The Role of Genital Nerve Afferents in the Physiology of the Sexual Response and Pelvic Floor Function

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Abstract

Introduction. Our understanding of genital and pelvic floor physiology is rapidly expanding. Penile erection is a neurovascular event controlled by spinal autonomic centers, the activity of which is dependent on input from supraspinal centers and the genitalia. Genital afferent stimulation excites spinal autonomic nuclei and supraspinal sexual centers of both genders.

Aim. To present a detailed understanding of the functional importance of genital afferent neuroanatomy and neurophysiology.

Methods. English-written articles of diverse disciplines from 1980 to 2010 that contained information on genital anatomy, pudendal/dorsal/perineal/cavernous nerves, vibratory stimulation, reflexogenic erection, peripheral/central nervous system-mediated erectile and micturition pathways, and sexual arousal in animals and humans were reviewed.

Main Outcome Measures. Analysis of supporting evidence for the role of genital afferents in the physiology of erectile response and pelvic floor function.

Results. Basic science and clinical studies support the concept that pudendal nerve circuitry serves an essential purpose for sexual behavior, erectile function, penile rigidity, ejaculation, and micturition. Males and females share a comparable pattern of genital afferent neuroanatomy and neurophysiology, and sexual and micturition reflexes are similar in both genders. Pudendal nerve branches communicate with the cavernous nerves and are nitric oxide synthase positive. Genital afferents activate multiple spinal reflexes that modulate erection and micturition. Genital sensory information is transmitted to supraspinal centers important for sexual function.

Conclusions. There is expanding support for the critical role of genital afferent neurophysiology in the mechanisms of erectile function and micturition. Genital afferent stimulation is a safe and natural modality that can be harnessed to amplify autonomic and somatic activity within the penis, female genitalia, spinal cord, and higher centers via established neurological principles. Such physiological adaptive processes may be beneficial in improving sexual response, erectile function, and micturition in many disease states, including in men after radical pelvic surgery. Well-designed and executed studies in each specific population are needed to authenticate such prospects.


Key Words. Penis; Erectile Dysfunction; Vibratory Stimulation; Sexual Reflex; Genital Afferent Neurophysiology; Micturition

Penile erection is controlled by spinal autonomic centers, the activity of which is dependent on input from supraspinal centers and genitalia. From a neurophysiological viewpoint, scientists believe that penile erection is a culmination of multiple successful nerve reflexes that initiate a vascular event [1,2]. The maintenance of erection and rigidity is an intriguing combination of neurovascular cavernosal reactivity, venous occlusion, and rhythmic perineal muscle contraction [3]. These mechanisms have
been passionately debated by anatomists, physiologists, psychologists, and urologists for many decades. The dorsal nerve of penis (DNP) is considered by some experts to be the single most important nerve in male sexual function and satisfaction [4]. The cavernous nerve (CN) is very important, although it is a conduit for brain-induced and reflexogenic instructions to reach the penis. This efferent system cannot function independently, and afferent pathways play a critical role. Most recent attempts to devise a treatment plan for erectile dysfunction have focused on pharmacological manipulation of the efferent system and vascular events that lead to penile fullness [5].

Neuromodulatory therapy, in the form of neurotrophins [6], neuroprotective agents [7], electrical stimulation [8], autologous vein to CN nerve graft [9], and novel biochemical compounds (erythropoietin [10], statins [11]) is an exciting new frontier in our attempts to promote erectile health and restore function after nerve trauma, as often occurs as a result of pelvic surgery.

In this article, we present multidisciplinary experimental and clinical data on the role of penile afferent circuitry and stimulation in mechanisms of erectile function and penile rigidity. We will also discuss important male and female genital afferent research to support our current understanding of sexual reflexes and micturition, which are similar in both genders. Briefly, we will speculate on several important clinical applications of genital/penile afferent stimulation for the treatment of several disease states, including post-pelvic surgery erectile dysfunction, diminished sexual arousal, orgasmic dysfunction, and pelvic floor dysfunction in both genders.

Neuroanatomy

Our analysis of more than three decades of published research on genital afferent neuroanatomy and neurophysiology reveals that both males and females share a comparable pattern of genital receptors and innervation. Despite obvious gross anatomical differences between the genders, neuroanatomical pathways within the pelvis, spinal cord, and the brain also show a great deal of resemblance (see Figures 1 and 2).

