Introduction

The essential feature of a substance use disorder (SUD) is a cluster of cognitive, behavioural, and physiological symptoms indicating that the individual continues using the substance despite significant substance-related problems Substance use disorder occur in a broad range of severity, from mild to severe, with severity based on a number of symptoms criteria endorsed ***(DSM-5,2013).***

Opiate dependence is a severe form of drug dependence characterized by early onset, chronic course, and high rates of psychiatric comorbidity. Thus, children of opiate addicts would be expected to be at risk for a variety of psychiatric disorders for which early diagnosis and treatment would be important. ***(Brooner et al., 1997).***

In a study of children of substance use disorder parents, found that 54% of children admitted to an inpatient psychiatric unit had preadmission histories of parental substance abuse. ***(Gabel et al., 1993)***

The published studies of psychiatric diagnosis by direct, structured interview in children of a mixed sample of opiate and cocaine addicts ***(Luthar et al., 1998)*** found rates of disorders higher than those of children in a community sample ***(Cohen et al, 1993)***

Children of addicted parents exhibit depression, anxiety and elevated rates of psychiatric and psychosocial disorder more frequently than do children from non-addicted families ***(Fitzgerald. et al., 1993).***

Families in which one or both parents use illicit drugs, particularly opiates and cocaine are much more likely to be living in poverty, and also, it's associated with criminal activities and places the parents at risk for arrest and imprisonment. Moreover drug-abusing families have more problems in areas known to influence children's adjustment, including poorer dyadic adjustment and higher levels of partner violence ***(Kelly & Fals-stewart, 2002).***

As compared to their peers, children of substance abusing parents (COSAPs) are at greater risk for a variety of problems, including internalizing symptoms such as depression and anxiety ***(Hussong et al., 2008)***

Compared to families in which neither parents were dependent on alcohol or illicit drugs, the offspring of parents with alcohol or other drug illicit dependence were at least three times more likely to experience externalizing disorders (i.e., ODD, ADHD) ***(Marmorstein et al., 2009)***

Aim of the Work

1- To illustrate the psychiatric illness of children and adolescent of substance dependent parents.

2- Association between psychiatric illness in children and severity of drug addiction in their parents.

3- Comparison between psychiatric illnesses in children of substance use parents and between children of non-substance use parents.

Substance use disorder diagnosis and neurobiology

The essential feature of a substance use disorder (SUD) is a cluster of cognitive, behavioral, and physiological symptoms indicating that the individual continue using the substance despite significant substance-related problems ***(DSM-5, 2013).***

Notable changes between the dsm-4 & dsm-5 in diagnosis sud include:

- In the DSM-4, substance use disorder was broken into two separate diagnoses of substance abuser and substance dependence. In the DSM-5, they combined these two diagnoses into one, to create a single diagnostic category of substance use disorder.
- The substance use disorder criterions of legal problems from DSM-4, was dropped in favor of cravings or a strong desire or urge to use a substance in the DSM-5.
- In addition, three categories of disorder severity were formed, using the number of patient symptoms. Out of 11 potential symptoms, 2-3 symptoms are diagnosed as a mild substance use disorder, 4-5 symptoms as moderate, and 6 or more symptoms as a severe substance use disorder.

In the DSM-4, patients only needed one symptom present to be diagnosed with a substance abuse, while the DSM-5 requires two or more symptoms to be diagnosed with substance use disorder.

- The DSM-5 eliminated the physiological sub-type and the diagnosis of poly substance dependence.

So, here are the diagnostic criteria of SUD in DSM-5:

It is a maladaptive pattern of substance use leading to clinically significant impairment or distress, manifested by the following occurring within 12 month period.

1. Recurrent substance use resulting in a failure to fulfill major at work, school or home.
2. Recurrent substance use in physically hazardous situations.
3. Continued substance use despite persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance.
4. Tolerance as defined by either of the following:
   - A need to markedly increase amount of the substance to achieve intoxication or desired effect.

- Markedly diminished effect with the continued use of the same amount of the substance.

