Script for the Virtual Cocaine Lab Tutorial

Cocaine and Dopamine

http://www.mind.ilstu.edu

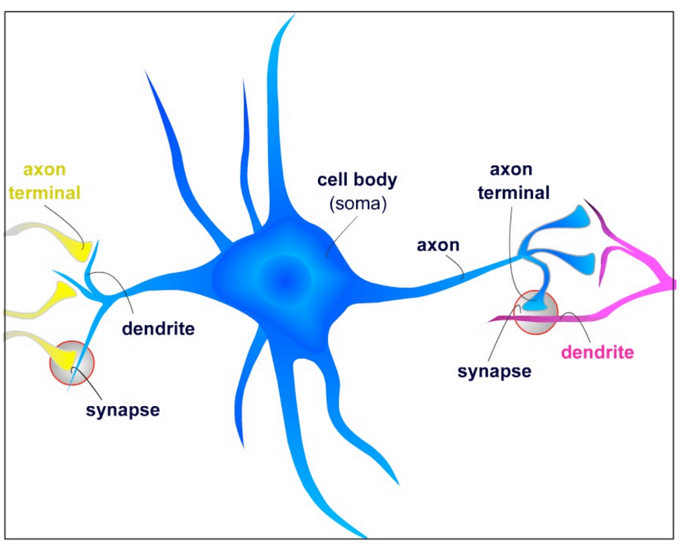
Introduction

This tutorial is for "The Virtual Neuroscience Lab #1: Cocaine Study," a free virtual lab available from The Mind Project. It contains a shortened summary of the content helpful for completing this virtual lab. This tutorial could be used as a supplement, or replacement for the reading required in the desk area within the virtual lab.

This tutorial includes background on the following content areas:

- role of neurotransmitters
- dopamine neurons
- motivated behavior
- measuring dopamine levels
- connection between dopamine and cocaine
- rat research
- experimental design of the virtual lab experiment.

Role of Neurotransmitters



There are four basic structures of a neuron.

The first is the cell body. This is where a majority of organelles and therefore where metabolism is controlled and structures are manufactured and recycled.

Dendrites are extensions of the neuron that receive incoming signals. Neurons generally have thousands of dendrites.

The Axon of a neuron is how signals are sent out to adjacent cells. Neurons only have one axon.

The axon terminal is where vesicles filled with neurotransmitters are located. Neurotransmitters are essential to the ability of neurons to communicate with one another and send signals quickly.

This animated graphic of a “Classic” chemical neurotransmission is available in the desk area of the virtual lab in Book 1.

1. An action potential arrives at the axon terminal and

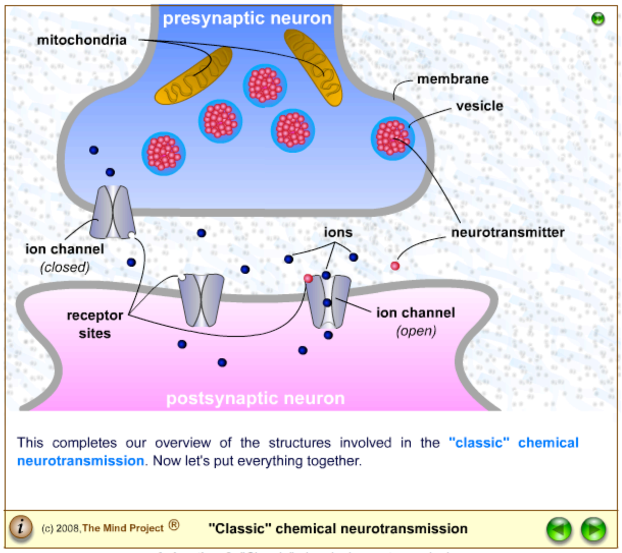
2. triggers release of neurotransmitter from a vesicle into the synaptic cleft.

3. These neurotransmitters bind to receptor sites on ion channels on the post synaptic neuron

4. This allows ions to cross the membrane through open channels

5. This influx of ions produces a synaptic potential in the postsynaptic neuron.

6. Chemical neurotransmission is ended by the removal of neurotransmitters from the synaptic cleft. This usually occurs via a process called uptake, where a transporter protein acts as a pump to move neurotransmitters back inside the axon of the neuron.



