The Neurobiological Effects of Substance Abuse

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**Why I Chose to Write on My Topic**

I chose to write on my topic in order to better comprehend how different kinds of drugs affect the various human neurobiological processes. It is usually easy to see when a person has abused a drug recently through different visual and behavioral cues. Their appearance may seem different than usual or they may act in a strange manner. Although we can easily see the external effects, what we don’t often see is just how that drug is specifically affecting their brain and neuronal functioning.

I felt that exploring this topic was important for me because there is a history of substance abuse, particularly alcohol, on my dad’s side of the family. None of my immediate family members abuse alcohol, but I know that I still have certain genetic predispositions that could put me at risk. Even though I have never abused any kind of psychoactive drug, I felt that researching this topic would give me deeper insight about how they affect behavior, emotions, thinking, and perceptions on a neurobiological level.

I have met people before who have abused certain kinds of substances and I also wanted to write on this topic to understand what was happening to them on a neurobiological level. When these people have explained their experiences with their preferred drug, I have always wanted to know on a scientific level what was happening to them when they abused it.

I also felt that this topic would give me a basic foundation needed for understanding the complex functions and interactions of various neurotransmitters and how they affect us neurobiologically and the roles they play in substance abuse. I also wanted to explore the possible effects of using multiple drugs at the same time and see what kinds of neurological side effects that type of abuse might have. I speculated that there might be some very adverse effects to this. I feel
that all of this will not only help me to continue to avoid abusing substances myself, but also allow me to help others avoid or overcome their addictions in a clinical setting.

**What the Research Says About My Topic**

The neurobiological effects that substance abuse can have are wide and varied. Since substances can have such a dramatic effect on brain and neuronal functioning, it is important to note how easily it can be to succumb to addiction, which will only act to continue the compulsive abuse of the preferred drug whether the substance is illegal or not. Many substances of abuse directly affect the pleasure circuitry of the brain by influencing the release of neurotransmitters. Commonly targeted neurotransmitters include dopamine (DA), serotonin (5-HT), gamma-Aminobutyric acid (GABA), and glutamate. Substances can influence these associated transmitter systems by acting as either an agonist or an antagonist on receptors, or by affecting reuptake of neurotransmitters, thereby increasing their effects on cognition and/or behavior.

One of the ways that cognitive functioning is affected by drug exposure is through interference of hippocampal information processing. Since the hippocampus is centrally involved in processing declarative memory and associative learning, any kind of drug-induced disruptions in this area will significantly alter cognitive abilities and behavior (Hernandez-Rabaza, Navarro-Mora, Velazquez-Sanchez, Ferragud, Marin, Garcia-Verdugo, Renau-Piqueras, & Canales, 2010). The hippocampus is one of many structures directly involved in the reward circuitry of the brain, and thus it is usually significantly influenced by drug-induced neurotoxicity that affects neurogenesis.

There is evidence that shows neurogenesis does indeed occur in the hippocampus, although the full interactions have not been entirely discovered as of yet (Sudai, Croitoru, Shaldubina,
However, it has been implicated that neurogenesis in the hippocampus may play a significant role in the process of creating and recalling certain types of memory (Sudai et al., 2011). Regarding the effects of cocaine-induced reduction in neurogenesis and memory cognition, Sudai et al. (2011) noted, “Furthermore, we believe that the difficulty in creating new memories could eventually evoke memories of past drug-induced behavior and as a result increase the propensity for drug relapse” (p. 259). There is quite a large body of literature that supports the idea that drug-induced neurotoxicity can greatly affect the hippocampal processes involved in memory.

A variety of neurobiological effects can stem from substance abuse. Most substances of abuse target areas associated with the reward circuitry of the brain and cause certain neuroadaptations that lead to addiction. Sudai et al. (2011) explains in their study, “It has been demonstrated that repeated exposure to substances of abuse result in brain region-specific neuroadaptations that correlate with the loss of the ability to control drug use” (p. 251). Sudai et al. (2011) continues to point out, “Accrued experimental evidence shows that addictive substances, such as alcohol, opiates, and amphetamines can negatively affect the self-renewal capacity of the hippocampus by impairing the long-term survival of neural precursors, or both” (p. 252). In their study, they found that cocaine in particular reduces cognitive performance by inhibiting the development and survival of newly generated neurons in the pre-frontal cortex and the hippocampus.

