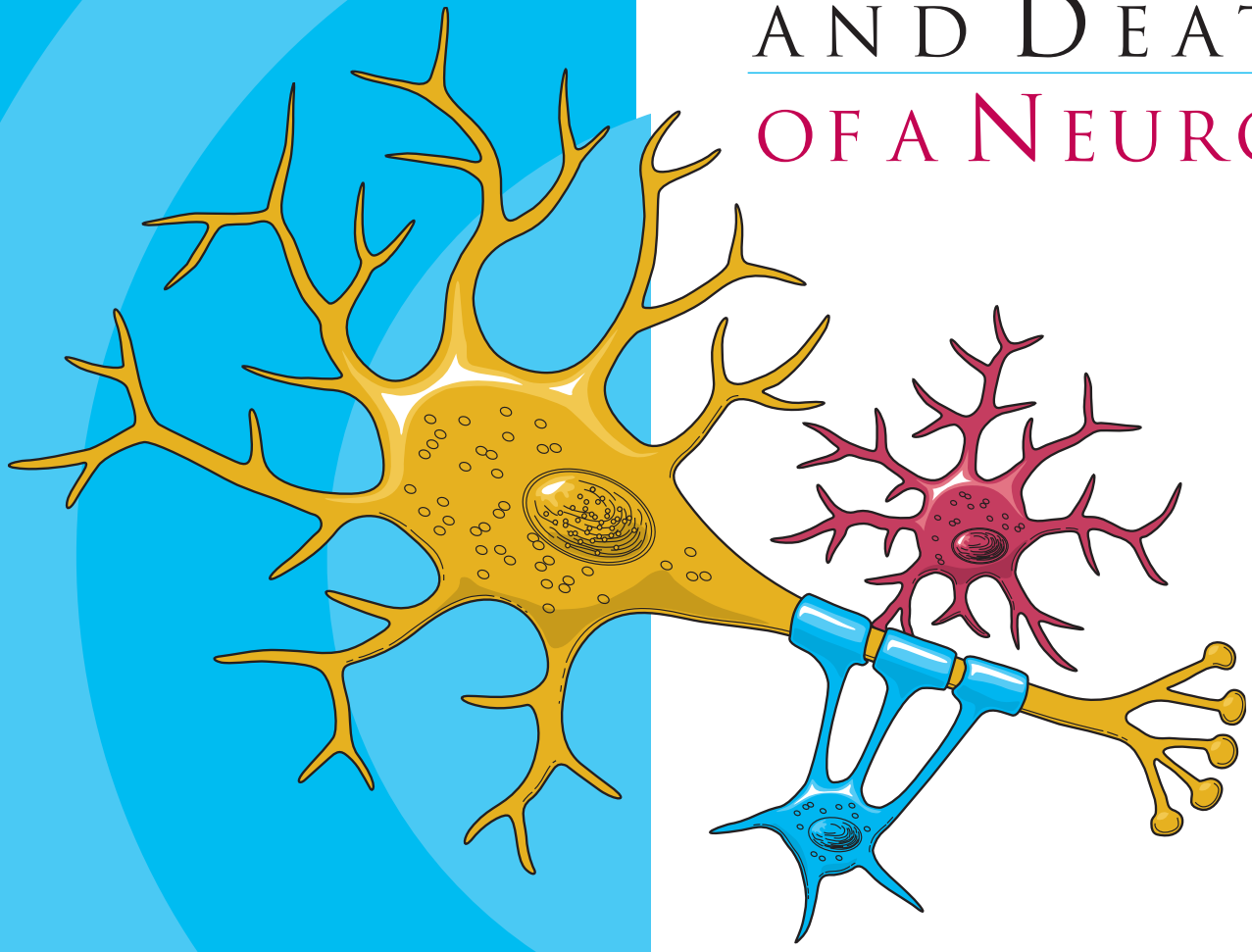
The Life and Death of a Neuron



National Institute of Neurological Disorders and Stroke

Brain Basics

Introduction

Until recently, most neuroscientists thought we were born with all the neurons we were ever going to have. As children we might produce some new neurons to help build the pathways – called neural circuits – that act as information highways between different areas of the brain. But scientists believed that once a neural circuit was in place, adding any new neurons would disrupt the flow of information and disable the brain's communication system.

