

Name _____ Class _____ Date _____

The Mind Project's

Virtual Parkinson's Disease Lab: Vocabulary Sheet

Compensatory Model (theory):

Dopamine (abbreviated DA):

Dopamine Transporters (abbreviated DAT):

Denervation:

Dopamine Tone: (sometimes called dopanergic tone)

Innervation:

Lesioning:

Parkinson's Disease (abbreviated PKD):

Presymptomatic:

Uptake:

Voltametry System:

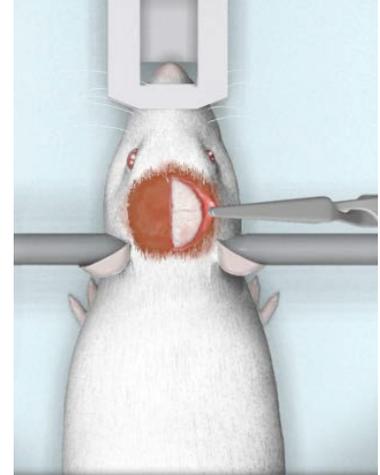
Volume Transmission:



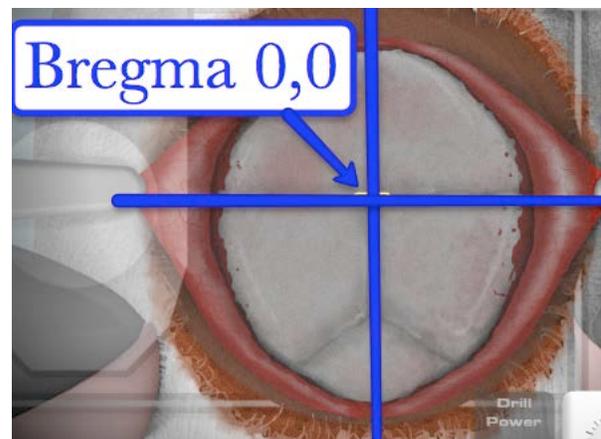
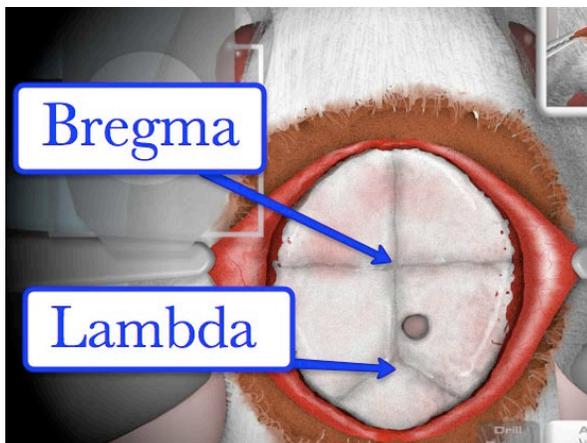
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Brain Coordinates & Reading a Rat Atlas

The Big Picture: In order to study Parkinson's Disease, you will be performing a virtual brain surgery on a rat. The goal of surgery is to lesion (kill) neurons in the part of the rat's brain to reproduce Parkinson's like conditions in our rat. To do this, we must be able to locate specific locations in the rat's brain so we put the neurotoxin (poison) in only the places we want. Therefore, we must know how to read a rat atlas. When you do surgery, you will shave the rat's fur, slice open the skin and muscle to reveal the top of the skull.



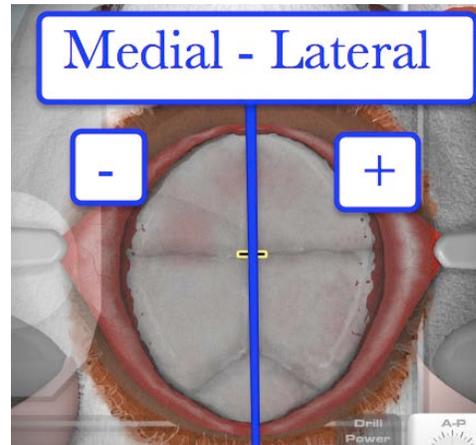
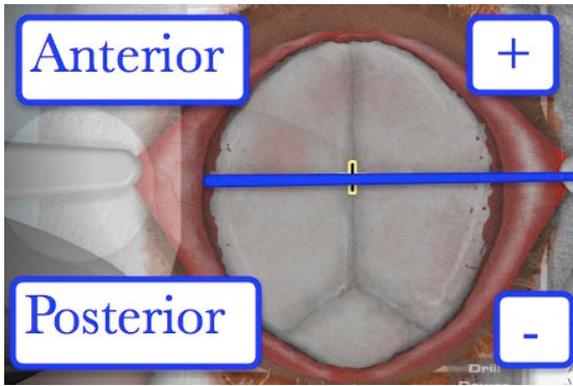
The **stereotaxic machine** have is a machine that holds skull of small animals in one place so that researchers can precisely align items like drills, needles, and electrodes to specific areas of the brain. It allows researchers to locate identified anatomical structures. A map, or atlas, is used to locate anatomical locations within the rat's brain. Researchers carefully record these coordinates and share them with others who can use them as a reference point to repeat the experiment.



