Autism and its Connections to the Nervous System Curriculum

Lesson 1
Temple Grandin Movie Guide
  Answer Key
Temple Grandin: Discussion Questions
DSM-IV Criteria for a Diagnosis of Autism
Autism Fact Sheet
Misconceptions about Autism Chart
Misconceptions about Autism Fact Sheet
10 Myths about Autism
Vaccines, Autism, & Bad Science

Lesson 2
Sheep Brain Dissection

Lesson 3
Glial Reading Guide

Lesson 4
The Potential to Change Challenge
Rate Your Reaction

Lesson 5
PowerPoint Presentation – Understanding Basal Ganglia
Synapse Foldable
Synaptical Transmission Model
Neurotransmitter List

Lesson 6
New Light on the Brain
The Birth of Optogenetics

*Also Provided:
Explanation of Curriculum
“Sugar and Fat Bingeing Have Notable Differences in Addictive-like Behavior” PDF
Autism and its Connections to the Nervous System

When Teaching Anatomy Physiology, we traditionally start from the bottom and work our way up. This means we introduce the smallest parts (molecules → cells) and how they work and gradually teach how those smaller parts fit together into larger parts (organs) and eventually how all of these parts work together to perform the ultimate function of a particular organ system. We generally then discuss how malfunctions in any portion of this process equates with disease states. It makes sense; lay the foundation and build upon it. Students understand how anatomy and physiology works and how diseases can manifest and affect human health.

In this module, a slightly different approach is being taken to teach the nervous system. We start with introducing the disease state Autism. While not well understood, we do know that patients with Autism experience some phenomena that impair their ability to demonstrate what we might identify as “normal human behavior”. While behaviors may be thought to be some type of psychological condition, Autism provides the perfect opportunity for students to learn that all behavior, just as all other functions in the human body, stem from physiological processes that can be understood, and eventually, if necessary, treated.

This module focuses specifically on the Central Nervous System (CNS), but includes components of the Peripheral Nervous System (PNS) and sensory organ Anatomy and Physiology, specifically general neuron structure and function and the impact of light stimulus on the nervous system. This provides a segue for teaching both of these components of the nervous system.

To teach this module, it is necessary to understand Autism in general. While Autism encompasses a wide range of behavior manifestations, it is widely accepted that specific behaviors are indicative of Autism. These behaviors are called Restricted, Repetitive Behaviors or RRBs. Similar RRBs, also called stereotypies manifest in animals kept in captivity. While the evolutionary origin of these behaviors may provide an opportunity for discussion, these behaviors are used to focus on the anatomy and physiology of the CNS in this module. It is important to understand general brain anatomy and the specific brain anatomy of the Basal Ganglia (BG). While the depth of knowledge of the BG passed on to students relies directly on those students in that classroom, the general notion that the BG contains specific areas with specific cells that produce and are stimulated by different neurotransmitters is important. These different areas and cells, in concert, regulate direct and indirect pathways that coordinate both motor control and decision making activities. Changes in the balance between these two pathways manifest as RRBs/stereotypies. Imbalances as a result of anatomical changes in the BG are also seen in Parkinson’s disease, Huntington’s disease, Tourette’s Syndrome and Attention Deficit Hyperactivity Disorder (ADHD). (H.S. Singer, 1992) (Peter, 2005)

The complexity of the BG includes similar cells in specific anatomical areas of the BG that may have different receptors and produce different neurotransmitters despite otherwise identical cellular structure. (neuroanatomy.wisc.edu, 2006) This makes identification of the causes, and ultimately the treatments, for specific abnormal behaviors difficult. The need for ongoing research in the field of neurobiology becomes apparent as students move through this module. The final lesson for this module
invites students to propose and design an experiment that might lead to greater insight into how behaviors, like those seen in Autism, manifest and might be treated.

This module includes activities to meet the needs of all students. Extensions are included for more in-depth analysis; activities and daily lessons may be deleted or included to meet the specific needs of your students in your classroom.

**Works Cited**


Jackson, M. (Director). (2010). *Temple Grandin* [Motion Picture].


Volumetric MRI changes in basal ganglia of children with Tourette's syndrome

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Abstract

To define the site of pathology in Tourette's syndrome (TS), we performed a volumetric MRI study of basal ganglia structures and lateral ventricles on 37 children with this disorder and 18 controls. There were no statistically significant differences in the size of the right or left caudate, putamen, globus pallidus, or ventricles in these populations. In contrast, there were significant differences for measures of symmetry in the putamen and the lenticular region. Virtually all controls (17 right- and one left-handed) had a left-sided predominance of the putamen, whereas in 13 of 37 TS subjects, a right predominance exceeded that of any control. Statistical comparisons among TS patients, with (n = 18) or without (n = 19) attention-deficit hyperactivity disorder (ADHD), and controls showed significant differences for the volume of the left globus pallidus and for lenticular asymmetry. Post hoc evaluations showed that in the TS + ADHD group, the volume of the left globus pallidus was significantly smaller than the volume of the right and that lenticular asymmetry was due to a greater right-sided predominance in the TS + ADHD group. This study lends further support to proposals that claim the basal ganglia is involved in the pathogenesis of TS and also suggests that the comorbid problem of ADHD is related to regional changes that differ from those primarily associated with tics.

Footnotes

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Is the ADHD Brain Damaged?

Posted by Peter on February 14th, 2005 | Comments off

This will be a long post as it seems that researchers can find numerous parts of the ADHD brain that seem dysfunctional. A major flaw in virtually all of this research is that they use very small groups that cannot depict the vast spectrum brain variability among the human species. This published research confuses many people as it seems the brains of those with ADHD are smaller, have damage in the basal ganglia, putamen, frontal lobes, cerebellum, and brain stem. This amounts to little more than neophrenology.

Small Brains

“It’s strong support for a very strong biological contribution to what causes ADHD.” Dr. Judith Rapoport, National Institute of Mental Health

(AP) Hyperactive children and teens have slightly smaller brains than those without the disorder, a study shows.

Exactly why this is so is not clear, but the researchers said the smaller brain volume does not appear to be related to the use of hyperactivity drugs such as Ritalin, as some parents had feared.

The finding could be reassuring to parents in another respect as well: It suggests that hyperactivity is biological in origin, not a product of bad parenting.

The researchers said it appears that the brains of hyperactive children develop at a normal pace but never entirely catch up in size with the brains of other youngsters. However, they said that people with smaller brains are not necessarily less intelligent.

The findings were reported in Wednesday’s Journal of the American Medical Association.

Other studies also have suggested biological differences in the brains of people with attention deficit hyperactivity disorder.

“It’s strong support for a very strong biological contribution to what causes ADHD,” said one of the researchers, Dr. Judith Rapoport, chief of child psychiatry at the National Institute of Mental Health in Bethesda, Md.

The 10-year study used MRIs to look at 152 patients ages 5 to 18 who had the disorder, and 139 people in about the same age range who did not. It also compared patients who were on medication and those who were not.
The study found the disorder is associated with about a 3 percent to 4 percent decrease in volume throughout the brain. The smaller their brains, the greater their symptoms.

“The first thought people have is that this is a product of bad parenting” or that it is environmental, said Dr. Daniel Coury, a professor of clinical pediatrics at the Ohio State University College of Medicine who was not involved in the research. “Having clear biological findings that this is something beyond the control of parents or the child themselves helps to remove that stigma.”

Dr. Bennett Leventhal, professor of psychiatry and pediatrics at the University of Chicago, said the findings regarding the effects of medication “should be reassuring to parents that you can treat your kids and not hurt their brains.”

The research was conducted between 1991 and 2001 at the National Institute of Mental Health, which funded it.

ADHD is one of the most common childhood psychiatric disorders. Its symptoms include short attention span, impulsive behavior, difficulty focusing and fidgetiness. The American Academy of Pediatrics estimates 4 percent to 12 percent of school-age children are affected.

**Bad Basal Ganglia**

Reading and attention disorders both seem to stem from the same primitive part of the brain that governs thinking and muscle control, Yale researchers have found.

A study of 27 people ages 18 to 24 revealed that participants with attention deficit and hyperactivity disorder, and those with reading disorders, displayed low activity in their basal ganglia.

The study, which was published in the November issue of the American Journal of Psychiatry, is the first to use sophisticated functional magnetic resonance imaging to identify the neural circuits involved with ADHD.

When both groups were given the drug methylphenidate (brand name Ritalin) activity in the basal ganglia was normal, said Keith Shafritz, lead author.

Shafritz performed the work as a Yale graduate student and is now a research associate at the Duke University Medical Center.

Shafritz said the results suggest that Ritalin does not produce a unique effect in people with ADHD and that ADHD and reading disorders are in some way equivalent.

Nationally about 5 percent of children have reading disorders, characterized by reading at a lower level than expected.
About 3 to 5 percent of children show symptoms of ADHD. These include inattention, impulsiveness, and hyperactivity.

Participants were placed in a functional magnetic resonance imaging unit where they saw and heard a mixture of real and nonsense words.

The normal control group was about 80 percent accurate. People with ADHD and people with reading disorders both scored about 70 percent, Shafritz said.

Basal ganglia activity was higher in the control group.

When participants with ADHD or reading disorders were given methylphenidate and repeated the test their basal ganglia function rose to normal levels.

Shafritz said the basal ganglion is an inhibitory organ that can also activate areas of the brain. The neurotransmitter dopamine regulates the basal ganglion.

Ritalin apparently increases the inhibitory effect, dropping people with ADHD to a calmer and more attentive state.

The drug blocks the dopamine transporter, a system that clears away dopamine. With the transporter turned down dopamine accumulates.

“One driving question was, ‘Were the effects of Ritalin on the brain unique to kids with ADHD?’” Shafritz said. “The results suggest that Ritalin has similar effects in ADHD and other conditions. The idea that Ritalin is acting in a certain way in ADHD appears not to be the case.”

“The study also suggests that ADHD brains are not that different from everyone else’s brains,” Shafritz said.

Shafritz said the study was not designed to measure classroom behavior or reading skills. Also, medical ethics prevented giving Ritalin to the control group.

**Bad Putamen**

An inverse index of regional cerebral blood flow, T2 relaxometry (an fMRI procedure), was used to indirectly assess blood volume in the striatum (caudate and putamen) of boys ages 6 to 12 in steady-state conditions (Teicher et al., 2000). Boys with ADHD had higher T2 relaxation times bilaterally in the putamen than controls. Relaxation times strongly correlated with both the individual’s capacity to sit still and error performance on an attentional task. Daily treatment with methylphenidate significantly changed T2 relaxation times in the putamen of boys with ADHD, although the magnitude and direction of the effect was strongly dependent on unmedicated baseline activity.

**Bad Frontal Lobes**
Investigators at UCLA used magnetic resonance imaging (MRI) to compare the brains of 27 children with ADHD to those of 46 children without the disorder. They found that the region of the brain associated with attention and impulse control, located on the bottom of the frontal lobes of the brain, was smaller in the ADHD kids than in the other children.

“We would expect that the abnormalities would be in this region, and this is what we found,” lead investigator Elizabeth Sowell, PhD, tells WebMD.

The researchers also found that children with ADHD had larger areas of the outer layers of the brain.

Previous research has indicated that the differences were limited to the right side of the brain, but Sowell and colleagues found that they occurred on both sides.

**Bad Cerebellum**

Symptoms of ADHD in adults may include reading difficulties, poor concentration, clumsiness, and low self-esteem. Our research has shown that a medical condition we refer to as Cerebellar Developmental Delay (CDD) is a likely culprit of ADHD in adults. In CDD, the cerebellum is under-developed and not able to process information going to and coming from the cerebrum (often known as the “thinking brain”) efficiently. DORE has developed specific exercises that stimulate the cerebellum, thus allowing it to process information faster.

**Bad Brain Stem and Other Parts**

U.S. researchers reported brain scans of children with attention deficit hyperactivity disorder show anatomical abnormalities beyond a chemical imbalance.

The study by North Shore-Long Island Jewish Health Center was presented at the annual meeting of the Radiological Society of North America.

A second study by the same authors showed stimulant medications prescribed to balance brain chemistry appear to normalize some of these brain irregularities.

“We found abnormality of the fiber pathways in the frontal cortex, basal ganglia, brain stem and cerebellum,” said lead author Manzar Ashtari.

“These areas are involved in the processes that regulate attention, impulsive behavior, motor activity and inhibition – the key symptoms in ADHD children.”

The study used diffusion tensor imaging to compare 18 children with diagnosed ADHD with 15 control children to evaluate the brain’s white-matter fiber development. Researchers found differences in the brain fiber pathways that transmit and receive information among brain areas.

**Bad Reticular Formation**
Usefulness of QEEG neurometrics in a clinical setting.

Chabot and colleagues found that generalized or focal theta/alpha excess was present in 76.2% of their sample of ADD, ADHD, and children with attentional problems. These theta and alpha excess children can be divided into two distinct neurophysiological subgroups.

The first and most common group consisting of 46.4% of the sample was characterised by theta and/or alpha excess, mostly at frontal and/or central regions with normal alpha mean frequency.

Excessively high output of thalamocortical alpha generators can result from (a) overactivation of the thalamus. The primary dopamine pathways originate in the substantia nigra in the brainstem and innervate the caudate nucleus and putamen and are largely responsible for sensorimotor integration. Down-regulation of nigrostriatal dopaminergic neurons results in overstimulation of the midbrain reticular formation and the production of excess alpha (b) underactivation of the prefrontal cortex resulting from disinhibition from nucleus reticularis.

**Bad Cerebrum**

The authors report a study to compare regional brain volumes at initial scan and their change over time in medicated and previously unmedicated male and female patients with ADHD and healthy controls. The case-control study was conducted from 1991-2001 at the National Institute of Mental Health, Bethesda, Md, of 152 children and adolescents with ADHD (age range, 5-18 years) and 139 age- and sex-matched controls (age range, 4.5-19 years) recruited from the local community, who contributed 544 anatomic magnetic resonance images. Using completely automated methods, the main outcome measures were initial volumes and prospective age-related changes of total cerebrum, cerebellum, gray and white matter for the 4 major lobes, and caudate nucleus of the brain were compared in patients and controls.

**Summary**

It’s both significant and tragic to note that one can use a search engine and type in ‘ADHD’ and virtually any particular portion of the brain and find clinically controlled research that indicates related brain damage or abnormality.

Brain scans and QEEG are relatively nascent technologies that are currently more art than science when used to determine the source of ADHD. Obviously, the publishing of data on small groups may assist researchers in garnering grant funds. It may even help them retain their position at university in a publish or perish world. However, publishing of such data is not only unethical, it is also highly misleading if it does not explicitly define itself as highly preliminary. Even then it is questionable.

Publication of this neophrenology allows media to portray ADHD individuals as irreparably brain damaged which is both harmful and flagrantly untrue.
http://www.playattention.com/is-the-adhd-brain-damaged/
NIH Curriculum: Autism and its Connections to the Nervous System

Lesson 1: Different Not Less

AT A GLANCE

While observing people with autism and animals with stereotypes (restricted, repetitive behaviors, AKA RRBs) students will recognize a similarity in these behaviors. Causation of these behaviors lies in the physiology of the Central Nervous System (CNS). This lesson will also give students the opportunity to recognize pseudoscience and its potential to impact human health.

FOCUS

Students will investigate the myths and realities surrounding Autism. This opportunity will be used to help students recognize pseudoscience and its potential impact on human health. Students will understand the need to pursue scientific discovery to continuously provide information that will offer the opportunity to improve the quality of life. Students will then watch the movie (or clips from) Temple Grandin. The purpose is to introduce autism as a disorder of the CNS. Autism will be used as an umbrella under which students will understand the structure and function of the nervous system. Students will become familiar with the characteristics of autism and identify similar characteristics (stereotypies) in animals and autistic children. Students will recognize that understanding how structure and function works in animals models can lead to understanding the structure and function of human systems. The use of animal models can also lead to the treatment of anomalies in human systems. Students will also recognize that continuous scientific research is necessary to insure appropriate diagnosis and treatments for diseases continue to be available.

MAJOR CONCEPTS

Neural pathways in the human CNS are similar to neural pathways in animal models. Unlike pseudoscience, scientific knowledge is based on empirical evidence that is both reliable and valid. Scientific knowledge is a continuously evolving as technology improves, leading to better technology and greater knowledge.

OBJECTIVES

- Students will be able to identify behaviors associated with Autism Spectrum Disorders (ASDs).
- Students will be able to describe stereotypes and the role they play in autism.
- Students will be able to infer how animal behaviors may lead to insight into human autistic behaviors.
- Students will be able to infer the role of the CNS (brain) in these behaviors.
• Students will be able to evaluate whether or not information they encounter related to health and wellness constitutes science or pseudoscience.
• Students will be able to recognize the difference between pseudoscience and real science and the potential for either to affect public opinion and/or the treatment of human disease.

PREREQUISITE KNOWLEDGE

• General overview of organ systems (general structures and functions).
• General cell structure (cell membrane with membrane bound proteins as receptors).
• Basic chemistry and concept of molecule interactions. This includes basic atomic and molecular structure, ions and their charges and macromolecule structure and function. Students should also understand how interaction between molecular structures constitutes normal metabolism.
• Basic biological concepts: use of energy to maintain homeostasis, growth, development, reproduction, adaptation, response to environment, organization of structures as related to function.
• Basic premise of the scientific method.

OVERALL TIME ESTIMATE

1-3 50 minute class periods, depending on video usage

VOCABULARY

Autism: Autism spectrum disorder (ASD) is a range of complex neurodevelopment disorders, characterized by social impairments, communication difficulties, and restricted, repetitive, and stereotyped patterns of behavior. (NIH, 2011)

Stereotypies: Stereotypies are repetitive, purposeless actions that are most commonly seen in childhood. Stereotypies do not have a clear definition due to the wide range of possible stereotyped behaviors and the overlap with other movement or behavioral disorders. (Medscape Reference, 2010)

Restricted repetitive behavior (RRBs): Stereotypic behaviors that fall into one of two categories:
• Low Order RRB= Sensory motor behaviors such as hand wringing, clapping, waving
• High Order RRB= Insistence on sameness behavior: routines

Valid: having some foundation or truth, cannot be denied without contradiction.

