal cortex in facial attractiveness. Neuropsychologia, 41, 147–155.

Panksepp, J. (1998). Affective neuroscience: The foundations of human and animal emotions. New York, NY: Oxford University Press.

Panksepp, J., & Biven, L. (2012). The archaeology of mind: Neuroevolutionary origins of human emotions. New York, NY: Norton.

Panksepp, J., Normansell, L., Herman, B., Bishop, P., & Crepeau, L. (1988). Neural and neurochemical control of the separation distress call. In J. D. Newman (Ed.), The physiological control of mammalian vocalization (pp. 263–299). New York, NY: Plenum.

Peterson, C. K., & Harmon-Jones, E. (2012). Anger and testosterone: Evidence that situationally-induced anger relates to situationally-induced testosterone. Emotion, 12, 899–902. doi: 10.1037/a0025300

Reynolds, S. M., & Berridge, K. C. (2008). Emotional environments retune the valence of appetitive versus fearful functions in nucleus accumbens. Nature Neuroscience, 11, 423–425.

Reynolds, S. M., & Berridge, K. C. (2002). Positive and negative motivation in nucleus accumbens shell: Bivalent rostrocaudal gradients for GABA-elicited eating, taste "liking"/"disliking" reactions, place preference/avoidance, and fear. Journal of Neuroscience, 22, 7308–7320.

Reynolds, S. M., & Berridge, K. C. (2001). Fear and feeding in the nucleus accumbens shell: Rostrocaudal segregation of GABA-elicited defensive behavior versus eating behavior. Journal of Neuroscience, 21, 3261–3270.

Schulkin, J. (1991). Sodium hunger: The search for a salty taste. New York, NY: Cambridge University Press.

Seymour, B., Daw, N., Dayan, P., Singer, T., & Dolan, R. (2007). Differential encoding of losses and gains in the human striatum. Journal of Neuroscience, 27, 4826–4831.

Stewart, J., De Wit, H., & Eikelboom, R. (1984). Role of unconditioned and conditioned drug effects in the self-administration of opiates and stimulants. Psychological Review, 91, 251-268.

Wacker, J., Mueller, E. M., Pizzagalli, D. A., Hennig, J., & Stemmler, G. (2013). Dopamine-D2-receptor blockade reverses the association between trait approach motivation and frontal asymmetry in an approach-motivation context. Psychological Science, 24(4), 489–497. doi: 10.1177/0956797612458935

Whalen, P. J. (1998). Fear, vigilance, and ambiguity: initial neuroimaging studies of the human amygdala. Current Directions in Psychological Science, 7, 177–188.

CHAPTER 10: 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.

10.1: INTRODUCTION

The complexity and capabilities of a well-functioning human brain are truly 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 to control 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 causing various dysfunctions. 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 are easily damaged by force or by 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 the many types of 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. In this chapter, we'll cover three common ones–Parkinson's disease, Alzheimer's disease, and Multiple Sclerosis.

10.2: 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.

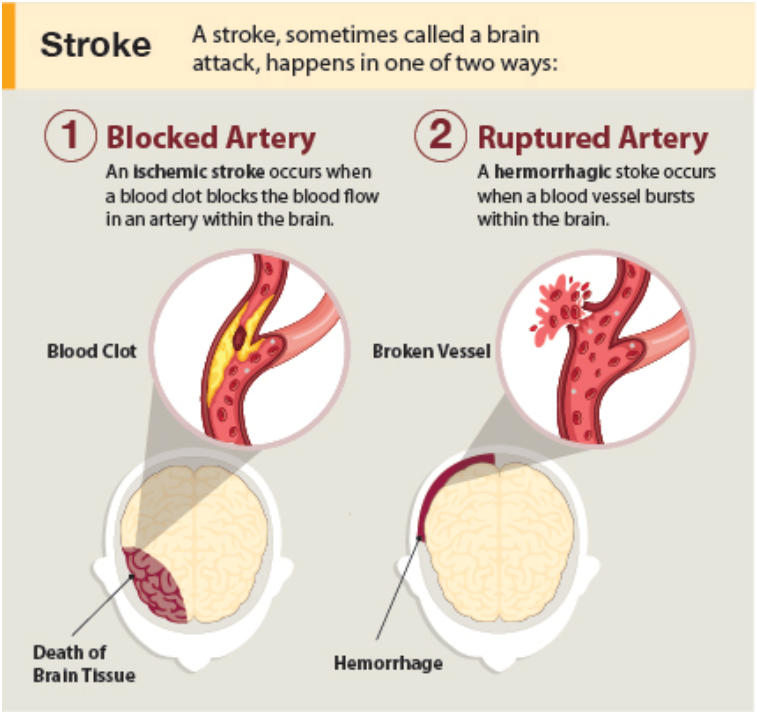

Figure 1. A stroke, sometimes called a brain attack, happens in one of two ways: 1) ischemic strokes occur when an artery is blocked, and 2) hemorrhagic stroke occurs when a blood vessel ruptures.

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 own glutamate reserves, which starts the process over in nearby cells. This glutamate excitotoxicity repeats itself in a vicious cycle that spreads quickly and kills many neurons in a matter of 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 useful 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 can 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 and 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. Risk factors of stroke that are nonmodifiable are 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 have been linked to a higher risk of hypertension, stroke, 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 public health and sensible public policy that mitigates risk factors.

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10.3: 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 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). Retrospectively, he said he may have had some coordination deficits (e.g., causing him to lose to his brother in golf); the tumor was surgically removed and he has resumed "trouncing" his brother in golf.

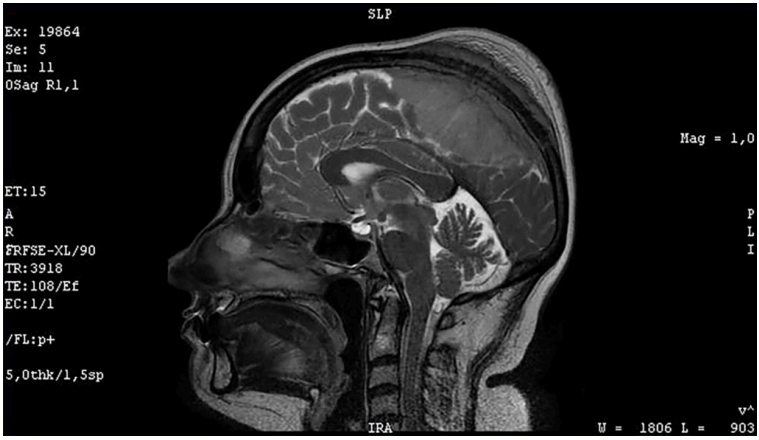

Figure 3. A meningioma, a benign tumor that developed in the meninges (thin membrane covering the brain), has caused a large hyperostosis (excessive bone growth of the skull).

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 very 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 surgically removed.

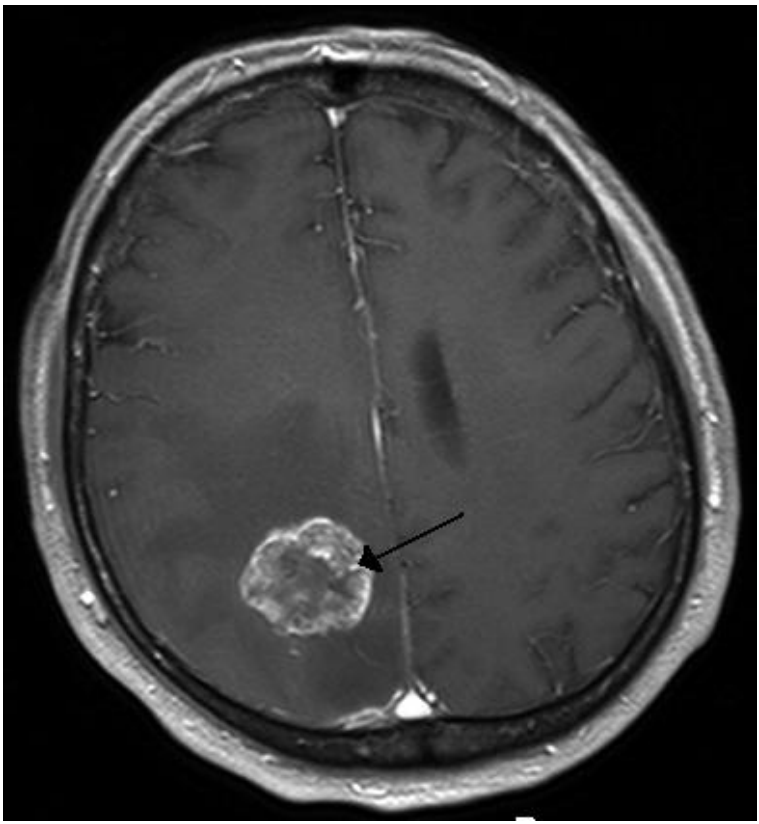

Figure 4. A metastatic tumor in the cerebral hemisphere from lung cancer, shown on magnetic resonance imaging.

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National Institute of Neurological Disorders and Stroke (NINDS) (2023c). Brain and Spinal Cord Tumors. https://www.ninds.nih.gov/health-information/disorders/brain-and-spinal-cord-tumors Public Domain.

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10.4: 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 various types of bleeding and tearing forces that injure nerve fibers and cause inflammation, metabolic changes, and brain swelling (NINDS, 2023d). Some examples include:

- Diffuse axonal injury (DAI), one of the most common types of brain injuries, refers to widespread damage to the brain's myelinated white matter tracts. DAI usually results from rotational forces (twisting) or sudden forceful stopping that stretches or tears these axon bundles (see Figure 5). DAI can disrupt and break down communication among neurons. It also leads to the release of brain chemicals that can cause further damage.

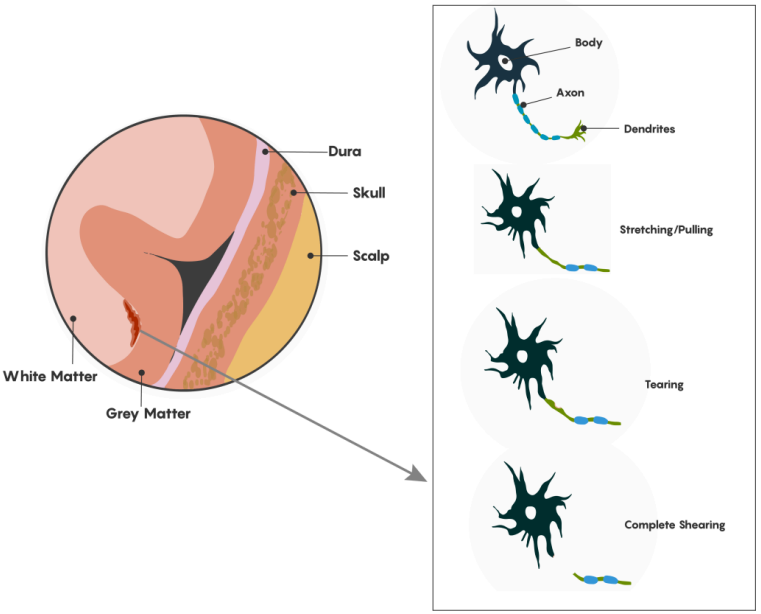

Figure 5. Diagram of diffuse axonal injury following TBI/concussion. Many types of damage can occur along the length of the axon, including stretching/pulling of axons which may affect myelination and localization of axonal channel proteins, and tearing and shearing, which will cause loss of axonal integrity.

- 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 a reason why concussion-monitoring protocols in sports are critical).

- 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 a bruising or swelling of the brain that occurs when very 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**).

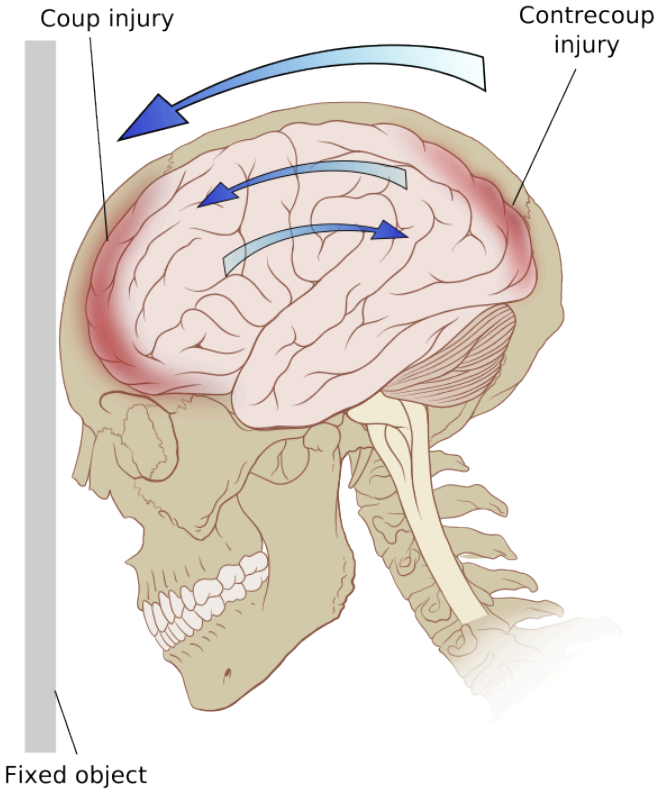

Figure 6. A diagram of the forces on the brain in a coup-contrecoup injury.

