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Review Article

Substance Abuse and Sexual Functioning: An Overview of Mechanisms

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Abstract

Sexuality remains a subject of ongoing debate, with significant implications for self-perception and self-esteem, and addiction is a factor that can adversely affect it. Sexual dysfunction heavily burdens people with substance use disorders, as it can cause severe issues such as erectile dysfunction, loss of libido, dyspareunia, and delayed ejaculation. These issues can be caused by hormonal imbalances, loss of vaginal lubrication, lowered blood flow to the penile tissue, and problems with other organs, such as the liver. There could be some therapies to resolve such issues at least partially, for example, medication (oral and injectable), low-intensity focused shockwave therapy, vacuum constriction device, promoting exercise, and testosterone replacement therapy. Utilizing such methods could be helpful, but we could not be sure of their effectiveness. The current review aims to give a brief overview of sexual function, substance use disorders, and their impact on sexuality.

Keywords: Substance use disorder, Addiction, Sexual dysfunction, Erectile dysfunction, Testosterone replacement therapy

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Introduction

Reproductive medicine has long faced significant challenges related to the issue of infertility. Infertility is a distinct disease, according to the World Health Organization, and because it is so common, it should be treated as a social disease.[1] Fertility rates are falling globally for several reasons. The causes of infertility can affect both men and women, occasionally even both, causing issues at every step of the sexual response.[2,3]

Common risk factors for sexual dysfunction include the person's overall health and non-communicable diseases such as cardiovascular diseases, diabetes mellitus, psychiatric/psychological disorders, genitourinary diseases, and chronic diseases.[4]

Substance use disorders are a significant cause of mortality and morbidity and are especially prevalent in young adults.[5,6] These disorders are a widespread issue that contributes to avoidable morbidity and mortality. According to estimates, 18.4% of adults worldwide used alcohol heavily or intermittently in 2015. Similarly, 15.2%, 3.8%, and 0.37% of people reported using tobacco, marijuana, or opioids, respectively.[7]

It is becoming more widely acknowledged that substance abuse and dysfunctional sexual activity are related.[8] Considering the importance of the reproductive system for the health of the family and society, as well as the increasing prevalence of substance use disorders, we attempt to look at the relationship between sexual dysfunction and substance use disorders caused by consumption of alcohol,[9] nicotine,[10] marijuana,[11] hallucinogens,[12] stimulants[13] and sedative substances[14] (Figure 1, Table 1).

Definition of substance use disorder

Substance abuse, a significant and escalating issue of this century, involves the use of various chemical substances that can end in addiction through diverse means. It is a chronic, multidimensional ailment affecting social, psychological, physical, and sexual health.[45] The use of substances like marijuana, alcohol, and nicotine, which are considered drugs, can cause alterations in mood, perception, cognition, brain function, and behavior, resulting in an inability to control their consumption, be it legal or illegal.[46] This leads to adverse consequences encompassing social, economic, legal, and health aspects for those addicted.

