REVIEWS

Effects of Cannabinoids on Female Sexual Function

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ABSTRACT

Introduction: With the legalization of both medical and recreational marijuana in some countries and a few US states, its use has become more widely prevalent. Both exogenous cannabinoids such as tetrahydrocannabinol (THC) and endogenous cannabinoids (endocannabinoids) have been shown to affect female gonadotropin pathways and female sexuality. Yet, our understanding of the mechanisms and effects on female sexual function is limited.

Aim: To review the literature regarding the effects of both endogenous and exogenous cannabinoids on female sexual function in both animals and humans.

Methods: We performed a PubMed search for English-language articles in peer-reviewed journals between 1970 and 2019. We used the following search terms: "cannabinoids," "endocannabinoids," "marijuana," "cannabis," and "female sexual function" or "sexual function." The main outcomes of the papers were reviewed.

Main Outcome Measure: The main outcome measure was sexual function in females.

Results: A total of 12 human studies and 8 animal studies that evaluated the relationship between cannabinoids and female sexual function were included. Study types in animals were blinded, prospective, placebo-controlled trials. Human studies were based primarily on questionnaire data. The data indicate dose-dependent effects on female sexual desire and receptivity, such that low doses generally facilitate or have no effect but high doses inhibit.

Conclusions: More research is needed to develop a better understanding of the effects of cannabinoids on female sexual function. There does appear to be an effect on both animals and humans, but whether the effect is positive or negative along dose and species lines requires more study. With the legalization of marijuana occurring in more countries and more US states, there needs to be more well-controlled studies evaluating the effects. Lynn B, Gee A, Zhang L, et al. Effects of Cannabinoids on Female Sexual Function. J Sex Med 2019; XX:XXX—XXX.

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Key Words: Endocannabinoids; Cannabis; Marijuana; Female Sexual Function; THC; Endocannabinoid System

INTRODUCTION

Marijuana use has become more widely prevalent over the last decade. Its use has been decriminalized in México and has been accepted into law for both medical and recreational purposes in

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Canada and for use by the general population in several US states. As of the publication of this paper, 33 states and the District of Columbia had legalized marijuana for medical use, and 10 of those states legalized marijuana for recreational use. Good-quality research has long been lacking on the effects of marijuana on sexual function due to the illegality of the drug. The effects of marijuana on physiological mechanisms and behaviors that drive sexual function have been studied primarily in rodents, and human research has had to depend on retrospective questionnaires. This paper aims to review the published data assessing the effects of cannabinoids on female sexual function.

METHODS

A literature review was performed in PubMed for publications in English with the keywords "marijuana," "cannabis,"

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"endocannabinoids," and "sexual function" or "female sexual function." We found 190 articles with these search qualifications, and the abstracts of these 190 articles were reviewed. Articles were included if they featured a study or survey that measured the impact of marijuana usage on female sexual function in animals and/or humans. Citations in these articles were then also reviewed for relevance. Given the scarcity of research done on humans relating to marijuana usage and sexual function, any relevant article was selected. No particular type of study was excluded or sought out. Twelve articles were identified relating to human research and were reviewed; of these 12 articles, 11 were retrospective surveys, and 1 was a prospective cohort study. Eight prospective, randomized, blinded animal studies were included. No particular animal species was included or excluded, but the animal studies relevant to this review were largely done on rats. Our main outcome measure was sexual function in females.

Endocannabinoid System

The first biologically active component of cannabis was identified in the 1960s as Δ^9 - tetrahydrocannabinol (THC), a

potent drug classified as a sedative-hypnotic. This was followed by the discovery of 2 cannabinoid receptors, CB1 and CB2, in the early 1990s.² Both are G-protein-coupled receptors and serve as the primary site of action for THC. Together, they are involved in a major neuromodulatory system known as the endocannabinoid system (ECS). The primary goal of the ECS is to promote homeostasis.³ The main components of the ECS are the receptors CB1 and CB2; their endogenous ligands, anandamide (AEA) and 2-arachidonoylglycerol; and the enzymes that modulate their breakdown (fatty acid amide hydrolase and monoacylglycerol lipase). They are synthesized by fatty-acid metabolism and located in neurons, where they are released on demand by simple diffusion (Figure 1).⁴

