Afferent Pathways Arising from the Lower Urinary Tract after Complete Spinal Cord Injury or Cauda Equina Lesion: Clinical Observations with Neurophysiological Implications

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Key Words

Spinal cord injury • Neurogenic dysfunction of the urinary bladder • Afferent neurons • Visceral afferents • Cauda equina syndrome

Abstract

Background: Afferents from the urinary tract transmit bladder sensations to the central nervous system. Spinal cord injury (SCI) may affect both efferent motor and afferent sensory pathways. Presence/absence of bladder sensations in patients with complete spinal cord, conus or cauda equina lesions was compared with neurologically unimpaired patients. **Methods:** During urodynamics, bladder sensations were studied and compared in 59 patients: 21 patients with complete SCI below T6 and above Th12, 7 patients with a complete lesion of the conus medullaris, 11 patients with a complete lesion of the cauda equina, and 20 patients without neurological deficit. **Results:** Two of 7 patients with complete conus lesion had a preserved filling sensation. Ten of 11 patients with complete lesion of the cauda equina reported a bladder filling sensation. Sensations are perceived at a similar pressure threshold but at a higher volume threshold. **Conclusions:** In patients with a complete cauda or a lower conus lesion, a sensory input from the bladder is preserved.

These findings imply that the preserved bladder filling sensation in complete cauda or lower conus lesions is possibly transferred through the intact hypogastric plexus to the thoracolumbar segments of the spinal cord.

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Introduction

Voluntary control of bladder function strongly depends on the perception of sensations arising from the lower urinary tract. Conscious perception and processing of these sensations are imperative for appropriate urine storage and voiding at a socially accepted time and place. Adequate perception requires the integrity of the afferent axis including the urothelium, the peripheral (pelvic, hypogastric, pudendal) nerves, the spinal cord, the pons and the mesencephalon and the sensory cortex.

The urothelium is involved in the afferent axis by releasing neurotransmitters and expression of receptors. Afferent ascending fibers from the lower urinary tract travelling via the pelvic, the hypogastric and the pudendal nerves convey information from the bladder and the proximal urethra to the lumbar and sacral segments of the spinal cord. Afferents originating from tension re-

ceptors in the bladder wall transmit information about bladder filling to the sacral segments. Nociceptive impulses from the pelvic organs are transmitted by the hypogastric and pelvic nerves. Somatic afferent pathways from the striated sphincter and the urethra convey the sensations of temperature, pain and urine passage as well as the imminence of micturition via the pudendal nerve to the sacral spinal cord. Lower urinary tract afferents mainly travel in the lateral and dorsal columns to several higher structures within the central nervous system [1].

According to the International Continence Society classification a normal bladder sensation can be judged by three defined points noted during filling cystometry and evaluated in relation to the bladder volume at that moment and in relation to the patient's symptomatic complaints [2]. The first sensation of bladder filling is the feeling the patient has, during filling cystometry, when he/she first becomes aware of the bladder filling. First desire to void is defined as the feeling, during filling cystometry, that would lead the patient to pass urine at the next convenient moment, but voiding can be delayed if necessary. Strong desire to void is defined, during filling cystometry, as a persistent desire to void without the fear of leakage. Also increased, reduced and absent bladder sensations can be described according to this standardization report.

Traumatic spinal cord lesions usually affect both afferent sensory and efferent motor nerve fibers. Afferent pathways arising from the urinary bladder transmit bladder filling sensation and the sensation of desire/urge to void to the central nervous system. However, what routes and pathways are involved in the transmission of the different afferent sensory impulses to the spinal cord and higher nervous centers is largely unknown in humans. In this study, it was hypothesized that comparative observations of bladder sensations in patients with complete spinal cord and cauda equina lesion at various levels can assign bladder sensations to separate ascending pathways. To do this, the presence/absence of bladder sensations in patients with complete spinal cord, conus or cauda equina lesions were compared to neurological unimpaired patients.

Patients and Methods

Fifty-nine patients were included: 21 patients with complete spinal cord injury below T6 and above Th12, 7 patients with a complete lesion of the conus medullaris, 11 patients with a complete lesion of the cauda equina, and 20 consecutive patients without neurological deficit, who were examined for stress urinary

Table 1. Patient population

Spinal cord injury	n	Gender, M/F	Mean age $\pm$ SD, years	Lesion age $\pm$ SD, months
Thoracic SCI	21	9/3	36.8 $\pm$ 10.6	49.9 $\pm$ 32.7
Conus lesion	7	4/3	39.9 $\pm$ 13.4	40.4 $\pm$ 27.2
Cauda lesion	11	6/5	41.8 $\pm$ 14.0	58.2 $\pm$ 42.6
Normal controls	20	4/16	64.7 $\pm$ 9.9	n.a.

incontinence. For patient details, see table 1. Patients with spinal cord injury above the level of T6 were excluded, because symptoms of autonomic dysreflexia may interfere with bladder sensation. Patients with spinal cord lesion were out of the spinal shock and performed clean intermittent catheterization for bladder emptying. All patients underwent a detailed neurological examination according to the American Spinal Injury Association (ASIA) protocol to re-define the segmental level of spinal cord injury [3]. All patients with thoracic lesions were on anticholinergic medication that was not stopped for the urodynamic studies. These patients with suprasacral injuries were studied during routine check-up urodynamics which were intended to ensure a well-balanced and safe management of neurogenic bladder dysfunction. In all patients urinary tract infections were excluded before the examination.

