Neurobiology of Addiction

By
William Santoro, MD FASAM, DABAM

Addiction, now often referred to as “substance use disorder,” is a primary, 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. The brain circuitry addiction effects are those of reward, motivation, learning, judgment, and memory. The dysfunction of addiction leads to characteristic biological, psychological, sociological and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use. Addiction can be defined as a chronically relapsing disorder, characterized by compulsion to use a substance, loss of control in limiting the use of a substance, and emergence of a negative emotional state, withdrawal, when access to the substance is prevented. DSM-5 combined two separate disorders, substance abuse and substance dependence, into substance use disorder (Addiction) with a range of mild, moderate, to severe.

Addiction is characterized by the inability to consistently abstain from use, impairment in behavioral control, craving, diminished recognition of problems with behaviors, and diminished recognition of problems with interpersonal relationships. To separate addiction from other neurological disorders, four factors must be present. These four factors, compulsion, craving, consequences and control, are simply referred to as the 4 C's. Although no other chronic disease has the 4 C’s, addiction does have a lot in common with other chronic diseases. Like other chronic diseases, addiction involves cycles of relapse and remission. Like any other chronic disease, including diabetes, cancer, and heart disease, addiction is caused by a combination of behavioral, psychological, environmental, and biological factors. While genetics play a key role, it is estimated that they are responsible for only about half of a person’s risk of developing a substance use disorder. Without treatment or engagement in recovery activities, addiction is very often progressive and can result in disability or premature death. Addiction is considered a disease by most medical associations, including the American Medical Association and the American Society of Addiction Medicine.

People feel pleasure when basic needs, such as hunger and thirst, are satisfied. In most cases, these feelings of satisfaction are caused by the release of certain chemicals in the brain. Dopamine is believed to be the neurotransmitter (hormone) responsible for addiction, due to its role in producing euphoria. The difference between normal activity, other neurological disorders, and addiction is that substance use disorder causes the brain to release high levels of dopamine that causes extreme feelings of pleasure. Continued substance use causes the brain to release more dopamine, which ultimately results in changes in the brain’s reward and motivation systems as well as memory. Dopamine rewards the individual and as the individual commits the experience to memory, it sets the individual up to repeat the behaviors that produce those feelings. This is no different than how healthy habits are formed. In this sense, humans are no different than Pavolvian dogs or Skinner pigeons.

The normal developmental changes might result in higher risk for drug use at some stages of a person's life than other stages. Experimentation, and a path toward addiction, often begins in adolescence, a time when the brain undergoes important developmental changes. Beginning in preadolescence and continuing into the mid-20s, cortical grey matter volume decreases, part of the normal pruning process and white matter volume increases, resulting in increasing connectivity. Drug exposure during adolescence is associated with more chronic and intensive use and greater risk of a substance use disorder than when the use is started at a later age. Normal adolescent-specific behaviors such as risk-taking, novelty-seeking, and sensitivity to peer pressure, increase the liklihood to experiment with legal and illegal drugs. These activities may be due to incomplete development of brain regions that are involved in executive control and motivation. Heavy alcohol use during adolescence is associated with a range of neurobehavioral problems, including impairments in visuospatial processing, attention, and memory. Adolescents who drink heavily have had faster declines in the grey matter and smaller increases in white matter volumes than adolescents who were not heavy drinkers.

Certain environmental factors such as low socioeconomic status, weak social support systems, parental drug use, parental depression, general poor parenting, and drug availability due to poor neighborhoods have been associated with increased risk of drug use. Stress is also a common feature that increases the risk for drug abuse. The mechanisms responsible for increased risk of drug use due to stress are not yet well understood but is likely due to the stress-responsive neuropeptide, corticotropin releasing factor (CRF) through its effects in the amygdala and hypothalamic-pituitary-adrenal axis, part of the pleasure center of the brain.

As a person continues to use substances, the brain tries to get back to a balanced state by reacting less to those rewarding chemicals. This is called adaptation. As a result, a person may need to use more of the substance just to feel the same way they felt with lower amounts. This is called tolerance. Neuroadaptation refers to the processes by which initial drug effects are either enhanced (sensitization) or attenuated (counteradaptation) by repeated drug exposure. Drug-related responses (reinforcement) are modulated by the neuroadaptive changes that occur with repeated drug exposure. Addiction alters the brain's mesolimbic dopamine pathway, also known as the reward circuit, which begins in the ventral tegmental area (VTA) above the brain stem. Dopaminergic neurons arise in the VTA, and their axons extend to the nucleus accumbens. Disruptions in these three areas of the brain, the prefrontal cortex, the VTA, and the nucleus accumbens are particularly important in the onset, development, and maintenance of substance use disorders.

Adaptation and tolerance result in a person having strong desires or urges to continue to use a substance to revisit the sensation the release of dopamine will give, even if there are harmful or dangerous consequences. Furthermore, with many substances a person may continue to use simply to avoid feeling sick (withdrawal). As the pattern of use causes more dopamine to be released and used, the result is a lower baseline of dopamine. When the use stops, the deficit of dopamine causes the reverse sensation that the substance use caused. This is called withdrawal. Once this damage has occurred, the brain can heal, but it takes time. Normal,

healthy dopamine production depends on a wide variety of factors, but many medical professionals believe that the brain's dopamine production will return to pre-substance misuse levels over a period of about 90 days. Because of the time needed, those with a substance use disorder are at risk of returning to use due to triggers. A common term to describe triggers used by those in recovery is, “people, places and things.” A trigger can be meeting up with a person who the patient has used with in the past, going to a restaurant or bar the patient used to frequent, or simply seeing a glycine envelope from a package. Many people can be triggered to use by seeing substance use in a movie or hearing a song associated with their previous drug use.

The goal for someone with an SUD may be to stop them from using substances entirely. However, it is important to take whatever steps needed to reduce the risks associated with substance use. In the case of opioid use disorder these strategies include the use of fentanyl test strips, needle exchange programs, expanding the access to naloxone, and even the creation of safe injection sites along with medication such as naltrexone, buprenorphine, or methadone.

Some people think addiction is not a disease because it is caused by the individual’s choice to use substances. While it is true that a person’s first use, and even into a person’s early use, there may be a choice, however, once the brain has been changed by addiction, the person loses control of their behavior. Choice does not determine whether something is a disease. Heart disease, diabetes and certain skin cancers involve personal choices like diet, exercise, and sun exposure. A disease is what happens as a result of those choices. Others argue that addiction is not a disease because some people with addiction get better without treatment. Most people who engage in substance use do not develop addiction, and many young people tend to reduce their use once they take on more adult responsibilities. People with a mild SUD may recover with little or no treatment. People with the most serious form of SUD usually need intensive treatment followed by lifelong management of the disease. However, some people experiencing addiction stop drinking or using other substances without treatment. Others achieve recovery by attending self-help meetings without receiving much, if any, professional treatment. Still, about 25-50% of people with a substance use problem develop a severe, chronic disorder. A chronic disease is a long-lasting condition that can be controlled but not cured.

In all cases, professional treatment and recovery supports should be made available to anybody who develops a substance use disorder. Addiction is a brain disease resulting in long-lasting changes in brain structure and function, specifically in the reward system. Advances in neurobiology have provided crucial insights into how addiction works, leading to the development of effective treatments. A combination of pharmacological and behavioral approaches offers the best chance for individuals to overcome addiction and lead fulfilling lives in remission or recovery. Remission is when a person decreases their use to a level that they no longer reach the criteria for substance use disorder. Recovery includes an improvement in the social determinants such as employment and a reconnection to family. Recovery occurs after remission. Bottomline… addiction is a treatable disease.