The ECS is widespread throughout the body, including the central and peripheral nervous systems. The cannabinoid receptors differ in their location of distribution. CB1 receptors are found throughout the central nervous system and some peripheral tissues. CB2 receptors, on the other hand, are primarily found in peripheral tissues and immune cells. Centrally, these receptors are more densely expressed in the neurons of

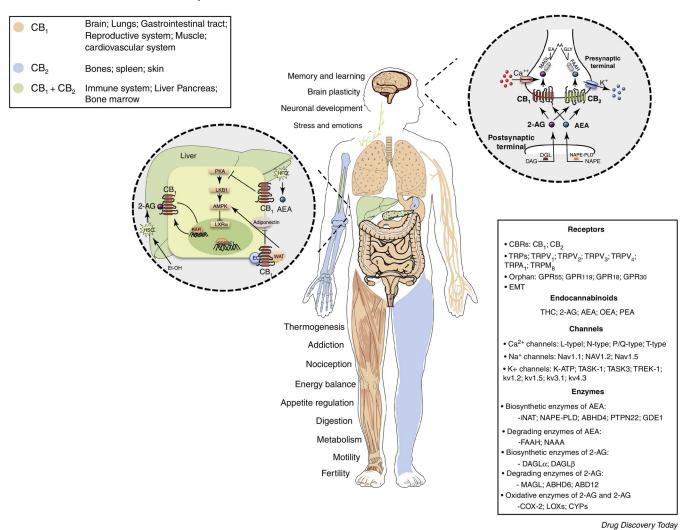


Figure 1. The endocannabinoid system: its functions, distribution, and components. Figure 1 is available in color online at www.smr. jsexmed.org.

hypothalamus, hippocampus, amygdala, cerebral cortex, parts of the basal ganglia, and cerebellum. Peripherally, cannabinoid receptors are found in organs responsible for producing sex hormones, such as the adrenals, which provide a source of androgens, and the ovaries, which provide a source of estrogen, progesterone, and androgens.⁵ Other biologically active cannabinoids (reviewed in Cohen et al⁶) have been discovered in marijuana, including cannabidiol, which is beginning to show promise in blocking pain and inflammation and for use as an antiepileptic medication; cannabigerol, which can treat the intraocular pressure associated with glaucoma; cannabichromene, which blocks pain and inflammation and shows encouraging anticancer effects; and tetrahydrocannabivarin, which acts as an effective appetite suppressant, reduces anxiety without altering mood, and shows efficacy in maintaining blood sugar levels and reducing insulin resistance. However, in addition to their interaction with CB1 and CB2 receptors, these molecules modulate the binding affinity of other neurotransmitter receptors (eg, dopamine, serotonin). Importantly, the effects of these molecules have not yet been tested on sexual behavior.

ECS and the Hypothalamic Pituitary Axis

Studies have shown that a relationship exists between the ECS and gonadal hormones. The ECS has been implicated in certain physiologic functions and behaviors that are known to be regulated by gonadal hormones. Many of the receptors and metabolic enzymes of the ECS are located extensively in the structures involved in the hypothalamic-pituitary-gonadal axis. In animal models, studies show that THC suppresses gonadotropin release through the blockade of gonadotropin-releasing hormone from the hypothalamus. This in turn causes decreased luteinizing hormone and follicle-stimulating hormone release from the anterior pituitary, resulting in decreased estrogen release from the ovaries and decreased progesterone release from the corpus luteum. Thus, overall, THC blunts the activation of hormones that affect female sexual function.

Cannabinoids and the Neurotransmitters That Affect Sexual Function

CB1 is a presynaptic receptor that results in inhibition of neurotransmitter release when activated. CB1 receptors are located in the axon terminals of GABAergic, dopaminergic, adrenergic, glumatergic, and cholinergic neurons. Haring et al also found evidence of CB1 receptors in a subset of serotonergic neurons. Of importance, dopamine and serotonin play key roles in sexual functioning. Dopamine and norepinephrine play a role in excitatory processes of sexual function, such as desire and arousal, and serotonin plays a role in inhibitory processes, such as loss of desire. These neurotransmitters interact with testosterone, estrogen, melanocortins, progesterone, prolactin, and oxytocin to modulate the female sexual response. Dopamine and control of the processes of the sexual response.