In 1962, scientist Joseph Altman challenged this belief when he saw evidence of neurogenesis (the birth of neurons) in a region of the adult rat brain called the hippocampus. He later reported that newborn neurons migrated from their birthplace in the hippocampus to other parts of the brain. In 1979, another scientist, Michael Kaplan, confirmed Altman's findings in the rat brain, and in 1983 he found neural precursor cells in the forebrain of an adult monkey.

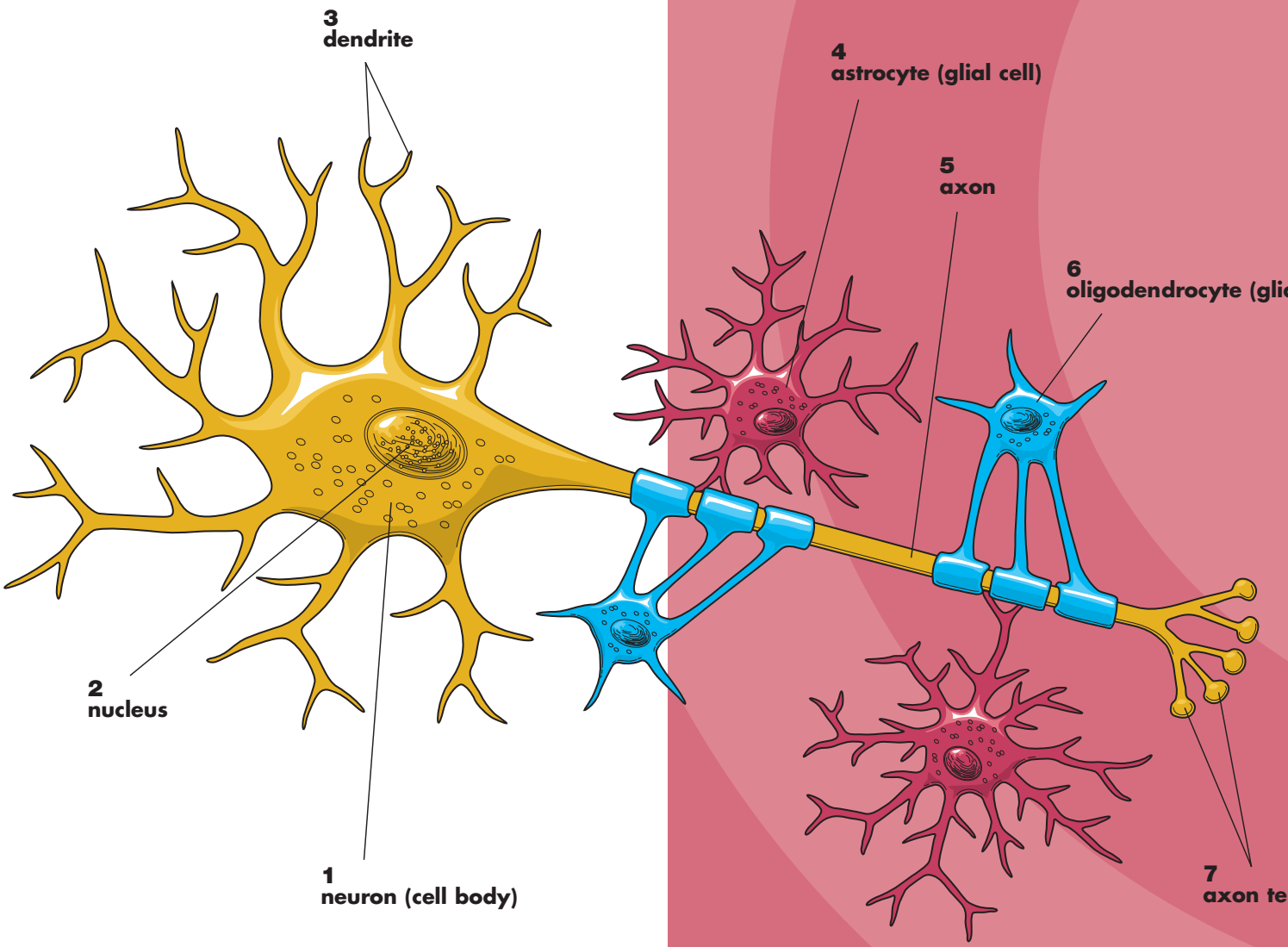
These discoveries about neurogenesis in the adult brain were surprising to other researchers who didn't think they could be true in humans. But in the early 1980s, a scientist trying to understand how birds learn to sing suggested that neuroscientists look again at neurogenesis in the adult brain and begin to see how it might make sense. In a series of experiments, Fernando Nottebohm and his research team showed that the numbers of neurons in the forebrains of male canaries dramatically increased during the mating season. This was the same time in which the birds had to learn new songs to attract females.

