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Introduction

Welcome. Brain Basics provides information on how the brain works, how mental illnesses are disorders of the brain, and ongoing research that helps us better understand and treat disorders.

Mental disorders are common. You may have a friend, colleague, or relative with a mental disorder, or perhaps you have experienced one yourself at some point. Such disorders include **depression, anxiety disorders, bipolar disorder, attention deficit hyperactivity disorder (ADHD)**, and many others.

Some people who develop a mental illness may recover completely; others may have repeated episodes of illness with relatively stable periods in between. Still others live with symptoms of mental illness every day. They can be moderate, or serious and cause severe disability.

Through research, we know that mental disorders are brain disorders. Evidence shows that they can be related to changes in the anatomy, physiology, and chemistry of the nervous system. When the brain cannot effectively coordinate the billions of cells in the body, the results can affect many aspects of life.

Scientists are continually learning more about how the brain grows and works in healthy people, and how normal brain development and function can go awry, leading to mental illnesses.

Brain Basics will introduce you to some of this science, such as:

- How the brain develops
- How genes and the environment affect the brain
- The basic structure of the brain
- How different parts of the brain communicate and work with each other
- How changes in the brain can lead to mental disorders, such as depression.



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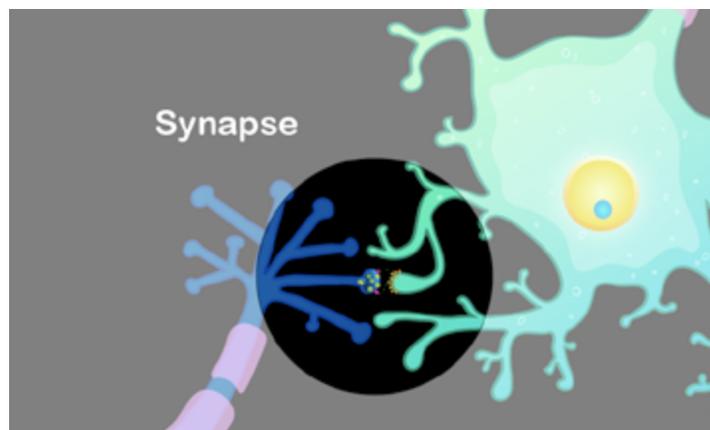
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Inside the Brain: Neurons & Neural Circuits

Neurons are the basic working unit of the brain and nervous system. These cells are highly specialized for the function of conducting messages.

A neuron has three basic parts:

- **Cell body** which includes the nucleus, cytoplasm, and cell organelles. The nucleus contains DNA and information that the cell needs for growth, metabolism, and repair. Cytoplasm is the substance that fills a cell, including all the chemicals and parts needed for the cell to work properly including small structures called cell organelles.
- **Dendrites** branch off from the cell body and act as a neuron's point of contact for receiving chemical and electrical signals called impulses from neighboring neurons.
- **Axon** which sends impulses and extends from cell bodies to meet and deliver impulses to another nerve cell. Axons can range in length from a fraction of an inch to several feet.



Each neuron is enclosed by a cell membrane, which separates the inside contents of the cell from its surrounding environment and controls what enters and leaves the cell, and responds to signals from the environment; this all helps the cell maintain its balance with the environment.

Synapses are tiny gaps between neurons, where messages move from one neuron to another as chemical or electrical signals.

The brain begins as a small group of cells in the outer layer of a developing embryo. As the cells grow and differentiate, neurons travel from a central "birthplace" to their final destination. Chemical signals from other cells guide neurons in forming various brain structures. Neighboring neurons make connections with each other and with distant nerve cells (via axons) to form brain circuits. These circuits control specific body functions such as sleep and speech. The brain continues maturing well into a person's early 20s. Knowing how the brain is wired and how the normal brain's structure develops and matures helps scientists understand what goes wrong in mental illnesses.

Scientists have already begun to chart how the brain develops over time in healthy people and are working to compare that with brain development in people with mental disorders. Genes and environmental cues both help to direct this growth.

