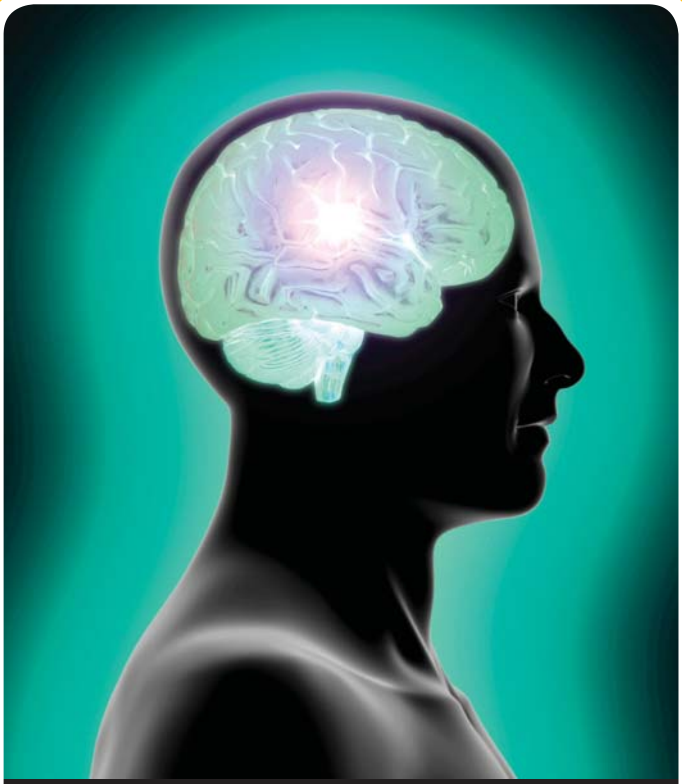
The Brain's Inner Workings



A GUIDE FOR STUDENTS

From the

National Institute of Mental Health

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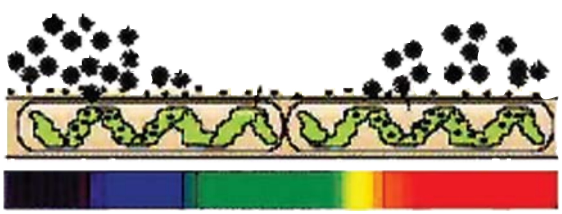
I. SIGNALS, SENSES, AND SURVIVAL

Have you ever watched tiny animals, like ants, walk across a sidewalk? Even if individual ants can't see one another, they seem to "get the message" and follow one another to food. By responding to their environment in a coordinated way, ants survive and thrive by sending chemical messages to one another.

Even single-celled organisms can respond to environmental signals such as light, gravity or chemicals. They can also coordinate their responses in a way that helps a group of organisms act together for their mutual advantage.

Are the messages ants send to one another visual, physical or chemical? Put a physical block (like a pebble) in their way. Can they make their way around it? Try disturbing them with noise. Then wash the surface carefully with window cleaner on a cotton swab to eliminate a chemical trail. Which kind of barrier confused their coordination?

Studying how single-celled organisms communicate can help us understand how the cells within larger organisms might coordinate their responses. One experiment that explored this problem was done in 1883, by biologist Theodor Engelmann. He took a long strand of the green alga Spirogyra and spread it across a microscope slide. Then he used a prism to create a spectrum (rainbow) of colors across the slide, so some parts of the alga got red light, some green, and some blue. Finally, he looked for tiny bacterial cells called *E. coli* in the water. These bacteria need oxygen to survive. He found that even the simplest bacterial cells could respond to chemical signals—and act together! They swarmed to the parts of the alga with the fastest rate of *photosynthesis*. They could sense the chemical oxygen that the algal cells released, and move toward it in a coordinated way. (Bacteria move by twirling whip-like flagella.)



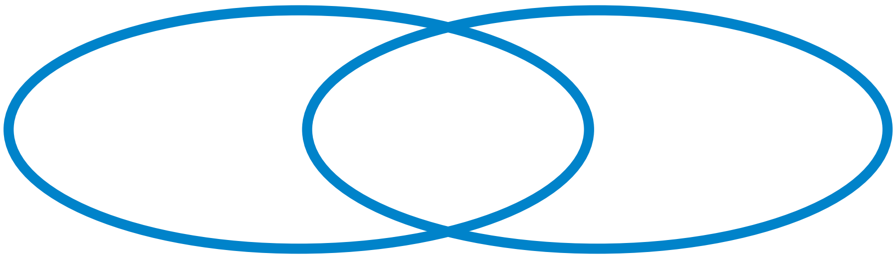
Ants, bacteria, and some 50 trillion cells in your own body must work together to survive. When cells respond to signals (stimuli), they help the organism maintain balance (homeostasis) despite challenges from the environment. In the next few pages, in video and experiments, you'll explore how these cells communicate and coordinate for survival. You'll explore the nervous system through amazing images in two videos, read about current research, and experiment on your own. When you have completed the activities in this module, you will have a better understanding of how your own cells communicate to survive, and how to make good decisions for your brain and your body's health.

Image source: *http://www8.nos.noaa.gov/coris_glossary/index.aspx?letter=f*

THE BRAIN'S INNER WORKINGS VIDEO PART I: STRUCTURE AND FUNCTION

Study Guide

1. Watch the beginning of the video carefully. Can you play an instrument? Kick a ball? Play chess? Are these inborn or learned skills? ____________
2. Why should we study normal brain function? ____________
3. If you could see the cerebrum, what structural features would you note? ____________
4. How many connections does a single nerve make? ____________
5. Why is the cortex folded? ____________
6. What is a dendrite? ____________
7. What is an axon? ____________
8. How are dendrites similar to axons? How are they different? Use a Venn diagram.



9. What is a synapse? ____________

____

10. Label the parts of the synapse shown at the right:
    1. ____________
    2. ____________
    3. ____________

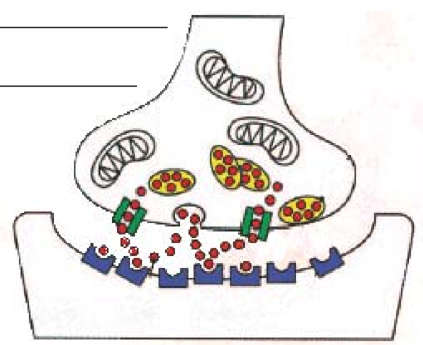


Image source: *http://www.nida.nih.gov/NIDA_notes/NNvol21N4/cell.gif*

11. Why should we study a synapse? ____________
12. What is a synaptic vesicle? ____________
13. What happens when a stimulus reaches a synaptic vesicle? ____________

____

____

14. What happens if an error occurs in this process? ____________
15. What new information do you want to know about the brain? ____________

____

KEEPING IN TOUCH

It's easy to imagine how a dozen ants, or even a thousand bacterial cells, might communicate. It's harder to imagine how trillions of different kinds of cells inside an organism might be coordinated for survival. The job of coordination is accomplished by the *nervous system* and the *endocrine system*. This module and the videos you'll see emphasize the nervous system, but you'll see connections to hormonal messages, too.

While the nervous systems of animals, from hydra to human, are different, they have many similarities too. Almost all animals have a *nervous system*, made of cells with highly specialized membranes working together. The basic functional cell is a neuron. Most neurons have small cell bodies and long extensions called axons and dendrites. Axons send information to target cells, while dendrites are the sites for receiving information. The nervous system also contains glial cells that support and nourish neurons. Some glial cells produce an insulating material called myelin. There may be ten times as many glial cells as neurons.

