Adult and Pediatric Neuromodulation

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Dedication/Acknowledgments

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Jason P. Gilleran

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Seth A. Alpert

Preface

Throughout medical history, surgical treatments of various conditions involve removal of abnormal tissues and reconstruction of normal (or nearly normal) anatomy in order to improve a patient's functional status. Such invasive procedures are highly morbid and may not accomplish the goal of correcting organ dysfunction. With the advent of neuromodulation, clinicians are now armed with minimally invasive techniques to identify and modify abnormal nerve conduction impulses to organ systems, which in turn provide either symptom relief or improvement.

The technology of neuromodulation continues to advance, and its applications are ever expanding. While this modality is currently indicated to treat a limited number of diseases and/or organ dysfunction, we hope this textbook demonstrates the depth and breadth of conditions that can respond to neuromodulation. We also look forward to the future of neuromodulation and its interface with modern digital technology, which can lead to noninvasive approaches that can be used at home and empower patients of all ages to manage these difficult conditions.

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Part I

Adults

1 Basic Neuroanatomy and Neurophysiology of the Lower Urinary Tract

Lauren Tennyson and Christopher J. Chermansky

Key Points

- Review normal sympathetic and parasympathetic neural connections within the lower urinary tract.
- Review pathophysiology of urologic dysfunction that results from common neurologic disorders, such as cerebrovascular accident, Parkinson's disease, multiple sclerosis, and spinal cord injury.
- Review landmark basic science studies and relevant animal studies on neuromodulation from the last 10 years.

Overview of the Lower Urinary Tract Neural Activity During Bladder Storage and Voiding

The lower urinary tract (LUT) serves to store and periodically eliminate urine through complex mechanisms coordinated by local, spinal, and brain circuits. These neural circuits coordinate the activities of the bladder and urethra, alternating between two primary modes of operation: urine storage and urine elimination [1]. The bladder remains in storage mode for the majority of the time, where it accommodates increasing volumes of urine at low pressures. Continence is maintained through neural reflexes that inhibit detrusor contractions and promote external urethral sphincter (EUS) activation. To initiate voiding, the neural reflex switches to allow EUS relaxation and bladder contraction, resulting in the flow of urine. This switch is triggered by the sensation of bladder fullness, and it is mediated by a long loop spinalbulbospinal reflex pathway [1]. Three sets of peripheral nerves are responsible for the coordination of events involved in urine storage and expulsion: pelvic parasympathetic nerves, lumbar sympathetic nerves, and pudendal somatic nerves. These nerves contain afferent (sensory) fibers, which monitor bladder volume and the amplitude of bladder contractions.

Discrete neurologic lesions typically result in predictable patterns of LUT dysfunction. The nature of the dysfunction depends on the nervous system area affected, the function of that area, and whether the neurologic lesion is destructive, inflammatory, or irritative [2]. The pathophysiology of the neurologic disorders commonly affecting LUT function will be described later in this chapter.

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Neural Connections to the Lower Urinary Tract

Efferent Innervation to the LUT

Efferent pathways of the LUT include the pelvic, hypogastric, and pudendal nerves (Fig. 1.1). The motor innervation to the bladder is through pelvic parasympathetic nerves, which originate in the intermediolateral gray matter of the sacral spinal cord (S2–S4) and promote bladder emptying and urethral relaxation [3]. Both pre- and postganglionic parasympathetic nerves release acetylcholine (ACh), an excitatory neurotransmitter that acts on muscarinic receptors (M2 and M3) within the detrusor to result in bladder contraction. Detrusor contraction and resultant urinary flow is mediated primarily by M3 receptors.

