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Normal male sexual function: emphasis on orgasm and ejaculation

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Abstract

Orgasm and ejaculation are two separate physiological processes that are sometimes difficult to distinguish. Orgasm is an intense transient peak sensation of intense pleasure creating an altered state of consciousness associated with reported physical changes. Antegrade ejaculation is a complex physiological process that is composed of two phases (emission and expulsion), and is influenced by intricate neurological and hormonal pathways. Despite the many published research projects dealing with the physiology of orgasm and ejaculation, much about this topic is still unknown. Ejaculatory dysfunction is a common disorder, and currently has no definitive cure. Understanding the complex physiology of orgasm and ejaculation allows the development of therapeutic targets for ejaculatory dysfunction. In this article, we summarize the current literature on the physiology of orgasm and ejaculation, starting with a brief description of the anatomy of sex organs and the physiology of erection. Then, we describe the physiology of orgasm and ejaculation detailing the neuronal, neurochemical, and hormonal control of the ejaculation process.

Keywords

Erectile function; male sexual function; ejaculation; orgasm

Ejaculatory dysfunction is one of the most common male sexual dysfunctions that is often mis-diagnosed or disregarded. At present, there is no definitive cure for ejaculatory dysfunctions (1). New research on the physiology of ejaculation keeps emerging to identify targets of treatment. However, knowledge about this topic is still lacking. In the present article, we summarize the current literature on the physiology of ejaculation. We describe the anatomy of the organs involved and the erection physiology. We discuss the physiology of orgasm and ejaculation as two separate physiological processes. In addition, we describe the neurochemical and hormonal regulation of the ejaculation process.

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FUNCTIONAL ANATOMY OF THE MALE GENITAL ORGANS

The male genital system consists of external and internal reproductive and sexual organs such as the penis, prostate, epididymis, and testes. Figure 1 shows the gross anatomy of the ejaculatory structures. Table 1 provides a summary of the functional anatomy of these organs (2–5).

PHYSIOLOGY OF ERECTION

The penile erection results from complex neurovascular mechanisms. Several central and peripheral neurological factors in addition to molecular, vascular, psychological and endocrino-logical factors are involved, and the balance between these factors is what eventually determines the functionality of the penis. In this section, we summarize some of those mechanisms.

Cerebral Control

Cerebrally controlled penile erections are induced through erotic visual stimuli or thoughts. The main cerebral structures involved in erection are contained within the medial preoptic area (MPOA) and paraventricular nucleus (PVN) in the hypothalamus (6). Dopamine is the most important brain neurotransmitter for erection, likely through its stimulation of oxytocin release (7). Another important neurotransmitter is norepinephrine, which is demonstrated through the erectogenic effect of the α -2 agonist (Yohimbine) (8). Several other brain neurotransmitters are involved in the erection process to varying degrees such as nitric oxide (NO), α -melanocyte stimulating hormone (α -MSH), and opioid peptides (9).

Autonomic Control

Parasympathetic stimulation is the main mediator for penile tumescence, although central suppression of the sympathetic nervous system also plays a role. Parasympathetic supply to the penis is derived from the sacral segments S2-S4 (10). However, patients with sacral spinal cord injury still maintain erections through psychogenic stimulation, although of less rigidity than normal. These psychogenic erections do not occur in patients with lesions above T9 (11), suggesting that the main mechanism for these erections is central suppression of sympathetic stimulation (12). Patients with lesions above T9 still may maintain reflexogenic erections. This implies that the main mechanism for reflexogenic tumescence is the preservation of the sacral reflex arc, which mediates erection through tactile penile stimulation (13, 14).

Molecular Mechanisms

The penis at baseline is in a flaccid state maintained by the contraction of corporal smooth muscles and constriction of cavernous and helicine arteries leading to moderate state of hypoxia with partial pressure of oxygen of 30–40 mm Hg (15). During sexual arousal, NO is released from cavernous nerve terminals through the action of neuronal NO synthase (16). The NO activates guanylate cyclase, which in turn converts guanosine triphosphate to cyclic guanosine monophosphate (15, 17), leading eventually to smooth muscle relaxation and vasodilation (18). Although the initiation of tumescence is through neuronal NO synthase,

the maintenance of erection is through endothelial NO synthase (19). The eventual smooth muscle relaxation and vasodilation results in blood flowing into the paired corpora and filling of the sinusoids, with increased intracorporal pressure (to >100 mm Hg during full erection) and compression of the subtunical venules, markedly reducing the venous outflow (13).

