

# The Endocrinological Effect of Illicit Drugs on the Reproductive System

Dr .Clairmont Griffith<sup>1</sup> and Professor Bernice La France<sup>2\*</sup>

<sup>1,2</sup>Howard University Hospital and Howard University School of Medicine, 2041 Georgia Ave. NW, Washington, DC 20059

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**\*Corresponding author:** Professor La France in Lieu, Howard University Hospital and Howard University School of Medicine, 2041 Georgia Ave. NW, Washington, DC 20059, Tel: (202) 865- 6741 E-mail: bemore1576@gmail.com

## Abstract

Hormones make the human reproductive system to function normally through tighter regulation in levels of their secretion. However, many drug compounds can alter the secretion of these hormones and impair the entire reproduction system. Today, many young adults indulge in illicit drugs, and this has contributed to increased cases of infertility in the world. By conducting a retrospective review of scientific journals published between 2014 and 2019, this paper shows that commonly abused illicit drugs such as cocaine, marijuana, and barbiturates act on the human reproductive system by interfering the normal release of major hormones such as luteinizing hormone and testosterone to result in infertility and other problems related to human reproduction.

**Keywords:** Illicit drugs; Cocaine; Marijuana; Barbiturates; Hormones; Human reproduction;

## Introduction

Drug abuse has become commonplace in many societies today. Young adults are increasingly abusing alcohol, marijuana, cocaine, and other mood-altering drugs. A large percentage of women of childbearing age use illicit drugs on a regular basis with some categorized as heavy alcohol drinkers [1]. The Mental Health Services Administration (SAMHSA) published a report in 2014 indicating that at least 27 million people above the age of 12 years abused drugs. The SAMHSA's National Survey on Drug Use and Health report showed that up to 140 million people used alcohol with about 61 million people engaging in binge drinking. The report also indicated that approximately 67 million people abused tobacco products [2]. Although some people report no signs of compulsion, cravings, and addiction, many individuals using illicit drugs are at high risks of addiction and damages to various systems in the body such as the reproductive system. While research on the Endocrinological effect of illicit drugs on the reproductive system is still in its infancy, this paper seeks to justify that existing data point to potential and serious dangers of such drugs to fertility in both males and females.

## Methodology

A search for online databases for scientific journal articles published between 2014 and 2019 was performed. Popular databases such as Google Scholar, Jstor, ProQuest, Science Direct, and PubMed Central were used to obtain the most relevant and credible sources for review. The Google Scholar search yielded 17,500 articles, but only those that qualified the search criteria were selected. PubMed Central had 1,280 articles about the topic, but only those articles with full preview were considered. Examples of keywords and phrases used in the search included "illicit drugs," "Endocrinological effects of illicit drugs" "illicit drugs and human reproductive system," and "drug abuse and human endocrinology" to identify the most relevant published articles on the topic. Exclusion criteria in the search comprised of the avoidance of general works focusing on human endocrinology, drug abuse, and human reproduction system. The search also excluded websites or like sources that were not authoritative. After obtaining the required sources, a retrospective review of the published works was performed to derive at the conclusions of the papers.

It was not humanly possible to consider all articles that contained one keyword as there were thousands and thousands of them and therefore to obtain articles that would fit the description, the researcher decided to look for articles that contained a combination of the listed keywords. An aggregate of about 300 articles emerged and from the different databases and the researcher restricted himself to articles published between 1995 and 2019. There were over 150 articles that were published between the aforementioned dates and from this, just about 70 articles were found to be relevant for this specific study. About 47 articles have been used directly in this paper whereas the others have been consulted on different areas to expand knowledge for this research.

## Results

Preliminary results indicated a significant Endocrinological association between illicit drugs such as opioids, marijuana, cocaine, and barbiturates and human reproduction in both males and females. The effects observed in most of the publications were both reversible and irreversible with gonadotropin-releasing hormone (GnRH), follicle-stimulating hormone (FSH) and luteinizing hormone (LH), progesterone, and testosterone being the common hormones most affected. Illicit drugs interfere with the normal balance of hormones such as LH, FSH and lower sperm motility, sperm count, and sperm morphology. Similarly, *Sema7A* KO mice have lower expression of gonadotropin-releasing hormone (GnRH) neurons and low plasma concentration of testosterone [3]. Similar effects are observed in individuals using illicit drugs such as marijuana, cocaine, and barbiturates. These

effects result in poor sexual behaviors such as opposite-sex attraction as shown in Fig 1(a) and (b) below.