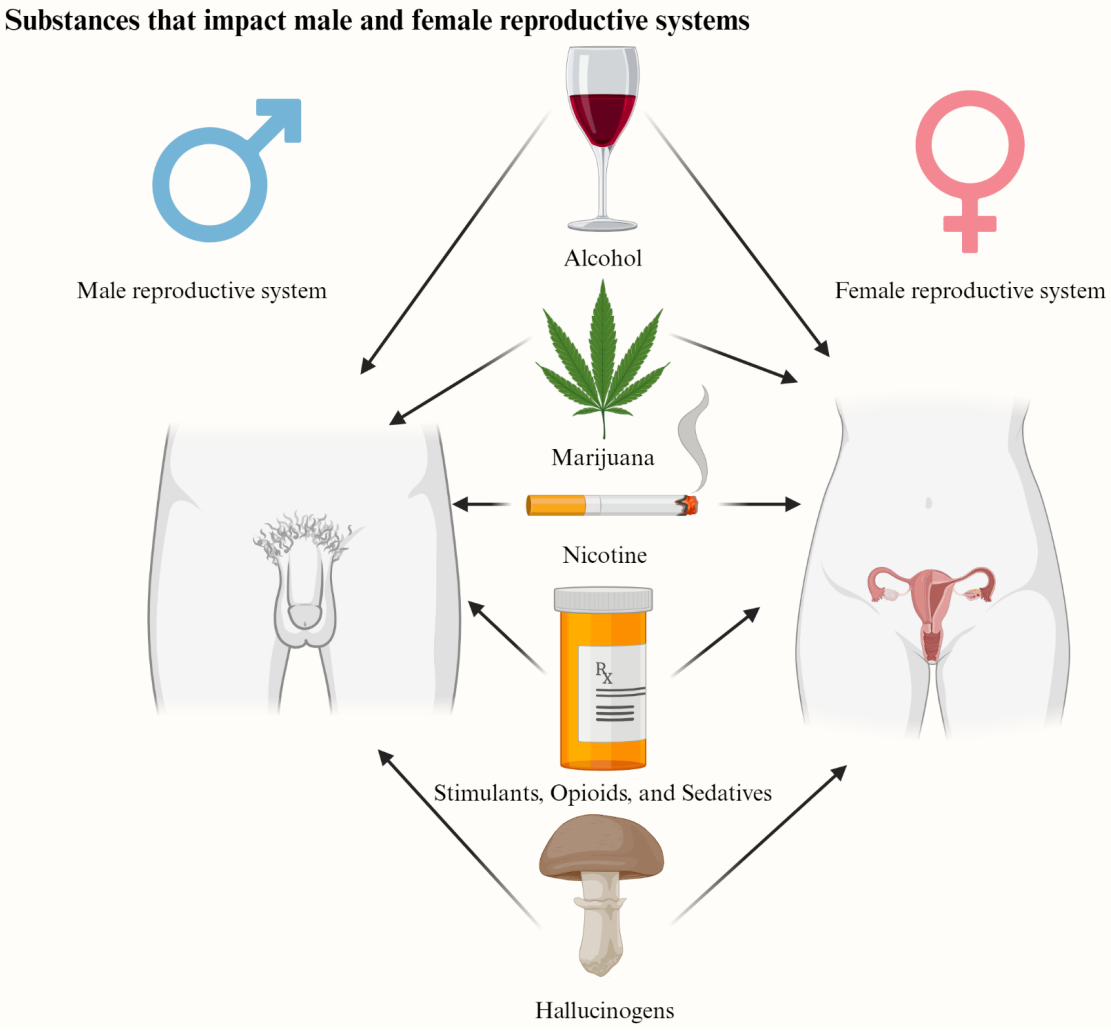

Figure 1. Common substances of abuse impacting the reproductive tract in both men and women. Created with BioRender.com.

Initiation of psychoactive substance use typically begins in adolescence and may start with experimental use in social settings. For some, particularly with opioids, addiction initiates with prescribed medications or medications obtained from those with prescriptions. The risk and speed of addiction vary based on the drug; opioid painkillers, for instance, pose a higher risk and induce dependence more rapidly.[46]

In the context of substance use, discussing sexual function and dysfunction is vital, as substances like alcohol, opioids, and cannabis are often used with the anticipation of improving sexual functioning. However, studies indicate that chronic substance use negatively impacts sexual function, leading to various forms of sexual dysfunction in both men and women.[10,47]

Substance use disorder is clinically diagnosed as per the *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition (DSM-5). It is defined as persistent and problematic substance use resulting in significant impairments or distress. It encompasses a wide range of substances such as alcohol, stimulants, opioids, cannabis, tobacco, and others. DSM-5 outlines specific criteria for diagnosing substance use disorders, including risky use, social impairment, impaired control over substance use, and pharmacological indicators like tolerance and withdrawal symptoms.[48] The DSM-5[49] defines substance use disorders as the presence of at least two of 11 criteria over a year, with the severity of the disease being indexed by the number of endorsed criteria (2–3 = mild; 4–5 = moderate; 6 = severe). Substance use disorder criteria in DSM-5 widely relate to the existence of substance-related issues, such as increased use, unsuccessful stops or reductions in use, continued use despite adverse physical, psychological, and social effects, persistent craving, tolerance development, and withdrawal symptoms.[49]

The severity of substance use disorder can be classified as mild, moderate, or severe based on the number of criteria met. A comprehensive understanding of substance use disorders considers biological, psychological, and social factors. Genetic predispositions, neurological changes, brain reward pathway alterations, peer pressure, family dynamics, socioeconomic status, and substance availability all contribute to the risk of developing this disorder.[50]