The male genital sensory pathway originates with its receptors in the glans and shaft of the penis. Similar to other areas of human skin, the most numerous afferent terminations of the penis are free nerve endings (FNE) of thin myelinated Aβ, and unmyelinated C fiber type [12]. They penetrate the epidermis and end in the stratum granulosum. Pacinian corpuscles, Ruffini’s corpuscles, and so-called genital end bulbs are also observed [12,13]. The physiology of these receptors will be discussed in the next section.

The brain and spinal cord also receive sensory information from mechanoreceptors located in the urethra, muscle spindles/golgi tendons of ischiocavernous (ICM), bulbospongiosus (BCM) and external urethral sphincter (EUS) muscles, tunica albuginea (TA), and corpora [13]. This sensory input is crucial in the central regulation of micturition, erection, and ejaculation.

Human and animal studies demonstrate a unique dual innervation of the penis. Afferent receptors converge and form bundles that enter the main branch of the pudendal nerve (PN) via dorsal (DNP) and perineal (PerN) nerves [13–17]. The dorsal surface of the penis is supplied by DNP. The sensation from the ventral surface and frenulum of the penis are conveyed mainly by the PerN. Although separate, there are overlapping areas of distribution. The female equivalent of the DNP is the dorsal nerve of the clitoris, and the PerN branches out to become the posterior nerves of labia majora and labia minora. These nerves join to become the PN.

Dual sensory innervation of the penis was recently tested using sequential blocking of the dorsal and ventral surface components [18]. Several adult and fetal cadaveric and electrophysiological studies also confirm such special nerve distribution [15–17]. The afferent supply to the urethra is also quite unique. Lateral arborizing fibers of the DNP innervate the distal urethral lumen, and the PerN supplies the proximal bulbar and membranous urethra [15].

Both the DNP and PerN join and become the PN nerve at the ICM and BCM junction [15]. The latter enters the spinal cord through S2-S4 roots to terminate on spinal neurons and interneurons in the gray commissure and central region of the lumbosacral segment. Spinthalamic and spinoreticular pathways relay sensory information (pain, touch, temperature, etc.) from the spinal cord to the thalamus, hypothalamus, medial reticular formation (MRF), sensory cerebral cortex, and other centers. In addition, penile afferent nerves interact with autonomic centers located in the sacral intermediolateral cell columns to modulate reflexogenic erection and micturition [19,20].
Figure 1 Male genital neuroanatomy. Gray’s Anatomy.

Figure 2 Female pelvic neuroanatomy (permission granted by Elsevier).
Penile Efferent Pathways

Onuf’s nucleus (S2-4) is the center of pelvic somatomotor integration [21]. Efferent motor neurons from this nucleus travel via the PN branches that innervate striated perineal muscles (ICM, BCM) and the EUS. Inferior rectal branch of the PN innervates the external anal sphincter (EAS) [15,22,23]. The major nerve supply to the levator ani muscle includes the levator ani nerve (from sacral segment S4) and contributions from the PN [24,25].

The sympathetic nervous system relays information to the penis that originates in the lower thoracic and upper lumbar (T12-L2) segments of the spinal cord. These fibers travel through the superior hypogastric and inferior hypogastric plexuses to join parasympathetic nerves from the sacral spinal cord (S2-4) to form the pelvic plexus. The chain ganglia specifically projecting to the penis are located in the sacral and caudal ganglia [26].

Parasympathetic nerves originate within intermediolateral cell columns of the sacral spinal cord (S2-4). Preganglionic fibers pass through the pelvic nerves to the pelvic plexus, where they are joined by sympathetic neurons. Efferent autonomic fibers to the penis form the CN on each side of the prostate [26]. Stimulation of the pelvic plexus and CN induce penile erection, whereas activation of the sympathetic trunk causes detumescence.

Due to the close proximity of the CN to the prostate and rectum, one or both of its trunks may be injured during pelvic surgery. On the contrary, the PN are mostly protected from iatrogenic injury by traveling beneath the levator ani muscle on their way to the penis [27,28]. In the case of bilateral CN neuropraxia, it can be assumed that the PN become the only reliable neuronal communication between the penis and the central nervous system (CNS).

