# YOUR WORLD
## BIOTECHNOLOGY & YOU

a magazine of biotechnology applications in healthcare, agriculture, the environment, and industry

Volume 6, Issue No. 1

# Investigating

YOUR WORLD
BIOTECHNOLOGY & YOU

**Volume 6, Issue No. 1**

*Your World/Our World* describes the application of biotechnology to problems facing our world. We hope that you find it an interesting way to learn about science and engineering.

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**In the past few decades scientists have made incredible advances in studying the brain. This issue of *Your World/Our World* provides:**

- **a glimpse of what we know about the way normal brains work and about brain disorders,**
- **how research and technology help us learn about the fundamental molecular workings of the brain,**
- **how this understanding can lead to the discovery of new medicines to treat brain disorders.**



***On the Cover: Seeing the Brain in Action***
*Computerized PET scan images show which regions of the brain are used for different tasks: hearing words (top) and speaking words (bottom). Different colors represent different levels of brain activity. Blue = low activity; Green = intermediate activity; Yellow = high activity; Red = intense activity; White = maximum activity.*

*Photo credit: Marcus E. Raichle, M.D.; Washington University School of Medicine*

# Investigating the Brain!

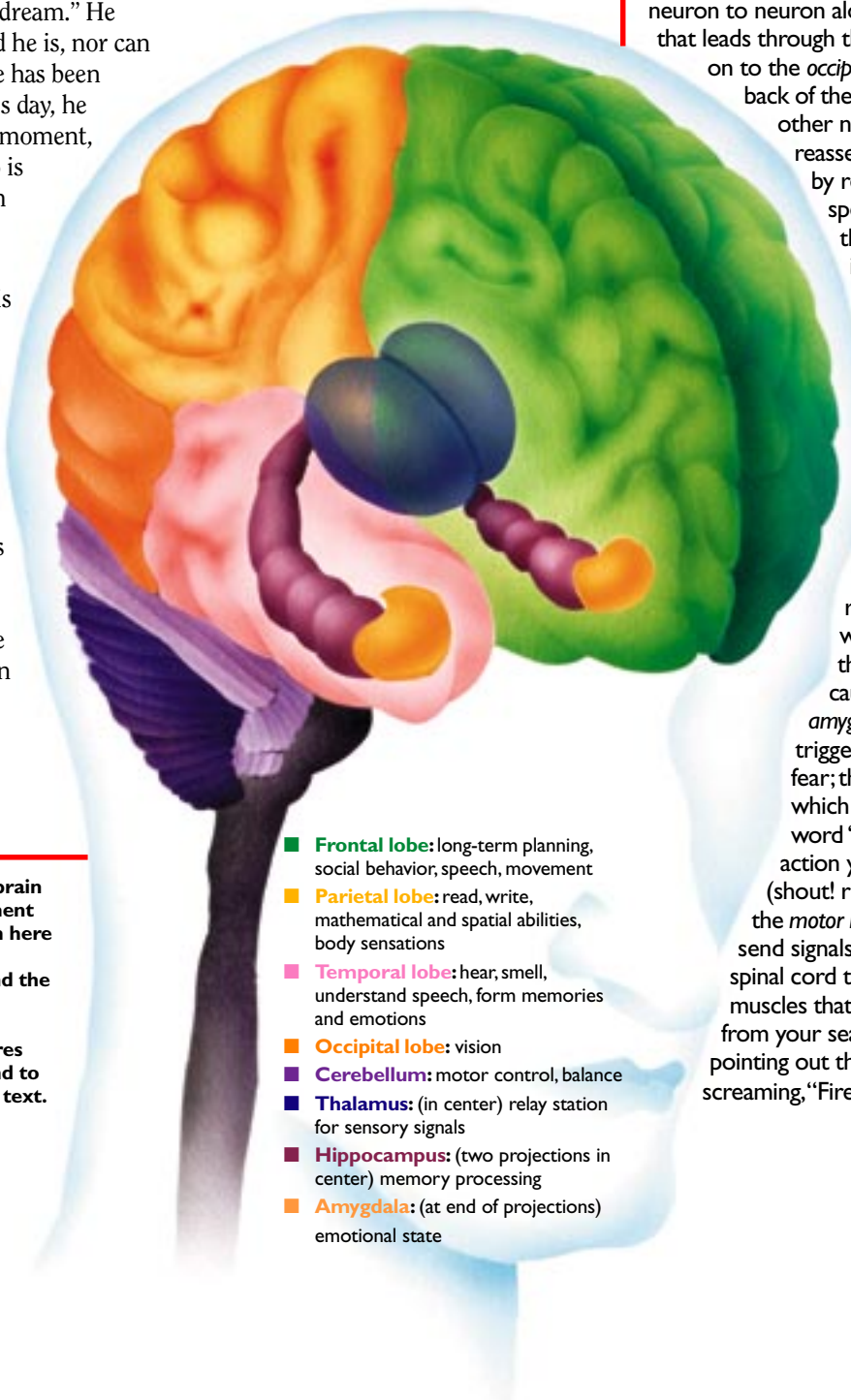
Over 40 years ago, Henry M. suffered from epileptic seizures so severe that he could not work. To stop his seizures, surgeons removed a brain structure called the hippocampus. The results of this surgery were both tragic and astonishing: Henry cannot remember anything new. He can easily recall events from before the operation, but nothing that has happened since. Henry says his world is "like waking from a dream." He does not know how old he is, nor can he recognize people he has been seeing for years. To this day, he lives from moment to moment, a 70 year old man who is forever 27 years old "in memory."

Your brain, a three-pound cluster of cells is the most complex living structure that we know of in the universe. It allows you to see, smell, taste, hear, feel, and respond to the world around you. It enables you to think, learn, remember, speak, feel emotions and have appetite, and it plays an important role in fighting disease.

In short, our brains define us. By studying the brain, we can learn more about who we are, both as individuals and as a species. Everything we learn about the brain can help us prevent or cure the many devastating brain disorders that kill, cripple, or deprive us of our personality, intelligence, and memories. ■

## FIRE!!!

Imagine you are gazing out the window. Suddenly you see flames shooting out of the roof of the building next door! This image – a pattern of light, shape, and movement – falls on *neurons* (nerve cells) at the back of your eyes that are sensitive to light. Signals race from neuron to neuron along a pathway that leads through the *thalamus* and on to the *occipital lobes* in the back of the brain. Here, other neurons reassemble the image by responding to specific features of the fire, such as its movement or its shape. These neurons, in turn, send messages to other parts of the brain, such as the *hippocampus,* which is involved in remembering what a fire is and the injury it can cause; the *amygdala,* which triggers the feeling of fear; the *frontal lobe,* which formulates the word "fire"; and the action you will take (shout! run!) and finally, the *motor neurons,* which send signals down the spinal cord to stimulate the muscles that will propel you from your seat, frantically pointing out the window and screaming, "Fire!"▼



- **Frontal lobe:** long-term planning, social behavior, speech, movement
- **Parietal lobe:** read, write, mathematical and spatial abilities, body sensations
- **Temporal lobe:** hear, smell, understand speech, form memories and emotions
- **Occipital lobe:** vision
- **Cerebellum:** motor control, balance
- **Thalamus:** (in center) relay station for sensory signals
- **Hippocampus:** (two projections in center) memory processing
- **Amygdala:** (at end of projections) emotional state

