REVIEW ARTICLE

Cannabis Abuse and Addiction: a Contemporary Literature Review

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Abstract

Introduction: *Drug addiction, particularly among teenagers and young adults, has become a serious public health problem globally. Drugs with addictive potential include the non-therapeutic drugs that are licit/legal (caffeine, tobacco or nicotine, alcohol) and those that are illegal/illicit for common use such as benzodiazepines, amphetamines, cocaine and crack, heroin and cannabis. Worldwide, the challenge of cannabis abuse and addiction is particularly devastating, nay in Nigeria. Despite this ugly scenario, the use of cannabis continues unabated and its control remains enigmatic. The aim of the present review is to provide a contemporary comprehensible overview of exciting recent developments in the understanding of brain circuits related to the nature and effects of cannabis abuse and addiction as well as to highlight the current therapeutic approach to effective management.*

Method: *A thorough manual literature and internet (Medline and HINARI databases) search were conducted.*

Result: *It was found that recent advances in the neurobiology of drug abuse and addiction have led to the identification of neuronal substrates (eg dopamine, 5-hydroxyltrypytamine etc) as being responsible for the rewarding effects of cannabis and are also crucial to the addictive process/behaviour. There is increasing evidence that prolonged exposure to drugs of abuse including cannabis, produces long-lasting effects in cognitive and drug-rewarding brain circuits. Hence, addiction is now generally considered a chronic brain disease. Chronic use of cannabis impairs cognitive functions, perception, reaction time, learning, memory, concentration, social skills and control of emotions. There may also be panic reactions, hallucinations, paranoid states with fixed delusions and even acute psychosis. These impairments have obvious negative implications for the operation of a motor vehicle or machinery and performance at school or workplace as well as the development of a healthy family, a strong national economy and a secure society. Complications of use, including psychosis and withdrawal effects, can be treated. Psychosocial measures and rehabilitation, together with effective prevention initiatives are essential in the management of individuals with drug-related problems.*

Conclusion: *Cannabis abuse and addiction is destructive and may affect all of our lives and the fabric of the society. The development of long-term management strategies based on medication, psychosocial support and continued monitoring as well as preventive initiatives to reduce risk factors and strengthen protective factors against drug abuse is a challenging clinical goal.*

Key Words: *Cannabis, Abuse, Addiction, Contemporary, Literature, Review*

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Introduction

Worldwide, drug problems are as old as drugs themselves. Addictive drugs whether licit/legal eg caffeine, tobacco or nicotine, alcohol or illicit/illegal because they are used in ways that are not medically approved eg benzodiazapines, amphetamines, cocaine and crack, heroin and cannabis, have the unique ability to perpetuate their use by compromising rationality and wrecking havoc on the faculty of self preservation. This causes a molecular brain disease which inevitably leads to disorder, dysfunction or perhaps destruction.[1-3]

Drug addiction is a chronic relapsing disorder in which compulsive drug-seeking and drug-taking behaviour persists despite serious negative consequences. Addictive substances induce pleasant states (euphoria in the initial phase) or relieve distress. Continued use induces adaptive changes in the central nervous system (CNS) that lead to tolerance, dependence, sensitization (reverse tolerance), craving and relapse. Drug or substance abuse refers to the use of drugs (amphetamine, cocaine, cannabis, narcotics/opioids etc) despite their harmful social and medical manifestations. Government agencies regard the use of any illegal substance as drug abuse. Medically, however, drug abuse refers to the use (usually by self

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medication) of any drug in a manner that deviates from the approved medical or social patterns. The term refers to the abnormal use of drugs for purposes other than their legitimate medical indications. Drug misuse means the inappropriate use of drugs.[2-7]

