



Stress and Drug Addiction: Neurobiological Mechanism, Pharmacological and Psychological Management of Substance Use Disorder Patients in Nigerian

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ARTICLE INFO

Article's History

Received: 20/10/2023

Revised: 14/02/2024

Accepted: 07/03/2024

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ABSTRACT

The menace of substance use disorders (SUDs) has eaten deep into the fabric of the society and has caused a great deal to individuals and society. Little progress has been made in the management SUDs/condition due to dearth of mental health professionals namely Clinical Psychologists, Psychiatrists etc. and the increasing teeming population of youths/individuals engage on drug use and dependence. Individuals who do drugs engage in it for different purposes. The factor that led one to do drugs may be quite different from the other. In this work, one of the major reasons/contributing factors to drug use implicated in stress. In many who do drugs, drug use is a stress-driven behavior. Neurobiological mechanism as relates to stress were buttressed and therapeutic measures including psychological management techniques, pharmacological measures and treatment implications in the management of this menace were addressed.

Keywords:

Drug

Addiction/Dependence;

Substance Use Disorder;

Substance Use Disorder
Patients;

Substance Abuse;

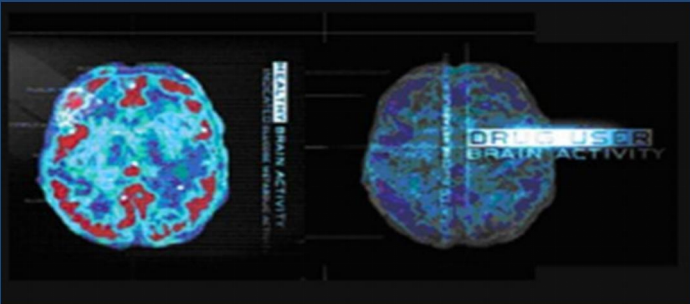
Stress

Introduction

Drug addiction otherwise refers to as substance use disorders [SUDs] is a chronic relapsing brain disease, characterized by compulsive drug seeking and use despite negative consequences (United Nation Office on Drugs and Crime [UNODC], 2018, 2020; Volkow, Fowler and Wang, 2003 and Volkow & Li, 2004). Literatures may have it as a chronically relapsing condition that is characterized by an inability to self-regulate drug consumption. Other characteristics of drug addiction includes; compulsive, reward or pleasurable and loss of

control in limiting intake. In any substance use disorder (SUD) person, drug use is compulsive and occurs in spite of negative social, legal, financial and medical consequences. Drug addiction has caused individual and society a great deal and little progress has been made in the management of substance use disorder patients. One of the things that have made addiction difficult to treat/manage is that not all SUD patients use drugs for exactly the same purposes. Thus, the factors that led to one doing drug may be quite different from another.

***What is Addiction?
Addiction is A Brain Disease***



- Characterized by:
 - Compulsive Behavior
 - Continued abuse of drugs despite negative consequences
 - Persistent changes in the brain's structure and function

Figure 1 Characteristics of addiction

According to Shalev, Grimm and Shaham (2002) and Mantsch (2010), in many individuals, drug use is a stress-driven behaviour. Hans Selye, the father of stress, in 1936, defined stress as the “nonspecific response of the body to any demand”. Psychologists defined stress in a variety of different ways. Stress is regarded as the external environmental stressor (e.g., problem at work), the response to the stressor as stress or distress (e.g.,

the feeling of tension), and the concept of stress as something that involves biochemical, physiological, psychological and behavioural changes. In all these definitions, stress involves an interaction between stressor and distress. This stress driven behaviour, can have its stressor as e.g., financial, economic, social, emotional, physical and psychological. Others include; negative life events, poverty, unemployment, anxiety-provoking