In the early 1970s, interest grew in studying the effects of marijuana on sexual function. It was known that marijuana had

effects on reproductive function. Marijuana was found to lower testosterone, decrease the weight of the testes, and affect spermatogenesis in male rats. ¹¹ In female rats, marijuana was shown to decrease the luteinizing hormone surge and inhibit ovulation. ^{12–14} It was therefore postulated that, due to its influence on reproductive hormones, marijuana and other endocannabinoids might diminish sexual function. At that time, however, work on the effects of marijuana on sexual behaviors was limited; therefore, studies were done with animals, primarily rodents, to further elucidate the link between cannabinoids, including marijuana and sexual function.

Preclinical Studies of the Effects of Cannabinoids on Sexual Function

In 1978, Gordon et al¹¹ evaluated the effects of THC on female lordosis, a posture assumed by some female mammals during mating, in which the back is arched downward. In rats, lordosis is a measure of female sexual receptivity. One goal of the study by Gordon et al was to determine if THC acted like estrogen or progesterone. When these hormones were absent, these researchers found there was no effect on lordosis; however, when these hormones were present, THC enhanced lordosis, although at very high doses it did not.¹¹

In 1981, Turley and Floody¹⁵ found that THC stimulated lordosis (receptivity) and sexual solicitation of a male (proceptivity), along with precopulatory vocalizations, in ovariectomized, estrogen-primed hamsters. These results showed that the effects of THC could be extended to other species and other sexual behaviors. Mani et al¹⁶ found that THC infused into the third ventricle of the rat brain enhanced lordosis. This effect was blocked by the cannabinoid antagonists SR141716A and SR144528. The endocannabinoid antagonists were found to block progesterone-induced lordosis, also. Mani et al further evaluated receptivity when progesterone and dopamine were blocked and showed that receptivity was inhibited. These results imply that THC-induced receptivity is mediated by dopamine and progesterone.

Selective endocannabinoid receptor agonists and antagonists have also been examined with regard to sexual responses in female rodents. Memos et al¹⁷ carried out a series of experiments evaluating the effects of the endocannabinoid antagonist SR141716 and the effects of the endocannabinoid agonist AEA on partner preference when compared with a placebo in rats. Sexual motivation was measured by the number of visits the female rats made to the male rats. They showed that AEA enhanced sexual motivation as measured by more visits from the female rats, and SR141716 inhibited it. They also found that AEA and SR141716 did not affect lordosis. Zavatti et al¹⁸ had somewhat different results, finding that SR141716 inhibited lordosis but not motivation in female rats.

Not all animal studies have yielded similar results. Ferrari et al¹⁹ evaluated the effects of a potent cannabinoid receptor agonist, HU-210, in female rats and found that administration

Sexual motivation [runway test] Decreased Increased ncreased (ultrasound vocalization or hops and darts) **Proceptivity** Decreased (high dose) Receptivity (lordosis) Increased (low dose) Decreased Simonsen Sprague-Dawley rats Sprague-Dawley rats Golden hamsters Long-Evans rats Long-Evans rats _ong-Evans rats Long-Evans rats Type of animal Wistar rats Antagonist/reverse Mechanism Antagonist of action Agonist Agonist Agonist Agonist Agonist Agonist CP 55,940 SR141716 HU-210 Drug 모 Turley and Floody (1980) Chadwick et al (2011)²² Ferrari et al $(2000)^{19}$ Lopez et al $(2009)^{20}$ Gordon et al (1978)¹¹ Memos et al (2014)¹ Mani et al (2000)¹⁶

Table 1. Summary of preclinical studies

 $\Delta \mathsf{EA} = \mathsf{anandamide}; \ \mathsf{THC} = \mathsf{tetrahydrocannabinol}.$

decreased both lordosis and the intensity of lordosis movements. The effect was dose and time dependent. Lopez et al²⁰ evaluated receptivity, proceptivity, and sexual motivation as measured by a runway test. The runway test measures how fast a female rodent runs to a male rodent after being released from a chamber and is used as a surrogate for sexual motivation. They found that AM-251, an endocannabinoid antagonist/reverse agonist, enhanced these sexual behaviors. Lopez et al²¹ then evaluated a different cannabinoid receptor agonist, CP55,940, and found that sexual behaviors and motivation were decreased. Another study by Chadwick et al²² showed similar results with CP55,940. In rats, it decreased sexual motivation. Interestingly, female rats in this study showed no preference for a female or male mate when treated with CP55,940 but showed a male preference in the control group.