The neuronal communication between the autonomic CN and the PN circuitry has been described in multiple studies. Baskin and colleagues studied 18 fetal human specimens and found extensive distribution of both DNP and PerN fibers along the corporal bodies which communicated with CN branches [16]. Other adult human studies also confirmed multiple anastomotic bundles identified bilaterally between the autonomic CN and somatic DNP/PerN at regular intervals [27–29]. A study in 2008 showed both DNP and CN communicating with each other along the TA [30].

Neurophysiology

The glans penis and the clitoris are important sources of sensory information to the CNS for induction and maintenance of sexual and micturition reflexes. In fact, desensitization of the glans of rats severely impairs erectile ability and successful penile intromission [31]. The most numerous genital receptors of both sexes are FNE [12].

FNE are known to express polymodality [12], which implies their ability to perceive different stimuli, such as temperature, mechanical (touch, pressure, stretch, vibration), and pain. This physiologic capacity is called “dissociated sensibility” by some authors [12]. FNE receptors can translate multiple sensory inputs to excitatory signals. This information is rapidly transmitted by genital afferents to the spinal cord and higher centers to produce sexual arousal, erection, ejaculation, and pleasure.

Several receptors, including FNE are suspected to be receptive to vibration. Pacinian corpuscles are rapidly adapting mechanoreceptors and are especially sensitive to vibration [32–34]. They are found in deep and subcutaneous tissues of the penis, clitoris, and vulva.

During sexual arousal, corporal engorgement distends the glans penis and exposes its hidden sensors located in its deep rugae to further tactile stimulation. This is thought to augment mechanical and thermal tissue compliance [12,33]. Vibratory stimulation can activate receptors buried in the ridges of deep rugae that are only responsive after glans erection.

Mechanoreceptors in the canine model are capable of encoding a variety of skin motions. Two receptor classes include rapidly adapting (RA) and slowly adapting [33]. These nerve sensors have the ability to respond to electrical, mechanical, and thermal stimuli. Warm receptive-field temperatures (35–45°C) have been shown to increase their sensitivity.

Repetitive stroking of the male and female genitalia during coitus and self-stimulation is an integral aspect of sexual behavior in human and higher mammals. Rapid thrusting action during intromission activates RA mechanoreceptors similar to animal experiments. Penile afferents transmit these excitatory oscillating nerve impulses to the spinal cord and higher centers, such as the thalamus [35], which will be discussed later.

Melanocortin receptor-4 (MCR4) has been detected close to PN mechanoreceptors [36]. MCR4 is expressed in the rat and human penis, rat
spinal cord, hypothalamus, brainstem, and pelvic ganglion. Activation of MCR4 receptors increases erectile activity in rats via oxytocinergic pathways [37,38].

**Pudendal Nerve (PN) and Branches**

PN circuitry is increasingly being recognized as a mixed nerve, composed of both somatic (sensory, motor) and autonomic components [39]. This stems from evidence that both DNP and PerN are neuronal nitric oxide synthase (NOS) positive in the distal shaft and glans penis [16]. In the canine model, neuronal NOS (n-NOS) immunoreactivity is observed throughout pudendal circuitry [40]. NOS activity and its neurotransmission is considered autonomic in origin and is considered a critical component of sexual and eliminative reflexology [39].

To assert that DNP and PerN have autonomic function is a controversial topic. Some scientists postulate that communicating nerve fibers between PN branches and the CN could be nNOS-carrying autonomic highway exits from the CN serving to reach regions of the penis that cannot be reached directly by it, such as the glans penis, corpus spongiosum and the distal parts of the corpora cavernosa (CC) [4].

A direct efferent contribution of the DNP and PerN for penile erection is not proven. Perhaps these nerves are part of auxiliary or redundant pathways that become activated in times of circuitry disconnection. Some critics suggest that nNOS positivity of the DNP and PerN are mere autonomic control of penile skin vascular constriction and dilation. However, the study by Baskin et al. showed the perineal nerve to be nNOS negative in its scrotal distribution and become nNOS positive as it travels on the penile shaft [16].

In male rats, copulatory and reflexogenic erection was studied before and after unilateral and bilateral CN transection and sham [41]. After bilateral transection, no penile body erection was observed, but glans erection remained intact. Partial glans erection has been described in men after non-nerve sparing prostatectomy [42].