Some of the simplest organisms on Earth have neurons. One of the favorites of biologists is *Caenorhabditis elegans*, a tiny roundworm only about a millimeter long. It only has about 1000 cells, and about 300 neurons. Like much larger animals, C. elegans can respond with simple reflexes.

The message that passes down the dendrites through the cell body, and then away from the cell along axons is electrical. Cells are filled with charged ions, electrically charged molecules, like Na^+, Cl^-, K^+, and Ca^{2+}. When the cell is at rest, the inside contains more negative ions than the outside. We say the membrane is *polarized* like a battery. When the membrane senses a stimulus, the charge is temporarily reversed. The membrane immediately works to restore the original charge, but the next section breaks down. (Imagine a flame moving down the fuse of a firecracker.) From dendrite to axon, an electrical message travels through the cell at a speed of from 1 to over 100 m/s.

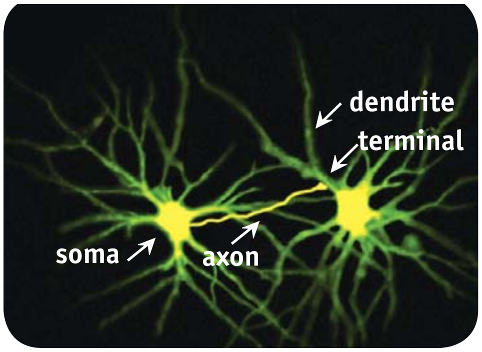


Image Source: *http://www.nida.nih.gov/*

At the end of the axon, the message changes. Between the terminal of one cell's axon and the dendrite of the next cell there is a tiny gap, called a synapse. The membrane there is able to release specialized chemicals called neurotransmitters. These chemicals jump the gap to the next cell, exciting the membrane of the nearest dendrite(s). That stimulus creates another electrical response, and the chain message continues. While you can't see the electrical signals that move down your nervous system, there are some great simulations. Begin with the video *The Brain's Inner Workings Part I*. Then review the structure of the neuron in the "Nerves" animation on the companion CD. Explore the speed of a nervous impulse in the "How Fast" animation on the companion CD.

Did You Know?

The platypus has thousands of electrical receptors on its bill. It senses the electrical signals from the nerves of its prey that way.

WALKING THE TIGHTROPE

Imagine you are snorkeling in the ocean, watching the sea life beneath you. Among the organisms you watch are sponges and sea anemones. A fish moves between them. Individual tiny cells of the sponge are probably responding by waving their flagella, too, but they are too small to see. It has no nervous system. The only communication between distant parts of the sponge would be through the slow movement of chemicals.

The anemone's response is different. It is coordinated. While it doesn't have a brain—a "front end"—to control its response, it has a way to send messages from cell to cell. It has neurons, arranged in a net to help the individual cells of the organism respond to the environment in a coordinated way. Unless the fish is a clownfish (protected by a special mucus) the anemone is likely to react by stinging the fish. The fish has a brain and complex nervous system. It learns. The sponge and the anemone are very simple examples of multicellular organisms. Comparing them provides good examples of how coordination can be an advantage in survival, and why the nervous system is so crucial. As animals (the Kingdom Metazoa) become more complex, their ability to respond in a coordinated manner increases too. More neurons are connected in more complex ways. They have more capacity to learn.

In the next four activities, you will examine how neurons help humans respond to their environment. You'll look at the structure of the neuron (one of the two basic kinds of cells in the nervous system). You will also compare what biologists can learn about the fine structure of a cell with different types of stains. Then you can explore sensory neurons in your skin. You won't have to use a microscope, or break your skin to find them. With a simple test, you can determine the distribution of the receptors for touch. Finally, you can test your own reflexes and compare them to learned responses in two separate activities. As you analyze your results, you will be asked to make inferences. Three ideas will help you do this.

- ? Structure and function are closely related even at the simplest unit of life, the cell. The neuron's ? cell membrane is very specialized.
- ? How do cells differentiate? A fertilized egg cell (zygote) divides and changes. They all still have ? the same genes, but not all the genes are expressed in all the cells. So soon it's easy to distinguish different kinds of tissues, each with its own role in the developing organism.
- ? The structures we observe in living things almost always have a survival advantage for living ? things. In the words of Charles Darwin, they make the organism "more fit" in some way.

ACTIVITY

The Neuron

Can you imagine the size of a single neuron? They look quite large in the video *The Brain's Inner Workings*. The tip of a dull pencil is about 2 mm across. Make a dot in the space above. The cell body of a neuron is closer to 0.02 mm. Can you calculate how many average cell bodies would fit in the dot you've drawn? Use an arrow and label your dot: "_______ neurons could fit in this spot." Of course, your estimate can't be very accurate. Neurons aren't dots. They are highly differentiated cells with membranes and processes that are specifically adapted for their function.

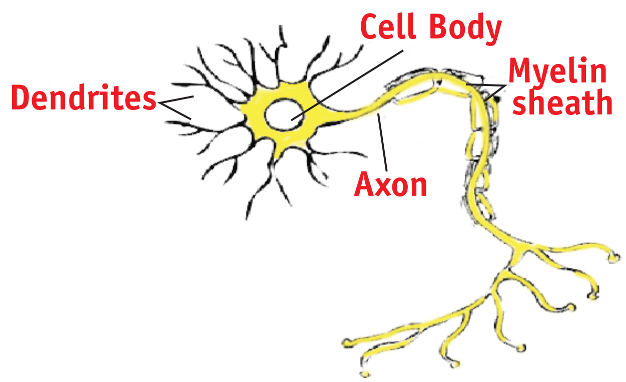


Image Source: *http://www.nida.nih.gov/JSP4/MOD1/images/neuron1.gif*

To see the bodies of cells under the microscope, we normally use special chemicals called stains that bind to specific organelles in the cell. The first effective stain for neurons was developed by German neurologist Franz Nissl about 1880. A few years later, an Italian histologist, Camillo Golgi, discovered another stain that could reveal neurons. But with Golgi's stain, the neurons looked very different. Look at the chart below. Compare the structures revealed by the methods of Nissl and Golgi. Then form a hypothesis: Why are they different? What organelles are shown?

Stain	Appearance	Chemical	Organelles
Nissl		Cresyl violet	
Golgi		Silver nitrate and potassium chromate	

Golgi's student, Spaniard Ramon y Cajal, helped find an answer to that question. In an amazing series of dissections, he revealed the structure of much of the nervous system. Golgi and Cajal shared the Nobel Prize in 1906, but they often disagreed. Golgi believed that neurons were all linked (like blood vessels). Cajal believed that brain cells touched one another, but only at specific locations called synapses. Who was proved right in the end? What evidence can you give for your answer?

DOES THE NOSE KNOW?

How do you sense the world? The simple answer, from your observations and your experience, is "through your cell membranes"—especially those specialized membranes on cells called neurons. But that doesn't explain it all.

Let's start by getting physical. There's a signal in the environment. It could be a chemical (like the trail the ants follow), a mechanical change (a touch or a vibration), or a form of energy like light or heat. That signal causes a change in a cell membrane.

Most complex animals have a variety of sensory cells in their skin—heat, pressure, light, pain, or sound. One small patch of skin might have receptors for all of these signals (except light). The receptors aren't just "on" or "off." They fire at a slow rate all the time. A stimulus changes the rate of that firing. This causes a change in the distribution of electrical ions on either side of the membranes of a specialized cell—a neuron. An "action potential" is generated, and a message begins to travel from neuron to neuron, to the spinal cord and then to the brain.

