The Brain's Inner Workings

A GUIDE FOR TEACHERS

From the

National Institute of Mental Health

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MODERN NEUROSCIENCE EDUCATION

Most biology courses begin by asking students to define "life"—a task that challenges even the most experienced researchers. Students often offer descriptions of structures they've seen ("cells") or physiological processes ("breathing") that reflect their limited experience with the diversity of the living world.

Yet the most essential elements of living things are often the hardest for beginning life science students to conceptualize. At the most basic level, the list includes:

- Living things use energy to maintain their organization and structure;
- Living things can replicate themselves;
- Living things can evolve; and
- Living things respond to their environment to preserve balance (homeostasis).

The fourth characteristic, response (or more technically, irritability), is crucial. It is intuitive once students begin to consider their own observations of the natural world. Yet it is the one that is covered least thoroughly in most secondary programs. The framers of the National Science Education Standards clearly defined behavior as one of the most important goals of secondary life science:

CONTENT STANDARD C: As a result of their activities in grades 9-12, all students should develop understanding of:

- The cell
- Molecular basis of heredity
- Biological evolution
- Interdependence of organisms
- Matter, energy, and organization in living systems
- Behavior of organisms

THE BEHAVIOR OF ORGANISMS

- Multicellular animals have nervous systems that generate behavior. Nervous systems are formed from specialized cells that conduct signals rapidly through the long cell extensions that make up nerves. The nerve cells communicate with each other by secreting specific excitatory and inhibitory molecules. In sense organs, specialized cells detect light, sound, and specific chemicals and enable animals to monitor what is going on in the world around them.
- Organisms have behavioral responses to internal changes and to external stimuli. Responses to external stimuli can result from interactions with the organism's own species and others, as well as environmental changes; these responses either can be innate or learned. The broad patterns of behavior exhibited by animals have evolved to ensure reproductive success. Animals often live in unpredictable environments, and so their behavior must be flexible enough to deal with uncertainty and change. Plants also respond to stimuli.
- Like other aspects of an organism's biology, behaviors have evolved through natural selection. Behaviors often have an adaptive logic when viewed in terms of evolutionary principles.
- Behavioral biology has implications for humans, as it provides links to psychology, sociology, and anthropology.

http://www.nap.edu/readingroom/books/nses/6e.html#ls

The National Science Education Standards emphasize that important concepts should be explored in depth, over time, and in a variety of contexts. Students should learn about behavior by relating structure to function, using the processes of inquiry and aiming toward the goals of scientific literacy. Information about behavior, from the basics of the nervous system to memory and learning often comes in small, discrete packages, without the sorts of scaffolded connections that would make it meaningful and authentic.

A strong foundation in the structure and function of the human nervous system offers students the framework for not only constructing understanding of physiology and homeostasis, but the ability to make good personal and community decisions about their behaviors in the future. It helps them look at the "implications for humans," including the role of the nervous system in learning and community health.

A thorough background in the function of the nervous system can also lead to a better understanding of brain disease, from chronic behavioral syndromes like ADHD to degenerative conditions like Parkinson's Disease. Since almost every family is challenged to care for and get appropriate medical help for members with brain disease at some point, building knowledge, skills and attitudes about these topics is important.

Constructing an Understanding of Behavior

In order to provide the environment and experiences through which students can construct strong and authentic concepts about behavior, most secondary programs need supplemental materials beyond the textbooks.* This module is intended to support traditional curricula in the middle and secondary schools, to achieve that goal. Included in the program are:

- This Teacher's Guide, with content background and a proposed pedagogy for the use of the material;
- Student pages available in text and on an accompanying CD ROM. The student pages include both text and activities;
- Two outstanding video supplements from NIMH, *The Brain's Inner Workings I* and *II*, introducing the structure of the nervous system and the role of neurotransmitters in health and disease;
- Student activities to complement the visuals on the NIMH video;
- Formative and summative assessments;
- Additional resources on CD including animations;
- A short computer program on the CD called "React," which can be used to support the laboratory activities in the Student Resource or to help students extend their understanding by conducting independent research of their own.

*Correlations to the major secondary textbooks are provided in the Appendix.

I. SIGNALS, SENSES, AND SURVIVAL

At the most basic level, organisms must respond to survive. Signals can be physical (light, touch, pressure, gravity), chemical, or electrical. The primary structure that is responsible for response is the cell membrane. Even the simplest cells that exist today have specialized membranes that respond to changes in the environment. (It's primarily differences in the structure of membranes that separates life into its three great domains, Archaea, Bacteria and Eukarya.)

The first reading in the Student Guide asks students to consider the familiar situation of ants that follow a chemical trail. It's a phenomenon many students will have observed, even though they may not have thought much about what was actually happening. Ants follow a set pattern unless the trail is disrupted. The student guide asks: "What sort of messages are they sending? How could you test your hypothesis?"

Allow students to brainstorm before they continue to read the text. While some students may know that the signals are chemical (and of course, there are hints in the sidebar) there are other reasonable hypotheses:

- Students may know that bees communicate by a "dance" and may suggest the ants communicate in the same way.
- Students may assume that the ants are not following one another, but are following another signal in a uniform way, such as a scent, visual, auditory, or even magnetic signals.

Safety Note

The sidebar in the student guide suggests using window cleaner as a potential solvent for a hypothetical chemical signal between the ants. We have not suggested anything stronger for safety reasons. Remember that all chemicals in classrooms require MSDS information.

Once students have discussed potential signals among ants, ask them if they know of any other animals that send chemical signals to one another. Common examples are musk (tail glands in deer), urine (marking territory in dogs), and odors (like primates in heat).

Of course, ants are multicellular organisms and individuals. Their ability to coordinate response is quite different than cells. But this familiar process can provide a simple analogy to the chemical signals that cells send to other cells. This example is used to stimulate discussion and to help students analyze their preconceptions before they begin to look at how the cells of complex organisms such as humans work together. Encourage students to speculate not only on how ants communicate, but on what sorts of experiments might be done to explore this function.

From tiny animals to tiny cells, the analogies continue. Students look at the classic experiment of Theodor Engelmann. This is described in order to illustrate how individual cells can respond to chemical messages. This experiment is difficult to replicate in the classroom because few students have the microscope skills to discern the *E. coli* while maintaining the depth of field needed for filamentous algae. But it's worth exploring in depth, both because it shows coordination and control among individual cells, and because you can use it to review the basics of cellular response.

After students have observed the experiment in enough detail to understand its variables and results, ask students: "How can the *E. coli* sense the area of the algae that is photosynthesizing most quickly?" Students may first suggest either that the bacteria "see" the light or "taste" the products of the photosynthesis reaction. Review the general (net) reaction for photosynthesis:

Carbon dioxide + Water — Oxygen + (Sugar)

Then ask students if they could taste oxygen in water. (This may require a bit of thought; "flat" water that has been heated then cooled does taste different, and when students recognize that they often realize that dissolved oxygen is very important in water.) Another equally likely possibility, from the standpoint of student understanding, is that water with less carbon dioxide in it tastes different. (Remind students of the difference between "flat" soda and fresh.) Once they are clear that the stimulus is a chemical analogous to a taste, students can brainstorm how responding together (like ants) is an advantage to bacteria.