Animation 2: "Classic" chemical neurotransmission.

Dopamine Neurons

Dopamine neurons are specialized neurons and therefore function a bit differently from “classic” chemical neurotransmissions.

Dopamine neurons are involved in motor control and motivated behavior, as well as in mediating the effects of drugs of abuse.

The neurotransmitter for dopamine neurons is dopamine along with two others.

One major difference between classic neurons and dopamine neurons is that the dopamine released at the synaptic cleft is not restricted to the post synaptic neuron. This means that dopamine diffuses out and can bind to other neurons with dopamine receptors.

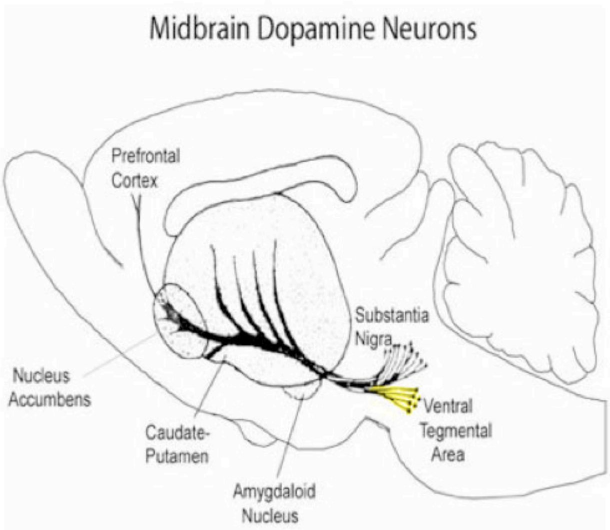
This is why dopamine levels in the brain can be measured more easily than other neurotransmitters.

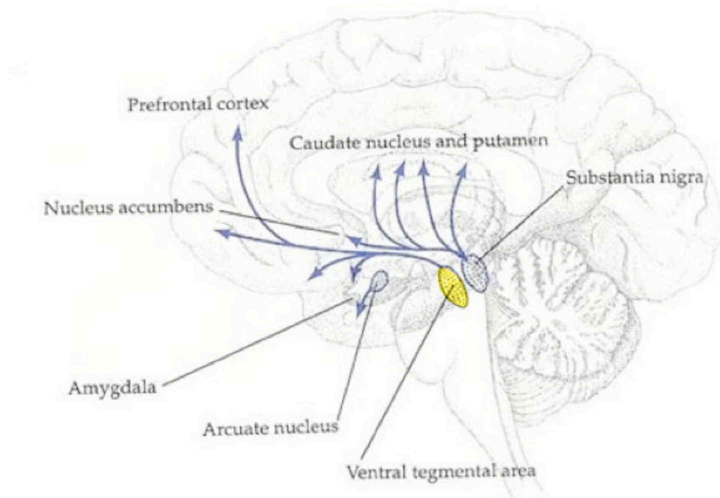
Dopamine Neurons in the Brain

While Dopamine neurons in the brain are located in several areas, this lab will be focusing on just one location.

Rats are good subjects for experiments because of the extensive overlap in brain anatomy and function, as well as similar dopamine neuron systems.

Dopamine neurons within this midbrain area start in a part of the brain called the ventral tegmental area. The neurons end in a location called the nucleus accumbens. Notice how these two areas of the brain are similar for both rats and humans.