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The Changing Brain—Effects of Genes and the Environment

There are many different types of cells in the body. We say that cells *differentiate* as the embryo develops, becoming more specialized for specific functions. Skin cells protect, muscle cells contract, and neurons, the most highly specialized cells of all, conduct messages.

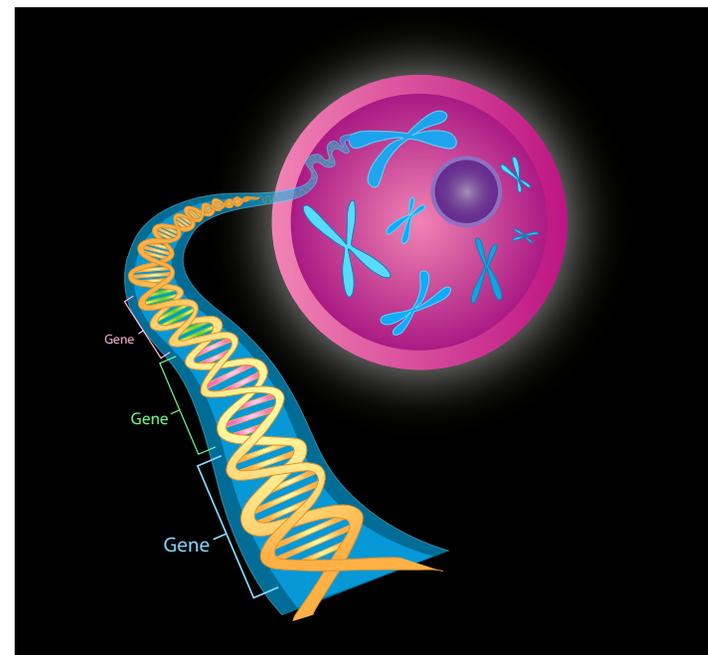
Every cell in our bodies contains a complete set of DNA. DNA, the “recipe of life,” contains all the information inherited from our parents that helps to define who we are, such as our looks and certain abilities, such as a good singing voice. A gene is a segment of DNA that contains codes to make proteins and other important body chemicals. DNA also includes information to control which genes are expressed and when, in all the cells of the body.

As we grow, we create new cells, each with a copy of our original set of DNA. Sometimes this copying process is imperfect, leading to a gene mutation that causes the gene to code for a slightly different protein. Some mutations are harmless, some can be helpful, and others give rise to disabilities or diseases.

Genes aren’t the only determinants of how our bodies function. Throughout our lives, our genes can be affected by the environment. In medicine, the term *environment* includes not only our physical surroundings but also factors that can affect our bodies, such as sleep, diet, or stress. These factors may act alone or together in complex ways, to change the way a gene is expressed or the way messages are conducted in the body.

Epigenetics is the study of how environmental factors can affect how a given gene operates. But unlike gene mutations, epigenetic changes do not change the code for a gene. Rather, they effect when a gene turns on or off to produce a specific protein. Scientists believe epigenetics play a major role in mental disorders and the effects of medications. Some, but not all mutations and epigenetic changes can be passed on to future generations.

Further understanding of genes and epigenetics may one day lead to genetic testing for people at risk for mental disorders. This could greatly help in early detection, more tailored treatments, and possibly prevention of such illnesses.



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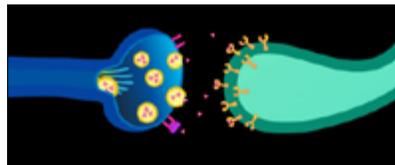
Neurotransmitters

Everything we do relies on neurons communicating with one another. Electrical impulses and chemical signals carrying messages across different parts of the brain and between the brain and the rest of the nervous system. When a neuron is activated a small difference in electrical charge occurs. This unbalanced charge is called an action potential and is caused by the concentration of ions (atoms or molecules with unbalanced charges) across the cell membrane. The action potential travels very quickly along the axon, like when a line of dominoes falls.