Dual innervation of the dorsal and ventral surfaces of the penis has been studied in stimulation experiments. After dorsal nerve block, healthy human male cortical evoked responses were elicited after electrical stimulation of the PerN which were of different wavelength from that of DNP stimulation [17]. Simultaneous sensory stimulation of the DNP and PerN appears to have an additive response. Vibrotactile stimulation of both surfaces of the penis increases ejaculatory response in men with spinal cord injury [43]. Penile vibratory stimulation (PVS) is the first choice for treatment of anejaculation in men with spinal cord injury [44] and men without spinal cord injury with orgasmic dysfunction [45]. [Correction added after online publication 16-Feb-2011: In the previous sentence, an ejaculation has been updated as anejaculation.]

**Supraspinal Sexual Centers**

Genital afferent nerves relay critical sensory information from the genitalia to supraspinal sexual centers, which include medial pre-optic area (MPOA) and paraventricular nucleus (PVN) nuclei of hypothalamus, hippocampus, medial amygdala, thalamus, MRF, and several areas of forebrain. There is growing support for their role in initiation of sexual behavior, penile erection, orgasm, and ejaculation at the supraspinal level.

**Hypothalamus**

Neurologists believe that the hypothalamus plays a critical role in human drives. Here, socially appropriate sexual urges are coordinated with the “four Fs” of human behavior, i.e., fear, feeding, fighting, and frustration [46]. It is thought that the hypothalamus processes relevant sexual stimuli, and activates somatomotor and autonomic mechanisms responsible for penile erection [47]. The PVN and the MPOA of the hypothalamus are both excited by genital afferent stimulation.

**Paraventricular Nucleus (PVN)**

The neuropeptide oxytocin is synthesized in the PVN of the hypothalamus [48]. It is released either from neurohypophyseal terminals into the blood, or as a neurotransmitter to regions of CNS that regulate emotional, cognitive, and social behaviors. Oxytocin also acts on specific receptors at the lumbosacral level that influences NOS activity [49]. In male rats, oxytocin produces penile erection, intracavernosal pressure (ICP) elevation, and yawning when it is injected into the lateral cerebral ventricle, the PVN, or the hippocampus [50].

Studies show direct anatomical and functional connectivity of the PVN and supraoptic nucleus with sacral parasympathetic centers [49]. C-Fos expression in PVN is increased during male rat sexual behavior [51]. Oxytocin appears to activate its own descending neurons [50]. NOS-containing neurons also exist in the PVN [52]. Inhibitors of NOS prevent oxytocin-mediated erection and yawning in the rat model [53].

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The dorsal nerve of the penis greatly communicates with both oxytocin-rich PVN and supraoptic nuclei [54,55]. In two studies, electrical and repetitive stimulation of the rat penis produces excitation in about 60% of PVN oxytocin cells, and less than 20% of vasopressin cells. In women, suckling or vaginocervical stimulation increases oxytocin production by similar mechanisms [56].

**Medial Pre-Optic Area (MPOA)**
MPOA of the hypothalamus is considered closely associated with supraspinal command and control of erection. Stimulating the MPOA, especially the posterior part, has been shown to result in ICP elevation by NOS-mediated mechanism. Alteration in nitric oxide/cyclic guanosine monophosphate (NO/cGMP) levels in MPOA effect erectile response [57,58].

In the rat model, penile afferents influence the MPOA. Direct DNP stimulation activates 80% of MPOA neurons: 50% stimulatory and 30% inhibitory [59].

An interesting rat study showed that the MPOA may modulate penile erection independent of the CN and perhaps via an ancillary penile nerve [60]. To test this theory, electrical stimulation of the MPOA was performed before and after bilateral CN transection. Bilateral CN transection did not completely ablate the MPOA-mediated erectile response, but severing bilateral pelvic nerves completely inhibited this response. This raises several interesting questions about the complexity of descending pathways to penile corporal tissues.

**Medullary Reticular Formation**
The MRF is located in the brainstem. It is essential for governing some of the most basic functions of higher organisms, including somatic motor and cardiovascular control, pain modulation, and sleep/consciousness [61–63]. Neurons in the MRF receive a vast array of inputs from somatic sensory neurons of the external genitalia and visceral autonomic input from lower urinary and gastrointestinal tracts [62].

In a study by Kaddum et al. electrophysiologic recordings were used to investigate MRF's responses to pelvic input [63]. Mechanical and electrical stimulation of rat pelvic organs was performed. Fifty percent of MRF neurons responded to bladder distension, 80% to colonic distension, and 70% to urethral infusion. Interestingly, all (100%) of MRF neurons responded to penile afferent mechanical and electrical stimulation.