PHYSIOLOGY OF ORGASM

There is no standard definition of orgasm. Each specialty such as endocrinology or psychology examines this activity from each one's perspective, making it difficult to reach a consensus on the definition. Orgasm is generally associated with ejaculation, although the two processes are physiologically different (20). Certain physiological features are associated with orgasm, including hyperventilation up to 40 breaths/min, tachycardia, and high blood pressure (21). In fact, faster heart rate was found to be an indicator of "real" male orgasm during intravaginal intercourse, differentiating it from "fake" orgasm (22). Orgasm is also associated with powerful and highly pleasurable pelvic muscle contractions (especially ischiocavernosus and bulbocavernosus) (23), along with rectal sphincter contractions and facial grimacing (21). There is also an associated release and elevation in PRL and oxytocin levels after orgasm; however, the significance of this elevation is not entirely clear (24).

Studies using positron emission tomography, which measures changes in regional cerebral blood flow, have identified areas of activation in the brain during orgasm. Primary intense activation areas are noted to be in the mesodiencephalic transition zones, which includes the midline, the zona incerta, ventroposterior and intralaminar thalamic nuclei, the lateral segmental central field, the suprafascicular nucleus, and the ventral tegmental area. Strong increases were seen in the cerebellum. Decreases were noted at the entorhinal cortex and the amygdale (25).

Quality and intensity of orgasms are variable. For instance, short fast buildup of sexual stimulation toward orgasm is associated with less intense orgasms than slow buildup. Early orgasms are less satisfying than later orgasms in life as the person learns to accept the pleasure associated with orgasms. Lower levels of androgen are associated with weaker orgasms, such as in hypogonadism or in older age (20). It has been suggested that pelvic muscle exercises, particularly the bulbocavernosus and ischiocavernosus muscles, through contracting those muscles 60 times, 3 times daily for 6 weeks will enhance the pleasure associated with orgasm (20). However, the effort and time associated with such exercises prevent their utilization. The orgasm induced through deep prostatic massage is thought to be different from the orgasm associated direct penile stimulation. Although penile stimulation orgasms are associated with 4–8 pelvic muscle contractions, prostatic massage orgasms are associated with 12 contractions. Prostatic massage orgasms are thought to be more intense and diffuse than penile stimulation orgasms, but they require time and practice and are not liked by many men (20, 26, 27).

Following orgasm in men is a temporary period of inhibition of erection or ejaculation called the refractory period. This is a poorly understood phenomenon, with some investigators suggesting a central rather than spinal mechanism causing it (28). Elevated levels of PRL

and serotonin after orgasm have been suggested as a potential cause; however, there is much debate about their exact role (29). More research is still needed in the area of male orgasm (20).

PHYSIOLOGY OF EJACULATION

Ejaculation is a physiological process heavily controlled by the autonomic nervous system. It consists of two main phases: emission and expulsion. The main organs involved in ejaculation are the distal epididymis, the vas deferens, the seminal vesicle, the prostate, the prostatic urethra, and the bladder neck (30).

Emission

The first step in the emission phase is the closure of bladder neck to prevent retrograde spillage of the seminal fluid into the bladder. This is followed by the ejection of prostatic secretions (10% of the final semen volume) containing acid phosphatase, citric acid, and zinc, mixed with spermatozoa from the vas deferens (10% of the volume) into the prostatic urethra. Subsequently, the fructose-containing seminal vesicle fluid alkalinizes the final ejaculatory fluid. The seminal vesicle fluid constitutes 75%–80% of the final seminal fluid. Cowper's glands and periurethral glands produce a minority of the seminal fluid (1, 31). The organs involved in the ejaculation process receive dense autonomic nerve supply, both sympathetic and parasympathetic, from the pelvic plexus. The pelvic plexus is located retroperitoneally on either side of the rectum, lateral and posterior to the seminal vesicle (32). It receives neuronal input from the hypogastric and pelvic nerves in addition to the caudal paravertebral sympathetic chain (33). The sympathetic neurons play the predominant role in the ejaculation process. Their nerve terminals secrete primarily norepinephrine, although other neurotransmitters such as acetylcholine and nonadrenergic/noncholinergic also play important roles (34). The role of the hypogastric plexus in emission is best demonstrated clinically by the loss of emission after non-nerve sparing para-aortic lymph node dissection for testicular cancer (35), and induction of emission in paraplegic men through electrical stimulation of superior hypogastric plexus (35). Input from genital stimulation is integrated at the neural sacral spinal level to produce emission (36). The emission phase of ejaculation is also under a considerable cerebral control, and can be induced through physical or visual erotic stimulation (37).