- 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

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.

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 therapies, such as neuroprotective agents and stem cell therapy, are under active research and hold promise for future treatment possibilities.[2]

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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.

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 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]

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.

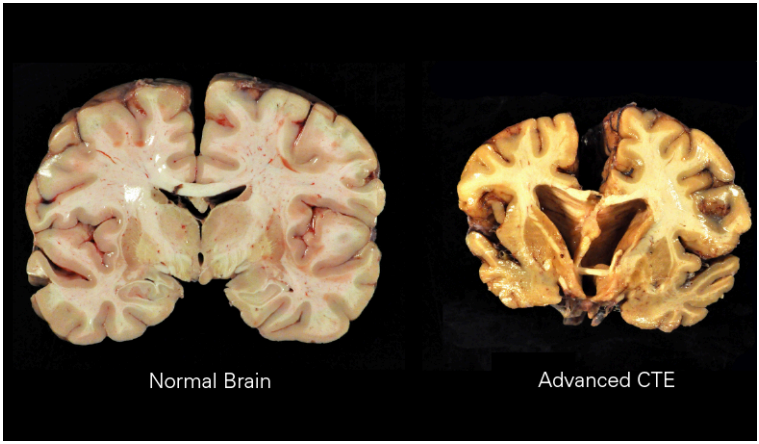

Figure 7. A normal brain (left) and one with advanced CTE (right).

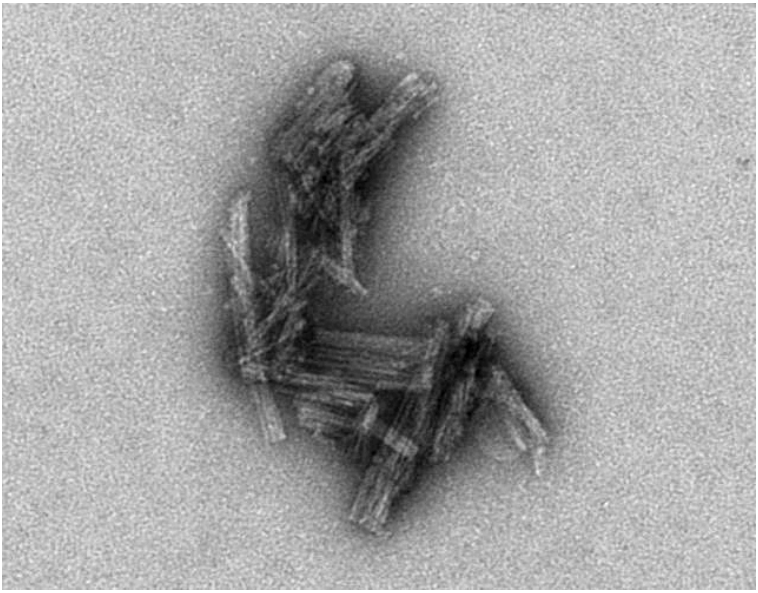

Figure 8. Electron micrograph of tau protein clusters that occur in Alzheimer's Disease and CTE.

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 (DV) is often used interchangeably with IPV, DV 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 I like to consider "concussion+". In the only study to examine the effects of strangulation-related AICs on cognitive and psychological outcomes, 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).

Preventing intimate partner violence. Intimate partner violence is preventable. A number of factors may increase or decrease the risk of perpetrating and experiencing 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. Efforts such as these and others 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.[4]

4. 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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10.5: 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 of them 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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10.6: 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.

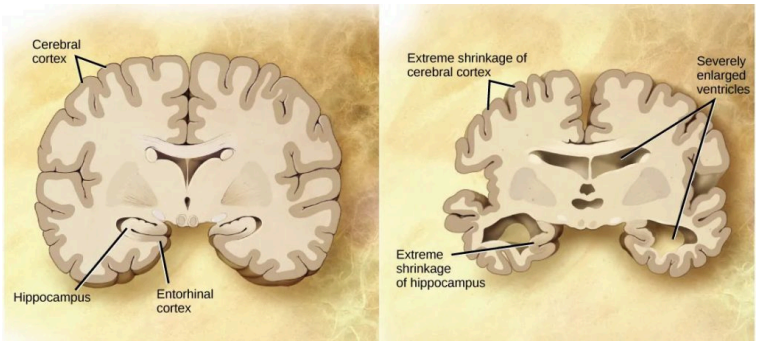

Figure 10. Compared to a normal brain (left), the brain of a patient with Alzheimer's disease (right) shows a dramatic neurodegeneration, particularly at the shrunken hippocampus and enlarged ventricles.

Amyloid plaques and neurofibrillary tangles are the two main biological markers associated with Alzheimer's (The Brain from Top to Bottom, n.d.). Both amyloid plaques and neurofibrillary tangles 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 better understand how and at what stage of the disease the various forms of beta-amyloid influence Alzheimer's disease symptoms.

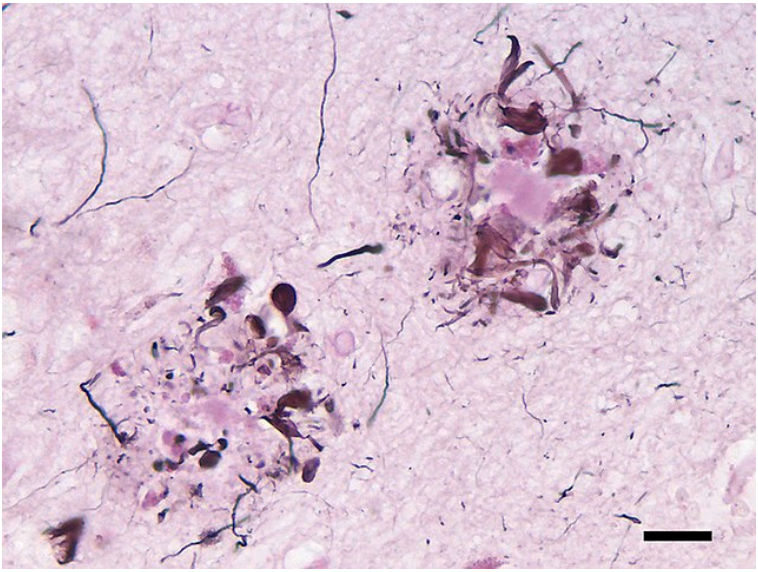

Figure 11. Two amyloid plaques from the brain of a patient with Alzheimer's disease. In this photomicrograph, neurites are darkly stained, and the elements stained pink include the plaque cores. The black bar is 20 microns (0.02mm) in length.

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, which harms the synaptic communication between neurons.

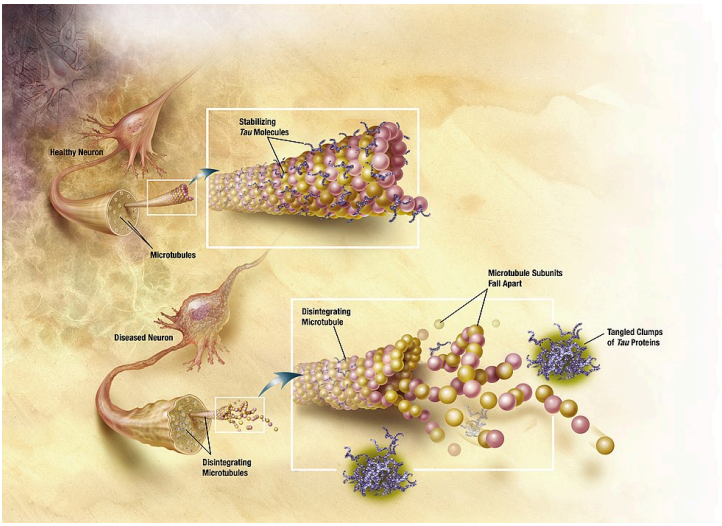

Figure 12. Diagram of how microtubules disintegrate with Alzheimer's disease. Source: National Institute on Aging.

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 likely also has a genetic component, although research has not been able to narrow down the 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. Current 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, research into prevention 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. Some studies have shown that people who remain intellectually active by playing games that are mentally stimulating, such as crossword puzzles, as well as reading, playing musical instruments, and being socially active in later life, have a reduced risk of developing the disease.

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10.7: 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 as well as 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 important for 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 (the ventral intermediate nucleus of the thalamus or VIM) 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.

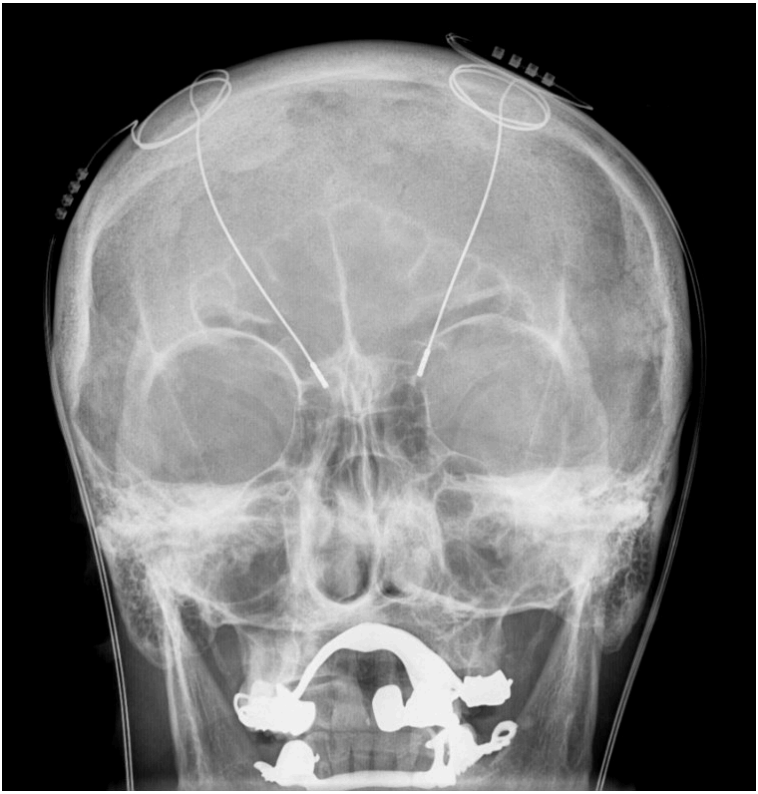

Figure 14. Deep Brain Stimulation probes shown in an X-ray of the skull.

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National Institute of Neurological Disorders and Stroke (NINDS) (n.d.). Deep brain stimulation (DBS) for the treatment of Parkinson's disease and other movement disorders. https://www.ninds.nih.gov/about-ninds/impact/ninds-contributions-approved-therapies/deep-brain-stimulation-dbs-treatment-parkinsons-disease-and-other-movement-disorders Public Domain.

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10.8: 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 with symptom onset generally occurring between the ages of 20 to 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.

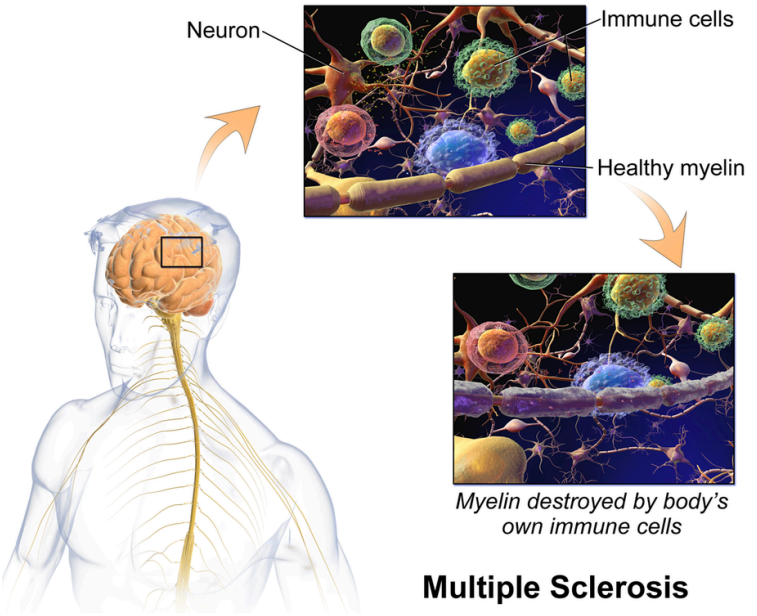

Figure 16. In MS, the immune system cells that normally protect us from viruses, bacteria, and unhealthy cells mistakenly attack myelin in the central nervous system.