An odorant is a specific molecule that binds to a very specific receptor site on a cell membrane. Humans depend more on vision, but dogs may have more than 40 million nerve endings per square centimeter in their nose.

Sensory neurons also are inside your body. Chemical signals are especially important to the regulation of basic body functions. You have probably experienced the way dissolved carbon dioxide lowers the pH of soda and makes it more sour. ("Flat" soda is sweeter.) That change is a vital measurement for your survival. Here's a real-world example: When you run or swim hard, you produce a lot of carbon dioxide because you are burning sugar fuel quickly. A specialized mass of neurons near your neck, called chemoreceptors, sense that the pH of your blood is lower, and sends a signal to your brain. (Remember Englemann's experiment? The bacteria are sensing just the opposite!) Subconscious signals go to your brainstem, and your respiratory rate increases.

This is a simple reaction. Many other reactions are far more complex. When chemoreceptors respond to an odor that we haven't sensed since we were small children, it might trigger memories or even emotions. Many odors stimulate the release of neurotransmitters from the brain that are subconscious but very powerful. "Mom's Chicken Soup" might remind a person of pleasant memories, while another odor might remind you (subconsciously) of a terrifying childhood experience.

ACTIVITY

Signs and Signals

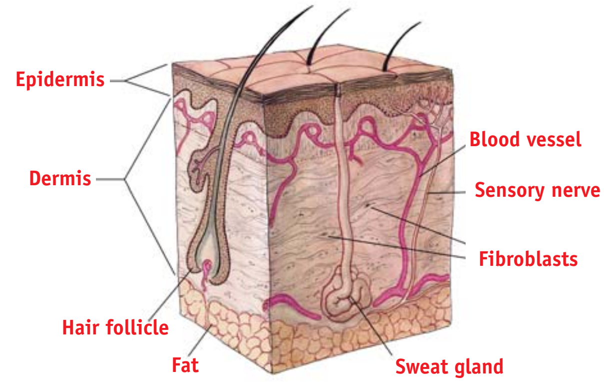


Image source: *http://www.nigms.nih.gov/NR/rdonlyres/0037E7BB-97A3-4EC6-904A-61CEEE4352EF/0/skin2.jpg*

Every organism must be able to sense the environment. This almost always occurs through cell membranes. You'll learn more about membranes in the next reading. But before you do, you can explore one special system of sensation in a simple yet accurate way.

In your skin, some of the specialized sensory neurons have membranes that respond to touch through receptor cells for pain, heat, and cold. Here's a way to measure them experimentally with a ruler marked in millimeters and a large paper clip. Separate the points of the paper clip by 2 cm. Ask a subject to cover his/her eyes and ask if he/she can feel one or two points on various areas of their body. Repeat the experiment with the points of the paper clip separated by 1 cm, .5 cm, and .25 cm.

Area	2 cm	1 cm	0.5 cm	0.25 cm
Forearm				
Cheek				
Index Finger				
Palm of Hand				

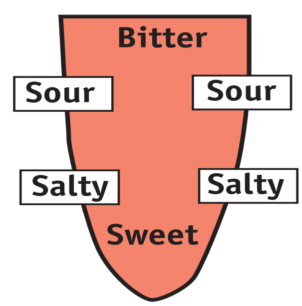
1. In what area were the touch receptors closest? ______________________________

____

2. What survival advantage might this difference have? ______________________________

____

Have you ever seen a "tongue map" that shows different tastes on different parts? Would you be surprised to know it doesn't exist? The 'tongue map myth' was based on a mistranslation of a German paper that was written in 1901 by a Harvard psychologist. Though small differences, which can be measured with highly specific instruments, occur in sensation in parts of the tongue, all taste buds can respond to all types of taste. But some people can taste much more sharply than others.



MEMBRANES AND MESSAGES

You may have studied *passive models* of cell membranes, but biologists know that membranes are very active indeed. The pores and permeability of membranes constantly change through the action of enzymes and energy.

Take a look at the diagram of a cell membrane on the right. Review what the membrane is made of: proteins and phospholipids. The outside ends of each molecule are slightly polar (slightly charged like the water molecule). The inside ends are non-polar. The membranes are studded with pores, vesicles, and special receptor sites.

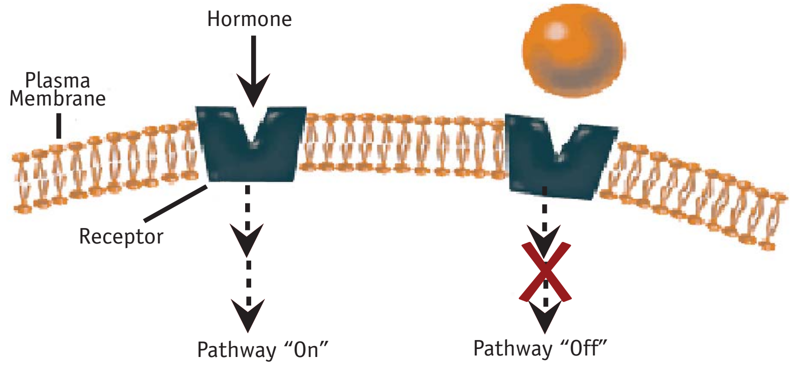


Image Source: *http://publications.nigms.nih.gov/chemhealth/images/ch4_party.gif*

Next look at the openings in the membrane first. One type of opening in a cell membrane that's very important in passing messages is an ion channel. There are many kinds. Potassium channels only allow K^+ ions to pass; calcium channels only allow Ca^{++} ions, and sodium channels Na^+. When an axon is in the resting state, the membrane is a little more permeable to potassium than to sodium or calcium. But enzymes use energy to create a difference in the amount of ions—a voltage—across the membrane. An enzyme system called the sodium-potassium pump transports ions from a lesser concentration to a greater concentration (just the opposite of diffusion) using energy to create and maintain this difference in charges.

Now imagine that something touches the cell membrane—something it recognizes like touch, pain, odor, or taste. Then special channels open and sodium ions flow inside the cell carrying their positive charges along. Those charges are just the opposite of what it would be if the cell weren't touched. So much flows in that the inside of the cell becomes more positively charged than the outside. We call this an action potential.

It hits a peak, then another channel opens and for a microsecond potassium flows freely. Potassium flows out until the cell is again negatively charged on the inside. Finally, the sodium-potassium pump goes to work and restores that portion of the cell to its normal resting state. But meanwhile the next section of the cell is affected and goes through the same process like flame down a fuse.

Soon the message hits the synapse. Then the message must be translated. Think again about the video *The Brain's Inner Workings Part I*. Did you see the action potential move down the axon? What happened at the synapse? How would you describe it to a friend?

ACTIVITY

Take That!