5. Withdrawal, as manifested by either of the following:
   - The characteristic withdrawal symptoms for the substance.
   - The same (or closely related) substance is taken to relieve or avoid withdrawal symptoms.
6. The substance is often taken in larger amounts or over a longer period than was intended.
7. There is a persistent desire or unsuccessful efforts to cut down or control substance use.
8. A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects.
9. Important social, occupational, or recreational activities are given up or reduced because of substance use.
10. The substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.

11. Craving or a strong desire or urge to use a specific substance ***(DSM 5, 2013).***

Substance-related disorders are not limited to any particular country or world region. Focusing on Egypt during the last few decades, and to be more specific during the past five decades, the changes that have affected the Egyptian society from socio-economic changes and the low level of awareness among the Egyptians about the seriousness of drugs, not only on the health side, but on all aspects of life ***(Amin, 2007)*** Contributed to increase the proportion of Egyptians population below 20 years using drugs significantly from 30% in 1987 to 48.2% in 2006 ***(Egyptian Population Report, 2006),*** also Egypt's geographic location at the junction of 2 continents and bordering on Europe is an important factor as life change that makes it a likely transit point and market for illicit drugs grown in the region ***(Hamdi et al., 2013).*** The current situation of substance use in Egypt indicated it as the second common mental disorder especially for males with prevalence 2% of general population ***(GSMHAT, 2017).*** In the area of drug addiction, the General Secretariat of Mental Health and Addiction Treatment undertakes continuous efforts to remove the stigma

surrounding addiction and increase public awareness of addiction as a mental disorder ***(Sabry, 2017).***

Neurobiology of the substance use:

All addictive substances have powerful effects on the brain. These effects account for the euphoric feelings that people experience during their initial use of substances, and these feelings motivate people to use those substances again and again, despite the risks for significant harms. Moreover these brain changes endure long after an individual stops using substances. Theses may produce continued, periodic craving for the substance that can lead to relapse ***(Hubbard et al., 2003).***

A- Brain areas that are involved in Substance Use Disorders:

In the brain there are three areas and it is communication is so important in the addiction progression and they are the most areas also affected in the disorder**,** the link between neurobiology of brain and substance use disorder and the area included in processing of the disease explained below and the areas are illustrated in figure 2 ***(USDHHS, 2016).***

The brain has many regions that are interconnected with one another, forming dynamic networks that are responsible for specific functions, such as attention, self-regulation, perception, language, reward, emotion, and movement, along with many other functions. Here focus on the three regions that are the key components of networks that are intimately involved in the development and persistence of substance use disorders: **Basal ganglia, extended amygdala,** and **the prefrontal cortex (USDHHS, 2016)** as shown in figure 1.

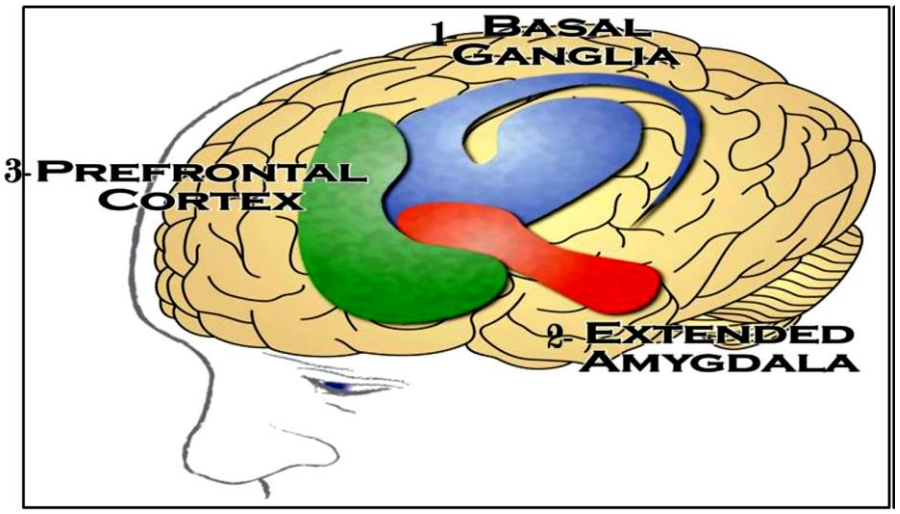

Figure (1): Areas of the Human Brain that Are Especially Important in Addiction, 1-Basal ganglia, 2- Extended amygdala, 3- prefrontal cortex ***(USDHHS, 2016).***

1- The Basal Ganglia:

The basal ganglia control the rewarding or pleasurable effects of the substance use and are also responsible for the formation of habitual substance taking.

