HOW MARIJUANA AFFECTS YOUR BRAIN

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Is marijuana addicting?

Do you think marijuana is addicting? Many people do not believe it is, however, it is addicting. What does it mean when you say a drug is addicting? In simple terms it means that the drug has taken over your brain and is driving you to use it. People addicted to a drug, continue to use, often despite all kinds of negative consequences such as health problems, legal problems, school problems, work problems, or family problems. Addiction can be thought of as "Chemical Slavery".

Not everyone who uses a drug becomes addicted to it. There are several things that can cause someone to becoming addicted including the potency of the drug or how strong it is, being exposed to the drug when your brain is developing, and experiencing trauma or abuse when growing up. These are important things to know so you can be fully informed before using a drug that can cause you to become addicted.

Drugs that can cause addiction include anything that works immediately to change the way you feel. These include things like alcohol, tobacco, marijuana, cocaine, methamphetamines, benzodiazepines, and opioids such as heroin. There may be nothing wrong with wanting to change the way you feel if the use of the substance happens only occasionally however, many people want to stay in that altered state of feeling so they continue to use regularly.

When someone starts using an addicting drug regularly, the time depends on the drug, the amount that used to work, does not work anymore and you must use more to get a similar feeling. This is called developing tolerance to the drug. If you are using regularly and then are not able to get the drug for whatever reason, you can start to experience withdrawal, which can be extremely uncomfortable. Many people become convinced that the drug was "helping them" and that is why they feel so bad without it. They do not realize that their body has become dependent on it and they are suffering withdrawal.

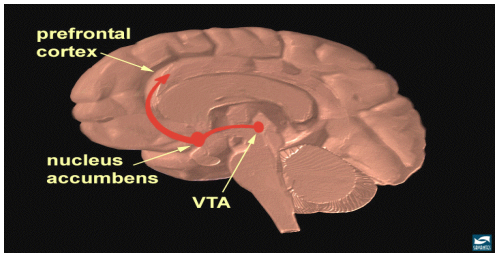
Symptoms of withdrawal from an addictive drug are exactly opposite of what the drug is supposed to do for you. If it helps with pain, withdrawal is very painful. If it helps with anxiety, withdrawal is very anxiety provoking. Withdrawal symptoms are time limited, the time depends on the drug, however, they can be so uncomfortable, the person just cannot quit without help.

The more potent a drug and the more often someone uses, the worse the withdrawal can be. Heavy drinkers with high blood alcohol levels can experience life threatening withdrawal if they quit abruptly without medical help. Heroin is the most potent pain killer known to man. When someone is withdrawing from heroin, they feel severe pain, all over their body. The only relief is often using more heroin. There is medication that can help with this, but the person must be willing to ask for help.

It used to be thought that marijuana was not addicting because there did not seem to be a withdrawal when people quit, however, that was with the "old time" marijuana. Back in the 60s, 70s and 80s the THC (the component that gets you high) in marijuana was less than 2 %. Since the late 90s when states started legalizing medical marijuana, the cannabis industry has worked tirelessly to increase the potency of the THC and now the average potency in the plants is 20% and the concentrates like wax, shatter, dab, vape oil, have an even higher concentration, some up to 90%. This makes the drug much more

addicting and there is a definite withdrawal syndrome associated with quitting after using regularly. Marijuana withdrawal symptoms include irritability, anxiety, anger, insomnia, poor appetite, and strong cravings for marijuana. This can last for weeks to months depending on how much and how often the person was using because marijuana is fat soluble and sticks around for a while. There is no medication that has been approved to help with marijuana withdrawal, so people usually need support from others to help them quit.

How does addiction happen?



The reward pathway

All drugs of abuse work in a pathway in the brain called the Reward Pathway and these drugs can hijack the brain through this pathway. This is a pathway we have on purpose to help us to learn and remember important things. When you learn something new, dopamine is released in this pathway and your brain says “this is important” so you need to remember it. We have this pathway for survival as it helps us learn and remember to eat. Do you remember the first time you ate a big juicy hamburger? That caused a release of dopamine in your reward pathway that said, this is good, we need to remember this, and you do not ever forget that you like hamburgers.

