Activity 1
Is FLORATRYP Addicting?

Core Concept:

Addictive drugs affect dopamine levels in the reward pathway of the brain.

Class time required:

Approximately 60-80 minutes

Teacher Provides:

- Copy of student handout entitled "Is FLORATRYP Addicting" for each student.
- Safety goggles for each student
- Kit of lab materials for each team of 2-3 students that includes:
  - o One COLOR copy of "Color Chart for Dopamine Concentration." See page 5.
  - o 3 Microtubes (or small test tubes) each containing 1 mL of "brain fluid" samples (0, 30, and 60 minutes)—either for sugar, cocaine, or FLORATRYP. Prepare using information below.

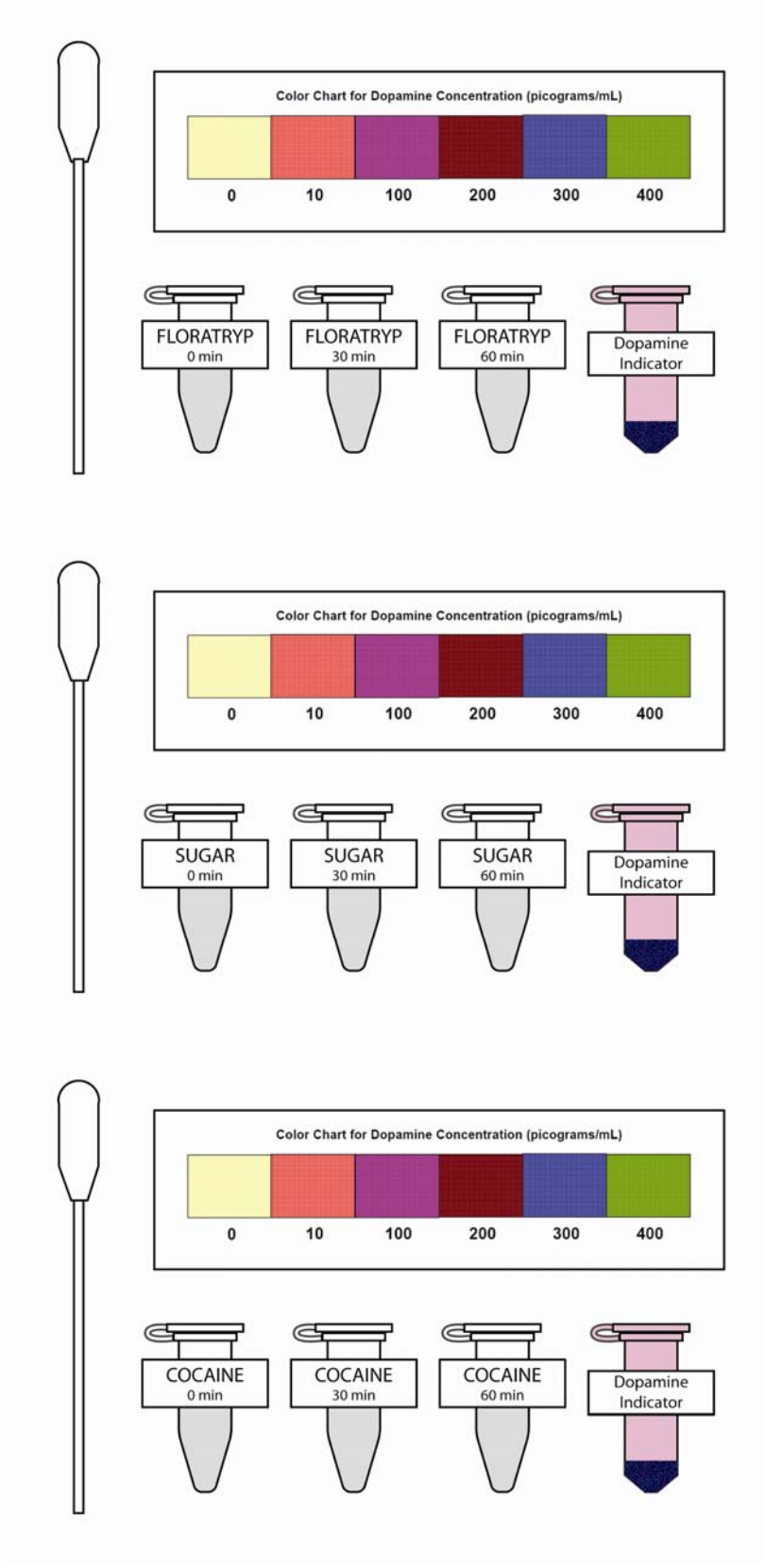
Label on Tube	Contents of Tube
Sugar 0 min	Buffer pH 2
Cocaine 0 min	Buffer pH 2
FLORATRYP 0 min	Buffer pH 2
Sugar 30 min	Buffer pH 6
Cocaine 30 min	Buffer pH 12
FLORATRYP 30 min	Buffer pH 8
Sugar 60 min	Buffer pH 2
Cocaine 60 min	Buffer pH 2
FLORATRYP 60 min	Buffer pH 6

