Part A: How does the brain communicate?
The human brain is the most complex organ in the body. This three-pound mass of gray and white matter sits at the center of all human activity - you need it to drive a car, to enjoy a meal, to breathe, to create an artistic masterpiece, and to enjoy everyday activities. In brief, the brain regulates your basic body functions; enables you to interpret and respond to everything you experience; and shapes your thoughts, emotions, and behavior. The brain is made up of many parts that all work together as a team. Different parts of the brain are responsible for coordinating and performing specific functions. Drugs can alter important brain areas that are necessary for life-sustaining functions and can drive the compulsive drug abuse that marks addiction.

The brain is a communications center consisting of billions of neurons, or nerve cells. Networks of neurons pass messages back and forth to different structures within the brain, the spinal column, and the peripheral nervous system. These nerve networks coordinate and regulate everything we feel, think, and do.

- **Neuron to Neuron**
  A neuron has three main parts. The cell body directs all of the neuron’s activities. Dendrites, short branches that extend out from the cell body, receive messages from other neurons and pass them on to the cell body. An axon is a long, single fiber that transmits messages from the cell body to the dendrites of other neurons or to other tissues in the body, such as muscles. A protective covering called the myelin sheath covers the axons of many neurons. Myelin insulates the axon and helps messages from nerve signals travel faster, farther, and more efficiently. Each nerve cell in the brain sends and receives messages in the form of electrical impulses. Once a cell receives and processes a message, it sends it on to other neurons.

- **Neurotransmitters - The Brain's Chemical Messengers**
  The exchange of information from the axon of one neuron to the dendrites of another is called neurotransmission. Neurotransmission takes place through the release of chemicals, called neurotransmitters, into the space between the axon of the first neuron and the dendrites of the second neuron, called the synapse. Our body produces many different types of
neurotransmitters. Each neurotransmitter has a specific role to play in the functioning of the brain.

- **Receptors - The Brain's Chemical Receivers**
  When neurons communicate, an electrical impulse traveling down the axon causes neurotransmitters to be released from the end of the axon into the synapse. The neurotransmitters cross the synapse and bind to special molecules on the other side, called receptors. A neurotransmitter and its receptor operate like a "key and lock," an exquisitely specific mechanism that ensures that each receptor will forward the appropriate message only after interacting with the right kind of neurotransmitter. A specific neurotransmitter only binds to certain receptors. Receptors are found on the dendrites and cell bodies of all neurons. These receptors convert the information into chemical and/or electrical signals for processing in the neuron.

- **Transporters - The Brain's Chemical Recyclers**
  Once the neurotransmitter has bound to a receptor, a series of events follow. First, the message carried by the neurotransmitter is received and passed on to the receiving nerve cell. Second, the neurotransmitter is inactivated and either broken down by an enzyme or reabsorbed from where it was released. The reabsorption is completed by other molecules called transporter molecules or reuptake pumps. These molecules are located in the cell membranes of the axon that releases the neurotransmitters. They pick up specific neurotransmitters from the synapse and carry them back across the cell membrane into the axon thereby shutting off the signal between neurons. The neurotransmitters are then recycled for use at a later time. Note that this process is true for most neurotransmitters, but not for all of them.

To complete Part A of this lab, fill in the boxes on the following page (How Do Neurons Communicate?), outlining the major steps in neurotransmission. Then use this outline as a guide and make physical models of the process with your box of clay. You must include two neurons, a presynaptic vesicle, a neurotransmitter, a receptor for the neurotransmitter and a transporter. More details on the process are on page 4 of this handout. Once you have constructed your clay model, you must get your TA to sign your copy of How Do Neurons Communicate.
Neurotransmission
Neurons Communicate by Neurotransmission

Neurons communicate using both electrical signals and chemical messages. Information in the form of an electrical impulse is carried away from the neuron’s cell body along the axon of a presynaptic neuron toward the axon terminals. When the electrical signal reaches the terminal, it cannot cross the synaptic space, or synaptic cleft, to reach the postsynaptic neuron. Instead, that electrical signal triggers chemical changes that can cross the synapse to affect the postsynaptic cell. When the electrical impulse reaches the presynaptic axon terminal, it causes membranous sacs, called vesicles, to move toward the membrane of the axon terminal. When the vesicles reach the membrane, they fuse with the membrane and release their contents into the synaptic space. The molecules contained in the vesicles are chemical compounds called neurotransmitters. Each vesicle contains many molecules of a neurotransmitter. The released neurotransmitter molecules drift across the synaptic cleft and then bind to special proteins, called receptors, on the postsynaptic neuron. A neurotransmitter molecule will bind only to a specific kind of receptor. The binding of neurotransmitter to its receptor causes a change in the postsynaptic neuron that in turn causes that neuron to generate an electrical impulse. The electrical impulse then moves away from the neuron ending toward the cell body. After the neurotransmitter binds to the receptor to transmit the signal to the postsynaptic neuron, it comes off of, or releases from, the receptor into the synaptic space. Specific proteins called transporters or reuptake pumps carry the neurotransmitter back into the presynaptic neuron. When the neurotransmitter molecules are back in the presynaptic axon terminal, they can be repackaged into vesicles for release the next time an electrical impulse reaches the axon terminal. Enzymes present in the synaptic space degrade neurotransmitter molecules that are not taken back up into the presynaptic neuron.
Part B: How do drugs work in the brain?