Making Our Own Misconceptions

Many of the experiments students do in class actually contribute to student misconceptions. One example is building "all purpose" models of animal cells. Another is the use of passive materials like egg shell membrane or dialysis tubing to illustrate cell membranes. In fact, very few of the functions of membranes are passive. The pores of membranes expand and contract based on the environment, and this requires enzymes and energy for response.

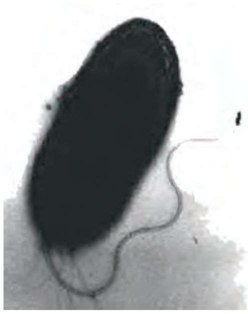


Image Source: *http://www8.nos.noaa.gov/coris_glossary/index.aspx?letter=f*

For students who suggest that the *E. coli* may be reacting to the light rather than the photosynthetic reaction, ask them to suggest an experiment. (The bacteria do not move to various areas when the alga is not there.) Finally, ask students how the bacteria move toward the stimulus. If students are not familiar with the ultrastructure of the bacterial cell, a picture will help the discussion. (Remind students that bacteria have flagella, but these are not controlled by contractile proteins like the more complex flagella of *Euglena*.)

Probe Further:

How specifically might the bacterial cells react to this change in their environment? With a little consideration, students who have studied the parts of a general cell might be able to offer some general suggestions:

- The environment changes the membrane;
- Changes in the membrane result in changes inside the cell;
- Changes inside the cell result in changes in the movement of the bacterial flagellum.

This is a good place to challenge students with an open question: If individual bacterial cells can work together to respond to signals, how can the individual cells in your body work together for the same purpose? To provide wait time, ask students to journal their responses or contribute to an online discussion thread before the class moves on.

VISUALIZING THE NERVOUS SYSTEM

Continue with the 5-minute video *The Brain's Inner Workings Part I*. This introductory video narrated by Leonard Nimoy provides outstanding visuals to introduce students' study. The following brief summary can provide some suggestions for discussion: The video begins with a collage of learned responses. This is a good segment to view, discuss, then repeat. It sets the tone for the more technical material that follows. A student plays piano, kicks a ball, plays chess. Brainstorm: What are the stimuli involved? (Sight, sound) What are the responses? (Muscle movements, higher cognitive functions) What must be learned? Is any of the activity inborn or instinctive? (A blink or a reflex as a ball approaches could be inborn, but most of the actions are learned.)

The narrator then speculates on what "makes humans human?" and attributes that quality to the brain's cerebral cortex. This is another great place for students to brainstorm their own definitions of activities that might be functions of a human brain:

- **Tool use?** It's also found in other primates and birds.
- **Culture?** The passing down of behaviors through social connections has been documented in many animals including cetaceans.
- **Emotions?** Many new studies show emotional responses in animals such as dogs and elephants.

Yet all of these animals, like humans, have complex brains with folded cerebral cortexes. The extent of folding seems to correspond at least to some degree with intelligence. The narrator suggests that the folding is a way to create more surface area in a limited space. First, ask students: "Why is the space limited?" Two logical reasons will easily be generated: There is a physical limit to the weight of the head, and the size of the head is limited by the need to pass through the birth canal in hips which are functional for walking. Students may suggest other reasons, such as to turn the head for defense.

The video next moves to show the structure of neurons within the brain. Students may be familiar with a drawing of a neuron with one long axon and one or two short dendrites; they may be surprised by the many contacts among these cells. Key terms in the video (Cerebrum, cortex, neuron, axon, dendrite, process, synapse and synaptic vesicle) are defined in the glossary. The video ends with a summary of why this research—and the student explorations which will follow—are important. Ask students if they've had any experience with brain disease, and indicate that they will learn more in the activities that follow. The student guide helps focus their work on decision-making skill.

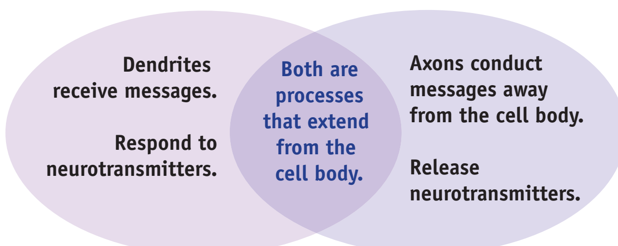
Don't expect students to get every detail of the video on first viewing. Its five-minute format makes it ideal for repeat viewing. The worksheet provided on the next page only asks for general observations. Then return to the video again. Students will undoubtedly find more to notice on second viewing. You can review the structure of the neuron in the "Nerves" animation on the companion CDROM.

Finally, the students can explore simple reflexes in the activity *Take That!*

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? **Learned skills.**
2. Why should we study normal brain function? **To understand abnormal/disease.**
3. If you could see the cerebrum, what structural features would you note? **The surface is "grey matter," two hemispheres, (myelinated) with many folds to increase surface area.**
4. How many connections does a single nerve make? **Thousands.**
5. Why is the cortex folded? **To increase surface area in a limited space.**
6. What is a dendrite? **A process (extension) of a neuron that receives messages.**
7. What is an axon? **A process (extension) of a neuron that sends messages.**
8. How are dendrites similar to axons? How are they different? Use a Venn diagram:



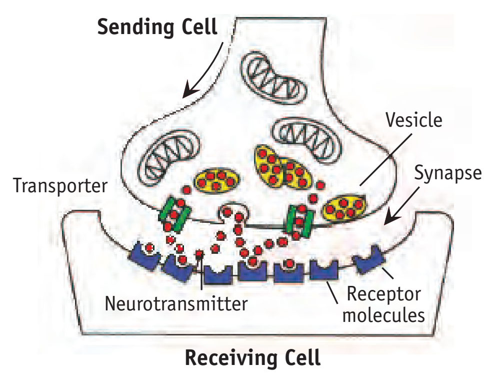


Image source: *http://www.nida.nih.gov/NIDA_notes/NNvol21N4/cell.gif*

9. What is a synapse? **A gap.**
10. Label the parts of the synapse. **See labels on diagram.**
11. Why should we study a synapse? **Many diseases seem to be related to malfunction of synapses.**
12. What is a synaptic vesicle? **A structure that contains a neurotransmitter.**
13. What happens when a stimulus reaches a synaptic vesicle? **Neurotransmitters are released; chemical messages are sent.**
14. What happens if an error occurs in this process? **The message may be garbled; disease occurs.**
15. What new information do you want to know about the brain? **Answers will vary.**

KEEPING IN TOUCH

Next, students move from coordination among organisms to coordination with the cells of multicellular organisms—with an emphasis on animals. Almost* all animals coordinate their responses through the action of specialized cells called neurons. These are cells that are specialized to receive information, encode it into electrical or chemical signals, and transmit that information to other cells. They are the most basic units of structure within the nervous system.

*Almost All Animals?

The simplest animals (Kingdom Metazoa) are the Placazoans, and we know almost nothing about them. They've been found on the walls of aquaria but never in the wild. Poriferans don't have nervous systems, but most other animals do.