Cocaine abuse has been known to induce certain neuroadaptations that could lead to the inability to cope with stressful situations and any resulting anxiety, particularly after withdrawal (El Hage, Rappeneau, Etievant, Morel, Scarna, Zimmer, & Bérod, 2012). This further supports
evidence that suggests that cocaine abuse changes brain morphology. El Hage et al. (2012) noted that “Interestingly, neuroimaging studies in abstinent cocaine dependent patients and studies in rodents have consistently pointed to persistent structural and functional alterations not only within the mesolimbic dopamine reward system, but also in the PFC (especially in the orbitofrontal, cingulate and insular cortices) and some of its connected subcortical areas (amygdala, thalamus and hippocampus) (p. 1). We can see that the substances of abuse don’t just affect one area of the brain. They can set off a multitude of side effects since most brain areas are closely connected to one another.

Methamphetamine is a particularly dangerous drug when abused. Bortolato, Frau, Piras, Luesu, Bini, Diaz, Gessa, Ennas, & Castelli (2009) said in their study, “Methamphetamine (METH) is a highly addictive synthetic psycho-stimulant, which acts by enhancing the release and reducing the synaptic reuptake of the major monoamine neurotransmitters, including dopamine (DA) and serotonin (5-HT)” (p. 231). Their study found that acute administration of METH has been shown to cause a broad range of neurotoxic effects, particularly on 5-THergic and DAergic systems. Serotonin and dopamine systems in the brain are both central to emotional reaction to various stimuli. METH-induced damage to these neurotransmitter systems can cause a variety of altered behaviors including a reduction in novelty-seeking behavior, apathy, and a persistent lack of motivation (Bortolato et al., 2009). Their study found that discontinued METH abuse could lead to anxiety, social phobia, paranoia, as well as the inability to feel pleasure several months after discontinuation. METH-induced alterations to serotonin transporters are also associated with a negative change in stress threshold (Bortolato et al., 2009).
Like many other drugs, METH affects these systems by inducing neurotoxicity. Bortolato et al. (2009) supports evidence that neurotoxic effects lead to neuronal changes that induce long-term neuropsychiatric effects including chronic mood and anxiety alterations, psychotic disorders, and severe cognitive deficits. In the same study, they found that acute and chronic cognitive deficits usually include a reduction in attentional and mnemonic competence. They also note that the ability to perform goal-directed tasks is inhibited in METH abusers. These behavioral and cognitive deficits are all related to the negative effect METH abuse has on dopamine levels and dopamine transporter (DAT) density in the striatum (Bortolato et al., 2009). The striatum has a direct connection to the cerebral cortex, which could further explain why METH has such a strong effect on behavior and cognition. In fact, Bortolato et al.’s (2009) study shows that there is a strong correlation between METH-induced DAT damage in the nucleus accumbens and the aforementioned behavioral deficits.

Some significant findings show that oxidative and nitrosative stress play key roles in neurotoxicity induced by METH abuse. Venkatasen et al. (2011) explain in their study:

Although METH was initially thought to selectively damage monoaminergic nerve terminals, recent studies have consistently shown that widespread neuronal cell death results. Cell death involves not only the striatum and cortex, but the hippocampus as well. Although the molecular mechanisms underlying METH neurotoxicity are likely multifactorial, several key findings support a significant role for both oxidative and nitrosative stress (p. 1).

This implicates the more broad effects of METH abuse and how neurotoxicity can greatly affect cognition and memory. Within the same study they also found that, “Within the hippocampal dentate gyrus (DG), neurogenesis occurs in the subgranular zone and granule cell layer. New
neurons formed here are functionally incorporated into the hippocampus and may participate in the formation of hippocampal-dependent memory” (p. 2). Neurogenesis in the hippocampus is directly impaired by METH abuse. The reduction of newly generated neurons in the hippocampus negatively affects learning, memory, and cognition.