From the reports of Ariel et al[8] and other authors[9-10] as well as information garnered from *Cannabinews*[11] and the National Household Survey on Drug Abuse (NHSDA),[12] it is estimated that 141 million people (2.5%) of the world's population use cannabis. It has been particularly observed that the consumption is higher among young people. In Nigeria, the problem of cannabis use appears to be on the increase judging from the reports of Lambo[13] and other authors[14-16] in the 1960s to 1980s as well as recent newspaper reports, clinical and epidemiological surveys.[17-23] Healthcare professionals have expressed grave concern about the above phenomenon. According to Emafo,[24] the situation had become sufficiently disturbing such that the defunct Federal Military Government in a bid to remedy the situation enacted Decree 48 (1989) which established the National Drug Law Enforcement Agency (NDLEA).

The above reports have shown that cannabis use cuts across various age groups (the adolescents and young adults being in the majority) and social classes. Some of the common reasons for taking to drugs include peer pressure, mere curiosity, desire to perform well in studies, parental deprivations as well as parental substance abuse, compensation for personality defects, need for excitement and social pressures as well as unemployment and environmental stressors.[8-14, 17, 21, 23]

The health effects of cannabis use is incalculable as it has been known to be linked with short-term damage to the memory, distortion of perceptions, impairment of judgment and complex motor skills, alteration of heart functions, exhibiting a high potential of anxiogenesis, paranoia and lethargy.[9,12,16, 23, 25] Psychosis is one of the more severe psychopathological conditions associated with cannabis use that has been well documented.[23, 25-27]

In spite of the above adverse effects, many have not considered it necessary to quit the practice. Furthermore, the difficulties in management and rehabilitation of victims in terms of definitive treatment, logistics and resources have only succeeded in yielding high morbidity and mortality.[8-27] It is in this unsalutary state of affairs that this review is solicited to address the issue of paucity of information as regards the understanding of the nature and effects of cannabis abuse and addiction as well as thecurrent approach to effective management.

Nature and Effects of Cannabis Abuse and Addiction

Cannabis: Classified as a hallucinogen (psychodysleptic, psychedelic, psychotogen or psychotomimetic), it is obtained from the annual plant *Cannabis sativa* and its varieties *Cannabis indica* and *Cannabis americana* that grow wild but can be cultivated. The term "cannabis" includes all the preparations that are either smoked or eaten. Cannabis is also referred to as Marijuana (the smoked preparation that is variously called Indian hemp, grass, pot, weed, ganja, spliff, riefer, igbo, garri etc). Hashish (dried resin preparation) is cannabis that is smoked or eaten. It contains several pharmacologically active alkaloids called cannabinoids which include a powerful psychoactive substance?^{9}-tetrahydrocannabinol (THC).[7, 28-29]

Neurobiology and mechanism: G-protein coupled cannabinoid CB_1 receptors, which are richly distributed in basal ganglia and cerebral cortex regions, are implicated in cannabis abuse and addiction. Endogenous cannabinoids that act as neurotransmitters include 2-arachidonyl glycerol (2-AG), anandamide and noladin, all of which bind to CB_1 receptors. These very lipid-soluble compounds are released at the postsynaptic somatodendritic membrane, and diffuse through the extracellular space to bind at presynaptic CB_1 receptors where they inhibit the release of either glutamate or GABA. Because of such backward signaling, endocannabinoids are called retrograde messengers. In the hippocampus, release of endogenous cannabinoids from pyramidal neurons selectively affects inhibitory transmission and may contribute to the induction of synaptic plasticity during learning and memory formation.[7]

Exogenous cannabinoids eg THC, increase the efflux of dopamine (DA) in the nucleus accumbens and cell firing in the ventral tegmental area (VTA) by their actions on CB_1 receptors in glutamatergic and GABA-ergic neurons associated with the nucleus accumbens and VTA.[2-3, 7, 27, 30] As a general rule, all addictive drugs activate the mesolimbic DA system. The behavioural significance of this increase of DA is still debated.[7] There is considerable evidence that addiction results in neuroadaptive processes within the brain circuits that oppose the acute reinforcing actions of drugs of abuse. These changes lead to impairment in the mechanisms that mediate positive reinforcement and to the development of affective changes such as anxiety, dysphoria and depression during withdrawals.