Expulsion

Expulsion follows emission as the process of ejaculation climaxes, and refers to the ejection of semen through the urethral meatus. The semen is propelled through the rhythmic contractions of the pelvic striated muscles in addition to the bulbospongiosus and ischiocavernosus muscles (23). To achieve antegrade semen expulsion, the bladder neck remains closed, whereas the external urethral sphincter is open. The external sphincter and the pelvic musculature are under somatic control; however, there is no evidence that voluntary control plays a role in the expulsion process (30). The exact trigger for expulsion is unknown. It has been suggested that a spinal center is triggered during emission of seminal fluid into the prostatic urethra (38). However, there is mounting evidence through clinical and experimental studies to suggest that this is not the case. For instance, men can

still have rhythmic contractions during orgasm despite “dry ejaculation,” for example, due to prostatectomy (23, 39, 40). This, in addition to the identification of spinal generator for ejaculation (SGE) in rats, led to the postulation that the process of expulsion is a continuum of the process initiated through emission, after reaching a certain spinal activation threshold (30, 41).

NEURONAL CONTROL OF EJACULATION

Ejaculation is heavily controlled by the nervous system. Figure 2 summarizes the reflex circuit necessary to elicit ejaculation.

Peripheral Nervous System

Afferents—The main sensory input from the penis comes from the dorsal nerve of the penis, which transmits sensation from the glans, prepuce, and penile shaft. It transmits signals to the upper and lower segments of the sacral spinal cord (42). The glans contains encapsulated nerve endings, termed Krause-Finger corpuscles, whereas the remaining penile shaft contains free nerve endings. Stimulation of these corpuscles potentiated by stimulation from other genital areas, such the perineum, testes, and penile shaft, play an important role in the ejaculation process (43). A secondary afferent route is through the hypogastric nerve, which runs through the paravertebral sympathetic chain to enter the spinal cord through the thoracolumbar dorsal roots (44). The sensory afferents terminate in the medial dorsal horn and the dorsal gray commissure of the spinal cord (45).

Efferents—The efferent peripheral nervous system constitutes of sympathetic, parasympathetic, and motor nervous components (46). The soma of the preganglionic sympathetic cell bodies involved in ejaculation are located in the intermedio-lateral cell column and in the central autonomic region of the thoracolumbar segments (T12-L1) (47). The preganglionic sympathetic fibers emerge from the ventral roots of the spinal cord and travel through the paravertebral sympathetic chain to relay either directly through the splanchnic nerve, or through relaying first in the celiac superior mesenteric ganglia and then through the intermesenteric nerve, to the inferior mesenteric ganglia (48). The hypogastric nerve then emanates from the inferior mesenteric ganglia to join the parasympathetic pelvic nerve to form the pelvic plexus, which then sends fibers to the ejaculation structures (49). The preganglionic parasympathetic cell bodies are located in the sacral parasympathetic nucleus. The sacral parasympathetic nucleus neurons travel then in the pelvic nerve to the post-ganglionic parasympathetic cells located in the pelvic plexus. The motor neurons involved in ejaculation are located in Onuf’s nucleus in the sacral spinal cord, which projects fibers through the motor component of the pudendal nerve to reach the pelvic musculature, including the bulbospongiosus, ischiocavernosus, and external urethral sphincter (50).

Central Nervous System

Spinal network—The thoracolumbar sympathetic, sacral parasympathetic (mainly sacral parasympathetic nucleus), and somatic sacral Onuf’s nucleus ejaculatory spinal nuclei play an important role in the integration of peripheral and cerebral input and coordinating output to the pelvip erineal structures involved in ejaculation (46). An additional spinal center is the

SGE located in laminae X and VII of L3-L4 spinal segments (51). The SGE contains spinal interneurons called lumbar spinothalamic cells, which project fibers to the parvocellular subparafascicular nucleus of the thalamus in addition to preganglionic sympathetic and parasympathetic neurons innervating the pelvis (41). The SGE stimulation elicits a complete ejaculatory response resulting in collection of motile spermatozoa in anesthetized rats (52). Further research on the SGE spinal center is still needed, and it is unclear whether it contains other cells than lumbar spinothalamic cells.