Most substances of abuse affect cognition in one way or another. Ecstasy is a psychoactive drug that can inhibit visuospatial cognition by affecting the transport of serotonin in the brain. Murphy, Bruno, Ryland, Wareing, Fisk, Montgomery, & Hilton (2012) notes:

The dominant chemical constituent of ecstasy (3,4-methylenedioxyamphetamine, or MDMA) is known to be neurotoxic with regard to serotonergic neurons in the brains of rats and primates, and although the nature and duration of its effects on human brains has been hotly debated, it is evident from scanning and imaging studies that the functioning of serotonergic neurons in a number of brain areas in ecstasy users can be altered in comparison with non-users (p. 113). The implication of MDMA-induced visuospatial impairment is extremely significant. A network of different brain areas processes visuospatial cognition. The dorsolateral prefrontal cortex along with occipital areas has been shown to process spatial information and monitors the flow of information (Murphy et al., 2012). Evidence shows that spatial information is partially processed in the parietal cortex (Murphy et al., 2012). Temporal cortical areas “may also be seen to contribute to visuospatial working memory processing, where information about object features and location needs to be brought together” (Murphy et al., 2012, p. 114). We can easily see that MDMA has a dramatic and widespread effect on different critical areas of the brain.

MDMA seems to affect visuospatial abilities more than other kinds of drugs. The reasoning is that MDMA reduces serotonin transporter binding that is essential to visuospatial processing in
the dorsolateral prefrontal cortex. Interestingly, evidence shows that changes in serotonin transporter binding may be reversible by abstaining from further use of ecstasy. However, damage may not recover cognitive abilities to pre-abuse levels (Murphy et al., 2012).

Alcohol is another substance of abuse that can significantly alter brain morphology. Different reactions occur in the brain during alcohol abuse. A protein known as p75 neurotrophin is necessary for the development, survival and function of neurons. Alcohol abuse seems to lower p75 neurotrophin receptors expression, which leads to cell damage in brain tissue (Skuja, Groma, & Kleina, 2011). Studies that were done on post-mortem subjects revealed that neurotoxicity brought on by alcohol abuse was the most likely risk factor to induce “global changes in brain morphology” (Skuja et al., 2011, p. 369). Another way alcohol damages brain tissue is by negatively influencing neuronal and glial cells and leads to neurodegeneration in the basal ganglia, which is a contributor in voluntary motor control, emotion, and cognition (Skuja et al., 2011). Of particular interest is evidence from Skuja et al. (2011): “Neurons and astroglial cells are sensitive to alcohol consumption, which promotes an apoptotic pathway of neurodegeneration. Endothelial cell apoptosis allows considering a possibility of the blood-brain barrier disfunction” (p. 376). A process known as programmed cell death is essential for normal tissue homeostasis. Chronic alcohol abuse increases the amount of apoptic cells in the striatum through oxidative stress (Skuja et al., 2011).

Considering all the effects that just one drug can do to the cognitive abilities of an individual, it is important to note that abusing combinations of substances at a time can lead to extremely adverse effects. For instance, Hernandez-Rabaza et al. (2010) demonstrated that “the simultaneous use of several psychoactive drugs among adolescents and young adults has also been
linked to adverse health outcomes, including enhanced propensity to suffer neuropsychiatric problems and cognitive deficits” (p. 413). Their study notes that memory impairments were correlated with granule cell depletion and that large doses of alcohol have been shown to inhibit the survival of newborn hippocampal cells. Hernández-Rabaza et al. (2010) noted that, “data suggested that threshold elevations in blood ethanol levels are required to affect the survival of newborn hippocampal neurons as shown previously in dose-dependent studies” (p. 420).

The effects of alcohol become exaggerated when taken in conjunction with MDMA at different combinations of doses, leading to severe memory deficits. Evidence from Hernandez-Rabaza et al. (2010) show, “Alcohol, MDMA and combinations thereof significantly decreased 5-bromodeoxyuridine labeling in the dentate gyrus (DG), indicating reduced survival of neuronal precursors” (p. 413). The dentate gyrus is an important hippocampal formation that is susceptible to neurotoxicity caused by simultaneous exposure to alcohol and MDMA, which can lead to continuing memory problems. Their study also notes, “Drugs of abuse induce impairments in several processes implicated in adult neurogenesis, thus potentially disrupting at least some of the mechanisms that underlie the encoding, consolidation and transfer of information within and beyond the hippocampal network” (p. 414).

