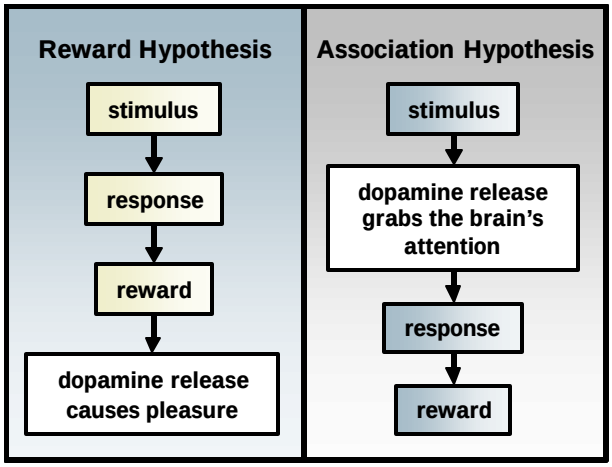
The Dopamine Debate

Evidence and Explanations for the Role of Dopamine in the Brain[1]

There is nothing pretty about becoming addicted to a harsh drug like heroin. The habit involves risky behavior, such as using needles, and the image of a person shooting heroin is not very appealing. How can we explain why people use drugs when the drawbacks are so obvious? For many years people have thought that being addicted simply means the person does not have enough will power to quit a bad habit—even scientists and doctors accepted this idea. A more recent theory is that the high produced by a drug is such a pleasurable experience that it overshadows everything else.

The Reward Hypothesis

In the 1970s, scientists found experimental evidence supporting this explanation. When they gave rats a chemical that blocked dopamine receptors in the brain's reward center, the rats stopped taking drugs when they were offered[2]. This suggested that drug-addicted rats could be "cured" of their drug habit by disabling their reward system. This idea was further tested by a second group of scientists who surgically disconnected the reward cells in the brain[3]. When these few cells in the brain were disconnected, the rats' brains did not receive a reward for having cocaine in their systems. The scientists used this evidence to conclude that dopamine was the rats' reward for taking cocaine. Whatever "pleasure" came from taking cocaine seemed to go unnoticed when dopamine was removed from the equation.



For twenty years, neuroscientists have accepted this **reward hypothesis** to explain addiction. The explanation for drug abuse has been that dopamine is a reward transmitter that produces feelings of pleasure. This pleasure is so powerful that it overshadows the dangers associated with obtaining and using a drug. This hypothesis provides one explanation for why organisms take such huge risks just to get a fix.

An Alternative Explanation

As you know, changes in scientific knowledge can lead to new explanations. One thing that makes scientific knowledge reliable is the fact that it is continually tested and questioned by scientists. Consequently, when a scientist proposes a new explanation it is not seen as a threat. Instead the idea becomes a way to test the current explanation. One example of this process is the development of an alternative explanation for dopamine's effects. Scientists could not explain some of the new experimental data using the reward hypothesis and so developed an alternative explanation. The new competing explanation will be called the **association hypothesis**.

Dopamine is still central to the association hypothesis. However, this explanation suggests that instead of just producing pleasure signals in response to a reward, dopamine signals the brain to pay attention to important events. This would mean that dopamine has a role in learning.

According to the association hypothesis, dopamine acts like a finger snapping. The chemical alerts the brain to what's going on so that something important, like food or some other reward, doesn't go unnoticed. Reward is still involved, but the release of dopamine encourages the sorts of response that would lead to the reward. Instead of dopamine becoming part of the reward, it nudges the brain to respond so that a reward can be obtained.

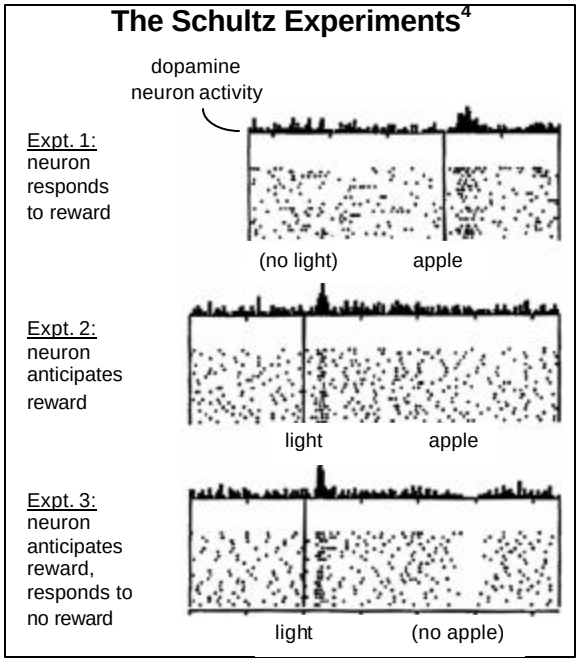
You might be asking which of these two ideas is right. Rather than making you believe something without any evidence, you are going to have the chance to evaluate the two hypotheses. Summaries of five experiments related to dopamine appear below. Your task is to consider which explanation seems to be more reasonable.