Note: Each team of students gets <u>three</u> microtubes: Sugar (0, 30, and 60 min) <u>or</u> Cocaine (0, 30, and 60 min) <u>or</u> FLORATRYP (0, 30, and 60 min)

  - o 1 disposable dropper--graduated to measure 1 ml.
  - o 1 microtube (or small test tube) labeled "Dopamine Indicator". Place 1 tiny scoop (approximately 1/16th of a teaspoon) of "Red Cabbage Extract" into each tube. Using the dry powder means that the kits do not need to be refrigerated. The "Red Cabbage Extract" can be ordered from Educational Innovations http://www.teachersource.com/Chemistry/pHIndicatorsAndThermometers/RedCabbageExtract.aspx .

This project was generously funded by Science Education Drug Abuse Partnership Award R25DA021697 from the National Institute on Drug Abuse. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute on Drug Abuse or the National Institutes of Health.

Quick Guide:



Suggested Class Procedure:

1. Distribute copies of the student handout entitled "**Is FLORATRYP Addicting**?" to each student.

2. Read the information in the box on page 1 aloud to the class. Students should complete the question at the bottom of page 1 of the student handout.

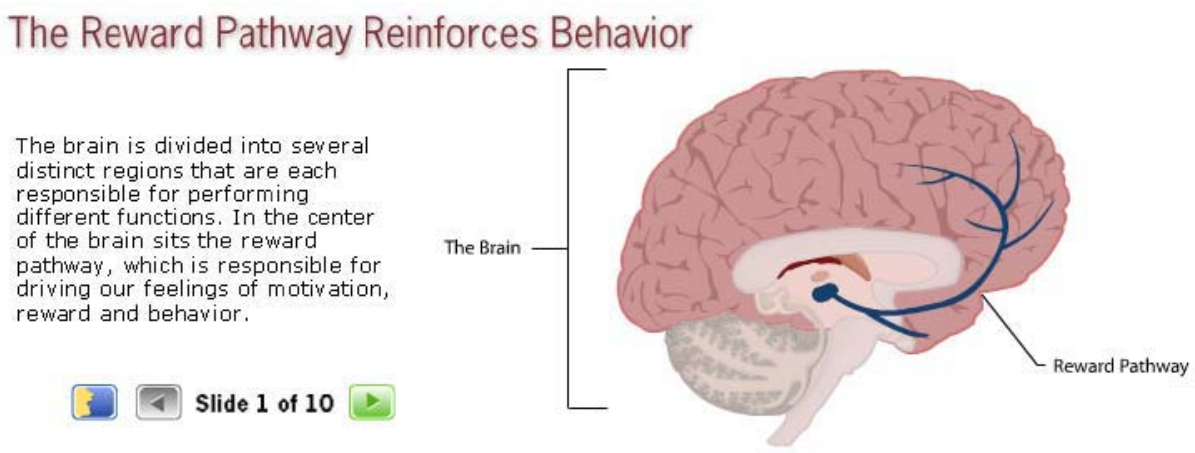
3. Explain that FLORATRYP is a fictitious ("fake") drug.