The varied findings in the animal studies likely reflect a series of factors. Different strains of animals, different types of agonist and antagonists, and different surrogate markers of sexual function (proceptive vs receptive vs locomotor measures of motivation) have been used. In addition, different compounds have different affinities for cannabinoid receptors. Routes of administration are varied, as well (intracerebral vs systemic). Finally, the hormonal milieu in the animals varied among natural hormonal fluctuations, lack of hormones, or hormone replacement. Despite these limitations, animal studies provide some evidence that cannabinoids play a role in female sexual function, both directly and through interaction with the hypothalamic-pituitary-gonadal axis (Table 1).

Clinical Studies of the Effects of Cannabinoids on Female Sexual Function

Compared to the animal literature, there have been far more studies of the effect of marijuana on human female sexual function, although, to date, these findings have been limited to self-reported data. Despite the inability to conduct legal double-blind, randomized, placebo-controlled trials at this point in time in the United States, some data have been published to support the hypothesis that female sexual function is improved when women use marijuana in moderate doses.^{23–25} These studies are based on questionnaires, which are potentially fraught with bias.

Surveys of Males and Females Evaluating Effects of Marijuana Use on Sexual Function

In one of the earliest studies, the National Commission on Marihuana and Drugs²³ reported findings from an informal survey of about 200 marijuana users who were asked, "Do you think being high on marijuana stimulates your sex interest, or not?" Among these 200 users, 44% reported "definitely increases their sexual desire," with 50% of those being women. They found that women were more likely than men to report an increase in desire. They also looked at rare, frequent, and heavy everyday marijuana use. Frequent but not daily marijuana use when compared to heavy everyday use and rare use (less than 1

joint a week) was associated with increased sexual pleasure in around 70% of users.

In 1974, Koff²⁶ performed a survey of 251 college-aged students, who were asked about the amount of marijuana smoked each time the drug was used (1 joint or less, 2-4 joints, or more than 4 joints) and whether their sexual desire increased, decreased, or remained the same. He also asked whether sexual activity was more or less enjoyable after marijuana use. Of the 251 college students surveyed, 128 were female. The results of the survey indicated that 39.1% of males reported an increase in sexual desire, whereas 57.8% of females reported an increase—a significant difference (P = .048). Also, 43% of the female participants reported heightened sexual pleasure. Additionally, Koff found that the effects of marijuana appeared to be dose dependent, noting that, although 71% of female participants reported increasing sexual motivation after 1 joint, the percentage of women reporting increased desire decreased after a larger consumption of marijuana (greater than 4 joints) (49.5%). This study supports the idea that the effect of marijuana on sexual function is dose dependent, such that low doses of marijuana (1 joint) can be sexually stimulating but high doses of marijuana can have the opposite effect.

In 1976, Chopra and Jandu²⁷ interviewed 275 chronic marijuana users (smoked for 6 months to several years) from India and Nepal about the effects of marijuana and included some questions evaluating its effects on sexual function. This study observed similar dose-dependent effects and speculated that sexual inhibition is caused by an increased sedative effect seen at higher doses of marijuana intoxication. They did not divide their findings by gender.

A survey of 84 graduate students of health sciences in the southeastern United States was conducted by Dawley et al²⁸ (78% male and 22% female). This survey included 57 multiple-choice and true/false questions that were developed to determine the attitudes of individuals regarding the effects of marijuana use on sexual function. The 84 graduate students were categorized as "experienced" (having had a sexual experience while under the influence of marijuana), "non-experienced" (those who have been under the influence of marijuana but have not concurrently had a sexual experience), and "non-smokers." The study found that the "experienced participants" reported increased sexual pleasure (88%), sensations (48%), and satisfaction when both partners used marijuana (76%), as well as an increase in the intensity of the orgasm (58%). However, this study did not explore any differences between males and females, specifically.

These findings were further replicated in a 1982 survey done by Halikas et al.²⁹ One hundred regular marijuana users (37 female users) with an average smoking experience of 2 years were systematically interviewed to assess the psychosocial effects of marijuana use, including effects on sexual function. This study demonstrated that 76% of females reported an increase in sexual pleasure and satisfaction (14% of women reported variable feelings), and 63% of women reported feelings of emotional

closeness and intimacy. Additionally, 32% of women reported an enhanced quality of orgasm, and the other 8% and 60% reported variable or no effects, respectively. Overall, 81% of people (men and women) reported pleasure-enhancing effects associated with marijuana use.

