The Neurobiology of Addiction

For Beginners

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One Step Rehab

Learning Objectives

By the end of this module you should:

I. Have an understanding of how the brain's reward system drives addictive behavior

II. Understand the working definitions of addiction according to two prominent medical bodies:
   - The American Society of Addiction Medicine.
   - The National Institute on Drug Abuse

III. Understand the primary and chronic nature of addiction as a disorder

IV. Have a basic understanding of the role that brain plasticity plays in addiction

V. Have a basic understanding of why treatment is necessary for addicted people.

Contents

1. Is Addiction Really a Disease?

The idea that addiction is a genuine medical disease is a controversial one. Nevertheless, two of the world's largest medical bodies researching addiction - The National Institute on Drug Abuse (NIDA) - and The American Society of Addiction Medicine (ASAM) - both define it in this way. While they use slightly different terminology they are saying approximately the same thing.

According to NIDA;

> *"Addiction is defined as a chronic, relapsing disorder characterized by compulsive drug seeking and use despite adverse consequences. It is* ***considered a brain disorder, because it involves functional changes to brain circuits*** *involved in reward, stress, and self-control. Those changes may last a long time after a person has stopped taking drugs."*[1]

And according ASAM;

> *"Addiction is a treatable,* ***chronic medical disease involving complex interactions among brain circuits****, genetics, the environment, and an individual's life experiences. People with addiction use substances or engage in behaviors that become compulsive and often continue despite harmful consequences. Prevention efforts and treatment approaches for addiction are generally as successful as those for other chronic diseases."*[2]

One definition (NIDA's) uses the word 'disorder', and the other (ASAM's) uses the word 'disease'. But these terms are virtually interchangeable.

2. Addiction as a Brain Disease/Disorder.

In order to define something as a disease, three conditions need to be present. There needs to be;

1. A specific location in the body
2. A specific dysfunction within that part of the body
3. A specific set of symptoms that marks this illness as distinct from other illnesses

With addiction all three of these are well known. Firstly, as ASAM and NIDA make clear in their definitions **addiction is a brain based illness.** This is sometimes difficult for people to accept because they can't see it. We can only see what's happening on the outside. we can see that addicted people's behavior is out of control, and the physical signs of them getting sicker, such as overeaters who have become obese, alcoholics who have liver disease, or injecting drug users who have blood borne viruses. What we can't see is the thing that's causing them all to behave this way, because that's on the inside.

To get really specific, addiction is predominantly a **limbic-brain** illness. The limbic brain is an ancient part of the brain that regulates basic instincts and survival drives. Think of it as the 'emotional brain' or 'animal brain'. The part of the limbic-brain that is dysfunctional with addiction is a group of brain cells that are connected by a pathway called the **reward circuit**. The reward circuit also influences other limbic-brain functions like **motivation, memory,** and **learning.**

As well as the limbic brain, addiction also affects another more recently evolved brain structure called the **cortex** which is sometimes called the 'mammalian' or 'human' brain because it only exists in mammals and is only highly developed amongst the higher mammals likes apes (including humans). The cortex regulates things like **decision-making** and **impulse control.**

The reward circuit begins in the limbic brain and works its way up to the cortex. A good way of thinking about addiction is to imagine the older, instinctive animal brain gaining the upper hand over the more newly evolved, rational human brain. As addictive behavior progresses these brain regions stop communicating with each other and the 'animal instincts' take over.

This brain malfunction (non-communication between limbic and cortical brain structures) causes some of the **external symptoms** of addiction that we all know so well:

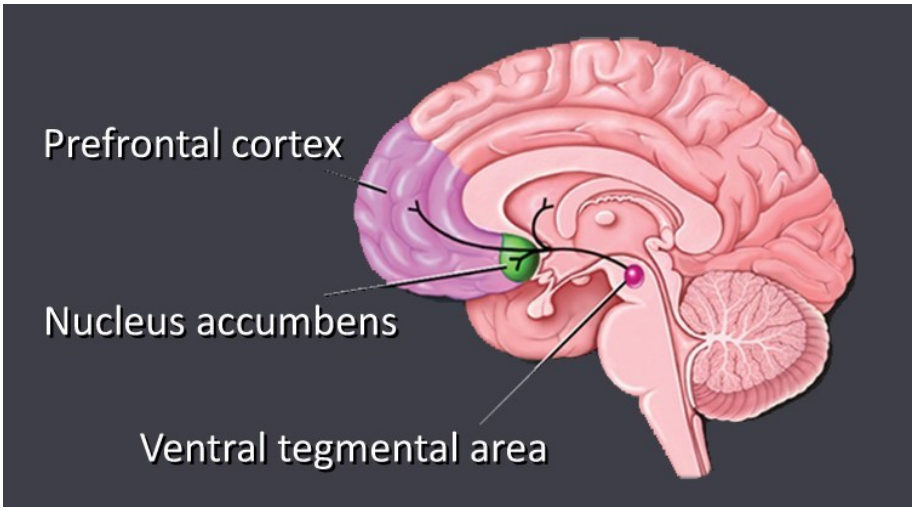
- Compulsive reward seeking
- Impaired decision making
- Dysfunctional emotions
- Inability to stop despite harm

3. The Reward Circuit & Dopamine

So how exactly does the limbic brain 'take over' or 'h□ack' the cortex? As you can see in Fig. 1. there are three distinct brain areas that make up the reward circuit and influence addictive behavior. These are;

- The ***Ventral tegmental area*** (VTA)
- The ***Nucleus Accumbens*** (NA)
- The ***Prefrontal cortex*** (PFC)

Fig 1. The brain's dopamine pathway (or reward circuit)



The reward circuit begins in the VTA which manufactures a **neurotransmitter** called **dopamine**.[3] Dopamine gets released from the VTA whenever we anticipate or actually experience something useful for our survival. So whenever we are in the presence of a reward like food or sex, lots of dopamine gets fired off from the VTA and works its way up to the Nucleus accumbens. Whenever a big shot of dopamine hits your Nucleus accumbens you will experience a feeling of reward, like something important is happening that you should take notice of. Dopamine evolved for this reason. It helps us to notice rewards and then move towards them. Without it we wouldn't notice anything that was necessary for our survival and we would die.

4. Natural Versus Unnatural Rewards

Things which human beings experience as highly rewarding are usually things which were present in our ancestral environment. We call these things "natural rewards".

- Calorie dense foods (such as sweet or fatty foods)
- Sex and nurturing (or other useful social interactions)
- Resource gathering & status. (Winning in competition, being high up in the pecking order, or getting your hands on useful 'things')

There are however, a long list of *unnatural rewards* which have also managed to 'hack' our brain's reward circuit. Below are the most common examples of unnatural rewards that addicted people use. You will notice that they are a kind of fake substitute for natural rewards;

- Drugs (are a kind of fake 'resource' or energy source)
- Gambling (wins)
- Gaming (wins)
- Smartphones + social media (likes)
- Pornography (sex)
- Money (status)

Dopamine rewards us for engaging in these behaviors regardless of whether they are natural or unnatural. Our brain's dopamine system can't tell the difference between pornography and sex, or indeed, between candy and heroin. All it cares about is the dopamine. If a thing gives us energy, status, resources, calories, love or sex then it's worth noticing in evolutionary terms. Dopamine **reinforces** survival behavior.

5. Brain Plasticity & Addiction

Specifically, dopamine reinforces the association between a particular 'thing' (a drug for example) and the sequence of behaviors that led to acquiring and consuming that thing. Those brain areas that were active when the drug was encountered are literally bathed in dopamine. In this way dopamine helps to associate people, places and things (and even sights and sounds and smells) with the drug.

Now, remember that NIDA saw addiction as a brain disorder because it involved "**functional changes to brain circuits.**" Well every time the connection is made between the useful 'thing' (the 'drug' in this case) and the sequence of behaviors associated with getting it, the connection between them gets stronger.

Neuroscientists refer to this process as '**long-term potentiation**' or LTP. LTP is a process whereby the messages between brain cells gets quicker and stronger. You can remember this with the following phrase:

"Brain cells that fire together, wire together"[4]

The following analogy might help you to understand it in more simple terms.

