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Neurobiology Using BOTH Sides of the Brain

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Introduction

Are you right-brained or left-brained? At one time it was thought that a person in whom the left cerebral hemisphere was dominant would be more logical and mathematically inclined. If a person was right-brain dominant, they would be talented at creative activities like art and music. Things are not that simple, but I am using this title for my unit on neurobiology to emphasize the idea that I want my students to learn about the nervous system by using a variety of activities where they can put their creativity to work, and by exploring how scientists are using scientific methodology to investigate the nervous system. This unit will incorporate historical research on the nervous system as well as cutting edge research being done using the latest imaging techniques. My hope is students will see that scientists must often find creative ways to explore areas of interest, such as the brain, that are difficult to access directly.

This unit is designed for a class of International Baccalaureate (IB) III Biology students, but would also be applicable for AP Biology students, or even a Psychology class. As one of the IB focused curriculum units, called options, each year I choose to cover Neurobiology and Behavior. This unit will span about three weeks, in which I meet with students every other day for ninety minutes. Just as it is difficult for scientists to get into the inner workings of the nervous system, it has been difficult for me to find good ways to bring the nervous system to life for my students. They can see the effects of nervous system action—reflexes and behavior—but since there aren't a lot of moving parts or easily distinguished pathways in a brain, they do not view the brain as particularly interesting. In developing this unit, I have included activities and labs that will add interest to the topic and help students see the relevance of the topic to their lives and maybe to their future careers.

IB students are also required to design and carry out their own investigations in biology, and yet, even though they are seniors, they always seem to have difficulty accounting for more than one or two variables, or designing an experiment that collects sufficient data. I believe that by exposing them to research methods being used by real scientists in the field, they will begin to see the importance of designing experiments with full consideration for conflicting variables, using proper controls, repeating trials and all other aspects that go into collecting meaningful data to test a hypothesis. As part of this unit, students will read about current research being done in neuroscience, then "dissect" and discuss the papers in terms of how the experiment was designed and how data was collected and analyzed. A behavior experiment will be replicated by the students after analysis of the original report. Having read, analyzed, discussed, and replicated various

experiments they will then design and conduct their own experiments exploring some area of neurobiology or behavior, with the expectation that they will apply the lessons learned about experimental design.

Background Information

I have been teaching much of the background information that follows, but during my research of the topic, I learned the answers to many of the questions I had about how neurons work, how imaging techniques of the brain are done, how disease affects the brain, and how plastic the brain is. In addition, as I was looking for research examples for my students to use, I learned a great deal more about what we still do not understand about the brain. So read on for the things your biology text left out about the nervous system!

The nervous system is divided into the central nervous system (CNS), containing the brain and spinal cord, and the peripheral nervous system (PNS), which connects the CNS to the rest of the body. The basic unit of the nervous system is the neuron. Its function is to transmit signals to other neurons, muscle cells, or glands. The integration of signals, carried out by the central nervous system, is used to regulate body processes, and perceive and respond to the world around us.

Neurons

Although there are many types of neurons, they (almost) all have some similar characteristics. Each neuron has a cell body or soma containing the nucleus of the cell and other organelles necessary for carrying out the cell's function. Extending from the cell body are two types of processes (cellular extensions). A neuron may have one or many dendrites, which are branching processes that receive incoming signals. One axon, often with branching ends, leaves the cell body. It is this special process that sends an electrical signal—the action potential—which is transmitted down its length to the next cell. At the terminating end of the axon is a gap, the synapse, between it and the target cell.

Before beginning a discussion of how an action potential is propagated, it is a good idea to review membrane structure, the properties of the lipid bilayer, membrane proteins, and passive and active transport across the membrane with students. Students should recall that ions cannot cross the lipid bilayer, but must cross through transmembrane proteins. Some of these proteins are simple gated channels, which change shape to allow the ions through, and some are pumps which require energy in the form of ATP to pump ions across the membrane against their concentration gradient. Some of these channels are permeable to cations, some to anions, and some are specific to only one type of ion. [1] Some of these channels are open for longer periods of time or open more frequently, such as K^+ and Cl^- channels, and must be deactivated to close. Others are more likely to be found closed, and must be activated to open. Some channels are stretch-activated, and open when the cell membrane is mechanically disturbed. Other channels are voltage-gated and open or close in response to changes in membrane potential. Still others are ligand-activated, meaning a specific chemical, called a ligand, binds to the membrane protein, either extracellularly or intracellularly, causing it to open. An example of this kind of activation is when calcium channels in the postsynaptic membranes of muscle cells are opened by the binding of the neurotransmitter acetylcholine. [2] The important point is that when these channels open and allow ions through, the concentration of ions inside and outside the cell changes, changing the membrane potential.

In addition to ion channels, other proteins in the membrane of neurons—along dendrites, the cell body, or even the axon—are important as receptors for neurotransmitters released by other neurons. The binding of these neurotransmitters, can lead to a change in the membrane potential. [3] Some neurons may have many such connections with other neurons, especially in the brain, where the development of connections between neurons is crucial to how the brain functions.