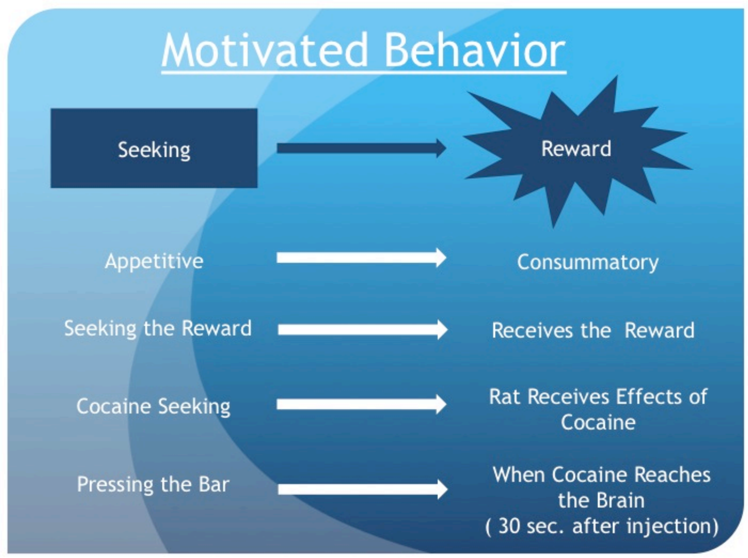


Two Phases of Motivated Behavior

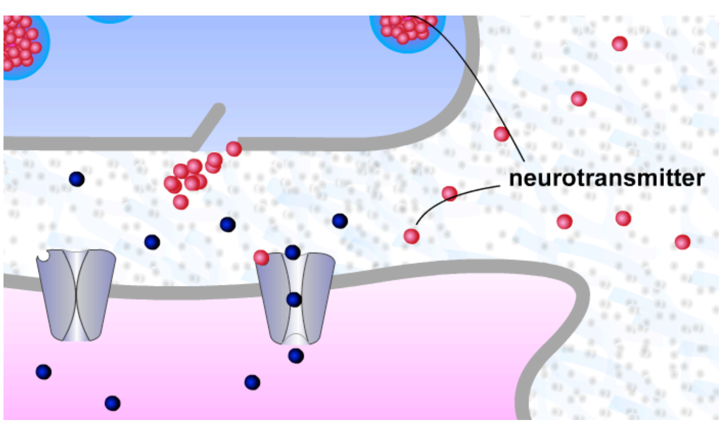
Motivated behavior refers to behavior related to receiving a reward or reaching a goal. There are two phases of motivated behavior.

One is called the appetitive phase that include behaviors of approaching or seeking the reward. The other is called the consummatory phase and represents when the reward is received.

In our virtual cocaine experiment, the appetitive phase refers to a rat when it is anticipating or seeking cocaine. And the consummatory phase refers to when the rat receives the effects of the cocaine.



Connection Between Dopamine and Cocaine Use



From The Mind Project http://www.mind.ilstu.edu

How does cocaine affect dopamine neurons?

Cocaine molecules binds to the dopamine transporters which shut down the neuron's ability to uptake the extra dopamine within the synaptic cleft. This results in increased levels of the neurotransmitter dopamine present in the extracellular spaces among these neurons.

Cocaine also binds to the transporters of the neurotransmitters norepinephrine and serotonin, affecting their uptake and therefore increasing the concentration of three neurotransmitters in the brain.

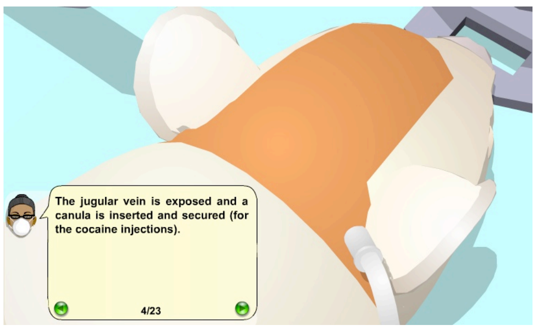
This increases heart rate and causes blood vessels to constrict. Large doses can result in cardiac failure.

The known connection between dopamine levels and cocaine is that 30 seconds after cocaine enters a rat's circulatory system, the level of dopamine rises in the nucleus accumbens portion of the brain. Therefore, it is commonly believed that cocaine is associated with the consummatory phase of motivated behavior. What is not clear, though, is whether or not the levels of dopamine rise in the cocaine seeking or appetitive phase.

Measuring Dopamine in the Rat Brain

Dopamine levels can be measured accurately with microelectrodes because of the diffusing nature of dopamine in between cells—instruments do not need to be able to fit within synaptic clefts, only in the area of the brain in which the neurons terminate.