**Thalamus**
The thalamus is considered an important sensory and motor relay center [64]. It has bidirectional connectivity to the MPOA. Activation of neurons in the parvicellular part of the caudal thalamus has been recorded during sexual behavior in rats [65]. Deep stimulation of the thalamus as a therapeutic modality to reduce tic episodes in men with Tourette's syndrome has shown changes in penile erection during and after therapy [66].

Hubscher et al. investigated responses of thalamic nuclei to fast repetitive input from the rat male genitalia [35]. All DNP-responsive neurons were activated by both ipsilateral and contralateral stimulation. Bilateral DNP stimulation augments thalamic response in an additive fashion. Interestingly, the authors observed that nearly all (97%) of DNP-responsive neurons also were activated by autonomic visceral pelvic nerve stimulation.

Thalamic neurons require “wind-up” firing to reach a response threshold [35,67]. Gradual build up of genital sensory activity or repeated fast exposure to a stimulus was a prerequisite for detection of convergent inputs in the rat thalamus. In a functional context, a gradual build up of neuronal activity produced by repetitive exposure of penile cutaneous receptors to sexually relevant input or vibratory stimulation can produce such “wind-up” responses. This is a possible scientific explanation for evolutionary observation of repeated fast sensory stimulation of the glans penis during vaginal intercourse and manual stimulation to achieve sexual climax.

**Cerebral Cortex**
Until recently, very little was known about how genital afferent input from the penis is conveyed and processed within the brain. A positron emission tomography imaging study measured regional cerebral blood flow (rCBF) of healthy men at rest and during manual penile stimulation by their female sexual partner [68]. Increased rCBF was observed in the right posterior gyrus, sensory SII cortex. Decreased rCBF was detected in the right amygdala. Other studies have confirmed a similar pattern, including increased rCBF in the interhemispheric postcentral gyrus [69,70].

The amygdala region of the brain plays a major role in modulating motivation and mood [71]. Imaging studies of men who suffer from war or combat-related post-traumatic stress disorder (PTSD) has revealed persistently increased rCBF or “hyperactive” amygdala [72]. These men often suffer from poor motivation, sexual difficulties,
and erectile dysfunction. Inability to deactivate amygdala may negatively impact the supraspinal contribution to erectile function.

Whether men after prostate cancer diagnosis, pelvic pain, or stress of prostate surgery exhibit PTSD-like “hyperactive amygdala” is not known. Furthermore, clinical observation of deactivation of the amygdala (decreased rCBF) by penile afferent stimulation [68] is very intriguing and deserves further clinical investigation.

**Spinal Reflex Loops**

The spinal cord is the epicenter of autonomic and somatic pathways to erectile tissues and related striated muscles [73]. Stimulation of the DNP in the male rat [74] and the female cat [75] elicits firing of pelvic, hypogastric, and the CN. Afferent/efferent projections overlap and interact in producing physiologic responses that prepare both genders for sexual intercourse. The most important reflex loops are the following:

**Pudendo-Cavernosal Reflex Loop**

This somatic-autonomic reflex involves the DNP and PerN as the afferent, and the CN as the efferent limb. Genital stimuli are conveyed via DNP and PerN to the dorsal horn of the lumbosacral gray commissure. They stimulate autonomic centers via interneurons. The efferent CN sends nNOS-mediated signals back to the genitalia to initiate penile corporal and clitoral/labial vasodilation.

For decades, the male rat has served as the principal model for the study of erectile function [76]. To test reflexogenic erection, conscious male rats were restrained on their backs. Telemetric devices were implanted into the corpus cavernosum to measure ICP [1]. Preputial sheaths covering the penis were retracted with a metal loop and stroked. This stimulation led to penile erection and glans engorgement. In anesthetized rats, electrical stimulation of the DNP also leads to ICP elevation [77,78]. This reflex response is abolished by switching off the parasympathetic output with bilateral CN transection.

Stimulation of the clitoris or urethral distension also elicits consistent increase in vaginal blood flow and clitoral engorgement. In the cat model, bilateral pelvic nerve transection significantly reduces vaginal flow after genital stimulation [75]. Sympathetic disconnection with hypogastric nerve transection cuts did not affect genital responses to afferent stimulation. The efferent output of this reflex is therefore an increase in parasympathetic vasodilatation, and not a decrease in sympathetic vasoconstriction. In women, vaginal or clitoral stimulation initiates a strong sexual response similar to findings in animal studies [79].