Why did these bird brains add neurons at such a critical time in learning? Nottebohm believed it was because fresh neurons helped store new song patterns within the neural circuits of the forebrain, the area of the brain that controls complex behaviors. These new neurons made learning possible. If birds made new neurons to help them remember and learn, Nottebohm thought the brains of mammals might too.

Other scientists believed these findings could not apply to mammals, but Elizabeth Gould later found evidence of newborn neurons in a distinct area of the brain in monkeys, and Fred Gage and Peter Eriksson showed that the adult human brain produced new neurons in a similar area.

For some neuroscientists, neurogenesis in the adult brain is still an unproven theory. But others think the evidence offers intriguing possibilities about the role of adult-generated neurons in learning and memory.

The Architecture of



THE NEURON

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The central nervous system (which includes the brain and spinal cord) is made up of two basic types of cells: neurons 1 and glia 4 & 6. Glia outnumber neurons by a substantial amount – some scientists have estimated it to be as large as nine to one – but in spite of their smaller numbers, neurons are the key players in the brain.

Neurons are information messengers. They use electrical impulses and chemical signals to transmit information between different areas of the brain, and between the brain and the rest of the nervous system. Everything we think and feel and do would be impossible without the work of neurons and their support cells, the glial cells called astrocytes 4 and oligodendrocytes 6.

It would take 30,000 neurons just to cover the head of a pin.

Neurons have three basic parts: a cell body and two extensions called an axon 5 and a dendrite 3. Within the cell body is the nucleus 2, which controls the cell's activities and contains the cell's genetic material. The axon looks like a long tail and transmits messages from the cell. Dendrites look like the branches of a tree and receive messages for the cell. Neurons communicate with each other by sending chemicals, called neurotransmitters, across a tiny space, called a synapse, between the axons and dendrites of adjacent neurons.

There are three classes of neurons:

1) **Sensory neurons** carry information from the sense organs (such as the eyes and ears) to the brain.

2) **Motor neurons** have long axons and carry information from the central nervous system to the muscles and glands of the body.

3) **Interneurons** have short axons and communicate only within their immediate region.

Scientists think that neurons are the most diverse kind of cell in the body. Within these three classes of neurons are hundreds of different types, each with specific message-carrying abilities.

How these neurons communicate with each other by making connections is what makes each of us unique in how we think, and feel, and act.

Birth

The extent to which new neurons are generated in the brain is a controversial subject among neuroscientists. Although the majority of neurons are already present in our brains by the time we are born, there is evidence to support that neurogenesis (the scientific word for the birth of neurons) is a lifelong process.

Neurons are born in areas of the brain that are rich in concentrations of neural precursor cells (also called neural stem cells). These cells have the potential to generate most, if not all, of the different types of neurons and glia found in the brain.

Neuroscientists have observed how neural precursor cells behave in the laboratory. Although this may not be exactly how these cells behave when they are in the brain, it gives us information about how they could be behaving when they are in the brain's environment.

The science of stem cells is still very new, and could change with additional discoveries, but researchers have learned enough to be able to describe how neural stem cells generate the other cells of the brain. They call it a stem cell's lineage and it is similar in principle to a family tree.

Neural stem cells increase by dividing in two and producing either two new stem cells, or two early progenitor cells, or one of each.