Chemical microsensors are used to measure dopamine levels in our virtual experiment. This fast-scan cyclic voltammetry system monitors dopamine several times a second. The carbon-fiber microelectrode is extremely small and, because of the way it works, is less intrusive and does less damage to surrounding tissues than other methods of measuring dopamine.

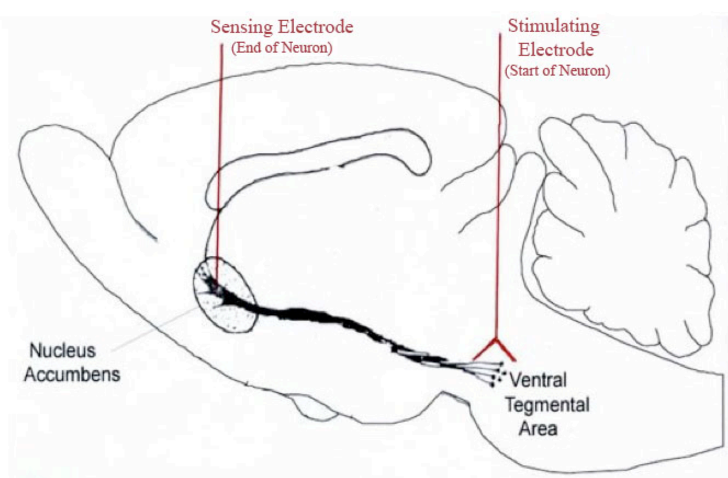


There are two important procedures that must be completed during surgery in order to perform this experiment. The first is to insert a tube called a cannula, into the jugular vein, as a way for cocaine to be directly injected into the rat's circulatory system. The second is to carefully lower electrodes into the brain so that dopamine can be measured.

There are three different electrodes that must be implanted into the brain in order to measure changes in dopamine levels. The first is the reference electrode, which acts as a chemical control, stabilizing the brain's environment so that the other electrodes can work properly. The second is the stimulating electrode. This is placed in the part of the brain where the dopamine neurons begin, or near their cell bodies. This electrode can be used to stimulate the neurons to stimulate dopamine release, and is therefore used to ensure that the sensing electrode is placed in the proper location.

The third electrode is the sensing electrode, which is placed in the part of the brain where the dopamine neurons end, at their dendrites. This electrode is what measures the levels of dopamine being released by the neurons.

This image is a cross section of a rat's brain. It shows the location of the where the stimulating electrode and the sensing electrode are placed during surgery.



The stimulating electrode is lowered into the Ventral Tegmental Area of the brain, which is where dopamine neurons begin. This allows the researcher to send an impulse to these neurons to produce dopamine.

The sensing electrode is lowered into the Nucleus Accumbens area of the brain, which is where dopamine neurons end. This allows the level of dopamine to be measured and recorded.

Rat Research

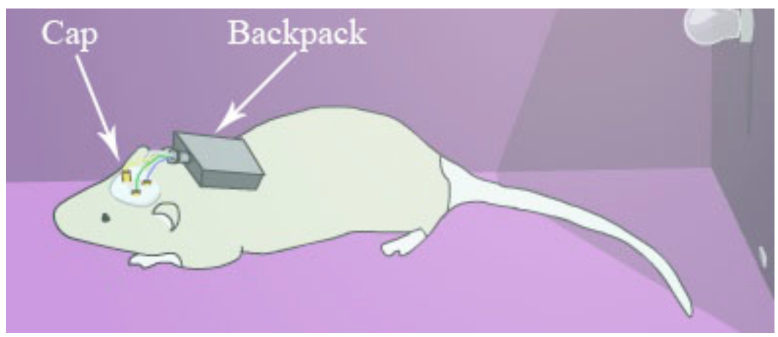
In this virtual lab, you proceed directly from surgery to experimentation. In reality, it takes several weeks for rats to recuperate from a surgery like the one just described. In addition, the rats must be trained to self-administer cocaine before actual experimentation begins.