Most textbooks discuss the nervous systems of higher animals, but rarely offer discussions of the simplest nervous systems. Students will benefit by beginning with the genetics of the roundworm Caenorhabditis elegans. This organism is a favorite of biologists because it has only a few cells (~1000). Great details of research about this popular organism can be found at *http://weboflife.nasa.gov/celegans/questionsshow.htm*.

Most students have studied a generic model of an animal cell. But they may not realize that there are at least 100 distinct types of differentiated cells in the bodies of most higher animals. (We actually create misconceptions by stressing a generic cell model and de-emphasizing differentiation.) Neurons are the most recognizable cells in the nervous system, but not the most numerous. In many animals, there are perhaps ten times more glial cells than neurons. They come in many forms and have a variety of functions; they may support and orient neurons, or insulate them from the environment. Oligodendrites and Schwann cells wrap around axons nourishing them. They produce myelin, a covering that insulates the axon and makes the tissue appear white (i.e., "white matter" vs "grey matter").

Researchers are exploring the potential of oligodendrites to differentiate into neurons. Clinical trials are underway to see if cultures of nasal oligodendrites can be transplanted to repair damage to the nerves in spinal cord injuries.

WALKING THE TIGHTROPE

The essential challenge of multicellular life is coordination. The reading *Walking the Tightrope* begins with a comparison among very simple Metazoa, the sponge and the anemone. Like the examples of bacteria and ants, these images are meant to help students think about responses in a very simple way, and to isolate the function of irritability so that they can develop deeper understanding of the content. Then four explorations are provided for students. While completing all of them is ideal, students can explore all the core concepts by completing two: *The Neuron and Take That!*

The activity *The Neuron* is meant to accompany either microscope or video observations of neurons, experiences included in almost every middle and high school course. If the facilities exist, allow students to view prepared microscopic slides of neurons in conjunction with the reading passage *Membranes and Messages,* which provides a very brief introduction to the action potential and its relationship to the neuronal membrane.

> Safety Note:
> Make sure students understand they are looking for touch—not pain—receptors.
>
> Take very great care that students' eyes are protected in the *Take That!* activity.

During the observation it is assumed that students have some knowledge of microscopic stains. (If they have only used iodine, it's worthwhile to explain that stains bond to specific kinds of molecules and highlight specific parts of cells and tissues.) It is also assumed that students have a rudimentary knowledge of cell ultrastructure, including organelles such as nucleus, mitochondria, endoplasmic reticulum, and cell membranes. A review is included below if you don't have one in your textbook. Emphasize the difference between free ribosomes and those that are bound to the endoplasmic reticulum, and the link between free ribosomes and membrane proteins.

The reading selection, *Does the Nose Know?* provides background on how stimuli affect cell membranes. Remember, many of the textbooks and lessons your students will have experienced will have shown membranes as passive structures. In fact, when asked "What is the most important part of the cell?" most students say "the nucleus." But the most essential component of a cell is its membrane and *most cells on Earth lack nuclei*. Even a few cells in human bodies (mature red blood cells) lack nuclei. They can't repair themselves, but can survive and even thrive for relatively short periods of time. But without a membrane to control its internal environment and allow it to respond, the cell cannot live at all.

Next, students explore the distribution of their own sensory neurons in their skin in the activity *Signs and Signals*. This activity asks students to look at the distribution of touch sensors in various areas of their skin. The "two point discrimination test" is not highly accurate, but the range of differences among areas of the body is so great that good results are usually easy to obtain.

Finally, students can explore the "simple" reflexes in the activities *Take That!* and *It's the Thought that Counts*. This section of the module includes two simple computer programs for measuring reaction time. They are only roughly accurate, but again the results are proportional to those obtained by more specialized equipment. Professional researchers know that the display of most personal computers creates inherent errors in reaction time measurement, but these errors are too small to contribute to misunderstandings at this level.

Some reflexes are coordinated in the spinal cord, where grey matter (unmyelinated neurons) connect sensory and motor neurons. Other reflexes like blinking are coordinated in the midbrain. While scientists hesitate to classify reflexes as "simple" any more, reflexes are defined as "instantaneous," so autonomic responses that take longer (like the "butterfly" reaction that occurs a few moments after a scare, due to less blood flow to digestive system) are technically not reflexes but the results of neurotransmitters.

There are also many types of movement that scientists consider "stereotypical," that defy easy classification for beginning students. For example, animals with their spinal cord completely transected have been observed to make well coordinated walking movements as a result of exposure to certain neurotransmitters—without any conscious control by the brain. The mystery of how molecules interact with cells to produce the most basic behaviors necessary for an organism to survive is far from solved.

These activities are meant to help students transition from an understanding of simple and relatively linear responses to the more complex balance of responses that occur in the nervous system as the result of the interaction of many neurons and neurotransmitters. They can also form the basis for more extensive independent research with the help of the computer programs.

Explore the speed of a nervous system in the "How Fast" animation on the companion CDROM, and then see how a simple reflex works in the "Reflexes" animation on the companion CD. Then return to a discussion of the very complex cognitive functions that were first introduced in the video. There is a great deal of difference between a blink or reflexive defense and a complex action like playing piano, making a goal in soccer or checkmating one's opponent. Yet they are all built of the same basic chemical and electrical messages that are represented in the model of a simple reflex.

TEACHER'S GUIDE TO ACTIVITY

The Neuron

Can you imagine the size of a single neuron? 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."

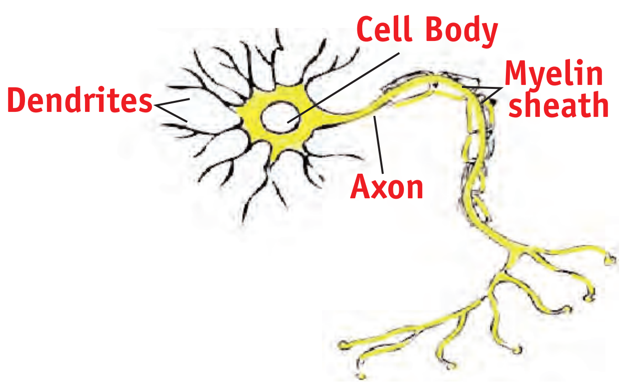


Image Source: *http://www.nida.nih.gov/JSP4/MOD1/images/neuron1.gif*

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. Biologists didn't always understand that, though.

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 that a different sort of stain would also 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. What cell organelles are binding to the two very different stains?

Stain	Appearance	Chemical	Organelles
Nissl		Cresyl violet	**Nissl bodies include granular endoplasmic reticulum and ribosomes.**
Golgi		Silver nitrate and potassium chromate	**Stains membranes of (some) axons and dendrites.**

Golgi's work was revolutionary, but it was left to a younger researcher, Spaniard Santiago Ramon y Cajal, to use the technology to its fullest. In an amazing series of dissections, he revealed the structure of much of the nervous system. 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? **Modern microscopes have more resolution; they show that the axon of one dendrite does not quite touch the dendrite(s) of the next. At the synapse the signal changes from electrical to chemical in most nervous systems. (Teacher note: This is not true in every nervous system. There are some where the gap junction is electrical. Electrical synapses are common in invertebrates, but found in only a few locations in mammals where coordination must be extremely fast and well coordinated).**

EXTRA BACKGROUND

Reviewing Neuron Ultrastructure

Many students can benefit from a review of the structure of the highly differentiated neuron.