Two sub-regions of the basal ganglia are particularly important in substance use disorders:

- The nucleus accumbens, which is involved in motivation and the experience of reward.
- The dorsal striatum, which is involved in forming habits and other routine behaviors ***(Kalivas and Volkow, 2005). (Azzam et al., 2018).***

2- The Extended Amygdala:

The extended amygdala is involved in stress and the feelings of unease, anxiety, and irritability that typically accompany substance withdrawal ***(Davis et al., 2010).*** And dysregulation of this brain emotional systems that mediate arousal and stress is a key component of the pathophysiology of drug addiction and its activation is hypothesized to be a key element of the negative emotional state produced by dependence that drives drug-seeking through negative reinforcement mechanisms ***(Koob, 2009).***

3- The prefrontal cortex:

The prefrontal cortex, is responsible for complex cognitive processes described as "Executive function". Executive function is the ability to organize thoughts and activities, prioritize tasks, manage time, make decisions, and regulates one's actions emotions and impulses ***(Ball et al., 2011).***

The imaging studies in addictive behaviors have identified a key involvement of the prefrontal cortex (PFC) both through its regulation of limbic reward regions and its involvement in higher-order executive function (for example, self-control, salience attribution and awareness) ***(Goldstein and Volkow, 2012),*** This function may explain its association with vulnerability to substance misuse ***(Cheetham et al., 2016).***

B- The Reward center in the brain:

This area of the brain is primarily concerned with basic survival. The term "reward system" refers to a group of structures that are activated by rewarding or reinforcing stimuli (e.g. addictive drugs). When exposed to a rewarding stimulus, the brain responds by increasing release of the neurotransmitter dopamine and thus the structures associated

with the reward system are found along the major dopamine pathways in the brain.

The mesolimbic dopamine pathway is thought to play a primary role in the reward system. It connects the ventral tegmental area (VTA), one of the principal dopamine-producing areas in the brain, with the nucleus accumbens, an area found in the ventral striatum that is strongly associated with motivation and reward. Another major dopamine pathway, the mesocortical pathway, travels from the VTA to the cerebral cortex and is also considered part of the reward system. So, the reward system is generally considered to be made up of the main dopamine pathways of the brain (especially the mesolimbic pathway) and structures like the VTA and nucleus accumbens, which are connected by these dopamine pathways.

Addictive Substances "Hijack' Brain Reward Systems:

All addictive substances produce euphoric feelings. These "rewarding effects" positively reinforce their use and increase the likelihood of repeated use. The rewarding effect of the substances involves activity in the nucleus accumbens, including activation of the brain's dopamine and opioid signaling system. Many studies have shown that neurons that

release dopamine are activated, either directly or indirectly, by all addictive substances, but particularly by stimulants such as cocaine amphetamine, and nicotine ***(Nestler, 2005).***

In addition, the brain's opioid system, which includes naturally occurring opioid molecules (i.e. endorphins, enkephalins, and dynorphins) and three types of opioid receptors (i.e., mu, delta, and kappa), plays a key role in mediating the rewarding effects of the addictive substances, including opioid and alcohol) ***(Koob and Volkow, 2010).***

Activation of the opioid system by these substances stimulates the nucleus accumbens directly or indirectly through the dopamine system. Brain imaging studies in humans show activation of dopamine and opioid neurotransmitters during alcohol and other substance use (including nicotine) ***(Koob and Volkow, 2010).***

Other studies show that dopamine antagonists and opioid receptors can block drug and alcohol seeking in both animals and humans ***(Swift and Aston, 2015).***