Membrane potential refers to a difference in charge across the cell membrane. The cytoplasm of the neuron is filled with proteins, anions such Cl^-, and cations such as Na^+, K^+, and Ca^{2+}, but is generally negative compared to the ionic concentration of the extracellular fluid. The membrane is permeable to potassium ions, with some open ion channels, and potassium reaches a state of equilibrium between the concentration gradient driving it to diffuse out and the potential gradient attracting the ions into the cell. (The K+ ions will diffuse out, down their concentration gradient, but are also being pulled in because they are attracted to the negatively charged interior of the cell.) At rest, the concentration of potassium ions is greater inside the neuron [120mM] than in the extracellular fluid outside the neuron [4mM]. The concentration of sodium ions outside the cell [145mM] is greater than inside the cell [15mM]. This sets up an electrochemical gradient for sodium ions to potentially enter the cell if more sodium channels open. [4] The resting potential of most neurons is about -70 millivolts, meaning the inside of the cell has a potential 70 millivolts less than the extracellular fluid. That is the starting point, or resting potential, for some stimulus to begin the events that lead to an action potential.

Propagation of the action potential is clearly described in most AP Biology textbooks. What is often not clear is how the signal is propagated from the dendrites, across the cell body, and to the axon. Bring in the Localized Graded Potential (LGP)! It is localized because it is a change in the membrane potential in one small area; graded, because the amount of change in the potential varies according to the strength of the stimulus. (This will not be the case with an action potential! Action potentials can be propagated over long distances with no variation in the amount of change in the potential, or its duration. [5]) A localized graded potential is initiated by some stimulus. As one example, neurotransmitters released at a synapse between an interneuron and the dendrite of a motor neuron will produce an LGP when ion channels open in the membrane of a dendrite, raising the membrane potential, and depolarizing a small area of the cell. [6] However, the change only lasts as long as the neurotransmitter is bound to the receptor. [7] Since neurons have very high resistance to the conduction of electricity, if no further input is provided, the current fades out quickly. This change in membrane potential would never make it down the axon, but since the distance that it must travel down the dendrite or through the cell body is very short, it may make it to the beginning of the axon, the hillock. [8] The cumulative effect of multiple LGPs contributed by multiple dendrites, may result in enough voltage-gated sodium channels opening that the threshold membrane potential is reached, triggering an action potential at the hillock of the axon. At the hillock, there is a higher concentration of sodium channels and a lower threshold for the initiation of an action potential. (So that's why the hillock is important!) Action potentials may also start in dendrites and lead to the initiation of an action potential in the axon, or in cell bodies, where the threshold level is higher. [9]

When the threshold level has been reached at the proximal end of the axon, usually about -55 millivolts, voltage-gated sodium channels change shape due to the change in charge and open, allowing sodium ions outside the cell to diffuse rapidly down their electrochemical gradient into a small section of the axon. (See Figure 1.) The inward flow of sodium causes the membrane potential to rise, becoming positive for a short time. This rising phase of the action potential is called depolarization. At this point the membrane potential has been reversed: the inside of the axon is now positively charged and the outside is now negatively

charged. When the membrane potential reaches its peak, about +40mV, the voltage-gated sodium channels begin to close, but voltage-gated potassium channels open, allowing K^+ ions to rush out down their concentration gradient and down the new potential gradient toward the negatively charged exterior of the axon. As more potassium ions diffuse out of the cell, the membrane potential falls, and the potential reverses again. This phase is called repolarization. During a brief period of time, called the refractory period, sodium channels are inactivated by the change in potential, and are unable to be opened by another threshold potential. So many potassium ions diffuse out through, not only the normally open K^+ channels, but also the voltage-gated K^+ channels, that the membrane potential drops below its original resting potential, resulting in a brief period of hyperpolarization. During this time the voltage-gated K+ channels close. The original resting potential is restored as potassium ions reestablish their equilibrium. Resting membrane potential is restored, but the position of the ions has been reversed, with more Na+ ions on the inside and more K+ ions on the outside of the axon than there were at the resting state. Although it does not take a lot of these ions to cross the membrane for these voltage changes to occur, the ions must be returned to re-establish equilibrium. They are pumped back across by another membrane protein, the sodium-potassium pump. This protein pump works continuously throughout the action potential, and the periods between the action potentials, to actively pump three sodium ions out for every two potassium ions it brings in, restoring the ionic concentrations to their original state. [10] At this point, this location in the axon is reset and ready to receive another stimulus.