The typical neuron is about 20 µm in diameter. Like most other cells, it has a nucleus that is about 5-10 µm in diameter.

In the cell, proteins are synthesized on ribosomes. Some float free in the cell; others are bound to the membranes of "rough" endoplasmic reticulum (ER). Both types of ribosomes are involved in protein synthesis, but the proteins that are destined to be bound to the cell membrane are normally produced on the rough ER.

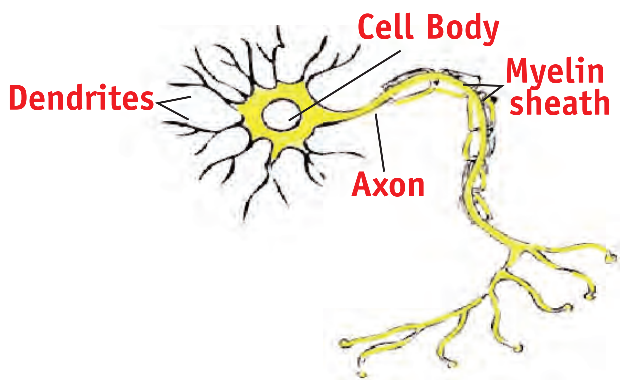


Image Source: *http://www.nida.nih.gov/JSP4/MOD1/images/neuron1.gif*

The cytosol of neurons is especially rich in rough ER. (That's what makes many neurons very reactive to the Nissl stain). That's a clue that the production of membrane proteins and neurotransmitters is a key function in neurons. It's a great example of structure providing clues to function. (Ask students: "If Nissl stain shows a great deal of rough endoplasmic reticulum, what does that suggest about the neuron's metabolism?)

Proteins that will eventually end up in the axon are further processed by the Golgi apparatus, since there is no protein synthesis in the cell processes. So Golgi are also notable in neuron ultrastructure.

Neurons are high-energy cells, and accordingly have a high level of mitochondria. Relatively large microtubules run down the length of the cell helping it maintain its overall structure. A specific change to the microtubule-associated protein, Tau, is associated with the dementia that accompanies Alzheimer's disease. Tau holds the microtubules in order; without it the shape of the dendrites change.

Neurons can be classified by the general shape determined by their dendrites: pyramidal or stellate (star shaped). They can also be classified by their connections: sensory or motor; or classified by the neurotransmitter released by their synapses.

But the most remarkable functions of neurons are directly associated with their membranes. That's the content summarized in the Student Reading *Membranes and Messages*.

TEACHER'S GUIDE TO ACTIVITY

Signs and Signals

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.

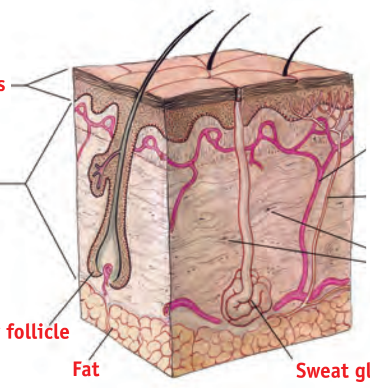


Image source: *http://www.nigms.nih.gov/NR/rdonlyres/0037E7BB-97A3-4EC6-904A-61CEEE4352EF/0/skin2.jpg*

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	X			
Cheek	X	X		
Index Finger	X	X	X	
Palm of Hand	X	X		

1. In what area were the touch receptors closest? **Fingers, hands and cheek.**
2. What survival advantage might this difference have? **Anthropologists believe that manual dexterity (use of hands for tools and communication) was an important survival factor in early hominids. Facial sensitivity is also important for communication and as a sexual stimulus.**

EXTRA BACKGROUND

Membranes and Messages

To understand the way neurons work, students must have a good understanding of the dynamic nature of the cell membrane. The specializations that occur in cell membranes are especially important for communication within multicellular organisms. As explained above, the standard exercises that students do in elementary or middle school to explore the permeability of membranes can even add to these misconceptions.

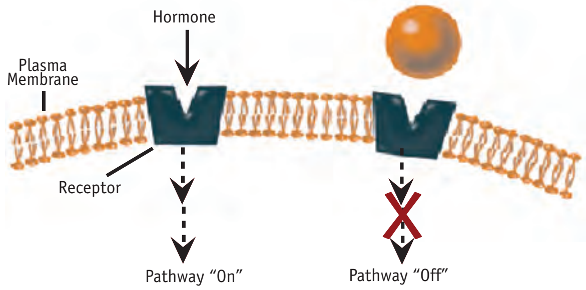
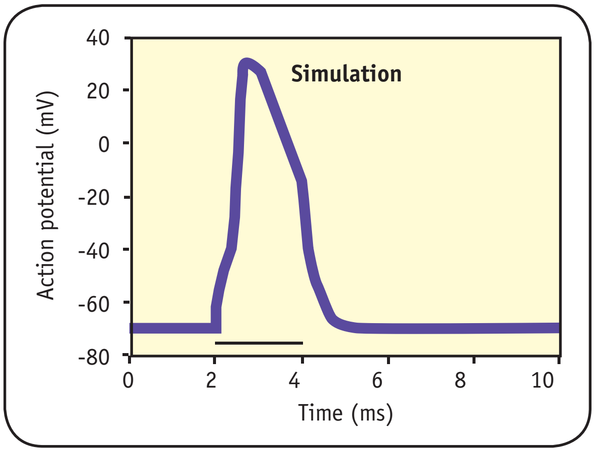


Image Source: *http://publications.nigms.nih.gov/chemhealth/images/ch4_party.gif*

Cell membranes are very active, indeed. If your students have already done experiments with passive models, it's a good idea to start there, reviewing the fact that passive transport is not the norm. The picture in the student guide can illustrate how a neurotransmitter changes the size of pores on a cell membrane.



The size of the pores in cell membranes changes constantly depending upon their environment and internal metabolism. Some are voltage-gated; that is, they open or close in response to a change in the voltage across the plasma membrane. Chemically-gated channels respond to chemicals such as neurotransmitters.

The reading selection *Membranes and Messages* provides a very simple description of an action potential. This is really all secondary students need to understand. The charge across the membrane of a neuron is controlled in part by *ion channels.* The control of channels requires both enzymes and energy. As an analogy, any static electricity demonstration might be used. But remind students that the signal in a neuron is voltaic (involving charged ions), not directly analogous to circuit electricity.

The example which is provided for control of respiration is one that can become the basis of many anecdotes and short student explorations. The carotid and aortic bodies contain chemoreceptors which respond to the oxygen and carbon dioxide concentrations in arterial blood. A carbon dioxide partial pressure of more than approximately 5kPa, (40mmHg) (depending on age or health), results in an immediate and marked increase in breathing. Athletes learn about this phenomenon without the basis of physiology. They learn that they must concentrate on breathing out (more than breathing in) to control blood pH and to prevent hyperventilation.

Remind students that the signal sent by the pacemaker of the heart is also electrical; it can be sensed from one end of the body to the other as it stimulates and coordinates the contractions of the heart. But that's more like current electricity.