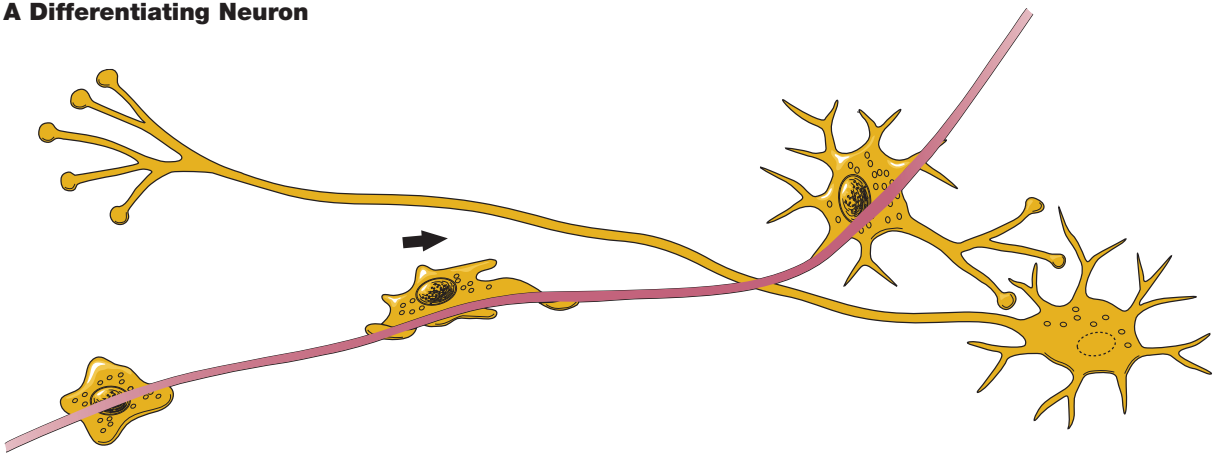
The axon of a single nerve cell can run half the length of a human body.

When a stem cell divides to produce another stem cell, it is said to self-renew. This new cell has the potential to make more stem cells.

When a stem cell divides to produce an early progenitor cell, it is said to differentiate. Differentiation means that the new cell is more specialized in form and function. An early progenitor cell does not have the potential of a stem cell to make many different types of cells. It can only make cells in its particular lineage.

Early progenitor cells can self-renew or go in either of two ways. One type will give rise to astrocytes. The other type will ultimately produce neurons or oligodendrocytes.

A Differentiating Neuron



Some neurons migrate by riding along extensions (radial glia) until they reach their final destination.

Migration

Once a neuron is born it has to travel to the place in the brain where it will do its work.

How does a neuron know where to go? What helps it get there?

Scientists have seen that neurons use at least two different methods to travel:

1) Some neurons migrate by following the long fibers of cells called radial glia. These fibers extend from the inner layers to the outer layers of the brain. Neurons glide along the fibers until they reach their destination.

2) Neurons also travel by using chemical signals. Scientists have found special molecules on the surface of neurons – adhesion molecules – that bind with similar molecules on nearby glial cells or nerve axons. These chemical signals guide the neuron to its final location.

Not all neurons are successful in their journey. Scientists think that only a third reach their destination. The rest either never differentiate, or die and disappear at some point during the two to three week phase of migration.

Some neurons survive the trip, but end up where they shouldn't be. Mutations in the genes that control migration create areas of misplaced or oddly formed neurons that can cause disorders such as childhood epilepsy. Some researchers suspect that schizophrenia and the learning disorder dyslexia are partly the result of misguided neurons.

Differentiation

Once a neuron reaches its destination, it has to settle in to work. This final step of differentiation is the least well-understood part of neurogenesis.

Neurons are responsible for the transport and uptake of neurotransmitters – chemicals that relay information between brain cells.