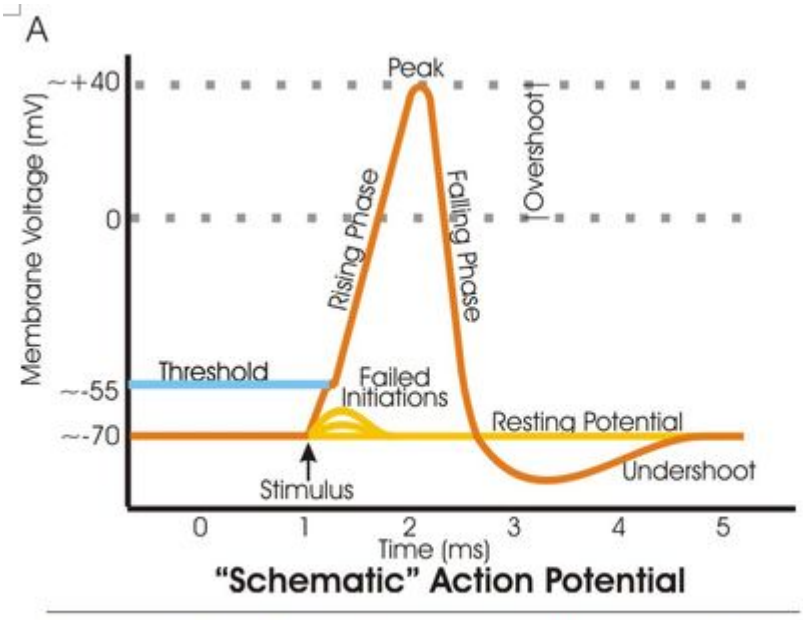

Figure 1--From: http://en.wikipedia.org/wiki/Action_potential

When the first action potential occurs at the axon hillock, the localized change in membrane potential caused by depolarization, raises the membrane potential in adjacent sections of the axon, downstream from the original axonal section that was stimulated, initiating a new action potential there that is as strong as the previous one. This section's action potential initiates an action potential in the next section and so on. In this sequential fashion, action potentials are propagated all the way down the axon. Action potentials travel faster in axons with wider diameters, such as the giant axons in squid. The reason for this is that the propagation of the action potentials down the axon is dependent on how far down the axon the next action potential can be initiated by the depolarization phase. The positive charge of the depolarization can travel locally through the axon or across the membrane through open membrane channels. A larger diameter axon has lower surface area to volume, and therefore more of the positive charge of the depolarization flows through the axon,

resulting in depolarization of the membrane farther ahead of the action potential. [11]

All axons cannot be big or we would need a much bigger skull to hold them. So axons have other mechanisms for speeding signal propagations. Some axons are insulated with a myelin sheath composed of Schwann cells, in peripheral neurons, and oligodendrocytes, in the central nervous system, wrapped around the axon at intervals. These glial cells produce an insulating fatty layer of myelin that surrounds axons and restricts the movement of ions into or out of the axon. Interspersed along the myelin sheath are sections of the axon that are not covered by the sheath, called the nodes of Ranvier. This intermittent insulating layer speeds up the movement of the action potential down the axon, because as the impulse passes through the part of the axon covered by the myelin, the potential is maintained because no ions can escape, and so it travels by diffusion the short distance covered by the myelin, to the nodes, where the action potential is propagated once again. [12,13] The speed of a signal down an axon varies depending on the diameter of the axon and whether or not the axon is myelinated, but the size of the action potential does not vary. The intensity of the stimulus that initiates the action potential is measured by the number of action potentials that occur in a neuron over time and is also indicated by the number of neurons firing. [14]

When the action potential reaches the terminal end of the axon, the impulse is converted from an electrical signal to a chemical signal. At the axon terminal, the change in membrane potential triggers voltage-gated calcium channels to open, and calcium ions flood into the terminal. Here in the axon terminal, vesicles filled with neurotransmitters are waiting near the presynaptic membrane. When calcium ions enter the cytoplasm, proteins in the vesicle membranes change shape and fuse with the presynaptic membrane, forming a pore, through which the neurotransmitter is released into the synapse. The pore widens and the entire vesicle membrane is incorporated into the presynaptic membrane. Endocytosis of the membrane is used to reform vesicles which are refilled with neurotransmitters. When calcium channels are close to the site of vesicle-binding to the presynaptic membrane, neurotransmitter release is very fast. When they are farther away, release is slower and may even delay until a threshold level of calcium ions is reached. [15]

After being released from vesicles, neurotransmitters diffuse the short distance across the synapse to the post-synaptic neuron. There are two types of neurotransmitter receptors that may be found on postsynaptic cells: transmitter-gated ion channels and G-protein-coupled receptors. When a neurotransmitter binds to a transmitter-gated ion channel, the channel changes shape slightly and opens to allow ions to diffuse into the postsynaptic neuron. If it allows sodium ions in, the resulting depolarization creates an excitatory post-synaptic potential (EPSP). The neurotransmitters acetylcholine and glutamate activate EPSP ion channels. If the channel that opens lets in Cl-, the resulting hyperpolarization creates an inhibitory post-synaptic potential (IPSP). The transmitter-gated channels that bind the neurotransmitters glycine and GABA cause an IPSP. [16] Both EPSPs and IPSPs are forms of localized graded potentials. The summative effect of the binding of different neurotransmitters from many different pre-synaptic neurons will result in the activation or inhibition of an action potential in the post-synaptic neuron.

G-protein-coupled receptors bind neurotransmitters and activate small molecules called G-proteins (guanosine triphosphate binding proteins) that move along on the inside of the post-synaptic membrane and activate either G-protein gated ion channels, or enzymes that produce second messengers which then trigger other enzymatic activities controlling ion channels or cell metabolism. [17] The neurotransmitter acetylcholine causes an EPSP in skeletal muscle cells, but is inhibitory in heart muscle and slows heart rate. The reason is that ACh binds to G-protein receptors in the membranes of heart muscle cells which activate G-proteins. These small proteins then bind to and open potassium channels, resulting in hyperpolarization of the muscle cells. [18]

Activated G-proteins can also begin a cascade of enzymatic reactions inside the post-synaptic cell that result in the opening of many ion channels instead of just one, extending the signal to wider and more distant areas of the membrane. [19]

To stop the signal to the post-synaptic cell, neurotransmitters must be removed from the synapse. Some simply diffuse away. Some are reabsorbed by transporter proteins in the membrane of the presynaptic neuron and either destroyed, or repackaged in vesicles to be used over again. Glial cells surrounding the neurons may also reabsorb neurotransmitters. The neurotransmitter acetylcholine is destroyed in the neuromuscular synapse by an enzyme, acetylcholinesterase, produced by postsynaptic muscle cells. Interaction with synaptic transmission is the focus of many drugs—which act to either enhance or block the transmission of the neurotransmitter across the synapse. [20]

Evolution of the Brain

The only animals that lack any kind of nervous system are the sponges. Some, like the cnidarians, only have a network of neurons. Most invertebrates have a simple nerve cord with a cluster of neurons in the anterior region that serves as a coordinating region for the animals' responses to their environments. How brains evolved in vertebrate animals is still not fully understood. Brains, being soft tissue, do not fossilize. Therefore, fossil evidence of brain characteristics is mostly found by looking at casts of braincases. We can however, look at living vertebrates today and get an idea of the progression of brain development, and the different routes that it took in various lines.

