REVIEWS

Pathways of Sexual Desire

James G. Pfaus, PhD

Center for Studies in Behavioral Neurobiology, Department of Psychology, Concordia University, Montréal, Canada

DOI: 10.1111/j.1743-6109.2009.01309.x

ABSTRACT

Introduction. Sexual desire is controlled by brain systems involved in sexual excitation and inhibition. Hypoactive sexual desire disorder (HSDD) may result from hypofunctional excitation, hyperfunctional inhibition, or some mix of the two.

Aim. This study aimed to identify neurochemical and neuroanatomical systems involved in sexual excitation and inhibition, their role during normal, and hypoactive sexual expressions.

Methods. A comprehensive review of the human and animal literature is made, and a theory surrounding the ways that HSDD can be manifested and treated is presented.

Main Outcome Measures. Drug effects and neural systems derived largely from rat studies that are involved in the stimulation of sexual desire (excitatory system) vs. the stimulation of sexual reward, sedation, and satiety (inhibitory system).

Results. Brain dopamine systems (incertohypothalamic and mesolimbic) that link the hypothalamus and limbic system appear to form the core of the excitatory system. This system also includes melanocortins, oxytocin, and norepinephrine. Brain opioid, endocannabinoid, and serotonin systems are activated during periods of sexual inhibition, and blunt the ability of excitatory systems to be activated.

Conclusions. Drugs that stimulate the activation of hypothalamic dopamine or that blunt endocannabinoid or serotonin release and/or postsynaptic binding may be effective in stimulating sexual desire in animals and humans. The characterization of how those drugs work will help generate a rational approach to drug development in the treatment of HSDD. **Pfaus JG. Pathways of sexual desire. J Sex Med 2009;6:1506–1533.**

Key Words. Sexual Desire; Hypoactive Sexual Desire Disorder; Neuropharmacology; Treatment; Libido

Introduction

Sexual desire seems a straightforward concept, yet there is no agreed-upon definition of what it is or how it manifests itself. In the Diagnostsic and Statistical Manual of the American Psychiatric Association-Edition IV-Text Revision (DSM-IV-TR), the diagnosis of hypoactive sexual desire disorder (HSDD) is given when "desire for and fantasy about sexual activity are chronically or recurrently deficient or absent" [1]. By converse logic, then, sexual desire is the presence of desire for and fantasy about sexual activity. This definition appears coherent but is circular. Many clinicians and motivational theorists alike view desire as distinct from arousal in both animals and humans. This is apparent in the DSM's categorization of arousal disorders distinct from desire disorders, a distinction that generally reflects blood flow to the genitals and erectile tissues vs. a "psychological" sexual interest in which individuals "want" sex (as defined by Robinson and Berridge [2]). In practice, however, desire may well be informed or even confirmed by the presence of autonomic and central responses that define arousal, and there is a growing body of evidence that people regard desire and arousal as parts of one another, despite being given distinct

definitions (e.g., [3,4]). When an individual expresses sexual desire behaviorally, it follows that attention and behavior focus on obtaining some form of positive sexual reinforcement. This can occur alone in fantasies or together with others in goal-directed social and sexual behaviors. Thus, in addition to subjective appraisals of desire, the concept encompasses the effort, including risk, that individuals engage in to obtain sexual rewards, the excitement displayed in anticipation of such rewards, and the strength of the incentive value ascribed to a particular sexual stimulus.

All animals, including humans, manifest sexual desire behaviorally. Desire can be inferred from increased motor output in anticipation of copulation or other sexual behaviors or from the amount of work performed for the opportunity to copulate or to obtain primary or secondary (conditioned) sexual rewards associated with these behaviors. Animals, including humans, also choose between two or more sexual incentives based on the strength of the incentive cues and the their own internal drive state. What characterizes those behaviors is that they occur before copulation. Solicitation, courtship, operant responses, conditioned locomotion in anticipation of sex, time spent near a place associated with sexual rewards, and the choices made between two or more incentives can all be considered analogies of sexual desire. The strength of the behavior can be observed as increasing or decreasing or can be tested by increasing the criterion level of responding that animals must attain before they are given access to rewards. Simply put, animals with more "desire" will display more robust behavior than animals with less desire. Desire can also be inferred from certain behaviors that occur during copulation, for example, the amount of solicitation a female rat will perform toward a particular male rat or the degree of chasing behavior a male rat will perform to catch a pacing female rat. A growing body of evidence indicates that these aspects of sexual behavior are controlled by a common set of brain regions and altered in a relatively selective fashion by certain drugs that are known to alter desire in humans [5,6]. This, in turn, allows researchers to construct a neurochemistry and neuroanatomy of sexual desire that have predictive validity for humans and other animals. The elucidation of neurochemical pathways that control sexual desire thus generates a vehicle for the construction of rational approaches to pharmacotherapy to treat desire disorders.

Common Structure of Sexual Behavior

All behaviors have a beginning, a middle, and an end, and all organisms that engage in sexual behavior share a common set of principles and end points that define the behavior, along with particular neural mechanisms that make it successful [6]. We must be able to respond to hormonal and neurochemical changes that signal our own sexual arousal and desire. This ability underlies our moment-to-moment level of attention to sexual cues [7,8] and defines a large part of the internal state that is commonly referred to as "sex drive." The rest requires a complex mix of instinct, learning, and feedback, a neural organization that allows us to initiate and terminate interactions with external sexual incentives. We must be able to identify external stimuli that predict where potential sex partners can be found, to seek out, solicit, court, or otherwise work to obtain sex partners, distinguish external cues and behavioral patterns of potential sex partners from those that are not sexually receptive, and to pursue sex partners once sexual contact has been made. Neural mechanisms that allow sexual responding to become habitual or automated with practice exist, and such processes may underlie the ability of sexually experienced animals to be less affected by treatments that disrupt sexual responding in sexually naive animals. Similarly, neural mechanisms that allow the stimulation received during sexual contact to be perceived as rewarding exist. Such reward contributes to the formation of preferences for salient stimuli associated with positive sexual reinforcement and leads to a state of sexual satiety in which inhibitory neural systems are activated. Those inhibitory systems blunt the reactivation of desire, arousal, and sexual behavior for a period of time that depends critically on the intensity of the reward/satiety state, the context in which sexual arousal occurs, and the expectancy of the individual. In the "normal" human sexual response, this pattern flows from desire and excitement at the prospect of sexual interaction, to its initiation, to a rising "plateau" in which sexual responding is maintained or intensified on its way to an orgasm, and finally to resolution or refractoriness after an orgasm (as in Kaplan [9] and Masters and Johnson [10]). Many aspects of sexual desire are manifested before the opportunity to engage in sexual behavior becomes apparent. Thus, although some appetitive responses made prior to copulation are not specific to sexual behavior (e.g., bar pressing in rats or flower giving in people), they can be