ADDICTION - THE TRANSITION FROM USING TO ABUSING

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Substance dependence is a global problem because drug abuse is found all over the world. Drug abuse is characterized as a chronically relapsing disorder that causes the individual to become obsessed with seeking and using the drug. But why is it so difficult for individuals to stop using them, what is the biological reasons for the development of addiction?

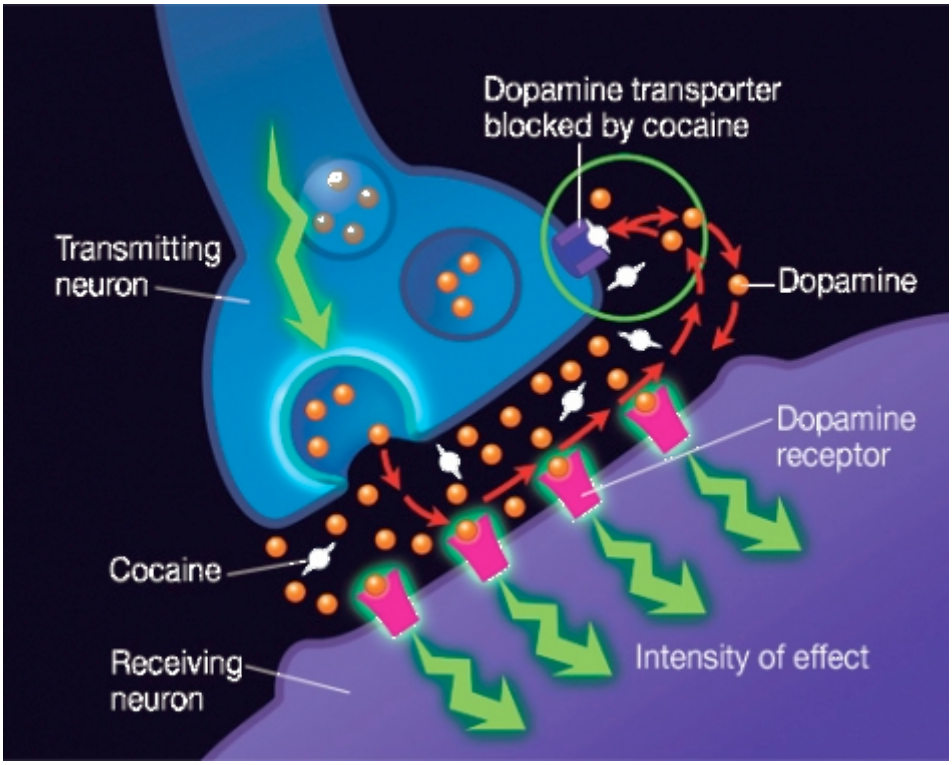
THE REWARD PATHWAY

There are a wide range of different psychoactive substances with different molecular structures and target areas, but what they all have in common is that they have the ability to increase the concentration of dopamine in the brain. This is a signal substance in the brain that causes a pleasant sensation in the reward pathway. This pathway is important in the human brain because it causes the individual to repeat biological profitable acts by giving the individual a pleasurable feeling when performing them. Drugs hijack the reward pathways and cause a sensational high that outshines those caused by natural rewards, but without giving any biological benefits. This will cause the abuser to ignore the natural rewards created by eating, drinking and sexual activity in order to obtain these euphoric, non profitable, highs caused by the drugs. When the natural rewards become neglected the individual will eat and drink less frequently which is why many substance abusers typically are malnourished.

Areas in the brain that make up the reward system and which are affected by substance abuse are the ventral tegmental area (VTA), where the DA is produced, the nucleus accumbens (NAc) an area that is involved in the creation of the pleasurable high feeling, the amygdala (A) where emotions are produced and which give rise to the negative effects caused by the withdrawal stage of addiction. The prefrontal cortex (PFC) where functions such as reasoning and rational thinking are found and the hippocampus (HC) which is important in the development and storage of memories. These structures, including other areas of the brain collaborate and give rise to cravings that leads to loss of self-control, which is one of the qualities that characterizes an addict.

