Cocaine: effects on the brain

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Cocaine is a drug refined from Erytroxylon cocoa bush leaves which grows in Peru and Bolivia. It is referred to using several names such as C, snow, flake, blow, or crack. Generally, it is sold on the streets as a hydrochloride salt. It has a fine, white crystalline powder appearance usually diluted with resembling substances such as talcum powder, or amphetamine. There are several methods of consumption. Snorting through the nostrils is most popular, but it also may be rubbed onto the mucous linings of the mouth, rectum, or vagina. German chemist Albert Niemann in the mid-19th century extracted and identified cocaine. It was first used as an elixir to treat a variety of illnesses. Later, aesthetic properties were discovered and was used for local anaesthesia for eye, ear and throat surgery.

Cocaine is an indirect-acting agonist. Indirect agonist drugs increase the release/action of an endogenous neurotransmitter but as they are in-direct, they do not participate in agonist activities at the neurotransmitter receptor itself. Transporter blocking, transmitter release, and transmitter breakdown inhibition is how indirect agonists act on synapses around the body.

Cocaine affects numerous neurotransmitters which include Dopamine, Serotonin, and Glutamate, among several others. The blockade of the dopamine transporter (DAT) protein is the most extensively studied effect of cocaine. During neural signalling, released Dopamine transmitters are recycled and made available through the transporter: the transporter binds itself to the dopamine transmitters and they are pumped out of the synaptic cleft directly into the pre-synaptic neuron. Here, they are stored in storage vesicles. When cocaine is present, it binds at the dopamine transporter. A complex is formed which impedes the transporter’s functionality. The re-

uptake of dopamine by the dopamine transporter is inhibited. This leads to the accumalation of dopamine in synaptic cleft. As a result, an enhanced and extended effect of dopaminergic signalling is observed at dopamine receptors on the receiving neuron. Through the down regulation of dopamine receptors and also, heightened signal transduction, the prolonged exposure to cocaine results in homoeostatic regulation of normal dopaminergic signalling. After chronic cocaine use, the decreased dopaminergic signalling may contribute to depression and sensitize the body to the reinforcing effects (e. g. enhanced dopaminergic signalling occurs only when cocaine is consumed) of cocaine. This sensitisation leads to the intransigent nature of addiction.

Cocaine’s effects on serotonin is visible across several serotonin receptors: the re-uptake of 5-HT3 is inhibited and this is shown to be an important contributor to the effects of cocaine. Cocaine conditioned rats exposed to cocaine displayed an over-abundance of 5-HT3 receptors, but the exact effects of 5-HT3 in this specific process are yet unclear. The evocation of hyperactivity is influenced by 5-HT2 receptors in cocaine usage. Furthermore, cocaine is also a sigma ligand agonist and the following sigma receptors are affected: NMDA, the D1 dopamine receptor, and The 5th subtype of the Metabotropic Glutamate Receptor(MGluR5). MGluR5 is known to be one of the main factors in cocaine self-administration and locomotor effects. Mice deficient in MGluR5 displayed the absence of the reinforcing properties of cocaine. In addition, an MGluR5 antagonist dose reduced cocaine self-administration. Cocaine also acts as a local aesthetic by blocking sodium channels, which consequently interferes with the propagation of

action potentials. Thus, when the drug is applied locally to tissue it can prevent transmission of nerve signals along sensory nerves. Furthermore, cocaine also has target binding to the site of the Kappa-opioid receptor and it was shown to inhibit monoamine uptake in rats with the ratio of about: serotonin_dopamine= 2: 3, serotonin: norepinephrine= 2: 5.

Cocaine affects the body wherever dopamine transporters are present through the build-up of dopamine. Euphoria and the loss of control can all be traced to the impact has on the limbic system which is composed of interconnected regions present in the front area of the brain. The system is known to be concentrated in dopamine-responsive cells. The control emotional response and links them with memories present in the brain. The nucleus accumbens, the main part of the limbic system, seems to be the most important part during a cocaine-induced high. Feelings of enjoyment and thrill are produced here when it is stimulated by dopamine molecules. The biological importance of the NAc is to promote survival and healthy reproductive functions. For example, during sexual intercourse when a person reaches an orgasm or when quenching thirst with water, dopaminergic cells flood the NAc with dopamine. The feeling of pleasure felt due to the receiving cells' response makes people want to repeat the experience to please themselves again. Cocaine yields a powerful control over feelings of pleasure through the artificial build-up of dopamine in the NAc as seen above. The amount of dopamine detected by the receptors can exceed the normal amount of dopamine associated with the activity in the NAc after a dose of cocaine, inducing a pleasure greater than which are felt

when eating after starving. Some experiments have shown that mice would rather remain starved and take cocaine when given a choice.

The limbic system also includes the hippocampus and amygdala, which contain important memory centres. The present memory centers allow us to remember the activities from which we experienced pleasure after a release of dopamine in the NAc. For example, locating a mate or finding water. These particular regions imprint the heightened pleasure and memories associated with the drugs such as the people present or the current location when someone is high on cocaine. Seeing images or revisiting a place where someone has consumed cocaine or seeing photographs of the cocaine-related paraphernalia generates the desire to repeat the experience after reviving emotionally filled memories. Scientists believe that repeated dopamine jolts, changes these cells in a way that they eventually begin to convert memory and desire into compulsion in response to the cues by seeking/taking cocaine.

Another limbic region named the frontal cortex is where the brain organises information and then weighs the different courses of action available. It acts as a control on the other regions of the limbic system when we decide to abstain from a certain pleasure in order to avoid the negative consequences. A non-addicted person with a healthy frontal cortex can avoid the destructive prognosis of prolonged cocaine abuse and suppress the urges to repeat drug-consumption from the NAc, hippocampus and amygdala. However, an addict will have an impaired frontal cortex and will less likely be able to overcome to urges

Ultimately, Cocaine can cause long-term effects on the CNS (central nervous system), including an increased chance of brain seizures, heart attacks, stroke, and convulsions, respiratory failures, and, death. Overdoses of cocaine raise blood pressure to unpredictable heights, which often results in permanent brain damage. Over the last two decades, scientists have determined how cocaine intoxicates with its initial effects in the brain’s limbic system, and now we are starting to understand the neuro-biological mechanism underlying the drug’s craving and vulnerability to addiction. The most important goal is to translate the knowledge we gained over the past decades, along with the future advances we make, into better treatments for addiction.