Imagine the top of a mountain as your VTA (which releases the neurotransmitter dopamine) and imagine that the bottom of the mountain is your *Nucleus Accumbens* (which receives the dopamine). Imagine that there is a ski-run that goes between the two. This is like the reward circuit that runs between the two brain areas. As any skier will tell you, the more you ski down the exact same route, the faster it becomes. This is how brain pathways work as well. The more we use them, then the faster and stronger they become. The opposite is also true. The less we use them, the weaker they become.

LTP is the active ingredient in 'brain plasticity'. Brain plasticity is the ability of the brain to mold itself and grow new connections in response to learning, or in

response to the environment. So with addiction, learning about which things are highly rewarding, and then doing them again and again actually changes the brain's structures.

In some scientific studies it has been shown that a single exposure to an addictive drug like cocaine can initiate the process of LTP in dopamine-releasing brain cells, particularly in the VTA (which manufactures dopamine, remember).[3]

This is why addicts can get a sudden 'rush' of excitement or anticipation when they see, hear, or smell something that reminds them of their drug. They are actually getting a big slug of dopamine because the process of LTP has strengthened the connections between the part of the brain that feels the effect of the drug – with the part of the brain that registers the environment it was taken in. **The drug and the things that are associated with it have become intertwined**.

In a way then, addicted people are actually more addicted to the processes, rituals and habits that are laid down and reinforced by the release of brain dopamine, than they are to the drug itself.

Of course, some people are physically addicted to drugs. But this is an entirely separate thing to addiction. **Physical dependence and addiction are not the same thing**. You don't need to be physically dependent on a drug to be addicted to it. Only some drugs (like alcohol, opioids and benzodiazepines) cause physical dependence, and there are many others drugs and addictive processes like gambling that do not create physical dependence. Physical dependence is not a criterion in deciding whether a drug or behavior is addictive or not. Psychological cravings are a far more reliable indicator of the presence of addiction than physical dependence.

6. Dopamine Depletion

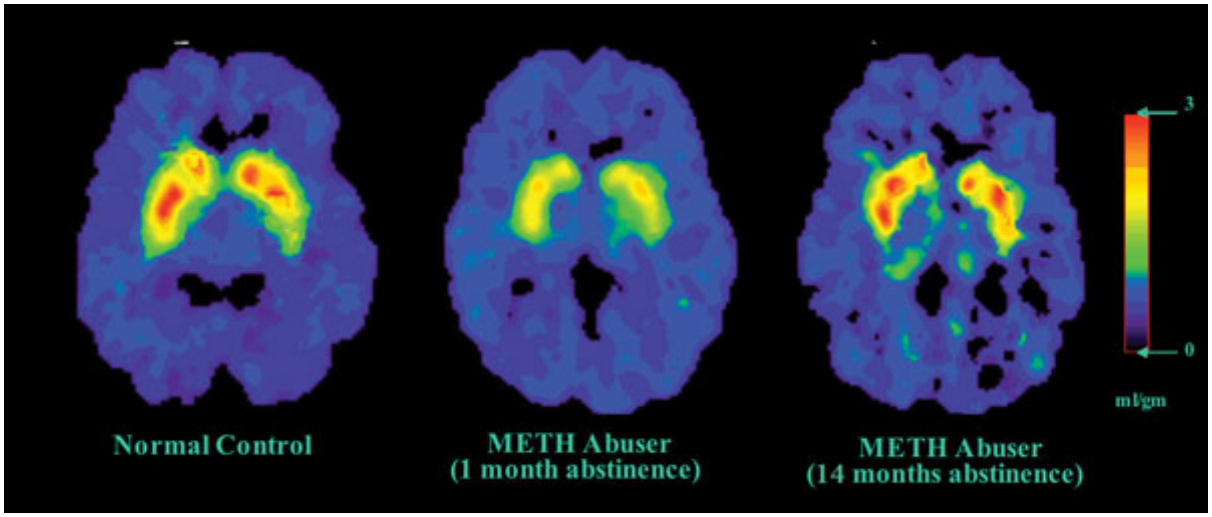
Other brain changes that occur through the process of becoming addicted include changes to the prefrontal cortex (PFC) and the way it sends messages back to the limbic brain.