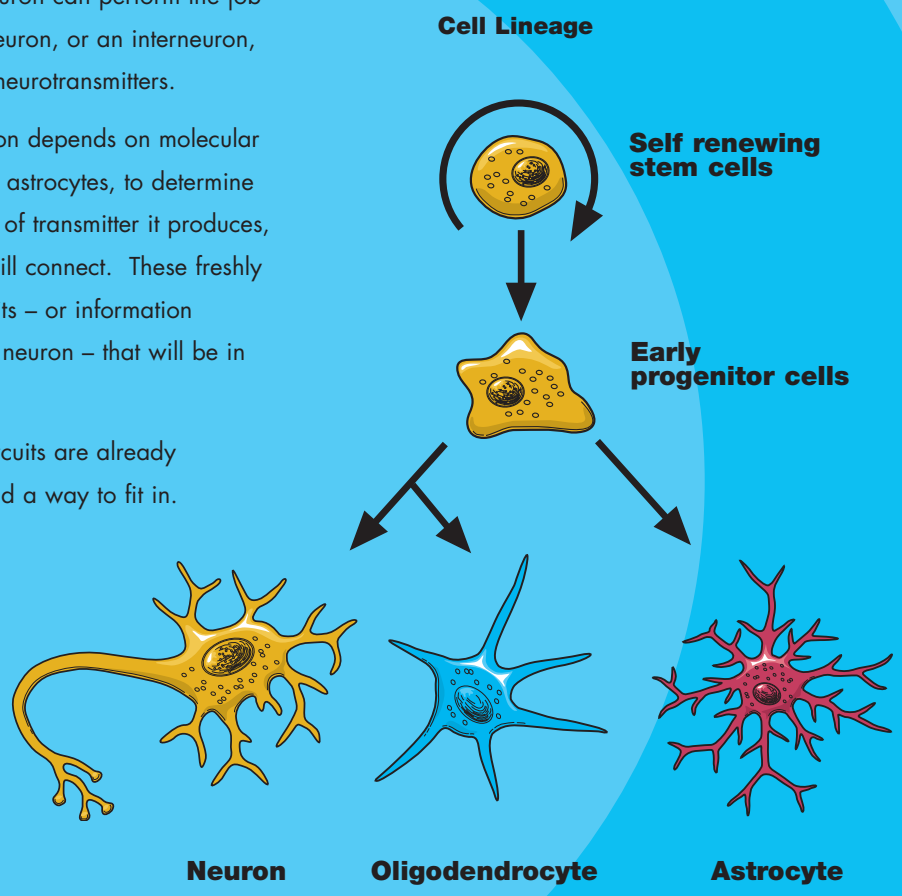
Depending on its location, a neuron can perform the job of a sensory neuron, a motor neuron, or an interneuron, sending and receiving specific neurotransmitters.

In the developing brain, a neuron depends on molecular signals from other cells, such as astrocytes, to determine its shape and location, the kind of transmitter it produces, and to which other neurons it will connect. These freshly born cells establish neural circuits – or information pathways connecting neuron to neuron – that will be in place throughout adulthood.

But in the adult brain, neural circuits are already developed and neurons must find a way to fit in.

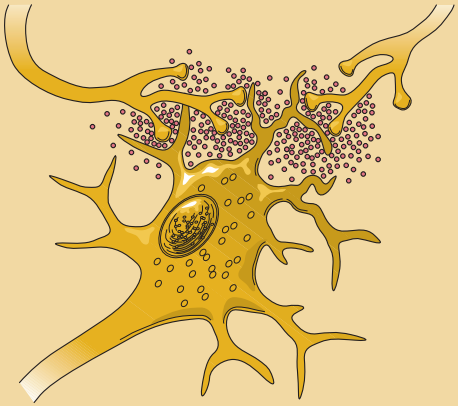
Researchers suspect that astrocytes play a similar role in the adult brain, actively regulating the function and synapse formation of new neurons.

As a new neuron settles in, it starts to look like surrounding cells. It develops an axon and dendrites and begins to communicate with its neighbors.



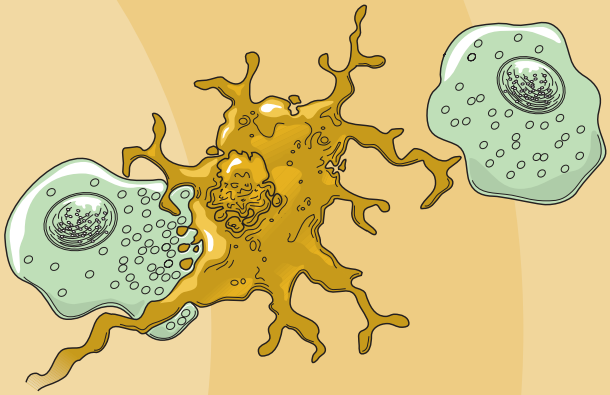
Stem cells differentiate to produce different types of nerve cells.

A Diseased Neuron



One method of cell death results from the release of excess glutamate.

A Dying Neuron



Macrophages (green) eat dying neurons in order to clear debris.

Death

Although neurons are the longest living cells in the body, large numbers of them die during migration and differentiation.

The lives of some neurons can take abnormal turns. Some diseases of the brain are the result of the unnatural deaths of neurons.