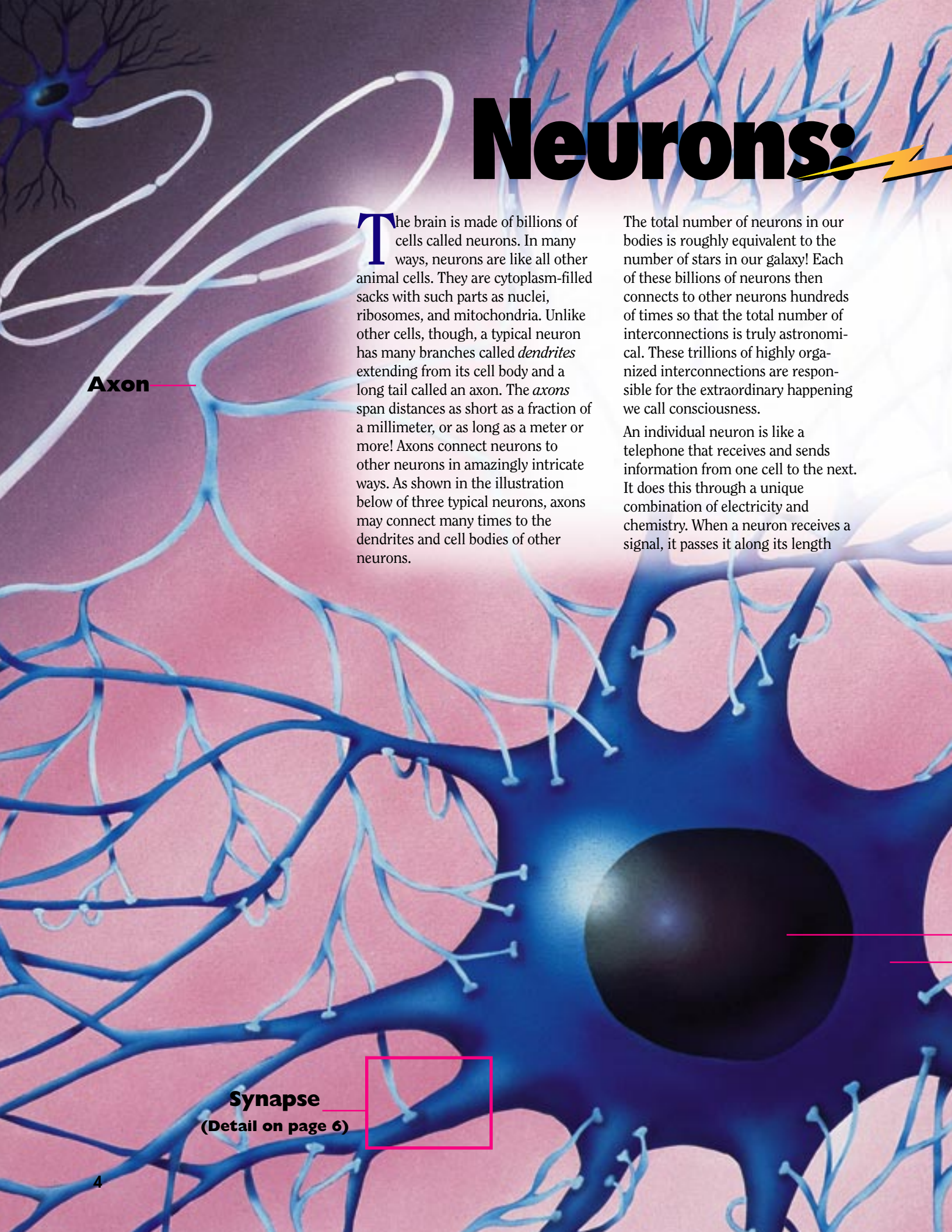
**This map of the human brain show the basic arrangement of some of its parts. Seen here are the two major hemispheres, left and right, and the internal brain structures mentioned in the stories above. The brain structures are colored to correspond to the colored words in the text.**

# Neurons:

The brain is made of billions of cells called neurons. In many ways, neurons are like all other animal cells. They are cytoplasm-filled sacks with such parts as nuclei, ribosomes, and mitochondria. Unlike other cells, though, a typical neuron has many branches called *dendrites* extending from its cell body and a long tail called an axon. The *axons* span distances as short as a fraction of a millimeter, or as long as a meter or more! Axons connect neurons to other neurons in amazingly intricate ways. As shown in the illustration below of three typical neurons, axons may connect many times to the dendrites and cell bodies of other neurons.

The total number of neurons in our bodies is roughly equivalent to the number of stars in our galaxy! Each of these billions of neurons then connects to other neurons hundreds of times so that the total number of interconnections is truly astronomical. These trillions of highly organized interconnections are responsible for the extraordinary happening we call consciousness.

An individual neuron is like a telephone that receives and sends information from one cell to the next. It does this through a unique combination of electricity and chemistry. When a neuron receives a signal, it passes it along its length



# An Electrifying Kind of Cell

electrically. To help speed this electrical signal, the axons of some neurons are surrounded by a special insulating sheath of cells called *myelin*. These electrical signals are easily detected and recorded. (See page 12.)

Then, at the end of the axon, the neuron transmits the signal to the next neuron by releasing a tiny amount of a chemical–called a *neurotransmitter*–into the gap, called the *synapse*, between neurons. When the neurotransmitter is released into the synapse, it is captured by a special protein, called a *receptor*, on the next neuron. The receptor then tells the neuron to start transmitting an electrical signal. There are many different neurotransmitters used by neurons and there is a different receptor for each neurotransmitter. Each receptor recognizes only one type of neurotransmitter, like a key fitting only one lock. The neurotransmitters dopamine, serotonin, and glutamate are discussed in following articles.

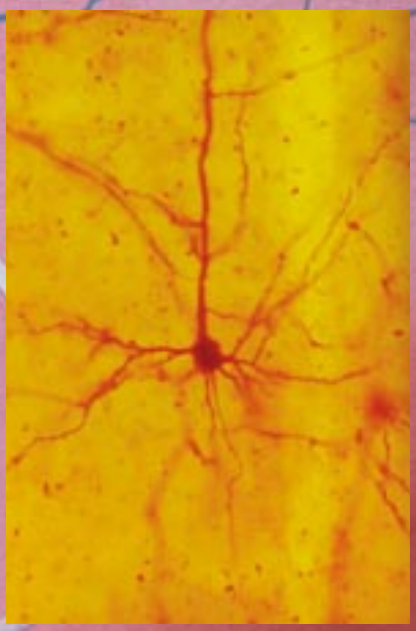
Later in this issue, you will learn how the events occurring during signaling across the synapse play a big role in the workings of our brain.