Brain network—Sensory and motor areas in the brain play an important role in the ejaculation, which requires a highly coordinated and integrated central process. The study by Holstege et al. (25) using positron emission tomography showed that certain areas in the brain are activated in the orgasm and ejaculation process. Furthermore, specific areas in the brain have been involved in the ejaculation process, as demonstrated in animal immunohistochemical studies examining Fos protein pattern of expression (53–56), and confirmed using a serotonin 1A subtype receptor agonist proejaculatory pharmacologic agent in rats (57). These are discrete areas within the posteromedial bed nucleus of stria terminalis, the parvicellular part of the subparafascicular thalamus, the posterodorsal preoptic nucleus, and the posterodorsal medial amygdaloid nucleus. There are reciprocal connections that link those areas to the MPOA of the hypothalamus, a brain area with a well-established role in controlling sexual behavior as demonstrated by anatomical and functional studies (54, 55, 58). Electrical or chemical stimulation of the MPOA elicited ejaculation (59–62), whereas an MPOA lesion was shown to abolish both phases of ejaculation (63). No direct connections of MPOA to the spinal centers for ejaculation were found on neuroanatomical studies; however, there are projections of MPOA to other regions in the brain involved in ejaculation, such as PVN, the periaqueductal gray, and the paragigantocellular nucleus (nPGi) (64–66).

The PVN projects to pudendal motor neurons located in the L5-L6 spinal segment in addition to autonomic preganglionic neurons in the lumbosacral spinal cord in rats (45, 67, 68). It also projects to nPGi in the brainstem (69). Bilateral lesions of the PVN with N-methyl-D-aspartate (NMDA) results in a one-third reduction of the seminal ejaculate material weight (70). The parvicellular part of the subparafascicular thalamus was found to send projections to bed nucleus of stria terminalis, medial amygdala (MeA), and MPOA (71, 72) and receives input from lumbar spinothalamic cells (51). The precise role of these regions is still unclear but they are likely involved in relaying genital signals to MPOA (53, 55). The brainstem regions (nPGi and periaqueductal gray) have recently received increasing attention. The nPGi nucleus likely plays an inhibitory role in ejaculation as evidenced through the urethro-genital reflex experimental model, a rat model for the expulsion phase of ejaculation (73, 74). Using the same model, the periaqueductal gray was found to be important for the ejaculation process, likely by acting as a relay between MPOA and nPGi (75). Midbrain structures have a significant role in ejaculation; however, much is still unknown about their exact role and further research is needed. Figure 3 summarizes the putative brain structures involved in ejaculation.

NEUROCHEMICAL REGULATION OF EJACULATION

Many neurotransmitters are involved in the ejaculation process. Defining the exact role of these neurotransmitters is difficult given the variety of sexual parameters affected, the different sites of action within the spinal and the supraspinal pathways, and the presence of multiple receptor types. Some of the molecules that received special attention for their role in ejaculation are mentioned later.

Dopaminergic Control

Dopamine is known to be important for normal male sexual response (76, 77). Two families of dopamine receptors exist, D1-like (D1 and D5 receptors) and D2-like (D2, D3, and D4 receptors) (46). In rats, D2-like receptors are known to stimulate ejaculation (78, 79), and trigger ejaculation even in anesthetized rats (80, 81). Systemic injection of the D3 receptor agonist 7-OH-DPAT has been shown to trigger ejaculation in rats without affecting arousal (82, 83). It also triggers ejaculation in anesthetized rats when injected directly into the cerebral ventricles or MPOA with the effect being specifically reversed by the D3, not the D2 antagonist (84, 85). The D3 receptor blockage has been shown to inhibit the expulsion phase of ejaculation and lengthen ejaculation latency in rats (86).

Serotonergic Control

Evidence suggests that serotonin (5HT) inhibits ejaculation (87). Selective serotonin reuptake inhibitors increase 5HT tone resulting in impairment of ejaculation, which led to their clinical use in premature ejaculation. This inhibitory effect is likely to occur in the brain (88), as 5HT effect on ejaculation in the spine is likely stimulatory (89). The amphetamine derivative p-chloroamphetamine leads to a sudden release of 5HT in synaptic clefts triggering ejaculation in anesthetized rats with complete spinal cord lesion (89). Intrathecal serotonin or selective serotonin reuptake inhibitor injection leads to enhancement of the expulsion phase of ejaculation (88). There are 14 receptor subtypes for 5HT, with 1A, 1B, and 2C being the ones involved in ejaculation (90). It is difficult to designate one influence for each receptor subtype, as each receptor could either activate or inhibit ejaculation depending on its location within the central nervous system (46).