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 gain initial entry into 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 have been linked to vulnerability to MS, and most of these genes are associated with immune-system function.
- Certain infections have been 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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10.9: REFERENCES

Parts of this chapter were adapted from:

Center for Disease Control and Prevention (CDC) (2022). Fast Facts: Preventing Intimate Partner Violence https://www.cdc.gov/violenceprevention/intimatepartnerviolence/fastfact.html

National Center for Complementary and Integrative Health (NCCIH) (2019). Multiple Sclerosis. https://www.nccih.nih.gov/health/multiple-sclerosis

National Institute of Neurological Disorders and Stroke (NINDS) (n.d.). Deep brain stimulation (DBS) for the treatment of Parkinson's disease and other movement disorders.

https://www.ninds.nih.gov/about-ninds/impact/ninds-contributions-approved-therapies/deep-brain-stimulation-dbs-treatment-parkinsons-disease-and-other-movement-disorders

National Institute of Neurological Disorders and Stroke (NINDS) (2023a). Stroke. https://www.ninds.nih.gov/health-information/disorders/stroke

National Institute of Neurological Disorders and Stroke (NINDS) (2023b). Multiple Sclerosis. https://www.ninds.nih.gov/health-information/disorders/multiple-sclerosis

National Institute of Neurological Disorders and Stroke (NINDS) (2023c). Brain and Spinal Cord Tumors. https://www.ninds.nih.gov/health-information/disorders/brain-and-spinal-cord-tumors

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

National Institute on Aging (NIA) (2017). What Happens to the Brain in Alzheimer's Disease? https://www.nia.nih.gov/health/what-happens-brain-alzheimers-disease

"The Brain from Top to Bottom" (n.d.). Retrieved on June 1, 2023 from https://thebrain.mcgill.ca/

References

Armstrong, M., & Strack, G. B. (2016). Recognition and documentation of strangulation crimes: A review. JAMA Otolaryngology–Head & Neck Surgery, 142(9), 891-897.

Asken, B. M., Sullan, M. J., DeKosky, S. T., Jaffee, M. S., & Bauer, R. M. (2017). Research gaps and controversies

in chronic traumatic encephalopathy: A review. JAMA Neurology, 74(10), 1255-1262.

Boehme, A. K., Esenwa, C., & Elkind, M. S. (2017). Stroke risk factors, genetics, and prevention. Circulation Research, 120(3), 472-495.

Catalano, S. M. (2012). Intimate partner violence, 1993-2010. Washington, DC: US Department of Justice, Office of Justice Programs, Bureau of Justice Statistics.

https://bjs.ojp.gov/content/pub/pdf/ipv9310.pdf

Center for Disease Control and Prevention (CDC) (2022). Fast Facts: Preventing Intimate Partner Violence https://www.cdc.gov/violenceprevention/intimatepartnerviolence/fastfact.html

Center for Disease Control and Prevention (CDC) (2023a). Leading Causes of Death. https://www.cdc.gov/nchs/fastats/leading-causes-of-death.htm

Center for Disease Control and Prevention (CDC) (2023b). Men and Stroke. https://www.cdc.gov/stroke/men.htm

Center for Disease Control and Prevention (CDC) (2023c). Traumatic Brain Injury & Concussion. https://www.cdc.gov/traumaticbraininjury/index.html

Center for Disease Control and Prevention (CDC) (2019). Answering Questions about Chronic Traumatic Encephalopathy (CTE). https://www.cdc.gov/traumaticbraininjury/pdf/CDC-CTE-FactSheet-508.pdf

Clark, M. A., Choi, J., & Douglas, M. (2018). Biology. OpenStax. https://openstax.org/books/biology-2e/

Compston, A., & Coles, A. (2008). Multiple sclerosis. The Lancet, 372(9648), 1502–1517.

Crea, F. (2021). Light and noise pollution and socioeconomic status: the risk factors individuals cannot change. European Heart Journal, 42(8), 801-804.

Delgado-López, P. D., & Corrales-García, E. M. (2016). Survival in glioblastoma: a review on the impact of treatment modalities. Clinical and Translational Oncology, 18(11), 1062-1071.

Departments of Defense and Veterans Affairs (2008). DOD/VA COMMON DEFINITION OF TBI. https://www.cdc.gov/nchs/data/icd/sep08tbi.pdf

Eagleman, D., & Downar, J. (2016). Brain and behavior: A cognitive neuroscience perspective. Oxford University Press.

Earhart, G. M. (2009). Dance as therapy for individuals with Parkinson disease. European Journal of Physical and Rehabilitation Medicine, 45(2), 231.

Faissner, S., Plemel, J. R., Gold, R., & Yong, V. W. (2019). Progressive multiple sclerosis: from pathophysiology to therapeutic strategies. Nature Reviews Drug Discovery, 18(12), 905-922.

García-Moreno, C., Pallitto, C., Devries, K., Stöckl, H., Watts, C., & Abrahams, N. (2013). Global and regional estimates of violence against women: prevalence and health effects of intimate partner violence and non-partner sexual violence. World Health Organization.

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

Hove, M. J., Suzuki, K., Uchitomi, H., Orimo, S., & Miyake, Y. (2012). Interactive rhythmic auditory stimulation reinstates natural 1/f timing in gait of Parkinson's patients. PloS one, 7(3), e32600.

Kuang, R. (2019). Glutamate Excitotoxicity and Ischemic Stroke. https://sites.bu.edu/ombs/2019/04/16/glutamate-excitotoxicity-and-ischemic-stroke

Lipton, M. L., Kim, N., Zimmerman, M. E., Kim, M., Stewart, W. F., Branch, C. A., & Lipton, R. B. (2013). Soccer heading is associated with white matter microstructural and cognitive abnormalities. Radiology, 268(3), 850-857.

Mark, L. P., Prost, R. W., Ulmer, J. L., Smith, M. M., Daniels, D. L., Strottmann, J. M., ... & Hacein-Bey, L. (2001). Pictorial review of glutamate excitotoxicity: fundamental concepts for neuroimaging. American Journal of Neuroradiology, 22(10), 1813-1824.

McGinley, M. P., Goldschmidt, C. H., & Rae-Grant, A. D. (2021). Diagnosis and treatment of multiple sclerosis: a review. JAMA, 325(8), 765-779.

Mez, J., Daneshvar, D. H., Kiernan, P. T., Abdolmohammadi, B., Alvarez, V. E., Huber, B. R., ... & McKee, A. C. (2017). Clinicopathological evaluation of chronic traumatic

encephalopathy in players of American football. JAMA, 318(4), 360-370.

National Center for Complementary and Integrative Health (NCCIH) (2019). Multiple Sclerosis. https://www.nccih.nih.gov/health/multiple-sclerosis

National Institute of Neurological Disorders and Stroke (NINDS) (n.d.). Deep brain stimulation (DBS) for the treatment of Parkinson's disease and other movement disorders.

https://www.ninds.nih.gov/about-ninds/impact/ninds-contributions-approved-therapies/deep-brain-stimulation-dbs-treatment-parkinsons-disease-and-other-movement-disorders

National Institute of Neurological Disorders and Stroke (NINDS) (2023a). Stroke. https://www.ninds.nih.gov/health-information/disorders/stroke

National Institute of Neurological Disorders and Stroke (NINDS) (2023b). Multiple Sclerosis. https://www.ninds.nih.gov/health-information/disorders/multiple-sclerosis

National Institute of Neurological Disorders and Stroke (NINDS) (2023c). Brain and Spinal Cord Tumors.

https://www.ninds.nih.gov/health-information/disorders/brain-and-spinal-cord-tumors

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

National Institute on Aging (NIA) (2017). What Happens to the Brain in Alzheimer's Disease? https://www.nia.nih.gov/health/what-happens-brain-alzheimers-disease

Omalu, B. I., DeKosky, S. T., Minster, R. L., Kamboh, M. I., Hamilton, R. L., & Wecht, C. H. (2006). Chronic traumatic encephalopathy in a National Football League player. Neurosurgery, 58(5), E1003-E1003.

Pinel, J. P., & Barnes, S. (2017). Biopsychology. Pearson.

Valera, E. M., & Berenbaum, H. (2003). Brain injury in battered women. Journal of Consulting and Clinical Psychology, 71(4), 797.

Valera, E., & Kucyi, A. (2017). Brain injury in women experiencing intimate-partner violence: neural mechanistic evidence of an "invisible" trauma. Brain Imaging and Behavior, 11(6), 1664-1677.

Valera, E. M., Cao, A., Pasternak, O., Shenton, M. E., Kubicki, M., Makris, N., & Adra, N. (2019). White matter correlates of mild traumatic brain injuries in women subjected to intimate-partner violence: a preliminary study. Journal of Neurotrauma, 36(5), 661-668.

Armstrong & Strack, JAMA OHNS 2016

Valera, E. M., Colantonio, A., Daugherty, J. C., Scott, O. C., & Berenbaum, H. (2022). Strangulation as an acquired brain injury in intimate–partner violence and its relationship to cognitive and psychological functioning: A preliminary

study. Journal of Head Trauma Rehabilitation, 37(1), 15-23.

Van Kempen, E., & Babisch, W. (2012). The quantitative relationship between road traffic noise and hypertension: a meta-analysis. Journal of Hypertension, 30(6), 1075-1086.

CHAPTER 11: 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

11.1: 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**. In this biopsych book, we focus more on biological factors, like brain function and genetics, that underlie psychological disorders and less on treatment-related aspects that may be covered in courses on clinical or abnormal psychology.

Psychological disorders emerge from a complex interaction of biological, social, and environmental factors. How exactly these factors interact to shape psychological disorders for different individuals remains a challenging question. The complexity of interacting factors and variability in symptom profiles across individuals complicates the diagnosis of psychological disorders. In order to promote consensus in diagnosing psychological disorders, psychological researchers and clinicians have developed classification systems. These classification systems traditionally focus on observable symptoms to diagnose a disorder. While it's widely recognized

that biological factors contribute to psychological functioning (Wyatt & Midkiff, 2006), biological evidence has been rarely used to inform diagnosis. In earlier years, this was partly due to technological limitations (e.g., in neuroimaging and genetic testing) that prevented scientists from adequately examining 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, may lead 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:

- **There are significant disturbances in thoughts, feelings, and behaviors**. A 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 who experiences them. For example, if an individual is uncontrollably preoccupied by thoughts of

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 License: CC BY 4.0 DEED.

germs and spends hours each day bathing, 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 are considered to reflect a psychological disorder if they cause the person considerable distress, or greatly impair their ability to function as a normal individual (often referred to as functional impairment, or occupational and social impairment). As an illustration, a person's fear of social situations might be so distressing that it causes the person to 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 in some ways culturally expected, the individual would not be assumed to signify a mental disorder.[2]

Understanding the Classification Systems of Psychological Disorders

A first step in the study of psychological disorders is systematically discerning significant signs and symptoms. Arriving at a proper diagnosis—that is, appropriately identifying and labeling a set of defined symptoms—is crucial. This process enables professionals to use a common language and aids in communication about the disorder with the patient, colleagues, and the public. For these reasons, classification systems that systematically organize

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 License: CC BY 4.0 DEED.

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.

Characterizing psychological disorders based on only symptoms is common for clinical purposes, but is limited for research purposes. For example, the variability of symptom profiles within and across psychological disorders, as well as comorbidity (the simultaneous presence of multiple disorders), makes it challenging for researchers to investigate the neurobiological mechanisms underlying a specific

disorder. Accordingly, the **Research Domain Criteria (RDoC)** is a research framework used to investigate mental disorders and is favored by granting agencies like the National Institute of Mental Health (NIMH) (Insel et al., 2010). Rather than using diagnostic categories (like "bipolar" or "schizophrenia"), the RDoC considers psychopathology in the context of six major domains of neurobehavioral functioning: arousal/regulatory systems, positive valence systems, negative valence systems, social processes, cognitive systems, and sensorimotor systems. Each domain is studied across the full spectrum of functioning in terms of molecular, genetic, behavioral, physiological, and self-report measures. The RDoC framework also prioritizes studying how biological and behavioral development and environmental and cultural factors may contribute to psychopathology. Ultimately, the RDoC framework advances our understanding about how constellations of different factors, both in isolation and together, may contribute to the development of psychopathology.