4. Discuss what is meant by the terms uncontrollable, compulsive, negative, and consequences.

5. Ask students to share their answer to the question at the bottom of page 1.

6. Explain that before a new drug can be classified as addictive, scientific evidence is needed.

7. Consider showing the class **The Reward Pathway Reinforces Behavior** (an outstanding series of 10 slides) at http://learn.genetics.utah.edu/content/addiction/reward/ . Encourage students to share the important things that they learned from this slide sequence.



8. Read (aloud) and discuss the "The Brain Reward Pathway." Allow time for students to answer questions.

9. Explain that in the next two parts of this activity, they will play the role of scientists who work for a company that conducts tests on new "designer drugs" to determine if they are addictive. Typically this type of research is done using animals such as rats or mice.

10. Explain to students that the lab tests they will be conducting are simulations. NO real drugs are used in these lab tests.

11. Distribute lab kits and safety goggles to teams of students. Explain that they will use the materials in the kits to determine if the "fake drug", called FLORATRYP, is addictive.

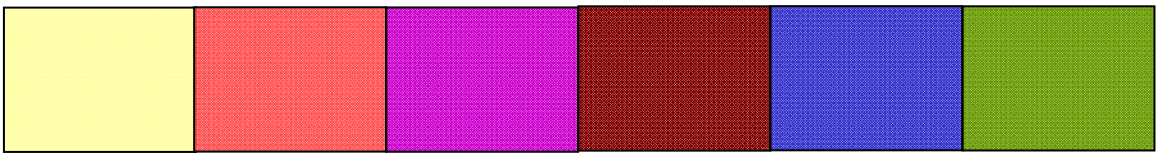
12. Ask students to complete "Part 1: Is FLORATRYP Like Other Addictive Drugs?" Be prepared to facilitate the sharing of data from different groups (sugar, cocaine, FLORATRYP) to complete the data table.

13. Ask students to read and complete “Part 2: Does FLORATRYP Cause Addictive Behavior?” Note: Part 2 may be done during class or as homework.

14. If time permits, have students share and discuss their answers to the questions in Part 1 and Part 2. Possible additional questions for discussion in class might include:

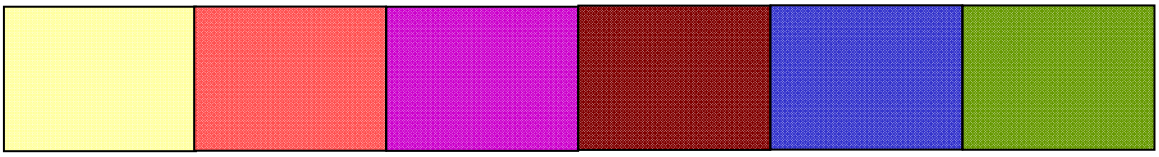
    - Why do they use rats, rather than humans, for these experiments?
    - Does the information from these rat experiments mean that FLORATRYP is addictive for humans too? Explain why or why not.

Color Chart for Dopamine Concentration (picograms/mL)



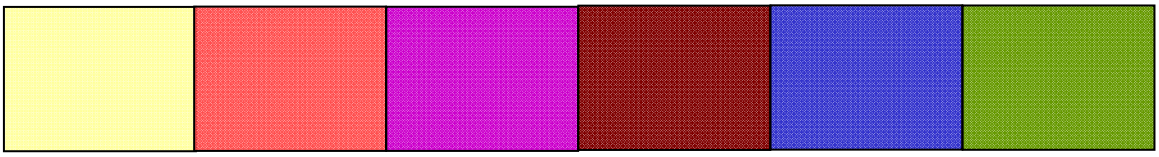
0 10 100 200 300 400

Color Chart for Dopamine Concentration (picograms/mL)



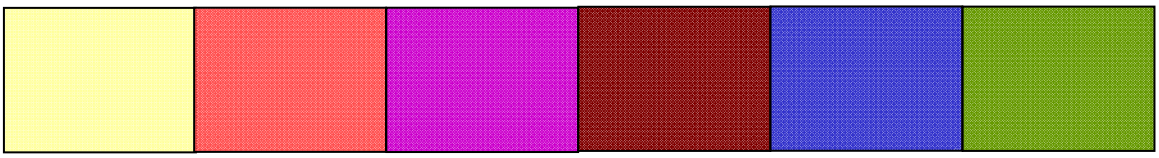
0 10 100 200 300 400

Color Chart for Dopamine Concentration (picograms/mL)



0 10 100 200 300 400

Color Chart for Dopamine Concentration (picograms/ml)



0 10 100 200 300 400

Is FLORATRYP Addicting?