Drugs are chemicals. They work in the brain by tapping into the brain's communication system and interfering with neurotransmission, but they can do this in different ways. Some drugs, such as marijuana and heroin, can activate neurons because their chemical structure mimics that of a natural neurotransmitter. This similarity in structure "fools" receptors and allows the drugs to lock onto and activate the nerve cells through specific receptors. Although these drugs mimic brain chemicals, they don't activate nerve cells in the same way as a natural neurotransmitter, and they lead to abnormal messages being transmitted through the network.

Other drugs, such as amphetamine or cocaine, can cause the nerve cells to release abnormally large amounts of natural neurotransmitters or prevent the normal recycling of these brain chemicals. This disruption produces a greatly amplified message, ultimately disrupting communication channels. The difference in effect can be described as the difference between someone whispering into your ear and someone shouting into a microphone.

Many illicit drugs act by altering levels of the neurotransmitter dopamine. You should know three things about dopamine:

1) Dopamine is critical to the way the brain controls our movements. Not enough dopamine -- can't move, or control our movements well. Too much dopamine? Uncontrollable/subconscious movements (like picking, tapping, repetitive moments, jerking, twitching). Remember that the heart is a muscle, too, and too much dopamine will result in increased pulse and blood pressure.

2) Dopamine controls the flow of information from other areas of the brain, especially memory, attention and problem-solving tasks. This becomes important when we talk about amphetamine-induced psychosis that is common in meth abusers.

3) When dopamine is released it provides feelings of enjoyment and reinforcement to motivate us to do, or continue doing, certain activities. Dopamine is released by naturally rewarding experiences such as food and sex. This pre-programmed reward system makes sure that people do eat, do desire to procreate, and basically survive. Without enough dopamine, people feel the opposite of enjoyment and motivation -- they feel fatigued and depressed, and experience a lack of drive and motivation.

Specifically:

1. **Nicotine** binds to specific receptors on the presynaptic neuron. When nicotine binds to receptors at the cell body, it excites the neuron so that it fires more action potentials (electrical signals) that move toward the synapse, causing more dopamine release (not shown in figure). When nicotine binds to nicotine receptors at the nerve terminal, the amount of dopamine released in response to an action potential is increased.

2. **Methamphetamine** alters dopamine neurotransmission in two ways. Methamphetamine enters the neuron by passing directly through nerve cell membranes. It is carried to the nerve cell terminals by transporter molecules that normally carry dopamine or norepinephrine. In the nerve terminal, methamphetamine enters the dopamine- or norepinephrine-containing vesicles and causes the release of this neurotransmitter. Methamphetamine also blocks the dopamine transporter from pumping dopamine back into the transmitting neuron. Methamphetamine acts similarly to cocaine in this way.

3. When **cocaine** enters the brain, it blocks the dopamine transporter from pumping dopamine back into the transmitting neuron, flooding the synapse with dopamine. This intensifies and prolongs the stimulation of receiving neurons in the brain's pleasure circuits, causing a cocaine "high."
How do drugs work in the brain to produce pleasure?
All drugs of abuse directly or indirectly target the brain's reward system by flooding the circuit with dopamine. Dopamine is a neurotransmitter present in regions of the brain that regulate movement, emotion, cognition, motivation, and feelings of pleasure. The overstimulation of this system, which rewards our natural behaviors, produces the euphoric effects sought by people who abuse drugs and teaches them to repeat the behavior. **All drugs of abuse target the brain’s reward system by flooding the circuit with dopamine.**

To complete Part B of this lab, you will alter your clay neurotransmission model three times, to show sequentially, the effect of methamphetamine, nicotine and cocaine. Read the description and it will tell you what to change. When you have each model completed, have your TA check it. Then return to your original model and alter it for the next drug on the list. Once you have had pictures taken of all three drug models, you may answer the following questions and submit it, along with your completed copy of *How Do Neurons Communicate*, as your lab report.

Post-lab Questions:

1. List at least four ways to administer a drug.

2. Postulate, based on your model, how the method of administration could affect the intensity of a drug's effect.

For more information, see:


http://www.drugabuse.gov/scienceofaddiction/brain.html

http://science.education.nih.gov/supplements/nih2/addiction/guide/lesson3-1.htm