

## SEXUAL MEDICINE REVIEWS

## Animal Models in Sexual Medicine: The Need and Importance of Studying Sexual Motivation

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## ABSTRACT

**Introduction:** Many different animal models of sexual medicine have been developed, demonstrating the complexity of studying the many interactions that influence sexual responses. A great deal of effort has been invested in measuring sexual motivation using different behavioral models mainly because human behavior is more complex than any model can reproduce.

**Aim:** To compare different animal models of male and female behaviors that measure sexual motivation as a key element in sexual medicine and focus on models that use a combination of molecular techniques and behavioral measurements.

**Methods:** We review the literature to describe models that evaluate different aspects of sexual motivation.

**Main Outcome Measures:** No single test is sufficient to evaluate sexual motivation. The best approach is to evaluate animals in different behavioral tests to measure the motivational state of the subject.

**Results:** Different motivated behaviors such as aggression, singing in the case of birds, and sexual behavior, which are crucial for reproduction, are associated with changes in mRNA levels of different receptors in brain areas that are important in the control of reproduction.

**Conclusion:** Research in animal models is crucial to understand the complexity of sexual behavior and all the mechanisms that influence such an important aspect of human well-being to decrease the physiologic and psychological impact of sexual dysfunctions. In other cases, research in different models is necessary to understand and recognize, not cure, the variability of sexuality, such as asexuality, which is another form of sexual orientation.

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**Key Words:** Sexual Dysfunction; Sexual Motivation; Non-Copulating Males; Asexuality; Brain Receptors

## INTRODUCTION

Over the years, different animal models to study sexual function have been developed and consistently used to understand the mechanisms that trigger sexual behavior and the origin and bases of different sexual dysfunctions in men and women. Unfortunately, the etiology of most sexual disorders remains unknown probably because, regardless of how good an animal model is, it cannot fully take into account the complexity of human disorders.<sup>1,2</sup> Despite their limitations, animal models are necessary to eventually understand the basic mechanism that triggers sexual behavior and the etiology of sexual dysfunctions. The advantages, disadvantages, and characteristics of animal

models have been described extensively<sup>1,2</sup> and are not being repeated here, but there are two factors that are worth pointing out. The first one is that animal models need to reproduce the behavioral characteristics of the dysfunction that is to be modeled. The second one is that human behavior is much more complex than any model can reproduce. For example, family, social, and cultural influences and personal beliefs, which are important in clinical practice, cannot be incorporated into animal models. Nevertheless, scientists working with animal models are aware of their limitations (see Ágmo<sup>1</sup> and references therein for a discussion).

Some reviews that have approached the study of sexual medicine have focused on the effects of various drugs on different models of sexual function.<sup>1,3,4</sup> In addition to animal models that have been used to develop drugs for clinical use, the effects of aphrodisiacs, including herbal and traditional medicines, have been tested in animal and human studies.<sup>5–7</sup> It is not surprising that a major focus in the study of sexual medicine is erectile dysfunction mainly because basic principles about the physiology of erection are shared among species. The diversity of animal

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**Table 1.** Reviews of different models to study sexual function

Main topic	Model	Other concepts	References
Pharmacology	Effects of drugs	Motivation, arousal	1
Pharmacology	Effects of drugs	Mounds, intromissions	3
General	Different behavioral paradigms	Arousal, desire	4
Hypoactive sexual desire	Several	Sexual response models	15
Hypoactive sexual desire and female sexual arousal disorder	Testosterone treatments	Cognitive factors	12–14
Animal models	Different behavioral paradigms	Sexual reinforcers	2
Aphrodisiacs	Plant and animal sources		6
Aphrodisiacs	Plants		7
Herbal and traditional medicine	Different compounds	Phytotherapy	5
Erectile dysfunction	Diabetic animals	Types 1 and 2	10
Erectile dysfunction	Traumatic, metabolic, aging	Castration, smoking	8
Erectile dysfunction	Animal models	Non-contact erections, reflexes	9
Erectile dysfunction	Hydrogen sulfide in erection	Angiogenesis, inflammation	11

models developed to evaluate erectile dysfunction<sup>8–11</sup> and the number of publications relating to this topic reflect its significant impact on the psychological and physical aspects of men's health and those of their sexual partners (see Chung et al<sup>8</sup> and references therein).

In addition, different models have been developed to study female sexual dysfunctions, including sexual arousal and hypoactive sexual desire disorder (HSDD).<sup>12–15</sup> However, it should be noted that the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)* has introduced changes in the sexual dysfunction chapter, including the merging of female HSDD and female arousal disorder into female sexual interest/arousal disorder.<sup>16</sup> Table 1 presents reviews of different models based mostly on pharmacology, aphrodisiacs, and erectile dysfunction. Because these topics have been covered extensively, this review focuses on models that measure, in one way or another, sexual motivation. This concept in humans is difficult to define because it involves awareness, goals, and intentions (see review by Toates<sup>17</sup>). The representation of sexual incentives (fantasies) and social learning also play a crucial role in human sexual motivation.<sup>18</sup> Evidently, some of these aspects are exclusively present in humans, such as awareness and fantasies, and therefore it would be very difficult, if not impossible, to create animal models to evaluate them. However, it is also well established that organisms displaying sexual behavior share similar behavioral characteristics and neural mechanisms (see Pfau et al<sup>2</sup> for a discussion). For example, it is clear that for many humans orgasm is rewarding. In some species, sexual behavior induces a positive affective state, as evaluated by the conditioned place preference paradigm, indicative of a reward state.<sup>19</sup> Several lines of evidence, using some of the models described below, have indicated that the rewarding aspects of sexual behavior in humans and rats, and probably other species, are mediated by opioids.<sup>20</sup> The many different behavioral models discussed offer the possibility of understanding the basic neuroendocrine, behavioral, and neural mechanisms involved in the sexual

response of animals. The challenge is to differentiate those aspects that correspond exclusively to the animal from those that could apply to humans. In the second part of the review, we discuss how recently developed models that use molecular techniques have been used in animal models that evaluate different aspects of sexual motivation.

## MODELS OF SEXUAL MOTIVATION

Since the classic study by Beach,<sup>21</sup> in which he classified sexual behavior as appetitive and consummatory phases, latencies to mount and intromit were considered possible measurements of sexual motivation, and the number of mounts and intromissions and ejaculation latency were considered parameters of the consummatory aspects of male sexual behavior. He later identified three behavioral characteristics displayed by female rats: attractivity, proceptivity, and receptivity.<sup>22</sup> Proceptivity was defined as a reaction by the female to the male's initiative toward establishing or maintaining a sexual interaction. For the female, attractivity and proceptivity were considered synonymous with sexual motivation, and receptivity was assumed to be a consummatory aspect of female sexual behavior. Although these ideas were useful for many years in the study of sexual behavior, it has become clear that the concept of sexual motivation in males and females is much more complex and difficult to define.<sup>22–24</sup> Extensive discussions have been presented to dissociate motivation from other concepts such as sexual arousal and sexual desire,<sup>1,2,4,17,25–27</sup> and they are not discussed in detail in the present review.

In an excellent article, Sachs<sup>26</sup> reviewed the different definitions given to male sexual arousal, making evident that this concept is frequently used interchangeably with sexual motivation. He proposed that sexual arousal in males should be inferred only when penile erection is observed in a sexual context.<sup>26</sup> Ågmo<sup>28</sup> proposed that sexual arousal could be defined as the enhancement of genital blood flow that causes erection in the

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