All coordinates start from the anatomical structure Bregma (0,0). Lambda is the other anatomical landmark.

It helps to think of the skull as a quadrant (Cartesian) graph. Bregma, is zero and all coordinates are made from this location. Two coordinates will tell you where to "plot" your point, and the third tells you how far into the brain you will need to go.





The Anterior/Posterior (A-P) number tells you to either move toward the nose (positive number) or toward the tail (negative number).

The Medial/Lateral number tells you to move left (negative) or right (positive).

Then, once you have that location, you also need to know how deep into the brain to go. This is the Dorsal-Ventral (D-V) coordinate and will always be negative.

Since the dopamine neurons that affect Parkinson's patients originate (start) in the part of the brain called the Substantia Nigra, we refer to the rat atlas to find out the coordinates so we know where to drill our hole into the rat's skull, and then how far into the brain we must go.

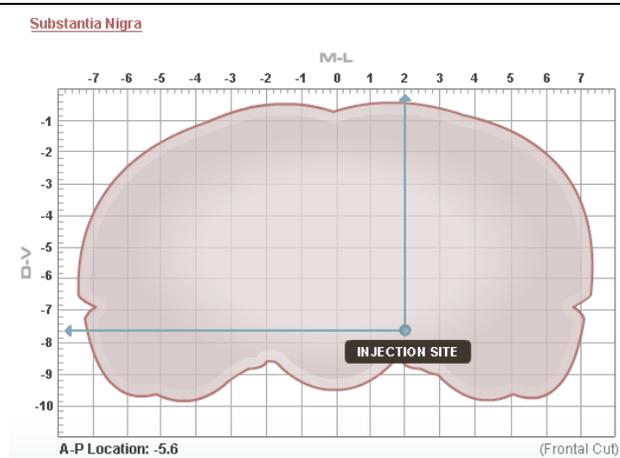
Rat Atlas Tells us the location of Substantia Nigra is:

A-P = -5.6

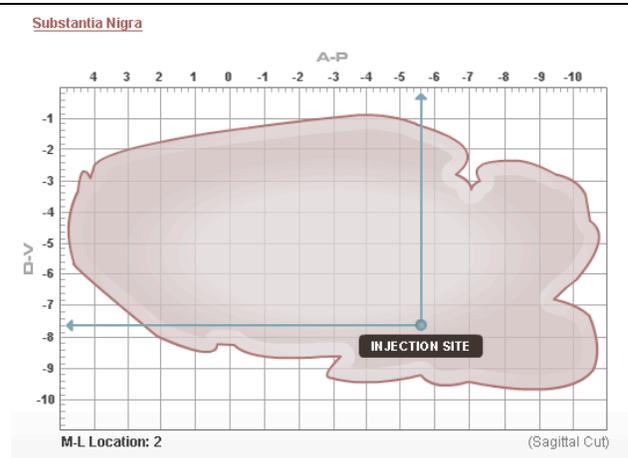
M-L = 2

D-V = -7.6

Frontal Cut of Rat's Brain



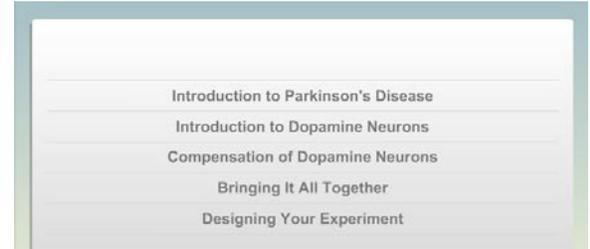
Sagittal Cut of a Rat's Brain



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The Mind Project's
Parkinson's Disease Virtual Lab: Part 1

First Tutorial: Introduction to Parkinson's Disease



1. What are the primary symptoms of Parkinson's Disease (PKD)?
2. What happens in the brain to cause the symptoms of PKD?
3. While PKD can't be cured, what treatments do patients usually receive to manage their symptoms?