Introduction:

Medical Report

Ray is at the medical clinic because he is feeling horrible. He is experiencing a variety of symptoms such as irregular heartbeats, headaches, nausea, and vomiting. He is having trouble sleeping. He also has been feeling very depressed and nervous.

He has experienced some of these symptoms in the past but they disappeared when he used "FLORATRYP", a mixture of over-the-counter and herbal medications. He tells the doctor that he has been using FLORATRYP for about a year.

Over the past few months Ray's use of FLORATRYP has increased from once a day to five or more times each day. He likes using FLORATRYP because it makes him feel happy and confident. "I only take it when I'm feeling low or stressed out. A little FLORATRYP and everything's better."

Ray has not been able to use FLORATRYP for the past few days because he ran out of money. He was recently fired from his part-time job because he skipped work a lot – especially after late nights of doing FLORATRYP with friends.

Ray explains that he doesn't think his symptoms are caused by FLORATRYP abuse. "Lots of people use FLORATRYP. It's not illegal. It's not addictive. What's wrong with feeling good?"

Drug addiction defined as "uncontrollable, compulsive drug seeking and use, even in the face of negative health and social consequences."
Scientists from the National Institute on Drug Abuse

1. Based on the information in the Medical Report, do you think that the Ray is addicted to FLORATRYP? Support your answer by listing <u>three</u> evidences from the Medical Report.

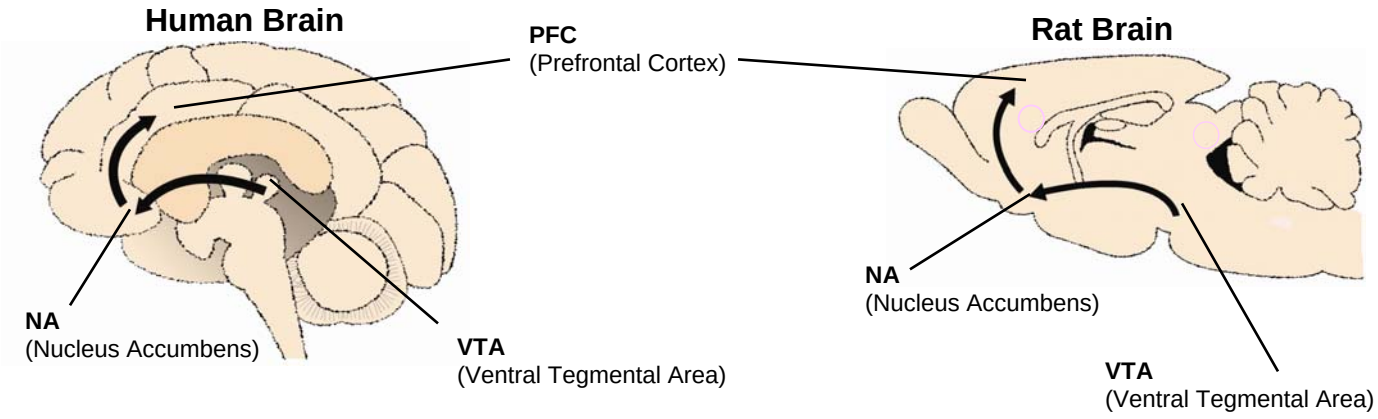
   Student answers may vary but should include the observation that the patient was using more of the drug and did not seem to be able to control his drug use.

The Brain Reward Pathway

The brain contains a **reward pathway** (also called a "pleasure-reward pathway") that causes animals to associate certain activities with pleasure or reward.

When an animal does something that is pleasurable (such as eating, sexual activity, or taking addictive drugs), nerve signals travel through the reward pathway and cause a sensation of pleasure. This pleasure sensation is a reward that causes the animal to learn to do this action again and again.

The arrows on diagrams below show the **reward pathway** in a human brain and a rat brain.



Dopamine is a chemical signal molecule in the brain reward pathway. Scientists know that a pleasurable or addictive activity will cause the amount of dopamine to increase in the reward regions of the brain.