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 broad classes that are prevalent and 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.

11.2: SCHIZOPHRENIA

Schizophrenia is a psychological disorder that is characterized by major disturbances in thought, perception, emotion, and behavior. About 1% of the population experiences schizophrenia in their lifetime, and the disorder is usually first diagnosed during early adulthood (early 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. Although presentation of schizophrenia varies widely, 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) occur in roughly two-thirds of patients with schizophrenia and are by far the most common form of hallucination (Andreasen, 1987).

Delusions are beliefs that are contrary to reality and are

firmly held even in the face of contradictory evidence. **Paranoid delusions** refer to the (false) belief that other people are plotting to harm them. For example, someone with schizophrenia may believe that their mother is plotting with the FBI to poison their coffee. People with schizophrenia also may hold **grandiose delusions**, which 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). Another type of delusion is **somatic delusion**, which is 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 in a way that is so disorganized and incomprehensible that it seems as though the person is 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 will exhibit **catatonic behaviors**, which show decreased reactivity to the environment, such as posturing, in which the person maintains a rigid and bizarre posture for long periods of time, or catatonic stupor, a complete lack of movement and verbal behavior.[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, showing brain shrinkage in schizophrenia (**Figure 1**) (Horga et al., 2011). Individuals with schizophrenia tend to have smaller brain volumes of some subcortical structures

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.

including the hippocampus, amygdala, and thalamus (van Erp et al., 2016) and thinner cortex especially in the frontal and temporal lobe regions (van Erp et al., 2018). Functional neuroimaging studies have 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 result in downstream dopamine circuit dysregulation, which may contribute to distorted interpretations of salience seen 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. In the rest of this section, we discuss the dopamine hypothesis and stress response in schizophrenia.

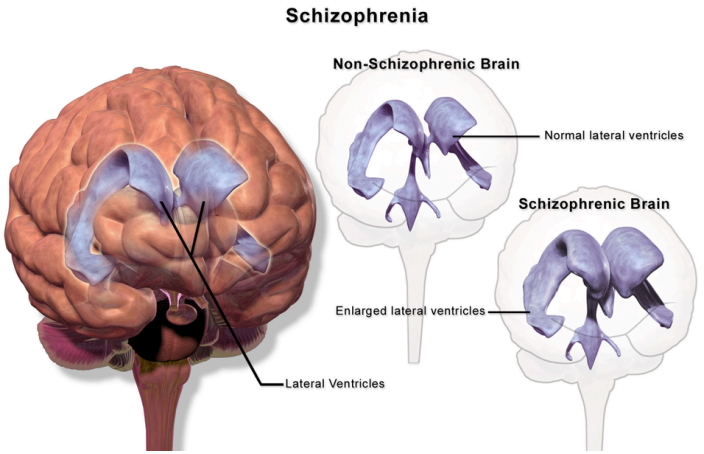

Figure 1. Image showing enlarged ventricles that are often observed in individuals with schizophrenia. Ventricles are cavities in the brain that are filled with cerebro-spinal fluid.

One of the earliest, and perhaps most influential, biological accounts of schizophrenia is the "**dopamine hypothesis of schizophrenia**." The dopamine hypothesis suggests that excessive **dopamine** activity may be related to schizophrenia (Meltzer & Stahl, 1976). This account was originally inspired by seminal 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). The dopamine hypothesis has undergone several iterations.

The second iteration of the dopamine hypothesis of schizophrenia (Dopamine Hypothesis: Version II) proposed that schizophrenia does not simply stem from excess dopamine

throughout the brain, but rather from region-specific dopamine activity. Researchers proposed distinctions between cortical and subcortical dopamine levels for negative and positive symptoms. Reduced dopaminergic engagement in the frontal cortex was linked to negative symptoms (e.g., social and emotional withdrawal) (Davis et al., 1991), whereas hyperactive dopaminergic engagement in the subcortical striatum was linked to positive symptoms (i.e., delusions, hallucinations) (Pycock et al., 1980). Ultimately, the Version II hypothesis proposed that reduced dopaminergic engagement in prefrontal areas led to hyperactive dopaminergic engagement in striatal areas, which contributed to the hallmark symptoms of schizophrenia.

Version III of the dopamine hypothesis departs from previous hypotheses in several ways. First, it proposes that dopamine dysregulation may be less relevant to schizophrenia as a whole, and instead contributes specifically to acute psychosis (a brief period of delusion, hallucination, or disorganized thinking that dissociates the individual from reality) (Howes & Kapur, 2009). Psychotic symptoms, such as delusions and hallucinations, could emerge from excessive dopamine in the striatum (a subcortical structure involved in processing salience) that causes neutral items and events to be interpreted as overly important or salient (e.g., "aberrant salience") (**Figure 2**) (Kapur et al., 2003).

Version III of the dopamine hypothesis also proposes that the main source of dopamine dysregulation may not be

exclusively at the dopamine type D2 receptor level. In line with this perspective, recent work shows that newer treatments that target glutamatergic and dopaminergic mechanisms, other than D2 receptors, are also effective at reducing schizophrenia symptoms (Krystal, 2021). Version III also highlights other dimensions driving schizophrenia, such as the environmental, sociocultural, and genetic risk factors that impact dopamine dysregulation and their influence on cognitive dysfunction and symptom profiles.

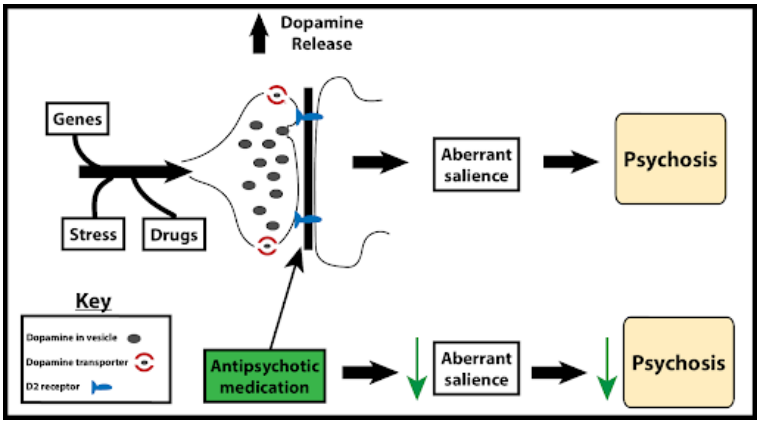

Figure 2. Visualizing striatal dopamine dysregulation's influence on psychosis: excessive dopamine in striatum could lead to "aberrant salience" (i.e., ascribing too much importance to a stimulus), and ultimately, psychosis. Current antipsychotic medication acts downstream of the primary dopaminergic dysregulation. [Image: Adapted from Howes, O. D., & Kapur, S. (2009). The dopamine hypothesis of schizophrenia: Version III—the final common pathway. Schizophrenia Bulletin, 35(3), 549-562.].

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 Chapter 8, 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.

Seminal work on neural diathesis-stress model of schizophrenia notes that stress worsens symptoms of schizophrenia and that the diathesis (or predisposition) is marked by a heightened stress response (Walker & Diforio, 1997). The model proposes that the hypothalamic-pituitary-adrenal gland (HPA) axis releases the hormone cortisol in response to stress and may mediate the effects of stress on schizophrenia symptoms. HPA-axis dysfunction may arise from hippocampal abnormalities in schizophrenia, exacerbate dopamine neurotransmission, and render a hypersensitivity to stress. Together, hippocampal, HPA axis, and dopamine dysfunction are thought to collectively promote a heightened stress response that marks a vulnerability to schizophrenia. To combat 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, it is important to note that diathesis-stress models (i.e., the important interaction between predisposition and stressful life events) also apply to other psychological disorders such as depression and anxiety (Arnau-Soler et al., 2019).

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11.3: 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 emotional states, 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. Depression is a heterogeneous mood state—it consists of a broad spectrum of symptoms that range in severity. People

with depressive disorders often feel sad, discouraged, and hopeless. These individuals lose interest in activities once enjoyed, often experience a decrease in drives such as hunger and sex, and frequently doubt personal worth. Depressive disorders vary by degree, but this chapter highlights the most well-known: major depressive disorder (sometimes called unipolar depression).

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 attempt to take on many tasks simultaneously. The most recognized of these disorders is bipolar disorder.[1]

Neural mechanisms underlying depression

Though depression involves an overall reduction in brain activity, some parts of the brain are more affected than others.

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.

In brain-imaging 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 primarily involved in cognitive control, which refers to the intentional selection of cognitive operations, such as attention, inhibition, and working memory, in order to carry out behavior. A situation that may require cognitive control is studying for an exam while resisting the urge to check social media. The **orbitofrontal cortex** is mainly involved in decision-making and reward valuation. This is especially relevant for deferring immediate gratifications in order to obtain greater long-term benefits. The **ventromedial prefrontal cortex** is implicated in a broad range of social and emotional processes such as value-based decision-making, regulation of negative emotions, and processing of self-relevant information. Indeed, disruption to these brain regions may contribute to hallmark characteristics of mood disorders, such as a bias toward negative affect and increased self-focus.

Some research indicates that the left prefrontal cortex is involved in establishing positive feelings and the right prefrontal cortex is involved in negative feelings. Typically, the left prefrontal cortex is thought to help to inhibit the negative

emotions generated by limbic structures such as the **amygdala**, which show abnormally high activity in patients with depression. In patients who respond positively to antidepressants, this amygdala overactivity is reduced. But when the amygdala remains hyperactive despite antidepressant treatment, that patient is likely to relapse into depression.

Emerging work has also begun to characterize the genetic contributions to depressive disorders. Studies have shown that 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]

Neural mechanisms underlying bipolar disorders

Research on the etiology (i.e., cause), course, and treatment

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 Down or Speed Up in Depression. Access for free at https://thebrain.mcgill.ca/ License: CC (Copyleft).

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 highly heritable (McGuffin et al., 2003). One may argue that high heritability demonstrates that BD is fundamentally a biological phenomenon. However, the course of BD varies greatly both within a person across time and across people (Johnson, 2005). The triggers that determine how and when this genetic vulnerability is expressed are not yet understood; however, evidence suggests that psychosocial triggers may play an important role in BD risk (Johnson et al., 2008; Malkoff-Schwartz et al., 1998). Additionally, growing research shows that bipolar disorders and schizophrenia share similar brain abnormalities and genetic substrates, which has prompted some researchers to suggest that bipolar disorders may be closer to psychotic disorders than to depression (Birur et al., 2017; Lichtenstein et al., 2009).

Biological explanations of BD have also focused on brain function. Many of the studies using fMRI to characterize BD have focused on processing emotional stimuli based on the idea that BD is fundamentally a disorder of emotion (APA, 2000). Findings show that regions of the brain involved in emotional processing and regulation are activated differently in people with BD relative to healthy controls (Altshuler et al., 2008; Hassel et al., 2008; Lennox et al., 2004). However, in individuals with BD, studies examining how different brain regions respond to emotional stimuli show mixed results.

These mixed findings are partly due to samples consisting of participants who are at various phases of illness at the time of testing (manic, depressed, inter-episode) and small sample sizes make comparisons between subgroups difficult. Additionally, the use of typical lab-based stimuli, such as facial expressions of anger, may not elicit a sufficiently strong brain response.

Within the psychosocial level, research has focused on the environmental contributors to BD. A series of studies shows that 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 substantially 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. People with BD suffer more manic symptoms after life events involving attainment of a desired goal (Johnson et al., 2008). Such findings suggest that people with BD may have a hypersensitivity to rewards.