Reliable: able to be trusted, dependable, predictable, and able to be repeated on successive trials.
NATIONAL SCIENCE EDUCATION STANDARDS:

12ASI2.2 Scientists conduct investigations for a wide variety of reasons. For example, they may wish to discover new aspects of the natural world, explain recently observed phenomena, or test the conclusions of prior investigations or the predictions of current theories.

12CLS6.1 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.

12CLS6.4 Behavioral biology has implications for humans, as it provides links to psychology, sociology, and anthropology.

12EST1.1 Identify a problem or design an opportunity. Students should be able to identify new problems or needs and to change and improve current technological designs

12FSPSP1.2 The severity of disease symptoms is dependent on many factors, such as human resistance and the virulence of the disease producing organism. Many diseases can be prevented, controlled, or cured. Some diseases, such as cancer, result from specific body dysfunctions and cannot be transmitted.

12FSPSP1.4 An individual’s mood or behavior may be modified by substances. The modification may be beneficial or detrimental depending on the motives, type of substance, duration of use, pattern of use, level of influence, and short- and long- term effects. Students should understand that drugs can result in physical dependence and can increase the risk of injury, accidents, and death.

12GHNS1.1 Individuals and teams have contributed and will continue to contribute to the scientific enterprise. Doing science or engineering can be as simple as an individual conducting field studies or as complex as hundreds of people working on a major scientific question or technological problem. Pursuing science as a career or as a hobby can be both fascinating and intellectually rewarding.

NEXT GENERATION FLORIDA SCIENCE STANDARDS:

SC.912.N.1.1 Define a problem based on a specific body of knowledge, for example: biology, chemistry, physics, and earth/space science, and do the following:
   1. pose questions about the natural world,
   2. conduct systematic observations,
   3. examine books and other sources of information to see what is already known,
   4. review what is known in light of empirical evidence,
5. plan investigations,
6. use tools to gather, analyze, and interpret data (this includes the use of measurement in metric and other systems, and also the generation and interpretation of graphical representations of data, including data tables and graphs),
7. pose answers, explanations, or descriptions of events,
8. generate explanations that explicate or describe natural phenomena (inferences),
9. use appropriate evidence and reasoning to justify these explanations to others, communicate results of scientific investigations, and evaluate the merits of the explanations produced by others.

SC.912.N.2.3: Identify examples of pseudoscience.

BASIC SCIENCE HEALTH CONNECTION

This activity introduces students to autism, the springboard for investigating the anatomy and physiology of the nervous system. As students discover how the nervous system works, they will develop an understanding that when we understand how organ systems work we are better able to develop ways to help correct anomalies in those systems.

INTRODUCTION

Autism is a disorder involving an imbalance in communication within the CNS, specifically the brain. Current research indicates an imbalance between the direct and indirect pathways within the basal ganglia in the brain. The direct and indirect pathways within the basal ganglia either excite (direct) or inhibit (indirect) sensory/motor responses or decision making impulses. Imbalances between these two pathways also appear to be responsible for the manifestations of behaviors associated with autism. Similar behaviors have been observed in animals kept in captivity. These behaviors (RRBs) can also be observed in people with damage to different areas of the basal ganglia (Parkinson’s disease, Huntington’s disease, brain trauma). (neuroanatomy.wisc.edu, 2006) By studying these behaviors and their physiological basis (in the CNS) in animal models, we gain a greater understanding of how physiology in the human brain works. Understanding brain physiology may eventually lead to better treatments of CNS anomalies like autism, Parkinson’s disease, Huntington’s disease, head trauma or even drug abuse.

This activity introduces autism as an umbrella under which the anatomy and physiology of the nervous system can be taught. Autism will be utilized to teach the role of the CNS (specifically the brain), nerve impulses, neurotransmitters and sensory stimuli in the nervous system. The specific cause of autism is still not clearly understood by scientists, hence the need for continued scientific research. As technology improves, greater scientific knowledge becomes available. Gaps in scientific knowledge leave opportunities for misconceptions to develop. Because understanding the physiology of the human brain is difficult at best, autism has provided a great opportunity for the development of misconceptions. From poor parenting techniques to vaccines, autism has provided many opportunities for pseudoscience to thrive.
The age of information allows greater access to what may be deemed ‘bad science’. This lesson will also take the opportunity to engage students in recognizing pseudoscience and the need to exercise thoughtful consideration when determining the value of any given piece of information encountered when researching scientific topics.

MATERIALS AND PREPARATION

- Movie *Temple Grandin* OR *Temple Grandin* video clips (times indicated on ‘as you watch’ worksheet)
- Temple Grandin ‘As You Watch’ work sheet
- Teacher access to Immunization Safety Review: Vaccines and Autism
  - Free download at: http://www.nap.edu/catalog.php?record_id=10997
- Teacher access to websites OR copies of:
  - Autism fact sheet
    Website: Autism Fact Sheet: National Institute of Neurological Disorders and Stroke (NINDS)
  - Autism misconceptions
    Website: http://gigli.tripod.com/welcome/misconceptions.htm
    Website:http://abcnews.go.com/Health/ColdandFluNews/story?id=6089162&page=1
    Website: http://www.autism-atss.com/misconceptions.htm
    Website: Portia Iversen http://www.dnalc.org/view/1074-Autism-Misconceptions-Bad-Parenting.html
  - Vaccines, Autism, and Bad Science
    Website: http://genome.fieldofscience.com/2008/03/vaccines-autism-and-bad-science.html
  - Immunization Safety Review: Vaccines and Autism
  - Animal stereotypy videos
    Website: http://www.aps.uoguelph.ca/~gmason/StereotypicAnimalBehaviour/library.shtml
  - Youtube videos autistic children
    http://www.youtube.com/watch?v=6DmzUmCFrrE&NR=1&feature=ffwp
    http://www.youtube.com/watch?v=-6blmKPiPe9c&feature=related
    http://www.youtube.com/watch?v=U35q146wMzo&NR=1&feature=ffwp
    http://www.youtube.com/watch?v=xeKKMkVgNPU&feature=related
    http://www.youtube.com/watch?v=PxH-Vubdzus&NR=1

PROCEDURE

Begin this lesson by asking students what they know or have heard about autism. Based on students’ responses, lead a discussion towards the characteristic behaviors of people with
autism. Guide students into identifying behaviors used to diagnose autism. Students should record these behaviors, via Cornell notes, in their notebooks. If necessary, utilize the Autism Fact Sheet (electronic or hard copy).

If the topic has not been breached, ask students what they know or have heard regarding the cause of autism. Use this opportunity to engage students in a discussion of misconceptions regarding the cause of autism over the years. Utilize Portia Iversen’s video: Autism Misconceptions: Bad Parenting as a beginning point if necessary. Use subsequent Portia videos to introduce misconceptions and discuss how misconceptions have been formed. Portia Iversen is not a scientist; however, as a parent of an autistic child, she had been engaged in efforts to raise funds and foundations whose purpose is to improve the lives of people with Autism. Utilize her words in the Socializing video to emphasize the need to separate the social perception of behaviors versus the physiological basis for behaviors as nervous system physiology will be the focus of this unit. Understanding the physiology of the nervous system, specifically the basal ganglia in the brain, lies at the center of behaviors that manifest in autism.

Guide students into recognizing the lack of scientific evidence supporting misconceptions regarding autism. If necessary, show or have students read your choice of “misconceptions” documents (as a link or hard copy). Have students record in Cornell notes misconceptions and reasons for those misconceptions regarding autism. Have students also describe why their chosen misconceptions are inaccurate, scientifically. Show and discuss the Vaccines and Autism video LAST. Show or have students read Vaccines, Autism and Pseudoscience. Engage students in a discussion weighing the positive and negative aspects of the lawsuit mentioned in the article. Have students develop potential consequences in the field of healthcare as a result of the decisions. Ask students to justify whether or not they believe the case was based on legitimate or pseudoscience. Show or have students read the SUMMARY of the Immunization Safety Review: Vaccines and Autism.

Students will watch the movie Temple Grandin. Utilizing the ‘As You Watch’ worksheet, students may be asked to complete the worksheet as the movie plays or the movie may be stopped to discuss the questions posed. Utilize the time marks to choose specific clips for discussion if time is limited. Students should be able to recognize that Temple is different from others. Her unique nature, however, does not equate with her being less competent that other people. Temple’s unique behaviors may be obvious to students.

Utilize Temple Grandin Discussion Questions as a guide for discussion. These questions should turn the discussion from a focus on scientific methodology to the characteristics of autism and similarities in animal behaviors.

Drive the focus of the discussion to behaviors, specifically, RRBs (stereotypies). Introduce the animal videos that show animals engaging in RRBs. Show several animal videos first pointing out the specific RRBs they are demonstrating. Emphasize these animals are considered under stress (in captivity). Repeat Portia’s words regarding the development of autism in children that were institutionalized due to lack of stimulation (Bad Parenting video). After you have shown a few of the animal videos, show students the paired videos of animal RRBs and autistic children
demonstrating similar RRBs. Point out the similarities in the sensory/motor behaviors. Emphasize that the nervous system, specifically the brain, is intimately involved in coordinating these movements. Emphasize that humans as well as these animals share similar brain structure and physiology. Emphasize that the study of animal models to understand brain structure and function may be valuable in understanding brain structure and function in humans.

Emphasis should be on similarities as brain structure (anatomy) will be examined in the next lesson.

NOTE: Additional lesson plans on Autism specifically may be found at http://www.dnalc.org/view/1354-Autism-lesson-.html

RESOURCES

Quick links

Vaccines, Autism, and Pseudoscience
http://genome.fieldofscience.com/2008/03/vaccines-autism-and-bad-science.html

Immunization Safety Review: Vaccines and Autism
http://www.nap.edu/catalog.php?record_id=10997

Portia Iversen videos

Misconceptions About Autism
http://gigli.tripod.com/welcome/misconceptions.htm

10 Myths About Autism
http://abcnews.go.com/Health/ColdandFluNews/story?id=6089162&page=1

Misconceptions of Autism
http://www.autism-atss.com/misconceptions.htm

Autism fact sheet

Autism diagnosis
http://www.autismspeaks.org/what-autism/diagnosis

Animal stereopathy:
http://www.aps.uoguelph.ca/~gmason/StereotypicAnimalBehaviour/library.shtml
Children with autism (RRBs) and suggested animal stereotypy video clips:

Boy in Supermarket = Asiatic Black Bear Head Swaying and Elephant Weaving
http://www.youtube.com/watch?v=6DmzUmcFrrE&NR=1&feature=fvwp

Boy spinning = mouse twirling
http://www.youtube.com/watch?v=-6blmKiPe9c&feature=related

Boy flapping and jumping, girl spinning = as squirrel monkey and mink
http://www.youtube.com/watch?v=U35q146wMZo&NR=1&feature=fvwp
http://www.youtube.com/watch?v=xeKKMkVgNPU&feature=related

Boy stimming in car, vocal noises = dog sucking flank
http://www.youtube.com/watch?v=PxHVubdzus&NR=1

Basal Ganglia
http://www.neuroanatomy.wisc.edu/coursebook/motor2.pdf

Bibliography


http://www.aps.uoguelph.ca/~gmason/StereotypicAnimalBehaviour/library.shtml


Hand Flapping, Walking in Circles and Spinning:
http://www.youtube.com/watch?v=xeKKMkVgNPU&feature=related


Jackson, M. (Director). (2010). *Temple Grandin* [Motion Picture].


Temple Grandin Movie Guide Answer Key

These are some of the expected answers to the questions asked. Answers may, of course, vary. Students may be asked to answer these questions as they watch the movie. This assignment may take place with a substitute teacher collecting student answers at the conclusion of the movie, or the movie may be stopped at the end of each segment (indicated by time mark) and discussed as a class. The Autism Fact Sheet (hard copy or internet access) may be referenced to help identify some of the answers, specifically those dealing with the characteristics of autism.

1. **00:15** What you think Temple means when she says she ‘thinks in pictures’?
   Language is a communication process that utilizes symbols. Temple uses pictures as her symbols. These pictures appear in her mind. They appear quite literally.

2. **Why does Temple call the hired hand a cowboy?**
   He was wearing objects her mind associated with pictures she had seen of cowboys.

3. **7:00** Who is Dr. Carlock? What role does he play in Temple’s life? Why is his role significant?
   Dr. Carlock is Temple’s science professor at the boarding school. Temple likes science and he is a scientist. He encourages Temple to utilize her way of ‘seeing’ things. Temple becomes able to use her way of seeing things to be successful.

4. **7:45** What was Temple seeing when she manipulated the air vent in her room? How was this significant?
   Temple was figuring out the relationship between the lever and the vent. This information was used to design the automatic gate opener.

5. **10:30** How does Temple know what the horse sees?
   Temple carefully observed the horse’s behavior. She was able to see what the horse saw and interpret its behavior.

6. **11:30** What is the cow clamper? Why is it used? 17:00 Why do you think the cow clamper helped Temple?
   It is a device use to hold cows in place while they are inoculated. Temple did not like human contact and the clamper calmed her as it did the cows by giving her the sensation of being ‘hugged’. Temple’s autism caused her to be uncomfortable with direct human contact (such as hugging).

7. **15:00** Why did Temple need to label pictures of her face displaying different emotions?
   Her autism does not allow her the ability to read emotion. This is related to the lack of social skills in people that are autistic.
8. **23:00** What characteristic behaviors does Temple display that are consistent with Autism? *Spinning (RRBs), lack of social skills, not speaking as a child.*

9. **27:45** Why does seeing pictures and connecting them cause problems for Temple? *Temple forms pictures in her mind literally. Getting up with the rooster’s, the guillotine and sliding doors, reading the French book all show how this literal interpretation often made communicating with humans confusing for Temple.*

10. **30:00** Explain the miscommunication regarding TEMPLE’S ‘HUGGING MACHINE? *The doctor interpreted it as a sexual device as a consequence of Temple’s answers to his questions. The doctor did not recognize Temple was interpreting his questions literally.*

11. **34:00** How is the ‘hugging machine’ issue resolved at Temple’s college? *Temple conducts legitimate scientific research on the effectiveness of the machine.*

12. **39:30** Explain what different not less means. *While Temple sees things differently, she is not less than a human being because of it.*

13. **44:47** Why wasn’t Temple sad when Chestnut died? *Chestnut wasn’t there anymore. People with autism often lack the ability to express emotion. Temple was, however, able to recognize that Chestnut was no longer there.*

14. **48:30** How does Dr. Carlock help Temple learn to use the way she “sees things”? *He challenged Temple with designing the perspective model.*

15. **52:45** What is animal husbandry? *Animal husbandry is the practice of taking care of animals.*

16. **52:00** How does a helicopter work? *The rubber band powered model has no wings and just one plane of resistance*

17. **53:30** When Dr. Carlock said “think of it as a door...”, how did this help Temple overcome her desire for sameness? *Temple was able to make the next step by simply stepping through the door. She had stepped through many doors before without harm. Once she saw different situations as nothing more than stepping through a door, she was able to overcome her fear of change (or desire for sameness).*

18. **57:30** Considering neurophysiology, what do Temple and her new roommate have in common? *They both process information utilizing perspectives that are different from others because of their autism/blindness.*

19. **62:25** Where and when did Temple go for her graduate degree?
20. **63:00** How many pounds do cattle put on while on the feed lot over a 3-4 month period? They start at 650+ pounds and must add on 400lb before slaughter.

21. **63:50** What is the potential problem for the dip vat? If cattle tip over they can drown.

22. **65:30** What observations did Temple make regarding how cows moved? Why did she say cows moved this way? How did she use this information in her dip vat design? Temple observed that cows like to move in circles. They were moving away from the handlers. It made them calm down. They felt they were returning to their starting point. She designed her dip vat to go along with the cows natural movements so they would remain calm for the dipping process.

23. **66:00** Why wasn’t Temple upset when she watched the cows being killed? Temple saw the cow as an animal and then as meat and wondered where the ‘cow went’.

24. **67:30** What was Temple’s master’s thesis on? What observations did she make regarding this type of behavior? Mooing, cows didn’t moo when walking in curves, since cows are prey animals, when a handler stepped into their natural flight zone they mooed louder, if handlers stepped into their flight zone, they got upset. She hypothesized that if handlers stayed out of the flight zone and allowed cows to move in their naturally curved flight zone, cows could be moved calmly to where handlers wanted them to go. She used this to design her dip vat.

25. **69:00** Why was temple unable to get back on to the yard? How did she resolve this issue? She is a female. She observed those entering the yard, bought a truck, clothes, got dirty and dressed up as a male.

26. **72:00** Why did temple have a problem with the automatic sliding doors at the store? She visualized them as a guillotine.

27. **73:30** how did temple figure out the cow’s experience in the dip vat? What distractions did she notice? She got on her hands and knees and crawled through the path to see what the cows saw. Light/shadow, reflections on puddles, chains moving, clothes.

28. **74:35** what upset Temple regarding the bull testicles left on her windshield? She had eaten them regularly and saw it as a waste of food.

29. **76:10** How did temple get Don Michaels to sign off on her Master’s Thesis? She didn’t; the ranch hand, who signs everything, signed off on it for her. He also suggested she observe cows in other ways (auctions, rodeos, etc).
30. **78:45** What happened as a result of Temple’s visit to a cattle auction?
   
   *She met someone from the Arizona Farmer-Ranchman magazine who published her thesis on ‘Mooing as a Guide to Cattle Agitation’ information prior to it being submitted to her professor.*

31. **80:30** why does temple have difficulty being around people?
   
   *She is unable to read people’s emotions*

32. **82:30** How did Temple get back on to the ranch to continue research after she completed her Master’s degree?
   
   *She got as press pass from the Arizona farmer-Ranchman magazine and write articles for them.*

33. **84:00** How did temple get her vat design job, how many days did she have to draft her design?
   
   *A ranchman from the Red River Feed Lot that happened to be in the magazine office asked her if she would like to put her work into practice and design a dip vat for him, 5 days.*

34. **85:30** how did temple get her design drafted on time?
   
   *She observed cow behavior to develop the design. Watched the draftsman do his work, purchased the materials and drafted the design herself.*

35. **86:30** How did temple know her design worked?
   
   *She did a demonstration for red Harris from Cattle magazine.*

36. **88:00** why did the ‘opening’ of Temple’s dip vat design fail?
   
   *How many cows were lost before she came and corrected this? The cow handlers took her design apart and ‘redesigned’ what they thought would work better. 3 cows.*

37. **91:30** what was temple’s next design job and how was she able to gain access?
   