**Dendrite**

**Nucleus**

**Cell Body**

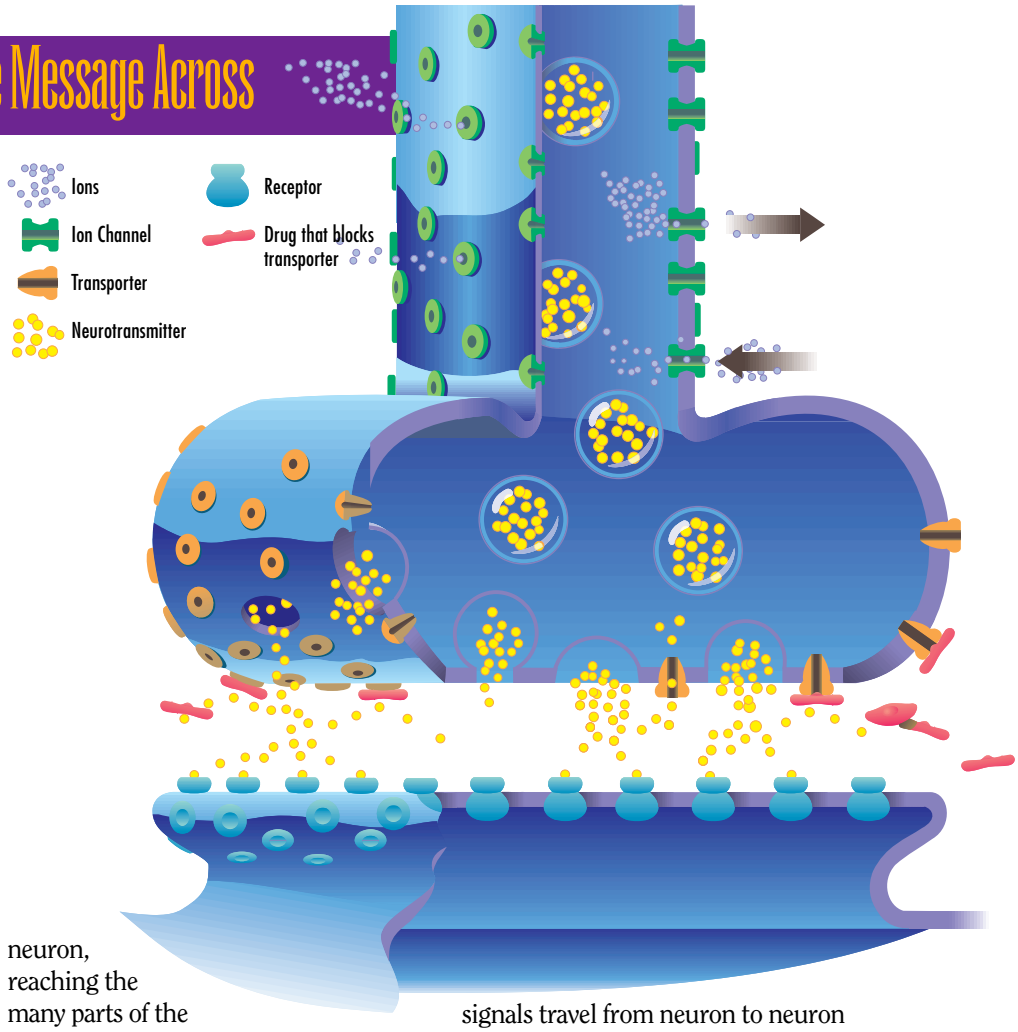
**Myelin Sheath**



Ronald F. Mertis, Ph.D., NeuroMetrix Research, Inc.

***A neuron from the cerebral cortex magnified 600 times. The neuron has been stained with a special dye that allows us to see the cell body and its many branching dendrites.***

# Synapses: Getting the Message Across




This illustration shows the end of an axon where it meets the next neuron–the synapse–as a signal is passed between the neurons.

Initially, neurons have an electrical "charge"–like a battery. This charge is caused by the accumulation of different ions (atoms with a positive or negative charge) on the inside and outside of the neuron. When neurons are in a resting state (not sending a signal), there are more negative ions on the inside of the neuron and more positive ions on the outside. When enough *neurotransmitter* crosses the synapse and attaches to *receptors*, a chemical reaction is triggered that lets ions move through openings or *channels* in the membrane. Positive ions flood into the neurons, causing a sudden reversal of the charge inside the neuron. This reversal of charge triggers nearby channels to open so that the opening of channels then flows along the length of the axon like a wave–much like a wave in a sports stadium. This has already happened to the top neuron.

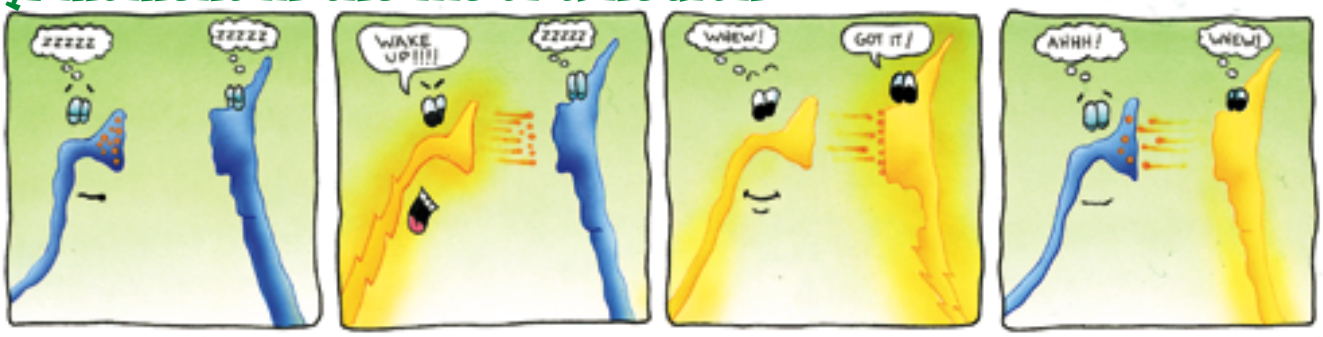
In the illustration, this wave, called an action potential, has reached the end of the axon, where it has caused the neurotransmitter to be released into the synapse. Some of the neurotransmitter has already bound to receptors on the next neuron stimulating the next neuron to "fire" electrically. This process continues from neuron to neuron, reaching the many parts of the brain involved in interpreting and reacting to these signals.

Neurotransmitter which is not bound to receptors may be taken back into the neuron through a protein called a *transporter*. Once the transporter removes the neurotransmitter from the synapse, the receptors are no longer exposed to the neurotransmitter.

Scientists who study the brain may use their knowledge of how these signals travel from neuron to neuron to design drugs. For example, they might design a drug that blocks ion channels and prevents the action potential so the sensation of pain is not transmitted to the brain; that is how a local anesthetic works.

Next you will read about two examples of drugs that enhance signals by blocking the transporter so neurotransmitters have more chance to stimulate receptors.▼

## A moment in the life of a neuron




***Resting state*** ***Action potential*** ***Receptor stimulation*** ***Neurotransmitter removal***

# DRUGS AND THE BRAIN

## Miracle or Menace?

Many drugs work by changing the way the synapse functions. For example, the drug may bind to a part of the synapse such as a receptor, channel or transporter. Other drugs affect other parts of the neuron. If a drug binds to a brain cell, it can affect the brain functions controlled by that neuron. Sometimes the results of this are good, and sometimes they are bad.

### The Good News

Ashley, a high school student, couldn't remember when she had last felt good about herself. She had been a busy, energetic teenager involved in the school yearbook, Drama Club, and year-round competitive swimming. She aced most of her courses and maintained an active social life.

Gradually, her energy disappeared, and it now seemed impossible to have ever felt so vibrant and happy. She no longer cared about school or swimming, and she thought her friends no longer cared about her. Her grades slipped to Cs.

Ashley's mother scheduled a doctor's appointment. The doctor diagnosed "clinical depression" and prescribed a drug to combat depression called Prozac®. Within a month, Ashley felt like herself again and renewed her activities with enthusiasm.

What happened? Ashley's depression probably resulted from a small shift in the biochemical activity of a region of her brain involved in emotion and motivation. Prozac® treats this effect by increasing the amounts of the neurotransmitter *serotonin* in her brain. It does this by blocking the serotonin transporter, so that the serotonin the neurons release has a longer time to stimulate their receptors. (See the discussion of the synapse on page 6.) From the ability of this drug to reduce depression, neuroscientists figured out that the neurons in the brain containing serotonin or serotonin receptors play a very important role in maintaining a healthy balance of emotions.