Compared to the drugs previously discussed, marijuana abuse showcases a different set of neurochemical interactions. Chemical compounds in the drug called cannabinoids influence the transmission of serotonin and GABA. Cannabinoids are well known to disrupt attention, memory, and information processing (Hoffman, Riegal, & Lupica, 2003). Endocannabinoids, which are produced naturally in the body, play an important role in regulating the synaptic transmission of GABAergic and glutamergic systems. GABA in particular is known for inhibiting the release of
dopamine. Through this process, cannabis abuse essentially inhibits an inhibitor. This reaction leads to an influx of dopamine. Hoffman et al. (2003) provides further evidence on the role of cannabinoids, “… the presynaptic actions of cannabinoids are consistent with their effects throughout the CNS and suggest that the inhibition of neurotransmitter release represents one of the hallmark marks of cannabinoid receptor activation in the mammalian brain” (pp. 524-525).

The hippocampus is again involved in marijuana abuse. Hoffman et al. (2003) noted in their study, “Because it has a well-established role in memory and learning and because it contains some of the highest levels of cannabinoid CB1 receptors in the brain, the hippocampus has been implicated as a specific target of cannabinoids” (p. 524). Venolovská and Fišar (2007) note, “Serotonin (5-hydroxytryptamine; 5-HT) is involved in many of the same processes affected by cannabis use and the serotonin transporter (SERT) plays a pivotal role in maintaining serotogenic function by regulating the 5-HT uptake” (p. 158). In addition to this, high doses or chronic ingestion of cannabinoids inhibit serotonin uptake, which can result in adaptive changes in serotonin transporter activity (Venolovská & Fišar, 2007). Interestingly, previous hypothesis suggested that cannabinoids inhibit both glutamatergic and GABAergic synaptic inputs. However, in their study, Hoffman et al. (2003) found that synthetic cannabinoid agonists did not significantly inhibit glutamatergic synaptic inputs. This finding adds to the current knowledge of the effects of cannabis abuse.

**What I Learned Personally, Interpersonally and Professionally**

I learned personally about many of the negative effects that substance abuse could have on my body and mind. I realized that I am in a very good position in my life and I am fortunate and
grateful that I am not exposed to any of these mind-altering substances in my personal life. I realize that no matter what, I would never want to ingest any of these substances.

I learned interpersonally about why it is that many people continue to abuse substances, despite the negative consequences substance abuse has. Understanding how substances of abuse affect brain chemistry, brain morphology, and neurological functions allows me to see that there are neurobiological factors as to why a person might continue abuse. I have met classmates who have admitted to me that they have abused certain drugs, and now I believe I understand what is happening to them on a neurobiological level.

I learned professionally that there are many different kinds of neurobiological interactions that occur when a substance is abused. If I am ever in a position of where I have employees under my supervision and one or more of them are abusing drugs, then I have better knowledge about what they are going through and why.

**How I Plan to Apply What I Learned Personally, Interpersonally and Professionally**

I plan to apply what I learned personally by continuing to abstain from any kind of substance abuse. My research helped me reinforce my personal position on avoiding drugs and reaffirmed to me to not closely associate with others who do, so as not to put myself at any kind of risk for abuse. I do not want my body and mind to be influenced and controlled by any of the substances I learned about.

I plan to apply what I learned interpersonally to anyone that might be abusing drugs, whether they are very harmful or not so harmful. I will use the knowledge I gained through this research to help others realize what is going on inside their body and how their minds are being affected. My
goal would be to help them stop abusing drugs and regain control of their own lives as I have control over my own.

I plan to apply what I learned professionally in my future career as a psychologist. I would love to use my knowledge to help patients. Helping them to understand how their substance abuse is affecting them on a neurobiological level could assist in either preventing addiction or getting over an addiction. As a future psychologist, it is important for me to ensure that I am correctly applying the type of information I learned in order to understand what kinds of therapy treatments would be available to patients, considering the complex chemical interactions in process.
References