When the action potential reaches the end of an axon, most neurons release a chemical message (a neurotransmitter) which crosses the synapse and binds to receptors on the receiving neuron's dendrites and starts the process over again. At the end of the line, a neurotransmitter may stimulate a different kind of cell (like a gland cell), or may trigger a new chain of messages.

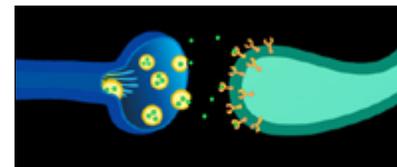
Neurotransmitters send chemical messages between neurons. Mental illnesses, such as depression, can occur when this process does not work correctly. Communication between neurons can also be electrical, such as in areas of the brain that control movement. When electrical signals are abnormal, they can cause tremors or symptoms found in Parkinson's disease.

- **Serotonin**—helps control many functions, such as mood, appetite, and sleep. Research shows that people with **depression** often have lower than normal levels of serotonin. The types of medications most commonly prescribed to treat depression act by blocking the recycling, or reuptake, of serotonin by the sending neuron. As a result, more serotonin stays in the

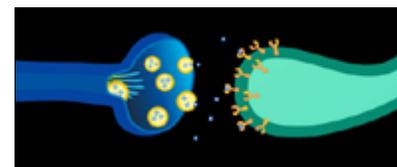


synapse for the receiving neuron to bind onto, leading to more normal mood functioning.

- **Dopamine**—mainly involved in controlling movement and aiding the flow of information to the front of the brain, which is linked to thought and emotion. It is also linked to reward systems in the brain. Problems in producing dopamine can result in Parkinson's disease, a disorder that affects a person's ability to move as they want to, resulting in stiffness, tremors or shaking, and other symptoms. Some studies suggest that having too little dopamine or problems using dopamine in the thinking and feeling regions of the brain may play a role in disorders like **schizophrenia** or **attention deficit hyperactivity disorder (ADHD)**.



- **Glutamate**—the most common neurotransmitter, glutamate has many roles throughout the brain and nervous system. Glutamate is an excitatory transmitter: when it is released it increases the chance that the neuron will fire. This enhances the electrical flow among brain cells required for normal function and plays an important role during early brain development. It may also assist in learning and memory. Problems in making or using glutamate have been linked to many mental disorders, including **autism**, **obsessive compulsive disorder (OCD)**, **schizophrenia**, and **depression**.



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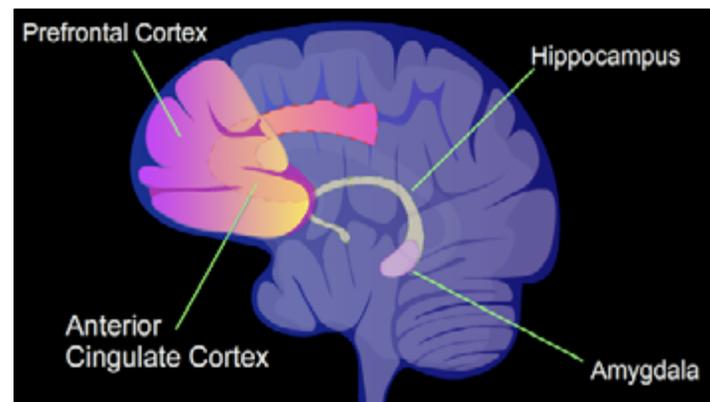
The Working Brain

Brain Regions

Just as many neurons working together form a circuit, many circuits working together form specialized brain systems. We have many specialized brain systems that work across specific brain regions to help us talk, help us make sense of what we see, and help us to solve a problem. Some of the regions most commonly studied in mental health research are listed below.