Image Source: *http://www.nida.nih.gov/pubs/teaching/Teaching2/largegifs/slide4.gif*

The simplest responses that organisms make to the environment are "hard wired" into their nervous systems. Some sensations trigger responses that occur without any analysis. They only involve the most primitive parts of the nervous system. You reach out and touch a thorn. You pull back without thinking about it at all! The message goes from sensory neuron to a connecting neuron in the spinal cord, and then to a motor neuron that moves a muscle. Explore:

1. Obtain two sheets of heavy, clear transparency acetate. You'll use these as your shield. Hold them up in front of a subject's face. Crumple a half sheet of paper into a ball (about the size of a ping pong ball) and toss it toward the subject's face. What is the reaction? ______________________________

2. Does the reaction change if the subject knows that the paper is coming toward his/her face? ______________________________

3. If the paper is aimed at one eye, does the other eye react in the same way? ______________________________

4. What is the survival advantage of this reflex? ______________________________

5. Next, lower the light in a room. Watch the size of your subject's pupils as you gently shine a small flashlight toward his/her eyes. What happens? ______________________________

6. Hold a note card parallel to your subject's nose. If you shine the light in one eye only, how does the other eye react? ______________________________

7. Now in full light, watch your subject's pupils again. This time, gently stroke the back of the subject's neck. How does this affect pupil size? ______________________________

8. Many of our simple reflexes are remnants of the time when humans were hunters. Think of the reactions you have to something that scares you (like a movie). What are your physical responses?

____

____

9. Which of the reactions above happen very quickly (in a second or less)? These are probably reflexes:

____

____

10. Which of the reactions you identified take a little longer (from seconds to minutes)? These are probably chemical signals. ____

____

Some reactions are completely unconscious. Explore how a reflex works in the "Reflexes" animation on the companion CDROM. Others aren't hardwired for survival, but are learned—mediated by our brains. Think of the first time you brushed your teeth. You probably thought "Left…right…up…down." But now it's almost unconscious. Your teacher will help you explore some learned responses using your classroom computer using the program "React."

ACTIVITY

It's the Thought that Counts

In the first section of this unit, you explored simple reflexes that were coordinated by unconscious connections, like the midbrain or the spinal cord. You observed them in the video, too. When you are stuck by a prickly cactus, you really don't think about it. The message goes from sensory neuron to spinal motor neuron. Use the first figure to show how that series of messages might travel. In the computer program "React" you explored how quickly you could recognize a signal and respond with a simple click. That required some "intervention" by your brain, but not much. Let's take the progression one step further. In the second section of "React" you will be asked to recognize and separate left from right, and different kinds of shapes. Compare the average speed for each task. Then outline the path of the stimulus and response for the actions in a simple reflex (such as touching something that hurts), responding to a signal and responding to a signal that requires prior knowledge.

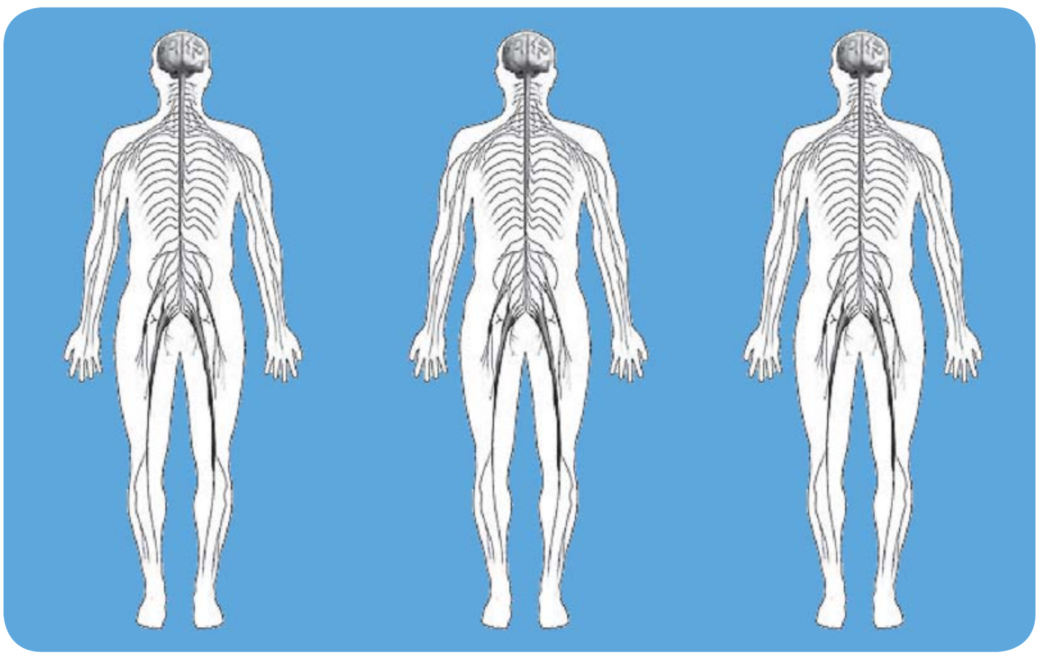


Image adapted from: *http://diabetes.niddk.nih.gov/dm/pubs/complications_nerves/images/fourparts.gif*

Take It Farther

Some biologists believe that the hardest task in sports is the action of a baseball batter hitting a ball. Think about it: The batter must not only react to an object approaching at over 90 miles per hour, but must have some knowledge of how that object moves through 3-dimensional space. (And if it's a curve ball, watch out!)

Web Search

The late, great biologist Steven Jay Gould was not only crazy about biology but was one of the most avid baseball fans ever. What can you find about his use of baseball stories to explain biology?

II. THE ALCHEMY OF LIFE

You've now read how electrical potential changes across a cell membrane, and watched a simulation of transmission of a message in the video. You've also learned that it's at the synapses—the places where neurons almost touch one another—where the situation becomes more complex. A cell can almost touch another, or thousands of other cells. In simpler animals and some higher animals, the electrical message can even cross the gap junction. But in most synapses in higher animals, the message that crosses the synapse is carried by a chemical called a neurotransmitter, released by synaptic vesicles. (This was simulated in the video as well.)

The simplest cells respond to chemical messages directly. (Remember Engelmann's experiment.) Even if an organism has several layers of cells (like a hydra or jellyfish) chemicals can diffuse from cell to cell, but this is a very slow way to communicate. In larger organisms, networks of nerves can speed up response. Your nose cells can respond to odors, and special receptors in your carotid arteries respond to the pH of your blood.

The many kinds of neurotransmitters don't just conduct messages but modify the way messages are transmitted. Many nerves release chemical messages in a coordinated way. Endocrine glands can release chemical messages, as well. So messages are continually transmitted and translated—like a complex United Nations debate—throughout the body. Here are a few of the neurotransmitters used by the human body:

- Glutamate is the primary neurotransmitter in the central nervous system that is released to increase the activity of neurons. It is especially important for memory and cognition.
- Gamma aminobutyric acid (GABA) is an inhibitory neurotransmitter, acting to reduce the activity of neurons.
- Norepinephrine is used by some brain neurons, and by peripheral nerves in the sympathetic division of the autonomic nervous system. It increases metabolism, respiration, and heart rate.
- Acetylcholine is released by motor neurons and some brain neurons. It is the primary neurotransmitter in the parasympathetic division of the autonomic nervous system.

In addition, these chemicals work in specific areas of the body to moderate physiology:

- Serotonin helps the brain moderate moods and aggression. Alcohol's effects on serotonin receptors are thought to be involved in the rewarding effects of alcohol.
- Dopamine is another reward neurotransmitter. It helps the brain and body relax, and appears to help coordinate muscles. Dopamine deficiencies are related to diseases like Parkinson's and overactive dopamine pathways involved in schizophrenia.
- Histamines, chemicals that cause your body to respond to cold viruses and allergens, are also neurotransmitters. Many more chemicals, including hormones like gastrin, gonadotrophins, endorphins, glucagons, thyrotropin, and insulin, don't necessarily connect nerve to nerve. They change the membranes of dendrites and thus coordinate body responses.