All vertebrates share three basic divisions in the brain—the hindbrain, the midbrain, and the forebrain. Fossils of fish from 500 million years ago show these three areas of the brain. [21] The hindbrain includes the medulla oblongata, pons, and cerebellum, located at the top of the spinal cord. The medulla oblongata is at the top of the spinal cord; it regulates respiration, breathing and blood pressure. The pons relays information to the cortex and is involved in alertness. The cerebellum coordinates movement, posture and balance. It is larger in terrestrial animals than in fish. The hindbrain is dominant in fish, with the midbrain, devoted to the optic lobes, and the forebrain mostly composed of the olfactory bulbs. [22]

In amphibians and reptiles, more of the sensory processing is done in the forebrain, which is divided into the diencephalon and the telencephalon. The diencephalon is composed of the thalamus, which integrates incoming sensory information and relays it to the cerebrum, and the hypothamus, which controls basic drives, emotions, and secretions from the pituitary gland. The telencephalon of reptiles and amphibians became the cerebrum in mammals. It is used for learning and memory. Birds have a larger cerebrum than reptiles, and in mammals, the cerebrum is the largest part of the brain. [23]

The cerebrum is divided into two hemispheres, following the bilateral symmetry of all vertebrates. And yet there is evolutionary evidence for lateralization—the specialization of functions in the two hemispheres of the brain. The fact that the left side of the brain controls the right side of the body and vice versa, might show a kind of symmetry. The fact that there is a preponderance of right-handedness in humans would indicate lateralization of that control. Studies have shown that humans are not alone in being predominately right-handed. Other primates show a preference for using the right hand when performing many tasks. [24] Beyond handedness, there is evidence that the left and right sides of the brain have evolved to take on a wide range of different tasks. As vertebrate brains evolved, each hemisphere became more specialized for certain kinds of tasks. The left hemisphere took over tasks that involved ordinary patterns of behavior that were self-motivated, such as feeding and language. The right hemisphere was then left to deal with unexpected stimuli,

and to take control when the environment threatened in some way, and a rapid response was needed. Many animals react more to predators that they see in their left field of vision—using the right side of the brain. [25] It makes sense that natural selection would have favored the compartmentalization of tasks in the brain rather than duplicating roles on both sides of the brain.

Humans have the largest brains in proportion to body mass of all vertebrates. The size of our cerebral cortex sets us apart from all other animals, even our closest relatives, the chimpanzees. [26] Animals are often used in neurological studies even though their brains are not nearly as complex as ours. There are differences in the size of various parts of the brain, but many of the structures are similar enough to make using animals to understand the workings of the brain valid. When trying to develop drugs and other treatments for neurological disorders, it is more cost-effective, not to mention safer, to test those treatments on animals first. However, results of studies with animals do not always translate readily to humans. [27]

Imaging Systems

One difficulty with understanding the brain is that it is protected inside the skull, out of view, with hardly any discernibly moving parts. It is also such a complex network of so many kinds of neurons and supportive cells that pathways for processes are difficult to find and follow. Since Camillo Golgi developed his staining technique for neurons in 1873, scientists have been trying to find ways to get at the information stored in the brain. One way to understand how the brain works is to look at how it is different when it doesn't work. Brain lesions are damaged areas of the brain as a result of injury or disease. Lesion studies have helped us understand how some parts of the brain function, when abnormalities or injuries have affected individuals in particular ways. Paul Broca discovered a language center in the left hemisphere of the brain by studying a man whose speech was affected when he incurred damage to that area of the brain. [28] The prefrontal cortex was shown to control decision making and control of emotions when an iron rod passed through the head of Phineas Gage in a construction accident, leaving him alive, but forever changing his behavior. [29]

Modern technology provides new ways to study brain function. An electroencephalogram (EEG) can be used to detect electrical activity in the brain and where that activity is located. An EEG is done by placing a network of electrodes over the head, which measure the electrical currents created by activation or timing of neuron signals in the cerebral cortex. The technique is noninvasive, and has been used in sleep studies, but is limited in its usefulness because the signal must pass through many layers to reach the electrodes, and the information generated is not very detailed. [30]

Positron Emission Tomography, or PET scans, trace radioactive molecules injected into patients as the isotopes decay. The radiation given off by the isotope in the tracer molecules is detected in a scanner and converted into an image. Depending on the isotopes used, blood flow, metabolic reactions, protein synthesis, or neurotransmitter synthesis can be traced to see what areas of the brain are active. This technique can be used to study receptor changes in diseased neurons, to determine what the response of the brain is to a drug, or to determine what the optimal dosage is for a particular drug. PET scans may be used to find actively growing tumors, or to diagnose disorders. [31]

Magnetic resonance imaging, or MRI, is a completely noninvasive technique that uses a combination of radio waves that pass through the brain, and a large magnet to create a detailed image of the soft tissues in the brain. Functional MRIs (fMRI) are used to map blood flow or oxygen consumption within the brain. Because fMRI can measure functional responses, like blood flow, they can be used to map activities in the brain, similar to PET scans.