Think of the limbic brain regions as the brain's 'GO" system (or green light) and think of the PFC as the brake (or red light).

The PFC's job is to be the brain's executive decision maker and exhibit good judgement and sound reasoning as to which behaviors are safe to engage in and which SHOULD BE STOPPED. In people who are actively addicted this process becomes impaired and they are increasingly unable to control their impulses OR STOP THEIR BEHAVIOR. Interestingly, this is only in relation to drugs and their cues, not in relation to other areas of life where the individual can often continue to display perfectly sound reasoning. This is because LTP has strengthened the neural connections in relation to taking rewards like drugs **but not to anything else**.

Another reason is that dopamine receptor sites which receive dopamine from the VTA start to die off with heavy drug use. This phenomenon is known as **dopamine depletion** (see fig. 2). Dopamine depletion (death of dopamine receptor sites) occurs because unnatural rewards like drugs produce much bigger bursts of brain dopamine than natural rewards like food. If we imagine rewards as sounds, then we can imagine that the dopamine signal coming from heroin or alcohol is much louder than the signal coming from other 'normal' rewards like eating or socializing. In response, the reward circuit begins to produce fewer brain cells that can receive dopamine (receptor sites) in an effort to "turn down the volume". This results in the person having less receptor sites, and therefore, a lowered feeling of reward. They will then need bigger and bigger doses of dopamine to get the same effect and become caught in a viscous cycle.

Fig. 2 Dopamine depletion in an active drug user.



Here we see a non-drug user (left) who has healthy dopamine function (indicated by red). An active drug user (center) has very little dopamine function. On the right is the same drug user in recovery with restored dopamine function. (Source: NIDA website)

So dopamine depletion (a lower density of dopamine receptor sites) leads to the phenomena of **tolerance**. Tolerance is a form of **neuro-adaptation** (brain change) where you need more and more of a drug to feel its effects. In reality, addicted people are becoming dopamine tolerant as well as tolerant to their specific drug of choice.

So this is where we see the ancient brain areas (limbic system) that control reward, gaining the upper hand over newer brain area (the cortex) that controls reasoning. This and this is how our brain evolved to work. It's just that in this situation (addiction) the natural evolved function of the brain is working against us.

So perhaps we should be asking another question. The question is "why do some people prioritize drugs as a survival need more than others?

7. Reward Deficiency

The dopamine depletion model put forward by NIDA assumes that the drug is causing the addiction. That may sound obvious, but there are many other models of addiction which, while agreeing on the neuro-anatomy we have already outlined, interpret the findings differently. Some models of addiction would maintain that "addiction" actually **precedes drug use**. That probably sounds pretty counter-intuitive and so it will need a bit of explanation.

In 1988, two Italian researchers called *Gaetano Di Chiara* and *Assunta Imperato* proved that regardless of the class of drug, all drugs (whether sedatives, stimulants, opioids or even nicotine) achieve their effect by releasing dopamine at the *Nucleus Accumbens*.[4] Multiple studies since seem to concur that all drugs and behaviors that are addictive, use the brains reward circuit (and therefore dopamine) to achieve their effects.

Then in 1990, *Ken Blum* and *Ernest Noble*, two American researchers, found that people who were low in dopamine receptor sites (presumably from birth) were more susceptible to alcoholism, drug addiction and numerous other compulsive behaviors.[5]

This led them to speculate that the 'disease' of addiction was actually more likely to be a genetic condition which preceded drug use. People who had less dopamine receptor sites felt more naturally unrewarded and were therefore more likely to get a medicinal effect from any drug they took and also more likely to repeat it.[6] *Blum* termed this condition, **Reward Deficiency Syndrome** (RDS).

In the RDS model, people are seen to use drugs in order to self-medicate a natural lack of mid-brain dopamine function, which leaves them feeling miserable and un-pleasured unless they can find a source of dopamine strong enough to fix it (like drugs).

It's worth noting ASAM's original definition at this point;

"Addiction is a treatable, chronic medical disease ***involving complex interactions among brain circuits, genetics, the environment****, and an individual's life experiences."*

Whilst some people may be born 'low-dopamine' due to genetic variation, the same condition might also be created by environmental conditions, including excessive drug use.