**Bulbocavernous Reflex (BCR) Loop**

This is a spinal reflex involving somatic afferent and somatic efferent neurons of the PN. This reflex has been demonstrated in animal and human studies [80–82]. The afferent limb is the DNP and PerN, which join fibers to relay their message to the sacral spinal Onuf’s nucleus S2-4. The efferent motor neurons then travel via the PN branches that supply ICM, BCM, EUS, and EAS. Stimulation of the human genitalia can activate the bulbocavernosus reflex (BCR), which is the basis of pelvic neurologic examination and electrophysiological latency testing [82]. Contraction of the ICM produces the rigid-erection phase [83], and rhythmic contraction of the BCM is necessary for ejaculation [84].

**Integrative Erectile Physiology**

Penile erection is a multifaceted vascular and mechanical response coordinated by the brain, spinal cord, and peripheral nervous system. Emotional and erotic stimuli (sexual thoughts, memories, smell, visual cues, sound, touch, etc.) activate excitatory descending pathways and shift the balance against sympathetic-mediated inhibitory signals. As discussed before, penile sensory stimulation also plays a critical role in sexual arousal and the erectile response. Their neuronal input excites both spinal autonomic nuclei and supraspinal sexual centers.

Genital afferent and erotic-mediated supraspinal erectile mechanisms appear to act synergistically [19]. In the psychology literature, penile erection can be inhibited when stressors such as guilt, hostility, shame, shyness, and nonsexual thoughts are present. Visual erotic stimulation facilitates the erectile response to PVS in men with and without erectile dysfunction [85–87]. Such cooperative nature of erectile pathways can explain how genital stimulation and erotic thoughts and fantasies are contributory during successful sexual encounters.

**Penile Tumescence**

Penile afferents play a direct role in penile tumescence via pudendo-cavernosal reflex [1]. Excitatory genital and supraspinal information coalesce and
launch a unified command via the CN to activate the erectile tissues of the penis [19]. Neurotransmitter release at CN terminals initiate the vasodilatatory phase of erection. Cavernosal smooth muscle relaxation is principally regulated by NO/cGMP [88,89]. The initial filling of blood by arterial vasodilation provides most of the blood to the corpora. Incoming blood is trapped between TA and peripheral sinusoids, which reduces venous outflow [3]. Emissary veins are further occluded by stretching tunica fibers. ICP is raised to around 100 mm Hg [3]. This event induces penile fullness, which is inadequate for sexual intercourse.

Penile Rigidity

To reach rigidity, ICP must exceed mean arterial pressure (MAP) by more than a hundred millimeters of mercury [90]. This large difference between ICP and MAP must be from another source of energy [91]. Penile afferent activation of BCR and rhythmic contraction of perineal muscles around the base of the penis is largely responsible for achieving such high suprasystolic pressures to develop [91].

The exact mechanism of penile rigidity is still widely debated. However, even critics of perineal muscle’s involvement in erectile function concede to intriguing clinical and laboratory observations of simultaneous penile rigidity and perineal muscle electromyographic (EMG) activity. Human electrophysiological studies have demonstrated that PN activity is responsible for rhythmic contraction of the ICM during rigid phase of erection [90]. Nerve blockage of penile sensory receptors appears to diminish such activity [90].

During initial filling of the corpora, ICP reaches MAP. At this stage, further ICP rise coincides with increasing ICM activity. If ICM is infiltrated by lidocaine, ICP rapidly decreases to MAP. ICM contraction helps clamp venous outflow by squeezing the proximal corpora and stabilizing TA in closing the emissary veins, which helps trap blood in the closed corporal system [92]. The unique anatomical location of the crura and the position of the ICM, which inserts on and surrounds them, provide an excellent force for such pressures to develop (see Figures 3 and 4).

A study of penile geometry and fluid deformation dynamics provides an explanation from a mechanical engineering perspective [93]. As the proximal corpora are filled with blood during the tumescence phase, the ICM begins to contract by a reflex mechanism. The fluid volume is diminished at the proximal corpora site pulled by the muscle. The blood has only two alternatives in the presence of corporal venous occlusion: to return to arterial circulation or to move to unfilled cavernosal sinusoids, which inflates the tunical envelope. The fluid adjustment with increased sinusoidal filling creates further tunical stretch-mediated reflexogenic ICM activity. A 15% circumferential squeezing of corpora by ICM contraction along 40% of its length increases ICP to 230 mm Hg. This pressure cannot be achieved by corporal filling and confinement by TA alone.