Abundant evidence exists implicating these changes with disturbances in DA and 5-hydroxyltryptamine (5HT) transmissions in the nucleus accumbens.[3, 7, 27, 30-31]

In addition, enhanced release of corticotrophin releasing factor (CRF) in the central nucleus of amygdala has been suggested to underlie the anxiogenic and stress-like consequences of withdrawal that are common to all substances of abuse.[31]

The causes of drug abuse are complex and multifactorial. These include social, economic and educational factors. Laboratory animals on whom social, economic and educational variables do not operate, voluntarily self-administer the same drugs human beings abuse but will not self-administer other drugs (non-drugs of abuse). These findings strongly suggest important biological basis for drug abuse.[32] The findings that laboratory animals will voluntarily self-administer the same drugs and secrete same into highly selective and specific brain loci and not others is indicative of the neurological nature of drug abuse. Neurochemical, neuroanatomical and pharmacological studies have identified dopamine-rich brain regions, including the basolateral amygdala, nucleus accumbens and prefrontal cortex as likely sites for mediation of motivating effects of drugs of abuse.[30-32]

The first experience of the use of drugs of abuse may be rewarding (producing pleasurable feelings) or unrewarding. Those individuals who find the experience rewarding are said to be susceptible to the rewarding effects of the drugs. Given the right conditions (environmental, physiological and other factors), susceptible individuals will want to repeat the drug-taking experience and a minority of these individuals will continue to use or abuse the drugs. Continued use of the drug may lead to drug dependence and addiction.[30-32]

Effects: The onset of effects of THC after smoking marijuana occurs within minutes and reaches a maximum after 1 2 hours. The most prominent effects are euphoria and relaxation. Users also report feelings of well-being, grandiosity, and altered perception of passage of time. Dose-dependent perceptual changes (eg visual distortions), xerostomia, drowsiness, smokers' cough, diminished co-ordination, memory impairment, and marijuana amotivational syndrome (loss of energy and drive to work), may occur. Cannabinoids can also create a dysphoric state, and following the use of high doses, visual hallucinations, depersonalization and frank paranoid psychosis may ensue. Additional adverse effects of THC include tachycardia, hypotension and a reddening of the conjunctiva (a bloodshot appearance characteristic of cannabis smokers) these resulting from peripheral vasodilation. The effects of increased appetite, attenuation of nausea, decreased intraocular pressure, bronchodilation and relief of chronic pain have led to the use of cannabinoids eg Dronabinol and Nabilone, in medical therapeutics. However, this issue has continued to solicit controversy mainly because of the founded fear that cannabis may serve as a "gateway" to the consumption of "hard drugs", just as cigarette and alcohol have done.[3, 7, 26-32, 33-34]

Chronic exposure to marijuana leads to dependence, manifested by a distinctive, but mild and short-lived, withdrawal syndrome that includes restlessness, irritability, mild agitation, insomnia, nausea and cramping.[7, 35] This syndrome, however, is not typically seen clinically except in persons who use marijuana on a daily basis and stop abruptly.[35] In fact, relative to the number of marijuana smokers, few patients, motivated by fear of withdrawal symptoms, seek treatment. Hence, the occurrence of this syndrome generates controversy. The relative risk for addiction of cannabis is 2.[7, 32, 37]

Effects of associated problems: These include cognitive deficits (lack of concentration, memory problems, impaired judgment); emotional problems (frequent negative emotions often filled with anger, hate and resentment); social problems (weakening of social interactions, problems at school, work and with family/friends, also legal and financial problems, engagement in risk behaviour that may result in infection with HIV and other sexually transmitted diseases, teenage pregnancy and unsafe abortions etc); psychiatric problems (depression, anxiety, low stress tolerance, low self-esteem, isolation and delusions); as well as poor spiritual health due to lack of spiritual purpose in life.[1, 12-23, 25-27]