- **Amygdala**—The brain’s “fear hub,” which activates our natural “fight-or-flight” response to confront or escape from a dangerous situation. The amygdala also appears to be involved in learning to fear an event, such as touching a hot stove, and learning not to fear, such as overcoming a fear of spiders. Studying how the amygdala helps create memories of fear and safety may help improve treatments for **anxiety disorders** like **phobias** or **post-traumatic stress disorder (PTSD)**.
- **Prefrontal cortex (PFC)**—Seat of the brain’s executive functions, such as judgment, decision making, and problem solving. Different parts of the PFC are involved in using short-term or “working” memory and in retrieving long-term memories. This area of the brain also helps to control the amygdala during stressful events. Some research shows that people who have PTSD or ADHD have reduced activity in their PFCs.

- **Anterior cingulate cortex (ACC)**— the ACC has many different roles, from controlling blood pressure and heart rate to responding when we sense a mistake, helping us feel motivated and stay focused on a task, and managing proper emotional reactions. Reduced ACC activity or damage to this brain area has been linked to disorders such as ADHD, schizophrenia, and depression.
- **Hippocampus**—Helps create and file new memories. When the hippocampus is damaged, a person can’t create new memories, but can still remember past events and learned skills, and carry on a conversation, all which rely on different parts of the brain. The hippocampus may be involved in mood disorders through its control of a major mood circuit called the hypothalamic-pituitary-adrenal (HPA) axis.



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Brain Basics in Real Life— How Depression affects the Brain

Meet Sarah

Sarah is a middle-aged woman who seemed to have it all. She was happily married and successful in business. Then, after a serious setback at work, she lost interest in her job. She had problems getting to sleep and generally felt tired, listless, and had no appetite most of the time. Weeks later, Sarah realized she was having trouble coping with the stresses in her life. She began to think of suicide because she felt like things weren't going to get better and that there was nothing she could do about it.

Worried at the changes he saw, Sarah's husband took her to the doctor, who ran some tests. After deciding her symptoms were not caused by a stroke, brain tumor, or similar conditions, Sarah's doctor referred her to a psychiatrist, a type of medical doctor who is an expert on mental disorders. Other medical professionals who can diagnose mental disorders are psychologists or clinical social workers.



The psychiatrist asked Sarah and her husband questions about Sarah's symptoms and family medical history. Epigenetic changes from stress or early-life experiences may have made it harder for Sarah to recover normally from her low mood. It's important to remember that everyone gets "the blues" from time to time. In contrast, major depression is a serious disorder that lasts for weeks. Sarah told the doctor that she had experienced long periods of deep sadness throughout her teenage years, but had never seen a doctor about it. She has faced a few bouts since then, but they have never been as bad as her current mood.

The psychiatrist diagnosed Sarah with major depression and gave her a prescription for a type of antidepressant medication called a selective serotonin reuptake inhibitor (SSRI). SSRIs are the most common type of medication used to treat depression.

SSRIs boost the amount of serotonin in the brain and help reduce symptoms of depression. Sarah also has several follow-up visits scheduled with the psychiatrist to check how she's responding to the treatment. She also begins regular talk therapy sessions with her psychiatrist. In these sessions, she learns how to change the way she thinks about and reacts to things that may trigger her depression. Several months later, Sarah feels much better. She continues taking SSRIs and has joined an online support group. Sharing her experiences with others also dealing with depression helps Sarah to better cope with her feelings.

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Modern research tools and techniques are giving scientists a more detailed understanding of the brain than ever before.

Brain Imaging

Using brain imaging technologies such as magnetic resonance imaging (MRI), which uses magnetic fields to take pictures of the brain's structure, studies show that brain growth in children with **autism** appears to peak early. And as they grow there are differences in brain development in children who develop bipolar disorder than children who do not.

Studies comparing such children to those with normal brain development may help scientists to pinpoint when and where mental disorders begin and perhaps how to slow or stop them from progressing. Functional magnetic resonance imaging (fMRI) is another important research tool in understanding how the brain functions.