Nitric Oxide

The role of NO in ejaculation has received special attention after the introduction of type-5 phosphodiesterase (PDE5) inhibitors and using them for premature ejaculation. Nitric oxide has an inhibitory role on the ejaculation process (1). Centrally, intrathecal sildenafil results in elevation of NO and cyclic guanosine monophosphate levels in MPOA causing a decreased peripheral sympathetic tone and inhibition of ejaculation (91). *N*-Nitro-L-arginine methyl-ester injection, an NO synthase inhibitor, was shown to increase the number of seminal emissions and reduce latency to first seminal emission in rats (92). Peripherally, nitroergic innervation and NO synthase were found in the seminal vesicle, vas deferens, prostate, and urethra (93–97). Therefore, drugs such as PDE5 inhibitors or NO donors are associated with reduced seminal vesicle contraction and inhibit seminal emission (92). The administration of NO inhibitors, such as L-nitroarginine-methylester, diminishes human seminal vesicle contraction (98), inhibits vasal contraction in guinea pigs (99), and decreases

latency to ejaculation in rats (100). Furthermore, reduced latency to emission was found in knockout mice for the gene encoding endothelial NO synthase compared with their wild-type counterparts (101).

HORMONAL REGULATION OF EJACULATION

Although male sexual function is heavily regulated by the hormonal system, there are few clinical studies performed to evaluate hormonal regulation of ejaculation, and the knowledge about hormonal effect on ejaculation is still lacking. We discuss some of the studies examining the effect of different hormones on ejaculation.

Oxytocin

Oxytocin is an oligopeptide synthesized in the supraoptic and PVN of the hypothalamus and released from the posterior pituitary gland. Oxytocin serum level increases after male ejaculation to levels ranging from 20%–360% of normal levels before reaching baseline at 10 minutes after ejaculation (102). Pharmacologic oxytocin administration in humans and animals results in increased ejaculated spermatozoa (103), confirming that oxytocin has a role in male genital tract motility. It was specifically found to augment powerful epididymal contractions and sperm motility (104), an important effect blunted by pretreatment with the oxytocin antagonist (des Gly–NH₂d(CH₂)₅–[d-Tyr₂,Thr₄] ornithine vasotocin) (105). Peripheral oxytocin receptors were found to be highly expressed in the epididymis and tunica albuginea (in smooth muscles more than epithelial cells), and to a lesser extent in the vas deferens and seminal vesicle (104). Oxytocin has a synergistic action on the epididymis with endothelin-1, where they augment epididymal contraction and propel spermatozoa forward (102, 106). Injection of oxytocin into the cerebral ventricles in male rats facilitated ejaculation by shortening the ejaculation latency and postejaculatory refractory periods (107), whereas these effects were curbed using the oxytocin receptor antagonist (d(CH₂)₅–Tyr(Me)–[Orn₈]vasotocin) injected into the cerebral ventricles (108). Despite these encouraging findings and some anecdotal evidence suggesting that intranasal oxytocin can facilitate orgasm in an anorgasmic male (109), a double-blind placebo-controlled clinical study (110) failed to demonstrate an effect of intranasal oxytocin on sexual behavior.

Prolactin

Hyperprolactinemia has a marked inhibitory effect on male sexual desire (111). A modest increase in serum PRL levels (15–20 ng/mL) has been detected in men after orgasm, and could be contributing to the after-orgasm refractory period (112). Some investigators have hypothesized that a low PRL level is a cause of premature ejaculation, where PRL levels were similarly low in those men with lifelong or acquired premature ejaculation (113). Further research is needed on this issue.

Thyroid Hormones

The relationship between thyroid hormonal abnormalities and ejaculatory dysfunction has been well documented (114–116). In rats, L-thyroxin administration has been shown to increase bulbospongiosus contractile activity and seminal vesicle contraction frequency (117). Clinically, the prevalence of suppressed TSH, which is a marker of hyperthyroidism,