Table 1. An overview of drugs of abuse and their impact on the reproductive tract

Type of drugs	Animal, human	Outcome	Reference
Opioids	Both sexes of human	Delayed male ejaculation and decreased vaginismus symptoms in women. hypogonadism in both sexes	15
Opioids	Both sexes of human	Erectile dysfunction and diminished libido in men, amenorrhea or oligomenorrhea in women, and infertility or bone loss in both sexes	16
Opioids	Both sexes of human	Induced hypogonadism, both in males and females	17
Marijuana	Both sexes of human	Feelings of sexual satisfaction and pleasure enhanced or variably improved	18
Tetrahydrocannabinol	Male mice	Blood testosterone first increased before falling back to baseline levels	18
Nicotine	Both sexes of human	Erectile dysfunction in males diminished vaginal lubrication and delayed orgasm in females	19,20
Nicotine	Men	Erectile dysfunction (decreased penile stiffness and degradation of various penile blood pressure measurements)	18,21
Nicotine	Both sexes of human	Many stages of the sexual response cycle impacted, depression	20
Cocaine	Men	Sustained utilization can reduce sexual desire and performance and lead to difficulties in achieving orgasm	22,23
Cocaine	Men	Decreased libido and sexual performance, difficulty achieving erections,	24
Cocaine	Females	Enhanced probability of sexual dysfunction and reduced sexual desire	25
Cocaine	Men	Priapism, a prolonged and painful erection	26
Cocaine	Both sexes of human	Risky sexual behaviors and psychological challenges	27
Amphetamine	Men	Heightened pleasure and reduced inhibitions Anorgasmia and diminished libido in high doses	28
Amphetamine	Both sexes of human	Delayed ejaculation and erectile dysfunction in men delayed orgasm in women	29,30
Methamphetamine	Men	Extended state of heightened sex drive in men but with inadequate erections	31
Sertraline and venlafaxine	Both sexes of human	Sexual dysfunction	32
Ecstasy	Men	Lower scores in the sexual desire, erectile function, and general satisfaction subscales, instances of priapism	33–35
Benzodiazepines	Both sexes of human	Reduced sexual desire and delayed orgasm	36,37
Benzodiazepines	Men	Decreased libido, erectile dysfunction	38
Clonazepam, Alprazolam, and Diazepam	Both sexes of human	Sexual dysfunction	39
Ketamine	Both sexes of human	Erectile dysfunction in men sexual dysfunction in women	40
MDMA	Men	Increased ejaculation latency, reduced sexual desire, and impaired sexual satisfaction	35
Alcohol	Men	Reduction in erection quality and ejaculatory function, drop in sexual arousal	41
Alcohol	Men	Hypogonadism, testosterone suppression, erectile dysfunction	10
Alcohol	Women	Decreased sexual function	42
Alcohol	Women	Low sexual desire, inability to achieve orgasm, dissatisfaction with orgasm, and low or nonexistent vaginal lubrication	43
Alcohol	Women	Delayed puberty, disrupted regular menstrual cycles, and sped up the anovulatory cycle	44

Effectively managing and treating substance use disorder often involves a combination of behavioral therapies, pharmacotherapy, and support groups. Behavioral therapies like motivational enhancement therapy, cognitive-behavioral therapy, and contingency management effectively assist individuals in modifying their behaviors and attitudes toward substance use. Pharmacotherapeutic interventions such as methadone for opioid use disorder or nicotine replacement therapy for tobacco use disorder help in reducing cravings and withdrawal symptoms.[51-53]

Sexual functioning and its origin

In the 1960s, Masters and Johnson were the first to investigate and write about both good and dysfunctional sexual function. The cycle of the human sexual response is broken down into four phases: stimulation, plateau, orgasm, and resolution.[54] For both men and women, this is the conventional, linear model of sexual function.[55] Sexual action that smoothly transitions from excitation to relaxation constitutes normal sexual functioning with a sense of fulfillment, joy, and contentment.[56]

Female sexual function

Increased vaginal lubrication, pelvic blood flow, and clitoral and labial engorgement are caused by neurotransmitter-arbitrated nonvascular and vascular smooth muscle relaxation, which starts the female sexual response cycle. Combinations of neuromuscular and vasocongestive processes mediate these mechanisms. Sexual arousal, genital sensation, vaginal lubrication, libido, and orgasmic capacity complaints are caused by physiological conditions that interfere with the normal female sexual response.[57]