Data by Green et al³⁰ support the previous finding by Halikas et al. Their review showed that approximately half of marijuana users reported increased aphrodisiac effects from marijuana use. Among regular marijuana users, 25% of them used marijuana in preparation for sexual intercourse. Of these users, over half reported increased sexual desire.

In 2004, Johnson et al³¹ conducted a survey-based, community epidemiological sample looking at the incidence and prevalence of sexual dysfunction in the general population (inhibited orgasm, functional dyspareunia, inhibited sexual excitement, and inhibited sexual desire). Out of the 3,004 participants, 60% were female. After controlling for multiple variables such as demographics, health status, and psychiatric comorbidities, marijuana was found to be associated with inhibited orgasm, as well as inhibited sexual excitement and desire. As opposed to the other studies mentioned in this review, Johnson et al asked survey questions specifically about sexual dysfunction, as opposed to general sexual function, and about comorbid drug and alcohol use. They did not ask questions about the potential benefits or experiences of marijuana usage, which perhaps played a role in why their results suggest a negative effect from marijuana.

Sumnall et al³² surveyed 281 sexually active volunteers regarding the effects of alcohol and drugs on their sexual behaviors; 131 (48.5%) of the volunteers were female. The most commonly reported drug used was marijuana (46.9%), although some individuals reported mixing alcohol with drugs. Their study reported that both marijuana and ecstasy were more frequently taken to improve the sexual experience than alcohol. Those who had taken illicit drugs reported greater sexual pleasure, increased mental/interpersonal contact with their sexual partner, greater willingness to sexually experiment, and a more satisfying sexual experience overall, indicating a greater total scale score for sex on drugs compared to alcohol (z = 5.696; P <.001). Although Sumnall et al found that it was not possible to distinguish the effects of different specific drugs, the overall effect was a more positive sexual experience on illicit drugs, including marijuana, compared to consuming alcohol.

In 2018, Palamar et al²⁴ evaluated self-reported sexual effects of marijuana, ecstasy, and alcohol use in a group of 679 men and women (ages 18–25); 38.6% of the respondents were women. When focusing on marijuana users, both male and female, the majority reported increased sexual enjoyment (53.5%), orgasm intensity (44.9%), sexual intensity (61.8%), body sensitivity (49.1%), and either an increase (31.6%) or no change (51.6%) in sexual desire. Although this study did not specifically analyze male and female differences, the authors did note that females in their survey were more likely than men to report sexual

dysfunction (30.6%), which was defined for survey takers as "vaginal dryness," after marijuana usage. They also noted that this definition of sexual dysfunction was limited and that participants may have experienced other forms of sexual dysfunction.

Female-Only Surveys Evaluating the Effects of Marijuana Use on Sexual Function

Sun and Eisenberg³³ surveyed 28,176 women via household laptops in 2002, 2006-2010, and 2011-2015. Women were asked, "Now please think about the past 4 weeks. How many times have you had sexual intercourse with a man in the past 4 weeks?" This was followed by, "During the past 12 months, how often have you smoked marijuana?" with the choice of responses being never, once or twice during a year, several times during the year, approximately once a month, approximately once a week, or at least once a day. They found that a higher frequency of marijuana usage was associated with increased sexual frequency. Although association does not imply causation and potential confounders existed in this study, including the exclusion of homosexual encounters and acknowledgment that those who use marijuana regularly might already be psychologically more disinhibited in general compared to those who do not use, the authors suggested that marijuana's impact on and potential benefit for sexual function should be further studied.

Lynn et al²⁵ conducted a survey of 373 women from 2016 to 2017 to evaluate women's perceptions of the effect of marijuana usage before sexual activity. Of the 373 women, 127 reported using marijuana before sex. The majority of women reported increases in sex drive, improvement in orgasm, and a decrease in pain. Specifically, women who reported regular marijuana usage before sexual activity had 2.13 higher odds of reporting satisfactory orgasms. Women with frequent marijuana usage had 2.10 times higher odds of satisfactory orgasms than those with infrequent usage. Lynn et al observed that there appears to be a link between marijuana usage and satisfaction with orgasm, as well as with improvements in other domains of sexual function, a better understanding of which may lead to the development of treatments for female sexual dysfunction.