Normal pleasurable actions result in small increases of dopamine in the reward regions of the brain. All known addictive drugs result in large increases of dopamine in the reward regions of the brain.

2. What is the function of the reward pathway of the brain?

   The reward pathway is a part of the brain that associates certain activities with pleasure or reward.

3. What chemical signal molecule is used to send messages within the reward pathway?

   Dopamine

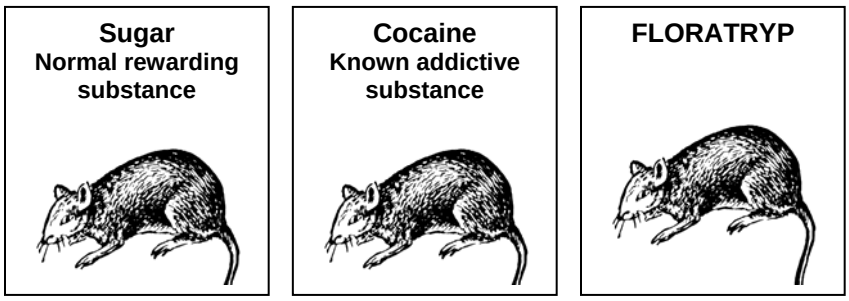
4. Predict which would result in the largest increase in the dopamine level in the reward regions of the brain - eating or taking an addictive drug.

   Taking an addictive drug.

Part 1: Is FLORATRYP like other addictive drugs?

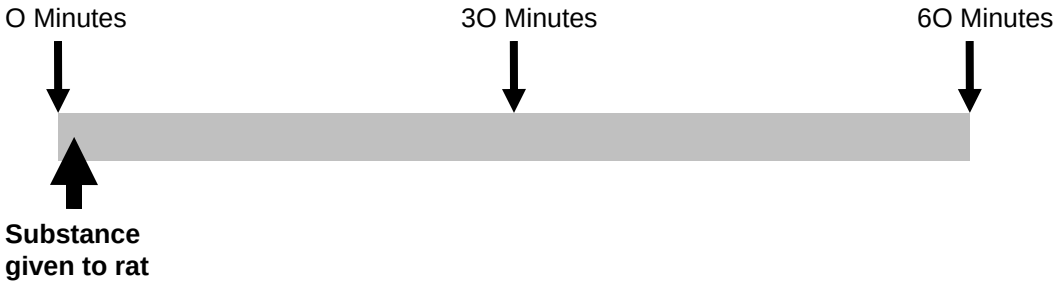
You work for a company that conducts tests to determine if "designer drugs" should be classified as addictive drugs. You have been asked to conduct animal tests to compare the levels of dopamine in samples of brain fluid collected from three rats.

The rats used in this experiment were given sugar, cocaine, or FLORATRYP.



The brain fluid samples were collected from the reward region of the brain at three times:

- 0 minutes (immediately before the substance was given to the rat)
- 30 minutes after the substance was given to the rat
- 60 minutes after the substance was given to the rat



You will be responsible for testing brain fluids samples collected from a rat that was given ONE of the substances (sugar, cocaine, or FLORATRYP). Other students in your class will be testing brain fluid samples collected from rats that were given the other substances.

1. Obtain three tubes (labeled 0, 30, and 60 min) from your teacher. These tubes contain brain fluid samples collected at different time points in the experiment.

2. Read the label on the three tubes. What substance was given to the rat that you are testing (sugar, cocaine, or FLORATRYP)?

   Sugar OR cocaine OR FLORATRYP

3. Prepare a Dopamine Indicator Solution by adding 1 mL of tap water to the tube labeled "Dopmaine Indicator" Put the cap on the tube, and shake gently for approximately 30 seconds.

4. Add 3 drops of "Dopamine Indicator" to each of the 3 tubes of brain fluid samples. Put the caps on the tubes, and shake gently for approximately 30 seconds.