To properly diagnose and treat female sexual dysfunction, one needs to have a comprehensive grasp of female pelvic anatomy. It is helpful to divide the female pelvic anatomy into two categories, even though it comprises a continuum of organs and systems connected in structure and function.[58]

Male sexual function

Numerous genital organs and structures play a part in male sexual function by producing fertilizing gametes and enabling female partner insemination. The testes are part of the reproductive and endocrine systems because they produce androgens and spermatozoa and are tightly controlled by the hypothalamopituitary axis. A complex and well-coordinated interaction between the somatic and autonomic nerve systems in various brain regions, the spinal cord, and pertinent peripheral organs regulates sexual reactions. The penis must have an erectile body to function, and penile tumescence results when the penis becomes engorged with blood. The relaxation of the smooth muscle cells of the erectile tissue and the endothelium of the penile arteries is what causes blood engorgement. When the ischiocavernosus muscles tighten, the penis becomes even more stiff. Penile erection is brought on by stimuli from peripheral or central sources that activate specific spinal nuclei. Ejaculation consists of two steps: emission and expulsion, which correspond to the distinct semen components being secreted by sex glands and the semen being forcedly expelled as a result of rhythmic contractions of the bulbospongiosus muscle, respectively. When the excitatory threshold is achieved, a spinal generator of ejaculation integrates genital sensations and sexual signals. It triggers ejaculation by coordinating the activation of autonomic and somatic pathways, controlling the peripheral events of ejaculation.[59]

The patient's identity, self-esteem, shame, and vulnerabilities are intimately entwined with their sexuality.[60]

The role of substance use disorders in sexual dysfunction

Opioid use disorder

Opium, which is made from the opium poppy's sap, is the source of opiates. The word "opiate" is used to describe both natural opium alkaloids like morphine and synthesized opium alkaloids like codeine and heroin.[61] Opioid use disorder is a chronic, curable condition marked by a lack of control over opioid use, compulsive usage, and persistent use despite adverse effects. Opioid use disorder is linked to severe morbidity and mortality if left untreated.[62] Initial opioid use delays male ejaculation and decreases vaginismus symptoms in women, giving the impression of improvement in sexual function. However, long-term use of opioids like morphine and heroin lowers luteinizing hormone release even further, which causes lower levels of testosterone and estradiol and an increase in free sex hormone-binding globulin, which results in hypogonadism.[15] While a shift in consciousness may occasionally lead to sexual enhancement in rare cases, opioid and opiate usage almost always results in a decrease in desire. Opioids like heroin lead to sexual disorders like erectile dysfunction and low libido.[16] Additionally, it has been demonstrated in the study done by Antony et al. that opioids have an impact on the secretion of prolactin and sex hormones, as well as opioid-induced hypogonadism both in males and females.[17]

Marijuana use disorder

Cannabis is the most commonly used illicit substance in the world, with 183 million users, or almost 4% of the world's population.[63]

Tetrahydrocannabinol, primarily produced in the plant's leaves and flower buds, is one of the cannabinoids thought to be responsible for the plant's psychoactive and behavioral effects.

Non-psychoactive cannabinoids like cannabidiol, cannabichromene, and cannabigerol, non-cannabinoid components belonging to several types of natural sources, and 9-tetrahydrocannabinol have a variety of medical uses. More than 560 components of cannabis have now been identified. Recent research has revealed the therapeutic benefits of cannabis and cannabinoids and some of the significant disorders they may be used to treat.[64]

There have been reports on both beneficial and adverse effects of marijuana on sexuality. It has been observed that high doses induce decline and impairment in libido.[65] In more reasonable dosages, it has been found to improve sexual performance.[66]

In a study on marijuana users, only 40% of the ladies reported that the quality of their orgasm was improved or variable, compared to 68% of the males. Thirty-nine percent of the males and solely 13% of the females mentioned that the intercourse duration was amplified or variably enhanced. Generally, 75% of the males and 90% of the females mentioned that feelings related to sexual pleasure and satisfaction were improved or variably intensified by marijuana.[18]