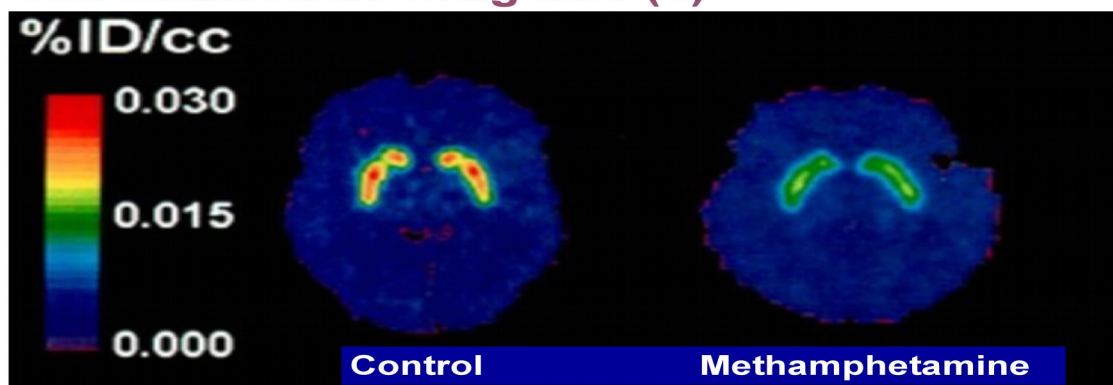
environment/condition, insecurity, suicide bombing, terrorism, kidnapping, aimed robbery, rape, ritual killing etc.

Stress is usually and especially problematic to SUD patients because the life of a SUD patient is particularly a stressful one; even though, many persons turn to drugs in order to help them cope with stress. To further strengthen that, drug use by its self can generate and/or aggravate stress responses. The relationship between stress and drug use appears to be a vicious cycle, in that, the onset of stress promotes drug use which in turn generates more stress and therefore leads to further drug seeking behaviour, thus, drug addiction/dependence. Managing addiction/self-perpetuating cycle, greatly requires eliminating/minimizing the stress and/or stressor(s) (including other factors), will probably provide a key to successful treatment of many SUD patients. The researcher has observed this especially, the role of stress/stressors in drug dependence, in the course managing SUD patients in the drug rehabilitation centre, Drug Addiction, Treatment, Educational and Rehabilitation [DATER] of Federal

Neuropsychiatric Hospital, Barnawa, Kaduna, where he works.

People use drugs because of pleasurable effect they have on brain. Suddenly, drugs produce pleasurable/euphoric effects through the “stimulation/activation of neural circuit that gives the pleasurable reward”. Often such effects offset the negative feelings associated with stress. “With repeated drug intake, changes in the neural circuit begins to emerge such that the brain of SUD patient functionally becomes different from that of a non-SUD patient or one who only occasionally use drugs”. To greater extent, when a drug is used consistently, the pleasure and neurobiological condition that propel drug use change such that the user enjoys the drug less but needs the drug more. These changes in brain function that emerge with consistent drug use are referred to as “neuroplasticity” and it appears to be “long-lasting, if not permanent (Volkow & Li, 2004)”. “The negative consequences of long-lasting neuroplasticity are a disease like condition that is associated with a high risk for relapse in many individuals”.

The Brain After Drug Use (1)



(Source: McCann et al. (1998). *Journal of Neuroscience*, 18, 2227)

Figure 2. Brain After Drug Use

For this reason, understanding the pathogenicity of neuroplasticity of addiction develops and can help in prevention and treatment of the condition. Besides, the involvement of stress, in addition to neuroplasticity is bidirectional. That is, stress promotes the onset of drug-induced neuroplasticity and the expression of which includes aggravated behavioural and hormonal stress responses.

Empirical/Clinical Proof

According to the works of Shalev, Grimm and Shaham (2002) and Volkow & Li, (2004), stress generally is a causative factor for drug use and inability to effectively cope with stress is predictive of relapse. In addition, Shalev, Grimm and Shaham (2002), indicated that “there is a high incidence of stress-related co-morbidity e.g., Post-Traumatic Stress Disorder (PTSD), panic attack and depression in drug dependent population”. For example, it has been reported “that up to 43% of cocaine-dependent persons met the diagnostic and statistical manual of mental disorders (3rd ed. Rev.; DSM 111-R and DSM V) criteria for lifetime PTSD”. In one study “95% of subjects with current PTSD and cocaine dependence reported a functional relationship between cocaine use and their PTSD symptoms, with 86.4% indicating that their PTSD symptoms have worsened with drug use”. More evidence that stress can lead to drug use is found in clinical laboratory studies demonstrating that stress can increase subjective measures of craving for cocaine and alcohol in recovering SUD patients.

Animal Research

Drug abuse studies have depended more on preclinical animal research. The use of self-administration procedures in which rats are

surgically implanted with intravenous catheters and required to perform behavioural task, has showed that drugs that are abused by humans are also self-administered by rats. In this animal studies, research has focused on the effect of stressors on the acquisition, escalation and reinstatement of drug seeking-behaviour.