5. Compare the color of the brain fluid samples with the "Color Chart for Dopamine Concentration" that is included in your lab kit. Record the estimated dopamine concentration in the data table below. *Note: 1 picogram is 1 trillionth of a gram.*

6. Share your results with others in your group and add their data to your table.

Data Table 1: Concentration of Dopamine in Rat Brain Fluid Samples

Substance Given	Time after being given substance	Concentration of dopamine (picograms/mL)
Sugar	**0 min**	***10***
	30 min	***100***
	60 min	***10***
Cocaine (a drug that causes addiction)	**0 min**	***10***
	30 min	***400***
	60 min	***10***
FLORATRYP	**0 min**	***10***
	30 min	***300***
	60 min	***100***

7. What was the purpose of testing samples of brain fluid from rats that were given sugar?

   These samples show what normally happens to dopamine levels when a rat is given a natural pleasurable substance.

8. What was the purpose of testing samples of brain fluid from rats that were given cocaine?

   These samples show what happens to dopamine levels when a rat is given an addictive drug.

9. Compare the levels of dopamine after 30 minutes in the rat given FLORATRYP with the levels of dopamine in the rat given sugar.

   The dopamine level in the rat given FLORATRYP increased more than the dopamine level in the rat that was given sugar.

10. Compare the levels of dopamine in the rat given FLORATRYP with the levels of dopamine in the rat given cocaine.

    - After 30 minutes:

      The dopamine level in the rat given FLORATRYP was similar to the dopamine level in the rat that was given cocaine.

    - After 60 minutes:

      The level of FLORATRYP remained above normal for longer period of time.

11. Do the results of your experiment support the hypothesis that FLORATRYP is an addictive drug? Support your answer with data collected in this experiment.

    FLORATRYP appears to be addicting because both cocaine and FLORATRYP cause an increase in dopamine levels in the rat brain.

12. Which substance (sugar, cocaine, or FLORATRYP) would you expect to have the most long-lasting effect? Support your answer with data collected in this experiment.

    FLORATRYP because its level remained above normal after 60 minutes.

13. Explain why drugs such as cocaine and FLORATRYP are more addictive than natural rewards (such as food or listening to music)?

    The level of dopamine with FLORATRYP use is much greater than the level with natural rewards.

Part 2: Does FLORATRYP cause addictive behavior?

To be considered addictive, FLORATRYP must activate the reward center and produce the repetitive drug seeking behavior associated with addictive drugs.

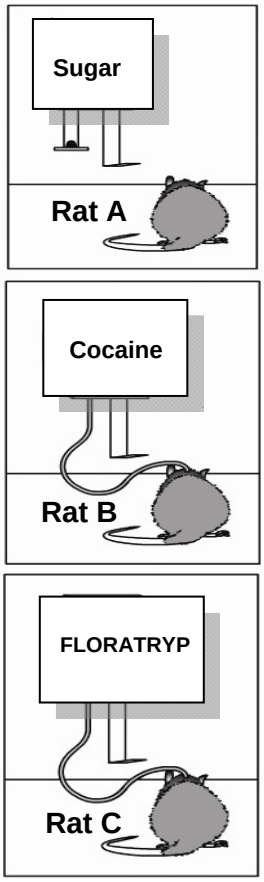
In this activity, you will analyze the data collected by a researcher who studied the drug seeking behavior in rats.

For this experiment, rats were placed in individual cages with a lever they could press that delivered a reward.

- When Rat A rat pressed a sugar lever, a pellet of sugar was released.
- When Rat B pressed a cocaine lever, it received an injection of cocaine (an addictive drug) into the reward region of its brain.
- When Rat C pressed a FLORATRYP lever, it received an injection of FLORATRYP into the reward region of its brain.

Each day (for 6 days), the rats were placed in the appropriate cages and scientists observed and recorded the number of times the rats pressed the levers in 5 minutes.

The results of the experiment are presented in Data Table 2 on the next page.



