The Adverse Effects of Cocaine on the Adolescent Brain

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BRIEF. Researches have observed the drastic consequences of cocaine to be greater when used during adolescence, as it stunts the development and growth of the brain.

ABSTRACT. Drug abuse, specifically cocaine, is a growing problem in several countries today. Cocaine use not only leads to numerous disorders and fatalities every year, but induces lifelong consequences on the brain and cognition. If the brain is in an ongoing state of development (e.g., adolescence), these damages are augmented, and the chance of recovery decreases. Neurobiologically, consistent cocaine use induces alterations in levels of gray and white matter in regions like the orbitofrontal cortex, amygdala, caudate nucleus, and others. In addition, these structural changes lead to impairments in cognitive functions including working memory and attention. Though treatments are being developed for addiction and cocaine use disorders, abstinence plays a pivotal role in the recovery of brain matter and function. However, individuals who begin using at an earlier age do not regain as much gray and white matter as older individuals do, demonstrating the idea that the brain is profoundly more vulnerable during its maturation.

INTRODUCTION.

The immaturity of the brain in individuals aged 12-17 plays a vital role in the risky and emotional behavior that tends to characterize teenagers. This period of learning, independence, and forming new relationships is also a period of vulnerability. At this age, kids become independent from their parents, and are faced with pressures and expectations from their family, friends, peers, and social media, while also going through physical changes. Because of the developing state of their brains, teenagers respond to stress differently than adults, as the areas of the brain that are especially sensitive to stress responses, and involved with memory, attention, and learning are all structures yet to mature [1]. Consequently, teenagers are more vulnerable when put under stress for a longer period of time, and their decision making and cognitive skills may be compromised.

The lack of proper decision making and rationality combined with numerous stress factors and pressure is part of the reason why substance abuse is a rising problem in adolescents today. The 2020 National Survey on Drug Use and Health showed that 1.9% (5.2 million people) of those 12 and under in the United States reported using cocaine within the past year. Additionally, 0.5%, or about 1.3 million people, had a cocaine use disorder [2]. In a different survey in 2021, about 0.2% of 8th graders, 0.6% of 10th graders, and 1.2% of 12th graders were found to be cocaine users within the past year. Aside from deaths, overuse of this drug causes serious and long-lasting health problems that affect a person's quality of life. In 2015, approximately 18,885 hospitalizations, and 9,401 Emergency Department (ED) visits occurred for cocaine-related poisonings in the U.S, and relapse rates for substance use disorders were found to be 40-60% [2], [3]. Not only is the use of this drug threatening to physical well-being, but it also induces adverse and long-lasting damages to the brain, especially if used in adolescence.

This paper provides an in-detail explanation of cocaine's effects on the developing brain, as well as long term disorders and treatments.

THE DEVELOPING BRAIN.

In the early years of life, the brain is highly susceptible to change as a result of external stimuli. The experiences that someone faces are crucial to the brain's proper functioning and behavior later in life. Though the plasticity of the brain - or its ability to change over time - is at its highest in infancy, the brain does not fully mature until about 25 years of age [4]. During these years, the brain undergoes different periods of growth, called critical periods, each period being important for a certain skill or function [5].

A critical period is a set time of heightened growth and plasticity during which the brain will modify itself to be fit for the environment that it is in. Different structures and brain functions will experience these periods at different times. For example, the critical period for vision may not occur at the same time as the critical period for smell or taste [5]. On a neurobiological scale, the brain is producing millions of neurons, and therefore synapses, both before and after birth. This excessive production of synaptic connections is soon followed by a gradual reduction of them in a highly experience-dependent process known as synapse pruning [4]. This is a series of weakening connections that the individual doesn't need or use, and strengthening ones that make them fit for their environment, also known as the "use it or lose it" principle [6]. The abilities that develop in the early years of life are a foundation to prepare the individual for the development of higher cognitive functions later in life [4].

Adolescence is a critical period for the maturation of several major areas of the brain, including the parts of the limbic system, which is composed largely of the hippocampus and amygdala, and the prefrontal cortex. In the teenage years, the limbic system is further developed than the PFC, which is yet to fully mature. This imbalance adds to the likelihood of teens to take risks and make impulsive decisions, and makes them vulnerable to drug abuse, and substance use disorders later in life [7].

THE EFFECTS OF COCAINE ON THE BRAIN.

Cocaine is most well known as a highly addictive stimulant drug that causes pleasurable sensations. Cocaine's major target is the mesolimbic dopamine system, which extends from a midbrain region called the ventral tegmental area to various other brain structures, including the amygdala, prefrontal cortex, and the nucleus accumbens, which is a primary reward region in the brain [2], [8]. In these regions, cocaine blocks dopamine transporters, so that they are activated for a prolonged period of time. The activity of the dopaminergic pathway strongly motivates behavior towards pleasurable experiences. In other words, this excessive stimulation of dopaminergic neurons reinforces the habit to continue taking the drug, and is what causes the euphoric feeling that drug users are looking for.