The mechanism of action of marijuana's adverse effects is unclear. One study indicated that plasma testosterone was decreased in chronic heavy marijuana smokers, but this finding was disproved in a follow-up investigation.[67,68]

A quick and sustained increase in serum testosterone

was produced by oral administration of low doses of tetrahydrocannabinol. After high-dose oral tetrahydrocannabinol delivery, blood testosterone increased before falling back to baseline levels.[69] This process may help to explain why low amounts of marijuana are linked to sexual enhancement. In contrast, high dosages are linked to sexual dysfunction in people, even though the relationship between blood testosterone levels and sexual arousal in humans is not well understood.[65]

Nicotine use disorder

The critical factor in continued tobacco smoking is nicotine. The foundation for the best smoking cessation therapy is knowledge of how nicotine keeps people smoking.[70]

Nicotine is extracted from the tobacco in cigarettes and inhaled as smoke. Nicotine is quickly absorbed into the pulmonary venous circulation after being carried into the lungs by smoke particles. The nicotine then quickly travels from the lungs to the brain via arterial circulation, where it binds to nicotinic cholinergic receptors (ligand-gated ion channels that typically bind to acetylcholine). Nicotine binding at the junction between two receptor subunits opens the track, enabling sodium or calcium to enter. More calcium can enter the cell due to the activation of voltage-dependent calcium channels by the entrance of these cations. The release of neurotransmitters is one of the results of calcium entering a cell.[71]

Smoking has long been known to affect sexual function, particularly in men. Erectile dysfunction is brought on by smoking and involves both erection initiation and maintenance. This is because nicotine has potent vasoconstrictor properties. Nitric oxide and other vasoactive molecules, like relaxing factors generated from the endothelium, are thought to be decreased by nicotine. Although the effects of smoking on female sexual function have not been well investigated, several studies have found that the vascular effects of nicotine lead to delayed orgasm and decreased vaginal lubrication. Smokeless tobacco users and people who only use nicotine alone can both experience these effects of tobacco on sexual function.[19,20]

According to a 1992 study by Hirshkowitz and colleagues on 314 smokers with erectile dysfunction, smoking more cigarettes per day was linked to a decline in several erectile function indicators.[21] Capacities include decreases in penile stiffness and degradation of various penile blood pressure measurements. Other evidence indicates that long-term nicotine usage may adversely affect some parts of male sexual function.[18,21]

Many stages of the sexual response cycle are impacted by nicotine use, which is directly related to sexual dysfunction. One-fourth of people who use tobacco also meet the prerequisites for depression. In addition to health education and awareness-raising, tobacco-related death prevention may be accomplished at a reasonable cost by using interventions as primary and primordial preventative measures.[20]

Stimulant use disorder

Stimulant use disorder is a type of substance use disorder characterized by the continued consumption of stimulants like amphetamines, cocaine, or related substances, resulting in mild to severe impairment or distress.[49] These stimulants can be ingested through various routes, such as inhalation, injection, insufflation, oral ingestion, mastication, or as a beverage, exerting influences on behavior, cognitive processes, and the physiological state of individuals. The normal functioning of the dopamine neurotransmitter system is notably impacted by stimulants,[25] ending in enhancement of free dopamine levels in the brain.[25,72-75]

Cocaine, a potent dopamine agonist, initially enhances sexual functioning in men, but prolonged use can reduce sexual desire and function and lead to difficulties in achieving orgasm.[22,23,47] Male users often strongly associate sexual arousal and cocaine use; however, this link tends to diminish as they seek treatment, resulting in challenges in sexual functioning while under the influence of cocaine.[76] Chronic cocaine abuse can decrease libido and sexual performance, with studies indicating that 66% of long-term cocaine users report difficulty achieving erections.[24] Moreover, regular cocaine users often exhibit heavy alcohol consumption, and a study on men addicted to both alcohol and cocaine reported issues such as low sexual desire (62%), erectile dysfunction (52%), and delayed ejaculation (30%).[24] In females, crack cocaine usage has been linked to reduced sexual desire and an increased likelihood of sexual dysfunction.[25] Cocaine can also lead to priapism, i.e., prolonged and painful erection,[26] and is related to risky sexual behaviors and psychological challenges.[27]