Acquisition

It is not everyone that tries a substance/drug for the first time will find it pleasant and will start using the substance on regular basis. Some individuals react/respond to drugs differently. The difference in response is due to a number of factors. Some persons are genetically predisposed toward drug use, whereas others are influenced by environmental factors such as stress. (Other factors may include; friends/peer groups, curiosity, personality, financial buoyancy, loneliness, unemployment, frustration, anger etc.). For many, individual susceptibility to addiction arises from complex interplay among genes, drug effects and environment. Preclinical factors that increase the likelihood that drug use will be initiated can be studied using acquisition self-administration model in which predisposition to engage in drug use is defined according to how readily drug naive subjects acquire the behaviour of drug self-administration. It was reported that using such model, a variety of stressful stimuli ranging from “very basic stressor (such as repeated tail pinch) to more complex stressors (such as social defeat) facilitate the acquisition of drug self-administration by rats”. Importantly, it is not just stress but the ability to control stress that is important for its effects on acquisition.

Escalation

Using drugs regularly does not mean that one is

addicted. It is the loss of control over drug use and its negative impact on other facets of a drug user's life that defines addiction. This aspect of drug addiction has been studied using rodent drug self-administration model in which progressive escalating patterns of drug intake emerge when daily access to a drug is prolonged. The onset of escalating the pattern is thought to reflect the transition from "control drug use to out-of-control drug addiction".

Reinstatement

In drug addiction, craving or the intense use of a drug, always leads to drug use. Starting of craving is often unpredictable and suddenly occurs even many months or years of abstinence. This can make management of addiction a difficult one. A preclinical study using reinstatement of self-administration procedures indicated how various stimuli can contribute in reinstating extinguished drug seeking behaviour. Using such procedures, has demonstrated that acute exposure to stressors can reinstate responding previously reinforced by a variety of abused drugs including cocaine, ethanol, heroin and nicotine. The studies on this, goes to show that "subjective stress imagery can increase measures of drug craving in recovery SUD patient". This may suggest that the inclusion of pharmacological and behavioural measures aimed to reducing stress during drug abstinence is important to the success of any drug rehabilitation program.

Neurobiological Process in Stress and Substance Use Disorders (SUDs)

Though, other factors exist that influence drug seeking behaviour, stressors exert their effects on

drug use by altering the activity of the neurobiological systems within the brain that is responsible for the motivated behaviour. To be precise, a critical role for a pathway on the brain consisting of nerve projection from medial prefrontal cortex that release the amino acid neurotransmitter glutamate into the nucleus accumbens has been identified for drug-seeking behaviour. This neural connection is closely modulated by the neurotransmitter dopamine, released from nerve that originates in the ventral tegmental area (VTA) of the mid brain. Like other stimuli that promote drug use, stress promotes drug-seeking behaviour through the activation that occurs during stress is not entirely clear, but it appears to require the stimulation of dopaminergic neurons in the VTA that project to the medial prefrontal cortex and almost certainly involves the neuropeptide corticotrophin releasing hormone (CRH).

Pertinently, stress can intensify the responsiveness of this motivational pathway to subsequent stimulation by inducing a form of cellular neuroplasticity in dopaminergic cells in the VTA called "long term potentiation (LTP)", thereby increasing susceptibility to the effects of abused drugs. See, figure 3 and 4 below.

Corticotrophin Releasing Hormone (CRH)

Apart from corticotrophin releasing hormone (CRH) initiating hormonal stress response through its actions in the pituitary gland, "CRH also exerts its effects within the brain, where it functions as a neuropeptide mediator of stress-related behavioral responses and anxiety". CRH administered directly into a number of regions, including the VTA reinstate extinguished drug seeking-behaviour,

whereas CRH antagonists prevent induced reinstatement. The exact mechanism through which CRH stimulates dopamine cells in the VTA is unclear, but “it appears to require the association of CRH with its binding protein and the activation of a specific subtype of the CRH receptor, CRH₁ receptor, which in turn facilitates cellular activation by the neurotransmitter glutamate”.