It is in the VTA that you find the cells (neurons) that produce the DA, these cells have axons, which are extended parts of the cells that can transport the DA to the end terminal of the cell. When the DA has reached the end terminal they are packed into small spherical vesicles. These vesicles will fuse to the membrane of the end terminal of the cell and cause a release of DA into the empty space between two neurons called the synaptic cleft. The DA will diffuse through the synaptic cleft and bind to receptors on the postsynaptic neuron; this will cause a cascade of events in the postsynaptic neuron. VTA neurons project to an area in the brain called the NAc, when a release of DA occurs, these signal molecules will bind to the neurons in the NAc and the individual will experience a pleasurable feeling.

When a psychostimulant is consumed the reward pathways are affected in that a massive increase of DA concentration in the NAc occurs. This will cause the individual to feel a sensational high feeling due to the large concentration of DA molecules that now are able to bind to the cell receptors. Despite different target areas all drugs of abuse can create an increase of DA concentration. One example is cocaine, which is a psychostimulant that has the ability to bind to dopamine transporters (DAT). These DAT play an important role in the reward system because they transport the released DA back into the presynaptic cell after being released. They therefore control the number of receptors that are being stimulated and the duration of time that the DA is present in the synaptic gap. Cocaine increases the DA concentration in the cell by binding to the DAT and preventing them from transporting the DA back into the presynaptic cell. This leads to the DA being able to stimulate additional receptors and for a longer time, causing an increased pleasurable feeling.



The figure shows how cocaine binds and interferes with the uptake of DA by the DAT.

Another drug that also has the ability to increase the DA concentration is heroin, which belongs to a class of drugs called opiods and is commonly used by many addicts. Heroin increases the amount of DA by interfering with the function of an inhibitor neurotransmitter called γ-Aminobutyric acid (GABA). One of GABAs functions is to regulate the release of DA, by binding to the terminal end of the presynaptic cell and preventing the release of DA. When an individual uses heroin GABAs inhibitory action is prevented by the binding of heroin to opiod receptors on the GABA containing cells. This action prevents the release of the inhibitory neurotransmitter.

Alcohol is a legal psycho stimulant that has been used by humans for centuries, it is the ethanol compound in alcohol that causes the soothing and often euphoric feeling. The ethanol causes its effect in the brain in two different ways, one is by preventing an excitatory neurotransmitter named glutamate from binding to its receptor and the other is by enhancing the inhibitory effect of GABA.

Taking these different psychostimulants creates different reactions in the user for example cocaine is a stimulant and thus causes mental alertness, decreased appetite and increased energy. While alcohol is a depressant that causes a temporarily soothing or drowsy effect heroin also has a soothing effect and creates a sudden rush of pleasure when taken. The negative effect of drug abuse is that the user becomes addicted, the drug is then no longer taken because it is desired, and instead it is a necessity in order for the addict to cope each day.

The transition from taking the drug in order to experience the pleasurable high feeling and instead using the drug in order to avoid experiencing the negative effects is what characterize an addict. The term negative effects refers to the down side of taking drugs, that is experiencing the hangovers followed by drinking too much, or the bone pains, insomnia and vomiting caused by the withdrawal effects of heroin. In cocaine it is the nausea feeling, the respiratory arrest and the disturbed heart rhythm that causes the user to feel ill when not being able to consume the drug. In addition to the different drugs that can be used there are also different methods to deliver the drug to the brain. The fastest way to deliver the drug to its target site (the brain) is by inhaling the drug, this will cause the drug to quickly transfer to the blood and reach the brain. Other ways are by injecting, snorting or consuming, the later is the slowest way which takes a couple of minutes before causing an effect, this is the reason why it takes a while before one realizes that the last glass of wine might not have been such a good idea.