Environments that are consistently unrewarding (especially in early childhood) may well have an effect on the development of dopamine receptors, and as we have already seen, repeated drug use can, in and of itself, destroy dopamine receptors sites. It all ends up with the same result. A person who feels catastrophically unrewarded, and who therefore needs to boost their mid-brain dopamine by any means necessary (drugs, food, sex etc.)

8. Why Do We Need Treatment?

Going back to NIDA and ASAM's definitions we should note that both definitions use the word the 'chronic' when describing addiction as a disease. So what does the word 'chronic' mean?

Unlike an acute illness (which can be eliminated by medicine or by the body's immune system) a chronic illness is one that doesn't go away. In other words - it's probably incurable. And while that sounds like bad news it's actually quite common. Many diseases are chronic conditions (such as diabetes for example). The good news is that when chronic diseases like addiction and diabetes are treated effectively the symptoms go into remission and the person can lead a relatively normal life (providing they continue treating the illness).

This is a very important point for people who are living with addiction to understand because it explains why people still relapse after years of sobriety. When you begin to unpack the reason for a person's relapse, it almost always comes down to the same thing. They stopped taking the illness seriously because they thought they were cured!

The two distinct areas of addiction treatment are:

- Medical interventions
- Ongoing psychological support (such as psychotherapy or mutual aid groups like Alcoholics Anonymous)

Obviously if an addicted person has been using a dependence forming substance like alcohol or opioids for some considerable time period, then they will most likely be physically dependent on that drug and will require medical supervision to reduce or taper themselves completely off that drug. But it is important to note that removing the physical dependency does not remove the addiction for all the reasons we have noted. Addiction is a condition that

most likely exists **before, during, and after** any relationship you might have with a particular drug. Ultimately, addiction is not to do with drugs. It is to do with self-medicating unrewarded feelings. If we don't address this underlying fact, then another source of brain dopamine will rapidly replace the one we have just removed (such as smokers who quit and then go on to gain massive amounts of weight due to overeating – just to give one example).

The prognosis (outcomes) for addiction treatment are actually very good. Studies have shown that abstinence results in bursts of neurogenesis (re-rowth of brain cells).[7] The important thing is that you understand that the addiction isn't gone in two weeks after having a detox. It will always be there due to the amount of dopamine driven cues and associations that are retained by your brains memory and learning systems. Should you be tempted to try a bit of 'controlled' drug use, you will most likely find that your brains reasoning faculties (PFC) let you down eventually. Therefore, it is best to come to terms with living with the illness, and working what is known as **a program**.

A program is way of living that seeks to find healthy, long-acting, and slow release sources of brain dopamine. This could include many things but below are a few common examples:

- *Boosting your self-esteem so you don't feel 'less than' others* - Stopping drug use is the first part of this process, and starting to re-build your life is the second.
- *Bringing an end to your isolation* - by belonging to a group of some sort that you can identify with, such as a support group or sporting activity*
- *Increasing feelings of meaning and purpose* – common examples would be spiritual or religious practice such as becoming interested in meditation retreats or re-connecting with your cultural faith.
- *Being of service to others* – helping others and locating our interest outside of ourselves seems to be highly dopamine reinforcing. It's as

though we are doing something of great importance. As the saying goes – “help one person – help the whole world”

**See Index for a list of self-help organizations relevant to addictive disorders.*

9. Summary

To summarize, in this module we have learned that:

- Addiction is a chronic (incurable) illness
- It is located in the brain
- It is predominantly a dopamine-based illness that affects our ability to feel reward.
- Other brain regions are affected too – especially memory, learning and impulse control.
- Dopamine helps us to target useful rewards like food, but this natural process has become dysfunctional in addicted people.
- When people start taking drugs, a process called LTP helps to strengthen the brain networks that are relevant to that drug (including environmental cues)
- People who have poor dopamine function from birth (or due to adverse early environments) are more likely to target drugs because the rewarded feelings they get when they take them compensate for poor mid-brain dopamine function.
- This can lead to dopamine depletion because the dopamine signal is "too loud" and causes the brain to kill off dopamine receptor sites leaving the person even more unrewarded than they were to begin with.
- Treatment is necessary because addiction is a chronic illness. Chronic illnesses need to be treated, they cannot be 'cured' (or rarely).
- Recovery activities work in a safer way than drugs to restore mid brain dopamine function. Being part of something, identifying with others, and finding potent sources of meaning are the most effective long term medicines for additive disorders.