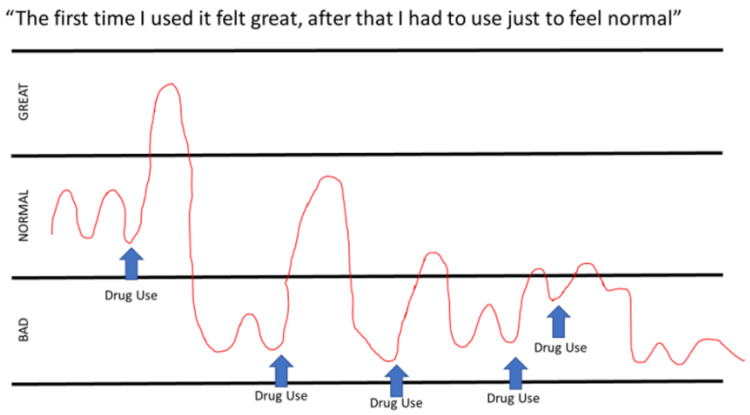
Do you remember the first time you learned to ride a bicycle? Do you remember how good that felt when you were successful? You had a release of dopamine in the reward pathway that said this is important, do not forget this. And even if you do not ride for some time, you never forget how to ride a bicycle; it is hard wired into your brain.

Natural rewards all cause a release of dopamine in the reward pathway. However, drugs of abuse cause even more powerful releases of dopamine and hijack the brain. While food can cause a one and half fold increase in dopamine, drugs like nicotine cause a two and a half fold increase, cocaine can cause a

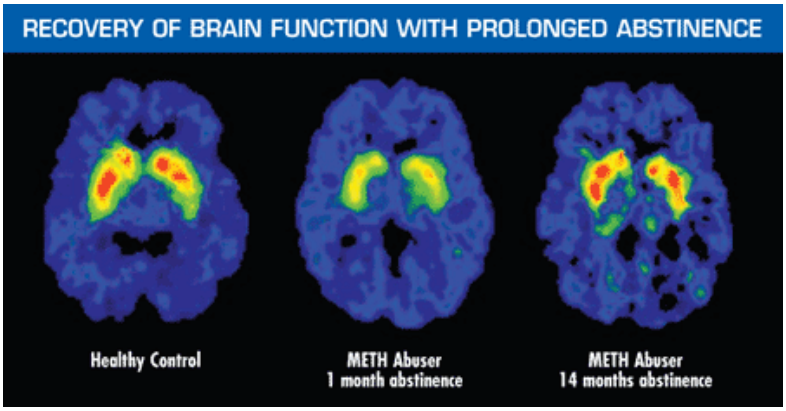
fourfold increase and amphetamines can cause an eleven fold increase in dopamine in the reward pathway, which is powerfully reinforcing. These drugs then make the brain believe they are **especially important, and you need to remember to use them.** The more often you use the use gets "hard wired" into your learning and memory system and you never forget.

Because natural rewards are limited in the amount of dopamine produced, the brain is always adjusting to changes in dopamine in a normal cycle of ups and downs. However, when the addictive drug produces more dopamine than the brain is used to naturally, the dopamine starts disappearing and the person no longer feels good when they use a drug. Addictive drugs can destroy dopamine in the brain and the person can feel miserable, even though they continue to use.