Serum Endocannabinoid Levels and Sexual Function

In 2012, Klein et al⁵ chose a more direct method of studying the endocannabinoid system and its effects on female sexual function. Their aim was to measure circulating endocannabinoid concentrations in relation to subjective and physiological indices of sexual arousal in women. They measured physiological sexual arousal with vaginal photoplethysmography, specifically measuring vaginal pulse amplitude, which reflects phasic changes in vaginal engorgement with each heartbeat. The overall concept is that higher amplitudes indicate greater genital engorgement. Endocannabinoid concentrations (AEA and 2-arachidonoylglycerol) in 21 healthy premenopausal women were measured immediately

prior to and following viewing of both neutral and erotic films. Results indicated that increases in both physiological and subjective measurements of sexual arousal were associated with significant decreases in levels of endocannabinoids. These findings support the hypothesis that the endocannabinoid system is involved in female sexual functioning and may well be inhibitory (Table 2).

DISCUSSION

Based on the above review of the literature, the most common sexual domains that have been evaluated include arousal, desire or "libido," orgasm, pleasure, dyspareunia, vaginal lubrication, and duration of intercourse. Several studies have evaluated the effects of marijuana on libido, and it seems that changes in desire may be dose dependent. Studies support that lower doses improve desire but higher doses either lower desire or do not affect desire at all. ^{23,26,27}

When evaluating sexual pleasure, most studies show that marijuana has a positive effect. ^{27,30,31} Marijuana use with sex has also been associated with prolonging orgasm or improving the quality of orgasm. ^{5,24,34} Only 1 study that we reviewed reported that marijuana use inhibits orgasm³¹; however, that study specifically looked at dysfunction as opposed to overall function. Although our search revealed no articles that found an association between marijuana use and vaginal lubrication, ^{35,36} this does not rule out such an effect, or an effect on vaginal blood flow, especially with a peripheral application.

Limitations

The body of evidence evaluating the effects of marijuana on female sexual function has several limitations. Although animal studies provide some information, there are no double-blind, randomized, placebo-controlled human trials from which to form a conclusion. The available human studies rely on recall and questionnaires. They are also quite different from each other. No validated questionnaires have been used, making it difficult to compare the results. Moreover, the specific wording of the questions regarding libido, orgasm, pleasure, and pain all differed in both content and positive or negative valence. Some studies used questionnaires, and some used interviews. Some focused on marijuana users specifically, whereas others focused on a general population. Populations ranged from university students to patients in an obstetrics and gynecology practice. Most studies focused on sexual function, but a single study evaluated potential sexual dysfunction. No human studies were able to evaluate the exact dose or timing of use. It is therefore difficult to make broad generalizations about the effects of marijuana on female sexual function based on available evidence.

It must be noted here that the other cannabinoids in marijuana have not been tested empirically with regard to their effect on the sexual behavior of female rats or humans, although a recent study by Carvahlo et al³⁷ reported an overall decrease in

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Table 2. Summary of clinical studies

Author	Type of marijuana usage	Gender	Sexual desire	Sexual pleasure	Other findings
US Commission on Marihuana and Drug Abuse (1972) ²³	Rare vs frequent vs heavy	Male and female (200 participants)	Definite increase in sexual desire reported by 44% (44, or 50%, of whom were female)	_	Frequent, but not every day, marijuana use (compared to usage every day) was associated with increased sexual pleasure in 70% of users
Koff (1974) ²⁶	One joint or less vs 2–4 joints vs >4 joints	Male and female (251 participants; 128 females)	Increase in sexual desire noted by 57.8% of females	Heightened sexual pleasure reported by 43% of female participants	Effects of marijuana appeared to be dose dependent; 71% of female participants reported increasing sexual motivation after 1 joint, but this percentage decreased after greater consumption (>4 joints) to 49.5%
Chopra and Jandu (1976) ²⁷	Chronic cannabis users (smoking 6 mo to several years)	Male and female (275 participants)	_	_	Dose-dependent effects with marijuana similar to the findings by Koff
Dawley et al (1979) ²⁸	Experienced (having had sex while under the influence of marijuana) vs non-experienced (under the influence but no sexual experience) vs non-smokers	Male and female (84 participants)	_	Increased sexual pleasure reported by 88% of participants	Increased sensations (48%) Increased satisfaction with both partners using (76%) Increase in the intensity of orgasm (58%)
Halikas et al (1982) ²⁹	Average smoking experience of 2 y	Male and female (100 participants; 37 females)	_	Increase in sexual pleasure and satisfaction reported by 76% of females	63% of women reported emotional closeness and intimacy
				Overall, 81% of participants reported pleasure-enhancing effects	32% of women reported an enhanced quality of orgasm
Green et al (2003) ³⁰	_	Male and female participants	Increased sexual desire reported by ~50%	-	-

