What Biological theme connects all of these Hollywood movies?
Understanding the Brain through Disease

Tammy Due
Masconomet Regional High School
Lecture Outline

• Brain Overview
• Neural Anatomy
• Neurological Diseases/Current Research
A Neuroanatomical Tour of the Human Brain
Cerebrum

- Makes up the left and right hemispheres of a vertebrate forebrain.
- Responsible for integrating memory, learning, emotions and other complex functions of the brain.
Hypothalamus

- Part of the forebrain involved with maintaining homeostasis.
- The hypothalamus is especially important in coordinating the endocrine and nervous systems.
- Secretes hormones of posterior pituitary which regulate the anterior pituitary.
Pituitary Gland

- Used to be called the “master” gland because so many of its hormones regulate other endocrine functions.

- **Anterior pituitary**: secretes hormones directly into the blood stream. The hypothalamus release inhibitory hormones.

- **Anterior pituitary hormones**: growth hormone (GH), insulin growth factors, prolactin (PRL), Follicle stimulating hormone (FSH), leutinizing hormone (LH), thyroid stimulating hormone (TSH), adrenocorticotropic hormone (ACTH), melanocyte-stimulating hormone (MSH), and endorphins

- Posterior pituitary: the two hormones released by the posterior pituitary are produced by the hypothalamus.

- Oxytocin and Antidiuretic hormone (ADH)
Brainstem

- Medulla or medulla oblongata: contains centers that control breathing, heart & blood vessel activity, swallowing, vomiting & digestion.
- Pons: have nuclei that regulate the breathing centers in the medulla.
- Brainstem is responsible for movement.
Cerebellum

- Part of the hindbrain
- Functions in unconscious coordination of movement and balance.

Return to Brain slide
Midbrain

- Develops into sensory integrating and relay centers that sends sensory information to the cerebrum.
Thalamus

• One of the integrating centers in the vertebrate forebrain.
• Neurons in the thalamus relay neural input to specific areas of the cerebral cortex and regulates what information goes to the cerebral cortex.
Ventricles

• Four spaces in the vertebrate brain that are filled with cerebrospinal fluid.

• Cerebrospinal fluid conveys nutrients, hormones, & white blood cells across the BBB to different parts of the brain.

• Fluid also is important in cushioning the brain.
Corpus Callosum

• Thick band of nerve fibers that connects the right & left hemispheres in placental mammals. This connection allows for the hemispheres to process information together.
Lecture Outline

• Brain Overview
• **Neural Anatomy**
• Neurological Diseases/Current Research
These cells control brain function on a cellular level. What are they called?

Image courtesy of Dr. Joshua Sanes, Harvard University, 2005
The Neuron comes in many shapes and sizes

http://www.mind.ilstu.edu/images/neuron_types.gif
“Typical” Neuron

http://www.mhhe.com/socscience/intro/ibank/ibank/0002.jpg
Osm-10 is a chemoreceptor found in *C. elegans*. This worm contains a transgene encoding the osm-10 promoter fused to GFP (Harvard Medical School).
Action Potential I

1. Resting state: -70mV
2. Neuron receives stimulus, gated ion channels open and sodium(Na+) moves into the cell, this is depolarization. The stronger the signal the more channels that open. When the threshold potential is reached (+55 to +50mV) an action impulse is triggered. This is an all or none event.

3. During repolarization the sodium channels close and potassium channels open. K⁺ moves out of the cell making the cell more negative than its environment.

4. The K⁺ gates are slow to close which may result in undershooting. This means that the negative voltage inside the cell goes lower than the resting state.
“Typical” Neuron

Dendrites

Direction of impulse

Soma (nucleus)

Direction of impulse

Axon

Myelin Sheath

Node of Ranvier

To next neuron

To next neuron

X

http://www.mhhe.com/socscience/intro/ibank/ibank/0002.jpg
The Synapse

Mitochondria

Synaptic Vesicle

Microtubule

Synaptic vesicle being transferred

Cisternae

Terminal end

Synaptic Cleft

Vesicle at synaptic cleft

Presynaptic Membrane

Postsynaptic Membrane

http://www.staff.city.ac.uk/c.r.legg/index.2.jpg
“Real” Synapses

From Dr. Venkatesh N. Murthy’s, Harvard University, 7/2005

Photo by T. Due, Harvard University, 7/2005

These C. elegans worms contain a transgene encoding unc-49 gene (GABA receptor) fused to its own promoter and GFP (Harvard Medical School)
Lecture Outline