Glucocorticoids

According to Koob, Ahmed and Boutrel, (2004); Shalev, Grimm and Shaham (2002) and Marinelli & Piazza (2002), in their respective studies, indicated that acute stress precipitates drug craving and use which is often problematic to SUD patients. However, it is chronic stress that can have a harmful/damaging effect on addiction process by producing or facilitating neuroplasticity that is pathogenic for addiction. Whereas the acute effect of stress on drug seeking behaviour appears to be mediated primarily through the action of CRH in the brain, many of the effects of chronic stress on drug use appear to involve the release of

glucocorticoids (such as cortisol in humans and corticosterone in rats) are critical “mediators of the physiological and behavioural responses that enables an organism adapt to and cope with stress”. Such responses are beneficial for short term adaptation for stressful stimuli but, with constant stimulation/activation, they can be detrimental to the organism, a consequence of chronic stress referred to as allostatic load. These allostatic effects appear to include adaptation in the motivational neurocircuitry of the brain that promotes illicit drug use. “Although glucocorticoids alone are capable of producing addiction-related neuroplasticity, it appears that in many cases these hormones work in concert with other stress-related molecules such as CRH to influence the addiction process”. They went further to indicate that many such interactions occur in the VTA, where stressor-induced neuroplasticity involving dopamine cells appear to be mediated by CRH and require glucocorticoid receptor activation. See, figure 3 and 4 below.

A Neurobiological Pathway Through Which Stress Influence Drug-Seeking Behavior.

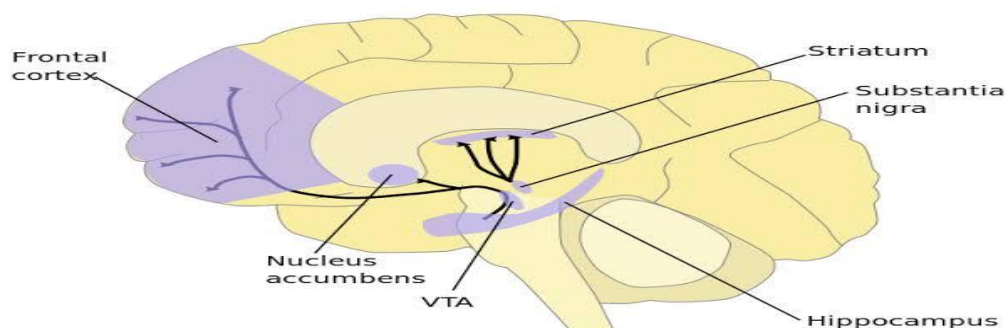


Figure 3. Source: National Institute on Drug Abuse (NIDA) (1999; 2014).

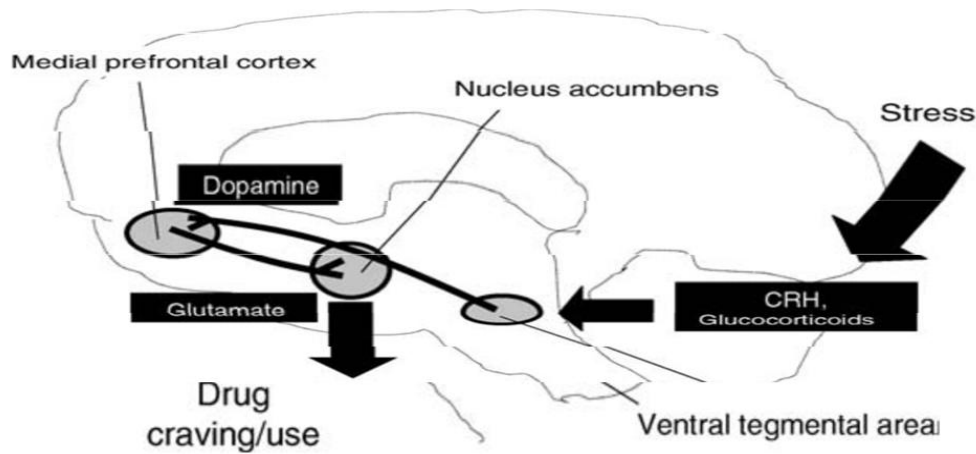


Figure 4. Source:National Institute on Drug Abuse (NIDA) (1999; 2014).

Figure 4. “The putative neurobiological pathway through which stressful stimuli may influence drug-seeking behaviour and addiction. The results of recent animal studies indicate that stressful stimuli increase brain corticotrophin releasing hormone (CRH) levels, which, in concert with elevated glucocorticoids, exert effects on cells in the ventral tegmental area of the brain to increase dopaminergic neurotransmission in the medial prefrontal cortex and nucleus accumbens and facilitate the activity of neurocircuitry that underlies motivation and natural reward”.

