Mini Review

BIOMEDICAL Journal of Scientific & Technical Research

ISSN: 2574 -1241

DOI: 10.26717/BJSTR.2022.47.007475

Neuroendocrine Control of Male Sexual Behavior

Elaine Hull*

Professor of Psychology and Neuroscience, Florida State University, USA

***Corresponding author:** Elaine Hull, Professor of Psychology and Neuroscience, Florida State University, Tallahassee, FL 32309, USA

ARTICLE INFO

Received: November 18, 2022

Published: November 23, 2022

Citation: Elaine Hull. Neuroendocrine Control of Male Sexual Behavior. Biomed J Sci & Tech Res 47(2)-2022. BJSTR. MS.ID.007475.

ABSTRACT

Abbreviations: SRY: Sex determining Region on the Y chromosome; T: Testosterone; AMH: Anti-Müllerian Hormone; E: Estrogen; DHT: Dihydrotestosterone; MPOA: Medial Preoptic Area; AVPV: Anteroventral Periventricular; VMN: Ventromedial Nucleus; VTA: Ventral Tegmental Area

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Sexual behaviors are critical for species to continue. Hormones control both the early sex differentiation and the later ability to engage in sexual behavior. Early in development it is not possible to distinguish male embryos from female embryos. However, as embryos develop, chromosomes in each cell control the production of proteins, including both structural proteins which make up most of our body, and enzymes, which control biochemical reactions. Normally, all humans have 46 chromosomes, two of which are sex chromosomes, referred to as X and Y. Females have two X chromosomes, which promote female differentiation as well as some non-sexual functions. The Y chromosome is much smaller and is mostly involved in male differentiation and function. One gene on the Y chromosome, the Sex determining Region on the Y chromosome (SRY) directs the undifferentiated gonads to become testes, which then secrete testosterone (T) and Anti-Müllerian Hormone (AMH), which blocks the development of the female reproductive tract. Without T and AMH, feminine development would occur, controlled by several X chromosome genes. T can be converted into either estrogen (E) or dihydrotestosterone (DHT), which is several times more potent at androgen receptors than T. It is DHT that is important for forming the male genitals. In addition to the gonads, there are two duct systems: the Wolffian ducts and the Müllerian ducts. In males T causes the penis and testicles to develop and causes the Wolffian ducts develop into the vas deferens, seminal vesicles, prostate, and epididymis. In females, genes on the X chromosome cause the Müllerian ducts to develop into oviducts (fallopian tubes in women) and uterus and cause the genitals to form the clitoris and labia.

In adulthood, T and E promote sperm and egg production and sexual behaviors. In both males and females, sensory input is sent either directly or indirectly to nuclei in the hypothalamus, which then activate appropriate behaviors. Studies on nonhuman animals have provided much of our information on brain control of sexual behaviors. In rodents, E is more important than T for controlling adult male sexual behavior, although in humans, it is T. For controlling male sexual behavior, one brain area is especially important. The medial preoptic area (MPOA), which is located above and slightly in front of the optic chiasm, controls male sexual behavior in essentially all vertebrate species. T in the MPOA can be converted by enzymes to E, which can attract microglia, immune cells that live in the brain. Microglia promotes cell survival and formation of synaptic connections. As a result, males have a larger MPOA than females. Thus, the MPOA is permanently masculinized and will promote male sexual behavior. This brain area is essential for male sexual behavior in all vertebrate species that have been studied, from fish through humans.

A separate area, slightly in front of the MPOA, controls menstrual cycles in women and estrous cycles in lower animals. Perinatal T actually decreases the anteroventral periventricular (AVPV) nucleus, which is therefore larger in females. In addition, the ventromedial nucleus (VMN) of the hypothalamus, which is behind the MPOA, is important for the control of female sexual behavior in lower mammals. The neurotransmitter dopamine is released in the MPOA as soon as a male rat detects the odor of a receptive female; release is further increased during copulation. Stimulation of dopamine D1 receptors in the MPOA can cause an erection in male rats. However, a large dose of a D2 receptor stimulant can inhibit erection and elicit an ejaculation. T promotes copulation, in part, by up-regulating nitric oxide synthase in the MPOA; the resultant production of nitric oxide gas increases both basal and female-stimulated dopamine release. In addition, glutamate release has been shown to increase by almost 300% in the MPOA when the male ejaculates. Glutamate is the major excitatory neurotransmitter in the brain.

The neurotransmitter serotonin is also released in the nearby anterior lateral hypothalamus at the time of ejaculation and contributes to the postejaculatory sexual quiescence. That occurs in part by decreasing dopamine release in the mesolimbic system, which is critical for motivated behaviors. That system has cell bodies in the ventral tegmental area (VTA) of the brain stem and sends axons up to the nucleus accumbens, which is in the basal forebrain. More recent research centered on the roles of dopamine and glutamate in the increase in sexual proficiency due to sexual experience. Similar mechanisms may underlie other forms of memory and drug addiction. Finally, we were interested in how certain mating-induced transcription factors in the MPOA interact to enhance future sexual behavior and decrease stress and anxiety.

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