The Challenge of Chemicals from the Environment

A delicate balance exists between neurotransmitters in the nervous system, and how they affect the body. Someone drops a book, or approaches you from behind when you are deep in thought. A rush of norepinephrine sets all your senses on alert. But dopamine usually moderates your response so that you don't panic. You tip a little, but regain your balance.

These reactions are essential for survival. But sometimes their function is impaired by things we do or experience. Imagine you've had a long day, and you finish a meal with coffee and chocolate. Like many rainforest products, the chocolate contains a whole pharmacy of chemicals. One, anandamide, is very similar to reward neurotransmitters in the brain and makes you feel happy. It also contains two mild stimulants, caffeine and theobromine. The coffee has caffeine too. Suddenly, instead of relaxing you are wide awake again!

Your teacher may suggest a challenge to your homeostasis. Can you do a concept map to show all the changes in neurotransmitters that might occur?

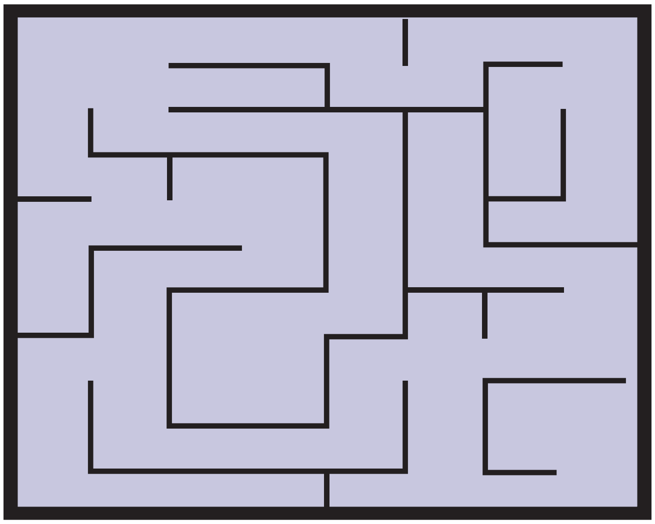
For most people, the effects of a single cup of coffee or a little chocolate are subtle and don't do much harm. But the effects of other drugs may be far more serious. They can mimic the action of neurotransmitters causing more serious reactions, or block the receptor sites for needed neurotransmitters, preventing the body from responding in the appropriate manner. Chronic use often changes the basic structure of neuron membranes—sometimes permanently. Here's an example. Scientists have known for many years that amphetamines affected the brain in ways that were very similar to symptoms of schizophrenia. We now know that they affect the neuron's sensitivity to dopamine (among other effects) by changing the function of receptor sites. The body's natural balance is altered.

Alcohol is another widely abused drug that changes neurotransmitter balance. Alcohol blocks reception of glutamate, preventing the hippocampus from changing short-term memories to more permanent ones. It also enhances receptor mechanisms for GABA. All these changes confuse a system that originally evolved for survival.

ACTIVITY

Use Your Brain!

In about 1300 grams, your brain has as many as 10 billion neurons and perhaps 10 times that many glial cells to nourish them. Each neuron can contact more than 1000 others across their synapses. Imagine all the connections you could make at one time! Somehow, you are able to concentrate and focus on a single task.



Here's an activity you can use to investigate how you learn, and your ability to concentrate. You will need colored pencils, a clock with a second hand, an MP3 player and a jar of crushed garlic. Appoint one of your team members to be the Principal Investigator. In a quiet setting ask each member of your team to try this maze.

Record the baseline time required for the maze. Next, go to the Web site *http://www.onebillionmazes.com/?t=0* and print out 4 copies of each of the first four mazes. Distribute them at random to the 4 subjects in your group upside down. Determine the time for each group member to complete the maze.

For step 2, you will redistribute the mazes so that each member gets a different version. You will also provide a distraction, in the form of music. Begin the music, then ask your subjects to again see how fast they can solve the mazes. For step 3, you'll again redistribute the mazes. But this time, each subject must sing his/her favorite song while they are doing a third maze. Finally, for step 4, the experimenter opens a jar of garlic to provide a strong odor to distract as the mazes are solved. Record the times on this chart:

Subject	Maze Only	With Music	While Singing	With Odor
Average Time				

1. The mazes from the Web site aren't guaranteed to be of equal difficulty. What technique did you use to try to minimize this source of error? ____

____

____

2. Use the diagram below to indicate which parts of the brain were involved in the tasks: shade the areas required to do the basic maze in grey (pencil), the area that analyzes music in red, the area that generates speech in blue, and the area that responds to odors in green.

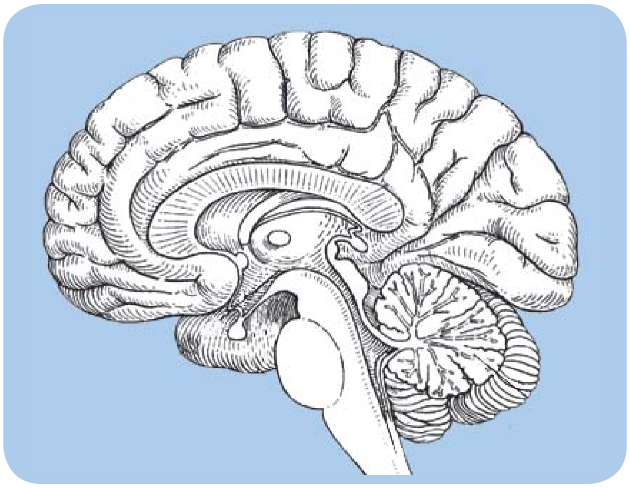


Image source: *http://pubs.niaaa.nih.gov/publications/arh284/images/tapert.gif*

THE BRAIN'S INNER WORKINGS VIDEO PART II: COGNITION

Study Guide

The first video traced the path of a message down a single row of neurons. In this video you learn about how neurons work together.

1. What is "higher order thinking?" ____

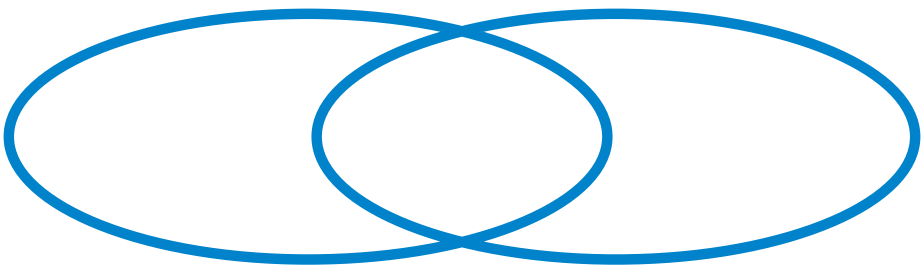
   ____

2. Give some examples of higher order thinking tasks that have challenged you today:

   ____

   ____

3. Many psychologists use laboratory rats to study behavior. Use the Venn diagram below to think about how rat behavior might be similar and different to that of humans in a maze.



4. The study of brain function has changed dramatically since scientists began to use functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) scanning. What advantage do these techniques give over previous "in vitro" examinations of human brains?

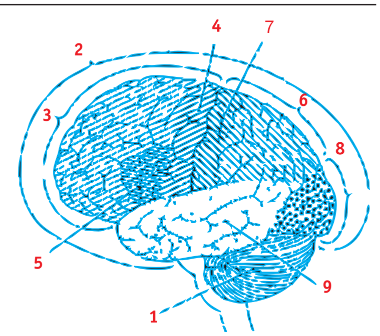
   ____

   ____

   ____

5. Use the video and outside sources to identify the parts of the brain.

   1. ____________ 6. ____________
   2. ____________ 7. ____________
   3. ____________ 8. ____________
   4. ____________ 9. ____________
   5. ____________



6. From a functional standpoint, how is the brain of a person with schizophrenia different? (You may wish to use the reading on page 25 for further information.)