— In **Parkinson's disease**, neurons that produce the neurotransmitter dopamine die off in the basal ganglia, an area of the brain that controls body movements. The brain can no longer control the body and people shake and jerk in spasms.

— In **Huntington's disease**, a genetic mutation causes over-production of a neurotransmitter called glutamate, which kills neurons in the basal ganglia. As a result, people twist and writhe uncontrollably.

— In **Alzheimer's disease**, unusual proteins build up in and around neurons in the neocortex and hippocampus, parts of the brain that control memory. When these neurons die, people lose their capacity to remember and their ability to do everyday tasks.

Physical damage to the brain and other parts of the central nervous system can also kill or disable neurons.

— **Blows to the brain**, or the damage caused by a stroke, can kill neurons outright or slowly starve them of the oxygen and nutrients they need to survive.

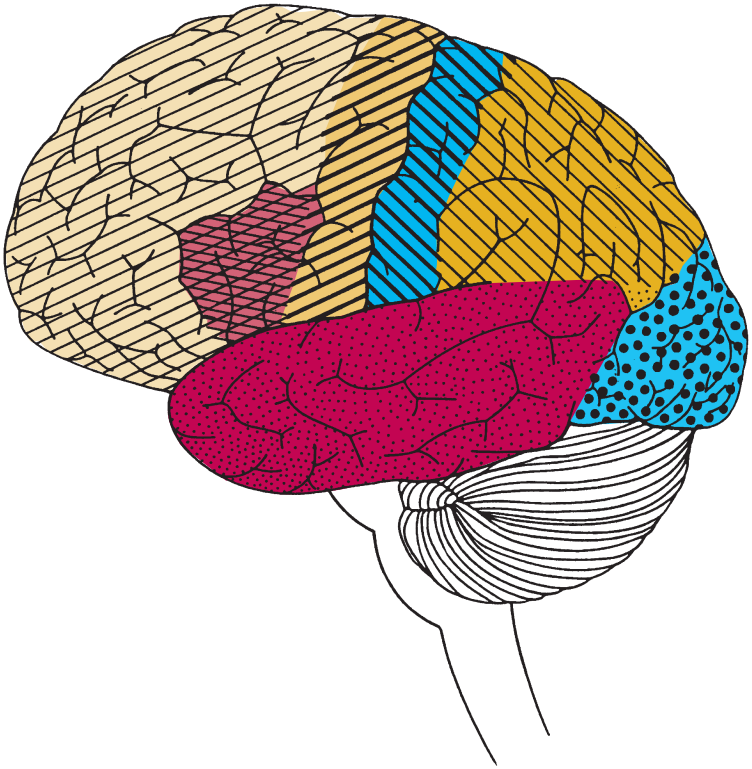
— **Spinal cord injury** can disrupt communication between the brain and muscles when neurons lose their connection to axons located below the site of injury. These neurons may still live, but they lose their ability to communicate.

Hope Through Research

Scientists hope that by understanding more about the life and death of neurons they can develop new treatments, and possibly even cures, for brain diseases and disorders that affect the lives of millions of Americans.

The most current research suggests that neural stem cells can generate many, if not all, of the different types of neurons found in the brain and the nervous system. Learning how to manipulate these stem cells in the laboratory into specific types of neurons could produce a fresh supply of brain cells to replace those that have died or been damaged.

Therapies could also be created to take advantage of growth factors and other signaling mechanisms inside the brain that tell precursor cells to make new neurons. This would make it possible to repair, reshape, and renew the brain from within.



"Know Your Brain," another brochure in this Brain Basics series, explains the anatomy and function of the human brain. For copies, contact the NINDS.

The National Institute of Neurological Disorders and Stroke

Since its creation by Congress in 1950, the National Institute of Neurological Disorders and Stroke (NINDS) has grown to become the nation's leading supporter of biomedical research on the brain and nervous system. Most research funded by the NINDS is conducted by scientists in public and private institutions such as universities, medical schools, and hospitals. Government scientists also conduct a wide array of neurological research in the more than 20 laboratories and branches of the NINDS itself. This research ranges from studies on the structure and function of single brain cells to tests of new diagnostic tools and treatments for those with neurological disorders. For more information, write or call the Institute's Brain Resources and Information Network (BRAIN) at:

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