Long-Term Effects of Drug Addiction

Part 1: Addiction is a chronic disease

Drug addiction is considered a chronic brain disease because drugs cause long-lasting changes in brain structure and function. Addiction is similar to other chronic (long lasting) diseases, such as heart disease. Both disrupt the normal, healthy functioning of an organ. Both drug addiction and heart disease may be prevented or treated but they cannot be cured. In most cases, chronic diseases cause long-term changes in body functions and will require a lifetime of regular treatment.

A positron emission tomography (PET) scan is a medical test that helps doctors identify abnormal from normal functioning organs and tissues. A PET scan can measure such vital functions as glucose metabolism - the use of sugar to produce energy for life activities. This information can help doctors determine whether organs are healthy or diseased.

1. Both drug addiction and heart disease are "chronic diseases." What is meant by the term "chronic disease?"

   _____

   _____

2. The top half of Figure 1 shows PET scans for the heart of a healthy person (on the left) and for a person with heart disease (on the right). Refer to the color scale for glucose metabolism shown on the bottom of Figure 1. Compare the metabolism of a healthy heart with the metabolism of a diseased heart.

   _____

   _____

   _____

   _____

   _____

In a PET scan:

- **Red and yellow** indicate **more active** regions with high metabolism (high use of food and oxygen to produce ATP needed for life activities).
- **Blue and purple** indicate less active regions with low metabolism (low use of food and oxygen to produce ATP needed for life activities).

3. The bottom half of Figure 1 shows PET scans for the brain of a person who does not use drugs and for a person who has abused drugs. Compare the glucose metabolism levels in the brains of the person who did not use drugs and the person who abused drugs.

_____

_____

4. Explain three ways in which heart disease and drug addiction are similar.

_____

_____

_____

Part 2: Drug abuse causes long-term changes in brain function

Scientists would like to know whether the brain can recover from drug addiction. They can use PET scan studies and gene studies to determine whether the brain returns to normal when an individual stops abusing drugs.

A. PET Scan Studies

Scientists can use PET scans to determine if drug addiction results in long-term changes to the brain. Figure 2 shows PET scans from:

- 3 individuals who never abused drugs
- 3 individuals who abused drugs for 6 months and then stopped using drugs for 10 days
- 3 individuals who abused drugs for 6 months and then stopped using drugs for 100 days

1. Based on the information in the brain PET scan photos, what conclusions can you draw?

_____

_____

B. Gene Expression Studies

Cells contain thousands of different genes. Not all of these genes are active (turned on) at any one time. Some genes are **expressed (turned on)** and others are **silenced (turned off).** Environmental factors, such as drugs, can influence which genes are expressed or silenced.

Scientists suspect that the long-lasting changes in brain function associated with drug abuse may be due to changes in **gene expression** in brain cells. If scientists can identify which genes are affected by long-term drug abuse, they may be able to use this information to develop treatments that could be used to restore normal brain functions.

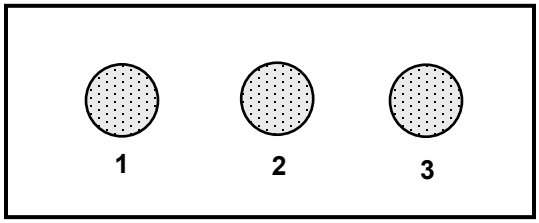
2. Scientists identified **three genes that they hypothesized might be responsible for the long-term brain damage in drug abusers**. They placed spots of DNA from these three genes on a strip of paper.

Rat Genes spotted on the paper:

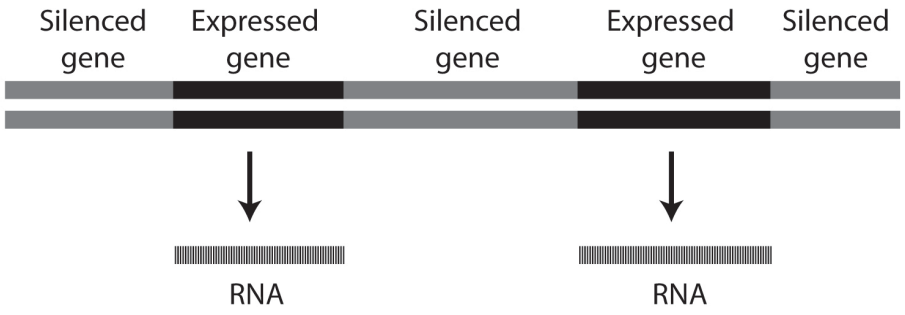
Gene 1: Makes an enzyme that is needed for the synthesis of dopamine