### The Bad News

Working with a rehab counselor, Tom recalled how he had slipped into a pattern of substance abuse that had ruined his future. His childhood had been happy and comfortable. He excelled in soccer and earned good grades in middle school.

When he was fourteen, he started sneaking drinks of alcohol and he soon tried other drugs. By the time he was a senior in high school, he was using marijuana and cocaine regularly. On the night of his senior prom, he lost control of his car and slammed into a telephone pole. The crash killed his girlfriend and left him paralyzed from the waist down. Tom tested positive for cocaine.

What happened? Abused drugs affect receptors or other proteins in the brain, just as medications do. Cocaine increases the levels of the neurotransmitter *dopamine* in much the same way that Prozac increases the level of serotonin, by blocking the *transporter*. One cluster of dopamine neurons in the brain enhances the pleasure we experience when we do something important to our survival, such as eating. When drugs like cocaine over-stimulate the release of dopamine in this region of the brain, the "user" can be overcome with the urge to pursue the pleasurable sensation and thus become dependent on the drug. ■

## The Pleasure Center

Scientists found evidence of a dopamine "pleasure center" by studying laboratory rats. The rats were trained to push a lever that electrically stimulated a part of their brains where dopamine is produced. The rats repeatedly pressed the lever for hours, ignoring food and water, to continue the stimulation. (In the same way, people addicted to drugs will neglect their health to stay high.) These findings led to the concept of "reward circuits" in the brain. Scientists have found that many different abused substances (such as cocaine, amphetamine, nicotine, and heroin) may directly or indirectly increase dopamine release in this part of the brain. Thus, these dopamine neurons may provide a common link to understanding the basis of dependence to a variety of drugs. You can read about more methods used to study brain functions on pages 12-13.▼

Elliot S. Valenstein, Ph.D.,University of Michigan

*A rat with a stimulating electrode implanted into its brain. The rat is pressing a lever that delivers a mild electrical current to a part of the brain that generates a pleasurable sensation.*

# Brain Careers

**PLUS**

People from many fields are involved in brain research, which has come to be known as *neuroscience*. The brain can be studied at every level, using almost every discipline from physics and mathematics to chemistry and psychology. If you are interested in one or more of the following areas, you could someday make an important contribution to the study of the brain.

- Molecular biology
- Biochemistry
- Medicine
- Endocrinology
- Physiology
- Pharmacology
- Psychology
- Experimental Psychology
- Clinical Psychology
- Cell biology
- Physics
- Computers
- Electronics
- Imaging

# Profile of Sandra Moon, *Neuroanatomist*

Sandra Moon knows that her profession, neuroanatomy or "anatomy of the brain," needs a bit of explanation. "If you want to know how a complex machine works, it helps to have a blueprint of it. It's the same with the brain. A neuroanatomist helps put together a blueprint of the brain."

Sandy earned her Ph.D. from M.I.T. and now works at Bristol-Myers Squibb in Wallingford, CT. Her department develops new medications for diseases and disorders of the nervous system. Over the past twelve years, she has worked on medications for anxiety, schizophrenia, depression, and learning and memory impairment. More recently, her lab is researching strokes. (See page10.) "The brain is a very hungry organ," Sandy explains. "It consumes 20% of all the oxygen in the blood. During a stroke, the source of oxygen is blocked and the brain suffers. Our ability to save injured brain cells will depend not only on the medications we are developing, but also on what part of the brain is damaged." That's where neuroanatomists come in. They help determine where a new chemical works in the brain so they can know whether it could become an effective medication.

***We will always depend on the new ideas and methods that young scientists contribute. In its study of the brain, science returns to one of humanity's oldest questions – Who are we? In seeking answers to this question, the tools of biotechnology are now playing a critical role.***

Sandy loves her job for several reasons. "First, it requires good manual skills just like my other hobbies: playing the piano, painting, and making paper. In addition, brain cells are very aesthetically pleasing. When I look at their shapes through the microscope, they remind me of a kaleidoscope. I also like the intellectual challenge of trying to figure out how the brain works. And last but not least, it's so exciting to know that my research will have an impact on people's lives in just a few years."■

# Brain Bogglers

## Neuroscientists are seeking answers to these questions:

1. How are memories formed and stored in the brain?
2. In what ways does learning change the brain?
3. In what ways do drugs change the brain?
4. What causes addiction to certain drugs?
5. What causes mental illness?
6. What causes aggressive or violent behavior?
7. Why do we sleep and dream?
8. Why and how do neurons die?
9. How can neurons be stimulated to regenerate after injury?
10. How does the brain give rise to thought and consciousness?

**DID YOU KNOW THAT...?**

***Neuropharmacology* is the study of how certain drugs affect the brain and other parts of the nervous system. A "drug" is a substance taken into the body that interacts with cells and changes the way they function.**

# Alzheimer's Disease: Fading Memories

***"I have recently been told that I am one of the millions of Americans who will be afflicted with Alzheimer's disease . . . I now begin the journey that will lead me into the sunset of my life."***

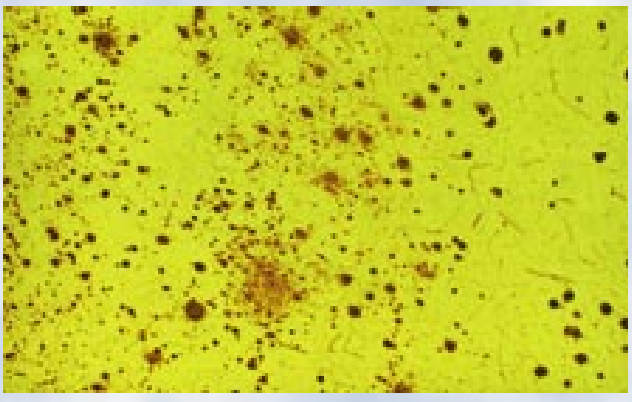
*President Ronald Reagan,*
*November 5, 1994*

Ronald Reagan's words brought home the realization that the devastating brain disease called Alzheimer's can happen to anyone, even a two-term president of the United States. Chances are you will know someone who has Alzheimer's. There is presently no effective treatment for Alzheimer's disease, but as researchers learn more about it, future treatments appear possible.

In Alzheimer's disease, neurons in the cortex and hippocampus that control higher mental functions such as learning, memory, and problem solving continually die. When they die, the connections between neurons are lost. These losses destroy the person's ability to reason and remember, and they cause changes in personality and emotion.

The brains of Alzheimer's patients are riddled with large deposits (called *plaques*) of an abnormal protein known as *amyloid*. Amyloid plaques accumulate around the neurons and within the walls of the blood vessels serving the brain. Researchers believe that these abnormal plaques may cause the neurons to die, so they are trying to learn exactly how amyloid is made and deposited around these brain cells. If they could understand the chemistry involved in this process, they might be able to design drugs to block the process that causes amyloid protein deposits to form.

Scientists are learning more about the chemical processes involved in the disease by analyzing the genes in Alzheimer's patients. Many cases of Alzheimer's disease clearly are inherited, and more than one gene defect seems to be related to the disease. This suggests that Alzheimer's disease is caused by several gene defects.



Robert Sitman, Ph.D.; Cephalon, Inc.