• Brain Overview
• Neural Anatomy
• Neurological Diseases/Current Research
ADHD

- **Symptoms:**
  Inattention, impulsivity, hyperactivity

- **Causes:**
  1. **Environmental Agents:** cigarettes, smoking, lead
     - May affect neuronal connections being formed in developing brain.
  2. **Brain Injury**
     - Evidence has shown that few with ADHD are the result of brain injury.
  3. **Food Additives & Sugar**
     - We once thought that refined sugar and food additives caused ADHD but in studies that restrict a patient’s diet there was little effect on behavior and learning.
4. Genetics:
   • 25% of close relatives of someone w/ ADHD also have ADHD. This rate is only 5% in the general public.
   • Twin studies show a strong genetic influence.
Brain Study Results

- Technology used: fMRIs, PET scans, single photon emission computed tomography (SPECT)
- ADHD children showed 3-4% smaller brain volume in all regions--frontal lobes, temporal gray matter, caudate nucleus and cerebellum.
- ADHD patients on medication showed no difference from controls in amount of white matter (connections).
- fMRIs show that there is less glucose used in the frontal lobes of patients with ADHD
In men who had ADHD, PET (positron emission tomography) scans showed that they processed a memory task in visual areas in the occipital lobe of the brain, as indicated by the yellow spots in the left image. Non-ADHD men used the temporal and frontal lobes, shown at right (ABCNEWS.com)

Brain Images: ADHD

Brain scan images produced by fMRI show differences between an adult with Attention deficit Hyperactivity Disorder (right) and an adult free of the disease (left).

*Zametkin, et. al., 1990*
Treatments

- **Medication**: shows positive results when appropriate medication and dosage is given
  - Ritalin, Adderall, Concerta: focus has been creating long lasting drugs with fewer side effects. All are stimulants and work in a similar manner to cocaine.
  - Strattera: a non-stimulant medication for ADHD
- Some side effects of medication: upset stomach, headaches, dizziness, decreased appetite, sleep issues
- **Behavioral Therapy** (not best when used alone)
  - Behavioral therapy, Psychotherapy
- **Combination Therapy**: medication and behavioral
Huntington’s Disease (HD)

- **Frequency**: 1/30,000 Americans

- **Symptoms of HD**
  - Uncontrolled movements
  - Loss of intellectual faculties
  - Emotional disturbances
  - Mood swings
  - Irritability
  - Depression
  - Difficulty driving
  - Concentration on intellectual tasks decreases with age.
Biological Basis

- Autosomal dominant disorder
- Gene located on chromosome 4
- Within the gene CAG repeats occur 11-30X in a normal person.
- A person with 36-125 CAG repeats will tend to develop HD between 30-40 years of age.
- If someone has >60 repeats they tend to develop HD much earlier, in their 20’s.
The result of CAG repeats

• The gene that is affected produces the Huntingtin protein in normal cells
• The protein that is created is a more polar molecule which tends to interact with other brain proteins differently. Ex. HAP 1
Molecular Basis of Huntington’s Disease

The gene’s DNA is translated into amino acids which form the abnormal huntingtin protein.

Possible "polar zipper" effect
What areas of the brain are affected by changes in Huntingtin protein?

- Neurons are damaged in the **basal ganglia**, especially the **caudate nucleus and globus pallidus**.

http://www.hdsa-wi.org/brain.gif
Treatment

- Medications are prescribed to decrease the symptoms of HD.
- Some medications treat fatigue, hyperexcitability, and restlessness.
- Other medications treat the control emotional and movement problems.
Current Research on HD

- Silencing of mutant gene, decreases protein production which results in decrease of HD symptoms. Gene was silenced using RNAi’s.
- Using rodent and primate models, scientists have transplanted fetal brain tissue into brains damaged by HD. The transplanted cells survived.