   ____

THE ARCHITECTURE OF THE BRAIN

Biologists often compare the brains of many species of animals. There are many similarities across groups, but the relative proportions of each section provide important clues to the way the brain functions.

The most basic divisions of the brain are forebrain, midbrain and hindbrain. The hindbrain is most like that of the simplest animals; it controls respiration and heart rate, and coordinates movement (the cerebellum). The amygdala is closely related to emotions. The hippocampus helps change short-term memories to longer memories.

The midbrain is the uppermost part of the brainstem, which controls reflexes and eye movement. In humans, the largest and most developed area is the forebrain. This includes the cerebrum.

The cerebrum is the largest part of the brain (85% by volume), with folds and wrinkles to increase its surface area. The corpus callosum connects the right and left hemisphere.

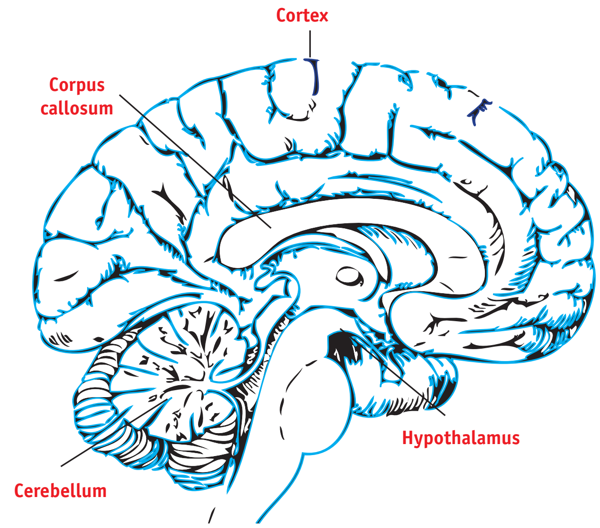
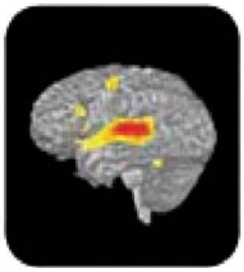


Image source: *http://pubs.niaaa.nih.gov/publications/arh284/images/tapert.gif*

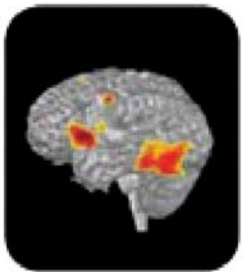
Each section of the cerebrum is specialized for specific function. Before the PET and MRI scan techniques came into common use, scientists could only probe cerebral functions during surgery or after accidents. Now we can look at the working brains of healthy people as they perform normal tasks. Here is a series of PET scans to show just a few of the revelations of these powerful new techniques.



Hearing Words

Speaking Words

Seeing Words



Thinking about Words

Learn more at *http://www.nia.nih.gov/Alzheimers/Publications/Unraveling*

All Together Now!

It's not enough for one part of the body to respond to a stimulus; the entire system must respond in a coordinated way. You can watch this happen in your own body. But first, let's think about what you expect to happen.

Imagine you are living in a primitive situation (Think "Lost!") Sometimes you are in great danger. An animal or a violent storm approaches. At other times, you can eat big meals and rest as you digest your food. Fill in the following chart with your hypotheses about what you would expect to happen to various systems of your body in a situation of stress or danger, and then in a situation of relaxation (like after a big meal).

System	Rest	Danger/Exercise	After Eating
Heart Rate			
Respiratory Rate			
Blood Pressure			
Blood Flow to the Skin			
Blood Flow to the Intestines			

1. Now let's test these hypotheses. To do that, you will first rest, then exercise, and finally examine your body after eating lunch. Take the first data set at the end of a morning class period, when you have been sitting quietly for at least 30 minutes.
2. Take the second data set after you've walked quickly around your school for at least 10 minutes.
3. Take the third data set after lunch while you are digesting your food.

You'll check your heart rate, your blood pressure, and your respiratory rate in each situation. There are three ways you can use to determine blood flow to skin. If you have a sensitive temperature probe, you can measure the skin temperature on the back of your hand. Another way to do it is to analyze the color of your skin. You can take two digital photos of the same place on your skin and compare them visually, or using a computer program called ImageJ from the National Institutes of Health. If you choose this second option, complete directions will be provided by your teacher.

System	Rest	Danger/Exercise	After Eating
Heart Rate			
Respiratory Rate			
Blood Pressure			
Blood Flow to the Skin			

1. Why does your blood pressure change when you exercise?

2. What's the survival advantage of being able to control the diameter of peripheral blood vessels?

3. In the experiment we have not measured blood flow to the intestines. But often you can feel a change in this area of your body. What does "danger" feel like in your small intestine?

4. What would happen if a chemical (like coffee or alcohol) changed the way in which your peripheral blood vessels reacted to chemical signals?

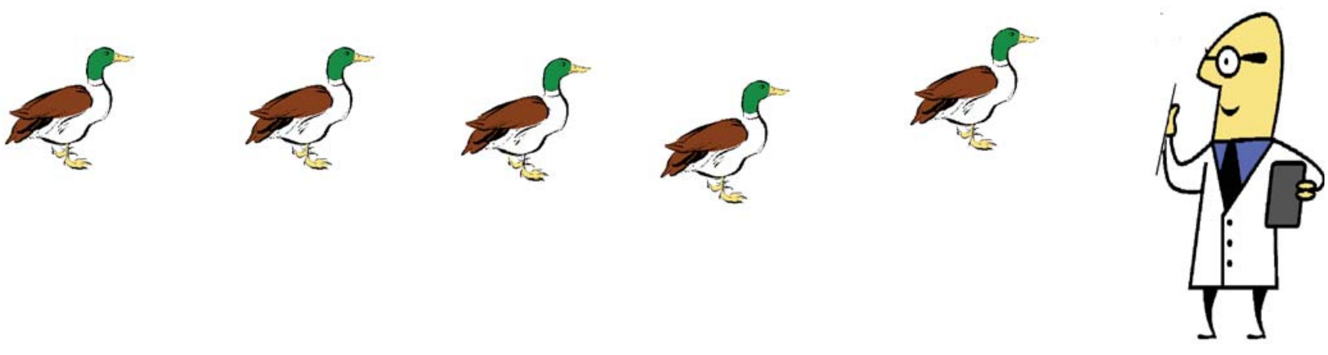
LEARNING FOR LIFE

Learning isn't something that happens only in school. You have learned every minute of every day of your life. And it's one of the biggest mysteries in neuroscience. In the videos you looked at several different kinds of learning, from simple responses to playing chess. You can certainly list many more.

Learning seems to be the result of long lasting changes in the synapses in your brain. New connections are constantly being formed. In your brain, each of billions of neurons might contact thousands of others. This happens most quickly when you are young. Because the plasticity of the nervous system is greater it's easier for a young person to learn to play a violin or speak a foreign language than for older people.

Learning also can occur in different ways. Some people find it easier to learn by reading, others by listening, and still others by handling physical objects. The reason is still a mystery to scientists, but some brains seem to give greater priority to some kinds of sensory input than others.