(continued)

Table 2. Continued

Author	Type of marijuana usage	Gender	Sexual desire	Sexual pleasure	Other findings
Johnson et al (2004) ³¹	Marijuana usage and comorbid alcohol/drug usage	Male and female (3,004 participants; 60% female)	Inhibited desire	-	Inhibited orgasm and sexual excitement
Sumnall et al (2007) ³²	Marijuana usage and comorbid drug usage	Male and female (131 participants; 48.5% female)	-	Increased sexual pleasure	Increased mental and interpersonal contact with sexual partner
				Increased satisfaction with sexual experience	Greater willingness to sexually experiment
Klein et al (2012) ⁵	Measured circulating serum endocannabinoid concentrations	_	_	_	Increases in both physiological and subjective measurements of arousal, which were associated with decreases in serum endocannabinoids
Sun and Eisenberg (2017) ³³	Never, once or twice a year, several times a year, once a month, once a week, or at least once a day	Female	_	_	Higher frequency of marijuana usage associated with increased sexual frequency
Palamar et al (2018) ²⁴	Marijuana, ecstasy, and alcohol	Male and female (679 participants; 38.6% women)	Increase or no change in sexual desire reported by 31.6%	Increased sexual enjoyment reported by 53.5%	44.9% reported increased orgasm intensity 30.6% of women reported sexual dysfunction (vaginal dryness)
Lynn et al (2019) ²⁵	Regular or frequent marijuana usage	Female	Increase in sex drive reported by majority of women	_	2.10 times higher odds of satisfactory orgasm with frequent marijuana usage; 2.13 times higher odds with regular marijuana usage

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fertility in female Swiss mice. It is also the case that the THC and cannabidiol content differs dramatically in different strains of marijuana,³⁸ particularly in the marijuana that has been used legally in research, relative to strains consumed recreationally.³⁹ This makes it impossible both quantitatively and qualitatively to compare the effects of laboratory-based intoxication with studies that examine retrospective experiences.

Clinical Implications

A better understanding of the role of the endocannabinoid system in female sexual function has important clinical implications. Sexuality is complex, and the ECS is only one small part of it. A clearer understanding may lead not only to the development of therapeutic options for women but also to a deeper understanding of the mechanisms involved in sexuality. With increasing legalization, there is the potential to carry out more rigorous trials evaluating the exact dosing and timing of use as opposed to using recall. This may lead to more substantive conclusions than the animal and human studies have allowed us thus far.

CONCLUSION

Female sexuality is a complex interplay of environmental, psychological, and physiological processes. Multiple neurotransmitters and hormones play a role in sexual excitation and inhibition. The information we have is limited to rodent studies and questionnaires that rely on memory, with none of the human studies yet being capable of delineating dose, timing, or other objective measures. Although there appears to be a dose dependency that separates putative excitatory effects from inhibitory effects on female sexual desire, orgasm, and reproductive function, and frequency of use also plays a role, it is not clear to what extent the psychoactive properties of the various cannabinoids play a role. For example, it is possible that the sedative hypnotic properties of THC and tetrahydrocannabivarin at low doses disinhibit sexual desire and arousal in response to erotic cues, but perhaps this occurs to a large extent in women who experience anxiety about sex or other interpersonal interactions. With recent decriminalization in México, and legalizations in Canada and certain US states, the Northern Hemisphere is now ripe to develop the high-quality, evidence-based studies necessary to answer important questions regarding marijuana and female sexuality. Like any drug, marijuana has risks and side effects and should be used with that in mind. A comprehensive understanding of the effects of marijuana and its constituent cannabinoids on female sexual function remains to be elucidated.

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