Quiz

Answer the following questions as True of False

1. Addiction is an acute illness?
2. Acute illnesses are usually curable?
3. Dopamine is a hormone that helps us to sleep?
4. Addiction is a chronic illness?
5. Dopamine is a neurotransmitter that helps us experience a feeling of reward.
6. Addiction affects memory and learning?
7. The pre-frontal cortex regulates impulse control?
8. Dopamine is manufactured in the Ventral Tegmental Area?
9. Heroin is a natural reward?
10. LTP is the process whereby synaptic connections between brain cells are strengthened in the brain
11. If someone is not physically sick when they stop taking a drug, then they can't be addicted?
12. Reward Deficiency Syndrome is a theory of addiction that states that some people have less dopamine receptor sites are more likely to become addicted
13. Treatment is necessary for addicted people because they are suffering from a chronic illness?
14. Medical interventions like detox are the only effective treatment for addiction?

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A List of Alcohol & Substance Abuse Programs

A List of Behavioral Addiction Programs

- Food Addicts Anonymous
- Food Addicts in Recovery Anonymous
- Gamblers Anonymous
- Kleptomaniacs & Shoplifters Anonymous
- Love Addicts Anonymous
- Obsessive Compulsive Anonymous
- On-Line Gamers Anonymous
- Overeaters Anonymous
- Self-Mutilators Anonymous
- Sex Addicts Anonymous
- Sex and Love Addicts Anonymous
- Sexaholics Anonymous
- Sexual Compulsives Anonymous
- Sexual Recovery Anonymous
- Spenders Anonymous
- Workaholics Anonymous

Non-12 Step Recovery Programs

- SMART Recovery
- Refuge Recovery

Resources & Further Reading

- Alcoholics Anonymous @ www.aa.org
- Gamblers Anonymous @ www.gamblersanonymous.org
- Overeaters Anonymous @ www.oa.org
- Narcotics Anonymous @ www.na.org
- Sex Addicts Anonymous @ www.sexaa.org
- Dual Recovery Anonymous www.draonline.org
- SMART Recovery @ www.smartrecovery.org
- Refuge Recovery @ www.refugerecovery.org

References

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2. www.asam.org/resources/definition-of-addiction

3. Zickler, Patrick, "Addictive Drugs and Stress Trigger Similar Change in Brain Cells, Animal Study Finds," NIDA Notes Research Findings, Vol. 18, No. 5 (December 2003).

4. See; Doidge, N. “The Brain that Changes Itself” (2007).

5. Di Chiara and Imperato “Drugs Abused by Humans Preferentially Increase Synaptic Dopamine Concentrations in the Mesolimbic System of Freely Moving Rats”. August 1988Proceedings of the National Academy of Sciences 85(14):5274-8

6. Blum K, et al. ‘Increased prevalence of the Taq I A1 allele of the dopamine receptor gene (DRD2) in obesity with comorbid substance use disorder: a preliminary report.’ Pharmacogenetics. 1996 Aug;6(4):297-305;

7. In 2006 Nora Volkow, the president of NIDA, also found evidence that people who have more dopamine receptors than the average person were less likely to become addicted than other people. See; Volkow ND, Wang G, Begleiter H, et al. High Levels of Dopamine D2 Receptors in Unaffected Members of Alcoholic Families: Possible Protective Factors. Arch Gen Psychiatry. 2006;63(9):999–1008. doi:10.1001/archpsyc.63.9.999

8. Crews FT, Nixon K. Mechanisms of neurodegeneration and regeneration in alcoholism. Alcohol Alcohol. 2009 Mar-Apr;44(2):115-27. doi: 10.1093/alcalc/agn079. Epub 2008 Oct 21. PMID: 18940959; PMCID: PMC2948812.