Much of what we know about learning originally came from animal studies—from simple mussels to chimpanzees raised with humans. In the 19th Century, Ivan Pavlov showed dogs some food and rang a bell over and over again. They would salivate (drool), responding to the odor. Eventually, they would drool when they heard the bell. They learned that the bell would be associated with a treat. In the 1930s biologist Konrad Lorenz looked at responses in ducks and geese. He found that newly-hatched ducks would memorize and "imprint on" the first visual image they saw, following it (mother, human or even another animal). They learned best by seeing at that stage in their life.



In the 1950s, psychologist B.F. Skinner studied how pigeons learned. He discovered that rewards were much more effective than punishments to shape behavior. Today's learning researchers are comparing internal rewards like dopamine to external ones.

Some behaviors are inborn (innate). Lorenz didn't have to teach his ducks to follow. Touch a baby gently on the cheek, and it begins to suck. These are behaviors that are absolutely necessary for survival. But you have been learning since you were born. You learned that smiling would get positive responses from your parents. You might also have learned that making a lot of noise got a response, too!

Your senses are constantly sending you information to learn. But what do you remember? That's the job of a specific part of the brain called the hippocampus. Your brain constantly receives information. But it must be filed and stored in such a way that you can find it again. Here's an analogy. Think of the "big box" store in your community. Trucks constantly bring stuff to the loading dock in the back. Employees have to take that stuff and put it in the right place in the store, so customers can find it. If they just put things in the store at random, the sporting goods in the drug department or the music CDs in the paint department, no one could find their materials and the store would be chaotic.

The job of storing information in places where you can find it again is done by a portion of your brain called the hippocampus. Short-term information is constantly received by your brain; your hippocampus has the job of converting short-term memories to long-term memories by making the right connections among the synapses in your brain.

Imagine you are at a big party. You are introduced to dozens of people, and provided many bits of information. Some of them are meaningful. They connect to questions you have wondered about, or you meet people whom you might need to know in the future. Your hippocampus stores those bits of information in places where you can find them again. Just as in your local "big box" store, it's easiest to retrieve stored information if it's meaningful to you. So if you already have some connections or some reason to make new ones, learning is easier. Think of the party again. If the new person you meet looks like Aunt Jane, or says "I have a job for you," you are more likely to remember the name.

That's easy to see in animals as well. To a dog (whose ancestors lived in dens and needed to keep those places clean to survive) it's easy to make the connection: "This house is my den. I can't make it dirty." But the ancestors of chimpanzees lived a migratory life, moving from one area of the forest to another. Despite the fact that most scientists think chimps are quite intelligent, it's very hard to teach them what places they can dirty and what spaces must remain clean. One more lesson from our "big box" analogy. What if many trucks came to the dock, but the store staff was working very slowly. The material would pile up on the loading dock, and might even fall into the road and be lost. Now think of a time when you had to read a long chapter in your science book. At first, the sentences might make sense. But soon, you might have found that you were reading paragraphs but not understanding them at all. Your hippocampus can reach a temporary limit!

These studies are done by cognitive psychologists. Your teacher studied cognitive science to become prepared to help you learn.

Are You Intelligent?

In many ways! Even though some school subjects only measure your learning with a few kinds of tests, psychologists like Howard Gardner know of many different ways to be "smart."

- Spatial (picture-smart)
- Logical/Mathematical (number-smart)
- Linguistic (word-smart)
- Kinesthetic (body-smart)
- Musical (music-smart)
- Interpersonal (people-smart)
- Intrapersonal (self-smart)
- Naturalistic (nature-smart)

IT TAKES A COMMUNITY

Nothing is so terrifying—or potentially devastating—to an organism as brain disease. Since coordinating your cells' response to the environment is absolutely necessary at every moment of life, anything that interferes with a properly functioning nervous system is serious.

People once believed that brain disease was caused by evil spirits, or by something bad that a person or their parents might have done. As recently as the 19th Century, scientists blamed many brain diseases on bad experiences or innocent mistakes in the way children were raised.

That changed when clear genetic links were found for some brain diseases. We now know that Huntington's Disease and the learning disabilities associated with Down's Syndrome are the result of interactions between genes and the environment. But for most brain diseases, both genes and the environment play roles in causing the problems and symptoms that victims encounter. That's why it takes a team of professionals with different areas of expertise to discover, diagnose, and treat brain diseases.

A Learning Challenge

Get a pack of cards. Think of a way to sort them into groups. It could be by color, number, suit, or a combination of those things. Then hand the cards to a partner, but don't tell him or her your scheme. Ask them to begin putting the cards in piles. If the subject puts a card on the right pile, say "OK." If not, "wrong." How long does it take to figure out your scheme? What sorts of intelligence does this task take?

You learned a bit about schizophrenia in the video. Read the history on the next page. Then form a team of five students. Each team will model the roles of professionals in diagnosing a brain disease, writing a medical history on the possible causes, and describing a treatment plan for the patient. Begin by inventing a name for Patient X, to insure privacy. You will write an imaginary, yet factual, report. Here are the members of your team and their individual assignments:

- A medical doctor, who will write a report describing the physical symptoms that the patient may encounter with the condition.
- A geneticist, who will research the genes that might contribute to the development of the condition.
- A public health researcher, who will describe the potential environmental factors that might have contributed to the development of the condition.
- A psychologist, who will describe the behavioral or learning conditions which might occur as a result of the condition.
- A medical social worker, who will prepare a report to the patient and family describing the treatment options that exist for the condition.

The assignment for each team member is expanded on the pages that follow, to help begin their work.

Schizophrenia: Yesterday and Today

Schizophrenia in History and Literature

In ancient Egypt, the heart was considered the center of the mind. An ancient document, the *Book of Hearts*, describes the symptoms of schizophrenia well. Plato called the symptoms "divine madness." Women in the Middle Ages who had the symptoms of brain diseases were sometimes called witches and punished severely.

The first scientific name of the condition we now call schizophrenia was *dementia praecox* (premature dementia). That name was misleading, since the term "dementia" usually refers to a condition that degenerates over time. Schizophrenia is a chronic condition, in which people sometimes hear voices or receive sensations that others don't. They may have delusions like paranoia (believing that others are threatening or controlling them). They may also withdraw, sitting immobile for many hours. Hallucinations, delusions, disorganized thoughts, and lack of emotion are all sometimes associated with the disease.

A person is more likely to develop schizophrenia if another relative has been afflicted. That has been known for at least 100 years. Part of the plot of the classic novel *Jane Eyre* involves a bride whose family does not tell the bridegroom of her family history of the disease. But that novel implies that the bride's disease was inevitable. That's certainly not true. Only about half of the identical twins of people with schizophrenia (who have exactly the same genes) get the disease. It's still not known what environmental triggers may contribute to expression of the gene(s), but scientists are getting closer to finding out.

Two lines of evidence link schizophrenia to an imbalance in the brain's dopamine systems. (Recall that dopamine is a reward neurotransmitter.) First, we know that amphetamines ("uppers") cause the release of dopamine, and that the symptoms caused by overuse of amphetamines are virtually identical to schizophrenia. We also know that the first drug found to treat the symptoms of the disease, chlorpromazine, prevents release of dopamine in the brain.

Today most patients respond to a combination of medication and psychosocial therapy to help them develop behavioral skills to cope with symptoms of the disease. There is no permanent cure.

IT TAKES A COMMUNITY: MENTAL HEALTH ASSESSMENT

Here are some tips on where to begin. Begin by brainstorming together the name, character and symptoms of your subject.

Medical Doctor:

Begin with the National Institutes of Health Web site *www.medlineplus.gov*. You will find a search box. Type in symptoms and the name of the condition you are researching. Remember, you are creating a medical history for a fictional patient. But you want to be as accurate as you can.