Amphetamines, including racemic amphetamine, d-amphetamine, and methamphetamine, are notorious for their high addiction potential and long-term usage links to severe cardiovascular and pulmonary disorders, depression, psychosis, and cognitive decline.[77] They are recognized as potent aphrodisiacs.[78] Human observational studies have revealed various sexual dysfunction patterns associated with amphetamine use, influenced by factors like dosage, route of administration, user habits, and social context.[79] Low doses can heighten pleasure and reduce inhibitions, potentially benefiting men with rapid ejaculation issues. Conversely, high doses may lead to anorgasmia and diminished libido.[28] Methamphetamine, a potent amphetamine, is notably linked to heightened sexual behavior due to increased social confidence, sexual disinhibition, and a heightened sense of physical energy, enhancing the overall sexual experience.[80,81] Prolonged use of amphetamine-based drugs has been associated with erectile dysfunction and delayed ejaculation in men in line

with delayed orgasm in women.[29,30] A distinct phenomenon associated with prolonged methamphetamine use is an extended state of heightened sex drive in men but with inadequate erections, colloquially known as "crystal dick".[31] Methamphetamine use is associated with a manyfold likelihood of participating in high-risk sexual behaviors, particularly among homosexual, bisexual, and heterosexual users, with potential implications for HIV and sexually transmitted infection transmission.[82,83]

Psychotropic drugs, including selective serotonin reuptake inhibitors, monoamine oxidase inhibitors, and tricyclic antidepressants, are frequently linked to the development of sexual dysfunction.[32,84] Antidepressant treatment is known to significantly contribute to sexual dysfunction in both men and women, with notable variations in effects observed among different drugs within this class.[84] A recent meta-analysis examining treatment-induced sexual dysfunction reported that medicines with a predominant serotonergic action, such as Selective Serotonin Reuptake Inhibitor (SSRIs) and venlafaxine, exhibited the maximum probability of causing treatment-associated Sexual Dysfunction (SD), ranging from 26% for fluvoxamine to 80% for sertraline and venlafaxine.[32] However, some points warrant consideration. The lower sexual dysfunction rates associated with fluvoxamine and escitalopram are unclear in terms of whether they stem from drug-specific characteristics or differences in investigative methodologies.[32] The mechanisms underpinning drug-induced sexual dysfunction are not fully understood. A prevalent hypothesis suggests that SSRIs and venlafaxine may reduce dopaminergic transmission through serotonin receptors in the mesolimbic area, impacting sexual desire and orgasm, aligning with the expected sexual dysfunction associated with these drugs.[85] This hypothesis gains further support by suggesting that serotonergic agents with antagonist rather than agonist action on 5HThR2, such as mirtazapine and nefazodone, do not induce sexual dysfunction.[86] Additional proposed mechanisms include the decrease of nitric oxidase synthase and anticholinergic effects related to paroxetine, which could also contribute to antidepressant-related sexual dysfunction.[85]

Ecstasy, also known as 3,4-methylenedioxymethamphetamine, is a synthetic psychoactive substance that shares chemical similarities with methamphetamine, a stimulant, and mescaline, a hallucinogen classified as an illicit drug; ecstasy functions as both a stimulant and a psychedelic, resulting in heightened energy levels and distortions in time perception, accompanied by increased enjoyment from tactile experiences.[87,88] While consuming ecstasy, many individuals report a sense of emotional closeness without a strong desire for penetrative sex.

On the other hand, some users, particularly men who experience sex with men and bisexual females, experience increased sexual arousal with ecstasy, and they specifically use the drug for sexual enhancement. Those engaging in sexual behavior during ecstasy episodes often display sexual risk-taking behaviors, such as several partners and sex without condoms.[89,90]

Research indicates that ecstasy users exhibit lower scores in sexual desire, erectile function, and general satisfaction subscales compared to control groups. Notably, ecstasy use has been associated with instances of priapism, i.e., prolonged and often painful erection.[33-35] Furthermore, studies suggest a stronger association of heightened perceived sexual effects, such as length of intercourse, perceived sexual attractiveness of self and others, sexual desire, and sexual outgoingness, with the combined use of alcohol and ecstasy.[91] Sexual dysfunction and its association with stimulant use disorder have been extensively studied in recent years.