Bladder sympathetic nerves arise from the thoracic and lumbar spinal cord between T11-L2 [3]. During bladder filling, these noradrenergic nerves provide inhibitory input to the bladder body and excitatory input to the urethra and bladder base, resulting in bladder relaxation and urethral contraction. Peripheral sympathetic nerves travel a complex route through the sympathetic

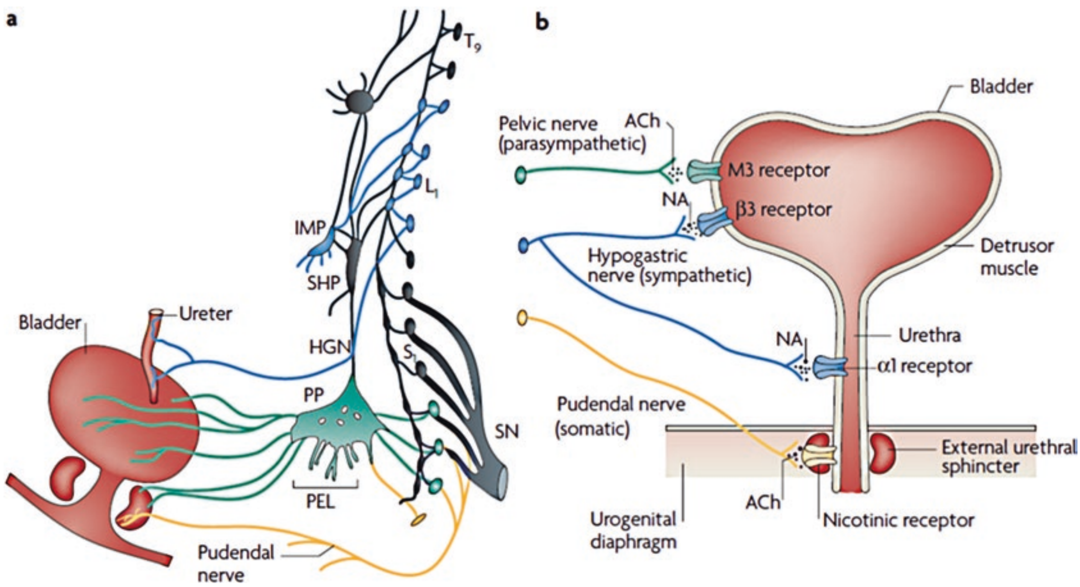

Fig. 1.1 Efferent pathways of the LUT. (**a**) Innervation of the female lower urinary tract. Sympathetic fibers (shown in blue) originate in the T11-L2 segments in the spinal cord and run through the inferior mesenteric ganglia (inferior mesenteric plexus, IMP) and hypogastric nerve (HGN) or through the paravertebral chain to enter the pelvic nerves at the base of the bladder and the urethra. Parasympathetic preganglionic fibers (shown in green) arise from the S2–S4 spinal segments and travel in sacral roots and pelvic nerves (PEL) to ganglia in the pelvic plexus (PP) and in the bladder wall. This is where the postganglionic nerves that supply parasympathetic innervation to the bladder arise. Somatic motor nerves (shown in yellow) that supply the striated muscles of the external urethral sphincter arise from the S2–S4 motor neurons and pass through the pudendal nerves. (**b**) Efferent pathways and neurotransmitter mechanisms that regulate the lower urinary tract. Parasympathetic postganglionic axons in the pelvic nerve release acetylcholine (ACh), which produces a bladder contraction by stimulating M_3 muscarinic receptors in the bladder smooth muscle. Sympathetic postganglionic neurons release noradrenaline (NA), which activates β_3 adrenergic receptors to relax bladder smooth muscle and activates α_2 adrenergic receptors to contract urethral smooth muscle. Somatic axons in the pudendal nerve also release ACh, which produces a contraction of the external sphincter striated muscle by activating nicotinic cholinergic receptors. Parasympathetic postganglionic nerves also release ATP, which excites bladder smooth muscle (not shown). L_1 first lumbar root, S_1 first sacral root, *SHP* superior hypogastric plexus, *SN* sciatic nerve, T_9 ninth thoracic root. From: de Groat WM. Neuroanatomy and neurophysiology: innervation of the lower urinary tract. In: Female Urology (Third Edition). Raz S, Rodríguez LV, eds. W.B. Saunders, Philadelphia;2008:26–46. Reprinted with permission from Elsevier