In a study of nine mongrel dogs, three transverse incisions were made in the penile shaft, completely dividing the TA of CC and corpus spongiosum [94]. Erection was produced by injection of papaverine. ICP of TA-covered and non-covered corporal areas were measured. No difference in ICP was observed.

Penile Elevation and Stability

Penile afferent activity and reflexogenic BCM and ICM contraction also play an important role in backward/upward elevation and stabilization of the rigid penis. Such anatomical adjustment is thought to help prevent injury during rapid intromission. ICM originates on the ischial tuberosity and ramus of ischeum just proximal to insertion at the sides and dorsum of the CC via TA [95]. During the flaccid state, penis lies horizontally and is prevented from falling toward the scrotum by the suspensory ligament of the penis that anchors the penile shaft to the symphysis pubis. As the penis is filled with blood, it begins to rise, and becomes more straight but is still in a horizontal position. Penile afferent activity and reflexogenic contraction of both ICM and BCM pulls the penis backward and against the pubic rami, and draws the penile root (two crura and bulb) inward [96]. They act as a lever to lift the rigid penis upward and backward toward the anus [97]. The suspensory ligament of the penis maintains stability during backward lever activity of these muscles. Cadaveric and EMG studies in healthy men have demonstrated anatomical and physiological entirety of the EAS and BCM. Median fibers of EAS continue to become the BCM [96].
micturition reflex involves afferent impulses from the urinary bladder to the sacral region of the spinal cord, and efferent parasympathetic and somatic PN efferent nerves to contract the detrusor muscle and relax the EUS, respectively [97]. Pelvic nerve afferents signaling bladder distension also stimulate ascending pathways to the brainstem and the cerebrum, which results in conscious desire to urinate. In the spinally intact animal, the bladder stores urine until descending inputs from the brain command the bladder to contract and the EUS to relax [98].

There is growing laboratory evidence that stimulation of genital afferents can also evoke spinal micturition-like reflex activity that is independent of descending control from supraspinal centers [99]. An intriguing somatic pudendal sensory-pudendal motor activity also exists in the control of urinary and anal sphincter function similar to the BCR as discussed in previous section [100].

Reflexes and somatic-autonomic responses have been thoroughly investigated in spinal cord-injured patients [101]. Multiple studies have exposed many profound and unanticipated benefits of penile afferent stimulation: relief of lower extremity spastic muscle contractions [102], increased bladder capacity [103], decreased detrusor irritability and improved continence [104], ejaculation [105], and reflexogenic erection [106].

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Figure 3 Anatomical relationship of penile corpora with ischiocavernosus (red color) and bulbocavernosus muscles.

Figure 4 Pudendal nerve innervation of perineal muscles and external anal sphincter.
**Rhabdosphincter**
Anatomical and functional integrity of the rhabdosphincter (EUS) is critical in preserving urinary continence after radical prostatectomy [107]. The PN delivers voluntary input from the corticospinal tract and involuntary reflexic input from nucleus reticularis in the caudal medulla [98]. Rhabdosphincter motor neurons are unique in receiving input from the PVN nucleus of the hypothalamus [98]. Penile afferent nerves also communicate with this nucleus [54].

**Animal Studies**
External urethral sphincter activity after PN stimulation appears to be frequency dependent. In a nonspinal male cat study, high frequency (1–10 kHz) electrical stimulation (ES) of PN causes reversible block of EUS contractions [100]. In another cat study, ES of the DNP either inhibits (low frequency) or activates (high frequency) detrusor contractions, promoting storage or emptying, respectively [108]. Evoked EMG activity of the EUS after DNP electrical stimulation was also observed.

Can sensory stimulation of a nerve with both sensory and motor function lead to contraction of striated muscles supplied by it? The PN appears to have this special characteristic. This functional coupling was studied recently in the cat [109]. ES of the PN lead to vaginal dilation and anal sphincter contraction.

**Human Studies**
Glans penis vibratory stimulation suppresses bladder activity and promotes higher capacity. This somatic sensory influence on autonomic bladder function appears to be durable and repeatable. Daily PVS of men with spinal cord injury (SCI) for a month demonstrated its safety and tolerability [103]. Its benefits persisted for at least 72 hours after the last vibratory stimulation. Such conditioning therapy is thought to minimize habituation of spinal reflexes. In fact, conditional stimulation has better effect on maximum cystometric capacity than continuous stimulation.