Management of Cannabis Abuse and Addiction

History and physical examination: These must be conducted to elicit specific symptoms and signs of drug abuse, dependence and addiction such as:

- Stereotyped drug-taking patterns despite adverse consequences on the patient, his family and the society.
- Physical signs eg the characteristic conjunctivitis, chronic bronchitis and cardiovascular problems.
- Impairment of cognitive functions eg distorted thinking including the denial that there is a drug problem, disorientation and loss of contact with reality.

- Emotional instability eg panic reactions, sinking sensations and
- Antisocial behaviour eg isolationism, disorganized behaviour[28]

A toxic confusional state can occur after heavy cannabis consumption as well as psychotic episodes especially in those with a family or personal history of schizophrenia.[28-29,32-33]

Laboratory investigations: Assay of pharmacologically active THC in biological fluids is still a problem but routine and other necessary investigations should be carried out as indicated.[28,32-34]

Treatment and rehabilitation: Cannabis abuse and addiction have no specific treatment.[38] Therapeutic approach include:

Counseling: This is to get the patient wish to stop using the drug. Since replacement therapy is neither necessary nor possible, it is essential to identify problems associated with the drug misuse which may serve to precipitate or maintain it and intervene where possible.

Intervention: This may be directed at physical ill health, psychiatric comorbidity, social problems like difficult interpersonal relationships, poor occupational and living conditions as well as family disharmony.[28, 33-39] Some patients self medicate with cannabis to treat emotional or psychological illness. Such should be effectively handled. Thus for patients with drug-induced psychosis, psychotherapy is required but iv Diazepam (or Chlorpromazine or Haloperidol) may be used for sedation. Hypotension usually responds well to iv fluids.[28-29] Accompanying depression, suffered by heavy users, may respond to antidepressant medication, but this should be decided on an individual basis considering the severity of the affective symptoms after the THC effects have dissipated.[38-39]

Referral: Relapsing patients and those with severe complications should be referred to specialist drug misuse services. Support can also be provided by self-help groups and voluntary bodies such as church groups, non-governmental organizations (NGOs) and Narcotic Anonymous in the UK.[28,39]

Prevention**:** Cannabis abuse and addiction is a preventable disease. Recent research findings[10, 12,25] particularly the National Institute on Drug Abuse (NIDA) funded research[25] have shown that prevention programmes that involve the family, schools, communities, the media and healthcare professionals are effective in reducing drug abuse. Prevention initiatives include reduction of risk factors and strengthening protective factors against drug abuse. Risk factors include peer pressure and parental antisocial behaviour; availability of marijuana through increased production of cannabis and through international criminal syndicates. Others are changes of attitude especially among young persons that have enhanced acceptability of drug consumption. Also implicated are social changes in many countries that encourage a weakening of family cohesion and of traditional values, poor educational system, the spread of urbanization, presence of disadvantaged sections of society (low socioeconomic status, high or low population density, high alienation of citizens); high crime rate; unemployment and lack of alternative forms of relaxation and recreation.[10, 12-26, 31-32] Protective factors include adoption of counteractive social measures and reduction of drug supply by discouraging illegal production. International control of drug smuggling as well as the appropriate national laws and resources of drug law enforcement agencies, eg NDLEA, within individual countries should be strengthened. Cannabis traders should be prosecuted to serve as a deterrent to others. Family bonding, cherished traditional and religious values should be encouraged. Effective education and public enlightenment, which should avoid dramatic or exaggerated accounts but must present the risks of drug abuse and misuse in a factual and honest manner that counteracts the biased misinformation and wrong attitudes available from drug peddlers, should be promoted.[10,12-26,31-33,39]

It is important to recognize cannabis users as being ill. Hence, they should not be condemned but be given sympathetic treatment and rehabilitation.[35,39]

Conclusion

Cannabis abuse and addiction is a major problem world-wide. As a chronic brain disease, it is among the most costly of such diseases in modern society. The DA reward system as well as other neurochemical systems involving 5HT and CRF are brain circuits implicated in the addictive process and behaviour.