   *Abbot slaughter house, she met the wife of someone from the slaughterhouse while exiting the store with the sliding door.*

38. **92:50** Why was Temple not upset over Dr. Carlock’s death? What did she leave for him?
   
   *She had just seen him and said good bye; he wasn’t there in the coffin; she left him one of her cow pins. Autistic people often have difficulty reading and/or expressing emotion (lack of social skills).*

39. **95:15** What surprising move did temple make at her professors funeral?
   
   *She moved to let her mother hug her. Temple’s autism generally made personal human contact uncomfortable for her.*
40. **98:00** How did temple convince the Abbot slaughterhouse people her design was better?

*She explains how her autism allows her to see what the cows will experience and that their experience will keep them calm and orderly as they walk towards slaughter, saving money in delays/backups/etc.*

41. **101:15** When did Temple become an autism ‘activist’?

*Temple began speaking publically about autism at the 1981 National Autism Conference when she spoke up as a member of the audience.*
Temple Grandin: Discussion Questions

1. Why would the Pediatrician recommend Temple’s mother have Temple institutionalized? *Children with autism often have difficulty with social interaction. During that time period children that were “retarded” were often left to be raised in institutions. Refer back to previous discussions regarding misconceptions.*

2. Describe how Temple’s behaviors fit the clinical diagnosis for ASDs. *Temple demonstrated many of the behaviors listed on the NDNIS Fact Sheet: How is Autism Diagnosed (NIH, 2011)*

   Very early indicators that require evaluation by an expert include:
   - no babbling or pointing by age 1
   - no single words by 16 months or two-word phrases by age 2
   - no response to name
   - loss of language or social skills
   - poor eye contact
   - excessive lining up of toys or objects
   - no smiling or social responsiveness.

   Later indicators include:
   - impaired ability to make friends with peers
   - impaired ability to initiate or sustain a conversation with others
   - absence or impairment of imaginative and social play
   - stereotyped, repetitive, or unusual use of language
   - restricted patterns of interest that are abnormal in intensity or focus
   - preoccupation with certain objects or subjects
   - inflexible adherence to specific routines or rituals.

3. How was Temple’s teacher able to give her the guidance needed to apply her talents? *He recognized that Temple ‘saw’ the world from a different perspective. He gave her an assignment that allowed her to use her special talent to solve a problem. This led Temple to gain confidence in her ability to be successful even though she knew she did not see or do things the same way others did. DIFFERENT, NOT LESS*

4. Consider the statement when a door opens, what does it mean? *Because people with autism are uncomfortable with new situations, Temple needed to see new situations as a door that you walk through. Because she had walked through doors previously without negative consequences, this vision led her to be OK with changes that might occur as she walked through the door. When the door was opened, Temple found opportunities available.*
5. Describe how Temple first began to develop her understanding of farm animals. *Because Temple was able to experience distractions in the same manner as the farm animals (she could ‘see’ what they saw), she was able to understand their behavior. Her initial contact with the horse is an example. She did this through careful observation.*

6. How might RRBs (stereopathies) be related to the behavior of farm animals (cattle)? *Repetitive behaviors lead to expected outcomes. The farm animals were able to calmly be directed where they needed to go because they were directed in a manner that led them to ‘understand’ they were going in a direction that was ‘known’ or expected.*

7. Describe how and why Temple was able to design the ‘dip’ and later the slaughterhouse? *Because Temple understood the natural movements of cows and why they moved that way (expected outcomes), she was able to design the dip and later the slaughterhouse. Both designs allowed cows to calmly be led through the dip or to the slaughter as they were free of distractions or objects that would ‘spook’ the animals as they were moved along.*

8. How has Temple’s autism helped her develop those designs? *Temple felt the same panic as the animals when confronted with change, distractions, and stimuli. She understood how the cows felt once she witnessed and later used the cow’s ‘hugging machine’ to calm down after encountering stress from such stimuli.*
DSM-IV Criteria for a Diagnosis of Autism

I. A total of six (or more) items from heading (A), (B), and (C), with at least two from (A), and one each from (B) and (C):

(A) Qualitative impairment in social interaction, as manifested by at least two of the following:
- Marked impairments in the use of multiple nonverbal behaviors such as eye-to-eye gaze, facial expression, body posture, and gestures to regulate social interaction.
- Failure to develop peer relationships appropriate to developmental level.
- A lack of spontaneous seeking to share enjoyment, interests, or achievements with other people, (e.g., by a lack of showing, bringing, or pointing out objects of interest to other people).
- A lack of social or emotional reciprocity.

(B) Qualitative impairments in communication as manifested by at least one of the following:
- Delay in or total lack of, the development of spoken language (not accompanied by an attempt to compensate through alternative modes of communication such as gesture or mime).
- In individuals with adequate speech, marked impairment in the ability to initiate or sustain a conversation with others.
- Stereotyped and repetitive use of language or idiosyncratic language.
- Lack of varied, spontaneous make-believe play or social imitative play appropriate to developmental level.

(C) Restricted repetitive and stereotyped patterns of behavior, interests and activities, as manifested by at least two of the following:
- Encompassing preoccupation with one or more stereotyped and restricted patterns of interest that is abnormal either in intensity or focus.
- Apparently inflexible adherence to specific, nonfunctional routines or rituals.
- Stereotyped and repetitive motor mannerisms (e.g. Hand or finger flapping or twisting, or complex whole-body movements).
- Persistent preoccupation with parts of objects.

II. Delays or abnormal functioning in at least one of the following areas, with onset prior to age 3 years:

(A) Social interaction.

(B) Language is used in social communication.

(C) Symbolic or imaginative play.
III. The disturbance is not better accounted for by Rett's Disorder or Childhood Disintegrative Disorder. Source: Diagnostic and Statistical Manual of Mental Disorders; Fourth Edition

Source:
http://www.autismspeaks.org/what-autism/diagnosis
What is autism?
Autism spectrum disorder (ASD) is a range of complex neurodevelopment disorders, characterized by social impairments, communication difficulties, and restricted, repetitive, and stereotyped patterns of behavior. Autistic disorder, sometimes called autism or classical ASD, is the most severe form of ASD, while other conditions along the spectrum include a milder form known as Asperger syndrome, and childhood disintegrative disorder and pervasive developmental disorder not otherwise specified (usually referred to as PDD-NOS). Although ASD varies significantly in character and severity, it occurs in all ethnic and socioeconomic groups and affects every age group. Experts estimate that six children out of every 1,000 will have an ASD. Males are four times more likely to have an ASD than females.

What are some common signs of autism?
The hallmark feature of ASD is impaired social interaction. As early as infancy, a baby with ASD may be unresponsive to people or focus intently on one item to the exclusion of others for long periods of time. A child with ASD may appear to develop normally and then withdraw and become indifferent to social engagement. Children with an ASD may fail to respond to their names and often avoid eye contact with other people. They have difficulty interpreting what others are thinking or feeling because they can’t understand social cues, such as tone of voice or facial expressions, and don’t watch other people’s faces for clues about appropriate behavior. They lack empathy. Many children with an ASD engage in repetitive movements such as rocking and twirling, or in self-abusive behavior such as biting or head-banging. They also tend to start speaking later than other children and may refer to themselves by name instead of “I” or “me.” Children with an ASD don’t know how to play interactively with other children. Some speak in a sing-song voice about a narrow range of favorite topics, with little regard for the interests of the person to whom they are speaking. Children with characteristics of an ASD may have co-occurring conditions, including Fragile X syndrome (which causes mental retardation), tuberous sclerosis, epileptic seizures, Tourette syndrome, learning disabilities, and attention deficit disorder. About 20 to 30 percent of children with an ASD develop epilepsy by the time they reach adulthood.

How is autism diagnosed?
ASD varies widely in severity and symptoms and may go unrecognized, especially in mildly affected children or when it is masked by more debilitating handicaps. Very early indicators that require evaluation by an expert include:
- no babbling or pointing by age 1
- no single words by 16 months or two-word phrases by age 2
- no response to name
- loss of language or social skills
- poor eye contact
- excessive lining up of toys or objects
• no smiling or social responsiveness.

Later indicators include:
• impaired ability to make friends with peers
• impaired ability to initiate or sustain a conversation with others
• absence or impairment of imaginative and social play
• stereotyped, repetitive, or unusual use of language
• restricted patterns of interest that are abnormal in intensity or focus
• preoccupation with certain objects or subjects
• inflexible adherence to specific routines or rituals.

Health care providers will often use a questionnaire or other screening instrument to gather information about a child’s development and behavior. Some screening instruments rely solely on parent observations, while others rely on a combination of parent and doctor observations. If screening instruments indicate the possibility of an ASD, a more comprehensive evaluation is usually indicated.

A comprehensive evaluation requires a multidisciplinary team, including a psychologist, neurologist, psychiatrist, speech therapist, and other professionals who diagnose children with ASDs. The team members will conduct a thorough neurological assessment and in-depth cognitive and language testing. Because hearing problems can cause behaviors that could be mistaken for an ASD, children with delayed speech development should also have their hearing tested.

Children with some symptoms of an ASD but not enough to be diagnosed with classical autism are often diagnosed with PDD-NOS. Children with autistic behaviors but well-developed language skills are often diagnosed with Asperger syndrome. Much rarer are children who may be diagnosed with childhood disintegrative disorder, in which they develop normally and then suddenly deteriorate between the ages of 3 to 10 years and show marked autistic behaviors.

**What causes autism?**
Scientists aren’t certain about what causes ASD, but it’s likely that both genetics and environment play a role. Researchers have identified a number of genes associated with the disorder. Studies of people with ASD have found irregularities in several regions of the brain. Other studies suggest that people with ASD have abnormal levels of serotonin or other neurotransmitters in the brain. These abnormalities suggest that ASD could result from the disruption of normal brain development early in fetal development caused by defects in genes that control brain growth and that regulate how brain cells communicate with each other, possibly due to the influence of environmental factors on gene function. While these findings are intriguing, they are preliminary and require further study. The theory that parental practices are responsible for ASD has long been disproved.
What role does inheritance play?
Twin and family studies strongly suggest that some people have a genetic predisposition to autism. Identical twin studies show that if one twin is affected, there is up to a 90 percent chance the other twin will be affected. There are a number of studies in progress to determine the specific genetic factors associated with the development of ASD. In families with one child with ASD, the risk of having a second child with the disorder is approximately 5 percent, or one in 20. This is greater than the risk for the general population. Researchers are looking for clues about which genes contribute to this increased susceptibility. In some cases, parents and other relatives of a child with ASD show mild impairments in social and communicative skills or engage in repetitive behaviors. Evidence also suggests that some emotional disorders, such as bipolar disorder, occur more frequently than average in the families of people with ASD.

Do symptoms of autism change over time?
For many children, symptoms improve with treatment and with age. Children whose language skills regress early in life—before the age of 3—appear to have a higher than normal risk of developing epilepsy or seizure-like brain activity. During adolescence, some children with an ASD may become depressed or experience behavioral problems, and their treatment may need some modification as they transition to adulthood. People with an ASD usually continue to need services and supports as they get older, but many are able to work successfully and live independently or within a supportive environment.

How is autism treated?
There is no cure for ASDs. Therapies and behavioral interventions are designed to remedy specific symptoms and can bring about substantial improvement. The ideal treatment plan coordinates therapies and interventions that meet the specific needs of individual children. Most health care professionals agree that the earlier the intervention, the better.

Educational/behavioral interventions: Therapists use highly structured and intensive skill-oriented training sessions to help children develop social and language skills, such as Applied Behavioral Analysis. Family counseling for the parents and siblings of children with an ASD often helps families cope with the particular challenges of living with a child with an ASD.

Medications: Doctors may prescribe medications for treatment of specific autism-related symptoms, such as anxiety, depression, or obsessive-compulsive disorder. Antipsychotic medications are used to treat severe behavioral problems. Seizures can be treated with one or more anticonvulsant drugs. Medication used to treat people with attention deficit disorder can be used effectively to help decrease impulsivity and hyperactivity.

Other therapies: There are a number of controversial therapies or interventions available, but few, if any, are supported by scientific studies. Parents should use caution before adopting any unproven treatments. Although dietary interventions have been helpful in some children, parents should be careful that their child’s nutritional status is carefully followed.
What research is being done?
In 1997, at the request of Congress, the National Institutes of Health (NIH) formed its Autism Coordinating Committee (NIH/ACC) to enhance the quality, pace and coordination of efforts at the NIH to find a cure for autism (http://www.nimh.nih.gov/health/topics/autism-spectrum-disorders-pervasive-developmental-disorders/nih-initiatives/nih-autism-coordinating-committee.shtml). The NIH/ACC involves the participation of seven NIH Institutes and Centers: the National Institute of Neurological Disorders and Stroke (NINDS), the Eunice Kennedy Shriver National Institute of Child Health and Human Development, the National Institute of Mental Health, the National Institute on Deafness and Other Communication Disorders, the National Institute of Environmental Health Sciences, the National Institute of Nursing Research, and the National Center on Complementary and Alternative Medicine. The NIH/ACC has been instrumental in the understanding of and advances in ASD research. The NIH/ACC also participates in the broader Federal Interagency Autism Coordinating Committee (IACC) that is composed of representatives from various component agencies of the U.S. Department of Health and Human Services, as well as the U.S. Department of Education and other government organizations.

In fiscal years 2007 and 2008, NIH began funding the 11 Autism Centers of Excellence (ACE), coordinated by the NIH/ACC. The ACEs are investigating early brain development and functioning, social interactions in infants, rare genetic variants and mutations, associations between autism-related genes and physical traits, possible environmental risk factors and biomarkers, and a potential new medication treatment.

Where can I get more information?
For more information on neurological disorders or research programs funded by the National Institute of Neurological Disorders and Stroke, contact the Institute's Brain Resources and Information Network (BRAIN) at:
BRAIN
P.O. Box 5801
Bethesda, MD 20824
(800) 352-9424
http://www.ninds.nih.gov
## Misconceptions About Autism

<table>
<thead>
<tr>
<th>Misconception</th>
<th>Reality</th>
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<tbody>
<tr>
<td>Autism is an emotional condition that is caused by a child's withdrawal from parents who are cold and unwilling to accept him/her.</td>
<td>Autism is a neurological disorder resulting in a developmental disability characterized by difficulties in social reciprocity, language acquisition, and attention to the normal range of environmental events. The cause of this neurological disorder is largely unknown. Recent evidence indicates that abnormalities of the cerebellum, the limbic system and of neuro-chemical transmitters may be involved. There is no evidence that autism is caused by an atypical parenting style. Families of children with autism exercise the same variations in parenting as families of typical children. Also, many children with autism have typical siblings without autism.</td>
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<td>Autism is a low-incidence disability.</td>
<td>According to recent statistics from the National Institute of Health, autism spectrum disorders represent the third largest developmental disability group in this country. This increased incidence is thought to be a function of improved methods for identifying children who present with symptoms.</td>
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<td>Dustin Hoffman’s character in <em>Rain Man</em> is a typical example of a person with autism.</td>
<td>People with autism present with an enormous range of individual differences. Dustin Hoffman’s character illustrates one point on a very wide continuum of personalities and skill levels. As in the typical population, some but not all individuals with autism excel in an area of interest (e.g. math, reading, music, art, etc.).</td>
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<tr>
<td>Children with autism lack the ability to form emotional attachments.</td>
<td>Many children with autism are normally attached to their parents and other members of the extended family. Some may present with sensory dysfunctions (e.g. overreaction to touch, vision, sound, etc.) which lead them to express and receive affection in unconventional way. However, the stereotype of a child with autism who is indifferent to the social world does not fit in most cases.</td>
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<tr>
<td>Autism is a life-long disability.</td>
<td>With appropriate treatment, almost 50% of individuals with autism will become indistinguishable from the mainstream population. Many others will develop independent living skills. A small number will require support throughout their lives.</td>
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<tr>
<td>There exists one single treatment that is appropriate for all children with autism at all times.</td>
<td>Autism is a spectrum disorder and children with autism appear to benefit from a spectrum of treatment options. Research suggests that a behavioral treatment approach is appropriate as a starting point. However, many children win benefit from additional treatment options (e.g., sensory integration, auditory processing, traditional speech-language therapy, pharmacological interventions, special diets, etc.). The diagnostic category of autism is less than 60 years old, and treatment efficacy research has not yet been completed.</td>
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MISCONCEPTIONS OF AUTISM

**Myth:** All individuals with autism possess special skills and genius abilities (e.g. are able to memorize license plates, complete complicated mental math, display exceptional musical/art skills)

**Truth:** Although the individual with autism depicted in the movie 'Rainman' possessed special abilities, the vast majority of people with autism do not. Individuals with autism who possess 'genius' abilities are often referred to as "savants" or "autistic savants". Approximately 50 percent of all savants have autism, while only about five to ten percent of individuals with autism possess extraordinary savant skills.

**Myth:** There is a cure for, or people grow out of autism.

**Truth:** People do not grow out of autism. Autism is a lifelong disorder, however the manifestation of symptoms may change over time. While there is yet no known cure, autism is definitely treatable

**Myth:** Poor parenting causes autism.

**Truth:** While there is no one known cause for autism, it is known the disorder is not caused by poor parenting.

**Myth:** Children with autism just need more love and a good spanking.

**Truth:** Autism is not caused by a lack of love and it is not cured by punishment. Parents need support to manage difficult behaviors with structure and consistency.

**Myth:** People with autism have to be in special programs for the 'autistic'.

**Truth:** Individually designed programs best meet the needs of a person with autism. Those with autism should be learning, living and working in settings where there is ample opportunity to communicate and interact with others who have the skills they lack.

**Myth:** All individuals with autism are withdrawn, avoid eye contact, engage in self-injurious behavior, rock, spin objects and avoid affection.

**Truth:** Individuals with autism tend to be diverse. Therefore, it is difficult to use words such as 'all' or 'none' when describing this group. Some individuals engage in eye contact, while others enjoy tickles and hugs. However, not all engage in rocking, spinning or self-abusive behavior. Individuals with autism do share common behavioral characteristics, and it is on this basis that a diagnosis can be made.

Source:

http://www.autism-atss.com/misconceptions.htm
10 Myths About Autism

By LARA SALAH ( @LaraSalahiABC ) and RADHA CHITALE
ABC News Medical Unit
Oct. 23, 2008

As the number of Americans diagnosed with autism spectrum disorders climbs, so, too, does the number of questions surrounding this disorder. Namely, what is autism, and what is causing a rise in autism diagnoses among adults and children nationwide?