At the cellular level, various dyes and staining techniques have been used to help visualize neurons. Antibodies designed to bind to specific proteins inside neurons, or on dendrites, axons or at synapses have been used to target and visualize particular processes in neurons. A gene for a bioluminescent protein from a jellyfish can be linked to promoters for the gene for GABA, injected into mice brains in order to visualize where the neurotransmitter is going in the brain.

Genetically altered "knock-out" mice, are designed to be deficient in a particular gene which gives them the characteristics of a human disorder, such as schizophrenia. These animals can then be used to study how the gene affects the nervous system and behavior, and how potential drugs or other treatments might alter these effects, before testing the drug on human patients. All of these new techniques offer hope for the understanding, treatment, and cure of nervous system disorders.

Strategies and Lesson Plans

The goal for this unit is to not only give students an understanding of the nervous system, but to also connect them to the kinds of research being done in universities they might be attending, and prepare them to participate in that research. In order for them to be ready, they must have an understanding of what it takes to design and conduct an investigation. During this unit students will read about research, "dissect" the research, replicate the research, and design their own investigation related to research in neurobiology. If you cannot access the journal articles used in this unit, find others that will be of interest to your students and prepare "dissection" guides for them.

Day 1—The unit will begin with a lecture on the structure of a neuron. Neurons are cells, and I will have students review cells by asking them to describe how this type of cell might be like the generic cell they diagrammed in IB Biology II. What organelles might it need and why? Where would organelles be found in a neuron? The lesson will continue with a lecture on the propagation of an action potential. To help students understand that the action potential does not involve movement of molecules down the axon, we will act out an action potential by doing "The Action Potential Wave". (See Activity 1)

Day 2— Students will review membrane structure and transport and relate it to the previous day's lecture on the action potential. In order for them to get a feel for how scientists might have studied the changes in membrane potential in a neuron, students will use conductivity probe-ware to measure the flow of ions as salt water diffuses through dialysis tubing. A good description of this type of lab can be found at http://cms.upb.pitt.edu/uploadedFiles/About/Sponsored_Programs/Science_In_Motion/Biology_Labs/bio019_%20Vernier%20-%20Diffusion%20Through%20Membranes.doc. After a lecture on synaptic transmission, students will investigate the effects of the drugs cocaine, amphetamines, benzodiazepines, nicotine, cannabis, THC, and alcohol on synaptic transmission and make short reports to the class on the effects of the drug they researched.

Day 3—Having looked at the smallest unit in the nervous system, students will be given a short introduction about the evolution of the brain. After going over the parts of the brain and their functions, students will be given pictures of various vertebrate brains and told to match them to the animal they came from based on what they know about phylogeny and the characteristics of the animals and what parts of the brain the animal might use most. Students will then make a three-dimensional model of the human brain from a series of MRI

images, labeling all important areas, and providing an annotated key with their model. (See Activity 2) For homework, students will read a Scientific American article, "Origins of the Left & Right Brain", and answer questions from a reading guide in preparation for dissecting and replicating an experiment described in the article. (See Activity 3)

Day 4—The article, "Origins of the Left & Right Brain" describes the evidence collected for the evolution of lateralization of the brain in vertebrate animals. Several behavioral studies are described in the article. Having read about them the previous night, I will give the students a copy of the one of the original reports—"Complementary right and left hemifield use for predatory and agonistic behavior in toads" by G. Vallortigara, L.J. Rogers, and others—along with "Dissection Instructions". (See Activity 4) There are a few vocabulary words in the report that students might not be familiar with, and we will go over these in class, trying to define them using context. Students will then work with lab partners to "dissect" the report and discover how the experiment was designed to control for variables, to test for the hypothesis, and to collect sufficient data.

Day 5—Students will replicate the predatory behavior experiment with toads described in the Vallortigara paper. The experiment involves presenting prey—worms or crickets—to toads from a clockwise or counter-clockwise direction and recording the point where the toad strikes at the prey. Having read, and thoroughly worked through the steps of the experiment, they should have a good idea about why they are doing what they are doing, and what outcome they should expect. Safety and animal care procedures must be reviewed before beginning the lab. We will discuss any deviations we will have to make from the methods described in the report due to budgetary, time, and equipment constraints, and come up with the methods for collecting data that each lab group will use. However, they will be working with live toads. I will have students do a test run of our procedures and make adjustments before going any further. We will discuss whether the adjustments might make a difference in the validity of our results. The toads will be kept in the classroom following the experiment.

Day 6—(Possible second day of the toad experiment) Following the collection and analysis of class data from the experiment, students will compare their results to the results reported in the original report, and discuss possible sources of error and ways to improve the procedure for classroom use.

Day 7—A power point presentation on various imaging techniques used to study the brain will be presented to the students, using several disorders as the focus of those images—schizophrenia, Parkinson's disease, and Alzheimer's disease. Students will then be given a summary of a study done at UNC on the effects of a cell membrane receptor protein—NCAM—involved in helping neurons in the pre-frontal cortex form synapses. Individuals with schizophrenia have unusually high levels of fragments of this protein in the brain. Transgenic mice, with a gene that creates similarly high levels of NCAM fragments, are being used to study the effects of these fragments on synapse development. [32] Because the article is very technical, I have summarized it for the students, leaving in the essential information on the methodology used. One of the authors provided me with images of neurons and brain tissue from the wild and knockout mice for my students to look at and compare. Students will identify and count the number of neurons on each slide, count the number of processes from each neuron and the number of branches, and come up with a branching index for each slide. They will then compare their results with the results reported in the article. For access to this activity, see Teacher Resources.