Conditional clitoral and perineal stimulation may strengthen EUS and improve pure stress urinary incontinence [110]. Frequent genital vibratory stimulation or transcutaneous mechanical nerve stimulation may help to tone and strengthen the EUS muscle via somatic afferent–efferent reflex mechanisms, such as the BCR. This pilot study (N: 25) is important in several aspects: safety, utility, and tolerability of vibratory stimulation in healthy patients without spinal cord injury.

Human genital afferents that project to sympathetic thoracolumbar neurons may also modulate activity at the bladder neck as seen in animal studies [111]. In a clinical study, men with complete spinal cord injury with neurogenic incontinence underwent PVS [112]. Both somatic EUS and autonomic bladder neck responses by PVS were recorded.

Dorsal genital stimulation may have modulatory effects on reducing detrusor irritability or overactive bladder in healthy women [113]. A regimen of percutaneous PN ES showed a >50% reduction in incontinence episodes and significant improvement in urgency. These results are comparable to FDA-approved sacral neuromodulation.

Restless Genital Syndrome is a newly recognized condition affecting both women and men [114–116]. It is characterized by neuopathy of the genital afferent nerves (DNP, PerN, dorsal nerve of clitoris). Patient’s complaints range from unwanted or unpleasant genital sensations, imminent orgasms, restless leg, and overactive bladder. Symptoms are aggravated by sitting, suggesting a possible pressure trigger on the nerve fibers of the PN or its branches. According to Waldinger et al. transcutaneous electrical nerve stimulation of genital afferents has resulted in significant reduction (>90%) of genital sensations and overactive bladder symptoms in a limited number of patients [115,116].

Genital afferent stimulation may modulate anal sphincter function [100]. The role of genital afferent stimulation on anal sphincter dysfunction was reported in a study of men and women with fecal incontinence [117]. They received ES of the penis or clitoris for 5 minutes, three times a day for 8 weeks. Significant improvement in subjective (>50% less accidents, pads) and objective (resting tone, maximal squeeze anal tone) parameters was demonstrated.

**Clinical Applications**
There is expanding laboratory and clinical evidence that support the critical role of genital afferent physiology in erectile function, sexual arousal, and pelvic floor function in both genders. Penile and female genital afferent stimulation may be utilized as a form of neuromodulation to amplify autonomic and somatic activity within the genita-
lia, spinal cord and higher centers via established neurological principles. Daily or on-demand genital afferent stimulation, perhaps in the form of vibratory method, may have therapeutic implications in many conditions, which include

1. Erectile dysfunction after pelvic surgery
   - Pudendal-cavernous reflex: Persistent stimulation of sacral autonomic centers to amplify CN activity, regeneration, and restoration of function.
   - DNP-PerN-CN connectivity: Activating auxiliary pathways and NOS activity between synaptic connections. This may enhance retrograde axonal regeneration and shorten recovery of CN neuropraxia.

2. Poor rigidity due to veno-occlusive dysfunction
   - Bulbocavernosus reflex: Strengthen rigidity of erection by optimizing ICM and BCM strength and tone.

3. Diminished libido/arousal and ejaculatory/orgasmic dysfunction in both sexes
   - Enhance sexual, erectile, and orgasmic response by shifting the balance between excitatory and inhibitory impulses from the CNS by up-regulating biochemical and neurophysiological signals in the spinal cord and higher centers.

4. Pelvic floor dysfunction: Stress urinary incontinence and/or detrusor irritability in both genders
   - Improve urinary control and symptoms by adaptive conditioning of bladder activity, rhabdosphincter tone, and strength.

Well-designed and dedicated studies in each population will shed light on its therapeutic prospects in the near future.

**Conclusion**

There is broad laboratory and clinical evidence that genital afferent stimulation may amplify autonomic and somatic activity within the penis, female genitalia, spinal cord, and higher centers via already established reflexogenic and neurophysiological principles. This safe and natural physiological adaptive process can be beneficial in improving erectile function, rigidity, sexual arousal, and control of micturition in many disease states, including erectile dysfunction and urinary incontinence after radical pelvic surgery. Well-controlled prospective studies are needed to authenticate current animal and human laboratory and clinical observations.

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