Mood disorders are also thought to be associated with abnormal levels of certain neurotransmitters, particularly serotonin and norepinephrine (Thase, 2009). These neurotransmitters are important regulators of the bodily functions that are disrupted in mood disorders, including appetite, sex drive, sleep, arousal, and mood. To treat major depressive disorders, one of the most common classes of medications are selective serotonin reuptake inhibitors (SSRIs). As their name indicates, SSRIs inhibit or block the

reuptake of serotonin back into the presynaptic cell, which in turn preserves high levels of serotonin in the synapse that may ultimately reduce depressive symptoms (**Figure 3**). However, recent findings show that while serotonin levels rise as quickly as an hour after taking an SSRI, it typically takes several weeks for SSRIs to actually improve symptoms.[3]

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

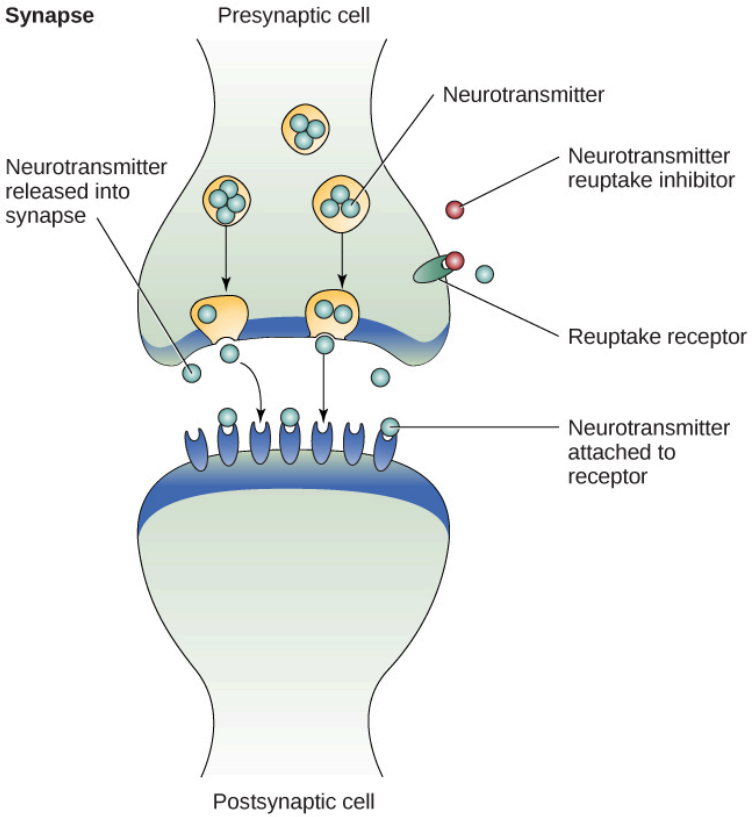

Figure 3. Many medications designed to treat mood disorders work by altering neurotransmitter activity in the neural synapse. Selective serotonin reuptake inhibitors (SSRIs), for example, inhibit the reuptake of serotonin back into the presynaptic cell, which preserves high levels of serotonin in the synapse.

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11.4: 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 4**).

Anxiety disorders are characterized by excessive and persistent fear and anxiety, and by related disturbances in behavior (APA, 2013). Although anxiety is universally experienced, anxiety disorders cause considerable distress. As a group, 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). Also, anxiety disorders are much more common in women than they are in men; within a 12-month period, around 23% of women and 14% of men will experience at least one 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]

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.

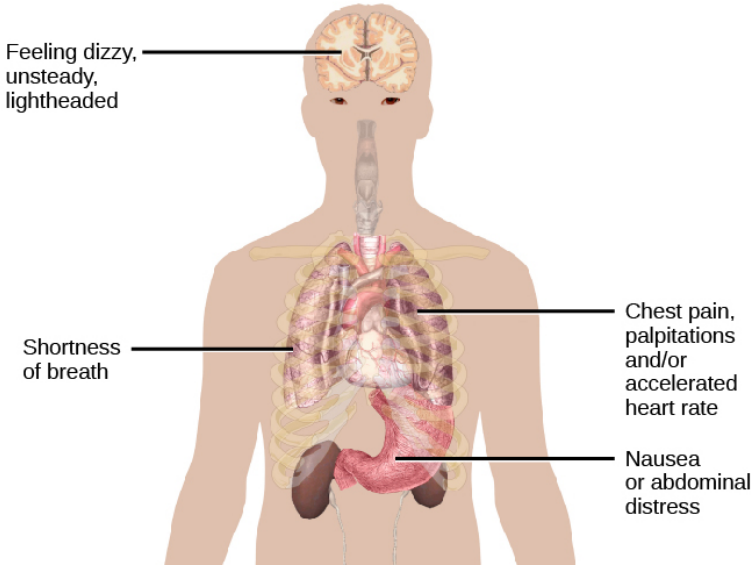

Figure 4. Common physical symptoms of anxiety are feeling dizzy, unsteady, and lightheaded; shortness of breath; chest pain, palpitations and /or accelerated heart rate; and nausea or abdominal distress. People may also experience sweating, trembling, feelings of faintness, or a fear of losing control, among other symptoms.

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). More than 200 genes are associated with anxiety disorders, and distinct gene clusters exist for different anxiety subtypes such as generalized anxiety disorder, social anxiety disorder, and panic disorder. The identified genes are expressed in brain regions (e.g., the basal ganglia, hippocampus, and amygdala) that are linked to anxiety and emotion processing (Karunakaran & Amemori, 2023).

The brain circuits underlying anxiety involve bottom-up signals from the amygdala that indicate 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, particularly 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 regulate emotion by inhibiting amygdala output; however, neuroimaging studies show that people with anxiety disorders have reduced

activation in prefrontal circuits (Etkin, 2010), and interestingly they required higher levels of prefrontal activation to successfully reduce negative emotions (Nuss, 2015).

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, injections of GABA agonists (activators) into the amygdala decreased measures of fear and anxiety (Sanders & Shekhar, 1995). GABA receptors can be modulated by a class of drugs called benzodiazepines, that include well-known brand names like Valium, Xanax, and Ativan. Benzodiazepines work by binding to the GABAA receptor complex, which increases the total conduction of chloride (Cl-) ions across the cell membrane. The increased concentration of negative chloride ions hyperpolarizes the neuron's membrane potential, thereby inhibiting it and making it less likely to fire. Through this increased neuronal inhibition, benzodiazepines can reduce anxiety and reduce the amygdala's response to aversive stimuli (Del-Ben et al., 2012).

Benzodiazepines were the most common pharmacological treatment for anxiety for many decades. But due to their highly addictive properties and lack of long-term effectiveness,

benzodiazepines are now recommended only for short-term treatments of anxiety (2-4 weeks). While GABA is an important target for modulating anxiety responses 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 (Nuss, 2015).

For non-pharmacological treatments, cognitive behavioral therapy (CBT) is well established, and successful CBT treatment of anxiety disorders has been shown to stop 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 activation in the amygdala, 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, anxiety can be reduced by decreasing activation in the amygdala or increasing activation in modulatory or emotion-regulating circuits, and ongoing research seeks to optimize how these networks can be targeted to manage anxiety.

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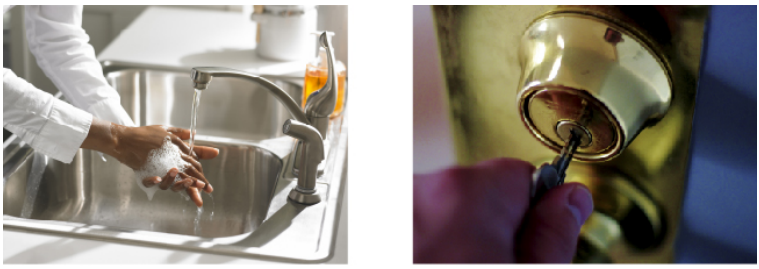
11.5: OBSESSIVE-COMPULSIVE AND RELATED DISORDERS

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 elevate the unwanted thoughts and repetitive behaviors to a status so intense that these cognitions and activities disrupt daily life. Included in this category are obsessive-compulsive disorder (OCD), body dysmorphic disorder, and hoarding disorder.[1]

1. This section contains material adapted from: Spielman, R. M., Jenkins, W. J., & Lovett, M. D. (2020). 15.5 Obsessive-Compulsive and Related Disorders. In Psychology 2e. OpenStax. Access for free at https://openstax.org/books/psychology-2e/pages/15-5-obsessive-compulsive-and-related-disorders License: CC BY 4.0 DEED.

OCD is marked by the presence of obsessions, compulsions, or both, that are time-consuming (e.g., more than 1 hour per day), and not attributable to a substance like a drug, another medical condition, or another mental disorder (APA, 2013). Obsessions are more than just unwanted thoughts that seem to randomly jump into our head from time to time, such as recalling an insensitive remark a coworker made recently, and they are more significant than the minor day-to-day worries we might have. Rather, obsessions are characterized as 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 urges that are aggressive or lustful. Usually, the person knows that such thoughts and urges are irrational and thus tries to suppress or ignore them, but has an extremely difficult time doing so. These obsessive symptoms sometimes overlap, such that someone might have both contamination and aggressive obsessions (Abramowitz & Siqueland, 2013).



(a) (b)

Figure 5. (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 that are typically carried out primarily as a means to minimize the distress that obsessions trigger or to reduce the likelihood of a feared event (APA, 2013). Compulsions often include such behaviors as repeated and 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 5**). Compulsions characteristic of OCD are not performed out of pleasure, nor are they connected in a realistic way to the source of the distress or feared event. Ultimately, a difficult cycle of obsessive thoughts, anxiety, compulsions, and temporary relief tends to deeply affect individuals with OCD (**Figure 6**). 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]

2. This section contains material adapted from: Spielman, R. M., Jenkins, W. J., & Lovett, M. D. (2020). 15.5 Obsessive-Compulsive and Related Disorders. In Psychology 2e. OpenStax. Access for free at https://openstax.org/books/psychology-2e/pages/15-5-obsessive-compulsive-and-related-disorders License: CC BY 4.0 DEED.

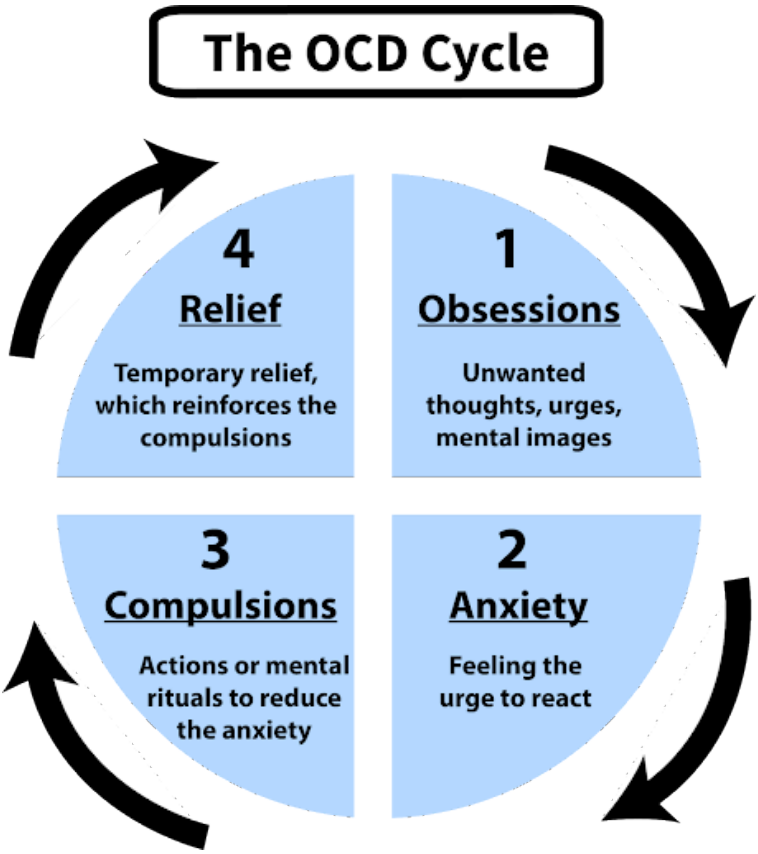


Figure 6. Visualizing the typical cycle of obsessive-compulsive disorder. [Image adapted from: https://psychcentral.com/ocd/ocd-cycle].

Body Dysmorphic Disorder

A disorder that shares similar features to OCD is **body**

dysmorphic disorder, wherein an individual is preoccupied with a perceived flaw in physical appearance that is either nonexistent or barely noticeable to other people (APA, 2013). These perceived physical defects cause people to think they are unattractive, ugly, hideous, or deformed. These preoccupations can focus on any bodily area, but they typically involve the skin, face, or hair. The preoccupation with imagined physical flaws drives the person to engage in repetitive and ritualistic behavioral and mental acts, such as constantly looking in the mirror, trying to hide the offending body part, comparisons with others, and, in some extreme cases, cosmetic surgery (Phillips, 2005). An estimated 2.4% of the adults in the United States meet the criteria for body dysmorphic disorder, with slightly higher rates in women than in men (APA, 2013).[3]

Hoarding Disorder

Although hoarding was traditionally considered a symptom of

3. This section contains material adapted from: Spielman, R. M., Jenkins, W. J., & Lovett, M. D. (2020). 15.5 Obsessive-Compulsive and Related Disorders. In Psychology 2e. OpenStax. Access for free at https://openstax.org/books/psychology-2e/pages/15-5-obsessive-compulsive-and-related-disorders License: CC BY 4.0 DEED.