In drug self-administration, the rat learns to associate pressing a lever or bar with the drug injection. The cocaine will be injected into the jugular vein through the cannula (that was inserted during surgery) and the cocaine is carried to the heart, which will then pump it to the brain in a matter of 30 seconds.

It takes several days of training for a rat to be fully prepared for the conduction of the experiment.

How Real is this Virtual Experiment?

While the data produced in the lab is based on actual experiments done with rats using similar methods, this virtual lab represents some of the latest technology, which is just being developed and employed. Notice how our virtual rat wears a "cap" that holds the electrodes in place. This allows the rat to move freely and for us to gather the electrode data wirelessly using radio waves, or telemetry. In actual experiments, electrodes coming from the rat's head must be hardwired or tethered to a computer, so the rat is not freely-moveable.



However, our rat must wear a back pack that houses both the cocaine for injections, and the voltommetry system for relaying data back to the computer.

Experimental Design of the Virtual Cocaine Lab

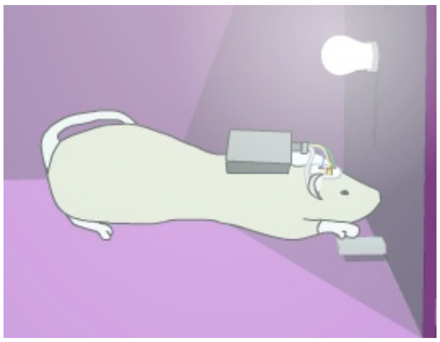
The overall objective of this virtual lab is to investigate the role of dopamine neurons in cocaine use.

The hypothesis we are testing in this virtual lab is: Dopamine is involved in cocaine seeking.

To test our hypothesis, we must make predictions regarding the outcome of our experiment. If our experiment agrees with the prediction, then our hypothesis is supported. The prediction for this experiment is: Dopamine release will increase during cocaine seeking—the appetitive phase.

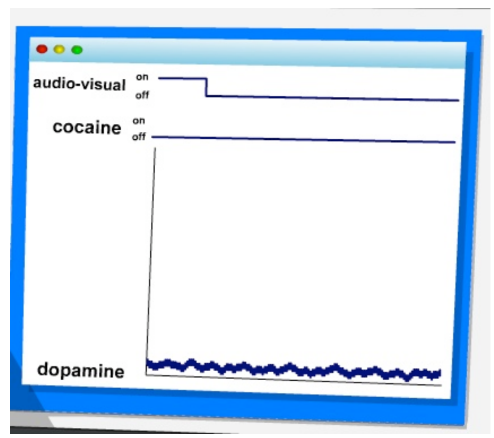
There are also additional questions we might be able to answer. They are: When during cocaine seeking is dopamine release increased? And does the increase in dopamine release cause a change in behavior?

The experimental design is divided into three parts. The first is to train a rat to self-administer cocaine. In our experiment any rat you will work with has already been trained to self-administer for cocaine. The second is preparation and surgery for voltammetry measurements of dopamine. First, you will select, weigh and anesthetize the rat. Then you will observe the surgery where the electrodes for monitoring dopamine have been implanted. And the last part is the monitoring the rat during cocaine seeking. You will observe the rat, as well as the computer monitor that will record the cues as well as dopamine levels in the rat's brain. Look for correlations between increased levels of dopamine during cocaine seeking behavior.



In actual experiments, data are collected for 120 minutes. However in our virtual lab, you will collect data for only 7 minutes.

With every bar press, several things occur. One is that the rat received a 6 second injection of cocaine. For 20 seconds, the light bulb within the containment area is lit and an audio cue is also sounded. During these 20 seconds, additional bar presses do NOT result in additional injections of cocaine.



This shows what the graph will look like when you begin your experiment. At the top, the audio and visual cues are indicated. Below that line is one that shows a record of when cocaine being injected. The majority of the graph is dedicated to recording the live readings of dopamine levels in the rat's brain that are being wirelessly transmitted to the computer.

Thank you for watching this tutorial of Background Content for the Virtual Cocaine Lab. We, here at The Mind Project, hope that watching this tutorial has helped you understand the basics of dopamine and cocaine. Enjoy yourself as you complete the virtual lab.