TEACHER'S GUIDE TO ACTIVITY

Take That!

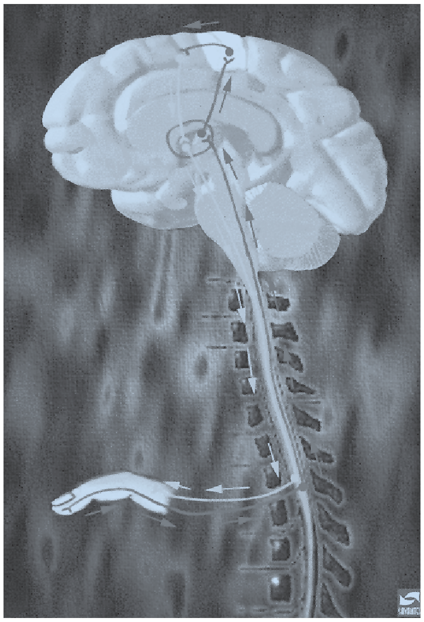


Image source: *http://www.nida.nih.gov/pubs/teaching/Teaching2/largegifs/slide4.gif*

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? **The blink reaction is a simple defensive reflex coordinated in the midbrain.**
2. Does the reaction change if the subject knows that the paper is coming toward his/her face? **Only a few people can control it.**
3. If the paper is aimed at one eye, does the other eye react in the same way? **Yes, in most cases.**
4. What is the survival advantage of this reflex? **It protects eyes.**
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? **The pupils constrict.**
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? **In healthy subjects they are coordinated.**
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? **Pupils dilate.**
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? **Sympathetic responses include dilated pupils, less blood to digestive system and more to muscles, increased heart rate and respiration rate.**
9. Which of the reactions above happen very quickly (in a second or less)? These are probably reflexes: **While all are autonomic, the pupil dilation is more rapid.**
10. Which of the reactions you identified take a little longer (from seconds to minutes)? These are probably chemical signals. **Changes in blood to digestive system are the result of neurotransmitters.**

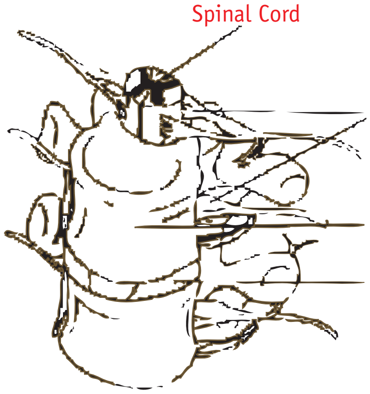
Some reactions are completely unconscious. Explore how a reflex works in the "Reflexes" animation on the companion CD. Others aren't hardwired for survival, but are learned—mediated by our brains. Think of the first time you brushed your teeth. You probably thought "Left…right…up…down." But now it's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

TEACHER'S GUIDE TO ACTIVITY

It's the Thought that Counts

In the first section of this unit, students explored blink reflexes that were coordinated by the midbrain. Researchers have found that this survival reflex is anything but simple. It is possible to develop a "conditioned" eye blink reflex; that is, to resist the impulse to blink and to learn to respond to new situations when blinking is necessary. In a series of experiments, researchers applied a puff of air near the eye of a rabbit and simultaneously played a distinctive sound. The rabbit quickly learned to blink when the sound was heard. This learning appears to be a function of the brain's cerebellum.

Section of the Spine



The second activity begins by describing a simple motor reflex: When you avoid a prickly cactus or a hot stove, the message goes from receptor to spine to motor neuron.

In the computer program "React" students explored how quickly they could recognize a signal and respond with a simple click. This is not a simple reflex, and students should be clear why it requires some "intervention" by the brain, but not much. Then they are asked to take the progression one step further. In the second section of "React" the subject recognizes and separates left from right, and then different kinds of shapes. Compare the average speed achieved 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.

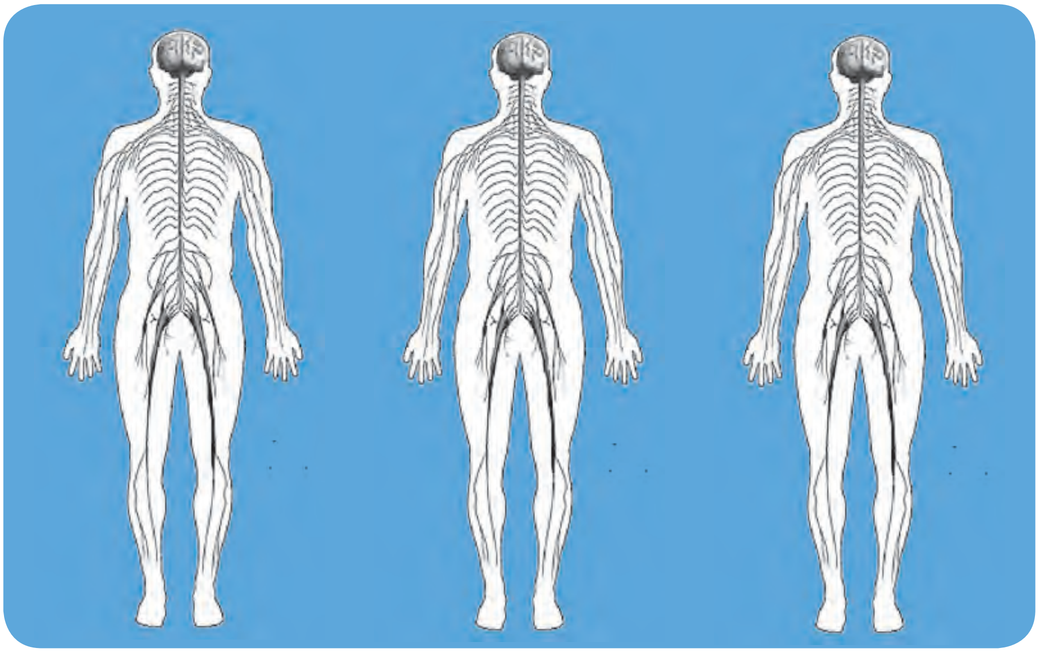


Image adapted from: *http://diabetes.niddk.nih.gov/dm/pubs/complications_nerves/images/fourparts.gif*

Students should note that a "simple reflex" involving a touch or pain sensor and a motor response moves from the sensory nerve to the spine, and back along a motor neuron to the muscle.

The three tasks in the React program require analysis and response by the brain at some level. Lines on the first diagram (showing a simple reflex) should go from finger to spine to finger; on the second diagram, from finger to spine to brain to finger; on the third, from finger to spine to cerebrum to spine to finger.

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!) Some novice players react to the oncoming ball by flinching or blinking. But like the rabbit in the experiment described above, a good ball player soon conditions his/her blink reflex.

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

While most units on neuroscience begin by discussing electrical signals, chemical messages are actually more common in multicellular animals. This module began by looking at how the simplest organisms communicate through chemical signals. Now students can explore the far more complex system of chemical messages in humans.