*Amyloid plaques in the cerebral cortex of a patient who had Alzheimer's disease.*

One of the major groups of neurons that die in Alzheimer's disease contains the neurotransmitter *acetylcholine*. One current treatment is the drug Cognex®, which increases the levels of acetylcholine by blocking the enzyme that normally degrades this neurotransmitter. Cognex® temporarily improves mental function for some patients, but does not slow the progress of the disease. Another approach being explored involves using *nerve growth factor*, a protein that helps neurons containing acetylcholine survive. Although this protein would not eliminate the cause of cell death in Alzheimer's disease, it might allow many of the affected neurons to survive. ■

# Wanted: Medical Breakthroughs

## Brain and Spinal Cord Injuries: Accidents Can Happen To Us All

In 1995, actor Christopher Reeve was thrown from a horse, crushing his spinal cord. During the assassination attempt on President Ronald Reagan in 1981, Press Secretary James Brady was shot in the head. Despite the best available medical care, Christopher Reeve is paralyzed from the neck down, and James Brady slurs his speech and has limited use of his arms and legs. Why were these injuries so severe, and what can researchers do to help?

More than two million Americans suffer brain or spinal cord injuries each year. About 100,000 of these injuries lead to life-long disabilities. Most of these victims are young, and many of them were injured in car or bike accidents. The good news is that research is leading to exciting new treatments.


Unlike many kinds of cells, which multiply to heal wounds, neurons can never be replaced. If they are lost, then the functions they control, such as sensation, movement, speech, or learning, are lost, too. Even if the neuron itself survives an injury, damaged or severed axons may destroy the communication pathway.

Currently, spinal injuries are treated with a drug that reduces the loss of neurons responsible for sensation and movement. However, there are presently no treatments that can restore the neurons lost to injury.

In July 1996, Swedish researchers announced an important breakthrough in treating injuries to the spinal cord. These scientists successfully restored some leg movement to rats that were partially paralyzed with a severed spinal cord. The scientists bridged the gap in the spinal cord with nerve grafts taken from the animal's chest. A growth factor added to the nerves promoted their growth. Over several months, the new nerves grew several centimeters down the spinal cord and re-established connections with some of the motor neurons that control the legs.

While treatments for these devastating injuries will be developed, the best weapon we have to fight them is prevention! Seat belts, helmets, and basic firearm safety practices would prevent thousands of injuries. For brain and spinal injuries, an ounce of prevention is worth tons of cure.

## Stroke: News of Success Against a Crippling Illness

Neurons are so sensitive to a lack of oxygen that interruption in the flow of blood to the brain for as little as 5 minutes can cause devastating injury. When this loss of blood flow is caused by blockage of the blood vessels serving the brain, the injury is known as a stroke. Each day, 1,200 Americans suffer strokes, and their injuries range from mild memory loss to extensive paralysis or death.

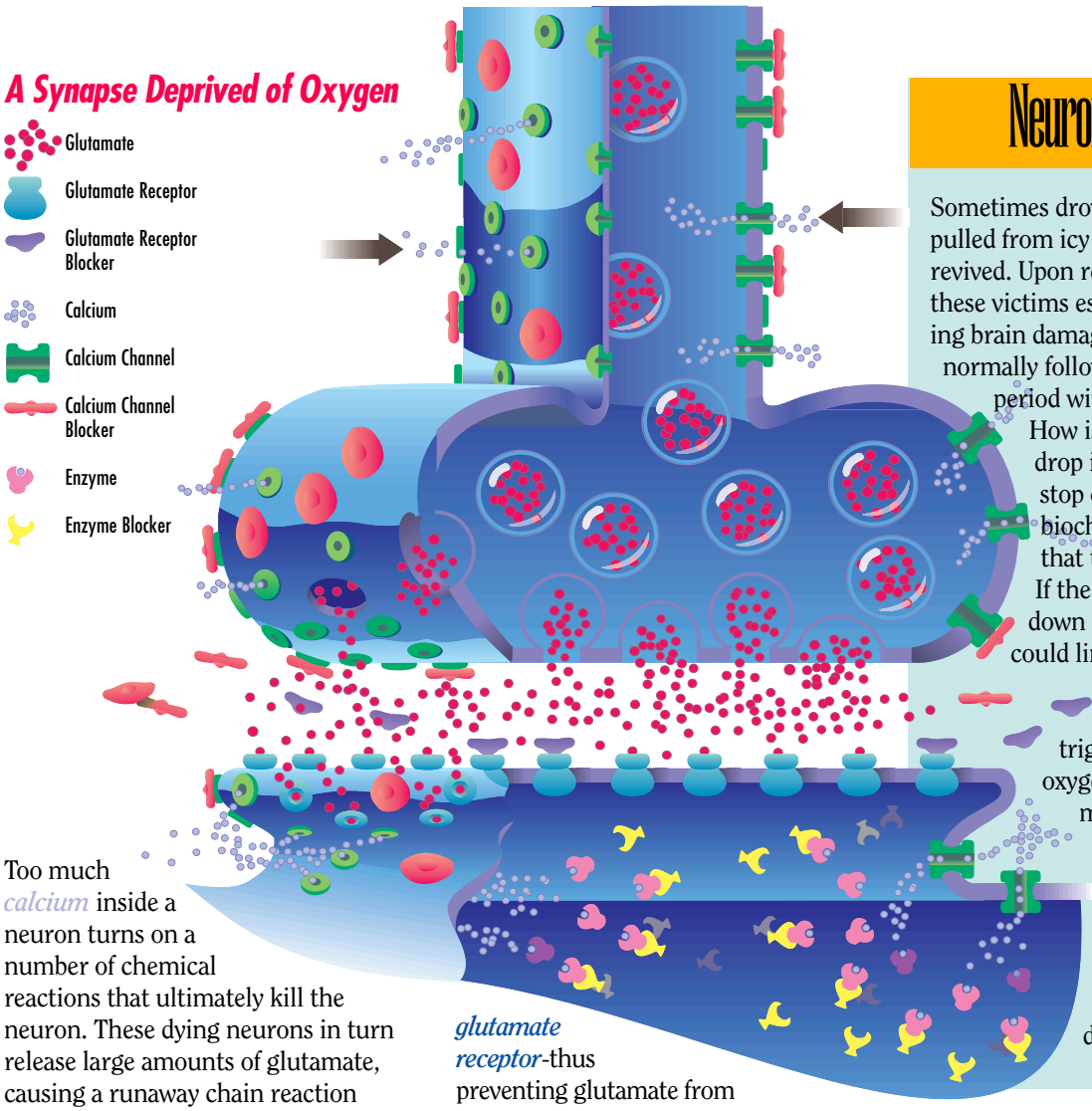
A recent test in the U.S. and Canada demonstrated the first successful treatment for stroke, based on a drug that disolves blood clots. Stroke patients with blood clots blocking one of the main arteries of the brain were given a genetically engineered enzyme called tPA within three hours of the first symptoms. This tPA treatment dissolved the blood clots and significantly reduced permanent disabilities in these patients. Researchers now hope to combine tPA with drugs that are being developed to reduce even more the damage caused by strokes.

## The Synaptic Switchyard

As researchers learn more about neurons and synapses, we can begin to use our understanding of the machinery of the synapse to design drugs that will let us switch some signals on and off or reduce their strength to control undesirable conditions. The synapse illustrated on page 11 shows many possible sites where we can alter the signals crossing the synapse.

For instance, strokes and many brain and spinal cord injuries deprive neurons of oxygen. When this happens, the neurons release large amounts of the neurotransmitter *glutamate*. Glutamate causes calcium ions to flood into neurons through *calcium channels*.

## A Synapse Deprived of Oxygen




Too much *calcium* inside a neuron turns on a number of chemical reactions that ultimately kill the neuron. These dying neurons in turn release large amounts of glutamate, causing a runaway chain reaction that spreads to more and more neurons. As a result, many more cells are destroyed than were originally damaged by the lack of oxygen.