Monkey Meets Apple: The Schultz Experiments[4]

Wolfram Schultz and his co-workers performed a series of experiments that led them to draw some interesting conclusions about the activity of dopamine neurons in monkeys. The scientists found that the neurons producing dopamine would become active when a reward - like a piece of apple - was given to a monkey.

Based on these observations, the Schulz team began a slightly different experiment. They trained the monkeys to recognize that a light would begin to blink as a signal that an apple was on its way. At first, the neurons would fire when the fruit was provided, just as they had observed in the earlier experiment. But over time, as the monkeys began to associate the blinking light with the fruit, the timing of the neuron activity changed. Instead of becoming active when the apple was given, the dopamine neurons became active when the light blinked to signal that the reward was coming. The dopamine neurons were working before the reward was supplied – to anticipate a reward just around the corner.

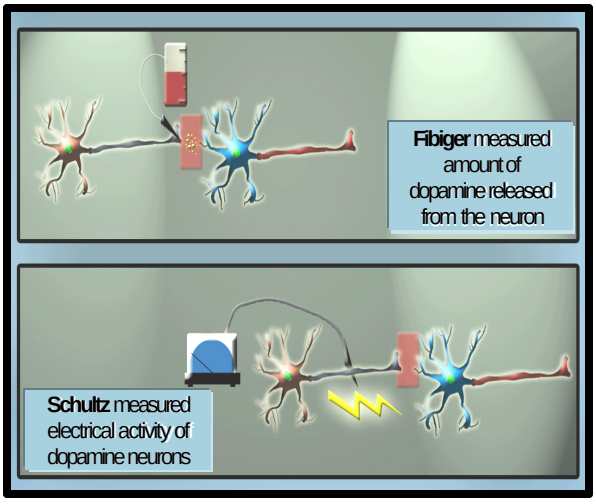
And that's not all. Once the monkeys had been trained to associate the light with the apple, the neurons would fire in response to the light, but if the monkey didn't receive the apple, dopamine levels would actually *decrease.*



A. **How do these results relate to the idea that dopamine is part of the reward sequence**?

Just Out of Reach: The Fibiger Experiments[5]

Like the Schultz group, Dr. Hans Fibiger and his research team performed a two-part experiment to study how dopamine levels in the brain change. However, the data they collected led them to different conclusions. Fibiger's group studied the levels of dopamine in rats' brains when they were presented with food. By taking tiny samples of fluid from a rat brain, Fibiger and his co-workers measured changes in dopamine levels, instead of changes in dopamine neuron activity. While these two ways of measuring dopamine usually lead to the same results, measuring electrical activity directly can sometimes pick up on small changes that don't produce a change in dopamine release.



The rats were quite hungry. Dopamine levels in the brain were low until the rats were fed. When food was given to them, they ate very quickly— and the levels of dopamine in their brains went up. Like the first experiment the Schultz team did, the animals weren't given the chance to anticipate the food until the experiment was changed a little bit.

In the second part of the experiment, the rats were allowed to see the food before they were allowed to eat. They were hungry but they couldn't reach the food because it was shielded by a wire mesh screen. The rats could see the food and tried to get to it. When the screen was lifted they ran to the food and began to eat it. The dopamine levels that Fibiger measured only went up as the rats ate, but not before. Even though the food could be seen and smelled, the dopamine levels in the brain did not increase until the reward was within reach.

B. Fibiger was measuring dopamine levels in the brain, while Schultz was measuring the activity of dopamine neurons. How can these differences lead to a more reliable explanation of dopamine's role?

A Cocaine High: The Volkow Experiments[6]

Another research team took a very different approach but came to similar conclusions about dopamine in the brain. Nora Volkow studied dopamine levels in the brains of cocaine users. Using brain-scanning technology she could study the brains without having to perform surgery.

Cocaine produces a high because it blocks dopamine from being reabsorbed into the neurons. Normally dopamine would be pulled out of the synapses but cocaine allows the dopamine to float about in the synapse longer than normal – keeping the neurons active.

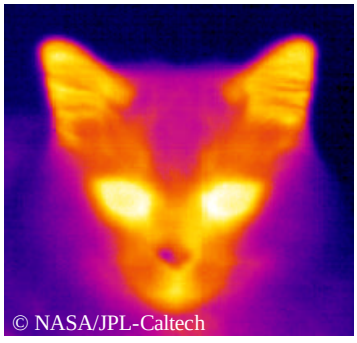
Volkow's research team administered a cocaine-like substance to the participants. They asked the people to report how intense the high was that they were experiencing. This information was compared to the brain scans that showed how much dopamine was circulating in the synapses. The correlation was quite clear: the more dopamine in the brain, the stronger the high that the people experienced.

C. Volkow was measuring dopamine levels, not the activity of dopamine neurons. Look at the graph from the Schultz experiment again. Based upon when the dopamine neurons were active, when would you expect to see a rise in dopamine levels? How could this explain why different scientists are creating different explanations?