OCD, considerable evidence suggests that hoarding represents an entirely different disorder (Mataix-Cols et al., 2010). People with **hoarding disorder** cannot bear to part with personal possessions, regardless of how valueless or useless these possessions are. As a result, these individuals accumulate excessive amounts of usually worthless items that clutter their living areas. Often, the quantity of cluttered items is so excessive that the person is unable to use their kitchen, or sleep in their bed. People who suffer from this disorder have great difficulty parting with items because they believe the items might be of some later use, or because they form a sentimental attachment to the items (APA, 2013). Importantly, a diagnosis of hoarding disorder is made only if the hoarding is not caused by another medical condition and is not a symptom of another disorder (e.g., schizophrenia) (APA, 2013).[4]

Neural and genetic mechanisms underlying

4. This section contains material adapted from: Spielman, R. M., Jenkins, W. J., & Lovett, M. D. (2020). 15.5 Obsessive-Compulsive and Related Disorders. In Psychology 2e. OpenStax. Access for free at https://openstax.org/books/psychology-2e/pages/15-5-obsessive-compulsive-and-related-disorders License: CC BY 4.0 DEED.

obsessive-compulsive and related disorders

The results of family and twin studies suggest that OCD has a moderate genetic component. The disorder is five times more frequent in the first-degree relatives of people with OCD than in people without the disorder (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 two dozen potential genes that may be involved in OCD; these genes regulate the function of three neurotransmitters: serotonin, dopamine, and glutamate (Pauls, 2010). Many of these studies included small sample sizes and have yet to be replicated, so additional research is needed.

A brain region believed to play a critical role in OCD is the orbitofrontal cortex (Kopell & Greenberg, 2008) (**Figure 7**). In people with OCD, the orbitofrontal cortex becomes especially hyperactive when they are provoked with tasks in which, for example, they are asked to look at a photo of a toilet or of pictures hanging crookedly on a wall (Simon et al., 2010). The orbitofrontal cortex is part of a group of brain regions that, collectively, is called the OCD circuit and influences the perceived emotional value of stimuli and the selection of both 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), which suggests that abnormalities in these regions may contribute to the symptoms of OCD (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).

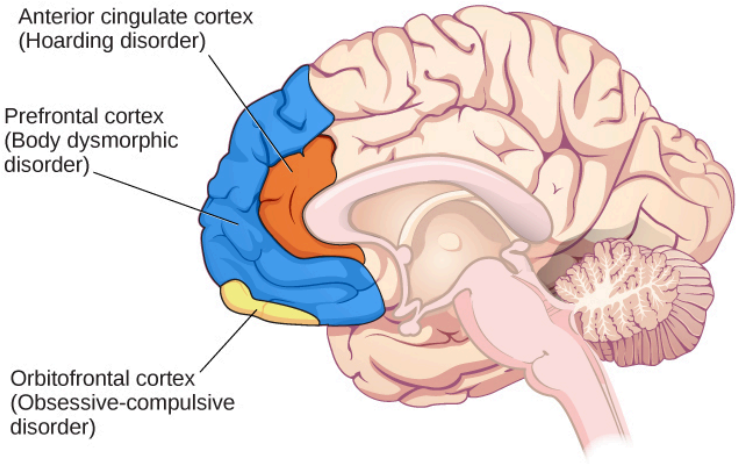


Figure 7. Different regions of the brain are associated with obsessive-compulsive disorder and related disorders–for example, the anterior cingulate cortex for hoarding disorder; the prefrontal cortex for for body dysmorphc disorder; and the orbitofrontel cortex for obsessive-compulsive disorder.

Neuroimaging studies have also highlighted the role of the prefrontal cortex in OCD and body dysmorphic disorder.

Individuals with body dysmorphic disorder often show abnormal perception of 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 is not evidence of causality (Abramowitz & Siqueland, 2013).

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 and 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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11.6: POST-TRAUMATIC STRESS DISORDER

Extremely stressful or traumatic events, such as combat, crimes, and natural disasters, place the people who experience them at an increased risk for 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 for instance, an upsetting but non-violent romantic breakup. Symptoms of PTSD include intrusive and distressing memories of the event, flashbacks (states that can last from a few seconds to several days, during which the individual relives the event and behaves as if the event were occurring at that moment [APA, 2013]), avoidance of stimuli connected to the event, persistently negative emotional states (e.g., fear, anger, guilt, and shame), feelings of detachment from others, irritability, proneness toward 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, including 10-12% of women and 5-6% of men, experience PTSD in their

lifetime (Goldstein et al., 2016; Olff, 2017), with higher rates among people exposed to mass trauma and people 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 suffered from 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 have been linked to PTSD (**Figure 8**). Individuals with PTSD show marked reductions in the 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). However, 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 is also known to alter hippocampal functioning, such that reduced hippocampal activity during states of high threat is a reliable neural signature in individuals with PTSD (Eichenbaum, 2001; Hayes et al., 2011). To clarify how threat may disrupt hippocampal functioning, a recent review proposed that threat-related arousal, through heightened NE release, disrupts hippocampal functioning by shifting information processing away from the hippocampus and toward other learning structures involved in emotional memories, such as the amygdala (Clewett & Murty, 2019).

The Advanced Understanding of RecOvery afteR traumA (AURORA) study is a multi-site longitudinal study that assesses individuals who present to US emergency departments within 72 hours of exposure to trauma and tracks their brain and cognitive development for the following year (McClean et al., 2020). This landmark effort will ultimately generate a comprehensive collection of brain, biospecimen, and behavioral measures to better characterize trauma-related disorders, such as PTSD.

To begin exploring the relationship between threat

reactivity, hippocampal functioning, arousal-related NE systems, and PTSD symptoms, one AURORA study measured responses to fearful faces in the fMRI scanner and fear-based startle responses to threat cues (a marker of arousal-related NE release) (Tanriverdi et al., 2022). People with more severe PTSD symptoms two weeks after trauma showed weaker hippocampal responses to threat, and hippocampus response was especially reduced in those with a greater fear-based startle. This suggests that excessive physiological arousal from threat may divert information processing away from the hippocampus. These findings emphasize the relationship between threat reactivity, arousal, and hippocampal functioning in understanding how PTSD may or may not emerge after exposure to trauma. Finally, whether or not PTSD emerges is also influenced by genetics, as genes play an important role in the fear and stress circuitry (Banerjee et al., 2017).

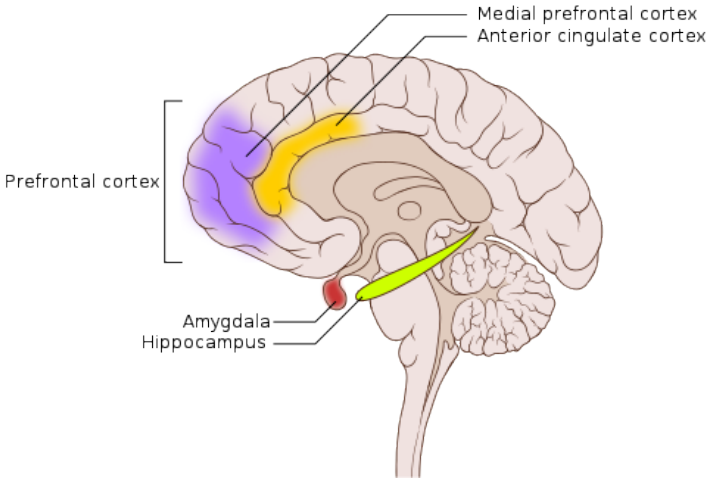

Figure 8. Brain regions typically associated with post-traumatic stress disorder include the prefrontal cortex, hippocampus, cingulate cortex, and amygdala.

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11.7: CONCLUSION

The biological perspective views psychological disorders as linked 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, and in turn may be targeted in future genetic-based therapies (e.g., Davidson et al., 2022). Sophisticated neuroimaging technology has revealed that abnormalities in brain structure and function are directly involved in many disorders. As imaging technologies continue to develop, they 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 many various forms.

11.8: 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

11.9: REFERENCES

Parts of this chapter were adapted from:

Barlow, D. H. & Ellard, K. K. (2023). 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

Gershon, A. & Thompson, R. (2023). Mood disorders. In R. Biswas-Diener & E. Diener (Eds.), Noba textbook series: Psychology. Champaign, IL: DEF publishers. Retrieved from http://noba.to/aqy9rsxe

Spielman, R. M., Jenkins, W. J., & Lovett, M. D. (2020). 10.4 Emotion. In Psychology 2e. OpenStax. https://openstax.org/books/psychology-2e/pages/10-4-emotion

Spielman, R. M., Jenkins, W. J., & Lovett, M. D. (2020). 15.1 What Are Psychological Disorders? In Psychology 2e. OpenStax. https://openstax.org/books/psychology-2e/pages/15-1-what-are-psychological-disorders

Spielman, R. M., Jenkins, W. J., & Lovett, M. D. (2020). 15.2 Diagnosing and Classifying Psychological Disorders. In

Psychology 2e. OpenStax. https://openstax.org/books/psychology-2e/pages/15-2-diagnosing-and-classifying-psychological-disorders

Spielman, R. M., Jenkins, W. J., & Lovett, M. D. (2020). 15.3 Perspectives on Psychological Disorders. In Psychology 2e. OpenStax. https://openstax.org/books/psychology-2e/pages/15-3-perspectives-on-psychological-disorders

Spielman, R. M., Jenkins, W. J., & Lovett, M. D. (2020). 15.4 Anxiety Disorders. In Psychology 2e. OpenStax. https://openstax.org/books/psychology-2e/pages/15-4-anxiety-disorders

Spielman, R. M., Jenkins, W. J., & Lovett, M. D. (2020). 15.5 Obsessive-Compulsive and Related Disorders. In Psychology 2e. OpenStax. https://openstax.org/books/psychology-2e/pages/15-5-obsessive-compulsive-and-related-disorders

Spielman, R. M., Jenkins, W. J., & Lovett, M. D. (2020). 15.7 Mood and Related Disorders. In Psychology 2e. OpenStax. https://openstax.org/books/psychology-2e/pages/15-7-mood-and-related-disorders

Spielman, R. M., Jenkins, W. J., & Lovett, M. D. (2020). 15.8 Schizophrenia. In Psychology 2e. OpenStax. https://openstax.org/books/psychology-2e/pages/15-8-schizophrenia

Duboc, B. (2002). The Brain from Top to Bottom (n.d.). Retrieved on June 1, 2023 from https://thebrain.mcgill.ca/

References for Psychological Disorders

Abi-Dargham, A., Moeller, S. J., Ali, F., DeLorenzo, C., Domschke, K., Horga, G., ... & Krystal, J. H. (2023). Candidate biomarkers in psychiatric disorders: state of the field. World Psychiatry, 22(2), 236-262.

Abramowitz, J. S., & Siqueland, L. (2013). Obsessive-compulsive disorder. In L. G. Castonguay & T. F. Oltmanns (Eds.), Psychopathology: From science to clinical practice (pp. 143–171). New York, NY: Guilford Press.

Ahmari, S. E., & Rauch, S. L. (2022). The prefrontal cortex and OCD. Neuropsychopharmacology, 47(1), Article 1. https://doi.org/10.1038/s41386-021-01130-2

Alonso, P., Cuadras, D., Gabriëls, L., Denys, D., Goodman, W., Greenberg, B. D., ... & Menchon, J. M. (2015). Deep brain stimulation for obsessive-compulsive disorder: a meta-analysis of treatment outcome and predictors of response. PloS one, 10(7), e0133591.

Altshuler, L., Bookheimer, S., Townsend, J., Proenza, M. A., Sabb, F., Mintz, J., & Cohen, M. S. (2008). Regional brain changes in bipolar I depression: A functional magnetic resonance imaging study. Bipolar Disorders, 10(6), 708–717. https://doi.org/10.1111/j.1399-5618.2008.00617.x

American Psychiatric Association. (2000). Diagnostic and

statistical manual of mental disorders (4th ed., text rev.). Washington, DC.