Treatment Implications

The recognition that stress is a key contributor to drug abuse/addiction highlights the need for the development and implementation of novel therapeutic strategies to the addiction process among SUD patients whose drug use is stress driven. The import of the above is strongly upheld. A look at our society and the world in general and how illicit drug use has eaten deep into the fabric of our society/world and the menace this has caused is a great eye saw. The negative consequences include; health problems, long term use of substances can

lead to long term neurological impairment leading to mental health problems. Others include liver damage, hypertension, excessive heartbeat, chronic bleeding and damage to unborn. Psychological or emotional consequences include; depression, anxiety, memory loss, aggression, mood swings, paranoia, psychosis, craving desires, withdrawal symptoms and premature death. Social consequences, for example, loss of job, family disintegration, expulsion from school, delinquency, criminal offences, stealing, assassination/murder, rape, armed robbery, kidnapping, destitution, prostitution and premature death. So, a look at the number of drug rehabilitation centres and dearth of mental health professionals especially Clinical Psychologists, Psychiatrists etc. are not good enough to manage the teeming population of youths (even adolescents and old adults) who are into addiction problems. The author seizes this medium to appeal to government for the establishment of more psychiatric centres/drug rehabilitation centres and inclusion of more Clinical Psychologists in the management of substance use disorders (SUDs).

Management of Stress in Substance use Disorder

Author is an experienced Chief Clinical Psychologist in the management of SUD patients. He works in Federal Neuropsychiatric Hospital, Barnawa, Kaduna, where he manages mental illness and do other psychological services including SUD patients in drug rehabilitation centre called Drug, Alcohol, Treatment, Educational and Rehabilitation Unit [DATER] of the same hospital. In the course of management of substance use disorder as indicted in this work, that stress is the key contributor to drug use and addiction. The author applied the following in the management of substance use disorders (SUDs).

The Use of Assessment Instruments:

a) Self-Report

Administration of drug assessment tools e.g., CAGE, AUDIT, TWEAK, Drug Abuse Screening Test (DAST), Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) etc.

b) Interview-this include the use of ASI- (Alcohol Severity Index) in conducting Intake interview. This comprises of 7 domains/areas- (General information, medical status, employment/support status, alcohol/drugs, legal status, family/social status and psychiatric status) pertinent in drug management.

c) Administration of questionnaire e.g., measures of individual distress e.g., Psychological and Behavioural Measures, Daily log Stress-Related Symptoms (Manuso, 1980), Symptom Distress Checklist-90-revised (SCL-90-R)- Derogatis and Savitz (1999), State Trait Anxiety Inventory (STAI) and State Trait Anger Expression Inventory (STAEI-2) and Minnesota

Multiphasic Personality Inventory [MMPI-2] and [MMPI-A], Wechsler Intelligent Scale for Children Fourth Edition (WISC-IV), Wechsler Adult Intelligent Scale Fourth Edition (WAIS-IV) and host of them.

Psychotherapy

This includes the following: cognitive behavioural therapy namely: Cognitive Restructuring; cognitive therapy, rational emotive therapy, thought stopping, Cognitive Behavioural Coping Skills; self-instructional training, relaxation training, systematic desensitization and stress inoculation training. Others include problem solving skills, life skill training, assertiveness training, psychodrama, debate, role playing, anger management, stress management and other stress coping skills, time management, relapse prevention, educational session, spiritual therapy etc. They are utilized and have proved effective in the management of SUD patients to enable them manage/cope with stress and remain abstinent.

Drugs (Medication)

Medications are used for the management of stress-related psychiatric conditions (e.g., antidepressants, (e.g., paroxetine (Seroxat) and benzothiazines are commonly prescribed to treat addiction.). For alcohol withdrawal symptoms, the following medications are prescribed; diazepam, thiamine and multivitamins, antiemetic, analgesia (e.g., paracetamol) and antidiarrheal. For post-withdrawal/detoxification management- you have; acamprosate, naltrexone and disulfiram. However, eventual development and approval of new drugs that block the action of CRH in the brain wall, it is hoped, will provide important tools, in addition to

psychotherapy, for the management of substance use disorders (SUDs).

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