Bells and Whistles: The Horvitz and Jacobs Experiments[7]

Jon Horvitz of Columbia University in New York City and Princeton University's Barry Jacobs tried to address the debate over the two hypotheses by removing the reward from the equation.

Cats are known for being very aware of their surroundings. In lab settings, researchers exposed cats to different stimuli – loud clicking sounds and bright blinking lights – that were not thought to be rewarding. Unlike other behavioral studies, these cats were not given any additional reward. They were simply exposed to the stimuli.



As the clicking or blinking occurred, the researchers measured the dopamine neuron activity. When the stimulus was presented at unpredictable times, the dopamine neurons were very active. The neuron activity seemed to be triggered by startling events, instead of a reward.

D. Were the lights and sounds causing the cats to experience pleasure? Or is there another explanation that can be drawn from this evidence?

Craving Another High: The Breiter, Rosen & Hyman Experiments[8]

Using the same kind of brain scanning technology that Nora Volkow used in her experiment, another team led by Hans Breiter and Bruce Rosen of Harvard Medical School in Boston and Steven Hyman, then director of the National Institute of Mental Health, studied the brains of cocaine addicts who were under the drug's influence. They wanted to find out what areas of the brain were active when the subjects felt the brief cocaine "rush." They also wanted to learn what areas remained active after the high wore off and the subjects were craving, or anticipating, another hit. The scientists were not surprised to find that the brain's reward system was active during the cocaine user's high. There was a lot of activity in the reward center – and the dopamine neurons located there. In addition, the reward system continued to be active during the craving stage. This finding suggests a role for the reward center in craving – or anticipating – the next hit.

The Breiter Experiments

Brain-scan images associated with rush (top) and with craving (bottom) indicate that the reward center was active in both the rush and the craving stage[9].

E. Does the activity of dopamine during the craving stage eliminate the possibility that it is also a pleasure transmitter? Is there another explanation that can be drawn from this evidence?

Conclusion

These experiments present different evidence and explanations for the role of dopamine in the brain. Since what scientists already know influences how they gather and interpret evidence, the different scientists came up with conflicting explanations for the same phenomenon. These debates are an important part of building scientific knowledge.

Fibiger's experiments (Just Out of Reach) did not record any rise in rat's dopamine levels until they were allowed to drink the liquid, but Schultz (Monkey Meets Apple) found that dopamine neurons in monkeys would fire in response to a stimulus that the monkeys had associated with reward. Neurobiologists aren't sure why the results obtained by direct recording from dopamine neurons don't always match up with data--like Fibiger's--that are based on dopamine levels. But the different time scales of the experimental techniques might explain the discrepancies. Because dopamine levels are measured over minutes, scientists may miss the tiny, momentary increases produced by dopamine-cell firing. "When the smoke clears, I think dopamine will be playing a role in learning the value of stimuli that are important in an animal's environment," predicts one neuroscientist[1].

This debate about the role of dopamine in the brain shows how scientific knowledge changes over time as new evidence is discovered. These new explanations also point to how dopamine might play a role in drug addiction. We know that dopamine can increase in response to a reward and that drug addiction can lead to depleted levels of dopamine in the brain. As a result, addictive drugs seem to be "hijacking" the reward system.

Since dopamine plays such a significant role in addiction, it is an important chemical for scientific research. If dopamine really does give an organism an incentive to act, or even just to get the brain's attention, how do you think this knowledge can be applied to understanding drug addiction? If a person has learned to associate a certain place or certain people with the reward of a drug, when would their dopamine neurons fire when they were in that environment or situation according to the reward hypothesis? If we tried to explain these behaviors using the association hypothesis, when would we expect for the dopamine neurons to be active?

References

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9. Reprinted from NEURON, Vol. 19, Breiter, H. et al. Acute effects of cocaine on human brain activity and emotion. 591-611 Copyright (1997), with permission from Elsevier.

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DIRECTIONS: Summarize the evidence from each experiment by describing what it says about the role of dopamine in the brain. Decide whether each experiment set supports the reward hypothesis, association hypothesis, or both and place a check in the appropriate blanks.

Experiments & Evidence	**Hypothesis**	
Write your explanation in the boxes below	Reward	Association
Experiment Set One: **Monkey Meets Apple** (Schultz)	___ Yes ___ No ___ Maybe	___ Yes ___ No ___ Maybe
Experiment Set Two: **Just Out of Reach** (Fibiger)	___ Yes ___ No ___ Maybe	___ Yes ___ No ___ Maybe
Experiment Set Three: **A Cocaine High** (Volkow)	___ Yes ___ No ___ Maybe	___ Yes ___ No ___ Maybe
Experiment Set Four: **Bells and Whistles** (Horvitz & Jacobs)	___ Yes ___ No ___ Maybe	___ Yes ___ No ___ Maybe
Experiment Set Five: **Craving Another High** (Breiter, Rosen & Hyman)	___ Yes ___ No ___ Maybe	___ Yes ___ No ___ Maybe