Amid these questions, television shows and magazines feature a barrage of stories and imagery -- families rallying for and against vaccines, debates between medical experts pointing to both genetic and environmental causes, and images of individuals diagnosed with autism who struggle to speak and function independently, while others can interact with others and are able to hold jobs. For many, these competing messages may make this already complex condition even more confusing.

Fortunately, doctors and researchers are learning more about the causes and characteristics of autism.

The following are answers to 10 common myths, that may help us better recognize the range of symptoms we call autism spectrum disorders.

Myth: Autism is an emotional or mental health disorder.
While physical or social behaviors of individuals with autism may suggest that they have a psychological disorder, autism is actually a biological illness that affects the brain's growth and development.
"In the case of autism, the parts of the brain that are most affected seem to impact three areas of functioning," said Michael Alessandri, executive director of the University of Miami's Center for Autism and Related Disabilities. "Social behavior, communication and restricted and repetitive rituals and routines are ways that the child or the adult with autism interact with the environment."
Although autism is now understood to be a neurodevelopmental disorder, Alessandri, an expert for ABCNews.com's OnCall+ Autism section, said autism can still be considered a complex disorder because its range of symptoms is so diverse.
"Scientists and clinicians now understand that autism is not a singular entity, but rather, a variety of syndromes that ... create the autism spectrum disorders," said Alessandri.

Myth: There is an autism epidemic.
The word "epidemic" often implies a sudden burst in the number of individuals within a fixed time who have, in this case, autism.
Although the CDC reports that one out of 150 children born have an autism spectrum disorder, some experts are quick to question whether a surge in autism cases is actually occurring. Some are more likely to link the upshot of numbers to the combination of a broader definition of autism, a wider spectrum, and an earlier diagnosis.

"The condition has not become more widespread, but there is more diagnosis of autism," said Dr. Bob Marion, director of Children's Evaluation and Rehabilitation Center at Albert Einstein College of Medicine in New York. Sheila Wagner, assistant director of the Autism Center at Emory University in Atlanta, added that more awareness of symptoms has allowed more people to identify individuals who have autism.

"There's a lot of media exposure to autism, in television and movies," said Wagner. "This has made [autism] more recognizable in the lay population."

Myth: Autism can be cured.
Some parents may allude to a certain diet, medicine, or set of behavioral treatments that have cured their autistic children, where other parents may try the same mode of treatment and see no results. While there are treatments created to improve an autistic child's ability, there is no known cure for autism.

"We do know that with early intervention with younger children and Applied Behavioral Analysis, we can improve a child’s functioning," said Marion. Applied Behavior Analysis, or ABA, is one form of therapy for newly diagnosed children. It includes repeating behavioral activities to improve a child's social and physical functions. According to Marion, there is no blanket treatment for autism, and it is up to the individual's doctor to assess what treatment will offer the best benefit for each autistic child. In some cases, Marion said, behaviors, including eye contact, interaction with others and development of language skills, will significantly improve -- but the underlying biological disorder will not change.

"And that is definitely not a cure," he said.

Myth: Autism is the result of cold and unemotional parents.
In the 1940s, Austrian doctor Bruno Bettelheim theorized that autism was a result of parents, especially mothers, who did not love their children. Children in such situations would withdraw and become autistic, Bettelheim believed.
However, researchers have thawed the "refrigerator mother" theory. According to medical experts, a child's autism diagnosis has nothing to do with how the child is raised. "We don't know if there are any things that a parent can do or not do, conclusively, will determine whether their child gets autism or not," said Dr. Daniel Geshwind, director of UCLA's neurogenetics program and center for autism research. "Most of the evidence right now points to there being a very strong genetic predisposition in most cases of autism, but not all."

Myth: Individuals with autism always have hidden or exceptional talents.
Stephen Wiltshire, 34, is best known as the human camera. He can replicate architectural designs and landscapes down to each blade of grass -- even if he is only given one opportunity
to observe the area he is drawing. Wiltshire has reproduced panoramic scenes of Tokyo, Rome and London by memory after one short helicopter ride over each of the cities.

Wiltshire is an autistic savant. That is, he has extraordinary cognitive skills that allow him to recall details of designs, numbers and measurements that are normally considered too difficult to remember.

The concept of an autistic individual as a savant may have been popularized by Dustin Hoffman's character in the movie "Rain Man."

But while Marion acknowledges that there is a minority group of individuals with autism who have unusual islets of skills, savants are an unrealistic portrayal of the majority of individuals on the spectrum. He said most do not have talents or skills that distinguish themselves by extraordinary talents.

"There are strengths and weaknesses in every child," said Marion. "It's important for every child with autism to have a multidisciplinary evaluation by health professionals who have experience in assessing a child’s skills and deficits, to come up with an educational plan that will benefit the child the most."

**Myth: Repetitive or ritualistic behaviors should be stopped.**

One of the classic indicators of autism is repetitive and ritualistic behaviors, according to the Diagnostic and Statistical Manual of Mental Disorders (DSM IV), a physician's tool to diagnose autism.

While these behaviors -- which can include hand flapping, banging on walls or rocking back and forth -- may seem odd, they do have a purpose: they can be calming; they can feel good; and they may help the individual communicate with others, said Wagner.

Repetitive behaviors may only pose a problem if they begin interfering in family life or if they prevent those with autism from functioning independently, Wagner added.

However, according to Dr. Pauline Filipek, associate professor of pediatrics and neurology at the University of California, Irvine, a child may learn to outgrow repetitive behaviors.

"Often, as an individual gets older, they learn that such behaviors make them stand out in society, and they learn to miniaturize those behaviors," said Filipek.

**Myth: Individuals with autism are unable to build social relationships.**

"This is a generalization and needs to be individualized because the spectrum is so wide," said Marion.

In short, social relationships are possible for some individuals on the autism spectrum, but not for others on the most severe end of the spectrum, Marion said.

The DSM IV, which includes diagnosing guidelines for autism, lists "impairment in social interaction" as one indication that an individual can have an autism spectrum disorder. But not every child on the autism spectrum will have the same degree of difficulty connecting with others.

"At the most severe end of the spectrum, yes, that's true," said Marion. "But there is a multitude of children who have friends, and even some who do have close relationships."

**Myth: Autistic individuals are a danger to society.**

"It is a disservice to think that all people with autism are dangerous," said Wagner.
The idea rises from numerous news stories of individuals diagnosed with Asperger's syndrome, a high form of autism, who have been accused of burglary and, at times, murder. However, if you look at the entire population of people on the autism spectrum, the number of people involved in crime is small, said Wagner. If someone with autism were to act out, it may be due to frustration or perhaps physical or emotional overstimulation, not necessarily malice, she said.
Vaccines, autism, and bad science

By Steven Salzberg on 3/07/2008 07:25:00 AM

The controversy over vaccines and autism just took a turn for the worse, due to an unfortunate decision by the U.S. vaccine court. For the first time, the court has awarded compensation to a family who claim their daughter’s autism was caused by vaccines. What the court actually decided was that an underlying disorder - in this case a genetic defect in the girl’s mitochondria - was made worse by the vaccine shots she received in July 2000, when she was 18 months old. Her parents say that her autism appeared soon after those shots.

This is bad news in several ways. First off, there is still no evidence that vaccines cause autism, despite this case. This is a legal ruling, not a scientific study. But the public won't understand the difference, and it's being reported all over the media (yesterday and today) as "evidence" that vaccines cause autism. I doubt that the public can make the distinction between legal evidence and scientific evidence.

The Institute of Medicine published EIGHT REPORTS examining the supposed link between vaccines and autism. They concluded that "the body of epidemiological evidence favors rejection of a causal relationship between thimerosal-containing vaccines and autism." This conclusion hasn't changed, but court rulings such as the one this week are likely to muddy the waters. Why? Because there are thousands of people out there, many of them parents of autistic children (perhaps some who will reply to this blog) who insist that there is a link.

This all started with some spectacularly bad science by a British doctor named Andrew Wakefield, who published a study in The Lancet in 1998 claiming to have discovered a link between vaccines and autism. This study was later revealed to be fraudulent in several ways, including the fact that the lead author, Wakefield, had recruited children to join the study through a small-time UK lawyer named Richard Barr, whose goal was to file a lawsuit against drug companies that manufactured the MMR vaccine. Wakefield was paid a large sum of money, 435,000 pounds (about $780,000), for consulting work supporting this lawsuit. There are many other blatantly fraudulent aspects to this study, summarized in a lengthy article by Brian Deer here. 10 of his 12 co-authors retracted the article when they learned of his fraud. Wakefield is under investigation for fraud in the UK, but he left long ago and set up shop in the U.S. (How nice that we are so friendly to medical frauds!) He travels the country promoting the vaccine-autism link, and unfortunately he continues to attract attention, much of it positive. He has convinced many parents that he is a hero, fighting the medical "establishment" who just won't see the truth of his claims.

Autism is a tragic illness, and the parents' tales are heartbreaking. Autism usually becomes evident in children at about the same time they get their vaccines, which means that many parents make the understandable - albeit erroneous - inference that vaccines caused the autism. However, study after study has shown that this just isn't true.
Now along comes this vaccine court case that has awarded compensation to the parents of an autistic child based on a supposed vaccine link. There are nearly 5000 other autism cases pending, and if the court starts awarding funds in many of them, the vaccine fund will quickly go bankrupt. This fund has been a tremendous success - it was created by Congress (along with the vaccine court) as a mechanism to compensate people who are, in very rare cases, hurt in some way by vaccines. Vaccines provide a tremendous public good, and in order to be successful, we need to have as many people vaccinated as possible. The vaccine fund sets aside federal money to achieve this public benefit, and to avoid scaring off vaccine manufacturers from producing vaccines (a very real possibility in our overly-litigious society).

The press and many parents are reporting this as a "landmark" case. It may be, but it isn't a good one. The impact on the public, sadly, is likely to be a decreased rate of vaccination among children whose parents hear about this. Most parents aren't going to investigate carefully, and even if they do, most of the media outlets are reporting this as if there is a genuine link that has now been discovered.

If fewer children are vaccinated, the result will be that hundreds, possibly thousands, of children will die from childhood diseases that are currently under control in the U.S. and Europe. Public memory is short, and no one with young children today is old enough to remember the (recent) era when children got ill - and some died - of a host of diseases such as measles, mumps, rubella, polio, and meningitis. I hope we don't have to experience a new epidemic of childhood deaths to re-educate people on the importance of getting their children vaccinated.

Source: http://genome.fieldofscience.com/2008/03/vaccines-autism-and-bad-science.html
Lesson 2: If I Only Had a Brain

AT A GLANCE

The nervous system coordinates incoming reception and interpretation of and outgoing responses to environmental stimuli. The brain is the major center for these activities. Students will become familiar with the general anatomy and physiology of the brain.

FOCUS

Students will identify the major anatomical structures and regions of the human brain and describe their functions. Students will compare the human brain to other mammalian brains. EXTENSION: students will dissect the cat brain (or other mammalian brain) OR students will compare structures of mammalian brains.

MAJOR CONCEPTS

The human brain has distinct structures that perform specific functions. Mammalian brains are similar in structure and function.

OBJECTIVES

- Students will be able to identify major anatomical portions of the mammalian brain.
- Students will be able to describe the general function of each anatomical portion.
- Students will be able to infer clinical manifestations in patients when damages occur to portions of the brain.
- Students will be able to describe similarities between mammalian brains.

PREREQUISITE KNOWLEDGE

- General overview of organ systems (general structures and functions).
- General cell structure (cell membrane with membrane bound proteins as receptors).
- Basic chemistry and concept of molecule interactions.

OVERALL TIME ESTIMATE

One class period (~50 minute class). With EXTENSION two class periods.

VOCABULARY

Cerebrum: see diagram for anatomy. The cerebrum is the main portion of the brain. It contains left and right hemispheres. This area of the brain controls conscious activities (thinking, learning, voluntary muscles, etc). In appearance, convoluted ridges (gyri) are separated by groves (sulci).
**Cerebellum:** see diagram for anatomy. The cerebellum is responsible for coordinating motor control.

**Brain stem:** see diagram for anatomy

**Diencephalon:**
- **Thalamus:** major center for coordinating input sensory information to cerebrum and output motor control leaving the cerebrum.
- **Hypothalamus:** regulates survival behaviors for homeostasis (feeding, fight, reproduction: controls portions of endocrine system). Regulates circadian rhythms.
  - **Pons** regulated breathing centers in medulla
  - **Medulla oblongata:** controls vital functions (i.e. breathing, cardiovascular functions, etc)

**Limbic region:** see diagram for anatomy. The limbic region consists of many structures. It is involved in reasoning, emotions and memory.

**Frontal lobe:** see diagram for anatomy. The frontal lobe is associated with motor function, planning, reasoning, problem solving, impulse control, judgement (to name a few).

**Parietal lobe:** see diagram for anatomy. The parietal lobe has areas associated with speech, hearing and taste.

**Occipital lobe:** see diagram for anatomy. The occipital lobe has areas associated with vision.

**Temporal lobe:** see diagram for anatomy. The temporal lobe has areas associated with hearing.

**Corpus callosum:** see diagram for anatomy. The corpus callosum attaches the left and right hemispheres of the brain. It has areas associated with eye movement and balancing arousal and attention.

**NATIONAL SCIENCE EDUCATION STANDARDS:**

**12CLS6.1** 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.

**12CLS6.4** Behavioral biology has implications for humans, as it provides links to psychology, sociology, and anthropology.

**12FSPSP1.2** The severity of disease symptoms is dependent on many factors, such as human resistance and the virulence of the disease producing organism. Many diseases can be
prevented, controlled, or cured. Some diseases, such as cancer, result from specific body dysfunctions and cannot be transmitted.

12FSPSP1.4 An individual's mood or behavior may be modified by substances. The modification may be beneficial or detrimental depending on the motives, type of substance, duration of use, pattern of use, level of influence, and short- and long-term effects. Students should understand that drugs can result in physical dependence and can increase the risk of injury, accidents, and death.

NEXT GENERATION FLORIDA SCIENCE STANDARDS

SC.912.L.14.27 Identify the functions of the major parts of the brain, including the meninges, medulla, pons, midbrain, hypothalamus, thalamus, cerebellum and cerebrum.

SC.912.L.14.21 Describe the anatomy, histology, and physiology of the central and peripheral nervous systems and name the major divisions of the nervous system.

BASIC SCIENCE HEALTH CONNECTION

In this activity, students will become familiar with the general anatomy and physiology of the human brain. They will be able to understand that brain function determines how well we are able to carry out all of the functions necessary to live a normal and healthy life. They will also recognize and understand why damage to any portions of the brain can have a devastating effect on our ability to function normally.

INTRODUCTION

In this activity students focus on the gross anatomy of the brain. Students will also learn general brain physiology based on that gross anatomy.

MATERIALS AND PREPARATION

Posterboard with a full size human brain
Full sized brain to fit posterboard. Your choice of anatomical brain parts should be cut out to fit onto the posterboard as a puzzle pieces. It is recommended you use the brain model associated with your textbook. If no model is available, check the resources section for links to a variety of models.
Brain dissection (Dissection may be live or virtual. For virtual dissection see link under resources):
  Dissection tools
  Sheep brain (or other mammal)
  Microtome for extension (producing cross sections of brain along frontal plane to mammalian comparisons)
  Virtual dissection (see resources)
Access to brain slides (online for mammalian comparisons)

**PROCEDURE**

**Jigsaw**
Utilize one of the diagrams of the brain (links below) or use your own diagrams to show students the general anatomy of the human brain.
In general, students will jigsaw anatomical portions of the brain (utilize waiting.com general physiology). Each group is responsible for correctly drawing their assigned brain ‘part’ and its associated physiology and damage symptoms on the posterboard brain.
As preparation for this activity, students will be split into groups to jigsaw the anatomy and physiology of the brain. The number of groups depends on the anatomical portions/regions of the brain you choose to have students understand. Each group will be assigned a different anatomical portion/region of the brain. Students in each group will be given a HOMEWORK ASSIGNMENT the day before this activity. In the homework assignment, each group members must bring a minimum of ONE function of their assigned brain ‘part’ to class the next day.
If your classroom has internet access, students may be split into groups and do their physiology research on the same day utilizing [http://www.waiting.com/brainanatomy.html](http://www.waiting.com/brainanatomy.html) as their resource.

On a posterboard, outline the human brain.
In class students will split into their groups and develop a mini lesson on the structure and function of their brain ‘part’. This may be done on computer, on whiteboard or on overhead transparencies. Students will use their research from the previous night’s homework or in class research at [http://www.waiting.com/brainanatomy.html](http://www.waiting.com/brainanatomy.html) to develop their mini lesson
Students must also construct their brain ‘part’ to fit the class posterboard utilizing materials of your choice (construction paper, white paper colored, or fancier materials if you wish).
This activity should take ~ 20 minutes.
Students will then teach each other the anatomy and physiology of their brain part and place their part on the class posterboard.

At the end of each presentation, generate student discussion utilizing the following question:
   How mould damage to this portion of the brain effect a patient?
   *Note: this discussion can lead to discussions regarding causes of brain damage (strokes via embolism, aneurysm, insults such as concussion and drug abuse).
The discussion can also lead to therapies that rely on brain plasticity to compensate for damages.

Students may access the brain match game or 3D brain as review for homework or in class.
(links in resources)

Utilize the 3D Brain Review (see link in resources) to review basic brain anatomy and physiology.
Virtual or live sheep brain dissection. See resources below.

Students will compare cross sections of mammalian brains utilizing slides from brainmuseum.org. This portion of the lesson may be as complex or as simple as you would like it to be. Students may be given the freedom to compare animal brains on their own as the tour the brain museum, or you may direct them to compare brain slides (coronal sections) or whole brain views (whole brain photographs) of your choice. Students should be able to recognize that mammalian brains are more similar than different.

Students may also independently, or teacher guided, participate in the virtual sheep brain dissection (see link in resources).

Extension: Students will perform the sheep brain dissection. See procedure in resources.

As students complete the brain dissections (any level), it is important to point out to students that studying damage to mammalian brains may provide answers regarding treatment of damage to human brains based on the similarity of structure and function.