was found to be twofold higher in patients with premature ejaculation than in patients who reported normal ejaculatory timing (118). In the first prospective multicenter study (114) on the topic, half of hyperthyroidism patients had premature ejaculation, whereas only 15% reported this symptom after cure of their thyroid dysfunction. Another single-center prospective study by Cihan et al. (116) demonstrated a prevalence of 72% of premature ejaculation in hyperthyroidism, which was reduced after treatment. It also identified a positive correlation of TSH with intravaginal ejaculation latency time. Öztürk et al. (119) found similar results. However, Waldinger et al. (120) found no correlation between TSH and intravaginal ejaculation latency time in a cohort of Dutch men with lifelong premature ejaculation. A meta-analysis by Corona et al. (102) demonstrated a threefold increase of hyperthyroidism in patients with premature ejaculation compared with controls, a finding that was more pronounced in patients with acquired rather than lifelong premature ejaculation. They also showed an increase in intravaginal ejaculation latency time by 84.6 ± 34.2 seconds ($P=.001$) upon treatment of hyperthyroidism. These findings suggest that thyroid hormones do not only affect the ankle reflex, but also the ejaculatory reflex, and screening patients with ejaculatory dysfunction for thyroid hormone abnormalities is warranted (102).

Glucocorticoids

Cortisol (F) levels in several animal studies were found to be elevated during arousal and ejaculation (121–123). In horses and donkeys, F was elevated 30 minutes after ejaculation, with unknown significance of this finding (124, 125). In addition, F levels were sharply elevated after electroejaculation in several anesthetized animal studies (126, 127). In humans, however, there was no change in F levels whether during sexual stimulation or orgasm (128–131). Although hypercortisolism in men was associated with reduced libido, no effect was identified on orgasm or ejaculation (132). Replacement of F in Addison disease was associated with improvement in overall sexual function including orgasm (133). Data in humans are still too preliminary to draw final conclusions, and further research is needed.

Estrogens

Estradiol plays an important role in the regulation of the emission phase of ejaculation through the regulation of epididymal contractility, luminal fluid reabsorption, and sperm concentration (134, 135). This role in the epididymis is the reason for recommending Tamoxifen as a first-line treatment for idiopathic oligospermia by the World Health Organization (136). Finkelstein et al. (137) showed that E_2 deficiency, along with androgen deficiency, contributes to decreased libido and erectile function.

Androgens

Testosterone, through its central and peripheral androgen receptors, has a well-known role on male sexual function, particularly on libido (138). Low T levels are associated with delayed ejaculation, whereas high levels were associated with premature ejaculation (102). This is likely because the emission phase of the ejaculation relies on the NO-PDE5 system, which is influenced by T (138, 139). Testosterone facilitates the control of the ejaculatory reflex through its androgen receptors in the MPOA and other areas in the central nervous

system (140). Furthermore, pelvic floor muscles involved in ejaculation are androgen dependent (141). There are likely multiple mechanisms involved in T action and further research is needed to identify specific targets for treatment in the ejaculatory reflex. Table 2 summarizes the neurochemical and hormonal regulation of ejaculation.

In conclusion, ejaculation is a complex process involving several anatomical structures and under extensive neurochemical and hormonal regulation. Orgasm, although associated with ejaculation, is a distinct physiological process, different from ejaculation. Many aspects of these physiological processes are still unknown and further research is needed to identify treatments for ejaculatory dysfunction.

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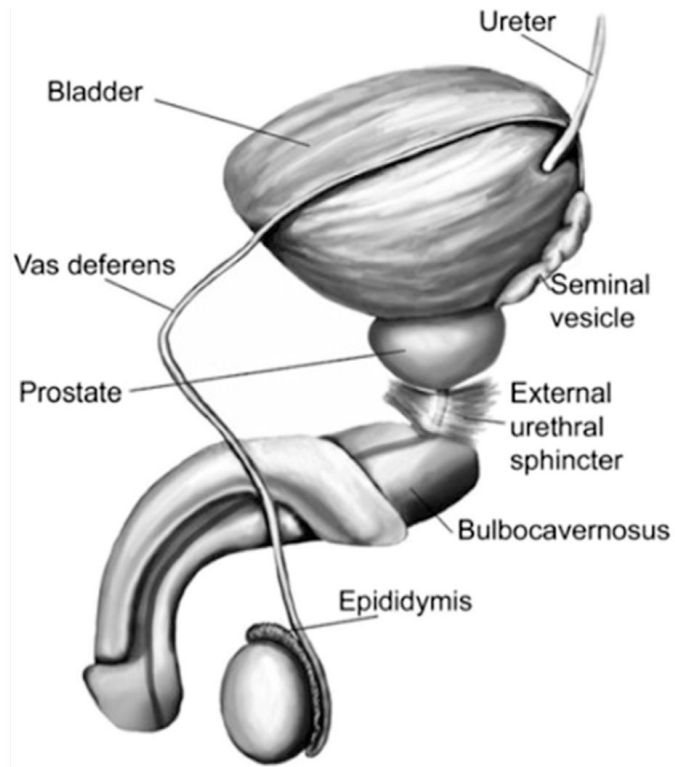


FIGURE 1. Gross anatomy of the ejaculation structures. (Reprinted with permission from Sheu G, Revenig LM, Hsiao W. Physiology of ejaculation. In: Mulhall JP, Hsiao W, eds. Men's sexual health and fertility: a clinician's guide. New York: Springer; 2014:15.)