Brain Dopamine Levels in Addiction



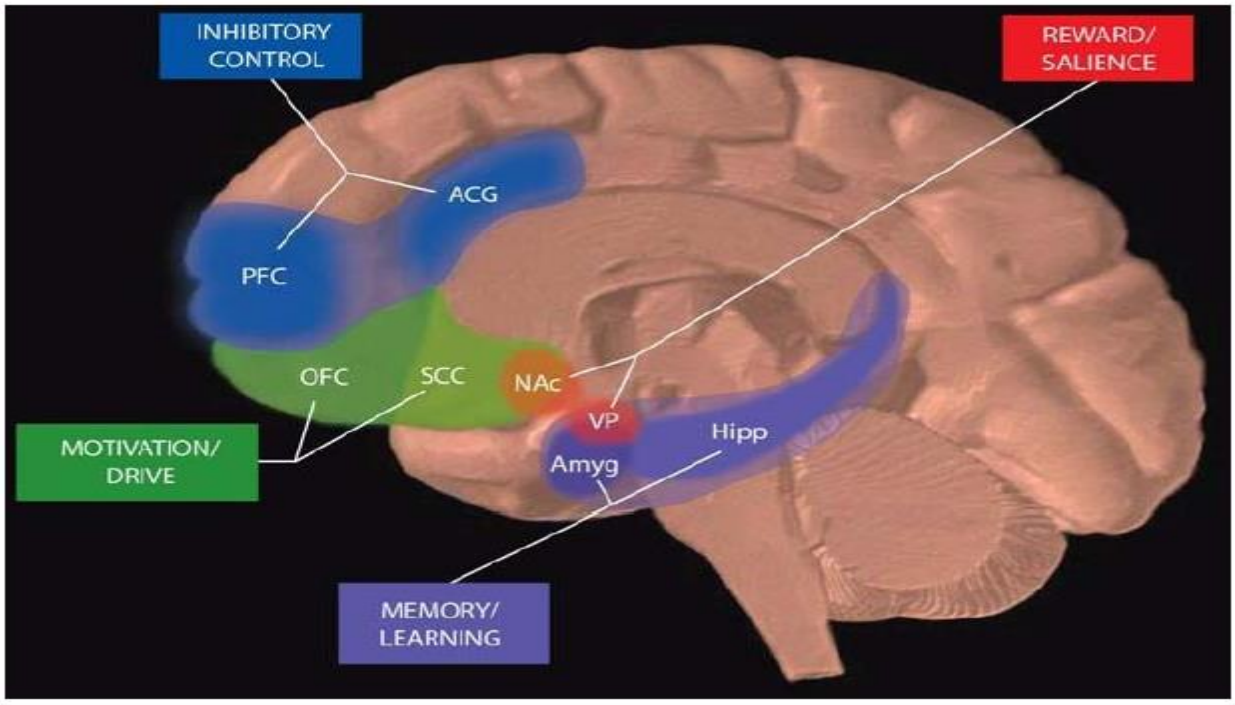
The good news is that when people quit using the addictive drug, the dopamine can recover.



These are pictures of human brains and the important thing to focus on is the red – these are the dopamine receptors in the reward pathway. The person on the left is a healthy person who has not been using addictive drugs. That person has a lot of dopamine. The person in the middle is someone who was abusing methamphetamines but quit for one month. That person has no red because the methamphetamine destroyed the dopamine and they usually do not feel particularly good. The person on the right is that same person 14 months later not using methamphetamines and the red is back. That means that the dopamine has recovered. However, it takes time for this to happen with the person eating a healthy diet and exercising without using addictive drugs.

So, dopamine plays a big role in learning and remembering things, and the drugs of addiction can hijack this learning and memory part of your brain. Dopamine is released in the part of the brain called the nucleus acumbens (NAc) in the reward pathway (see picture). The different parts of your brain then communicate via a chemical called glutamate. This is our major chemical that excites nerves in the brain and helps communicate between different parts of the brain. When you use a drug like marijuana for the first time your NAc gets a release of dopamine and sends a message, via glutamate, to your amygdala (Amyg), your hippocampus (Hipp) and your orbital frontal motor cortex (OFC) (see picture).

Your amygdala is the warning system in your brain, it is the "scout", always scanning the environment for anything important that might be a threat to you. The NAc says to the amygdala: "next time you see that guy that gave us that marijuana, warn us". Your hippocampus is where you put all your new memory and learning. The NAc says to the hippocampus: "next time the amygdala sees that guy, remember what he is good for." The orbital frontal cortex (OFC) is where you have your motivation and drive. The NAc says to the OFC: "next time the amygdala sees that guy, go get him because he has some good stuff." You just do this a few times and it becomes hard-wired into your brain and you never forget. That is why when people are put in jail for legal problems related to using addictive substances, they may be in there for 6 months without using anything, but once they get out and see their drug dealer, they may go right back to using. This is because the same neurons that were hard wired together, are now triggered to fire together. This especially happens if they have not done anything during that period to change their thinking and "wire in" other behaviors in their learning and memory system. This is what treatment does – it helps re-wire new memory and learning into the reward pathway.