Once dissections are complete, walk students through The Exploratorium link (resources) to help reinforce the link between anatomical similarities in mammalian brains and the ability to use knowledge gained from mammalian brains to understand human brain function. This portion of the lesson provides a segue into subsequent lessons.

As a final review, have students play the matching Brain Game (link in resources below). Students should be given these web addresses for independent practice on their own time.

RESOURCES

Quick links

Mammalian brain slides
http://www.brainmuseum.org/

Sheep brain dissection guide
www.biologycorner.com/anatomy/sheepbrain/brain_dissection_guide.doc

Virtual sheep brain dissection
http://www.biologycorner.com/anatomy/sheepbrain/sheep_dissection.html

The Anatomy of Memory virtual dissection
http://www.exploratorium.edu/memory/braindissection/index.html

3D brain review
http://www.pbs.org/wnet/brain/3d/index.html

General brain physiology
http://www.waiting.com/brainanatomy.html
Matching brain game
http://www.anatomyarcade.com/games/matchingGames/MatchABrain/matchABrain.html
(copypaste)

Bibliography

http://www.anatomyarcade.com/games/matchingGames/MatchABrain/matchABrain.html

http://www.exploratorium.edu/memory/braindissection/index.html


www.biologycorner.com/anatomy/sheepbrain/brain_dissection_guide.doc

http://www.biologycorner.com/anatomy/sheepbrain/sheep_dissection.html


http://www.brainmuseum.org/index.html

**Sheep Brain Dissection**

**Name** ______________________________

**Objectives:**
1. List and describe the principal structures of the sheep brain
2. Identify important parts of the sheep brain in a preserved specimen

**Materials:** Dissection tools and trays, lab glasses, lab gloves, preserved specimen

**External Sheep Brain:** The sheep brain is quite similar to the human brain except for proportion. The sheep has a smaller cerebrum. Also the sheep brain is oriented anterior to posterior whereas the human brain is superior to inferior.

1. The tough outer covering of the sheep brain is the **dura mater**, one of three meninges (membranes) that cover the brain. You will need to remove the dura mater to see most of the structures of the brain. Remove the dura mater while leaving other structures intact.

2. The most prominent feature of the brain is the **cerebrum** - which is divided into nearly symmetrical **left and right hemispheres** by a deep longitudinal **fissure**.

3. The surface of the cerebrum is covered with large folds of tissue called **gyri**. The grooves between the gyri are **sulci**. The deeper sulci are often termed **fissures**. The fissures are used as landmarks to divide the surface of the cerebrum (the **cerebral cortex**) into regions:

   - frontal lobes / parietal lobes / occipital lobes / temporal lobes

   * Locate each of the lobes of the brain.

4. The smaller, rounded structure at the back of the brain is the **cerebellum**. The cerebellum has smaller gyri that are roughly parallel to one another. Compare the gyri of the cerebellum to that of the cerebrum. Removing the dura mater from the cerebellum can be tricky business. Look for areas on the side of the brain that you can snip to peel the dura mater off.

5. Turn the brain over so that the cerebrum is down. The most prominent structure visible on the ventral side of the brain is the optic chiasma, where the two **optic nerves** cross over each other and form an “X” shape. Locate the **optic chiasma**.

6. The **pituitary gland** is a large round structure under the chiasma. If you removed this area with the dura mater, you may need to replace it to see the chiasma and pituitary gland.

7. Toward the front of the brain are two prominent round structures, the olfactory bulbs.
8. Toward the back of the brain, in order from the optic chiasma are bulges that indicate the **midbrain**, the **pons**, and the **medulla**.

9. Just behind the optic chiasma is a raised area or bump that indicates the **infundibulum** (also known as the **pituitary stalk**). This is where the pituitary was attached to (which was probably removed with the dura mater).

10. **Oculomotor nerves** may be visible to each side of the pituitary gland (or stalk). Or in some cases you may find them stuck to the dura mater that you removed with the pituitary gland.

11. Carefully bend the cerebellum to get an inside glimpse of the brain. The bumps you see (kind of resemble a “butt”) are the **superior colliculi**. The smaller ones underneath are **inferior colliculi**.

12. If you gently push those structures down, you can see the tiny nub of the **pineal gland**.

**Internal Sheep Brain.**

1. Use a knife or long-bladed scalpel to cut the specimen along the **longitudinal fissure**. This will allow you to separate the brain into the left and the right hemisphere. Lay one side of the brain on your tray to locate the structures visible on the inside. You should also cut through the cerebellum.

2. The **corpus callosum** had been connecting the two cerebral hemispheres and can now be clearly seen in the brain section.

3. The tiny space within the corpus callosum (which holds cerebrospinal fluid) is called the **lateral ventricle**. Underneath it, you can find the **third ventricle**. There are other ventricles
within the brain, but those are the easiest to locate in a preserved specimen. The white area between those two ventricles is the **fornix**. The **fourth ventricle** is the space under the cerebellum.

3. Inferior to the corpus callosum is a round structure known as the **thalamus**. It seems it almost perfectly centered. Just behind the thalamus is the **pineal body** (gland). The **hypothalamus** is also round shaped but is lower and toward the front of the brain.

4. The **pons**, **medulla**, **cerebellum** and **spinal cord** are also visible in the side view of the brain. Gently separate the cerebellum at the **transverse fissure**, which separates it from the cerebrum.

5. Within the cerebellum, you can see the **arbor vitae**, named such because the white lines resemble a tree.

6. Use a scalpel to cut a cross section of the cerebrum in the occipital lobe area. You should be able to see the color and texture differences of the **white matter** and the **gray matter**.

Lesson 3: The Players

AT A GLANCE

Students will understand the general structure of cells found in the CNS

THE FOCUS

Students will construct the cells of the brain. Special attention will be paid to the structures of neurons.

MAJOR CONCEPTS

The human brain relies on specific cells to carry our specific functions.

OBJECTIVES

- Students will be able to identify and describe the general structure and function of cells (neurons and glial cells) found in the CNS (and PNS).
- Students will be able to predict potential patient conditions based on malfunction of these cells.

PREREQUISITE KNOWLEDGE

- General overview of organ systems (general structures and functions).
- General cell structure (cell membrane with membrane bound proteins as receptors).
- General understanding that cells work together within an organ so the organ can function properly (function of tissues).
- Basic chemistry and concept of molecule interactions.

OVERALL TIME ESTIMATE

One class period (~50 minute class).

VOCABULARY

**CNS:** Central Nervous System, specifically the brain and spinal cord
**PNS:** The Peripheral Nervous System, the network of all neurons other than those in the CNS.
**ECM:** Extracellular Matrix, the external environment surrounding cells.
**Glial cell:** Cells surrounding neurons that support neurons chemically and physically. Glial cells do not conduct nerve impulses or release neurotransmitters.

The glial cells in the CNS include:
- **Astrocytes:** Astrocytes maintain the environment of the ECM in the brain around the neurons. Astrocytes also assist in repairing damage.
**Ependymal cell:** the ‘epithelium’ of the CNS. These cells form the restrictive barrier around the CNS cells and produce the cerebrospinal fluid (CSF) found in the meninges.

**Microglia:** These cells breakdown and recycle waste surrounding the cells in the CNS.

**Oligodendrocyte:** These cells form the myelin sheath surrounding the axons of neurons in the brain. They also provide the structural framework by holding the axons in place.

Glia: cells in the PNS include:

- **Schwann cell:** These cells form the Myelin sheath surrounding the axons of neurons in the PNS.
- **Satellite cell:** These cells maintain the external environment surrounding the soma of neurons in the PNS.

**Neuron:** A nerve cell. Neurons conduct nerve impulses and release neurotransmitters into a synapse.

**Axon:** The axon is the portion of a neuron that transmits an impulse away from the body (soma) of a nerve cell. At the end of the axon, telodendria end in a synapse. The telodendria release neurotransmitters into the synapse to initiate a post synaptic cell response to carry on the nerve impulse (post synaptic cell = another neuron) or a cellular response (post synaptic cell is not another neuron, i.e. muscle cell).

**Soma:** The soma is body of a neuron. The soma contains the nucleus of the cell.

**Dendrite:** Dendrites are projections radiating from the soma of a neuron. They receive stimuli from the environment and are used to receive incoming information (sufficient to stimulate a nerve impulse when necessary). The soma is often covered with hundreds of dendrites.

**Myelin sheath:** A myelin sheath is a portion of a cell that provides a protective covering for the axon of a neuron.

**Nodes of Ranvier:** These Nodes are spaces between Schwann cells in the PNS that allow a nerve impulse to bypass the myelin sheath to conduct a nerve impulse.

**CSF:** Cerebrospinal Fluid is fluid secreted by the ependymal cells to fill the space between portions of the meninges and the brain and spinal cord.

**Meninges:** The meninges are tissue layers that form a protective covering around the CNS (brain and spinal cord).

**NATIONAL SCIENCE EDUCATION STANDARDS:**

12CLS6.1 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.

12FSPSP1.2 The severity of disease symptoms is dependent on many factors, such as human resistance and the virulence of the disease producing organism. Many diseases can be prevented, controlled, or cured. Some diseases, such as cancer, result from specific body dysfunctions and cannot be transmitted.
12GHNS1.1 Individuals and teams have contributed and will continue to contribute to the scientific enterprise. Doing science or engineering can be as simple as an individual conducting field studies or as complex as hundreds of people working on a major scientific question or technological problem. Pursuing science as a career or as a hobby can be both fascinating and intellectually rewarding.

NEXT GENERATION FLORIDA SCIENCE STANDARDS:

SC.912.L.14.21 Describe the anatomy, histology, and physiology of the central and peripheral nervous systems and name the major divisions of the nervous system.

SC.912.L.14.27 Identify the functions of the major parts of the brain, including the meninges, medulla, pons, midbrain, hypothalamus, thalamus, cerebellum and cerebrum.

BASIC SCIENCE HEALTH CONNECTION

This activity helps students understand that the nervous system relies on very specifically constructed cells that perform very specialized functions. If the structure of cells in the nervous system is compromised, the nervous system cannot function properly. This may pose serious problems for people suffering from conditions that interfere with the structure of the cells in the nervous system.

INTRODUCTION

In this activity students focus on the cells of the brain (and nervous system in general).

MATERIALS AND PREPARATION

It is preferable to utilize the diagram of a neuron from your textbook. If no diagram is available, you may use the link in resources as a sample diagram of a neuron.
Glial reading guide (resources below)
Materials to construct neurons and glial cells. Materials may range from construction paper or white paper and crayons to clay, felt, string/yarn. This is an opportunity to be creative.
Students may be asked to bring in materials.

PROCEDURE

Show students a diagram of a labeled neuron. Identify the parts of the neuron and the general function of each part.
Give each student a single piece of paper (construction paper or white paper) to create a foldable. Have students fold the paper in half. On the ‘outside cover’ of the foldable, students will write “Cells of the Nervous System” The Players. After being shown a neuron and the major parts of the neuron, students will construct a neuron on the inside left side of their foldable utilizing the materials provided. Students need to color code the parts of their neuron so they
can use the color coding to describe the function of each cell part on the right side of their foldable. This should take approximately 20 minutes. Student will read the glial cells document. Students will then construct each of the glial cells and attach their glial cells appropriately to their neurons. Glial cells should also be color coded and their function described on the right side of their foldable.

When completed, students may use the following interactive website as review/homework: [http://www.mhhe.com/biosci/esp/2001_saladin/folder_structure/in/m1/s2/index.htm](http://www.mhhe.com/biosci/esp/2001_saladin/folder_structure/in/m1/s2/index.htm)
If time, this review may be completed in class.

**RESOURCES**

**Neuron diagram**

**Glial cells reading**
Text adapted from [http://www.sci.uidaho.edu/med532/neurons_neuroglial_cells_module3.htm](http://www.sci.uidaho.edu/med532/neurons_neuroglial_cells_module3.htm)
diagram from [http://classes.midlandstech.edu/carterp/Courses/bio210/chap11/lecture1.html](http://classes.midlandstech.edu/carterp/Courses/bio210/chap11/lecture1.html)

**CNS cell tutorial:**


Glial cells make up approximately 90% of the cells found in the CNS (brain and spinal cord).

**Glial cells of the CNS.**

**Astrocytes**, known for the many processes attached to their cell body, provide structural support and their processes often have 'end feet' that abut the basal lamina around the capillary endothelium or line the exterior surface of the CNS, where they contribute to the pial-glial external limiting membrane. Cell bodies of astrocytes are among the largest for the glia, but only overlap the lower end for size of neurons.

**Oligodendrocytes** form myelin sheaths around axons in the CNS. One oligodendrocyte can form myelin sheaths along more than one internode of more than one axon. They have smaller cell bodies than astrocytes and relatively fewer processes leaving the cell body. The electron micrograph shows the cell body of an oligodendrocyte. Its nucleus is at the upper right and processes extend around myelinated fibers toward the lower left. The relatively electron dense cytoplasm is characteristic.

**Microglia** are the main phagocytic cell and antigen-presenting cells in the CNS. They have the smallest cell bodies among the neuroglia.
Ependymal cells line most of the ventricular system of the CNS, which is an inner space or lumen. At least seven of them with nuclei are evident in this electron micrograph of spinal cord.

Glial cells of the PNS
The phrase 'neuroglial-like' is also used to account for cells found in the peripheral nervous system (PNS) that are not neurons and that have functions similar to the classically described neuroglia.

Schwann cells form myelin (one Schwann cell/internode/axon) in the PNS. In the photomicrograph, their nuclei are the dark, cigar-shaped structures among the myelinated fibers that occupy the center and bottom parts of the picture.

Satellite (capsule) cells surround cell bodies of neurons in ganglia (both sensory and autonomic ganglia, but especially the former). Their nuclei are the dark, round structures that surround the neuronal cell bodies at the top and right sides of the picture.

http://www.sci.uidaho.edu/med532/neurons_neuroglial_cells_module3.htm
http://classes.midlandstech.edu/carterp/Courses/bio210/chap11/lecture1.html
Lesson 4: Nerve Impulses

AT A GLANCE

This lesson narrows student focus to the physiology of nerve impulses. Students perform reaction time tests before looking at the physiology involved in making those reactions occur.

FOCUS

- Students will perform simple reaction time tests.
- Students will then explore the physiological processes that occur
- Students will watch
- EXTENSION: Students will then design and conduct a simple lab to calculate reaction time. Students will conduct their reaction time lab.

MAJOR CONCEPTS

The function of the human brain relies on specific cells carrying out specific functions.

OBJECTIVES

- Students will be able to utilize tools to measure nervous system reactions.
- Students will be able to form a hypothesis regarding how environmental factors may affect nervous system reaction times. EXTENSION: Students will design and conduct an experiment to test their hypothesis.
- Students will be able to explain/describe the process of an action potential.

PREREQUISITE KNOWLEDGE

- General overview of organ systems (general structures and functions).
- General cell structure (cell membrane with membrane bound proteins as receptors).
- Basic structure of neurons.
- Basic chemistry and concept of molecule interactions.

OVERALL TIME ESTIMATE

One class periods ~50 minute classes. With experimental design EXTENSION 2 class periods.

VOCABULARY

Membrane potential: In cells, intracellular fluid is slightly negatively charged with a higher concentration of K+ (potassium ions) while the extracellular fluid is slightly positively charged with a higher concentration of Na+ (sodium ions). This electrochemical condition constitutes the cells membrane potential.
Depolarization: Depolarization occurs when the membrane potential along a cell membrane changes due to the movement of charged particles across that membrane. In neural axons, sodium rushes into the cell.

Repolarization: Repolarization occurs in neural axons as potassium rushes out to correct the charge effect of depolarization.

NATIONAL SCIENCE EDUCATION STANDARDS

12ASI.2.2 Scientists conduct investigations for a wide variety of reasons. For example, they may wish to discover new aspects of the natural world, explain recently observed phenomena, or test the conclusions of prior investigations or the predictions of current theories.

12CLS.6.1 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.

12EST.1.1 Identify a problem or design an opportunity. Students should be able to identify new problems or needs and to change and improve current technological designs.

12FSPSP.1.2 The severity of disease symptoms is dependent on many factors, such as human resistance and the virulence of the disease producing organism. Many diseases can be prevented, controlled, or cured. Some diseases, such as cancer, result from specific body dysfunctions and cannot be transmitted.

12FSPSP.1.4 An individual’s mood or behavior may be modified by substances. The modification may be beneficial or detrimental depending on the motives, type of substance, duration of use, pattern of use, level of influence, and short- and long- term effects. Students should understand that drugs can result in physical dependence and can increase the risk of injury, accidents, and death.

12GHNS.1.1 Individuals and teams have contributed and will continue to contribute to the scientific enterprise. Doing science or engineering can be as simple as an individual conducting field studies or as complex as hundreds of people working on a major scientific question or technological problem. Pursuing science as a career or as a hobby can be both fascinating and intellectually rewarding.

NEXT GENERATION FLORIDA SCIENCE STANDARDS

SC.912.N.1.1 Define a problem based on a specific body of knowledge, for example: biology, chemistry, physics, and earth/space science, and do the following:
   1. pose questions about the natural world,
2. conduct systematic observations,
3. examine books and other sources of information to see what is already known,
4. review what is known in light of empirical evidence,
5. plan investigations,
6. use tools to gather, analyze, and interpret data (this includes the use of measurement in metric and other systems, and also the generation and interpretation of graphical representations of data, including data tables and graphs),
7. pose answers, explanations, or descriptions of events,
8. generate explanations that explicate or describe natural phenomena (inferences),
9. use appropriate evidence and reasoning to justify these explanations to others,
10. communicate results of scientific investigations, and
11. evaluate the merits of the explanations produced by others.

SC.912.L.14.22 Describe the physiology of nerve conduction, including the generator potential, action potential, and the synapse.

BASIC SCIENCE HEALTH CONNECTION

This activity introduces students to Autism, the springboard for investigating the anatomy and physiology of the nervous system. As students discover how the nervous system works, they will be able to develop ideas regarding how the anomalies experienced by people with Autism might be treated.

INTRODUCTION

In this activity, students focus on nerve impulses. Students begin calculating reaction times. Students then learn the mechanism of nerve impulses: action potential. Students make the link between the rapid chemical changes that occur in a neuron via action potential to the ability to respond to stimuli as experienced in their reaction test experiments.