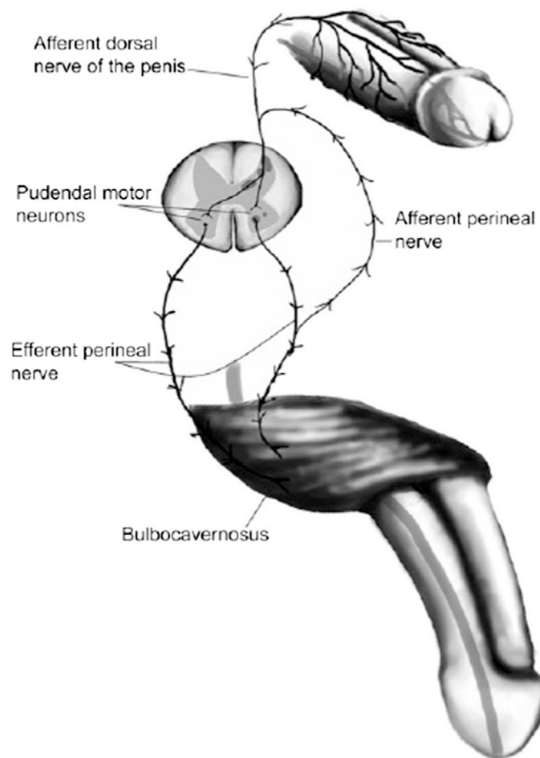
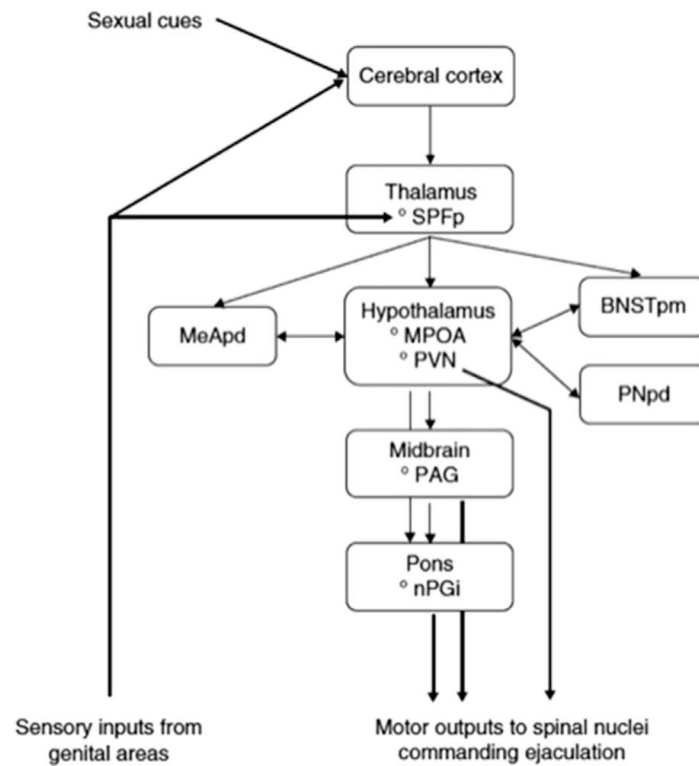


FIGURE 2. Reflex circuit needed to establish ejaculation. (Reprinted with permission from Sheu G, Revenig LM, Hsiao W. Physiology of ejaculation. In: Mulhall JP, Hsiao W, eds. Men's sexual health and fertility: a clinician's guide. New York: Springer; 2014:18.)