THE CHALLENGES OF ENDING AN ADDICTION

But why is it that so many addicts relapse, if the toxic effects of the withdrawal have passed shouldn't these individuals being able to cope just like us non-users? Scientist have tried to understand the biological reason for why so many people relapse back into addiction and have started to understand the complex molecular and cellular alterations in the brain that causes these. Excess flows of DA in the brain will after a while cause the brain to adapt to the increased flow by producing more receptors on the cells that can be stimulated by DA. But by adapting to the new concentrations of DA these users then must take a larger dose of the psychostimulant in order to produce the same high that was experienced during the first drug intake.

Due to the disturbance in the natural flow of neurotransmitters in the reward system, other areas in the brain become affected. One area called the frontal cortex is found in the anterior part of the brain. This area contains the control system for actions such as impulse control, behavior, attention, working memory and response to ones surroundings. Scientists have revealed differences in these areas in addicts which explain why they are more prone to risk-

taking behavior and show limited impulse control. The cells in these areas become in a sense rewired causing them to become more sensitive to the drugs and drug-associated stimuli, that is they feel the urge to take the drug when they are in a place that reminds them of taking it.

This stage of addiction has similarities to how we humans learn to perform an action that gives us a biological profitable outcome. When you drink a glass of water in order to quench your thirst, you experience a pleasurable feeling that tells you that you've done something good. The next time you feel thirsty you're brain will remember how good you felt when drinking water and you will then repeat the act. Addiction works in a similar way, when an addict experiences the anticipating stage of taking the drug and the pleasurable high that it gives rise to, strong emotional memories are formed and stored in the brains. Despite the fact that an individual can be freed from the chemical part of the addiction, that is the individual does no longer feel ill when not taking the drug, he or she is still vulnerable to the emotional part. These strong emotional memories are believed to be one of the reasons why so many addicts relapse.

It is quite hard for a non-user to understand how these sensational highs feel like but one way is to imagine a mood stage where you feel content, not happy or sad, and then call this the zero level. Thereafter imagine that someone puts your favorite dish in front of you, this causes your mood level to increases up to 50%. After returning to the basal level again the individual of your desire wants to engage in a sexual activity, this will cause a 200% rise in your mood from the basal level. And finally somebody offers you a drug that you take by inhalation which gives you a rapid delivery to the brain and gives rise to a 1000% elevation in your mood compared to the basal level. So if a biological profitable act such as eating gives rise to a 50% increase in mood and thereby will cause you to eat every time you feel hungry, then imagine how hard it is to resist an act that gives you a 20 times higher pleasurable feeling…

STARTING WHEN YOU'RE YOUNG

Being a teenager isn't easy, your body is developing and you seem to have no control over it, while at the same time your hormones are running high. Teenagers are often characterized as having poor judgment, reasoning and thrill seeking needs, to many parents distress. This is due to the fact that certain areas during adolescence are rapidly developing, and these areas are in the frontal cortex and are in charge of reasoning and complex adult behavior.

Critical periods of brain development have proven to be more sensitive to substance abuse than others, which is why there is a greater chance of developing an addiction if the individual starts using at a young age, before the brain is fully developed. Due the fact that drugs have the ability to effect the arrangement of neurons in different areas, it is therefore highly dangerous for young people to abuse drug, because it interferes with development of the young adult brain. Frontal cortical areas that are in charge of reasoning, talent and adult behavior are affected causing these areas to not develop in a normal way. This leads to the person being prone to engage in high risk behavior and never fully develop adult skills such as reasoning and judgment. This is one reason why it is more difficult to rehabilitate a person that started to abuse drugs at a young age.

By hijacking the reward system the drugs take over the individual's ability to make wise decision and in a sense makes the individual helpless and unable to control its need (to seek and take the drug). By better understanding the mechanism behind addiction, scientist can start creating new treatments that will cure both the chemical and emotional parts of the disease.

Further reading:

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