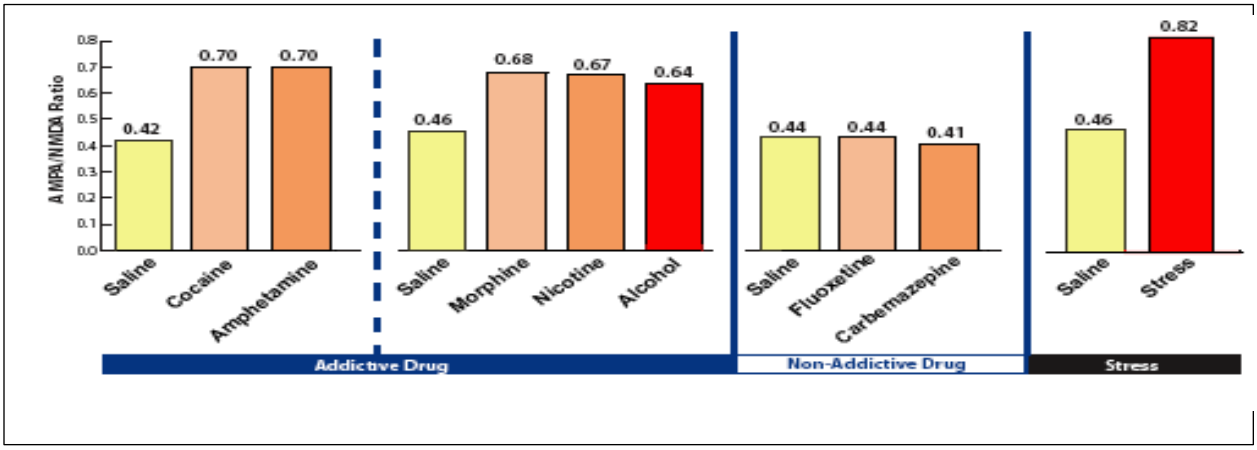
You can be in real trouble if you start using addictive drugs before your brain is fully developed. Adolescence is a time a major brain development and it is not fully developed until your mid-20s. That purple part in the picture (at the front of your brain) – the PFC or prefrontal motor cortex is the last part

of your brain to fully develop and is responsible for inhibitory control or your ability to put on the breaks and control impulsive behavior. As an adolescence, this part of your brain is not working very well, so it is difficult to say no when feeling pressured from friends to "try" some drug.

Long Term Potentiation – how to increase long term learning and memory

There is a concept in the learning literature called Long Term Potentiation (LTP). What this means in simple terms is that when you first learn something you get a dopamine release in the NAc, the next time you do it, you get an even more powerful dopamine release, that really reinforces the learning. LTP can be documented by measuring the glutamate receptor ratios in the brain after the drug has been introduced. In this study in mice (see picture), the normal glutamate receptor ratio is shown in the saline column (saltwater control).

All drugs of abuse do the same thing in the same way since the NAc communicates with all the different parts of the brain via glutamate after the NAc is stimulated by the drug to release dopamine. You can see here that addicting drugs such as cocaine, amphetamine, morphine, nicotine, and alcohol all increase the glutamate receptor ratio (AMPA/NMDA) causing long term potentiation which really reinforces the learning. Drugs that are not addicting like Fluoxetine (Prozac – a drug to treat depression) or Carbamazepine (Tegretol – a drug to treat bipolar disorder) do not work in the reward pathway and therefore do not cause LTP. That is why many people have difficulty remembering to take their psychiatric medications – there is no salience associated with their use. You do not take a Prozac and think "wow – that was great – really important".