MATERIALS AND PREPARATION

Reaction tests (see links below in resources)
Reaction rate lab (resources below) OR utilize lab format for student designed lab.
Meter stick
Outreach action potential website (resources below)
Potential to Change Sheet

NOTE: This activity may be used as an inquiry lab by having students design their own experimental method for determining reaction rates.

PROCEDURE

Students participate in reaction time tests. (online, see links in resources)
EXTENSION: Students will conduct the Rate Your reaction lab. OR, students will design (optional/INQUIRY) and conduct a reaction rate lab.

    NOTE: This is a simple lab. You may be able to conduct this lab on the same day. You know your students best.

Students will watch and take notes on the outreach nerve impulse video below to gain understanding on physiological processes that occur in transmission of nerve impulses.  
http://outreach.mcb.harvard.edu/animations/actionpotential.swf

Students should be encouraged to take notes (Cornell notes if this is your practice) as they are walked through the video.

Students participate in the Potential to Change activity (resources below). This activity may be done as a whole class or as a competition between groups. Cut the steps in the challenge into individual steps.

    Whole class: each student (or students in pairs) receive one of the steps in the challenge. Students must then arrange themselves in the correct order as an action potential.

    Group competitions: Students are separated into small groups. Each small group receives all of the steps in the challenge. Groups will compete to be the first to finish with the entire series of events in the correct order.
    *NOTE: Bold lettering indicates major events with unbolded following within those major events. Unbolded events may or may not require a specific order to be correct (this depends on the specific event).

Students will review using outreach interactive website or highered website animation. (see resources)

RESOURCES
Reaction rate test links
http://www.bbc.co.uk/science/humanbody/sleep/sheep/reaction_version5.swf
http://getyourwebsitewhere.com/jswb/rttest01.html
http://www.mathsisfun.com/games/reaction-time.html

Nerve impulses animations
http://highered.mcgraw-hill.com/sites/0072495855/student_view0/chapter14/animation__the_nerve_impulse.html
http://outreach.mcb.harvard.edu/animations/actionpotential.swf


**The Potential to Change Challenge**

<table>
<thead>
<tr>
<th>Normal resting potential</th>
</tr>
</thead>
<tbody>
<tr>
<td>sodium inside/potassium outside</td>
</tr>
<tr>
<td><strong>Intracellular negative/extracellular positive</strong></td>
</tr>
<tr>
<td><strong>Sufficient stimulus</strong></td>
</tr>
<tr>
<td><strong>Depolarization occurs</strong></td>
</tr>
<tr>
<td>Potassium channels close</td>
</tr>
<tr>
<td>Sodium rushes in</td>
</tr>
<tr>
<td><strong>Repolarization occurs</strong></td>
</tr>
<tr>
<td>Potassium rushes out</td>
</tr>
<tr>
<td><strong>Return to resting potential</strong></td>
</tr>
<tr>
<td>Sodium/potassium pumps pump potassium back into the cell and sodium back out of the cell</td>
</tr>
<tr>
<td>1/3 of total energy expenditure</td>
</tr>
<tr>
<td><strong>Impulse travels to end of axon</strong></td>
</tr>
<tr>
<td>Telodendria release neurotransmitters into the synapse</td>
</tr>
</tbody>
</table>
Rate Your Reaction

I. Purpose
The purpose of this lab is to observe the reaction rates of a person’s hand/eye coordination.

II. Materials
Metric ruler
Table (or solid foundation)

III. Diagram
Draw a picture of an elbow resting on a table with a meter stick suspended over the hand that is prepared to catch it between forefinger and thumb.

IV.
Students will catch a meter stick between their forefinger and thumb. The distance measured will be converted to reaction time utilizing a conversion chart.

V. Steps
1. Rest your elbow firmly on a table or other surface.
2. Have your partner suspend a meter stick above your open palm, thumb facing up. The 0 cm mark should be at the same level as your thumb.
3. Have your partner randomly release the meter stick and catch the meter stick.
4. Record the distance (uppermost part of your hand or fingers) on the meter stick at the point it was caught and record on your data table.
5. Repeat 4 more times and record
6. Calculate the average distance.
7. Utilizing the conversion table, convert the average distances to reaction time.

VI. Results

<table>
<thead>
<tr>
<th>Trial number</th>
<th>distance</th>
<th>reaction rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trial 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trial 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trial 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trial 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Conversion Chart Distance to Reaction Rate

<table>
<thead>
<tr>
<th>Distance</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 in (~5 cm)</td>
<td>0.10 sec (100 ms)</td>
</tr>
<tr>
<td>4 in (~10 cm)</td>
<td>0.14 sec (140 ms)</td>
</tr>
<tr>
<td>6 in (~15 cm)</td>
<td>0.17 sec (170 ms)</td>
</tr>
<tr>
<td>8 in (~20 cm)</td>
<td>0.20 sec (200 ms)</td>
</tr>
<tr>
<td>10 in (~25.5 cm)</td>
<td>0.23 sec (230 ms)</td>
</tr>
<tr>
<td>12 in (~30.5 cm)</td>
<td>0.25 sec (250 ms)</td>
</tr>
<tr>
<td>17 in (~43 cm)</td>
<td>0.30 sec (300 ms)</td>
</tr>
<tr>
<td>24 in (~61 cm)</td>
<td>0.35 sec (350 ms)</td>
</tr>
<tr>
<td>31 in (~79 cm)</td>
<td>0.40 sec (400 ms)</td>
</tr>
<tr>
<td>39 in (~99 cm)</td>
<td>0.45 sec (450 ms)</td>
</tr>
<tr>
<td>48 in (~123 cm)</td>
<td>0.50 sec (500 ms)</td>
</tr>
<tr>
<td>69 in (~175 cm)</td>
<td>0.60 sec (600 ms)</td>
</tr>
</tbody>
</table>

Source: [http://faculty.washington.edu/chudler/chreflex.html](http://faculty.washington.edu/chudler/chreflex.html)

### VII. Conclusion
Consider these questions
Did your reaction rate change with subsequent trials?
What body part was receiving the stimulus information?
What body part was responding to the stimulus?
Predict how interference with either incoming or outgoing information might affect reaction rates (and why?).
Determine what types of interferences might cause your predictions.

### EXTENSION
Generate a hypothesis and design an experiment to test your predictions.
Lesson 5: Synapses and Neurotransmitters

AT A GLANCE

Students will look at the interactions that take place in the synapses. Students will apply those details to the concept of neural pathways within the brain.

FOCUS

- Students focus on interactions that occur in the synapses.
- Students will learn about neurotransmitters in general.
- Students will utilize an interactive website to understand how environmental factors (specifically drugs) interrupt the proper communication functions that occur within the synapse and ultimately affect sensory/motor control or decision making pathways.

MAJOR CONCEPTS

The human brain relies on specific cells to carry our specific functions. Those functions include specific chemical interactions as a communication device between cells. Interference with these chemical interactions can cause the entire CNS to function improperly.

OBJECTIVES

- Students will explain the interactions that may take place within the synapse.
- Students will describe how environmental factors may influence these interactions.
- Students will describe how a balance between pathways, based on these interactions, determines how well sensory/motor or decision making behaviors/responses occur.

PREREQUISITE KNOWLEDGE

- General overview of organ systems (general structures and functions).
- General cell structure (cell membrane with membrane bound proteins as receptors).
- Basic chemistry and concept of molecule interactions.
- Understand the mechanism of neuron to neuron communication.

OVERALL TIME ESTIMATE

One class period (~50 minute class).
**VOCABULARY**

**Basal Ganglia:** This portion of the brain serves as a relay center for incoming and outgoing information. The balance between appropriate sensory/motor and decision making responses occurs as a result of a balance between direct and indirect pathways within the basal ganglia. Appropriate communication between neurons in these two pathways determines that balance.

**Direct pathway:** This is the excitatory pathway within the basal ganglia.

**Indirect pathway:** This is the inhibitory pathway within the basal ganglia.

**Neurotransmitters:** These are chemicals released from vesicles within the telodendria at the end of neural axons. Neurotransmitters are released into the synapse to cause some type of response (excitatory or inhibitory) by a postsynaptic cell. Major Neurotransmitters include:

- **Dopamine:** Dopamine is generally an excitatory neurotransmitter. It may be inhibitory to some cells.
- **Acetylcholine:** Acetylcholine is generally an excitatory neurotransmitter. It may be inhibitory to some cells. (neuromuscular junction)
- **Norepinepherine:** Norepinepherine is generally an excitatory neurotransmitter.
- **Serotonin:** Serotonin is generally an inhibitory neurotransmitter.
- **GABA:** GABA is generally an inhibitory neurotransmitter
- **Glutamate:** Glutamate is generally an excitatory neurotransmitter.
- **Endorphins:** Endorphins are released when the body is under stress. They are our body’s natural pain and stress relievers.

**Synapse:** A synapse is the space at the end of an axon where neurotransmitters are released.

**Postsynaptic cell:** This is the cell that receives neurotransmitters that are released into the synapse front the end of a neural axon.

**NATIONAL SCIENCE EDUCATION STANDARDS:**

**12ASI2.2** Scientists conduct investigations for a wide variety of reasons. For example, they may wish to discover new aspects of the natural world, explain recently observed phenomena, or test the conclusions of prior investigations or the predictions of current theories.

**12CLS6.1** 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.

**12CLS6.4** Behavioral biology has implications for humans, as it provides links to psychology, sociology, and anthropology.

**12EST1.1** Identify a problem or design an opportunity. Students should be able to identify new problems or needs and to change and improve current technological designs.
12FSPSP1.4 An individual’s mood or behavior may be modified by substances. The modification may be beneficial or detrimental depending on the motives, type of substance, duration of use, pattern of use, level of influence, and short- and long-term effects. Students should understand that drugs can result in physical dependence and can increase the risk of injury, accidents, and death.

12GHNS1.1 Individuals and teams have contributed and will continue to contribute to the scientific enterprise. Doing science or engineering can be as simple as an individual conducting field studies or as complex as hundreds of people working on a major scientific question or technological problem. Pursuing science as a career or as a hobby can be both fascinating and intellectually rewarding.

NEXT GENERATION FLORIDA SCIENCE STANDARDS

SC.912.N.1.1 Define a problem based on a specific body of knowledge, for example: biology, chemistry, physics, and earth/space science, and do the following:
   1. pose questions about the natural world,
   2. conduct systematic observations,
   3. examine books and other sources of information to see what is already known,
   4. review what is known in light of empirical evidence,
   5. plan investigations,
   6. use tools to gather, analyze, and interpret data (this includes the use of measurement in metric and other systems, and also the generation and interpretation of graphical representations of data, including data tables and graphs),
   7. pose answers, explanations, or descriptions of events,
   8. generate explanations that explicate or describe natural phenomena (inferences),
   9. use appropriate evidence and reasoning to justify these explanations to others,
   10. communicate results of scientific investigations, and
   11. evaluate the merits of the explanations produced by others.

SC.912.L.14.2 Relate structure to function for the components of plant and animal cells. Explain the role of cell membranes as a highly selective barrier (passive and active transport).

SC.912.L.14.6 Explain the significance of genetic factors, environmental factors, and pathogenic agents to health from the perspectives of both individual and public health.

SC.912.L.14.22 Describe the physiology of nerve conduction, including the generator potential, action potential, and the synapse.

BASIC SCIENCE HEALTH CONNECTION

Specific chemical reactions occur in the synapses in the brain. Specific stimulus/response pathways occur as a result of these interactions. When environmental substances interfere with
these interactions, the pathways become imbalanced. This may cause inappropriate responses to stimuli. By understanding the mechanisms of these pathways, it is possible to develop treatments to correct imbalances that occur as a result of environmental interference.

INTRODUCTION

In this activity, students focus on chemical interactions in the synapse once an action potential has occurred. Combined interactions make up specific neural pathways that, when in balance, allow for appropriate responses to stimuli to occur.

MATERIALS AND PREPARATION

Access to nerve impulse animations for review (see resources)
Access to Introduction to neurotransmitter video (see resources)
Synapse model (see resources)
List of neurotransmitters (see resources)
Basal Ganglia Power Point (see resources)

PROCEDURE

Make sure to include Ritalin, addiction patterns, cocaine, amphetamines, Parkinson’s
Review nerve impulse videos.
View the introduction to neurotransmitters video (see resources)
Students will generate a simple trifold foldable for the synapse and neurotransmitters. Fold one paper into a trifold paper. The center panel will be the diagram of a synapse. The left panel will be the labeled structures in a synapse. The right panel will be the neurotransmitters. Utilizing the synapse diagram and list of neurotransmitters (see resources), students will draw the synapse in the center panel. Students should label each synapse part A, B, C, D etc. You can give students a copy of the synapse if pressed for time and have them glue it in place.
Students will use the left panel of the foldable to identify each structure in the synapse with its function (front side = A / name of structure, back side = A / function).
Students will use right panel of the foldable to identify neurotransmitters as excitatory or inhibitory (front of panel excitatory, back of panel names of neurotransmitters behind the appropriate neurotransmitter type).
You may use the foldable sample provided or create your own.
Students will identify and discuss interactions of different neurotransmitters within the synapse.
Students will interact with mouse party website to determine how substances of abuse interfere with activities in the synapses of the brain.
http://learn.genetics.utah.edu/content/addiction/drugs/mouse.html

EXTENSION: Engage students in Drugs Alter the Brains Reward Pathway interactive website (or assign for homework) (see resources)
Introduce basal ganglia as the location of direct and indirect pathways in the relay center of the brain (sensory/motor and decision making). Utilize the Basal Ganglia power point to assist. (see resources) The power point includes the activity below as well as some Think, Pair, Share activities.

NOTE: You may simplify this by telling students there are direct and indirect pathways involved in receiving and sending appropriate responses to stimuli. Then have students form a hypothesis on how a specific drug may interfere with indirect and direct pathways in the basal ganglia. If you simplify, be sure to note that addictions involve constant stimulus of reward pathways (dopamine producing) by the environmental substances, including food. You know your students best.

RESOURCES
Review Nerve impulses animations
http://highered.mcgrawhill.com/sites/0072495855/student_view0/chapter14/animation_the_nerve_impulse.html (copy/paste)
http://outreach.mcb.harvard.edu/animations/actionpotential.swf

Intro to neurotransmitters
http://www.youtube.com/watch?v=r71Rolkftd4

Synapse
http://commons.wikimedia.org/wiki/File:Synapse_diag1.png

Mouse party
http://learn.genetics.utah.edu/content/addiction/drugs/mouse.html (copy/paste)

EXTENSION
http://learn.genetics.utah.edu/content/addiction/drugs/index.html

Cocaine and dopamine
http://www.encognitive.com/node/17156

Sugar and fat addiction article
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2714381/ (copy/paste)


http://www.encognitive.com/node/17156


See Power Point Presentation:

Understanding the Basal Ganglia

Direct and indirect pathways
<table>
<thead>
<tr>
<th>Synapse Labels</th>
<th>Draw Synapse in This Space</th>
<th>Neurotransmitters</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Fold the edge to the beginning of the synapse diagram</td>
<td>• Top</td>
<td>• Fold the edge to the right side of the synapse diagram.</td>
</tr>
<tr>
<td>• Cut and number flaps 1-8.</td>
<td>• Label parts with numbers 1-8</td>
<td>• Cat and label 2 flaps: excitatory inhibitory</td>
</tr>
<tr>
<td>• Correctly identify synapse parts under each numbered flap.</td>
<td>• Bottom</td>
<td>• List the excitatory and inhibitory neurotransmitters under the appropriate flaps</td>
</tr>
</tbody>
</table>
Synaptical transmission (chemical).
A : Neuron (Presynaptic) B : Neuron (Postsynaptic)
1. Mitochondria
2. Synaptic vesicle full of neurotransmitter
3. Autoreceptor
4. Synaptic cleft
5. Neurotransmitter receptor
6. Calcium Channel
7. Fused vesicle releasing neurotransmitter
8. Neurotransmitter re-uptake pump

http://commons.wikimedia.org/wiki/File:Synapse_diag1.png
Neurotransmitters

**Dopamine:** Dopamine is generally an excitatory neurotransmitter. It may be inhibitory to some cells.

**Acetylcholine:** Acetylcholine is generally an excitatory neurotransmitter. It may be inhibitory to some cells. (neuromuscular junction)

**Norepinephrine:** Norepinephrine is generally an excitatory neurotransmitter.

**Serotonin:** Serotonin is generally an inhibitory neurotransmitter.

**GABA:** GABA is generally an inhibitory neurotransmitter.

**Glutamate:** Glutamate is generally an excitatory neurotransmitter.

**Endorphins:** Endorphins are released when the body is under stress. They are our body’s natural pain and stress relievers.
Lesson 6: Skipping a Tick?

AT A GLANCE

In this lesson, student understanding of the physiology of the nervous system will be applied to the design of experiments that might lead to treatments of CNS disorders like Parkinson’s or Autism.

FOCUS

Students connect cellular physiology of brain to autism via comparative behaviors. Students will form a hypothesis regarding potential methods to correct imbalances between neural pathways in the BG. Students will also design an experiment testing their hypothesis using animal models.

MAJOR CONCEPTS

Anomalies in the physiology of brain cells may lead to behaviors that make it difficult for people to interact with the rest of society. When the physiological mechanisms for these behaviors are understood, scientists can develop ways to correct these anomalies.

OBJECTIVES

- Students will be able to identify similarities in neural physiology among mammals.
- Students will be able to develop a hypothesis regarding malfunctions that may occur in that physiology.
- Students will be able to generate an experimental design that can legitimately test their hypothesis.

PREREQUISITE KNOWLEDGE

- General overview of organ systems (general structures and functions).
- General cell structure (cell membrane with membrane bound proteins as receptors).
- Basic chemistry and concept of molecule interactions.
- Understanding of neural pathways, cell communication within those pathways and how imbalances in those pathways may affect behavior.
- General methodology for experimental design: formation of hypothesis, controlling variables, etc.

OVERALL TIME ESTIMATE

One class period (~50 minute class).
VOCABULARY

Optogenetics: The use of optics (light) and genetics to control biological events.

NATIONAL SCIENCE EDUCATION STANDARDS:

12ASI2.2 Scientists conduct investigations for a wide variety of reasons. For example, they may wish to discover new aspects of the natural world, explain recently observed phenomena, or test the conclusions of prior investigations or the predictions of current theories.

12CLS6.1 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.