Researchers, using animal models, are exploring ways to alter the chemistry of the synapse to prevent the chain reaction. In one approach, they may give the animals a *glutamate receptor blocker* - a drug that binds to the *glutamate receptor*-thus preventing glutamate from attaching to the receptors and starting the chain reaction. In another approach, they may give the animals a *calcium channel blocker* - a drug that blocks the entry of calcium into the neurons. A third approach is to give the animals an *enzyme blocker* - a drug that blocks the *enzyme* reactions triggered by calcium. All three approaches are demonstrated in the figure.

## Neurons on Ice

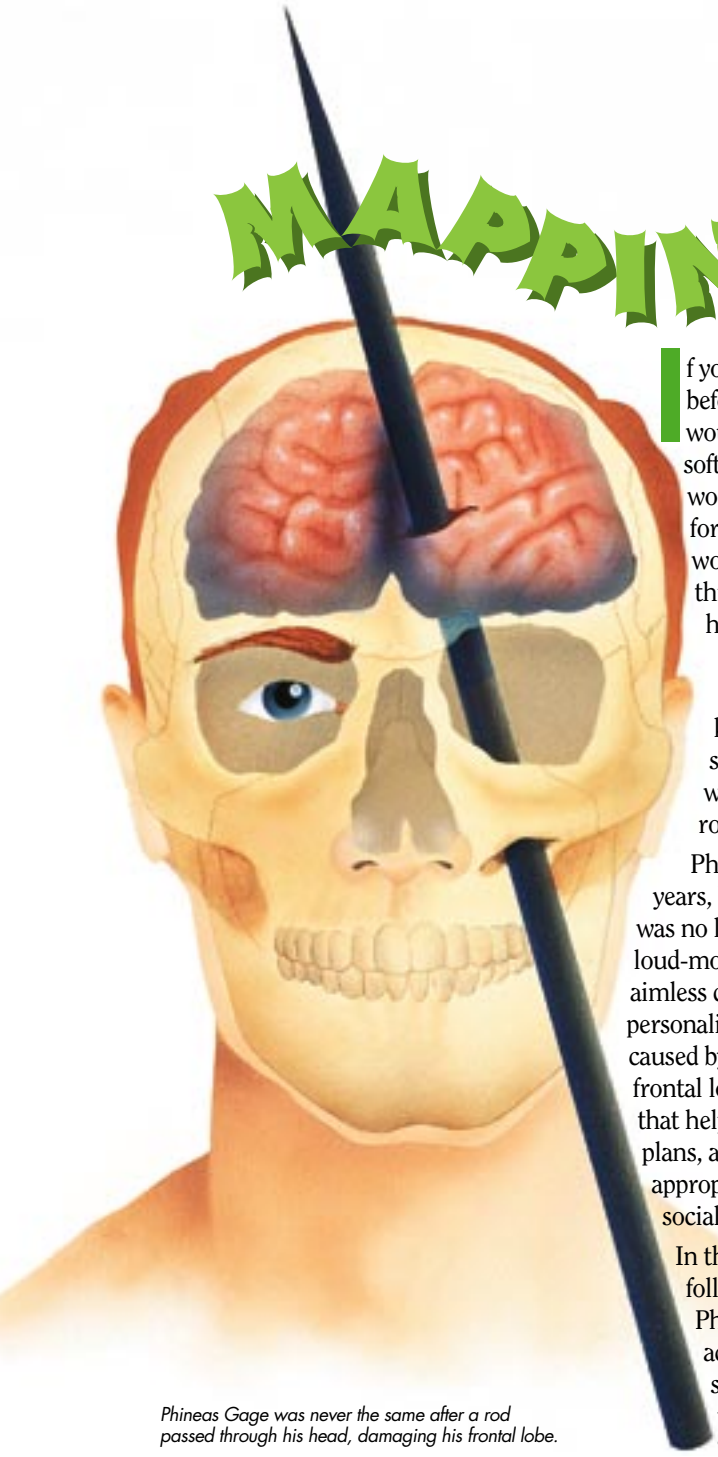
Sometimes drowning victims pulled from icy waters can be revived. Upon recovery, some of these victims escape the devastating brain damage that would normally follow such a long period without oxygen. How is this possible? A drop in temperature can stop or slow the biochemical reactions that take place in a cell. If the brain is cooled down quickly enough, it could limit the deadly glutamate chain reaction that is triggered by lack of oxygen. Some experiments with strokes in animals show that cooling the brain a few degrees below body temperature can prevent brain damage. ▼

The more we learn about the mechanisms that destroy neurons, the more hope scientists have of designing drugs to rescue neurons after a stroke or injury to the head or spine. These same methods may also help treat other diseases in which neurons die, such as Alzheimer's disease.
(See page 9.)

## The Death of a Neuron


*Resting state* *Glutamate attack* *Calcium flood* *Cell death*

# MAPPING THE MIND



*Phineas Gage was never the same after a rod passed through his head, damaging his frontal lobe.*

If you had met Phineas Gage before his accident in 1848, you would have liked him. He was a soft-spoken, dependable fellow working as a construction foreman until an explosion at work hurled a thirteen-pound, three-foot-long metal rod into his left cheek and out the top of his head.

Incredibly, Phineas was not killed! Instead, he sat up a short time later, rubbed his wound, and asked where his rod went.

Phineas lived another twelve years, but as a different man. He was no longer quiet and reliable, but loud-mouthed, obscene, and an aimless drifter. This dramatic personality change was probably caused by massive damage to his frontal lobe, the part of the brain that helps us make and carry out plans, and behave appropriately in social situations.

In the years following Phineas' accident, scientists began to develop a "functional map" of the brain that identified which parts of the brain controlled specific functions. Today, scientists continue to learn more details about what parts of the brain do. Here are some of the techniques they use to "map the brain."

## Brain Lesions

Lesions are places where a tiny part of the brain has been removed or destroyed. By making surgical lesions in anesthetized animals and then studying the changes in the animals' behavior, scientists can learn about the function of different brain areas. Scientists also use chemicals called *neurotoxins* that destroy specific types of neurons. What do you think would happen to the laboratory rats on page 7 if a neurotoxin destroyed the neurons that use dopamine as a neurotransmitter?

## Electrical Recording

By recording the electrical current flowing through individual neurons in the brain in active animals, scientists can study the brain's firing patterns as they happen. That's how scientists learned that different neurons respond to different small features of a visual scene. It is the combination of all these millions of features that recreate the scene in our brains and allow us to see the world around us. (See "Fire!" on page 3.)

**DID YOU KNOW THAT...?**

**... Brain tissue is insensitive to pain. In some cases, patients undergoing brain surgery may have only local anesthetics, so they can stay awake and talk with the surgeon during the operation.**


"Whoa! *That* was a good one! Try it, Hobbs — just poke his brain right where my finger is."