Saal et al. Neuron 2003;37:577-582

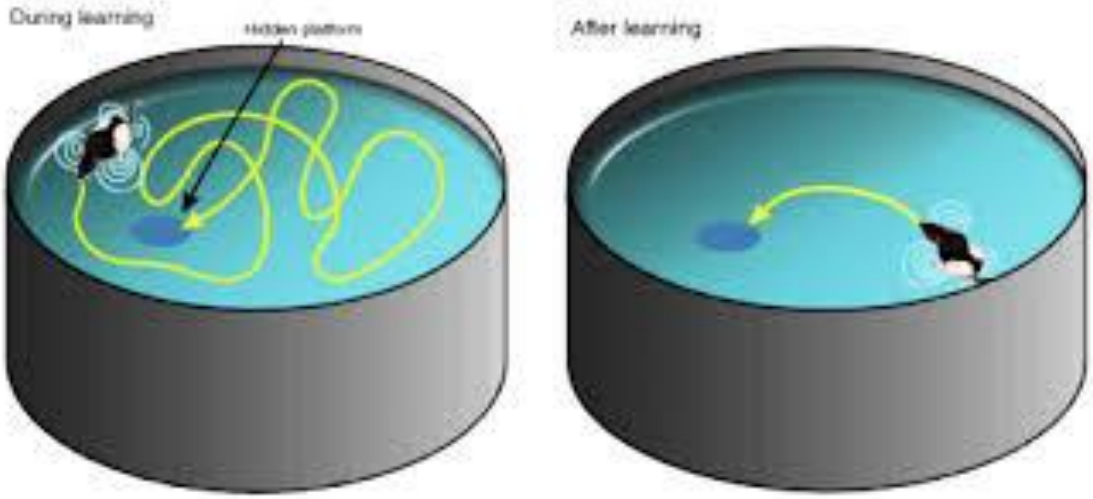
What causes the most LTP is stress or trauma. If someone has experienced abuse or incredibly stressful experiences growing up, that can cause LTP. That means that the first time they use an addicting drug, they already have LTP from the trauma, so they get a powerful release of dopamine from the drug, which really reinforces the learning to use the drug. They can be addicted from the first use.

Hippocampus and Neurogenesis

Another aspect of your brain required for learning and memory is a healthy hippocampus. This is a part of your brain that continually regenerates, and this is called neurogenesis. You have new stem cells that grow and differentiate all the time which makes sense. You are learning new things all the time and you must have new cells to help with this. However, if you use any addictive substance chronically, it can decrease neurogenesis and cause your hippocampus to shrink, making it difficult to learn new things. This is true for all addictive drugs including alcohol, cocaine, methamphetamines, heroin, nicotine, and THC.

Hippocampus from the Greek word hippos for horse and kampos for sea monster, because it was thought this part of the brain looked like a seahorse

A cool example of this are animals in a Morris Water Maze test. Animals such as rats or mice are put in an exceptionally large vat of water where somewhere, just under the surface, is a small block of wood they can stand on, so they do not drown. You put an animal in the vat and calculate how long it takes for it to bump into the block of wood. You then know the animal can learn because you have pictures all around the room it can see, and it can figure out where that block of wood is relative to the pictures. Then the next time you put it in the tank, it swims right to the block of wood and you think: "that is a smart animal".



But, you can give similar animals addictive drugs like nicotine or THC and after they have been using them for some time, the poor animals cannot find the block of wood to save their life, they have to just continue to swim until they bump into it. The constant drug use makes it so they cannot learn so easily.

The good news is they can recover their ability to learn if the drugs are taken away and the animals are allowed to be in a healthy environment with good food and where they can run to their hearts content on their little exercise wheels. After a period of recovery, they can find the block of wood. This is because one of the best things we know of to increase neurogenesis in the hippocampus is voluntary exercise.

Stopping Drugs and Exercising improves the ability to learn new things

Exposure to drugs during adolescence can get the brain ready for addiction

Exposure can happen actively where someone is being given the drug on purpose or passively where someone is exposed to the drug by others. This most often comes in the form of smoke. When someone smokes a drug, the drug is on the aerosolized tar droplets that make up smoke. They get into your lungs, through secondhand smoke. The drug then is absorbed in the blood stream in your lungs and then goes to your brain, whether you want it to or not. This is one of the reasons we no longer have smoking allowed on airplanes. When your parents flew in an airplane before you were born, people could smoke in the back of the plane. One time a test was done with a passengers on a 3-hour flight, those who were nonsmokers in the front of the plane gave a urine drug screen at the beginning and then again at the end of the flight. There was enough nicotine in their second urine as if they had smoked 3 cigarettes during the flight. If the drug is in your urine, then it was in your blood and was in your brain.