12CLS6.4 Behavioral biology has implications for humans, as it provides links to psychology, sociology, and anthropology.

12EST1.1 Identify a problem or design an opportunity. Students should be able to identify new problems or needs and to change and improve current technological designs.

12FSPSP1.2 The severity of disease symptoms is dependent on many factors, such as human resistance and the virulence of the disease producing organism. Many diseases can be prevented, controlled, or cured. Some diseases, such as cancer, result from specific body dysfunctions and cannot be transmitted.

12FSPSP1.4 An individual’s mood or behavior may be modified by substances. The modification may be beneficial or detrimental depending on the motives, type of substance, duration of use, pattern of use, level of influence, and short- and long-term effects. Students should understand that drugs can result in physical dependence and can increase the risk of injury, accidents, and death.

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3. examine books and other sources of information to see what is already known,
4. review what is known in light of empirical evidence,
5. plan investigations,
6. use tools to gather, analyze, and interpret data (this includes the use of measurement in metric and other systems, and also the generation and interpretation of graphical representations of data, including data tables and graphs),
7. pose answers, explanations, or descriptions of events,
8. generate explanations that explicate or describe natural phenomena (inferences),
9. use appropriate evidence and reasoning to justify these explanations to others,
10. communicate results of scientific investigations, and
11. evaluate the merits of the explanations produced by others.

BASIC SCIENCE HEALTH CONNECTION

This activity allows students the opportunity to apply their knowledge of the physiology of the CNS, specifically the brain, to resolve issues for people with neurological anomalies. Students will be able to recognize that the search for real knowledge can lead to the development of treatments that may be used to correct some of the conditions that plague many members of our society. Student will be able to recognize that they are able to access this knowledge and use it to make life better for others.

INTRODUCTION

In this activity students will use their knowledge of CNS neural physiology to design experiments to correct anomalies using animal models. Optogenetics will be introduced as an additional method of manipulating cell physiology.

MATERIALS AND PREPARATION

EXTENSION: Optogenetics papers (online below or download for hard copies)
Stereopathy and autism videos

PROCEDURE

Briefly review previous lesson regarding neurotransmitter activities in the CNS and the general pattern of Basal Ganglia (BG) circuitry. Emphasize the impact of materials, like drugs, on the ability of the CNS to function properly.

EXTENSION: If you did not view yesterday’s video Heavy metals and the synapse, this can be done now. (see resources below) mercury and neurons

EXTENSION: In addition, and as a segue into teaching students about the senses, have students read one of the articles on optogenetics. (see resources). You may do this by jigsawing any/all
of the articles. Most have abstracts. Students may be able to gain sufficient information from abstracts to discuss with each other. Once the jigsaw is complete, discuss potential application of optogenetics (and potentially other sensory input methods, like sound) in correcting anomalies on BG pathways.

Students view animal stereopathies. (see links below)

Students view autism videos with similar behaviors. (see links below)

Discuss the similarities in RRBs between animals and autistic children.

Students use previous knowledge to develop a hypothesis and design an animal model experiment that might be used to correct (or interfere) with stereopathies/autistic behaviors. The general lab format used previously can be used as a guideline.

RESOURCES

Heavy metals and the synapse
http://www.encognitive.com/node/16851

Animals:
Stereotypic Animal Behaviour
http://www.aps.uoguelph.ca/~gmason/StereotypicAnimalBehaviour/library.shtml (copy/paste)

Autism:
Links to 5 youtube videos of autistic children. Compare movements to animal RRBs (pacing, spinning, flipping, digging, etc)
http://www.youtube.com/watch?v=6DmzUmcFrrE&NR=1&feature=fvwp
http://www.youtube.com/watch?v=-6blmKiPe9c&feature=related
http://www.youtube.com/watch?v=U35q146wMzo&NR=1&feature=fvwp
http://www.youtube.com/watch?v=xeKKMkVgNPU&feature=related
http://www.youtube.com/watch?v=PxH-Vubdzus&NR=1

OPTPGENETICS LINKS

Original paper
optogenetics F1000
http://f1000.com/reports/b/3/11 (copy/paste)
http://the-scientist.com/2011/07/01/the-birth-of-optogenetics/ review article (copy paste)

NOTE: Access to AAAS articles (below) may require a paid subscription.
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By combining genetics with fiber optics, Karl Deisseroth has given researchers a powerful tool with which to probe our most enigmatic organ.

PART ELECTRICITY and part chemistry, the brain's language relies on precision in both wiring and timing. Technologies such as EEG and fMRI let researchers and clinicians eavesdrop on the brain's internal conversations, but they miss many of their subtleties. And because scientists can't always parse the brain's code, the source of the communication breakdown in disorders like autism, depression and Parkinson's disease continues to elude them. Compare that to, say, the heart, says Karl Deisseroth, in which the model of how the organ works—and what happens when it malfunctions—is relatively straightforward. "[With] congestive heart failure, the heart is not pumping well," he says. "We don't have that analogous understanding of the brain. What's really not working well in a disease state?"

As an associate professor of bioengineering and psychiatry at Stanford, Deisseroth bridges what some might call the study of the mind and the study of the brain. His work with clinical patients shows him the subjective, experiential side of the mind's maladies, but he is best known for his role in developing optogenetics, a new technology that gives scientists an extraordinarily precise tool for probing those disorders' biological origins.

In the murky world of neuroscience, optogenetics is literally a bright point. Using different wavelengths of light, delivered via fiber optic cable, scientists can control the activity of the cells that send and receive information in the brain. Blue light activates targeted neurons; yellow light quiets them. Think of it as a universal remote that operates the body's tiniest circuits.
Even better, because optogenetics can be used in living, behaving lab animals—rodents and primates so far—scientists can observe the effects of toggling brain circuits on disease symptoms. Turn these neurons off, and what goes wrong? What happens when you crank them back up? Establishing causal links between brain circuitry and symptoms could lead to highly targeted therapies—more effective drugs, perhaps, or a new class of less invasive brain implants to treat disorders like Parkinson's disease.

MAKING LIGHT WORK OF BRAIN RESEARCH: Deisseroth, center, with Shenoy and Henderson. Toni Gauthier

At Stanford, Deisseroth's lab has used optogenetics to investigate the roots of schizophrenia, and along with Stanford School of Medicine neurosurgeon Jaimie Henderson, the problems underlying Parkinson's disease. The work of colleague Krishna Shenoy, an associate professor of electrical engineering and bioengineering, could help those with paralysis and traumatic head injuries.

Yet as tantalizing as such potential applications are, Deisseroth's ultimate vision is focused less on cures, and more on gaining fundamental insight into the brain. Optogenetics may finally give scientists a way not only to better interpret its rapid-fire language, but also to start talking back to it using the speed and precision of light.

THE IDEA OF USING light to control the mammalian brain didn't originate with Deisseroth's lab; it had been considered, but not achieved, by many others. He keeps a copy of a 1979 issue of Scientific American on his desk, in which Francis Crick—of Watson and Crick, the team that first described DNA's double-helix—imagined such a precise tool. "He didn't say 'light,' but he said what we need is a way to control neurons specifically as they are embedded in intact tissue," says Deisseroth. "He later speculated that light or other things might be one way of doing it, but he had absolutely no idea of how that might be done."

For decades, a few researchers outside neuroscience had experimented with genes derived from algae and other microorganisms. Algae contain light-sensitive proteins called opsins that
act as tiny gatekeepers, regulating the flow of charged ions across cell membranes. For example, Channelrhodopsin-2, which responds to blue light, allows positive ions in, activating the cell. Another protein, Halorhodopsin, which comes from a bacteria-like single-celled organism, allows negative ions to enter in response to yellow light, silencing the cell.

But how to get these opsins into neurons? The genes for these proteins can be packaged inside a virus and delivered to an animal's brain by injection, making nearby neurons sensitive to light. Attaching snippets of DNA called promoter tags ensures that the genes only become activated within desired kinds of cells, so that those cells alone respond to light from the fiber optic cable.

Early attempts, including unpublished efforts by Roger Tsien's biology lab at UC-San Diego, didn't work—they'd chosen the wrong algae genes. When Deisseroth's lab took up the challenge in 2003, some considered it a waste of time. He was turned down for a foundational grant because funders doubted he could achieve convincing results. Even with the right genes, making algae opsins operate in animal tissue was a long shot. The opsins, Deisseroth explains, "come from these microbes that are not brains, or anything like brains. They don't have the same machinery, they don't operate on the same speed, they need chemical cofactors to get them to work." Using them posed two problems—finding those necessary chemical catalysts, and the possibility that the animal's cells would reject these foreign proteins.

Yet right away, Deisseroth says, "Several things happened that we had no right to expect. One is that we didn't have to add any chemicals to get it to work." Additionally, the neurons tolerated the opsins well.

Within two years Deisseroth's lab had published its breakthrough 2005 paper. Demonstrations of optogenetics' power were astounding. One widely circulated video shows a lab mouse with a fiber optic cable inserted into the part of its motor cortex that controls left-side movement; a thin wire protrudes from its skull. When the cable glows blue, the mouse circles left. When the light is turned off, it stops. Optogenetics had produced, in essence, a remote-controlled mouse.
OPTOGENETICS 101

1. The gene that makes cells light-sensitive is isolated from algae or other microorganisms.
2. A snippet of DNA is added to "address" the gene to a particular type of neuron.
3. The tagged gene is inserted into a harmless virus and injected into the mouse's brain.
4. Targeted neurons express the light-sensitive protein on their surface.
5. Light is delivered via a fiber-optic cable wired into the mouse's brain.
6. Different proteins respond to particular wavelengths of light, turning neurons on or off.

The ability to switch cells off and on lends itself to an extraordinary number of potential applications, and Deisseroth's lab readily shared its technology. One group at Stanford is using it to explore the brain's sleep-wake cycles to gain insight into sleep-related disorders. One at UC-San Francisco is investigating the neural circuitry involved in addiction. Because optogenetics works on any cell, not just those of the brain, it also has been applied to organs such as the heart and the eye. Deisseroth has collaborated with European researchers who hope to restore vision to those with retinitis pigmentosa by using light-sensitive opsins to reactivate the eye's photoreceptors. Perhaps the best-known optogenetics experiments are those exploring Parkinson's disease, possibly because they so clearly illustrate the contrast between the precision of optogenetics and older, more empirical, approaches. Doctors already have a highly successful implant technology for Parkinson's called deep brain stimulation (DBS) that ameliorates symptoms like tremor and rigidity. In this procedure, a metal electrode, sometimes referred to as a "pacemaker for the brain," is implanted into the subthalamic nucleus and pulses the area with electric current. (It's also in human clinical trials as a treatment for epilepsy and depression.) In Parkinson's patients, the results can be dramatic. "It reduces symptoms by anywhere from 50 to 80 percent and reduces patients' medication needs by about 60 percent," says Stanford neurosurgeon Jaimie Henderson, who has performed approximately 600 such operations. Improvement can be immediate. In a documentary video recording Henderson's operation on bike racer Davis Phinney, the cyclist's left arm shakes violently throughout the operation, but relaxes within seconds of the current being turned on. "That feels good," Phinney murmurs happily. "It's a relief, baby." Steven Gulie, who wrote about his own surgery under Henderson's care for Wired, described the flipping of the switch this way: "For more than five years my right hand hasn't felt the way it should. Suddenly, it's back. I can tap my fingers, move freely."

Yet DBS has drawbacks. Deisseroth has described electrodes as "fast but dumb." In the brain, different types of neurons are intermixed, and electricity floods them all. Neurons with the largest axons—the connective wiring that Henderson calls the "cabling of the brain"—absorb the most current, and electricity can take unexpected paths. That means side effects. "You can get tingling, muscle contractions, problems with speech, balance difficulties or cognitive problems," Henderson says. What's more, nobody knows exactly why DBS works. It's not even clear which cells it affects. "The electrode could be driving excitatory cells; it could be driving inhibitory cells," Deisseroth says. "When you drive it this hard you can exhaust cells, so you might actually be inhibiting excitatory cells or you might be inhibiting inhibitory cells. Or you might be having some more
complex effect like affecting synchrony or timing or the competition of two circuits for a third. With an electrode you just didn't know."
Most of all, it's not a cure. Even with treatment, patients deteriorate. DBS treats symptoms, but not their cause.
The ability to switch cells off and on lends itself to an extraordinary number of potential applications.
Optogenetics is helping doctors search for the underlying problem. In collaboration with Henderson, Deisseroth's lab used optogenetics to control Parkinson's symptoms in lab mice outfitted with fiber-optic implants. The researchers delicately toggled different neurons, and were surprised to find that the most therapeutic effect came not from stimulating a particular kind of cell, but from affecting the activity of their connective axons. When the axons were pulsed with light at high frequency, the mice behaved normally; when the pulse stopped, their symptoms returned. "This points to the concept that neuropsychiatric diseases may in large part relate to altered flow of activity between brain regions," says Deisseroth.
In other words, the problem isn't within the cells, it's in the informational flow among them. "One theory we are working with currently is that the brain communicates using different frequencies of oscillation," says Henderson. "Think of how radio works: There is a 'carrier' wave that is modulated by the sound that is to be carried, producing a complex waveform with lots of information. We think that the brain may get locked into rhythmical activity that blocks out that information and replaces it with a kind of 'hum,' as if fine-grained information in the radio waves is getting overwhelmed by a periodic repeating waveform. Once a circuit gets locked into that oscillation, you get abnormal behavior like seizures in epilepsy, and tremor and rigidity in Parkinson's."
Thanks in part to optogenetics, an emerging model of the brain holds that spatial specificity and millisecond timing are critical to information flow. If that's the case, then arrhythmia in the brain may be just as dangerous as it is in the heart. Deisseroth suspects that disruptions in timing and rhythm may underlie several brain disorders, including schizophrenia.
In one experiment, his group made a type of neuron called a fast-spiking cell light-sensitive. Rare in healthy brains, these neurons are even sparser in schizophrenics. But their function—and the ramifications of their deficiency—was not well understood. Using optogenetic controls, Deisseroth says, "We found that they play a role in a particular kind of brain wave called a gamma oscillation, which is a 40-times-per-second rhythm. They help maintain this rhythm, this synchronicity in the brain."
The group also demonstrated that this rhythmicity enhances communication in the brain; when the rhythm is off, messages are garbled. That's significant for schizophrenics, who have trouble processing sources of information and intent, often misreading the significance of objects and actions. Auditory hallucinations, or "voices in the head," also may be a result of misprocessed information, Deisseroth notes. "It may be a poorly recognized version of internal thoughts. Somehow the information that a thought is really coming from oneself is lost. It's viewed as a foreign thing, a voice speaking." Prior to the advent of optogenetics, he says, "There was no way to know this because there was no way to selectively control [the cells] on the right timescale."
The technique also may help restore communication in damaged brains. Stanford scientist Krishna Shenoy has spent the past 12 years working on brain-machine interfaces that enable
paralyzed people to move prosthetic devices. These interfaces "read out" the brain's movement instructions, bypass the damaged spinal cord and send them directly to, for example, a robotic arm.

'Optogenetics is the newest, most exquisite tool we have available as neuroscientists.' Interpreting the brain's signals is one thing, but "writing in" information about touch and the limb's location relative to the body is much harder. Imagine using a robotic arm to take a drink, he says: "When you move that arm out, all of a sudden you are immediately faced with the fact that you can't feel anything. If you squeeze on that glass too hard, you can shatter it. If you have a plastic water bottle, you may spill it. If you don't grip it hard enough, it may slip and fall."

Shenoy shares a $14.9 million DARPA grant to use optogenetics to develop a fundamental model of how the brain operates, and apply that insight to better understand how to write in information to the brain. While the grant's focus is on basic research, it could lead to very practical applications, such as more sensitive, naturally moving prosthetics, or perhaps treatments for traumatic head injuries. Learning how to write in the information that gets lost when a part of the brain is damaged could allow doctors to reroute signals around a damaged area.

In experiments with primates, Shenoy's lab is using tiny devices implanted atop the monkey's head that shine light down optical fibers implanted into the brain's surface. The light activates or silences neural circuits in the pre-motor and motor cortex, effectively giving instructions to the parts of the brain that initiate and control movement. "How are you going to inject information so precisely at the cellular level, talking to every type of cell in natural language?" Shenoy asks. "Optogenetics. That's certainly the newest, the most exquisite tool we have available as neuroscientists."

DEISSEROTH'S OFFICE, tucked into the Clark Center basement, is nearly empty. It was recently renovated, and he's put off unpacking because he's enjoying the minimalism of three walls of bare shelving. The only objects on display are a trophy called "The Golden Brain" shaped like, well, a brain, and four empty champagne bottles, one to celebrate each major paper his team published this year. Stacks of boxes crowd around the door—some hold additional champagne bottles from previous years. The team has been extraordinarily prolific.

Deisseroth's career has been one of rapid successes: He went to college (biochemistry at Harvard) at age 16, medical school (at Stanford) at 20, and published his key optogenetics paper just a year after establishing his own lab. "Starting things a little too early has been a common theme my whole life," he says. He has a humble, almost boyish demeanor. As he speaks, he balls his fists up inside the hem of his faded T-shirt, and stares thoughtfully down at the table. He's conscious of inhabiting an unusual middle ground between the abstraction of psychiatry and the precision of bioengineering. "They're worlds apart," he says. "Your average bioengineer has essentially nothing to say to your average psychiatrist and vice versa. But this is changing, and I think we’re helping a little bit with that, because there is a natural affinity there."

Psychiatry, he says, can benefit from a bioengineering approach: "We need new tools, we need new technology, we need a quantitative understanding of the dynamics of these tiny electrical devices which are neurons as they operate within an enormously complicated circuit."

Deisseroth still spends about 20 percent of his time seeing clinical patients, including those with autism and depression. This, he says, "keeps me grounded in clinical reality" and helps him
"maintain intuition for disease processes." He's hopeful that optogenetics could lead to new treatments—more accurately targeted drugs, better brain implants, perhaps more helpful talk therapy.

Functional brain imaging has shown physical differences in the brains of people who have, or have not, gone through therapy. "We may find that talk therapy can indeed, if it's done right, turn up or down particular brain circuits," he says. "So we might be able to even gain insight into what might be the best kind of talk therapy using optogenetic insight." He hopes that mental disorders will become less stigmatized as their origins are better understood.