Second Tutorial: Introduction to Dopamine Neurons

4. Where are dopamine neurons in the brain?
5. What is the structure of a dopamine neuron?

Launch the "Transmission of Dopamine" animation to learn about how dopamine neurons communicate.

6. How are dopamine neurons different than "classical" neurons?



7. What role do vesicles play in the dopamine neurotransmitter being released?

8. What two places might a free-floating DA molecule end up?

9. What is volume transmission?

10. What is dopamine tone?

Third Tutorial: Compensation of Dopamine Neurons

11. Fill in the blank.

The phenomenon scientists are trying to figure out is how the body is able to compensate for _____% neuron loss , while maintaining high overall dopamine tone. Patients only begin to show symptoms when the percentage of remaining neurons falls below _____%.

Launch the "Compensation of Dopamine Neurons" animated graphic and answer the following questions.

Refer to these definitions to help you understand the compensation model

Nerve innervation (inervated regions): the functioning nerves that appropriately connect and produce normal body functions

Denervated: death of the nerve

12. Zigmond's explanation of how dopamine tone is maintained in his *Increased Release Compensatory Model*. After watching the graphic, explain this theory, watching carefully the amount of DA released at each nerve ending.



Fourth Tutorial: Bringing It All Together

13. In what part of the brain are the cell bodies of DA neurons?
14. In what part of the brain do DA neurons end (terminate) and release DA neurotransmitters?
15. How does the motor cortex influence the body? What role does the basal ganglia play in the process?
16. In Parkinson's Disease, the loss of dopamine inhibits what parts of the brain?
17. What happens in the brain of a Parkinson's patient's that causes tremors?

Fifth Tutorial: Designing Your Experiment

18. What is the hypothesis we will be testing in this virtual lab?
19. How will we test our hypothesis? (experimental design)
20. What is our procedure?



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The Mind Project's
Parkinson's Disease Virtual Lab: Parts 2-5
 From The Mind Project's Virtual Parkinson's Lab



Prepping Rat and Performing Lesioning Surgery

Before you can begin surgery on your rat, you must weight, anesthetize your rat to put it to sleep, and also inject it with an analgesic to decrease pain after surgery.

To calculate the amount of
anesthesia needed

$$\frac{\text{Weight of the rat (g)}}{1000} = \text{mL}$$

To calculate the amount of
analgesic needed

$$\frac{\text{Weight of the rat (g)}}{1000} / 2 = \text{mL}$$

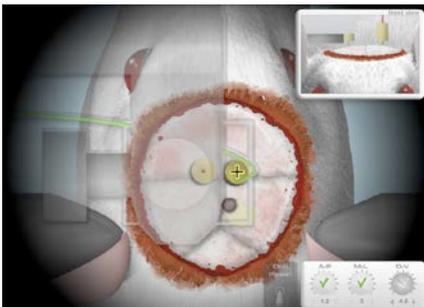
Rat Surgery Notes

1. Rat Weight _____ g
2. Anesthesia Amount _____ mL
3. Analgesic Amount _____ mL

In order to kill neurons in the substantia nigra, where dopamine neurons originate (start), we must use a Rat Atlas to determine the approximate coordinates. A-P = anterior/posterior; M/L = medial/lateral, and D-V = dorsal/ventral. The following is a completed version of the virtual clipboard you will find in the virtual lab.

	A-P	M-L	D-V
Bregma	0	0	0
Lambda	-9	0	0
Substantia Nigra	-5.6	2	-7.6

Surgery to Implant Electrodes in the Rat's Brain



After our rat has recuperated for 2 weeks, and the neurotoxin has had time to take affect, we perform another surgery to implant electrodes that will allow us to collect data on how much dopamine is released. This system is called **Voltammetry**. In this surgery we need to drill additional holes



in the skull for additional equipment. Three types of electrodes are listed below, along with the reason each is needed:

- **Recording electrode** = This electrode gathers the data we will be studying. We want to know how much DA is in the extracellular space in the striatum. Essentially we are measuring the amount of dopamine tone.
- **Stimulating electrode** = This electrode is inserted near the origin of the neurons (in the substantia nigra) so we can stimulate the neurons to fire, and therefore study the DA result of those firing neurons.
- **Reference electrode** = This electrode acts as the control

	A-P	M-L	D-V
Substantia Nigra	-5.6	2	-7.6
Reference Electrode	1.2	-3	-4
Recording Electrode	1.2	3	-4.5
Stimulating Electrode	-4.6	1.6	-8

Once you've drilled the holes for the additional electrodes, you'll insert the electrodes to the proper depth (D-V), then you'll detach the electrode and raise the stereotaxic arm.