Geneticist:

Begin at the National Center for Biological Information's Web site Online Mendelian Inheritance in Man, *http://www.ncbi.nlm.nih.gov/sites/entrez?db=omim*. You will probably find many suspected genes (loci) that have been statistically associated with the disease. Research a few of them. Since much of this is very active research, it's fine to say that a certain list of suspected alleles should be investigated. You can also create a pedigree chart of your fictional patient tracing one of the suspected genes through a family.

Public Health Researcher:

Search *www.nimh.nih.gov, www.medlineplus.gov or http://www.ncbi.nlm.nih.gov/sites/entrez* for your disease and "risk factors." Remember, some of the sources you find will be hard to read. Choose your sources carefully. Then create a list of questions that your patient should answer about past exposures to environmental factors.

Psychologist:

Look carefully at the symptoms that the medical doctor has identified. Some of them may impair cognitive function (thinking). Even if most of the symptoms of your disease are physical, there may be psychological effects of having a serious or chronic condition. Research what drugs and other treatments are used for the condition using the term "treatment." As you write a recommended treatment, don't forget to consider the side effects.

Medical Social Worker:

Your role is to summarize all of the material that has been collected in a way that the patient and his/her family can understand. You could create a written report, a PowerPoint, or a podcast with your explanations. Remember to be complete and honest, but understanding. Tell them what they can expect, and how they can best handle the disease as it progresses. Conditions to research:

- Depression
- Bipolar Disorder
- Schizophrenia
- Autism Spectrum Disorders
- ADHD
- Alzheimer's Disease

Neuroscience: Today, Tomorrow, and the Future

Since the beginning of medical science, we have sought to understand the mind. How do we learn? How do we use emotions and not be trapped by them? How do we conquer brain disease? These questions have challenged humans for tens of thousands of years, yet scientists have only made significant progress in the past two centuries.

Today's neuroscientists know the structure of the nervous system. They can monitor the electrical and chemical signals. With functional MRI and PET scans, they can measure the activity of the parts of the brain. Tests show variations in genes that are associated with variations in structure and behavior. And public health researchers have enormous databases to show what environmental factors might be connected to some diseases.

But much work remains. In most cases, a single cause or a single gene isn't always the cause of a specific disease. A single cure or solution seldom works for every patient.

So the challenge of understanding the brain and nervous system continues. Every healthy citizen should know the basics, to make good decisions about behaviors, habits and attitudes. These videos, activities and readings should be just the beginning.

This is also an area with many valuable and rewarding career opportunities. Some require only a few years of training; aides, group home coordinators and tutors provide invaluable help to those with brain diseases. Others, like psychiatrists and psychologists, require years of training. Whatever your goals are, don't stop here. Continue to explore your brain and to use its potential in the future.

RESOURCES

National Institute of Mental Health
Bethesda, MD
http://www.nimh.nih.gov

National Institute on Drug Abuse
Bethesda, MD
http://www.nida.nih.gov/students.html

National Institute of Neurological Disorders and Stroke
Bethesda, MD
Brain Basics: Know Your Brain.
http://www.ninds.nih.gov/disorders/brain_basics/know_your_brain.htm

National Institute on Aging
Bethesda, MD
Inside the Human Brain.
http://www.nia.nih.gov/Alzheimers/Publications/Unraveling

GLOSSARY

Acetylcholine	An excitatory neurotransmitter.
Action Potential	The temporary change in charge across a membrane caused by a stimulus.
Amygdala	One portion of the brain involved in emotions.
Axon	Processes that extend from the cell body and transmit messages.
Broca's Area	Part of the cerebral cortex on the left frontal lobe, which helps transform thoughts into words.
Cell Membrane	An essential part of every cell, composed of a double layer of lipids with pores and specialized receptors, that controls the cell's internal environment and its responses to outside stimuli.
Cerebellum	A portion of the brain involved in muscle coordination.
Cerebrum	The portion of the forebrain involved in conscious thought, memory and analysis of sensory signals.
Chemoreceptor	Receptors on membranes that receive chemical signals.
Dendrite	Processes that extend from the cell body and receive messages.
Differentiation	Changes in cells to make them more specialized.
Dopamine	A neurotransmitter that affects mood and helps control complex movements.
Endocrine system	The system comprised of glands that secrete hormones as chemical messages to other parts of the body.
Endoplasmic Reticulum	A cell organelle that looks like a channel, isolating and transporting materials.
Forebrain	The largest part of the human brain, composed primarily of the cerebrum.
GABA	Gamma-aminobutyric acid, a neurotransmitter with mostly inhibitory effects.
Genes	Segments of DNA containing the codes for specific enzymes or portions of enzymes or other proteins.
Glial cell	A cell in the nervous system that nourishes and protects neurons.
Glutamate	The major excitatory neurotransmitter in the brain.
Golgi body	A cell organelle that packages cell products for transport.
Hindbrain	The most primitive part of the brain, which controls the body's most basic functions such as respiration and heart rate.
Hippocampus	A portion of the brain involved in transforming short term memory to long term memory.
Histamines	A chemical signal in the body that causes a reaction to a foreign substance.
Homeostasis	The steady state that a cell or organism must maintain to stay alive.
Hormone	A chemical message produced by an endocrine gland which travels through the bloodstream to a target organ.
Hypothalamus	A portion of the brain that sends signals to the pituitary.

Ion Pump	Mechanisms in the cell membrane that use energy and enzymes to move ions across the cell membrane, establishing voltage (charge) across a membrane.
Ions	Charged atoms or stable groups of atoms.
Metazoa	Animals.
Midbrain	The upper part of the brainstem, which controls some reflexes and eye movements.
Motor Neuron	A nerve that causes a muscle to contract.
Myelin	A protective sheath around the axons of some neurons.
Nerve	A bundle of axons in the nervous system.
Nervous System	The system that coordinates an organism's response to the environment.
Neuron	The basic functional cell in the nervous system.
Neurotransmitter	A chemical messenger released from an axon and sensed by a dendrite.
Nissl Body	An organelle in a cell that responds to Nissl stain, primarily comprised of rough endoplasmic reticulum.
Norepinephrine	A neurotransmitter that increases the rate of metabolism and helps an organism respond to threats.
Nucleus	The area of some cells that protects the genetic material.
Occipital Lobe	Part of the cerebral cortex at the back of the brain, which processes images from the eyes and links it to memory.
Parietal Lobe	The topmost part of the cerebral cortex behind the frontal lobes which receives information about temperature, taste, touch and movement.
Plasticity	The ability to change during growth.
Potential	A voltage or difference in electrical charge.
Reflex (Simple)	A direct response to a stimulus like that controlled by the spinal cord.
Schizophrenia	A brain disease caused by defects in neurotransmitters (especially dopamine), characterized by delusions and severe behavioral changes.
Sensory Neuron	A neuron that receives a message from the environment.
Serotonin	A neurotransmitter involved in sleep, temperature regulation, pain and cognition.
Sodium-Potassium Pump	A mechanism in the membranes of neurons that can separate ions and create a voltage (charge) across a membrane.
Spinal Cord	The mass of nervous tissue along the axis of an animal (within the backbone of vertebrates).
Synapse	A gap between two close nerve cells.
Synaptic Vesicle	A structure in the membrane at the end of an axon that releases a neurotransmitter.
Temporal Lobe	The lateral part of the cerebral cortex in front of the visual areas, involved in receiving and analyzing sounds, arousal, memory and other functions.

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