## Diagnostic Brain Imaging

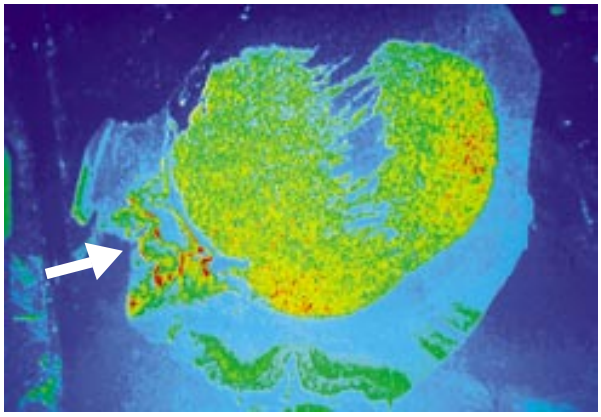
Positron emission tomography (or PET), provides a way of measuring brain function in awake people. First, patients are injected with a radioactive substance that concentrates in the most active parts of the brain. A brain scanning machine and a computer convert this information into a color-coded picture of brain activity, with the brightened colors showing the areas of the brain that are most active. The cover of this magazine shows PET scans of two people performing different tasks.

## Neurotransmitter and Receptor Mapping

To find where a specific neurotransmitter is located in the brain, scientists make antibodies to that neurotransmitter. (An antibody is a protein that binds to one specific molecule. In our bodies, antibodies block disease-causing microorganisms by binding to them.) Scientists spread the custom-made antibodies on a thin slice of the brain, and the antibodies attach to their matching neurotransmitters in the slice. Then, scientists add a specially treated protein that binds to the antibody, making a kind of triple-decker sandwich: protein on antibody on neurotransmitter. Before adding this protein, scientists treat it so it will glow or cause a color change after binding to the antibody. When they look at the brain slice under a microscope, scientists can see where the neurotransmitters are by the location of the glow or color. Scientists can use a similar process to locate specific receptors (the proteins that "receive" neurotransmitters). (See page 5.)

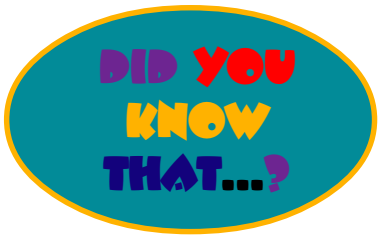
## Probing the Brain

Scientists have identified genes (the DNA sequence) for many proteins, such as neurotransmitter receptors and transporters, that influence brain functions. Using the DNA sequence, scientists can make a "probe"-a piece of DNA or RNA-that will attach to the "messenger" RNA (mRNA) responsible for making a specific protein inside a cell. They treat the probe with a chemical that makes it glow, and spread a solution containing many copies of the probe on a thin slice of the brain. Scientists can then determine if a particular gene is "turned on" (actively making the protein encoded by it) by finding the glowing probe on the slice. Using this technique, neuroscientists have learned that certain genes are turned on and off at different times in neurons, such as when the brain is being formed during fetal development, or when an animal learns something new.■



James H. Meador-Woodruff, M.D./University of Michigan

*A probe shows the mRNA for the dopamine receptor in a region of the human brain containing many dopamine neurons. The arrow points to a part of the brain that is associated with pleasurable sensations.(See "The Pleasure Center" on page 7.)*




**. . . If the connections between the two halves of the brain are cut, each hemisphere appears to function independently of the other, with its own distinct consciousness and abilities!**


**The brain "expresses" (turns on) more genes than any other tissue in the body. Why?**

## Gene "Knock Outs"

A modern version of the "lesion" experiment involves the use of genetically engineered mice. By making a selective mutation in the DNA within a fertilized mouse egg, scientists can now breed mice that are missing one particular gene. This deletion is call a *knockout*. A "knockout" experiment allows researchers to evaluate the effects produced by the absence of one specific protein (the one normally made by the gene that has been knocked out).

In a dramatic example of this technique, scientists deleted the gene for the dopamine transporter, the protein responsible for removing dopamine from the synapse and shuttling it back into the neuron that released it. Cocaine attaches to the dopamine transporter and increases the amount of dopamine in the synapse by preventing its removal through the transporter. (See page 7.) Normal mice injected with cocaine show a burst of hyperactivity caused by the increased levels of dopamine in the synapse. However, mice lacking the dopamine transporter are hyperactive all the time – because the excess dopamine stays in the synapse and continues to stimulate the dopamine receptors. When these animals are injected with cocaine, they show no response whatsoever! Why do you think this happens? ▼

# EXPERIMENT: Getting The Point

## Making Skin Sensory Comparisons

### Questions

Have you ever noticed that some areas of your skin are more sensitive to touch than other parts? What could account for such differences?

Can you determine differences in skin sensitivity by testing for the location of receptors in the skin?

### Make a hypothesis

Predict which skin areas are most sensitive to touch.

### Experiment

Work in groups of three; each team consists of a:

- **Subject:** Volunteers his/her skin for the sensitivity tests.
- **Measurer:** Touches a prepared card to the subject's skin surfaces.
- **Recorder:** Records plus or minus signs onto the data table for all six areas of the skin.

### Materials

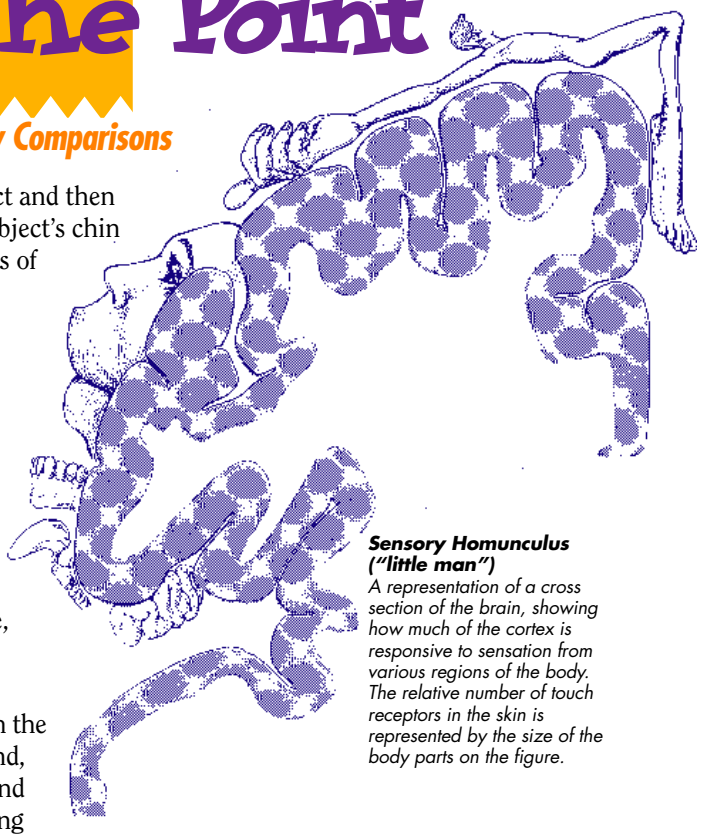
tape
toothpicks *cut in half*
note pad
metric ruler
blindfolds
index card

### Procedure

1 All teams use the following six skin areas to touch for sensitivity:

a. chin
b. forearm
c. back of hand
d. palm of hand
e. index finger
f. thumb tip

2. Tape pairs of toothpicks onto the index card as shown to the right so they are 2mm, 6mm, and 12mm apart. Make sure to label each pair of toothpicks. Tape a single toothpick to one end of the card.
3. Prepare a data table with the six skin areas listed down the lefthand column and the three toothpick distances across the top.
4. Blindfold the subject and then gently touch the subject's chin with one of the pairs of toothpicks. Make sure the two points touch the skin at the same time. Ask if s/he feels one point or two.
5. If the subject feels two points, record a plus in the data table. If s/he feels only one, record a minus.
6. Repeat this step with the forearm, back of hand, palm, index finger and thumb tip, alternating between the different pairs of toothpicks in random order. Occasionally use the single toothpick so the subject won't assume you are always using two points.
7. Remember to record a plus or minus for each measurement with a pair of toothpicks. (It is not necessary to record the response to the single toothpick.)