Stimulant use disorders involving substances like cocaine, methamphetamine, and amphetamines are strongly linked to sexual dysfunction. The impact on sexual functioning is evident in both males and females, affecting aspects such as desire, arousal, orgasm, and overall sexual satisfaction. Understanding this relationship is crucial for developing effective interventions to address both substance use disorders and associated sexual health issues. Stimulant use disorder and its effects on sexual function are critical areas of research that warrant further investigation for a comprehensive understanding of the interplay between stimulant use and sexual health. These findings emphasize the need for targeted interventions and support systems addressing both substance use disorders and their impact on sexual well-being.

Sedative use disorder

Sedatives, a class of drugs that depress the central nervous system, are widely used for their calming effects, with benzodiazepines for anxiety and barbiturates for sleep disorders being well-known examples. These substances enhance gamma-aminobutyric acid, an inhibitory neurotransmitter in the brain, effectively dampening neural activity and promoting relaxation. However, prolonged misuse can lead to dependence, resulting in a sedative use disorder.[92,93]

The association between sedative use disorder and sexual dysfunction is intricate, involving various neurobiological processes. Sedatives significantly influence critical neurotransmitters for sexual function, including gamma-aminobutyric acid, serotonin, and dopamine. This interference can disrupt normal sexual responses, causing sexual dysfunction. Specifically, benzodiazepines can hinder sexual arousal by altering dopamine, serotonin, and norepinephrine levels, ultimately reducing sexual desire and delaying orgasm.[36,37]

Furthermore, benzodiazepines are prevalent psychotropic drugs worldwide, commonly used for

various central nervous system-related disorders.[92] However, these properties are accompanied by various adverse effects.[94] Literature indicates that patients receiving benzodiazepines experience sexual dysfunction, including erectile dysfunction, decreased libido, and other unsought sexual urges.[38,95,96] Mechanistically, benzodiazepines induce sexual dysfunction mainly by enhancing GABAA receptor function, which dampens penile erection.[14] Additionally, diazepam's impact on serum cholesterol levels, a precursor for testosterone synthesis, may contribute to a decline in testosterone concentration.[97,98] Notably, patients using anxiolytic treatments such as alprazolam, clonazepam, and diazepam are associated with sexual dysfunction, with clonazepam being the most commonly used drug in these cases.[39]

In addition to neurobiology, sedative use profoundly affects psychological and emotional factors contributing to sexual dysfunction. Chronic use may induce anxiety, depression, or altered self-perception, all negatively impacting sexual desire, arousal, and overall sexual satisfaction. Sexual dysfunction encompasses a range of issues, from erectile dysfunction to reduced libido and delayed orgasm, arising from psychological, physiological, and environmental factors.[99] Anxiety, depression, relationship problems, chronic illness, and substance abuse, including sedative use, are known contributors.

Significantly, gender differences play a vital role in both sexual dysfunction and sedative use patterns. Males and females may experience variations in sexual desire, arousal, and satisfaction as a result of sedative use.[35] Understanding these gender-specific distinctions is crucial for tailoring effective treatments and interventions for sexual dysfunction in those with sedative use disorder.

Long-term sedative use can result in persistent sexual dysfunction even after discontinuation. The chronic alteration of brain chemistry and hormone levels can have enduring effects on sexual desire and performance. Withdrawal symptoms and the overall impact of addiction can exacerbate sexual dysfunction, emphasizing the need for comprehensive treatment strategies.[100]

Addressing both sexual dysfunction and sedative use disorder requires a multidimensional approach, including medical intervention, psychological counseling, and lifestyle modifications.[101] Cognitive-behavioral therapy, in particular, has shown promise in mitigating both sexual dysfunction and substance abuse.

In conclusion, the connection between sexual dysfunction and sedative use disorder involves a complex interplay of neurobiological, psychological, and emotional factors. Understanding this intricate relationship is vital for developing effective prevention and intervention strategies. Future research should focus on exploring the underlying mechanisms and identifying targeted treatments to improve the sexual health and overall well-being of individuals grappling with sedative use disorder and its associated sexual dysfunction. A holistic approach to treatment considering neurobiological and psychosocial aspects is necessary to address this pressing issue effectively.