### Effects of Illicit Drugs

Many scholars [4-16] have studied the effects illicit drugs have on mice. As noted by [17-19], illicit drugs tend to reduce the levels of testosterone and GnRH in plasma and this consequence is severe in males where sexual attraction declines with exposure to drugs. Using *Sema7A* ko mice that express low levels of GnRH neurons, scientists can determine the level of sexual attraction in both male and female mice as compared to the wild-type (wt) mice. *Sema7A* ko mice not only have reduced numbers of neurons expressing GnRH, but are also sub fertile and have smaller testicles than the wt mice. A similar observation is true when wt mice are castrated when they attain adult stage. Sexual attraction is regulated by the accessory olfactory bulb (AOB), which is the first central part of the vomeronasal system. AOB is involved in sexual behaviors such as opposite-sex attraction and cue preferences [3].

Some drugs such as performance-enhancing drugs, steroids, and opioids have direct effects on the endocrine system [20-22]. Such drugs have both reversible and irreversible effects such as male pattern baldness and beard growth among women and infertility and testicle shrinking in men [23]. While hormones are normally released in the body when required, some drugs often disrupt the normal process of their release. For instance, excessive use of alcohol interrupts the endocrine system by increasing the risks of loss of testosterone among men and boys. In particular, opioids affect the function of the hypothalamic-pituitary axis through the inhibition of gonadotropin-releasing hormone (GnRH) secretion. This resulting inhibition of both FSH and LH secretion leads to a reduced concentration of testosterone and impaired spermatogenesis in men [24]. Opioids affect various endocrine functions leading to loss of libido, irregularities in menstrual cycles, and increased risks of osteoporosis [25]. Endocrinological effects of opioids constitute of dysfunctions in hypothalamic-pituitary-adrenal axis and inhibition of gonadal and pituitary hormones [26-28]. Both males and females have increased risks of hypogonadism, which is associated with the suppression of GnRH secretion by the hypothalamus, decreased levels of LH, testosterone, and FSH, dehydroepiandrosterone, and oestra-diol and progesterone among women.

Scholars [29-34] have demonstrated that smoking marijuana or cannabis negatively affects fertility in men. This is because of the expression of cannabinoid receptors in testicular tissues, Sertoli cells, Leydig cells, and anterior pituitary that results in the impairment of sperm function, spermatogenesis, and hypothalamus-pituitary-gonadal axis. While existing results from human studies on the effect of marijuana on hormone

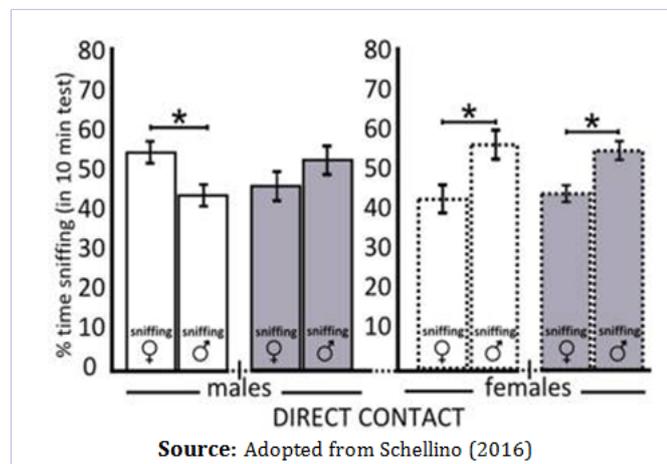


Figure 1: Sniffing time both wild-type and knockout mice in direct contact with pheromone

