Drug Addiction, Dopamine, and Liking vs. Wanting ES.S10, 2013-03-04

Major sources:

Food Reward: Brain Substrates of Wanting and Liking by Kent C. Berridge; <u>Neuroscience and</u> <u>Behavioral Reviews</u>, Vol. 20, No. 1, pp. 1-25, 1996.

Dopamine in drug abuse and addiction: results from imaging studies and treatment implications by Nora D. Volkow, et al.; <u>Molecular Psychiatry</u>, Vol. 9, pp. 557-569, 2004.

Note that "reward" usually refers to both liking and wanting.

	Liking:	Wanting:
Synonyms:	Euphoria, high, sensory pleasure,	Motivation, incentive salience,
	affective reaction, hedonistic value	appetite, drive, craving
Feel:	Sedating	Stimulating
Subjective:	Conscious	Often unconscious
Neurotransmitters:	GABA, opioids, DA	DA
Brain structures:	Ventral pallidum, paraventricular	Nucleus accumbens, ventral
	nucleus of hypothalamus	tegmental area, amygdala
Triggered by:	Taking drugs	Seeing drugs or taking drugs

Normal Person:	Drug Addict:	
Likes drugs more (experiences more euphoria when given drugs)	Likes drugs less	
Likes natural rewards more (food and sex)	Likes natural rewards much less	
Wants drugs less (no craving)	Wants drugs much more (very intense drug craving)	
Wants natural rewards more	Wants natural rewards much less (does not care hardly at all about food and sex)	
Good self control	Bad self control (very impulsive)	

Classic Stimuli:

Classic stimuli (normal stimuli) are both wanted and liked to a similar degree. Your favorite food is a good example – you like it and you want it. Both liking and wanting depend on context, such as how recently you ate.

Manipulation: Injecting opioid agonists such as morphine into the basal ganglia causes an increase in both liking and wanting. Opioids directly promote liking, but they probably promote wanting indirectly via dopamine and learning. (Note: Humans who have taken opioids often report enhanced enjoyment of sweet foods, and this may be directly due to the action of opioids on the liking pathways in the brain.)

Manipulation: Injecting benzodiazepine agonists such as diazepam (these stimulate GABA_A receptors) into the brainstem causes an increase in both liking and wanting. Benzodiazepines directly promote liking, but they probably promote wanting only indirectly via learning.

Excessively Wanted Stimuli:

The stimulus is wanted, so the person will expend great effort to get it, but it is not liked. Once attained, the stimulus brings little enjoyment.

Money is a good example. Money does not taste good or feel good, but people want it. This is because people are capable of abstract thought, and we realize that money can be used to buy food which tastes good and blankets which feel good.

Alcohol while taking naltrexone is another good example. Alcoholics normally both like and want alcohol. Naltrexone is an opioid antagonist, so it blocks the pleasurable effects of alcohol (naltrexone blocks liking). An alcoholic who is taking naltrexone will often have one or two shots, then they feel disappointed (because of the naltrexone), and then they remember that being an alcoholic sucks and they decide not to drink any more. Without naltrexone, one shot usually leads to twelve more shots and a full relapse.

Cocaine becomes an excessively wanted stimulus if you develop a cocaine addiction. As your addiction worsens, you want cocaine more and more and you like it less and less. This is true of all drugs of addiction, although cocaine is a particularly extreme example. Heroin addicts like heroin less than they used to, but they still like heroin a lot. Heroin still brings a lot of pleasure, because it acts directly on opioid receptors and opioids signal liking.

Female domestic cats want to mate, but they do not like to mate. It is clear that they want to mate because the females will seek out males and will assume the mating posture. It is clear that they do not like to mate because the male's penis has sharp spines, so the female often yowls in pain and swats at the male after being mounted.

(Debatable) Humans want to have children, but some evidence suggests that we do not like having children. When a survey asks "how happy are you", people with children on average report less happiness. However, when a survey asks "what makes you happy", people with children consistently (and paradoxically) say that their children make them happy. When you give a parent a smartphone that buzzes every hour and tell them to enter how happy they are at the moment when it buzzes, they will very often enter things like "I am very unhappy now because my daughter refuses to get dressed for school". When you compare the parents with non-parents, you see that parents on average say they are less happy in hourly reports, and the parents are often unhappy because of interactions with their children. These findings are controversial, mainly because parents staunchly claim that their children make them happy and they do not regret having children.

Manipulation: In rats, we can electrically stimulate the lateral hypothalamus. This will cause the rat to eat, but it does not enjoy eating, especially if the food is bitter and the rat is

not hungry. The rat eats because its brain is being stimulated, but it gapes its mouth and shakes its forepaws like a rat that is being force-fed unpalatable food.

Excessively Liked Stimuli:

The stimulus is liked, but it is not wanted so the animal will not seek it out.

The best examples of these stimuli come from rodent experiments where the rodent has brain damage in its wanting pathways.

Marijuana (which contains THC, a cannabinoid receptor agonist) is a possible example of an excessively liked stimulus. Humans, monkeys, and rodents all seem to like cannabinoids, but it is very difficult to train monkeys or rodents to self-administer cannabinoids. Furthermore, marijuana addiction is not very common when you consider how many people have tried marijuana. Nonetheless, marijuana can definitely induce addiction.

Manipulation: If you kill the dopamine-releasing cells in a rat's wanting pathway using the neurotoxin 6-hydroxydopamine, then the rat will no longer want food, but it will still like food. The rat will not eat, even though food is readily available and it is capable of performing the movements needed to eat the food. If delicious food is placed in the rat's mouth, it will show pleasurable responses (e.g. lip smacking). These dopamine-deficient rats also do not want drugs, they cannot be trained to self-administer cocaine or heroin.

Manipulation: If you kill the brain cells in the central amygdala using electric current, it destroys the wanting aspect of the salt appetite without affecting the liking aspect. Normal rats with normal blood chemistry do not like 3% salt solution in water, it is too salty and so gape and shake their paws. Normal rats with low blood sodium have a specific salt appetite, because their blood sodium is low they now want salty water and they now show pleasurable reactions when drinking salty water. Rats with a lesion in their central amygdala do not want salty water even when their blood sodium is low, thus the lesion has destroyed the wanting pathway. However, rats with this lesion still like salty water if and only if their blood sodium is low.

Caveat: "Wanting" Does Not Mean What You Think

When I say "wanting" on this handout, I am talking about a special kind of wanting, the kind that is mediated by your mesolimbic dopamine system. This kind of wanting is deep in your brainstem and basal ganglia, and you may not be consciously aware of it. Scientists can tell what you "want" even if you cannot, because scientists can look inside your brain with PET scans and fMRI, and scientists can track your eyeballs with cameras.

There is a different kind of "wanting" which is mediated by the conscious mind, and this wanting probably has much less to do with the mesolimbic dopamine system. I call this alternative form of wanting "thinking it is a good idea". Thus, I might think it is a good idea to get a root canal, but the prospect of a root canal probably does not prompt a burst of dopamine in my mesolimbic reward circuit.

ES.S10 Drugs and the Brain Spring 2013

For information about citing these materials or our Terms of Use, visit: http://ocw.mit.edu/terms.