The reading selection *The Alchemy of Life* begins by outlining the basic neurotransmitters that cross synapses to coordinate response in animals. Students may quickly jump to questions and speculations about other kinds of chemical messages sent by *hormones*. Technically, a neurotransmitter is a molecule that is *synthesized in a presynaptic neuron, and produces a response in a postsynaptic cell*. So while hormones are certainly chemical messengers, they aren't all neurotransmitters in the strict sense of that definition. The chart below illustrates just a few of the neurotransmitters currently studied in humans.

Many basic textbooks outline the functions of neurotransmitters one at a time, implying that they operate independently. But it's clear from modern research that to maintain homeostasis organisms must achieve a delicate balance among many types of chemical messages. That's why the section on "chemicals from the environment" includes a suggestion that students brainstorm a concept map showing the interaction between various neurotransmitters and body processes.

- 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.
- Serotonin (5-hydroxytruptamine) is a "reward" neurotransmitter. The brain cells that release serotonin help moderate mood swings, limit aggression, and help modify pain.
- 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 are implicated in schizophrenia.
- Histamines (the chemicals that cause your body to respond to cold viruses and allergens) are also neurotransmitters. And there are many more, including hormones like gastrin, gonadotrophins, endorphins, glucagons, thyrotropin, and insulin. These aren't necessarily used to connect nerve to nerve, but change the membranes of dendrites and thus help coordinate body responses.

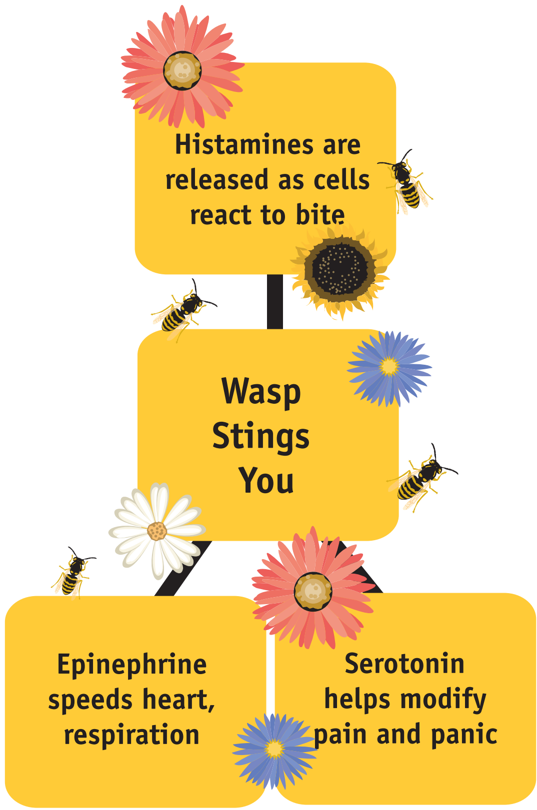
The Challenge of Chemicals from the Environment

One way to help students begin to conceptualize the dynamic relationship among neurotransmitters is to have them develop concept maps which include the responses to given environmental challenges. Offer each group a challenge card, with a situation such as these:

- Someone threatens you in a way that makes you very angry.
- You eat a very heavy meal, and you relax in front of a football game.
- You are surprised by a large spider on the back of your hand.
- You are stung by a large wasp.
- You exercise regularly, running a few miles each morning.
- You are sleeping soundly and an alarm rings.

Once groups have tried one concept map, they might be challenged to invent a situation for another group to analyze. They can then move on to the more specific hypotheses in the activity *All Together Now*. Note: Answers may vary somewhat. Even among individuals of the same species, the exact mix of neurotransmitters can vary. Students should understand that neurotransmitters must work in a coordinated way.

Sample Concept Map for the reaction to an insect bite:



The student reading progresses from a discussion of very mild chemical influences (like coffee and caffeine) to one that is potentially fatal alcohol abuse. It's important that students don't trivialize the comparison.

Apply and Extend

There are many authentic connections that can be made when students study neurotransmitters. They can monitor their own responses to common situations like eating, exercise, or scary movies by charting and comparing blood pressure and heart rate over time.

Another important extension should involve the way that drugs can alter the way in which neurotransmitters are released and sensed by cells. The diagram illustrates the interference of morphine and opiate receptors on the cell.

Another connection involves use of alcohol:

- Alcohol blocks reception of glutamate, preventing the hippocampus from changing short-term memories to more permanent ones.
- Alcohol enhances the receptor mechanisms for GABA, making most people sleepy. But when chronic drinkers try to quit, they can't relax because their nervous systems become used to the more intense effects.
- 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 a reward neurotransmitter. It's also one that helps us associate subtle environmental cues with pleasurable memories—like "mom's chicken soup." Some pharmacologists believe that the association of places with past drinking experiences contributes to craving.

All these changes confuse a system that originally evolved for survival.

Game On?

Researchers at Stanford University School of Medicine are studying how video games trigger the release of neurotransmitters in the brain. They have found that the responses of men to games was far stronger than the responses of women. The nucleus accumbens of their brains sometimes released levels of neurotransmitters comparable to addiction!

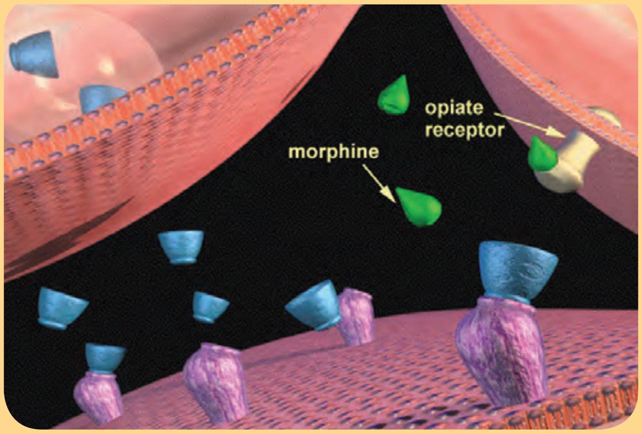
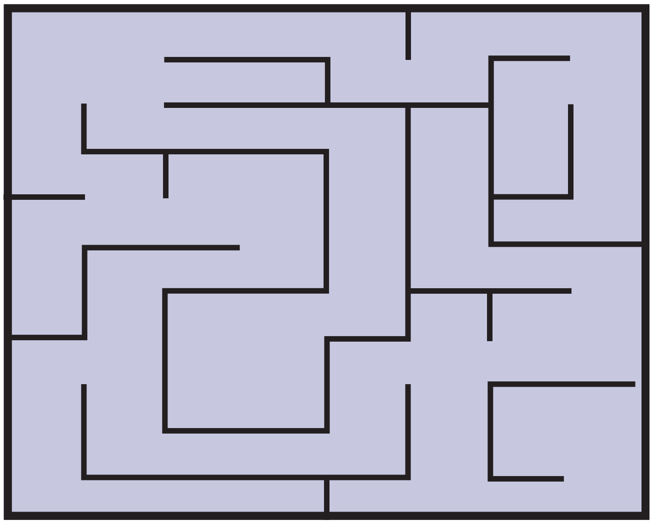


Image source: *http://www.nida.nih.gov/pubs/teaching/Teaching2/largegifs/slide17.gif*

For further information on the neurobiology of addiction, go to *http://www.nida.nih.gov/pubs/teaching/Teaching2/Teaching4.html.*

Use Your Brain!