Although there is at present no definitive treatment for the "molecular switch and the various components of the spiraling distress-addiction cycle", the adverse effects and complications of cannabis abuse and addiction can be adequately managed by interventions directed at restoring physical, mental, emotional, social and spiritual health as well as family harmony together with improved political and socioeconomic conditions. Since prevention is the key to successful management, urgent attention should be paid to reduction of risk factors and

strengthening of protective factors against this menace by the international community, governments, mass media, institutions of learning, religious groups, NGOs, parents and teachers, and more importantly healthcare professionals.

Thus, by mass mobilization and by many means, we can effectively reduce and remedy the tragic effects of cannabis abuse and addiction on individuals, families and society.

References

1. Atrens D. Drug addiction as a demonic possession. Overland 2000; 158: 19 24.
2. White FJ. A behavioural/ systems approach to the neuroscience of drug addiction. J Neuroscience 2002; 22(a): 3303 3305.
3. Cami J, Fame M. Mechanism of disease: Drug addiction. N Engl J Med 2003; 349: 975 986.
4. World Health Organization (WHO). The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines. Geneva: WHO, 1992.
5. American Psychiatric Association (APA). Diagnostic and statistical manual of mental disorders. 4th ed, text revision: DSM-IV-TR, Washington DC; APA, 2000.
6. Luscher C, Ungless MA. The mechanistic classification of addictive drugs. PLoS Med 2006; 3: e437.
7. Luscher C. Drugs of abuse. In: Katzung BG (ed). Basic and clinical pharmacology. 10th ed, Boston: McGraw Hill, 2007: 511 523.
8. Ariel LS, Lisa LL, Ning L, et al. Episodic heavy drinking and marijuana use among college students. Public Health and the Environment. APHA Washington DC, Nov 6 10, 2004.
9. Affinnih YH. A preliminary study of drug abuse and its mental health consequences among addicts in Greater Accra Ghana. J Psychoactive Drugs 1999; 31: 395 403.
10. Bell R, Wechster H, Johnston LD. Correlates of college students marijuana use. Results of a US national survey. Addiction 1997; 92: 571 -581.
11. Cannabinews. College marijuana use - a growing problem. Boston Globe. www.drugsense.org. (October 2000).
12. National Household Survey on Drug Abuse (NHSDA) Report: Marijuana use among youths, 2000.
13. Lambo TA. Medical and social aspects of drug addiction in West Africa with special emphasis on psychiatric aspects. Bulletin on Narcotics 1960; 17: 1 3.
14. Anumonye A. Drug use among young people in Lagos, Nigeria. Bulletin on Narcotics 1980; 32(4): 39 45.
15. Odejide AO. Problems of drug abuse in Nigeria: a review of the existing literature and suggestions on preventive measures. Nig Med J 1980; 10: 122 128.
16. Olataru M. Pattern of self-reported drug use among secondary school students in Bendel State Nigeria. United Nations' Office on drugs, United Nations, 1981.
17. Abiodun OA, Adelekan ML, Ogunremi OO, et al. Psychosocial correlates of alcohol, tobacco and cannabis use amongst secondary school students in Ilorin, Nigeria. W Afr J Med 1994; 13(4): 213 217.