American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). Washington, DC..

American Psychiatric Association. (2022). Diagnostic and statistical manual of mental disorders (5th ed., text rev.). Arlington, VA

Arnau-Soler, A., Adams, M. J., Clarke, T. K., MacIntyre, D. J., Milburn, K., Navrady, L., ... & Thomson, P. A. (2019). A validation of the diathesis-stress model for depression in Generation Scotland. Translational Psychiatry, 9(1), 25.

Banerjee, S. B., Morrison, F. G., & Ressler, K. J. (2017). Genetic approaches for the study of PTSD: Advances and challenges. Neuroscience Letters, 649, 139-146.

Barlow, D. H., Raffa, S. D., & Cohen, E. M. (2002). Psychosocial treatments for panic disorders, phobias, and generalized anxiety disorder. In A guide to treatments that work, 2nd ed (pp. 301–335). Oxford University Press.

Beucke, J. C., Sepulcre, J., Talukdar, T., Linnman, C., Zschenderlein, K., Endrass, T., Kaufmann, C., & Kathmann, N. (2013). Abnormally High Degree Connectivity of the Orbitofrontal Cortex in Obsessive-Compulsive Disorder. JAMA Psychiatry, 70(6), 619–629. https://doi.org/10.1001/jamapsychiatry.2013.173

Birur, B., Kraguljac, N. V., Shelton, R. C., & Lahti, A. C. (2017). Brain structure, function, and neurochemistry in

schizophrenia and bipolar disorder—a systematic review of the magnetic resonance neuroimaging literature. NPJ Schizophrenia, 3(1), 15.

Bolton, D., Rijsdijk, F., O'Connor, T. G., Perrin, S., & Eley, T. C. (2007). Obsessive–compulsive disorder, tics and anxiety in 6-year-old twins. Psychological Medicine, 37(1), 39–48. https://doi.org/10.1017/S0033291706008816

Bremner, J. D. (2006). The Relationship Between Cognitive and Brain Changes in Posttraumatic Stress Disorder. Annals of the New York Academy of Sciences, 1071(1), 80–86. https://doi.org/10.1196/annals.1364.008

Bremner, J. D., & Vermetten, E. (2004). Neuroanatomical Changes Associated with Pharmacotherapy in Posttraumatic Stress Disorder. Annals of the New York Academy of Sciences, 1032(1), 154–157. https://doi.org/10.1196/annals.1314.012

Carlsson, A., & Lindqvist, M. (2009). Effect of Chlorpromazine or Haloperidol on Formation of 3-Methoxytyramine and Normetanephrine in Mouse Brain. Acta Pharmacologica et Toxicologica, 20(2), 140–144. https://doi.org/10.1111/j.1600-0773.1963.tb01730.x

Castonguay, L. G., & Oltmanns, T. F. (2013). Psychopathology: From Science to Clinical Practice. Guilford Publications.

Clewett, D., & Murty, V. P. (2019). Echoes of Emotions Past: How Neuromodulators Determine What We Recollect.

ENeuro, 6(2), ENEURO.0108-18.2019. https://doi.org/10.1523/ENEURO.0108-18.2019

Correll, C. U., & Schooler, N. R. (2020). Negative Symptoms in Schizophrenia: A Review and Clinical Guide for Recognition, Assessment, and Treatment. Neuropsychiatric Disease and Treatment, 16, 519–534. https://doi.org/10.2147/NDT.S225643

Craik, F. I. M., Govoni, R., Naveh-Benjamin, M., & Anderson, N. D. (1996). The effects of divided attention on encoding and retrieval processes in human memory. Journal of Experimental Psychology: General, 125(2), 159–180. https://doi.org/10.1037/0096-3445.125.2.159

Davidson, B. L., Gao, G., Berry-Kravis, E., Bradbury, A. M., Bönnemann, C., Buxbaum, J. D., ... & Sahin, M. (2022). Gene-based therapeutics for rare genetic neurodevelopmental psychiatric disorders. Molecular Therapy, 30(7), 2416-2428.

Davis, K. L., Kahn, R. S., Ko, G., & Davidson, M. (1991). Dopamine in schizophrenia: A review and reconceptualization. The American Journal of Psychiatry, 148(11), 1474–1486. https://doi.org/10.1176/ajp.148.11.1474

Del-Ben, C. M., Ferreira, C. A., Sanchez, T. A., Alves-Neto, W. C., Guapo, V. G., de Araujo, D. B., & Graeff, F. G. (2012). Effects of diazepam on BOLD activation during the processing of aversive faces. Journal of Psychopharmacology, 26(4), 443-451.

American Psychiatric Association (2022). Diagnostic And Statistical Manual Of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR). https://doi.org/10.1176/appi.books.9780890425787

DiGrande, L., Perrin, M. A., Thorpe, L. E., Thalji, L., Murphy, J., Wu, D., Farfel, M., & Brackbill, R. M. (2008). Posttraumatic stress symptoms, PTSD, and risk factors among lower Manhattan residents 2–3 years after the September 11, 2001 terrorist attacks. Journal of Traumatic Stress, 21(3), 264–273. https://doi.org/10.1002/jts.20345

Easterbrook, J. A. (1959). The effect of emotion on cue utilization and the organization of behavior. Psychological Review, 66(3), 183–201. https://doi.org/10.1037/h0047707

Eichenbaum, H. (2001). The hippocampus and declarative memory: cognitive mechanisms and neural codes. Behavioural Brain Research, 127(1-2), 199-207.

Ellicott, A., Hammen, C., Gitlin, M., Brown, G., & Jamison, K. (1990). Life events and the course of bipolar disorder. The American Journal of Psychiatry, 147(9), 1194–1198. https://doi.org/10.1176/ajp.147.9.1194

Etkin, A., & Wager, T. D. (2007). Functional neuroimaging of anxiety: a meta-analysis of emotional processing in PTSD, social anxiety disorder, and specific phobia. American Journal of Psychiatry, 164(10), 1476–1488.

Etkin, A. (2010). Functional neuroanatomy of anxiety: A neural circuit perspective. In M.B. Stein and T. Steckler

(Eds.), Behavioral Neurobiology of Anxiety and Its Treatment (pp. 251-277). Springer-Verlag.

Fan, T., Hu, Y., Xin, J., Zhao, M., & Wang, J. (2020). Analyzing the genes and pathways related to major depressive disorder via a systems biology approach. Brain and Behavior, 10(2), e01502.

Feusner, J. D., Townsend, J., Bystritsky, A., & Bookheimer, S. (2007). Visual Information Processing of Faces in Body Dysmorphic Disorder. Archives of General Psychiatry, 64(12), 1417. https://doi.org/10.1001/archpsyc.64.12.1417

Goldstein, R. B., Smith, S. M., Chou, S. P., Saha, T. D., Jung, J., Zhang, H., Pickering, R. P., Ruan, W. J., Huang, B., & Grant, B. F. (2016). The epidemiology of DSM-5 posttraumatic stress disorder in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions-III. Social Psychiatry and Psychiatric Epidemiology, 51(8), 1137–1148. https://doi.org/10.1007/s00127-016-1208-5

Graybiel, A. M., & Rauch, S. L. (2000). Toward a Neurobiology of Obsessive-Compulsive Disorder. Neuron, 28(2), 343–347. https://doi.org/10.1016/S0896-6273(00)00113-6

Grillon, C., & Morgan, C. (1999). Fear-potentiated startle conditioning to explicit and contextual cues in Gulf War veterans with posttraumatic stress disorder. Journal of

Abnormal Psychology, 108, 134–142. https://doi.org/10.1037/0021-843X.108.1.134

Hassel, S., Almeida, J. R., Kerr, N., Nau, S., Ladouceur, C. D., Fissell, K., Kupfer, D. J., & Phillips, M. L. (2008). Elevated striatal and decreased dorsolateral prefrontal cortical activity in response to emotional stimuli in euthymic bipolar disorder: No associations with psychotropic medication load. Bipolar Disorders, 10(8), 916–927. https://doi.org/10.1111/j.1399-5618.2008.00641.x

Hayes, J. P., LaBar, K. S., McCarthy, G., Selgrade, E., Nasser, J., Dolcos, F., & Morey, R. A. (2011). Reduced hippocampal and amygdala activity predicts memory distortions for trauma reminders in combat-related PTSD. Journal of Psychiatric Research, 45(5), 660-669.

Herdade, K. C. P., de Andrade Strauss, C. V., Júnior, H. Z., & de Barros Viana, M. (2006). Effects of medial amygdala inactivation on a panic-related behavior. Behavioural Brain Research, 172(2), 316-323.

Hettema, J. M., Neale, M. C., & Kendler, K. S. (2001). A review and meta-analysis of the genetic epidemiology of anxiety disorders. American Journal of Psychiatry, 158(10), 1568-1578.

Horga, G., Bernacer, J., Dusi, N., Entis, J., Chu, K., Hazlett, E. A., ... & Buchsbaum, M. S. (2011). Correlations between ventricular enlargement and gray and white matter volumes of cortex, thalamus, striatum, and internal capsule in

schizophrenia. European Archives of Psychiatry and Clinical Neuroscience, 261, 467-476.

Howes, O. D., & Kapur, S. (2009). The Dopamine Hypothesis of Schizophrenia: Version III—The Final Common Pathway. Schizophrenia Bulletin, 35(3), 549–562. https://doi.org/10.1093/schbul/sbp006

Insel, T., Cuthbert, B., Garvey, M., Heinssen, R., Pine, D. S., Quinn, K., Sanislow, C., & Wang, P. (2010). Research domain criteria (RDoC): toward a new classification framework for research on mental disorders. The American Journal of Psychiatry, 167(7), 748–751. https://doi.org/10.1176/appi.ajp.2010.09091379

Isaacowitz, D. M., Gershon, A., Allard, E. S., & Johnson, S. L. (2013). Emotion in Aging and Bipolar Disorder: Similarities, Differences, and Lessons for Further Research. Emotion Review, 5(3), 312–320. https://doi.org/10.1177/1754073912472244

Johnson, S. L. (2005). Mania and dysregulation in goal pursuit: A review. Clinical Psychology Review, 25(2), 241–262. https://doi.org/10.1016/j.cpr.2004.11.002

Johnson, S. L., Cueller, A. K., Ruggero, C., Winett-Perlman, C., Goodnick, P., White, R., & Miller, I. (2008). Life Events as Predictors of Mania and Depression in Bipolar I Disorder. Journal of Abnormal Psychology, 117(2), 268–277. https://doi.org/10.1037/0021-843X.117.2.268

Johnson, S., Winett, C., Meyer, B., Greenhouse, W., & Miller, I. (1999). Social support and course of bipolar disorder.

Journal of Abnormal Psychology, 108, 558–566. https://doi.org/10.1037/0021-843X.108.4.558

Juárez Olguín, H., Calderón Guzmán, D., Hernández García, E., & Barragán Mejía, G. (2016). The Role of Dopamine and Its Dysfunction as a Consequence of Oxidative Stress. Oxidative Medicine and Cellular Longevity, 2016, 9730467. https://doi.org/10.1155/2016/9730467

Kapur, S. (2003). Psychosis as a state of aberrant salience: a framework linking biology, phenomenology, and pharmacology in schizophrenia. American Journal of Psychiatry, 160(1), 13-23.

Karunakaran, K. B., & Amemori, K. I. (2023). Spatiotemporal expression patterns of anxiety disorder-associated genes. Translational Psychiatry, 13(1), 385.

Kendler, K. S., Fiske, A., Gardner, C. O., & Gatz, M. (2009). Delineation of two genetic pathways to major depression. Biological Psychiatry, 65(9), 808-811.

Kensinger, E. A. (2009). Remembering the Details: Effects of Emotion. Emotion Review, 1(2), 99–113. https://doi.org/10.1177/1754073908100432

Kessler, R. C., Brandenburg, N., Lane, M., Roy-Byrne, P., Stang, P. D., Stein, D. J., & Wittchen, H.-U. (2005). Rethinking the duration requirement for generalized anxiety disorder: Evidence from the National Comorbidity Survey Replication. Psychological Medicine, 35(7), 1073–1082. https://doi.org/10.1017/S0033291705004538

Kessler, R. C., Ruscio, A. M., Shear, K., & Wittchen, H.-U.

(2010). Epidemiology of anxiety disorders. Current Topics in Behavioral Neurosciences, 2, 21–35.