Hallucinogen use disorder

The fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* of the American Psychiatric Association classifies hallucinogens as a diverse group of substances that, despite having various chemical structures and potentially involving multiple molecular mechanisms, produce comparable changes in users' perception, mood, and cognition.[49] This category includes a variety of substances, from naturally occurring plants to compounds created artificially. Ayahuasca, ketamine, ibogaine, 3,4-methylenedioxymethamphetamine (3,4-methyl enedioxymethamphetamine, lysergic acid diethylamide, and psilocybin (the active component in magic mushrooms) are a few examples.[102,103] Hallucinogens are known to have several adverse effects, including memory loss, anxiety, mood swings, and transitory paranoia. Two of the most often reported adverse effects were acute blood pressure rises and nausea.[103]

Additionally, they have adverse effects on sexual function. For example, Men who use ketamine are more likely to experience erectile dysfunction, with reports of erectile dysfunction varying between 30.8 to 52% of users. A lower score on the female sexual function index and, consequently, female sexual dysfunction and ketamine cystitis were associated with ketamine use. Finally, using ketamine was linked to less brain activity in response to sexual signals, which may partially reflect the neuronal origins of sexual dysfunction.[40] Based on a study by Kumsar et al, MDMA abuse was related to erectile dysfunction (ED), which increased ejaculation latency, reduced sexual desire, and impaired sexual satisfaction. MDMA users' International Index of Erectile Function total score was considerably lower than it was for the control group.[35]

Alcohol use disorder

Alcohol use disorders include those that are characterized by compulsive heavy drinking and a lack of control over alcohol intake. Alcohol use disorders are among the most common mental illnesses in the world, especially in high- and upper-middle-income nations. They are also linked to increased mortality and disease burden, primarily because of adverse effects on health, such as liver cirrhosis or damage.[104] The central and peripheral neurological systems are known to be harmed by chronic, excessive alcohol use. Dementia, peripheral neuropathy, delirium tremens, and autonomic neuropathy are a few examples of such symptoms.[105] For centuries, people have used alcohol as an aphrodisiac to increase sexual desire and performance. However, the variety of harmful

consequences of alcohol on sexual function has been documented in much research. Sexual arousal in men is just slightly increased. Higher doses, however, cause a reduction in erection quality and ejaculatory function as well as a drop in sexual arousal. Almost all types of male sexual dysfunction are brought on by prolonged alcohol consumption because of how it affects different organ systems.[41] It causes hypogonadism by inhibiting the hypothalamic-pituitary-adrenal axis, which lowers gonadotropin secretion.

Additionally, it results in testosterone suppression, which causes erectile dysfunction. Reduced gonadotropins or alcohol's direct effects on the testicles may suppress testosterone release, which would explain the lower testosterone levels. Reduced production of vasodilator molecules like nitric oxide and the harmful effects of the oxidants created during alcohol metabolism are two additional pathways that may be responsible for testosterone suppression. Erectile dysfunction may be brought on by alcohol-induced neuropathy or by the cardiovascular issues laid on by long-term alcohol usage.[10] One of the standalone risk factors for women's decreased sexual function is alcohol usage.[42] An equally significant risk factor for female sexual dysfunction is alcohol dependence. According to a research study focusing on women with alcohol dependence syndrome, sexual disorders like low sexual desire, inability to achieve orgasm, dissatisfaction with orgasm, and low or nonexistent vaginal lubrication are significantly more common in women with ADS than in women who stay away from alcohol.[43] Moreover, it has been reported that moderate alcohol use can delay puberty, disrupt regular menstrual cycles, and speed up the anovulatory process.[44]

Conclusion

Sexual dysfunction is a crucial matter, causing several problems for men and women worldwide. These problems range from erectile dysfunction to delayed orgasm and can cause severe distress for affected individuals. Substance use disorders are serious issues, especially among young individuals, and could lead to serious health issues such as sexual dysfunction. These disorders, including alcohol use disorder, marijuana use disorder, nicotine use disorder, and so on, could end in reduced desire for sex, ED, delayed orgasm, etc., via multiple pathways such as reduced blood flow to the penis, hormonal imbalance, and liver and other organs dysfunction. These issues could diminish the quality of life for impacted people with addiction; thus, we propose to use appropriate treatments for each case based on the substance of abuse comprising medication (oral and injectable), low-intensity focused shockwave therapy, vacuum constriction devices, promoting exercise, and testosterone replacement therapy. To conclude, it could be said that substance use disorders have serious sexual side effects, necessitating urgent attention to this issue due to their impact on patients' body image and quality of life.

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