18. Adelekan ML, Makanjuola AB, Ndom RJ, et al. 5 yearly monitoring of trends of substance use among secondary school students in Ilorin, Nigeria, 1988 1998. W Afr J Med 2001; 20(1): 28 36.
19. Fatoye FO, Morakinyo O. Substance use among secondary school students in rural and urban communities in southwestern Nigeria. E Afr Med J 2002; 79(6): 299 305.
20. Eneh AU, Stanley PC. Pattern of substance use among secondary school students in Rivers State, Nigeria. Nig J Med 2004; 13(11): 36 39.
21. Omigbodun OO, Babalola O. Psychosocial dynamics of psychoactive substance misuse among Nigerian adolescents. Ann Afr Med 2004; 3(3): 111 115.
22. Abasiubong F, Atting I, Bassey E et al. Gender difference in knowledge and pattern of psychoactive substance use amongst secondary school students in Akwa Ibom State, Nigeria. Nig Clin Rev J 2006; 10(5): 11 17.
23. Abiodun B, Afolayan AM. Pattern of marijuana use among male university students: a case study. J Med Sci 2007; 7(6): 1068 1072.
24. Emafo P. Drug regulation and social policy: narcotics, law and policy in Nigeria. 1990: 1 85.
25. National Institute on Drug Abuse (NIDA). Marijuana: Facts for teens. 1998. www.nida.gov.
26. Thornicroft G. Cannabis and psychosis: is there epidemiological evidence for an association? Br J Psychiatry 1990; 157: 25 33.
27. Florindo S, Celia RR, Jose SG. Drug Dependence, mental impairment and education. J Psychology 2008; 42(1): 143 150.
28. Jones AL, Karalliede L. Drugs of misuse: cannabis. In: Boon NA, Colledge NR, Walker BR (eds). Davidson's principles and practice of medicine. 20th ed, Philadelphia: Churchill Livingstone, 2006: 212.
29. Laurence DR, Bennet PN, Brown MJ. Cannabis. Clinical pharmacology. 8th ed, Endinburgh: Churchill Livingstone, 1997: 179 181.
30. Konipsky KL, Hyman SE. Molecular and cellular biology of addiction. In: Davis KL, Charney D, Coyle JT, Nemerof C. (eds). Neuropsychopharmacology: the fifth generation of progress. Philadelphia; Lippincott Williams & Wilkins, 2002; 1367 1379.
31. Weiss F, Ciccocioppo R, Person LH et al. Compulsive drug-seeking behaviour and relapse. Neuroadaptation stress and conditioning factors. Ann NY Acad Sc 2001; 937: 1 22.
32. Lowinson JH, Ruiz P, Miliman RB, Langrod JG (eds). Substance abuse: a comprehensive textbook. 3rd ed, Philadelphia: Williams & Wilkins, 1997: 19 40.
33. Rang HP, Dale MM, Ritter JM, Moore PK. Drug dependence and drug abuse. In: Pharmacology. 5th ed, Philadelphia: Churchill Livingstone, 2003: 594 611.
34. Mycek MJ, Harvey RA, Champe PC. CNS stimulants. In: Lippincott's reviews: pharmacology. Philadelphia: Lippincott Williams & Wilkins, 2000: 104 105.

35. Brunton LL, Parker KL, Blumenthal DK, Buxton ILO (eds). Drug addiction and drug abuse. In: Goodman & Gilman's Manual of pharmacology and therapeutics. Intl ed, New York: McGraw Hill, 2008:385-399.
36. Okpako DT. Drug abuse. In: Principles of pharmacology a tropical approach. 2nd ed. Cambridge: Cambridge University Press, 2002: 533-537.
37. Tripathi KP. Hallucinogens. In: Essentials of medical pharmacology. 4th ed. New Delhi: Jaypee Brothers Medical Publishers, 2001: 430-431.
38. O'Brien CP. Drug addiction and drug abuse. In: Hardman JG, Limbird LE. (eds). Goodman & Gilman's The pharmacological basis of therapeutics. 10th ed, New York: McGraw Hill, 2001: 636 638.
39. O'Brien CP. A range of research-based pharmacotherapies for addiction. Science 1997; 278: 66 70.