Another type of brain scan called magnetoencephalography, or MEG, can capture split-second changes in the brain. Using MEG, some scientists have found a specific pattern of brain activity that may help predict who is most likely to respond to fast-acting antidepressant medications. Currently available antidepressants usually take four to six weeks to reach their full effect, which can be a difficult wait for some people struggling with depression. However, recent research points to a possible new class of antidepressants that can relieve symptoms of the illness in just a few hours. Knowing who might respond to such medications could reduce the amount of trial and error and frustration that many people with depression experience when starting treatment.

Gene Studies

Advanced technologies are also making it faster, easier, and more affordable to study genes. Scientists have found many different genes and groups of genes that appear to increase risk or provide protection from various mental disorders. Other genes may change the way a person responds to a certain medication. This information may someday make it possible to predict who will develop a mental disorder and to tailor the treatment for a person's specific conditions.

Such brain research help increase the understanding of how the brain grows and works and the effects of genes and environment on mental health. This knowledge is allowing scientists to make important discoveries that could change the way we think about and treat mental illnesses.

The National Institute of Mental Health supports many studies on mental health and the brain. You can read about some of these studies online at www.nimh.nih.gov.



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action potential—Transmission of signal from the cell body to the synaptic terminal at the end of the cell's axon. When the action potential reaches the end of the axon the neuron releases chemical (neurotransmitters) or electrical signals.

amygdala—The brain's "fear hub," which helps activate the fight-or-flight response and is also involved in emotions and memory.

anterior cingulate cortex—Is involved in attention, emotional responses, and many other functions.

axon—The long, fiber-like part of a neuron by which the cell sends information to receiving neurons.

cell body—Contains the nucleus and cytoplasm of a cell.

cell membrane—The boundary separating the inside contents of a cell from its surrounding environment.

cytoplasm—The substance filling a cell, containing all the chemicals and parts needed for the cell to work properly.

dendrite—The point of contact for receiving impulses on a neuron, branching off from the cell body.

dopamine—A neurotransmitter mainly involved in controlling movement, managing the release of various hormones, and aiding the flow of information to the front of the brain.

DNA—The "recipe of life," containing inherited genetic information that helps to define physical and some behavioral traits.

epigenetics—The study of how environmental factors like diet, stress and post-natal care can change gene expression (when genes turn on or off)—without altering DNA sequence.

gene—A segment of DNA that codes to make proteins and other important body chemicals.

glutamate—The most common neurotransmitter in a person's body, which increases neuronal activity, is involved in early brain development, and may also assist in learning and memory.

hippocampus—A portion of the brain involved in creating and filing new memories.

Hypothalamic-pituitary-adrenal (HPA) axis—A brain-body circuit which plays a critical role in the body's response to stress.

impulse—An electrical communication signal sent between neurons by which neurons communicate with each other.

magnetic resonance imaging (MRI)—An imaging technique that uses magnetic fields to take pictures of the brain's structure.

mutation—A change in the code for a gene, which may be harmless or even helpful, but sometimes give rise to disabilities or diseases.

neural circuit—A network of neurons and their interconnections.

neuron—A nerve cell that is the basic, working unit of the brain and nervous system, which processes and transmits information.

neurotransmitter—A chemical produced by neurons that carries messages to other neurons.

nucleus—A structure within a cell that contains DNA and information the cell needs for growing, staying alive, and making new neurons.

prefrontal cortex—A highly developed area at the front of the brain that, in humans, plays a role in executive functions such as judgment, decision making and problem solving, as well as emotional control and memory.

serotonin—A neurotransmitter that regulates many functions, including mood, appetite, and sleep.

synapse—The tiny gap between neurons, where nerve impulses are sent from one neuron to another.

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National Institute of Mental Health (NIMH)

Publications, science news, and funding information related to Federally-supported research on mental disorders

NIMH Clinical Trials

Clinical trials funded by NIMH

Medline Plus

Consumer health information provided by the National Library of Medicine

NIH Office of Science Education

Science education resources developed or supported by the National Institutes of Health (NIH)

NIH RePORTER

Public database of active grants funded by the National Institutes of Health

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