In only about 1300 grams of tissue, 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! But somehow, you are able to concentrate and focus on a single task. Here's an activity students can use to investigate how they learn, and their ability to concentrate. It can also be used as a post-viewing activity for the second video, since research with rat mazes is featured.

To complete the activity, students will need colored pencils, a clock with a second hand, an MP3 player and a jar of crushed garlic (or other strong odor that is non-toxic and unlikely to stimulate allergies). Appoint one student in each group to be the Primary Investigator. In a quiet setting each member of the team tries a maze and records the baseline time required for completion. This step is to provide a standard and practice timing. From the Web site *http://www.onebillionmazes.com/?t=0* print out 4 copies of each of the first four mazes for each group. Mark the number of the maze on the back. The PI distributes mazes at random to the 4 subjects in the group upside down and determines the time for each group member to complete the first maze. For step 2, the PI times each subject on a different maze while providing a distraction, in the form of music. For step 3, each subject must sing his/her favorite song while solving a third maze. For step 4, the PI opens a jar of garlic to provide a strong odor as a distraction as the mazes are solved. Students 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?
   Averaging and random assignment of mazes minimizes error.

2. Use the diagram at the right 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.

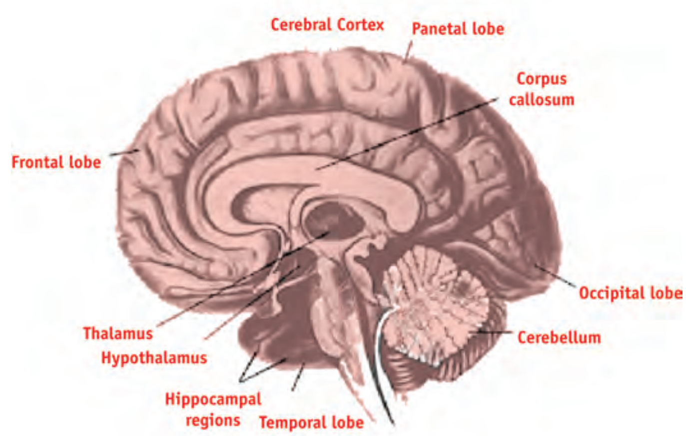


Image source *http://pubs.niaaa.nih.gov/publications/aa63/images/brain.gif*

Students should realize that many areas of the brain must work together to solve a maze. The occipital lobe is responsible for vision, the parietal lobe is the center of visual attention and goal-directed voluntary movements, and the cerebellum for fine motor coordination. Broca's area (for speech) is located in the inferior frontal gyrus. The temporal lobes are responsible for hearing. Odor is detected by the piriform cortex, a portion of the primary olfactory cortex.

It's also important for students to realize that the mazes may be only approximately equal in difficulty. Some subjects could be right- or left-dominant, and find certain turns easier to perceive than others. Only a large number of subjects would reduce this source of error.

Some of the first quantitative studies of the performance of rats in mazes were completed by American psychologist Karl Lashley in the 1920s. Lashley would allow a rat to complete a maze to get food again and again. He would then create lesions in various areas of the cerebral cortex, and then measure whether the rat could still complete the maze. But Lashley thought that all areas of the cortex were more or less equivalent. His student, Donald Hebb, began the work to localize specific cortical areas for vision, hearing, and spatial discrimination.

THE BRAIN'S INNER WORKINGS VIDEO PART II: COGNITION

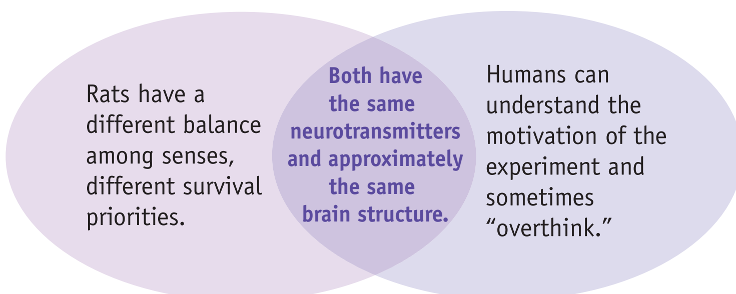
Study Guide

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

1. What is "higher order thinking?" **Problem-solving, creative thinking.**

2. Give some examples of higher order thinking tasks that have challenged you today: **Answers will vary; finding a route around a detour, passing a test, getting a new friend to respond, fixing a broken tool, writing a poem or an essay.**

3. Many scientists 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.



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? **We can now study healthy brains of people doing normal, every day functions.**

4. Use the video and outside sources to identify the parts of the brain.
   1. **cerebellum**
   2. **cerebrum**
   3. **frontal lobes**
   4. **motor area**
   5. **Broca's area (language)**
   6. **parietal lobes**
   7. **sensory lobes**
   8. **occipital lobes**
   9. **temporal lobes**

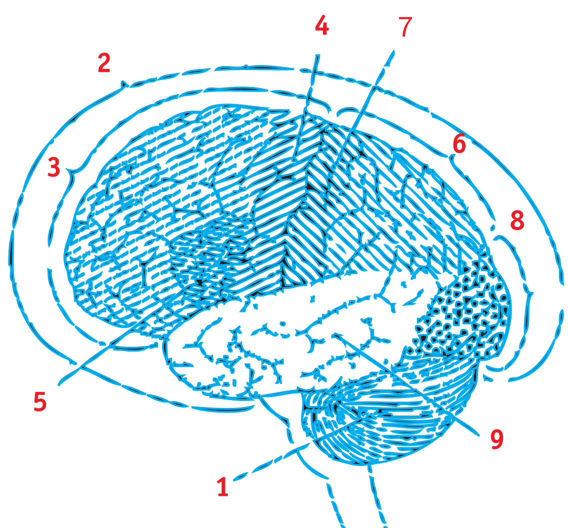


Image Source: *http://www.ninds.nih.gov/disorders/brain_basics/know_your_brain.htm#art*

5. 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 brain processes information differently. There are several lines of evidence that suggest malfunctions in dopamine transmission.**

A Note on Sensitivity and Stigma:

Whenever groups of students study brain disease, there is the possibility of reaching someone for whom the problems are very personal. Despite progress in society's recognition of the nature and challenges of brain disease, there is still stigma surrounding brain disease and those who suffer from it, and still some situations where information may be uncomfortable.

The video only begins to suggest the progress that has been made in this area. One of the most basic concepts in life science, the idea that individuals vary and that such variations make populations stronger, is an important foundational idea here and in the culminating activity *It Takes a Community*. Students may wish to contrast old ideas about mental illness with attitudes today.

TEACHER'S GUIDE TO ACTIVITY

All Together Now

This activity is structured as a partially open inquiry. Students begin with hypotheses, and then test them using procedures that they have developed themselves.

Students have a variety of options to measure these parameters, and in particular, several ways to measure blood flow to the skin. A visual evaluation using digital photos is generally effective. Blood oximeters can be purchased online for under $60. You can also use the NIH program referenced in the student guide, which measures the color saturation of a digital photo (see ImageJ at *http://rsb.info.nih.gov/ij/*). (But hint: crop a very small portion of each photo to analyze, since the program is very memory-intensive).