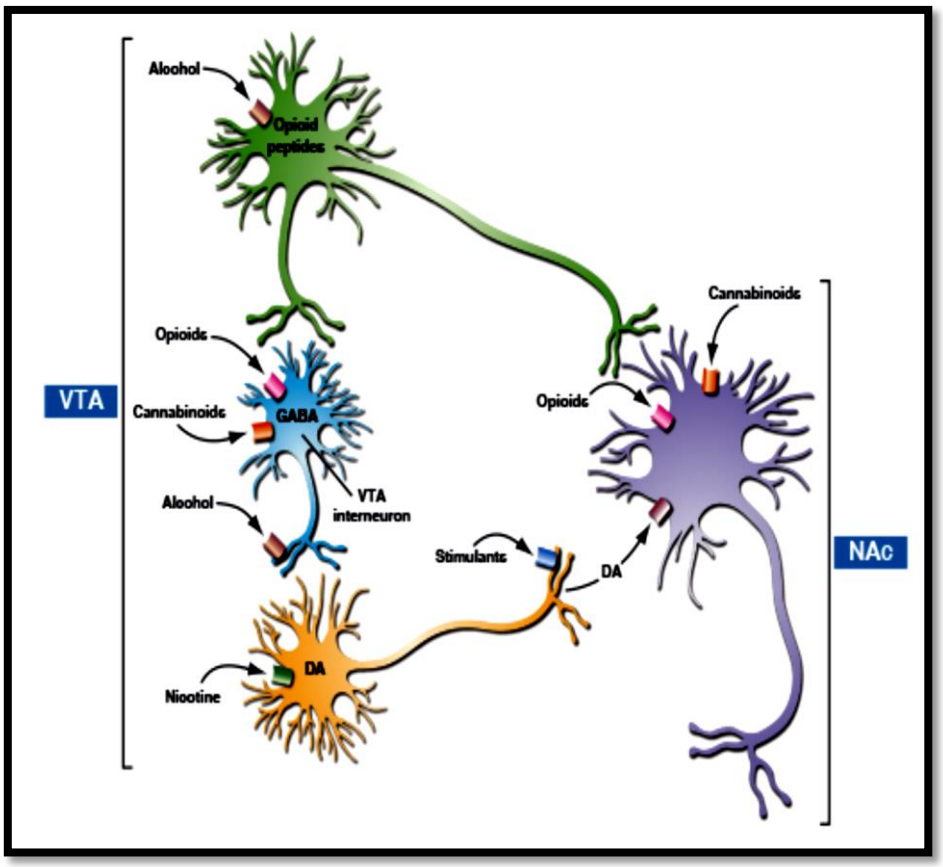

Figure (2): Actions of addictive substances on the brain

This is a simplified schematic of converging acute rewarding actions of addictive substances on the nucleus accumbens (NAc). Dopamine neurons that originate in the ventral tegmental area (VTA) project to the NAc. Opioid peptides act both in the VTA and NAc. Despite diverse initial actions, addictive substances produce some common effects on the VTA and NAc. Stimulants directly increase dopamine

(DA) transmission in the NAc. Opioids, alcohol, and inhalants (e.g., the solvent toluene) do the same indirectly. Alcohol also activates the release of opioid peptides. Heroin and prescribed opioid pain relievers directly activate opioid peptide receptors. Nicotine activates dopamine neurons in the VTA. Cannabinoids may act in the VTA to activate dopamine neurons but also act on NAc neurons themselves ***(US department of health and human services 2016).***

The addiction cycle:

Addiction can be described as a repeating cycle with three stages. Each stage is particularly associated with one of the brain regions basal ganglia, extended amygdala and prefrontal cortex (figure 2). This three-stage model provides a useful way to understand the symptoms of addiction, how it can be prevented and treated, and how people can recover from it ***(Koob and Volkow, 2010).***

The three stages of addiction are:

- **Binge/Intoxication,** the stage at which an individual consumes an intoxicating substance and experiences its rewarding or pleasurable effects.