Gene 2: Makes a dopamine Receptor protein

Gene 3: Makes an enzyme that triggers programmed brain cell death

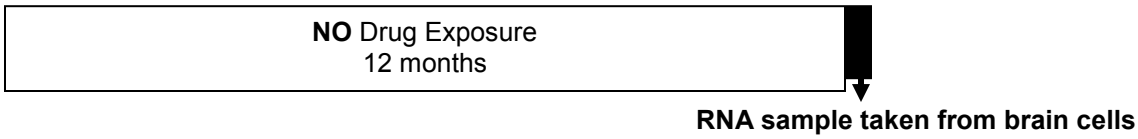


3. The scientists knew that active (expressed genes) produce RNA. Inactive (silenced genes) do not make RNA.

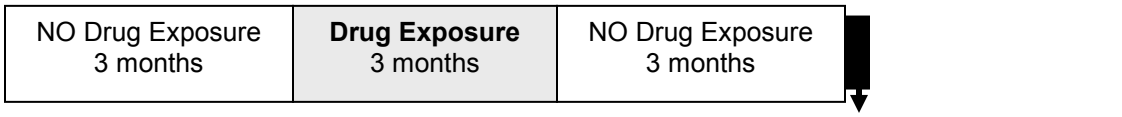


4. To compare the gene expression in rats that had been exposed to drugs with rats that had not been exposed to drugs, scientists isolated **RNA** samples from the brains of two types of rats.

   - Rats that were never exposed to drugs:



   - Rats that were exposed to drugs for 3 months and have been drug free for 3 months:



5. The RNA molecules in the samples from both types of rats were then labeled with a pink label.
   - If a gene is **expressed,** the RNA will stick to the corresponding spot on the paper causing a pink color.
   - If a gene is **silenced**, the RNA will not stick to the corresponding spots on the paper and the spot will remain white.

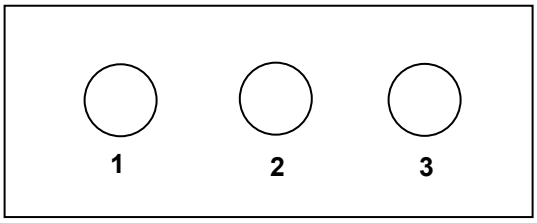
6. What color would a gene spot be if that gene in a brain cell is being expressed (turned on)?

   _____

7. Obtain a tube containing RNA from the brain cells of a rat that was **NOT exposed to drugs**.

8. Use the paper that is labeled "Use for RNA from Rat that was <u>NOT</u> exposed to drugs". Place one drop of this RNA onto each of the circles (DNA spots) on the paper. Record your observations in the diagram below.

Use for RNA from a rat that was NOT exposed to drugs



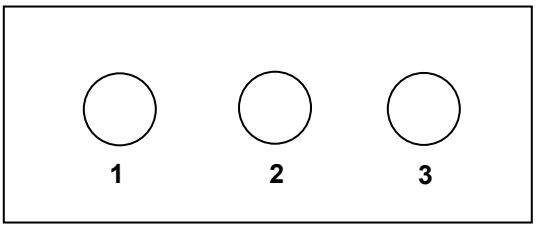
9. List the numbers of the genes that are **expressed** in the brain cells of a rat that was <u>NOT exposed</u> to drugs.

   _____

10. Obtain a tube containing RNA from the brain cells of a rat that was **EXPOSED to drugs and then was drug free**. This rat was exposed to drugs in the past, but has been drug-free for 3 months.

11. Use the paper labeled "Use for RNA from Rat that was EXPOSED to drugs". Place one drop of this RNA onto each of the circles (DNA spots) on the paper. Record your observations in the diagram below.

Use for RNA from a rat that was EXPOSED to drugs and is now drug free



12. List the number of the gene that is expressed **only in rats that were exposed** to drugs. Also describe the function of this gene.

_____

_____

_____

_____

Rat Genes spotted on the paper and their functions:

Gene1: Makes an enzyme that is needed for the synthesis of dopamine

Gene 2: Makes a dopamine Receptor protein

Gene 3: Makes an enzyme that triggers programmed brain cell death

13. How might expression of this gene affect the functioning of rat brain cells?

_____

_____

14. List the numbers and the functions of the genes that are **silenced only in rats that were exposed** to drugs.

_____

_____

15. How might silencing of these genes affect the functioning of rat brain cells?

_____

_____

16. Do the results of your microarray experiments support the conclusion that drug abuse causes long term changes in brain cells? Explain why or why not.

_____

_____

_____

17. Scientists hope to use information from this type of research to develop ways of preventing or treating brain damage that results from drug abuse and addiction. To do this they might try to identify drugs that turn off or turn on the expression of specific genes.

- What genes would they want to turn **on** to treat brain damage that results from drug abuse and addiction?

  _____

- What gene would they want to turn **off** to treat brain damage that results from drug abuse and addiction?

  _____