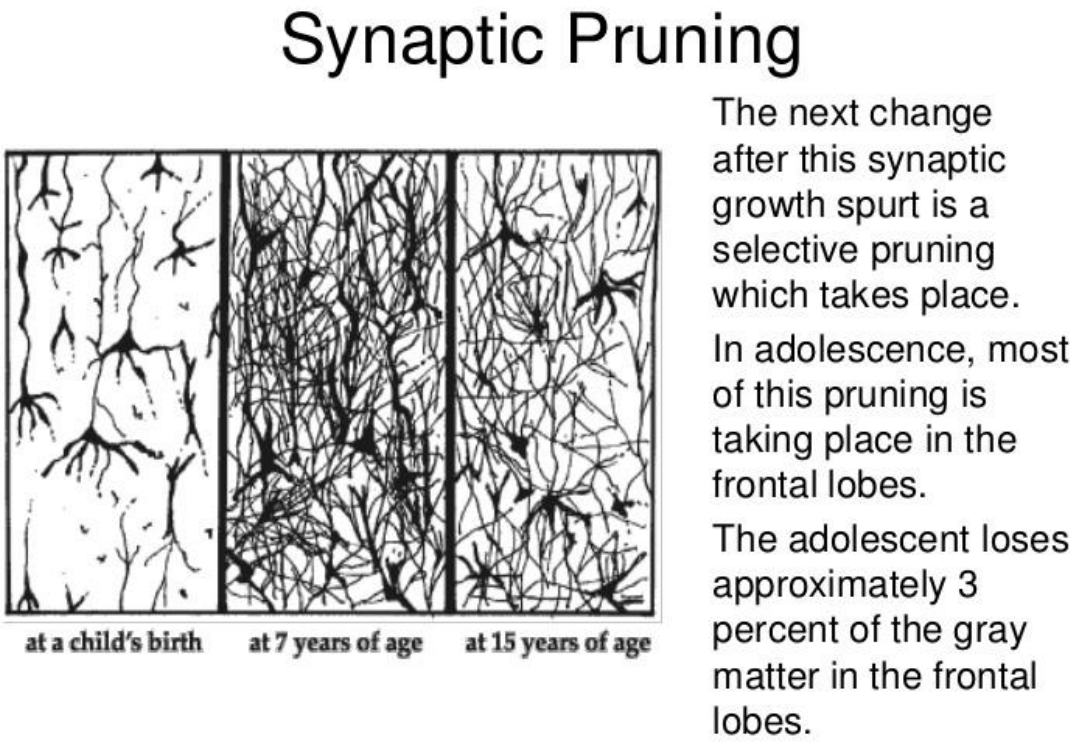
Studies in rats have shown us that when you give an adolescent rat nicotine, they are more likely to want to use nicotine as adults than when they are first exposed as adults. This correlates with what we know with humans, if you start smoking tobacco before your 20s it is much harder to quit than if you start smoking in your 20s. The brain is also cross-tolerant, meaning it sees all the addictive drugs the same, since they all work in the same place in the brain and in the same way. Studies have shown that if you give an adolescent rat nicotine, they are more likely to want to use cocaine than those that are exposed to nicotine as adults. Other studies show that when you give an adolescent rat Ritalin (medication used for ADHD), they are more likely to want to use cocaine than if they are given a placebo like salt.

This exposure as a child can get the brain ready for use and is a risk factor, however, it does not have to result in addiction. What allows the addictive drug to “hijack” the brain is the person engaging their

prefrontal motor cortex and making the choice to use the substance, or use it in a way other than recommended (snorting, smoking, IV) after their brain has been primed. This is a common story seen in adult smokers attempting to quit using tobacco. When asked when they started smoking it was usually around puberty, age 13-14. When asked why they started smoking, many say, "I don't know, I hated the fact that my parents smoked, I hated the smell and the smoke and I was always taking their cigarettes and trying to destroy them so they would stop." Then when asked what got them to smoke the first time, they state, "A friend gave me a cigarette and I was addicted that minute." This is entirely possible because their brain was primed by that passive exposure to smoke but then they made the conscious choice to smoke and the drug could hijack their brain and the behavior is hard to change.

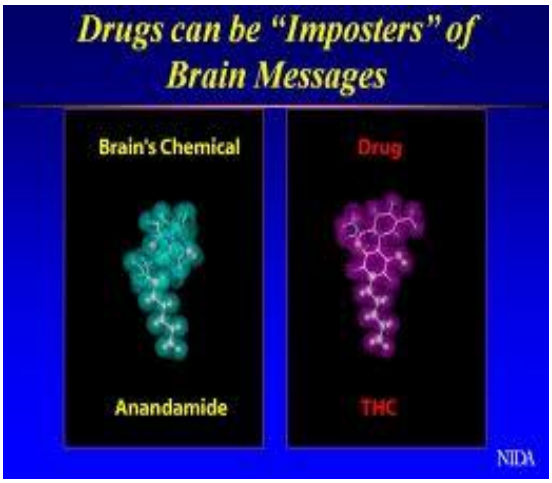
Why Adolescence is the time of greatest risk for using addictive drugs.