Day 8—A behavior study was also done with the mice in conjunction with the brain tissue analysis. Wild and knockout mice were made to swim in a T-maze to test the decision making ability of their pre-frontal cortex.

Students will be given a description of the experiment to dissect, and data from the experiment to analyze.

Day 9 and 10—Students will draw and label a diagram of the human eye, dissect a sheep eye and compare the structures in the two. Following a lecture on how vision occurs from the retina to the vision centers in the brain, students will explore a variety of visual tests and optical illusions. They will then be given an assignment to research the sensory organs and behavior of either crickets, mealworms, or earthworms.

Day 11-12—As a culminating activity, each students will design a lab testing or investigating the senses of the animal they have selected to research. They will be expected to incorporate all they have learned about good experimental design, conduct their experiment, analyze the results, and make a presentation to the class.

Activities

Activity 1—The Action Potential Wave

Ever been to a stadium where the crowd does the "wave"? No one moves from their seat, but the wave travels from one end of the stadium to the other. You can use this idea to help students understand how a signal can travel down a neuron without molecules actually moving down the axon. This could be done before or after a lecture on action potentials.

The Action Potential

Depending on the size of your class, divide the students into two groups. Have each group line up shoulder to shoulder, with a 2-3 foot gap between the two groups. Explain to the students that they are going to do the wave, but that if there is no one within 3 inches of them doing the wave, then they can not raise their arms. Have the first person in group 1 start the wave at a signal from you. The second group will not be able to continue the wave, because they will be too far from the last person in the first group.

Discussion: Why did the first person in the group start the wave off? Why did the wave only travel in one direction? Was anything physically passed down the "neuron"? How could the wave get passed to the second group if there is a gap?

Teacher's verbal signal—a stimulus that starts an action potential in a sensory neuron. If you say the "start" signal too quietly, the group will not begin the wave. The verbal signal has to reach a "threshold" level for the group to begin the wave. The signal can be given repetitively to start new wave action potentials in the student neuron. If the teacher gives the signal too rapidly, the first student in line will not be ready to start the wave again.

Students—Each student represents a section of the axon. When the threshold has been reached (a stimulus or an action potential has occurred next to them) the sodium gates open (arms go up—depolarization), then sodium gates close (arms go down—repolarization). A student's arms cannot start going back up when they are only half way down—representing the refractory period.

Synaptic Transmission

In order for this next step to go well, you should discuss this response with the two students involved before

the demonstration. The last student in the line represents the axon terminal. Give this student either a piece of candy or a rock. When the wave gets to that student they toss or pass this "neurotransmitter" to the first person in the "neuron" across the gap. When the student in the second row receives the candy or rock, they will either be excited and throw their hands up in the air, starting a second wave, or they will be sad, and their arms will stay down.

Discussion: How does the signal change as it goes across the gap? How do different "neurotransmitters" affect the post-synaptic neuron? What if one piece of candy was not enough to excite the receiver? (Be sure to note that neurons only release one kind of neurotransmitter, but that post-synaptic neurons will have receptors for both types of neurotransmitters. Also discuss that neurotransmitters are not taken up by the post-synaptic neuron, but are released from the receptor, destroyed by enzymes in the synapse, or reabsorbed by the pre-synaptic neuron.)

Saltatory Transmission

To represent an action potential down a myelinated axon, have students line up as before, but leave spaces between some of the students in the "axon". Students at the gaps will be connected to each other by a short piece of rope. When the student at the beginning of the space raises their hands, they will also raise the rope, which will be the signal for the student at the other end of the space to raise their hands for the wave. To compare the speed of the signal, have students create two parallel lines of equal length. One line of students might have only 4 students, because some will be replaced with sections of rope. The other line might have 10 students. Give both the start signal and observe which "neuron's" signal reaches the end first.

Discussion: Why does transmission of the signal happen faster down the myelinated neuron? If the arms going up represents sodium channels opening, then how is the signal moving through the rope sections?

Activity 2—MRI Model of the Brain

Students will construct and label a three dimensional model of the brain using layers of sagittal sections from MRI images of a normal brain. These images are available from The Whole Brain Atlas website: http://www.med.harvard.edu/AANLIB/home.html .

Teacher Preparation:

At the Whole Brain Atlas website, open Normal Anatomy in 3-D with MRI/PET (Javascript). Copy sagittal images 34, 38, 42, 46, 50, 54, 58, 62, 66, 68, and 69, into a Word document with all margins set at 0.5" and in landscape orientation. Enlarge each picture to 8" in order to bring the model closer to life size. Since this MRI was made through the brain from the left side through to the right, the images past the midline will need to be reversed to be seen from the right outside of the model. To do this, copy sagittal image 70 into MS Paint and under Image, select Flip/Rotate and flip the image horizontally. Then copy the reversed image to the word document and enlarge. Do the same for images 72, 76, 80, 84, 88, and 92. You may want to number the images to help students keep them in order. You may also want to trim away everything on the images except the brain, so that more than one image can be copied to a page, and to reduce the amount of black area on each image. Make a copy of the set for each student.