Deisseroth is acutely sensitive to the moral implications of giving scientists such fine-tuned control over brain function. "The specificity of optogenetics raises the question of how precisely could one tweak a brain to really create an individual with different needs, desires, priorities, feelings," he says. And while he sees the promise of using the technique to, for example, help the severely depressed feel enjoyment again, he acknowledges that "there is a disturbing aspect, too, which raises questions of free will." (Recall the mouse that feels compelled to turn left, but doesn't know why.)

Even though optogenetic applications for humans are still entirely hypothetical, for bioethicists, the possibility of tinkering so intimately with the brain raises profound questions. "We're very brain-centric in our culture," observes Dr. Debra Mathews, the assistant director for science programs at the Johns Hopkins Berman Institute of Bioethics. The idea of intervening directly with what we see as the seat of our identities, and being able to influence personality and how we perceive ourselves, our ties to others and our roles in the world, is a sensitive one, she says, particularly given the sometimes inglorious history of psychosurgery.

Although optogenetics' selling point is extreme precision, Mathews cautions that any attempt to influence the brain is inherently unpredictable. "The brain is an incredibly complex organ, vastly more complex than anything else we deal with, and we can't guarantee that plucking at one cell is only going to affect the cells that we think it will, or the system we think we will, or the phenotypes—the characteristics—we think it will. We're just not that good yet."

Still, Mathews calls the possibility of using optogenetics to better understand the brain and look for new therapeutic targets "awesome." For her, the most exciting part of Deisseroth's work is its utility as a research tool. The technique "has the potential to be a pretty powerful tool for basic science, certainly for interrogating previously inaccessible questions, systems and connections in the brain."

Deisseroth agrees: "Before treatments, we need understanding."

ADVANCING UNDERSTANDING means enabling others to use optogenetics, a multidisciplinary skill set that requires expertise in fiber optics, virology, and animal surgery and behavior, among other disciplines. Deisseroth's group started training researchers in 2006 and has shared the technology with more than 700 labs worldwide.

This summer, with support from Stanford's BioX program, the University launched its Optogenetics Innovation Laboratory, offering free three-day or three-week training sessions to scholars from other universities. Deisseroth compares it to a microlending approach: "People can go back to their own institutions and teach other people." The goal is to train at least 100 researchers per year.
Freely sharing skills will lead to "geometric expansion" of the field, says neurosurgeon Henderson. "Rapid dissemination means that this incredibly cool technology can now be in the hands of hundreds of researchers" who can use it to test their own ideas. It's a way of leveraging the brainpower of the entire scientific community, Deisseroth notes: "I can't do even a tiny fraction of what I would want to do, and so the more people we can help the better." Of course, there are potential roadblocks ahead. What works in mice and monkeys may not work in humans. There are also open questions regarding immune reactions, how deeply light spreads through brain tissue, and how well opsins will work over time. Optogenetics-derived therapies are far off, and will have to not only face the hurdle of FDA approval, but also prove superior to current treatments like deep brain stimulation.

But for Deisseroth, the ultimate goal is not using opsins in humans—it's gaining a fundamental understanding of the brain's complexities. Sitting in his near-bare office, with only a few commemorative champagne bottles to signify the accomplishments of the past few years, Deisseroth is proud of how far the field already has come in deciphering the brain's secret language. "If I had to shut down my lab tomorrow," he says, "I'd be a happy man."

Kara Platoni is a frequent contributor who lives in Oakland.

The Birth of Optogenetics:
An account of the path to realizing tools for controlling brain circuits with light
By Edward S. Boyden | July 1, 2011

Blue light hits a neuron engineered to express opsin molecules on its surface, opening a channel through which ions pass into the cell—activating the neuron.

For a few years now, I’ve taught a course at MIT called “Principles of Neuroengineering.” The idea of the class is to get students thinking about how to create neurotechnology innovations—new inventions that can solve outstanding scientific questions or address unmet clinical needs. Designing neurotechnologies is difficult because of the complex properties of the brain: its inaccessibility, heterogeneity, fragility, anatomical richness, and high speed of operation. To illustrate the process, I decided to write a case study about the birth and development of an innovation with which I have been intimately involved: optogenetics—a toolset of genetically encoded molecules that, when targeted to specific neurons in the brain, allow the activity of those neurons to be driven or silenced by light.
A strategy: controlling the brain with light
As an undergraduate at MIT, I studied physics and electrical engineering and got a good deal of firsthand experience in designing methods to control complex systems. By the time I graduated, I had become quite interested in developing strategies for understanding and engineering the brain. After graduating in 1999, I traveled to Stanford to begin a PhD in neuroscience, setting up a home base in Richard Tsien’s lab. In my first year at Stanford I was fortunate enough to meet many nearby biologists willing to do collaborative experiments, ranging from attempting the assembly of complex neural circuits in vitro to behavioral experiments with rhesus macaques. For my thesis work, I joined the labs of Richard Tsien and of Jennifer Raymond in spring 2000, to study how neural circuits adapt in order to control movements of the body as the circumstances in the surrounding world change.

In parallel, I started thinking about new technologies for controlling the electrical activity of specific neuron types embedded within intact brain circuits. That spring, I discussed this problem—during brainstorming sessions that often ran late into the night—with Karl Deisseroth, then a Stanford MD-PhD student also doing research in Tsien’s lab. We started to think about delivering stretch-sensitive ion channels to specific neurons, and then tethering magnetic beads selectively to the channels, so that applying an appropriate magnetic field would result in the bead’s moving and opening the ion channel, thus activating the targeted neurons.

By late spring 2000, however, I had become fascinated by a simpler and potentially easier-to-implement approach: using naturally occurring microbial opsins, which would pump ions into or out of neurons in response to light. Opsins had been studied since the 1970s because of their fascinating biophysical properties, and for the evolutionary insights they offer into how life forms use light as an energy source or sensory cue. These membrane-spanning microbial molecules—proteins with seven helical domains—react to light by transporting ions across the lipid membranes of cells in which they are genetically expressed. (See the illustration above.) For this strategy to work, an opsin would have to be expressed in the neuron’s lipid membrane and, once in place, efficiently perform this ion-transport function. One reason for optimism was that bacteriorhodopsin had successfully been expressed in eukaryotic cell membranes—including those of yeast cells and frog oocytes—and had pumped ions in response to light in these heterologous expression systems. And in 1999, researchers had shown that, although many halorhodopsins might work best in the high salinity environments in which their host archaea naturally live (i.e., in very high chloride concentrations), a halorhodopsin from Natronomonas pharaonis (Halo/NpHR) functioned best at chloride levels comparable to those in the mammalian brain.
Infographic: OPSINS: Tools of the Trade

I was intrigued by this, and in May 2000 I e-mailed the opsin pioneer Janos Lanyi, asking for a clone of the *N. pharaonis* halorhodopsin, for the purpose of actively controlling neurons with light. Janos kindly asked his collaborator Richard Needleman to send it to me. But the reality of graduate school was setting in: unfortunately, I had already left Stanford for the summer to take a neuroscience class at the Marine Biology Laboratory in Woods Hole. I asked Richard to send the clone to Karl. When I returned to Stanford in the fall, I was so busy learning all the skills I would need for my thesis work on motor control that the opsin project took a backseat for a while.

The channelrhodopsin collaboration
In 2002 a pioneering paper from the lab of Gero Miesenböck showed that genetic expression of a three-gene *Drosophila* phototransduction cascade in neurons allowed the neurons to be excited by light, and suggested that the ability to activate specific neurons with light could serve as a tool for analyzing neural circuits. But the light-driven currents mediated by this system were slow, and this technical issue may have been a factor that limited adoption of the tool. This paper was fresh in my mind when, in fall 2003, Karl e-mailed me to express interest in revisiting the magnetic-bead stimulation idea as a potential project that we could pursue together later—when he had his own lab, and I had finished my PhD and could join his lab as a postdoc. Karl was then a postdoctoral researcher in Robert Malenka’s lab (also at Stanford), and I was about halfway through my PhD. We explored the magnetic-bead idea between October 2003 and February 2004. Around that time I read a just-published paper by Georg Nagel, Ernst Bamberg, Peter Hegemann, and colleagues, announcing the discovery of channelrhodopsin-2 (ChR2), a light-gated cation channel and noting that the protein could be used as a tool to depolarize cultured mammalian cells in response to light.

In February 2004, I proposed to Karl that we contact Georg to see if they had constructs they were willing to distribute. Karl got in touch with Georg in March, obtained the construct, and inserted the gene into a neural expression vector. Georg had made several further advances by then: he had created fusion proteins of ChR2 and yellow fluorescent protein, in order to monitor ChR2 expression, and had also found a ChR2 mutant with improved kinetics. Furthermore, Georg commented that in cell culture, ChR2 appeared to require little or no chemical supplementation in order to operate (in microbial opsins, the chemical chromophore all-trans-retinal must be attached to the protein to serve as the light absorber; it appeared to exist at sufficient levels in cell culture).
Finally, we were getting the ball rolling on targetable control of specific neural types. Karl optimized the gene expression conditions, and found that neurons could indeed tolerate ChR2 expression. Throughout July, working in off-hours, I debugged the optics of the Tsien-lab rig that I had often used in the past. Late at night, around 1 a.m. on August 4, 2004, I went into the lab, put a dish of cultured neurons expressing ChR2 into the microscope, patch-clamped a glowing neuron, and triggered the program that I had written to pulse blue light at the neurons. To my amazement, the very first neuron I patched fired precise action potentials in response to blue light. That night I collected data that demonstrated all the core principles we would publish a year later in Nature Neuroscience, announcing that ChR2 could be used to depolarize neurons. During that long, exciting first night of experimentation in 2004, I determined that ChR2 was safely expressed and physiologically functional in neurons. The neurons tolerated expression levels of the protein that were high enough to mediate strong neural depolarizations. Even with brief pulses of blue light, lasting just a few milliseconds, the magnitude of expressed-ChR2 photocurrents was large enough to mediate single action potentials in neurons, thus enabling temporally precise driving of spike trains. Serendipity had struck—the molecule was good enough in its wild-type form to be used in neurons right away. I e-mailed Karl, “Tired, but excited.” He shot back, “This is great!!!!!”

Transitions and optical neural silencers
In January 2005, Karl finished his postdoc and became an assistant professor of bioengineering and psychiatry at Stanford. Feng Zhang, then a first-year graduate student in chemistry (and now an assistant professor at MIT and at the Broad Institute), joined Karl’s new lab, where he cloned ChR2 into a lentiviral vector, and produced lentivirus that greatly increased the reliability of ChR2 expression in neurons. I was still working on my PhD, and continued to perform ChR2 experiments in the Tsien lab. Indeed, about half the ChR2 experiments in our first optogenetics paper were done in Richard Tsien’s lab, and I owe him a debt of gratitude for providing an environment in which new ideas could be pursued. I regret that, in our first optogenetics paper, we did not acknowledge that many of the key experiments had been done there. When I started working in Karl’s lab in late March 2005, we carried out experiments to flesh out all the figures for our paper, which appeared in Nature Neuroscience in August 2005, a year after that exhilarating first discovery that the technique worked.
A neuron expresses the light-gated cation channel channelrhodopsin-2 (green dots on the cell body) in its cell membrane (1). The neuron is illuminated by a brief pulse of blue light a few milliseconds long, which opens the channelrhodopsin-2 molecules (2), allowing positively charged ions to enter the cells, and causing the neuron to fire an electrical pulse (3). A neural network containing different kinds of cells (pyramidal cell, basket cell, etc.), with the basket cells (small star-shaped cells) selectively sensitized to light activation. When blue light hits the neural network, the basket cells fire electrical pulses (white highlights), while the surrounding neurons are not directly affected by the light (4). The basket cells, once activated, can,
however, modulate the activity in the rest of the network.

Watch Video MIT McGovern Institute, Julie Pryor, Charles Jennings, Sputnik Animation, Ed Boyden

Around that same time, Guoping Feng, then leading a lab at Duke University (and now a professor at MIT), began to make the first transgenic mice expressing ChR2 in neurons. Several other groups, including the Yawo, Herlitze, Landmesser, Nagel, Gottschalk, and Pan labs, rapidly published papers demonstrating the use of ChR2 in neurons in the months following. Clearly, the idea had been in the air, with many groups chasing the use of channelrhodopsin in neurons. These papers showed, among many other groundbreaking results, that no chemicals were needed to supplement ChR2 function in the living mammalian brain. Almost immediately after I finished my PhD in October 2005, two months after our ChR2 paper came out, I began the faculty job search process. At the same time, I started a position as a postdoctoral researcher with Karl and with Mark Schnitzer at Stanford. The job-search process ended up consuming much of my time, and being on the road, I began doing bioengineering invention consulting in order to learn about other new technology areas that could be brought to bear on neuroscience. I accepted a faculty job offer from the MIT Media Lab in September 2006, and began the process of setting up a neuroengineering research group there. Around that time, I began a collaboration with Xue Han, my then girlfriend (and a postdoctoral researcher in the lab of Richard Tsien), to revisit the original idea of using the N. pharaonis halorhodopsin to mediate optical neural silencing. Back in 2000, Karl and I had planned to pursue this jointly; there was now the potential for competition, since we were working separately. Xue and I ordered the gene to be synthesized in codon-optimized form by a DNA synthesis company, and, using the same Tsien-lab rig that had supported the channelrhodopsin paper, Xue acquired data showing that this halorhodopsin could indeed silence neural activity. Our paper appeared in the March 2007 issue of PLoS ONE; Karl’s group, working in parallel, published a paper in Nature a few weeks later, independently showing that this halorhodopsin could support light-driven silencing of neurons, and also including an impressive demonstration that it could be used to manipulate behavior in Caenorhabditis elegans. Later, both our groups teamed up to file a joint patent on the use of this halorhodopsin to silence neural activity. As a testament to the unanticipated side effects of following innovation where it leads you, Xue and I got married in 2009 (and she is now an assistant professor at Boston University). I continued to survey a wide variety of microorganisms for better silencing opsins: the inexpensiveness of gene synthesis meant that it was possible to rapidly obtain genes codon-optimized for mammalian expression, and to screen them for new and interesting light-drivable neural functions. Brian Chow (now an assistant professor at the University of Pennsylvania) joined my lab at MIT as a postdoctoral researcher, and began collaborating with Xue. In 2008 they identified a new class of neural silencer, the archaerhodopsins, which were not only capable of high-amplitude neural silencing—the first such opsin that could support 100 percent shutdown of neurons in the awake, behaving animal—but also were capable of rapid recovery after having been illuminated for extended durations, unlike halorhodopsins, which took minutes to recover after long-duration illumination. Interestingly, the archaerhodopsins are light-driven outward pumps, similar to bacteriorhodopsin—they hyperpolarize neurons by
pumping protons out of the cells. However, the resultant pH changes are as small as those produced by channelrhodopsins (which have proton conductances a million times greater than their sodium conductances), and well within the safe range of neuronal operation. Intriguingly, we discovered that the \textit{H. salinarum} bacteriorhodopsin, the very first opsin characterized in the early 1970s, was able to mediate decent optical neural silencing, suggesting that perhaps opsins could have been applied to neuroscience decades ago.

**Beyond luck: systematic discovery and engineering of optogenetic tools**

An essential aspect of furthering this work is the free and open distribution of these optogenetic tools, even prior to publication. To facilitate teaching people how to use these tools, our lab regularly posts white papers on our website* with details on reagents and optical hardware (a complete optogenetics setup costs as little as a few thousand dollars for all required hardware and consumables), and we have also partnered with nonprofit organizations such as Addgene and the University of North Carolina Gene Therapy Center Vector Core to distribute DNA and viruses, respectively. We regularly host visitors to observe experiments being done in our lab, seeking to encourage the community building that has been central to the development of optogenetics from the beginning.

As a case study, the birth of optogenetics offers a number of interesting insights into the blend of factors that can lead to the creation of a neurotechnological innovation. The original optogenetic tools were identified partly through serendipity, guided by a multidisciplinary convergence and a neuroscience-driven knowledge of what might make a good tool. Clearly, the original serendipity that fostered the formation of this concept, and that accompanied the initial quick try to see if it would work in nerve cells, has now given way to the systematized luck of bioengineering, with its machines and algorithms designed to optimize the chances of finding something new. Many labs, driven by genomic mining and mutagenesis, are reporting the discovery of new opsins with improved light and color sensitivities and new ionic properties. It is to be hoped, of course, that as this systematized luck accelerates, we will stumble upon more innovations that can aid in dissecting the enormous complexity of the brain—beginning the cycle of invention again.

**Putting the toolbox to work**

These optogenetic tools are now in use by many hundreds of neuroscience and biology labs around the world. Opsins have been used to study how neurons contribute to information processing and behavior in organisms including \textit{C. elegans}, \textit{Drosophila}, zebrafish, mouse, rat, and nonhuman primate. Light sources such as conventional mercury and xenon lamps, light-emitting diodes, scanning lasers, femtosecond lasers, and other common microscopy equipment suffice for in vitro use.

In vivo mammalian use of these optogenetic reagents has been greatly facilitated by the availability of inexpensive lasers with optical-fiber outputs; the free end of the optical fiber is simply inserted into the brain of the live animal when needed,\textsuperscript{14} or coupled at the time of experimentation to an implanted optical fiber. For mammalian systems, viruses bearing genes encoding for opsins have proven popular in experimental use, due to their ease of creation and use. These viruses achieve their specificity
either by infecting only specific neurons, or by containing regulatory promoters that constrain opsin expression to certain kinds of neurons.

An increasing number of transgenic mouse lines are also now being created, in which an opsin is expressed in a given neuron type through transgenic methodologies. One popular hybrid strategy is to inject a virus that contains a Cre-activated genetic cassette encoding for the opsin into one of the burgeoning number of mice that express Cre recombinase in specific neuron types, so that the opsin will only be produced in Cre recombinase-expressing neurons. In 2009, in collaboration with the labs of Robert Desimone and Ann Graybiel at MIT, we published the first use of channelrhodopsin-2 in the nonhuman primate brain, showing that it could safely and effectively mediate neuron type–specific activation in the rhesus macaque without provoking neuron death or functional immune reactions. This paper opened up a possibility of translating the technique of optical neural stimulation into the clinic as a treatment modality, although clearly much more work is required to understand this potential application of optogenetics.

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http://the-scientist.com/2011/07/01/the-birth-of-optogenetics