The Big Idea: Notice that the stimulating electrode is placed very close to the location where we inserted the neurotoxin. The coordinates for the substantia nigra and the stimulating electrode are very close in proximity. Remember, we added the neurotoxin in order to kill the cell bodies of dopamine neurons within the substantia nigra so we can replicate on a cellular level what is going on in Parkinson's patients.

Lab Results

Reading the Dopamine Data from the Rat's Brain

4. Looking Back: What is the hypothesis we tested?

Lab Results

5. What are we looking to compare in our data?

6. What other data are we looking at?



7. Graph Title: _____

Use the space on the left, create a graph with the data from our experiment. Be sure to include a:

- a) title for the graph
- b) label for the y axis
- c) label for the x axis
- d) line that represents the data

8. Do the data support our hypothesis? How do you know?

Passive Stabilization Compensatory Model

9. What role does a glial cell have in the Passive Stabilization Compensatory Model?

10. What role does the concept of “Uptake” play in the Passive Stabilization Compensatory Model?



11. As you work through the **Passive Stabilization Compensatory Model** section, fill in following table as a way to compare two theories as to why Parkinson’s patients don’t show symptoms until they’ve lost 80% of their DA neurons!

Increased Release Compensatory Model Dr. Zigmond’s Theory	Agree	Passive Stabilization Compensatory Model Dr. Garis’ Theory

Passive Stabilization Program

A snapshot of the Passive Stabilization Program is shown below. This image shows 100% functioning neurons.



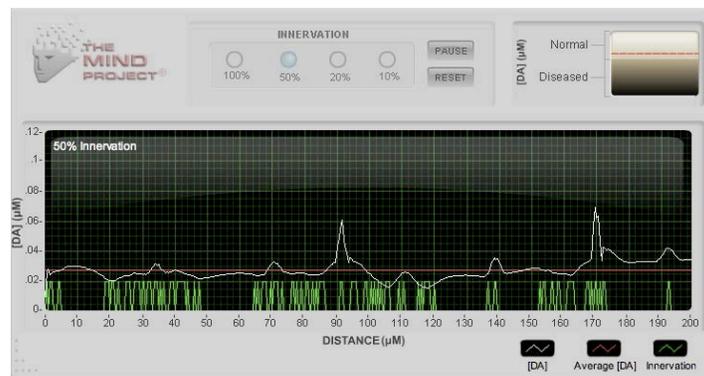
Describe what each colored line represents.

12. Green Line (closest to the bottom, appearing to go off the page)

13. White Line (wavy line that crosses all other lines)

14. Red Line (horizontal straight line)

The screen shot below shows 50% loss of DA neurons. Notice that the dopamine tone (the red straight line) is exactly the same, although the total number of DA neurons (the green bars) is halved.