The orbitofrontal cortex, which is a brain region responsible for decision making, is also influenced by exposure to cocaine. Research has found a strong negative correlation between gray matter volume in various brain regions, including the orbitofrontal cortex, and the duration of cocaine use [9]. These cocaine-induced adaptations in the orbitofrontal cortex are thought to lead to compulsivity, or a lack of control over decisions and processing of consequences. This contributes to continued drug use and addiction [10]. In rhesus macaques, there was found to be a decrease in GMD in the orbitofrontal cortex and the lateral parietal cortex, along with a correlated decrease in performance on cognition-related tasks after a period of self-administration of cocaine [11].

In this same experiment, a decrease of gray matter in the amygdala as a result of cocaine use was also observed. Since the amygdala is still in a developing stage during adolescence, drug use may result in stunted development and potentially cause serious deficits in emotional regulation if cocaine use is consistent.

After a 24-month period of abstinence, the GMD in the orbitofrontal cortex and the amygdala showed no significant change, implying that the cocaine-induced shrinking of these regions was permanent. Thus, the use of cocaine over several months or years has a direct and irreversible effect on the GMD in these regions, and is a contributing factor to the risk of relapse [11].

Other changes in gray matter after prolonged cocaine use include GMD decreases in the insula and temporal cortex, and increases in the caudate putamen. The volumetric change in the caudate nucleus is linked to attentional impairments in cocaine users [9]. The reason for this brain region having an increase in GMD, as opposed to other brain regions having a decrease in GMD is still unclear [11]. It has also been found that gender differences exist in cocaine users; female cocaine users demonstrated greater gray matter volume in regions such as the frontal gyrus, thalamus, and caudate after cocaine use compared to men [12].

Aside from gray matter, white matter changes have also been observed in relation to cocaine use. Greater duration of cocaine use is associated with decreased white matter volume in the inferior frontal region, which is part of the prefrontal cortex [13]. A study revealed that, in subjects who are unexposed to cocaine, white matter myelination in frontal and temporal regions continues to increase with age up to about 47 years, but this growth is stunted in cocaine-dependent individuals [14]. Cocaine abuse causes delayed white matter maturation because it slows down the expression of myelin-related genes, therefore resulting in fewer proteins being formed [15], [16]. Myelination of axons contributes to faster communication between neurons, so the speed of signals in certain brain regions of cocaine users may be decelerated.

In an adolescent brain, these changes in gray matter, white matter and cognitive abilities increase susceptibility for developing a substance use disorder. Moreover, the detrimental effects of cocaine use last longer on a teenager rather than an adult [17]. Changes other than gray and white matter alterations also exist as a result of cocaine use, but are beyond the scope of this review [18], [19]. As explored later, some of the cocaine induced cognitive impairments are partially reversible for adults, which highlights a principal difference between a developing brain and an adult brain.

HOW IS THIS BEING TREATED?

There is no existing medication to reverse the effects of cocaine use. However, advancements are being made in the pharmacological field for treatments for those struggling with cocaine use disorder. For example, a vaccine for cocaine users creates antibodies that prevent the drug from entering the brain, but is limited to people who have high enough antibody levels [2]. With further research, the vaccine has the potential to help recovering cocaine addicts lower their risk of relapse. Moreover, researchers are looking for medications that target dopamine, serotonin, glutamate, and gamma-aminobutyric acid (GABA), which are all neurotransmitters affected by cocaine. Disulfiram, a medication that is typically prescribed for alcoholism, is being researched to help reduce cocaine use [2], [20]. One of the drawbacks, however, is that the effectiveness of this treatment is influenced by the genes of the patient; it may not be as potent in some patients as it is in others [2].

Aside from addiction, impairments in cognition and brain structure are also consequences of cocaine use. To partially reverse these changes, studies have found abstinence to be the key. As Jedema and colleagues [11] discovered, abstainers showed increased gray matter levels in the frontal, occipital, and temporal cortex after several months. Moreover, these GMD changes correlated with improvements in working memory, decision making, and other cognitive tasks. This implies that some of the damages caused by cocaine are transient, and recovery is possible over time. However, brain regions such as the OFC, caudate/putamen, and amygdala showed no significant signs of recuperation following a period of abstinence, perhaps due to lower neuroplasticity. The main weakness of this study is that it fails to address effects on individuals of different ages and gender; the study only tests adult male monkeys. Females, as well as children and teenagers, have different brain chemistry, so these results may differ if tested on a more diverse group.

In adults and adolescents alike, increased cocaine use negatively correlates with working memory function. However, Vonmoos and colleagues [21] found that individuals who started using at an earlier age showed less recovery than those who started at a later age. These findings support the idea that drug use in adolescence has greater long-term repercussions than drug use in adulthood.

CONCLUSION.

During adolescence, certain brain structures including the prefrontal cortex, amygdala, and hippocampus are not fully mature yet, and do not completely support their related functions. Partially due to this, teenagers may indulge in risky behaviors, including the use of cocaine. Consistent use of this drug decreases gray matter levels in certain brain regions such as the orbitofrontal cortex, amygdala, lateral parietal cortex, and others, leading to impairments in cognition. Abstaining from the use of this drug has reversing effects, allowing individuals to at least partially regain certain cognitive abilities and gray matter volume. Most existing cocaine studies focus primarily on adult subjects, but an adolescent-based study may provide helpful insight on the unique state of the brain when exposed to cocaine during those years, and give researchers more information on adolescent drug addiction.

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