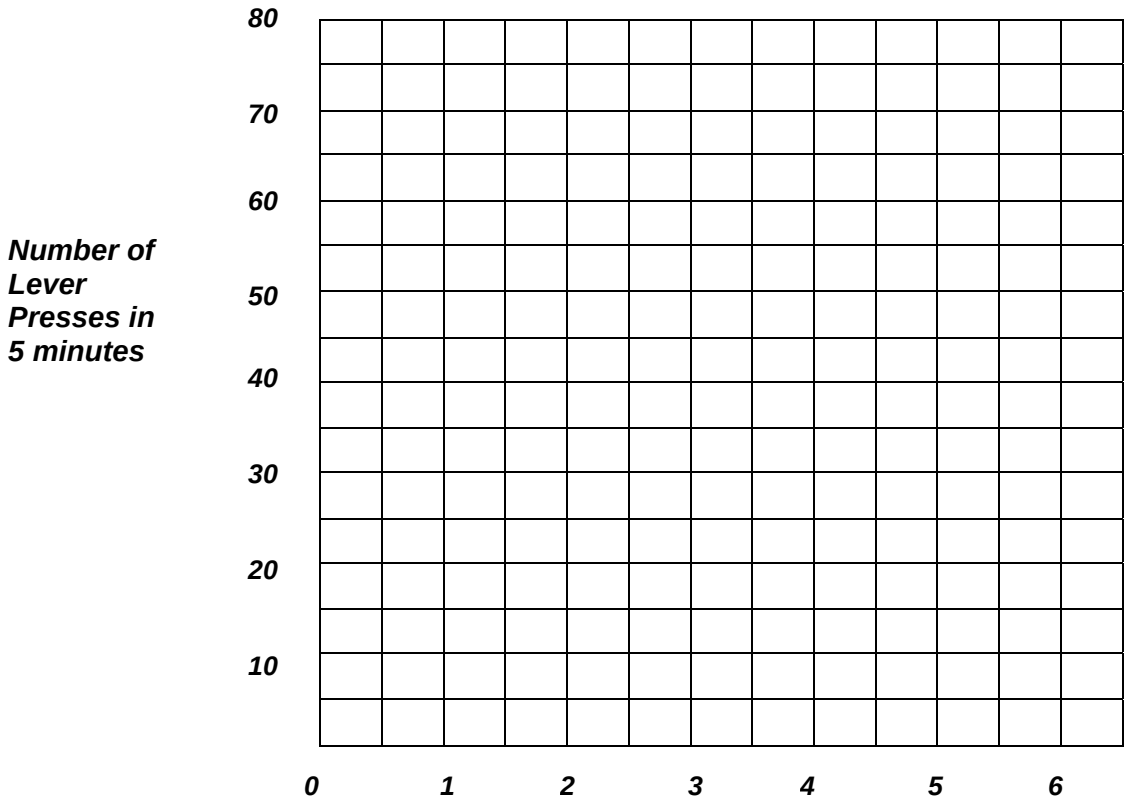
Data Table 2: Effect of Reward on Rat Lever Pressing Behavior

		Total number of lever presses during 5 minute observation					
	Lever	**Day 1**	**Day 2**	**Day 3**	**Day 4**	**Day 5**	**Day 6**
Rat A	**Sugar** (a natural reward)	1	3	4	5	7	8
Rat B	**Cocaine** (an addictive drug)	4	7	12	29	52	77
Rat C	FLORATRYP	3	8	14	20	47	70

1. Summarize the data from the experiment by plotting the total number of times that the each of the rats pressed the levers versus days.

   - Label the vertical axis
   - Mark an appropriate scale on both of the axes.
   - Plot the data using the legend provided.

Legend:
Rat A – Sugar
Rat B – Cocaine
Rat C - FLORATRYP



On the first day, the rats initially press a lever while they are exploring the cage. Whether the rat presses the sugar lever or the drug lever at first is usually random. Once the rats have learned that pressing a lever provides a pleasurable reward, they will repeat the lever pressing behavior more frequently.

2. Why does the number of lever presses for sugar increase?

   The rats have learned that pressing the lever delivers a pleasurable reward.

3. Compare the number of lever presses for FLORATRYP with the number of lever presses for sugar.

   Rats pressed the cocaine lever more often than the sugar lever.

4. Compare the number of lever presses for FLORATRYP with the number of lever presses for cocaine.

   Rats pressed the cocaine lever more often than the FLORATRYP lever.

5. Does the data support the claim that FLORATRYP is an addictive drug? Support your answer using information from the graph.

   Yes. Rats pressed the FLORATRYP lever more often than the sugar lever. Like cocaine, FLORATRYP activated the reward pathway in the brain and caused increased rat lever pressing.