Bucket Theory Analogy

15. What does each part of the Bucket Analogy represent?

- a. The water faucet
- b. Large central drain
- c. Small drain

d. Level of water in the bucket



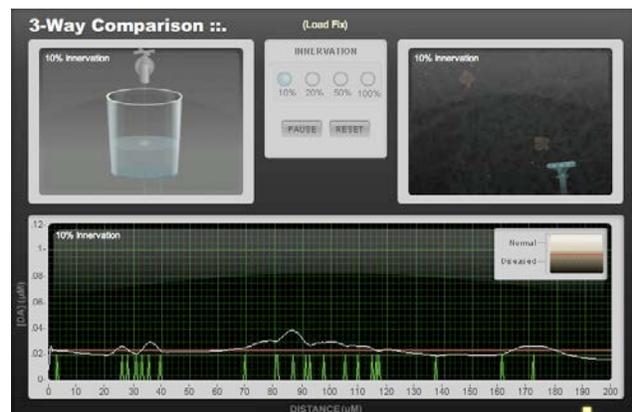
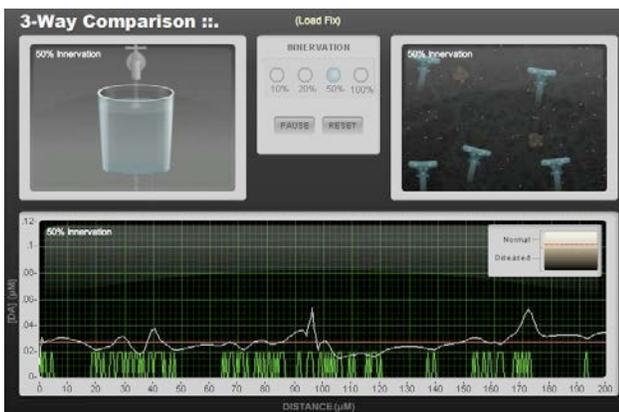
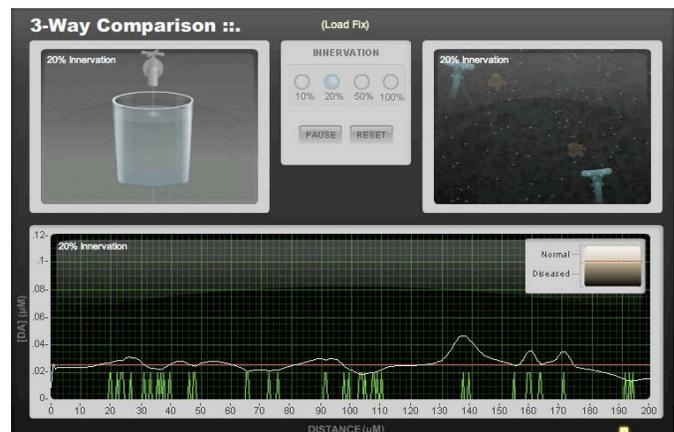
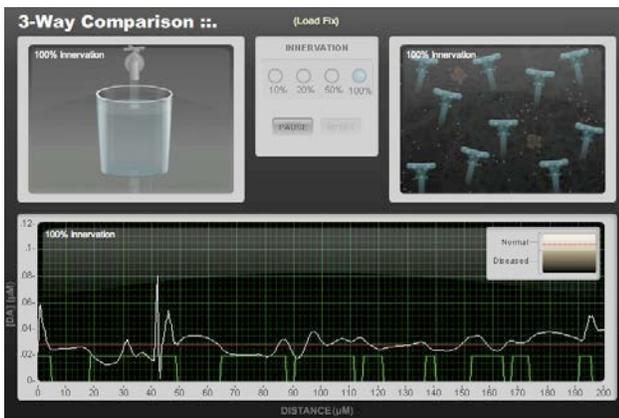
16. How are mathematical/computer models helpful to scientists studying neurobiology?

17. In the Bucket Theory Animation, what changes occur to the bucket when DA neurons die?

18. What changes occur to the bucket that account for why DA tone goes down only below 20% denervation?

3-Way Comparison

Here are screen shots of the 3 models side-by-side at 100% innervation, 50%, 20% and 10%.



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Word Drag: Read the following paragraphs, and use the word banks to fill in each blank. This matches the assessment in the virtual lab.

Parkinson's disease is a _____, neurological disorder of unknown causes. Early symptoms include a _____ (trembling of the hand while it's at rest) and _____ (muscle stiffness). Parkinson's disease is considered a _____ disorder as it affects the movement of the body.

Patients with Parkinson's disease suffer from the loss of _____ neurons in the _____. Known as the nigrostriatal pathway, these neurons have their cell bodies in the substantia nigra. Their axons run through the _____ and end in the _____.

WORD BANK

Degenerative

Dopamine

Mediastianatal Bundle

Motor

Resting Tremor

Rigidity

Striatum

Substantia Nigra

When dopaminergic neurons release dopamine, the dopamine molecules will _____ until they are taken up by a _____ or attach to a target cell. This is known as _____.

Volume transmission results in a background concentration of dopamine, known as _____. This allows for signals to pass smoothly from the _____ to the _____ and then out to the rest of the body.

WORD BANK

Diffuse

Dopaminergic Tone

Dopamine Transporter

Motor Cortex

Thalamus

Volume Transmission

Parkinson's disease patients do not show visible symptoms until _____ of the dopaminergic neurons in the striatum have died. Scientist don't know how dopaminergic tone is maintained until then. Dr. Zigmond has put forth the _____ model, which theorizes that the remaining dopaminergic neurons release _____ dopamine with each action potential.

WORD BANK

80%

Compensatory Release

More

Dr. Garris disagrees with this theory. He has proposed the _____ model, which theorizes that dopaminergic tone is maintained because of the relationship between dopamine release and _____. As a patient loses dopamine neurons, he or she not only loses a source of dopamine _____, but also a source of dopamine uptake. Therefore, the net concentration of dopamine molecules remains the _____. This stabilization is disrupted as the _____ begin to compete with the dopaminergic neurons for the uptake of dopamine molecules.

WORD BANK

Glial

Passive Stabilization

Release

Same

Uptake