Materials:

Brain image copies. Foam board or cardboard, glue sticks, scissors, straight pins

Student Instructions:

Cut out the MRI images of the brain and glue them to cardboard or foamboard pieces, trimmed to fit. On each layer, label the following parts of the brain that are visible: cortex, cerebellum, medulla, pons, hippocampus, corpus callosum, pituitary gland, hypothalamus, ventricles, occipital lobe, frontal lobe, temporal lobe, parietal lobe, and spinal cord. Use straight pins to put the sections of the brain together in order.

Activity 3—An Introduction to the Origins of the Left and Right Brain

Teacher Notes:

Distribute copies of the following article and the reading guide to students to complete for homework. Have them work in groups the next day to compare answers. Each group should come up with 2 questions they still have about the topic of hemispheric lateralization of the brain to discuss with the class. Lead a discussion on how the experiments described in the article might have been carried out, reviewing the parts of the scientific method as needed.

Reading Guide:

"Origins of the Left and Right Brain"—Peter F. MacNeilage, Lesley J. Rogers, and Giorgio Vallortigara. Scientific American, July 2009

Directions: Read the article and answer the following questions in complete sentences on a separate sheet of paper.

1. What does the left side of the brain control?
2. What does the right side of the brain control?
3. What did scientists believe about the brain 40 years ago?
4. What was once believed about the connection between right handedness and language?
5. The hypothesis of this paper about the evolution of left brain specialization is….
6. The hypothesis of this paper about the evolution of right brain specialization is….
7. What are the areas of control of the two hemispheres

The Left Hemisphere

8. What kind of evidence was collected to test the hypotheses?
9. Describe the brain specialization evidence for:
    a. Fishes, reptiles, and toads
    b. Chickens, pigeons, quails and stilts
    c. New Zealand wry-billed plover
    d. Humpback whales

Origins of Right-Handedness

10. What evidence is more supportive of the idea that human right-handedness evolved from some earlier ancestor?
11. How did William D. Hopkins test for handedness in apes and what were the results?
12. What would have been an evolutionary advantage for right handedness in human ancestors?

Communication and the Left Brain

13. What do the authors hypothesize about the specialization of the left hemisphere for language?
14. What are some other examples of left brain specialization for language in animals?
15. Describe exceptions to the idea that the right hemisphere controls under emotional circumstances?
16. What are some examples of left brain control of nonvocal communication?

Evolution of Speech

17. What is a syllable?
18. How would syllables lead to language?

Did the Syllable evolve from Chewing? (p65)

19. How does the evolution of syllabic utterances relate the left brain specialization?

The Right Hemisphere

20. What is the animal evidence that the right hemisphere specialized in detecting and responding to unexpected stimuli?
21. How has evidence for human hemispheric specialization been collected?
22. Which eye is most likely to be used to watch for predators or competitors?
23. What negative emotional behaviors in humans are the result of right-hemisphere activity?

Responding to Surprise (p66)

24. What happens when the toad is presented with a predator from different directions?

Recognizing Others

25. The right hemisphere is also involved in reacting to others of its own species in the environment, which led to the role of the right hemisphere in _____.
26. Some animals that exhibit the ability for individual recognition are _____.
27. What is prosopagnosia and what is the most common cause?

Photogenic Left

28. What might portraits reveal about right hemisphere control of facial emotion?

Global and Local

29. Which hemisphere is more global, which more local in analyzing spatial aspects of the environment?
30. Describe why chicks with vision only in the right eye focused only on a few specific features.

Division of Labor in the Hemispheres (p63)

31. Describe why the brain damaged patients in the experiment drew the H as they did.

Why do Hemispheres Specialize?

32. When an animal receives stimuli of different types from its environment, it must process the information in order to make an appropriate response. What would be the selective advantage of hemispheric specialization?
33. How did Rogers create chicks without hemispheric specialization for visual processing?
34. How did this affect the chicks' behavior?
35. How do these result support the idea that hemispheric specialization is an evolutionary advantage?

Social "Symmetry Breaking"

36. Why would it be more likely to see the same types of hemispheric specialization in a variety of animal species rather than a 50-50 distribution?
37. What might be an evolutionary disadvantage to hemispheric specialization?
38. Why might these disadvantages have not kept brain specialization from evolving in populations?

Activity 4—Dissection of an Experiment

A Lab Dissection of "Complementary right and left hemifield use for predatory and agonistic behavior in toads" by G. Vallortigara, L.J. Rogers, A. Bisazza, G. Lippolis, and A. Robins

Teacher Notes:

After students have read the article in Scientific American, distribute copies of the original paper described in the article: Vallortigara, G., L.J. Rogers, A. Bisazza, G. Lippolis, and A. Robins. "Complementary right and left hemifield use for predatory and agonistic behavior in toads." Neuroreport 9 (14) (1998): 3341-3344. Go over the vocabulary words students will need to know in order to understand the paper. They should be able to predict what many of the words mean. Have students work with a lab partner to "dissect" the paper and find out how the researchers designed their experiment and collected data. Live toads can be ordered from Carolina Biological Supply (http://www.carolina.com/home.do) for $ 17.95 for three live toads. They are only available from March through September, so this unit must be taught within that time frame. Crickets and worms can be purchased from local pet stores or bait shops.

Student Directions:

Read the original paper from Neuroreport about one of the experiments done with toads described in the article from Scientific American. As you go through the paper, you will "dissect" it to find the parts of the scientific method that the researchers used.