While many animals' brains are fully developed when they are born, human brains are continuing to develop and are not fully developed until the mid-20s. Adolescence is one of the times of the most active brain development. It is a time of active learning and movement, so there are a lot of stimulatory neurotransmitters (dopaminergic and glutaminergic) being produced and strengthened. At the same time there is a decrease in inhibitory neurotransmitters (GABAergic and serotonergic) which are mostly located in the prefrontal motor cortex. For this reason, you may experience some anxiety and depression during this time, and you may have impulse control problems, or difficulty putting on the brakes and saying no to offers of drugs from your friends. During adolescence there is active pruning of neurons going on in the brain.



Acetylcholine is another neurotransmitter in the brain that is responsible for helping us focus and concentrate. The receptors in the brain for this chemical are in the learning and memory area of your brain and are called nicotinic cholinergic receptors. This is not because we are supposed to smoke tobacco. They are called this because nicotine works on these receptors. The problem for adolescents is this receptor plays an important role in brain development as it is involved in promoting or preventing cell death, depending on the stage of development. These receptors essentially help determine what neurons to keep and what neurons to get rid of. If you put nicotine into your brain by vaping, smoking or oral tobacco use during this time it can disrupt the fine tuning of your brain.

Endocannabinoid receptors are present all over the brain and they also play a big role in brain development during adolescence. Even though marijuana has been around for centuries, we did not really know why people liked it until the 1960s when people working in a lab in Israel were injecting different cannabinoids from the plant into animals and when they gave aggressive Rhesus monkeys THC, they found that they became calm and sedate. They then discovered there was a receptor in the brain that THC fit into like a glove. They named it a cannabis receptor, and this is sad because that made people believe we have a receptor in our brain that means we are supposed to smoke cannabis. That is NOT TRUE! This same lab group then discovered in the 1990s why we have this receptor. They discovered that our brain makes chemicals, one of which they named “anandamide” which is a Sanskrit word for “supreme joy” or “bliss” and these chemicals are responsible for balancing us and regulating our mood. The endocannabinoid system is our homeostatic system, balancing excitatory and inhibitory neuronal activity. The brain makes the decision when these chemicals are needed, makes them locally and they are used and then destroyed. THC looks identical to anandamides but is a fat-soluble chemical that can sit in the receptor for a long time and not allow your natural anandamides to work. When you use marijuana during adolescence this can disrupt synaptic pruning in the prefrontal motor cortex, disrupting normal brain development.



What are the most important messages to remember?

Adolescence is an exciting time. You are learning new things every day and putting them into practice. However, you need to understand that your brain is not fully developed, especially the part that helps you make good decisions and control impulses that may get you in trouble. It is also a stressful time in that you are expected to become more independent from your parents and make choices on your own. You also have a peer group that can influence you in many ways, positive or negative, depending on the peers you chose. You are encouraged to make healthy choices which include:

1. Waiting on making the decision to use addictive drugs like alcohol, nicotine, and marijuana (and other drugs) until you are in your mid-20s and your brain is fully developed.
2. Recognizing if you have any things in your history that put you at higher risk of becoming addicted faster, such as being raised in an environment where you are exposed to people smoking drugs (tobacco, marijuana, or any other addictive drug) or having adverse childhood experiences such as trauma or abuse and asking people for help to deal with these things in your environment.
3. Focusing on ways to achieve natural highs – which release dopamine and help you feel good like sports, music, dance, crafts etc.
4. Choosing healthy peers to hang with, who you can turn to for support.
5. Learning a skill like mindfulness. This is an important skill to learn that helps you learn to focus on the present moment and at the same time being aware of what you are sensing and feeling in the moment without interpretation or judgement. Practicing mindfulness includes breathing methods and things like guided imagery that relax your body and mind and help relieve stress. This takes practice but works out better for you in the long run, rather than reaching for a “quick fix” from an addictive drug to relieve stress.