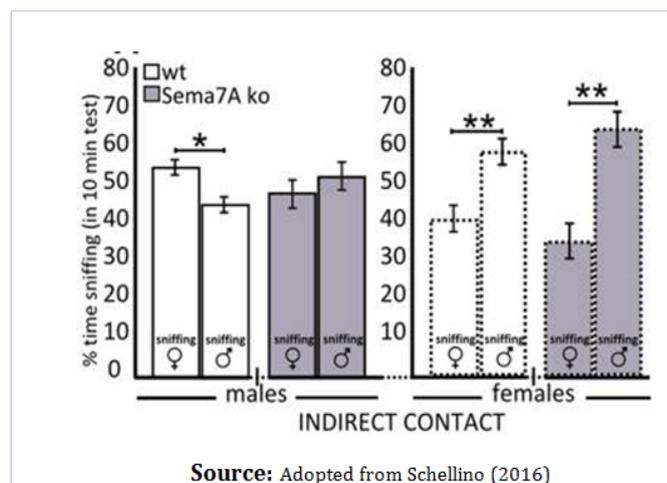


Figure 2: Sniffing time both wild-type and knockout mice in indirect contact with pheromone

levels are misleading, animal studies suggest that cannabis results in a decline in testosterone and LH levels. In one study involving 20 chronic cannabis smokers, researchers reported a decline in plasma testosterone levels among users. In the study, investigators noted a marked increase in testosterone levels in participants following stimulation with human chorionic gonadotropin hormone or abstinence from the use of the drug. These results have been contradicted with later findings showing no significant changes in plasma levels of testosterone among acute or chronic users of marijuana, including participants who used cannabis in tea. In another study involving 27 men, changes in plasma levels of testosterone before and after smoking were statistically insignificant. However, another study on four health subjects found a correlation between cannabis smoking and a significant depression in LH plasma levels and an increase in cortisol production. More studies in the future will provide clear data and conclusions regarding the Endocrinological effect of cannabis on reproduction.

Other illicit drugs such as cocaine have been shown to have negative effects on both male and female fertility [35-38]. Like marijuana, cocaine suppresses ovulation by altering the feedback loop that controls the ovarian cycle [39]. Cocaine's effect of increasing the levels of prolactin hormone leads to a disruption of the menstrual cycle and hormonal balance. Studies have reported a change in neurochemical and endocrine functions following chronic and acute cocaine administration. In one study investigating the effects of cocaine on gonadal and anterior pituitary hormones in human subjects, researchers observed that levels of LH and FSH increased after cocaine administration. Studies show that the reinforcing effects of cocaine are greater when women are in the follicular phase of the reproduction cycle compared to the luteal phase. This observation is consistent with other studies that have suggested progesterone production during the luteal phase attenuated the effects of cocaine. Other scholars [40-42] have shown that cocaine-dependent users exhibit greater levels of progesterone and lower ratios of estrogen to progesterone during the menstrual cycle. Maria et al. (2014) study show that although ovulation and cycle duration might remain constant among cocaine users, chronic use of cocaine or abstinence may significantly affect the hormonal milieu.

Illicit drugs such as barbiturates and methamphetamine (MA) alter the normal functioning of the hypothalamic-pituitary-adrenal axis [43-45]. Barbiturates are pharmacologically recognized as sedative-hypnotic substances and are depressants [46]. They act on the central nervous system (CNS), although their mechanism of action remains unclear. Their property as depressants makes them be popular substances of abuse. These drugs are often used as anesthetic agents on laboratory animals in reproductive studies. Laboratory studies have revealed the inhibitory effects

of barbiturates on various reproductive hormones, with most investigations reporting the neuroendocrine effects of the drugs on female reproductive cycles [47]. In general, barbiturates inhibit both FSH and LH and suppress the secretion of steroid hormones. In rats and hamsters, barbiturates both spontaneous and steroid-induced release of LH. These effects are similar in both male and female animals, as Phenobarbital has been shown to inhibit the secretion of gonadotropin and the increase in the serum levels of the hormone in male animals.

## Conclusion

The human reproduction system comprises one of the critical systems affected by commonly abused drugs such as cocaine, marijuana, and barbiturates. Young adults abuse these drugs on a regular basis to become addicts. While addiction is one of the problems of drug abuse, human fertility has become an important issue among healthcare practitioners and researchers. Although research on the Endocrinological effects of drug abuse is yet to expand, evidence point to a significant link between illicit drug use and impaired reproductive systems in both males and females. Using scientific journals published online, this paper has presented multiple findings from a wide range of studies showing the effects of illicit drugs on human beings and particularly with regard to how they affect different human systems, for instance, the human reproductive system. A majority of these drugs have adverse effects on the human reproductive system with some having extreme adverse effects.

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