

CONTRACTILE FUNCTION OF THE DENERVATED FEMALE LOWER URINARY TRACT**Aims of Study**

Histochemical and electromyographic studies indicate that partial denervation of the urethra is associated with stress urinary incontinence in women. In this investigation, we used an animal model to determine the effect of selective denervation on the function of the female lower urinary tract with specific emphasis on the external urethral sphincter (EUS) and bladder dome.

Methods

Young virginal female rats underwent selective denervation procedures designed to assess the relative impact of pudendal and pelvic neurectomy on function of the external urethral sphincter (EUS). First, local injury to periurethral nerves was achieved by microdissection and transection of pudendal and pelvic nerve branches 2-5 mm lateral to the urethra (**Peri-U**, n=8). Identical surgical procedures (except nerve transections) were performed in 5 sham-operated controls (**Sham**). Bilateral excision of proximal pudendal nerves was performed in a third group of animals (**Pud N**, n=4). To remove neuronal input from the pelvic plexus, a fourth group of animals underwent bilateral excision of main and accessory pelvic ganglia (**Pelvic N**, n=4). A final group of animals underwent periurethral nerve transection, bilateral ganglionectomy, and bilateral pudendal neurectomy (**Pud+Pelvic N**, n=4). After 2-3 weeks, striated external urethral sphincter (EUS) and smooth muscles of the urethra, bladder base, and bladder dome were dissected for neurophysiologic studies. Electrical field stimulation was used to study neural mediated contractions. Responses to KCl and muscarinic agonist were also analyzed.

Results

Peri-U nerve injury did not alter force of nerve-mediated smooth muscle contractions of urethra and bladder base. Nerve-mediated contractions of the bladder dome, however, were impaired (18.8 ± 1.9 compared with 31.9 ± 2.3 mN/mm², $p \leq 0.01$). Latency (time delay in initiation of force) was also significantly prolonged in both base and dome after Peri-U neurectomy. KCl-induced contractile force was not impaired, and, consistent with other models of bladder denervation, the bladder dome and base were more sensitive to muscarinic agonists after Peri-U. Thus, Peri-U nerve injury resulted in marked changes in lower urinary tract smooth muscle function. However, numerous parameters of striated EUS function remained intact (Table 1). To further investigate the effect of denervation on the EUS, experiments were conducted after pudendal neurectomy, bilateral pelvic ganglionectomy, or both. Twitch tension and peak force of contraction were similar in urethral sphincters from sham-operated controls and all denervated animals (Table 1). In addition, force-frequency curves were similar among all groups. In sphincters from Sham, Peri-U, and Pelvic neurectomy animals, contractile force fatigued to ~45% after 30 sec of maximal stimulation. However, muscle fatigue was significantly more pronounced in the EUS from animals that underwent pudendal neurectomy. Muscle fatigue was further exaggerated after combined pelvic and pudendal neurectomy.

Table 1. Contractile function of the denervated EUS.

	Sham	Peri-U	Pud N	Pelvic N	Pud+Pelvic N
Maximal force (mN/mm ²)	5.2 ± 0.3	6.1 ± 1.1	5.0 ± 0.3	6.4 ± 0.8	5.49 ± 0.6
Twitch tension (mN/mm ²)	1.8 ± 0.4	1.8 ± 0.4	1.2 ± 0.1	1.4 ± 0.1	1.5 ± 0.5
Fatigue, F _{30 sec} /F _{peak} (%)	48 ± 3.5	45 ± 1.2	30 ± 2.3*	45 ± 4	23 ± 5.7*

* $P < 0.02$ compared with Sham, ANOVA.

Conclusions

In this animal model, force-generating capacity of the EUS is surprisingly preserved 2-3 weeks after denervation injury. Local periurethral nerve injury results in decreased capacity of the dome to respond to neural stimulation without alteration of striated EUS function. Sphincter fatigability, however, is increased significantly after bilateral pudendal neurectomy; and, pelvic neurectomy exaggerates the adverse effect of pudendal nerve transection on muscle fatigue. These results suggest that (i) intact pudendal nerves are necessary for EUS resistance to fatigue, and (ii) pelvic denervation processes (such as those that occur with aging) may worsen the effect of pudendal neuropathy on EUS contractile function. Compromised nerve-mediated contractions in the dome with an intact, functioning EUS after periurethral nerve injury suggests that injury to peri-urethral neurons may be involved in voiding dysfunction and post-operative urinary retention that often complicates anti-incontinence procedures or radical pelvic surgery. On the other hand, increased

fatigability of the EUS after pudendal nerve injury provides a pathophysiologic basis for the association of pudendal neuropathy with stress urinary incontinence, particularly if complicated by pelvic nerve injury.