**FIGURE 3.**

Putative brain structures involved in ejaculation. BNSTpm = posteromedial bed nucleus of stria terminalis; MeApd = posterodorsal medial amygdaloid nucleus; MPOA = medial preoptic area; PAG = periaqueductal gray; nPGi = paragigantocellular nucleus; PNpd = posterodorsal preoptic nucleus; PVN = paraventricular thalamic nucleus; SPFp = parvicellular part of the subparafascicular thalamus. (Reprinted with permission from Clement P, Giuliano F. Physiology of ejaculation. In: Mulhall JP, Incrocci L, Goldstein I, Rosen RC, eds. *Cancer and sexual health*. New York: Springer; 2011:82.)

TABLE 1

Summary of the functional anatomy of the male genital organs.

Organ	Characteristics
Penis	<p>Composed of three chambers: paired corpora cavernosa (erectile bodies) and a midline ventral corpus spongiosum (contains urethra)</p> <p>Main blood supply: internal pudendal artery</p> <p>Somatic sensation: pudendal nerve (S2-S4)</p> <p>Autonomic nerve fibers: cavernous nerves (pelvic plexus) contain both sympathetic (hypogastric plexus) and parasympathetic nerve fibers (S2-S4)</p>
Urethra	<p>Four segments: prostatic urethra, membranous urethra (passes through the urogenital diaphragm), bulbar urethra, and penile urethra (ends with a small dilatation at the fossa navicularis near the meatus)</p> <p>Cowper's glands: located on both sides of the membranous urethra and open in the bulbar urethra</p> <p>Veromontanum: small elevation of the posterior wall of the membranous urethra, related to ejaculatory ducts, prostatic utricle, and prostatic ducts</p>
Testis	<p>It is divided by fibrous septa into many lobules containing seminiferous tubules</p> <p>Leydig cells: main source of T production</p> <p>Seminiferous tubules: contain germ cells and sertoli cells. Forms the rete testis inside the testis mediastinum</p> <p>Rete testis: gives rise to 15–20 efferent ductules</p>
Epididymis	<p>Posterior and superior to the testicle</p> <p>Composed of head, body, and tail</p> <p>Efferent ductules unite to form the convoluted duct of the epididymis</p> <p>Becomes the vas deferens at the end of the tail</p>
Vas deferens	<p>Muscular tube; typically 45 cm long and has a 2.5 mm diameter</p> <p>It is a continuation of the epididymis</p> <p>Joins the seminal vesicle duct to form the ejaculatory duct, which then drains into the veromontanum</p> <p>Supplied by the vasal artery, a branch of the inferior vesical artery</p>
Prostate	<p>Surrounds the prostatic urethra</p> <p>Composed of 70% glandular component and 30% fibromuscular component</p> <p>Arterial supply: inferior vesical and middle rectal arteries</p>
Seminal vesicles	<p>Paired structures; located lateral to the vas deferens</p> <p>Typically 5 cm long and 1 cm wide</p> <p>Joins the vas to form the ejaculatory duct</p> <p>Arterial supply: inferior vesical and middle rectal arteries</p>

TABLE 2

Neurochemical and hormonal regulation of ejaculation.

Neurotransmitter/hormone	Effect
Dopamine	Stimulates ejaculation through D2-like receptors (D2, D3, and D4 receptors, mainly D3)
Serotonin	Inhibits ejaculation in the brain and stimulates it in the spine through the receptors 5HT, with 1A, 1B, and 2C
Nitric oxide	Inhibits ejaculation through reduction of seminal vesicle contraction and seminal emission
Oxytocin	Synthesized in the supraoptic and PVN of the hypothalamus and released from the posterior pituitary gland Augments powerful epididymal contractions and sperm motility Acts in the CNS to stimulate ejaculation
Prolactin	Secreted from the pituitary gland Hyperprolactinemia has a marked inhibitory effect on male sexual desire, through inhibition of GnRH (therefore T production) and dopamine production
Thyroid hormones	Hypothyroidism and hyperthyroidism are associated with delayed and premature ejaculation, respectively
Glucocorticoids	Cortisol levels are elevated after ejaculation in animal studies No change in cortisol levels in humans Replacement of cortisol in Addison disease improves sexual function including orgasm
Estrogens	Regulates the emission phase of ejaculation through the regulation of epididymal contractility, luminal fluid reabsorption, and sperm concentration
Androgens	Low levels are associated with delayed ejaculation, whereas high levels are associated with premature ejaculation Facilitates the control of the ejaculatory reflex through its androgen receptors in the MPOA and other areas in the CNS Pelvic floor muscles involved in ejaculation are androgen dependent

Note: CNS = central nervous system; MPOA = medial preoptic area; PVN = paraventricular nucleus.