Kopell, B. H., & Greenberg, B. D. (2008). Anatomy and physiology of the basal ganglia: Implications for DBS in psychiatry. Neuroscience & Biobehavioral Reviews, 32(3), 408–422. https://doi.org/10.1016/j.neubiorev.2007.07.004

Kraguljac, N. V., McDonald, W. M., Widge, A. S., Rodriguez, C. I., Tohen, M., & Nemeroff, C. B. (2021). Neuroimaging biomarkers in schizophrenia. American Journal of Psychiatry, 178(6), 509-521.

Krystal, J. (2021). Potential Schizophrenia Medications Point to New Disease Model. Psychiatric News. https://doi.org/10.1176/appi.pn.2021.11.37

LaBar, K. S., & Cabeza, R. (2006). Cognitive neuroscience of emotional memory. Nature Reviews Neuroscience, 7(1), Article 1. https://doi.org/10.1038/nrn1825

Lennox, B. R., Jacob, R., Calder, A. J., Lupson, V., & Bullmore, E. T. (2004). Behavioural and neurocognitive responses to sad facial affect are attenuated in patients with mania. Psychological Medicine, 34(5), 795–802. https://doi.org/10.1017/S0033291704002557

Levy-Gigi, E., Szabó, C., Kelemen, O., & Kéri, S. (2013). Association Among Clinical Response, Hippocampal Volume, and FKBP5 Gene Expression in Individuals with Posttraumatic Stress Disorder Receiving Cognitive

Behavioral Therapy. Biological Psychiatry, 74(11), 793–800. https://doi.org/10.1016/j.biopsych.2013.05.017

Lichtenstein, P., Yip, B. H., Björk, C., Pawitan, Y., Cannon, T. D., Sullivan, P. F., & Hultman, C. M. (2009). Common genetic determinants of schizophrenia and bipolar disorder in Swedish families: a population-based study. The Lancet, 373(9659), 234-239.

Malkoff-Schwartz, S., Frank, E., Anderson, B., Sherrill, J. T., Siegel, L., Patterson, D., & Kupfer, D. J. (1998). Stressful Life Events and Social Rhythm Disruption in the Onset of Manic and Depressive Bipolar Episodes: A Preliminary Investigation. Archives of General Psychiatry, 55(8), 702–707. https://doi.org/10.1001/archpsyc.55.8.702

Mataix-Cols, D., Frost, R. O., Pertusa, A., Clark, L. A., Saxena, S., Leckman, J. F., Stein, D. J., Matsunaga, H., & Wilhelm, S. (2010). Hoarding disorder: A new diagnosis for DSM-V? Depression and Anxiety, 27(6), 556–572. https://doi.org/10.1002/da.20693

McGuffin, P., Rijsdijk, F., Andrew, M., Sham, P., Katz, R., & Cardno, A. (2003). The Heritability of Bipolar Affective Disorder and the Genetic Relationship to Unipolar Depression. Archives of General Psychiatry, 60(5), 497–502. https://doi.org/10.1001/archpsyc.60.5.497

McLean, S. A., Ressler, K., Koenen, K. C., Neylan, T., Germine, L., Jovanovic, T., Clifford, G. D., Zeng, D., An, X., Linnstaedt, S., Beaudoin, F., House, S., Bollen, K. A., Musey, P., Hendry, P., Jones, C. W., Lewandowski, C.,

Swor, R., Datner, E., ... Kessler, R. (2020). The AURORA Study: A Longitudinal, Multimodal Library of Brain Biology and Function after Traumatic Stress Exposure. Molecular Psychiatry, 25(2), 283–296. https://doi.org/10.1038/s41380-019-0581-3

Meltzer, H. Y., & Stahl, S. M. (1976). The dopamine hypothesis of schizophrenia: A review. Schizophrenia Bulletin, 2(1), 19–76. https://doi.org/10.1093/schbul/2.1.19

Naegeli, C., Zeffiro, T., Piccirelli, M., Jaillard, A., Weilenmann, A., Hassanpour, K., ... & Mueller-Pfeiffer, C. (2018). Locus coeruleus activity mediates hyperresponsiveness in posttraumatic stress disorder. Biological Psychiatry, 83(3), 254-262.

National Comorbidity Survey. (2007). NCS-R lifetime prevalence estimates [Data file]. Retrieved from http://www.hcp.med.harvard.edu/ncs/index.php

Nestadt, G., Samuels, J., Riddle, M., Iii, O. J. B., Liang, K.-Y., LaBuda, M., Walkup, J., Grados, M., & Hoehn-Saric, R. (2000). A Family Study of Obsessive-compulsive Disorder. Archives of General Psychiatry, 57(4), 358-363.

Norberg, M. M., Calamari, J. E., Cohen, R. J., & Riemann, B. C. (2008). Quality of life in obsessive-compulsive disorder: An evaluation of impairment and a preliminary analysis of the ameliorating effects of treatment. Depression and Anxiety, 25(3), 248–259. https://doi.org/10.1002/da.20298

Norrholm, S. D., & Jovanovic, T. (2018). Fear Processing, Psychophysiology, and PTSD. Harvard Review of Psychiatry, 26(3), 129. https://doi.org/10.1097/HRP.0000000000000189

Nuss, P. (2015). Anxiety disorders and GABA neurotransmission: a disturbance of modulation. Neuropsychiatric Disease and Treatment, 11, 165-175.

Olff M. (2017). Sex and gender differences in post-traumatic stress disorder: an update. European Journal of Psychotraumatology, 8(sup4), 1351204. https://doi.org/10.1080/20008198.2017.1351204

Petrovic, P., Dietrich, T., Fransson, P., Andersson, J., Carlsson, K., & Ingvar, M. (2005). Placebo in emotional processing—induced expectations of anxiety relief activate a generalized modulatory network. Neuron, 46(6), 957-969.

Phelps, E. A. (2004). Human emotion and memory: Interactions of the amygdala and hippocampal complex. Current Opinion in Neurobiology, 14(2), 198–202. https://doi.org/10.1016/j.conb.2004.03.015

Phillips, K. A. (2005). The Broken Mirror: Understanding and Treating Body Dysmorphic Disorder. Oxford University Press.

Pruessner, M., Cullen, A. E., Aas, M., & Walker, E. F. (2017). The neural diathesis-stress model of schizophrenia revisited: An update on recent findings considering illness stage and neurobiological and methodological complexities. Neuroscience & Biobehavioral Reviews, 73, 191-218.

Pycock, C. J., Kerwin, R. W., & Carter, C. J. (1980). Effect of lesion of cortical dopamine terminals on subcortical dopamine receptors in rats. Nature, 286(5768), 74-77.

Rotge, J. Y., Guehl, D., Dilharreguy, B., Cuny, E., Tignol, J., Bioulac, B., ... & Aouizerate, B. (2008). Provocation of obsessive–compulsive symptoms: A quantitative voxel-based meta-analysis of functional neuroimaging studies. Journal of Psychiatry and Neuroscience, 33(5), 405-412.

Rothschild, A. J. (1999). Mood disorders. In A. M. Nicholi, Jr. (Ed.), The Harvard guide to psychiatry (pp. 281–307). The Belknap Press of Harvard University.

Ruscio, A. M., Stein, D. J., Chiu, W. T., & Kessler, R. C. (2010). The epidemiology of obsessive-compulsive disorder in the National Comorbidity Survey Replication. Molecular Psychiatry, 15(1), Article 1. https://doi.org/10.1038/mp.2008.94

Rushworth, M. F. S., Noonan, M. P., Boorman, E. D., Walton, M. E., & Behrens, T. E. (2011). Frontal Cortex and Reward-Guided Learning and Decision-Making. Neuron, 70(6), 1054–1069. https://doi.org/10.1016/j.neuron.2011.05.014

Sanders, S. K., & Shekhar, A. (1995). Regulation of anxiety by GABAA receptors in the rat amygdala. Pharmacology Biochemistry and Behavior, 52(4), 701-706.

Saxena, S., Bota, R. G., & Brody, A. L. (2001). Brain-behavior relationships in obsessive-compulsive disorder. Seminars in

Clinical Neuropsychiatry, 6(2), 82–101. https://doi.org/10.1053/scnp.2001.21833

Scatton, B., Worms, P., Lloyd, K. G., & Bartholini, G. (1982). Cortical modulation of striatal function. Brain Research, 232(2), 331-343.

Simon, D., Kaufmann, C., Müsch, K., Kischkel, E., & Kathmann, N. (2010). Fronto-striato-limbic hyperactivation in obsessive-compulsive disorder during individually tailored symptom provocation. Psychophysiology, 47(4), 728–738. https://doi.org/10.1111/j.1469-8986.2010.00980.x

Southwick, S. M., Bremner, J. D., Rasmusson, A., Morgan III, C. A., Arnsten, A., & Charney, D. S. (1999). Role of norepinephrine in the pathophysiology and treatment of posttraumatic stress disorder. Biological Psychiatry, 46(9), 1192-1204.

Stewart, S. E., & Pauls, D. L. (2010). The Genetics of Obsessive-Compulsive Disorder. FOCUS, 8(3), 350–357. https://doi.org/10.1176/foc.8.3.foc350

Straube, T., Glauer, M., Dilger, S., Mentzel, H. J., & Miltner, W. H. (2006). Effects of cognitive-behavioral therapy on brain activation in specific phobia. Neuroimage, 29(1), 125-135.

Tanriverdi, B., Gregory, D. F., Olino, T. M., Ely, T. D., Harnett, N. G., Van Rooij, S. J. H., Lebois, L. A. M., Seligowski, A. V., Jovanovic, T., Ressler, K. J., House, S. L., Beaudoin, F. L., An, X., Neylan, T. C., Clifford, G. D.,

Linnstaedt, S. D., Germine, L. T., Bollen, K. A., Rauch, S. L., ... Murty, V. P. (2022). Hippocampal Threat Reactivity Interacts with Physiological Arousal to Predict PTSD Symptoms. The Journal of Neuroscience, 42(34), 6593–6604. https://doi.org/10.1523/JNEUROSCI.0911-21.2022

Thase, M. E. (2009). Neurobiological aspects of depression. Handbook of Depression, 2, 187-217.

Trevizol, A. P., Shiozawa, P., Cook, I. A., Sato, I. A., Kaku, C. B., Guimarães, F. B., ... & Cordeiro, Q. (2016). Transcranial magnetic stimulation for obsessive-compulsive disorder: An updated systematic review and meta-analysis. The Journal of ECT, 32(4), 262-266.

van Erp, T. G., Hibar, D. P., Rasmussen, J. M., Glahn, D. C., Pearlson, G. D., Andreassen, O. A., ... & Turner, J. A. (2016). Subcortical brain volume abnormalities in 2028 individuals with schizophrenia and 2540 healthy controls via the ENIGMA consortium. Molecular Psychiatry, 21(4), 547-553.

van Erp, T. G., Walton, E., Hibar, D. P., Schmaal, L., Jiang, W., Glahn, D. C., ... & Fatouros-Bergman, H. (2018). Cortical brain abnormalities in 4474 individuals with schizophrenia and 5098 control subjects via the enhancing neuro imaging genetics through meta analysis (ENIGMA) consortium. Biological Psychiatry, 84(9), 644-654.

Walker, E. F., & Diforio, D. (1997). Schizophrenia: a neural diathesis-stress model. Psychological Review, 104(4), 667.

Wang, Z., Neylan, T. C., Mueller, S. G., Lenoci, M., Truran, D., Marmar, C. R., Weiner, M. W., & Schuff, N. (2010). Magnetic Resonance Imaging of Hippocampal Subfields in Posttraumatic Stress Disorder. Archives of General Psychiatry, 67(3), 296–303. https://doi.org/10.1001/archgenpsychiatry.2009.205

Weinberger, D. R., Berman, K. F., & Illowsky, B. P. (1988). Physiological dysfunction of dorsolateral prefrontal cortex in schizophrenia: III. A new cohort and evidence for a monoaminergic mechanism. Archives of General Psychiatry, 45(7), 609-615.

Wyatt, W. J., & Midkiff, D. M. (2006). Biological Psychiatry: A Practice in Search of a Science. Behavior and Social Issues, 15(2), 132–152. https://doi.org/10.5210/bsi.v15i2.372

Yehuda, R., Teicher, M. H., Trestman, R. L., Levengood, R. A., & Siever, L. J. (1996). Cortisol regulation in posttraumatic stress disorder and major depression: A chronobiological analysis. Biological Psychiatry, 40(2), 79–88. https://doi.org/10.1016/0006-3223(95)00451-3

GRANT INFORMATION

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