***Sensory Homunculus ("little man")***
*A representation of a cross section of the brain, showing how much of the cortex is responsive to sensation from various regions of the body. The relative number of touch receptors in the skin is represented by the size of the body parts on the figure.*

### Results

1. Record results from each team on the board or overhead.
2. Analyze class data:
   - What areas of the skin appear to be most sensitive? Least sensitive?
   - What does the data tell you about the distribution of receptors in the skin?
   - How could you measure the magnitude (size) of the difference in sensitivity between different skin areas?

### Conclusion

1. How did the test results compare with your predictions?
2. Why are some skin areas more sensitive than others? ■

# Ethical Issues in Neuroscience

## HEAD GAMES

With many illnesses, it's pretty easy to tell when a drug treatment works and whether its benefits outweigh any negative side effects. For example, if you have strep throat, antibiotic medicines can make you "normal" again–make your flaming throat stop hurting. The benefits of the antibiotics are usually worth the small problems they can cause, such as an upset stomach. But if you have a disorder that affects your personality, mood, or thinking ability, it's hard to know when a drug makes you "normal." It's also hard to judge whether the effect of the drug is a beneficial "treatment" or an unintended/negative "side effect." The patient taking the drug may have very different views about it than the doctor, family, friends, or teachers.

### Case 1: Creative Chaos

A talented young artist has uncontrollable behavioral urges. She does socially unacceptable things, and as a result she cannot make or keep friends. She has trouble staying calm and focused in class, and can't get her school work done. Her doctor gives her a drug that calms her down. Her social behavior improves, and so does her school work. But she is not happy, because she feels she has lost the creative insights she once had and her artwork has gone downhill. She wants to stop taking the drug.

### Questions

Do the benefits of this treatment outweigh the side effects?

Who should make the decision? The artist? The doctor? The teacher? Family? Friends?

Are the girl's behavioral urges simply a "personality trait" or a "disorder?" What about the creative energy?

### Case 2: The Real Me

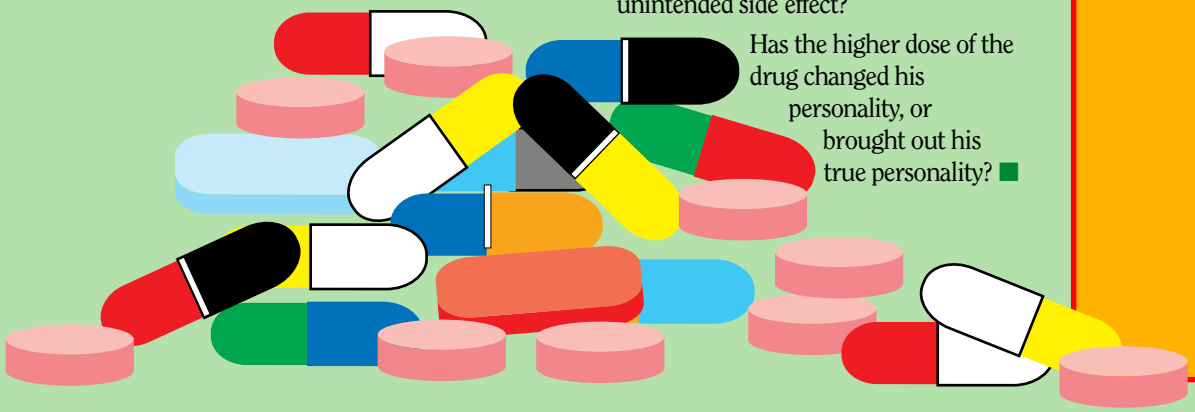
A teenage boy becomes clinically (medically) depressed, and is treated with a drug that increases his energy level and improves his mood. The doctor begins the treatment with a high dose of the drug. This high dose raises the boy's mood and energy levels above what they had been back when he felt "normal"– before the depression started. Once the depression is under control, the doctor lowers the dose. The boy is no longer depressed, but he misses the high energy and feeling of well-being that the higher dose gave him. He wants to keep that "edge," which he claims is "the real me." He asks his doctor to put him back on the higher dose because he doesn't feel "himself" at the lower dose.

### Questions

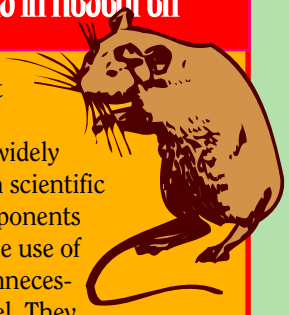
Should the doctor put the boy back on the higher dose?

Is the boy's feeling of high energy and well-being at the higher dose a desirable treatment effect? Or is it an unintended side effect?

Has the higher dose of the drug changed his personality, or brought out his true personality? ■



## Animals in Research



Despite great controversy, animals are widely used today in scientific research. Opponents claim that the use of animals is unnecessary and cruel. They believe scientists should be able to grow tissue in the laboratory or use computers to accomplish the same goals.

Scientific researchers, on the other hand, argue that current alternatives to animal testing are not sufficient. Complex brain functions cannot be imitated in a tissue culture dish or computer. Many in the research commuity believe that animal research must remain an option for now in order to test some drugs or surgical procedures on animals rather than on humans.

### Questions

1. Do we have the right to use other living creatures for our own benefit?
2. Is it right to use animals to save human lives?
3. Would it be preferrable to test new drugs or surgical procedures for the first time on humans or animals? ▼

# REFERENCES

## Read More About It!


**World of the Brain** by Alvin and Virginia Silverstein: ISBN 0-688-05777-2

**Understanding Your Brain** by Rebecca Treays; ISBN 07460 20147

**You and Your Body, Brain** by Douglas Mathers; ISBN 0-8167-2091-6

**Know Your Brain** available through NINDS (address below)

**Your World/Our World**:

Vol.4, No. 2 (Gene Therapy)

Vol. 5, No. 1 (Transgenic Animals)

Vol. 5, No. 2 (Human Genome Project)

**Organizations:**
**Society for Neuroscience**
11 Dupont Circle, N.W. Suite 500
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(202) 462-6688
http://www.sfn.org

**National Institute of Mental Health (NIMH)**
Information Resources and Inquiries Branch
5600 Fishers Lane, Room 7C02
Rockville, MD 20857
(301) 443-4513
http://www.nimh.nih.gov

**National Institute of Neurological Disorders and Stroke (NINDS)**
Building 31, Room 8A16
31 Center Drive, MSC 2540
Bethesda, MD 20892
(800) 352-9424
http://www.nih.gov/ninds/

**Internet Sites:**
Neuroscience for Kids: http://weber.u.washington.edu/-chudler/neurok.html

Shufflebrain: http://www.indiana.edu/-pietsch/home.html

Addiction: http://idir.net/-irvcohen/index.html

Your World/Our World: http://www.bio.com/pba


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NeuroQuest@AOL.com

# Dear Students:

We are pleased to provide you with this issue of *Your World/Our World* on the human brain. We hope you find it an interesting way to learn about biotechnology. Biotechnology can be important to you for two reasons:

1. During your lifetime there will be tremendous discoveries in this field, and you'll want to understand what these discoveries will mean for you, your friends and your family.
2. You can help make those discoveries if you decide to continue to study science and math.

Either way, we hope you join us in discovering the promise of biotechnology for the world. We are pleased to acknowledge the support of the companies listed.

Sincerely,

Jeff Davidson

Executive Director
Pennsylvania Biotechnology Association


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