- Vocabulary:
- Lateralization
- Hemifield
- Agonistic
- Conspecifics
- Complementary specializations
- Response competition
- Medial organs
- Lateral
- Anurans
- De novo

- Avian
- Modes of analysis
- Monocular

"The Introduction"

1. Describe the problem being addressed in this experiment.
2. Why would the answer to this problem be important to know?
3. What was already known that may relate to this problem?
4. What methods were used to find the answer to this problem?
5. Summarize the types of information included in the "Introduction"

"Materials and Methods"

Predatory behavior

6. List the materials used in the Predatory behavior experiment with B.bufo and B.viridis.
7. List the constants in this experiment
8. What were the dependent variables? How were they measured?
9. Describe the experimental groups.
10. Was there a control group?
11. Describe the testing apparatus or draw what you think it looked like.
12. Why was the outer cylinder white, and not clear like the inner cylinder?
13. Describe the procedure in your own words. Use diagrams if helpful.
14. What were the independent variables?
15. Why do you think the toads were isolated before the experiment began?
16. Why were they all males?
17. List the materials used in the predatory behavior experiment with B. marinus.
18. List the constants in this experiment.
19. What were the dependent variables? How were they measured?
20. Describe the experimental groups.
21. Describe the procedure in your own words. Use diagrams if helpful.
22. Why do you think crickets were chosen as the prey? Why were they all about the same size?
23. Why was the data from this experiment not combined with the data from the first experiment?

Agonistic behavior

24. List the materials used in the agonistic behavior experiment.
25. How did the scientists distinguish agonistic behavior form predatory behavior?
26. Describe the procedure in your own words.
27. How was the data collected?
28. How was the agonistic behavior of B. bufo different from that of B. marinus?
29. Was any data reported in the "Materials and Methods" section?

"Results"

Predatory behavior

30. Compare the number of strikes to the right and left visual fields.
31. Compare the rotation direction to the visual field interaction.
32. Compare the strike direction when the rotation was clockwise.
33. Compare the strike direction when the rotation was counterclockwise.

Agonistic behavior

34. Describe the results of the agonistic behavior experiment.
35. How are statistical tests helpful in analyzing data such as this?
36. How were the results processed and presented in this section of the report?

"Discussion"

37. How are toads' eyes different from birds and lizards? Why are the authors careful to avoid referring to left eye/right hemisphere and right eye/left hemisphere when discussing the toad data? (A diagram might aid your explanation.)
38. How can the experimental results be summarized?
39. What are two explanations proposed by the authors for the apparent lateralization seen in the experiments?

"Conclusion"

1. What is the conclusion of the authors about the data?
2. What two explanations do they suggest might account for the results?

Notes

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Teacher Resources:

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http://www.ndgo.net/sfn/nerve/ —Neuroscience Education Resources Virtual Encycloportal. Part of the Society for Neuroscience website. Links you to every possible site on the nervous system. You can search for sites on the nervous system by grade level, theme or format. One-stop shopping!

http://faculty.washington.edu/chudler/experi.html —Neuroscience for Kids. Lots of good activities for the classroom.

http://cms.upb.pitt.edu/uploadedFiles/About/Sponsored_Programs/Science_In_Motion/Biology_Labs/bio019_%20Vernier%20-%20Diffusion%20Through%20Membranes.doc -"Diffusion Through Membranes". Lab protocol for using conductivity probe-ware to measure diffusion of ions through dialysis tubing.

http://www.med.harvard.edu/AANLIB/home.html —The Whole Brain Atlas website. This site contains both normal and diseased brain images made using CT, MRI, and SPECT/PET imaging systems. I used this site to collect images for the MRI Brain Model activity.

http://www.sfn.org/baw/ —Society of Neuroscience website for Brain Awareness Week. Has great, free publications like Brain Briefings and Brain Facts.

http://outreach.mcb.harvard.edu/animations/actionpotential.swf —good detailed animation of an action potential.

http://www.learner.org/resources/series142.html?pop=yes&pid=1569# —Video clips on multiple topics dealing with the brain.

connie.woodcms.k12.nc.us —for access to a summary of the NCAM protein article as well as brain tissue and neuron images

Student Resources:

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http://www.ndgo.net/sfn/nerve/ —N.E.R.V.E, a great site for students, too!

http://www.ninds.nih.gov/index.htm —National Institute of Neurological Disorders and Stroke. Contains an encyclopedia of brain disorder information.

http://www.ncsu.edu/labwrite/ —the NC State University guide to writing a lab report. Use it to get A's on all your lab reports!

http://faculty.washington.edu/chudler/nsdivide.html —Neuroscience for Kids

http://www.kidskonnect.com/content/view/337/27/ —has links to many sites dealing with the nervous system as well as other systems in the body.

Appendix—Implementing District Standards

The specific aims of the International Baccalaureate science courses are to make students aware of how scientists work and communicate. Many of those aims are addressed in this unit. Students will learn more about the methods and techniques used by scientists, analyze and evaluate scientific data, develop the skills needed to conduct scientific investigations, and develop an "appreciation of the possibilities and limitations associated with science and scientists". [33] This unit meets the core requirements of International Baccalaureate Biology assessment statements 6.5.1-6.5.6 covering the structure of neurons, nerve impulse transmission and synaptic transmission, and 5.4.7 which deals with how natural selection leads to evolution. This unit also meets the requirements of Option E: Neurobiology and Behavior—specifically, assessment statements E4.1through E4.6 on neurotransmitters and synapses, E5.1 through E5.3 on the structure of the brain and its study, and E3.1 and E3.2 on animal behavior experimentation. In addition, the unit requires students to apply what they have previously learned about cell membrane structure and transport—concepts addressed in assessment statements 2.4.3 through 2.4.7.