Because these are very important concepts for student understanding, it is worth the time to allow students to determine their own step-by-step procedures. As they do, encourage students to talk about how to make their measurements as reliable as possible. Questions to consider include:

- How will subjects be selected? Should they be controlled for gender, age, athletic ability?
- How will safety be insured? Will parents be contacted (or the physical education department be consulted) to insure that the subjects can handle exercise?
- How will the definition of "lunch" be standardized? Some students have only a drink or fruit, while others eat carbohydrates and protein.
- How quickly after exercise and/or lunch will measurements be taken?

System	Rest	Danger/Exercise	After Eating
Heart Rate	Lower	Higher	Recovers to base rate over time.
Respiratory Rate	Lower	Higher	Recovers to base rate over time.
Blood Pressure	Lower	Higher	Recovers to base rate over time.
Blood Flow to the Skin	Greater	Less	Greater/may result in flushing to cool the skin more quickly.

Because each group will have different standardized methods, the results below are approximate:

1. Why does your blood pressure change when you exercise? **The body increases blood flow to muscles by constricting blood vessels and increasing heart rate.**
2. What's the survival advantage of being able to control the diameter of peripheral blood vessels? **The total volume of blood in the body is insufficient to function for both digestion and strong exercise at the same time.**
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? **The "butterfly" feeling is the narrowing of the blood vessels that serve the 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? **Chemicals often confound and counter the appropriate effects of neurotransmitters. For example, nicotine can constrict blood vessels raising blood pressure, while alcohol dilates the blood vessels in the skin, making you "feel warmer" which increases the risk of hypothermia.**

EXTRA BACKGROUND

Learning for Life

Students are often very interested in how they learn—and why some of them learn differently than others. This topic is far more important than its treatment in the standard textbooks would imply. That's why it's very important to encourage students in this section to respect diversity. The fact that they may learn differently doesn't mean they learn less or less well. Moreover, understanding one's strengths in learning can help a student plan for further education and a career.

The reading section *Learning for Life* includes basic information about neuroplasticity. This is especially important for students to understand. They often ask: "Why can children learn more easily than adults?" or "Why is drinking or drug use more dangerous when you are a teen?" The answer involves the plasticity of the growing brain.

There are several forms of memory. Immediate memory is often considered short term. Conversion from immediate to lasting memory is very much dependent on relevance and the processes that the learner uses to retain the information. In the classroom this has very important implications. We offer students massive "data dumps" every day. Only if they find the information relevant will they be motivated to organize, store, and remember it.

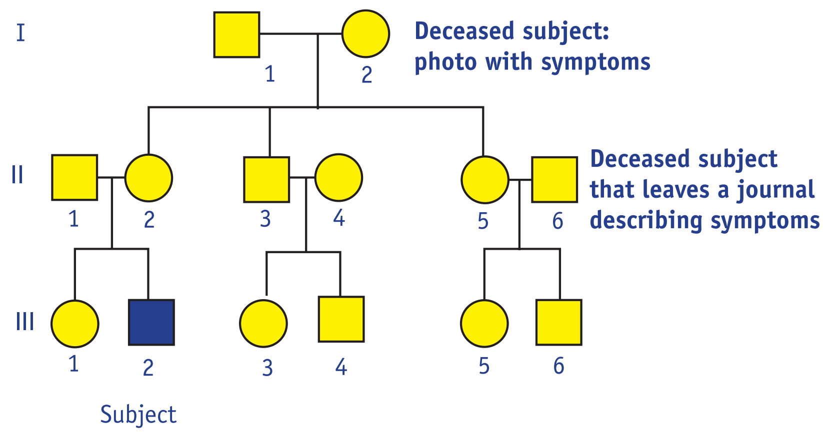
The reading passage uses an analogy of a "big box" store's delivery and stocking process. To extend this analogy a bit, consider that what's being stored (the information) must fit into a previously-established organizational scheme. In pedagogical terms, this means learning must be *authentic* in order to be long-lasting.

Another practical extension: If for some reason the trucks kept coming and coming to the loading dock, but the staff inside the store couldn't shelve them fast enough, the docks would overflow. Ask students if they've ever been reading and suddenly realized that they had blanked out for a few paragraphs. In effect, their "loading dock" (hippocampus) was too full and they couldn't effectively comprehend or store more information.

A second implication of the analogy explains the relevance of constructivist methods. The delivery persons can't stock the shelves in the store; the employees must do it. In the same way, the teacher can't force the students to use their hippocampuses to file their short-term information as long-term, retrievable memories. The learners must do that themselves.

TEACHER'S GUIDE TO SUMMATIVE ASSESSMENT

It Takes a Community



This open inquiry asks students to create a complete medical history, prognosis and treatment plan for an imaginary patient. It is best accomplished in sequence. First, students invent a patient. This might be done as a brainstorm session, where students first give the patient a name, a face (perhaps even a drawing or clip art), and then research the symptoms the patient might have experienced. While the responsibility for writing this history rests with the doctor on the team, using a brainstorming session helps speed up the rest of the work. Next, the geneticist and the public health researcher provide additional information. The geneticist might invent an imaginary pedigree like the one above.

A health researcher might begin with a questionnaire based on suspected environmental factors, then create the responses of the patient to the questionnaire. (Creative students may also wish to show the responses of family members to the same questions.)

Finally, the psychologist and medical social worker collaborate for a treatment plan. Remind students that every treatment plan involves the family, not just a single patient. The activity could also be expanded by adding a pharmacologist to the team to research medications. Activities like this are best assessed with a rubric, which might begin like this and then be expanded with student participation:

Criterion	Incomplete	Novice	Intermediate	Professional
Patient profile is complete and consistent.	The profile is missing a major component such as symptoms, and consistent medical history.	The profile has only a few details on symptoms or medical history.	The profile has many details, but some of them are inaccurate or inconsistent.	The profile is complete, detailed, accurate.
Reports reflect accurate research.	No evidence research was used.	Some evidence research was used, but sources are poor.	Evidence of use of a small number of good sources.	Evidence that each team member used good sources.

Today, Tomorrow, and the Future

This last section of the module suggests the importance of this content material for students. First and foremost, knowledge of one's brain and nervous system can lead to better decisions about health and social relationships. This is an ideal time to assess not only student knowledge, but potential changes in their decision-making skills and attitudes. Second, this brief exposure to research might provide the opportunity for students to explore new careers, at every level from technology to research.

APPENDIX

Correlation to Common Middle and Secondary Textbooks

Title	Publisher	Date	Pages
BSCS Biology—An Ecological Approach	Kendall/Hunt	2008	488-494, 501-502
BSCS Biology—A Human Approach	Kendall/Hunt	2008	230-241
Biology	Prentice-Hall/Pearson	2008	897-915
Holt Modern Biology	Holt McDougal Littell	2009	1004-1024
Holt Biology	Holt McDougal Littell	2008	Various Pp, including 936-967
McDougal-Littell Biology	McDougal-Littell	2008	816-846, 872-895

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