REVIEW

Physiology of Women's Sexual Function: Basic Knowledge and New Findings

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DOI: 10.1111/j.1743-6109.2010.01810.x

ABSTRACT

Introduction. Data concerning the physiology of female sexual functioning are still obtained from animal studies, but an increasing amount of novel evidence comes from human studies.

Aim. To gain knowledge of psychological and biologic physiology of women's sexual functioning, mainly addressing sexual arousal and orgasm.

Methods. A broad-based literature review of current knowledge of the psychological and biologic physiology aspects of women's sexual functioning.

Results. A comprehensive understanding of the anatomical, neurobiological, and psychological mechanisms behind sexual function and responses is of paramount importance. A biopsychological paradigm was considered when reviewing currently available data, thus considering aspects of: (i) sexual differentiation of the brain, which is critical for sex differentiation in behavior; (ii) central neurobiology of sexual function, highlighting specific and innovative findings from neuroimaging methods that enable visualization of active brain areas during arousal and orgasm; and (iii) peripheral functional anatomy, mainly addressing genital arousal and orgasm. Translational science was also covered, providing data about the actual role of sexual arousal in women in both procreation/reproduction and recreation/pleasure. The interaction between physiological and psychological states of women's sexual response, nonspecific sexual response, interoceptive awareness, and flexibility of sexual interests have also been addressed.

Conclusion. Further research on normal physiology of women's sexual function is needed in order to expand and "translate" current knowledge into the pathophysiological clinical setting. This manuscript encompasses data presented at the 3rd International Consultation on Sexual Medicine in Paris, France, July 10–13, 2009. **Salonia A, Giraldi A, Chivers ML, Georgiadis JR, Levin R, Maravilla KR, and McCarthy MM. Physiology of women's sexual function: Basic knowledge and new findings. J Sex Med 2010;7:2637–2660.**

Key Words. Female; Arousal; Orgasm; Physiology; Biology; Brain

Introduction

Since the early descriptions of the sexual response cycle by Masters and Johnson [1] and, later, Kaplan [2], the stages have been challenged [3]; substantial advances have occurred in the understanding of physiological aspects of female sexual function (FSF) and dysfunction (SD), mainly driven by more and more sophisticated methods of their measurement. The recent application of neuroimaging methods has significantly improved our knowledge of central mechanisms; similarly, research on peripheral pathways and the interaction between central and peripheral

mechanisms have provided a better understanding of female desire, arousal, and orgasm. Likewise, an increased awareness of the interaction between anatomical, physiological, neurobiological, and endocrine mechanisms, along with psychological/behavioral factors and their influence on FSF, has grown in parallel.

By reviewing the most recent peer-reviewed data, according to the basic principles of evidence-based medicine, whenever possible, this manuscript addresses central and peripheral anatomical and physiological aspects of *women's sexual arousal* and *orgasm*, also highlighting their interactions with psychological factors in a "biopsychological paradigm." Because of ethical constraints and experimental limitations, much of our current knowledge is still obtained from animal studies; these have been included in the article when no human data are available.

Physiology of Women's Sexual Function

Definitions of Female Sexual Arousal and Orgasm

When describing the physiological fundamentals of arousal and orgasm, it is noteworthy to stress that it is difficult to retrieve an exhaustive definition for *female sexual arousal (FSA)* [4]; in the literature, this is often based on what is considered dysfunctional. It is mandatory to stress that in women, changes in physiology do not necessarily induce SD, while sexual problems may occur despite an apparent normal sexual physiology. In this context, it has been suggested to subdivide FSA into an objective (namely, both genital and "extra-genital") and a subjective part. Genital sexual arousal may be described as "a combination of objective and subjective signs; the bodily reactions as vulvar swelling, vaginal lubrication, heavy breathing and increased sensitivity of the genitalia, combined with the subjective experience of feeling pleasure and excitement" [4]. Orgasm, in contrast, may be defined as "a variable, transient peak sensation of intense pleasure, creating an altered state of consciousness, usually accompanied by involuntary, rhythmic contractions of the pelvic striated circumvaginal musculature, with concomitant uterine and anal contractions and myotonia that resolves the sexually induced vasocongestion (sometimes only partially), usually with an induction of well-being and contentment" [5].

Development and Determination of Female Sexual Physiology and Anatomy

Biological Principles of Sexual Behavior

Understanding the physiology of adult female sexual behavior requires knowledge of events that occur early in development and the understanding of brain regions essential to motivation, consummation, and reward. The basic principles of the neural control of sexual behavior apply to an impressively broad range of species, from fish to nonhuman primates; the importance of the biological mechanisms regulating reproduction in animals is much greater than that in humans. Stereotyped sexual behavior and coitus occur normally only in estrous, while human female receptivity or proceptivity can occur over the entire ovarian cycle, during pregnancy, and in the postmenopausal period, thus demonstrating first the relative freedom from hormonal control [6], and, second, the epigenetic influence of both cognitive and sociocultural factors. In this context, several basic cellular mechanisms establishing the physiological and neuronal parameters upon which other variables act to influence human female sexuality may be often only available from studies in animals, by means of observation, experimentation, and hypothesis testing.

Sex Determination and Differentiation. In mammals, phenotypic sex is determined by a single gene—called *Sry*—on the Y chromosome. This sex-determining region of the Y chromosome codifies for the protein tdf, for testis determining factor, a transcription factor which initiates a cascade of gene expression and protein products that will direct the development of the bipotential gonadal anlage toward a testis [7]. In the absence of the *Sry* gene, this same gonadal anlage will become an ovary. The brain is also sexually differentiated in males and females by gonadal steroid hormones and this process occurs during a restricted developmental window termed the *sensitive period*. In rodents, the sensitive period is during the last few days of gestation and first week of life, and the critical hormone for masculinization is estradiol (E_2), derived from testicular androgens. In primates, including humans, the sensitive period is largely prenatal, beginning in the 2nd trimester, and the critical hormone for masculinization is testosterone (T).

Female Sex Behavior is Controlled by a Hormonally Responsive Neuronal Network. Sexual behavior represents a complex set of behaviors which includes motivation to seek partners, evaluation of critical stimuli, motor execution of the behavior, and rewarding physiological processes, which eventually reinforce the behavior so it will be subsequently repeated. Each component of the behavior involves multiple brain regions, with a number of