Standardized video-urodynamic investigations in supine position were performed using a MMS Solar system (Medical Measurement Systems B.V., Enschede, The Netherlands). Bladder filling was realized with body warm contrast medium via a double lumen water-perfused 8F cystometry catheter at a constant filling speed of 20 ml/min. Bladder filling was stopped at a maximum of 600 ml to avoid overdistension. Bladder sensation during cystometry namely bladder filling sensation, first desire to void and strong desire to void were studied and compared within the patient groups. Urodynamic studies were performed according to the recommendation of good urodynamic practice as published in 2002 [4]. Bladder sensations during urodynamic investigations were recorded in a standardized manner according to the standardization of the International continence society as published in 2002 [2]. First sensation of bladder filling is the feeling the patient has, during filling cystometry, when he/she first becomes aware of the bladder filling. First desire to void is defined as the feeling, during filling cystometry, that would lead the patient to pass urine at the next convenient moment, but voiding can be delayed if necessary. Strong desire to void is defined, during filling cystometry, as a persistent desire to void without the fear of leakage. Reduced bladder sensation is defined, during filling cystometry, as diminished sensation throughout bladder filling. Absent bladder sensation means that during filling cystometry, the individual has no bladder sensation. Nonspecific bladder sensations, during filling cystometry, may make the individual aware of bladder filling, for example, abdominal fullness or vegetative symptoms. According to this description, bladder volume and bladder pressure were compared in all three groups at the moment when patients reported first filling sensation, at the moment of first and of strong desire to void. Details of the urodynamic results are shown in table 2.

Table 2. Urodynamic data in 30 patients with spinal cord injury and 20 controls with stress urinary incontinence

Patients	Thoracic lesion	Conus lesion	Cauda lesion	Normal controls
Number	21	7	11	20
Mean volume at FFS $\pm$ SD, ml	n.a.	467 (SD n.a.)	452.0 $\pm$ 52.6	266.7 $\pm$ 47.7
Mean p det at FFS $\pm$ SD, cm H ₂ O	n.a.	3.5 (SD n.a.)	2.7 $\pm$ 0.9	3.2 $\pm$ 1.6
Mean volume at FDV $\pm$ SD, ml	n.a.	n.a.	n.a.	381.25 $\pm$ 50.6
Mean p det at FDV $\pm$ SD, cm H ₂ O	n.a.	n.a.	n.a.	6.05 $\pm$ 1.6
Mean volume at SDV $\pm$ SD, ml	n.a.	n.a.	n.a.	447.5 $\pm$ 47.4
Mean p det at SDV $\pm$ SD, cm H ₂ O	n.a.	n.a.	n.a.	8.8 $\pm$ 1.9

FFS = First filling sensation; FDV = first desire to void; SDV = strong desire to void; p det = detrusor pressure.

Results

Urodynamic data are summarized in table 2. All patients without neurological impairment reported normal bladder sensations. First filling sensation occurred at mean 267 ml (SD 47.6 ml), first desire to void at mean 381 ml (SD 50.6 ml) and strong desire to void at mean 447 ml (SD 47.4 ml). In neurogenic patients, the neurological examination according to the ASIA protocol confirmed completeness of the spinal cord lesion at the previously described level. During cystometry none of the 21 patients with complete lesions above Th12 reported any filling sensation or desire to void. Fourteen patients had involuntary detrusor contractions during cystometry. Four of them did not report any sensation, even with strong involuntary detrusor contractions up to 85 cm H₂O. Five patients perceived increased spasticity of the abdominal and lower limb muscles as indirect indicator for a full bladder.

Two of 7 patients with complete conus medullaris lesion had a preserved filling sensation at 445 and 489 ml, respectively; both were diagnosed with an acontractile detrusor. Ten of 11 patients with complete lesion of the cauda equina reported a bladder filling sensation at a mean bladder volume of 452 ml (SD 42.6 ml). Sensations of first or strong desire to void were not reported. Bladder sensation in these patients met the criteria of nonspecific bladder sensations according to [2]. They made the individual aware of bladder filling, without corresponding to physiological sensations and more related to abdominal fullness or vegetative symptoms. Individual descriptions of the sensation included the following terms: weak, mild, located somewhere in the lower abdomen, non-noxious, fullness, pressure, displacement and malaise.

Discussion

Afferent pathways arising from the pelvic organs including the lower urinary tract transmit sensory impulses from these organs to the spinal cord and higher centers. Numerous studies in animals examined these afferents and their reflex connections. In several species including cat, rat and mouse afferent axons in the pelvic, hypogastric and pudendal nerve were found to convey impulses from the urinary bladder to the lumbosacral spinal cord. During bladder filling, tension receptors within the detrusor muscle become activated by increases in bladder volume or detrusor contraction, and then low-level firing in small myelinated pelvic afferents starts. These impulses are transmitted to the sacral spinal cord; some afferents connect directly to Onuf's nucleus, others project into Lissauer's tract while still others ascent to the thoracolumbar spinal cord [5–7].

In mice, at least four mechanosensitive both myelinated and unmyelinated afferents have been described. Some afferent axons originate from the urothelial layer, some from the detrusor muscle and others receive impulses from both layers [8–11]. Sacral afferents spread more in the muscle layer than in the suburothelium and have a more uniform distribution throughout the bladder dome and the trigone. In contrast, lumbar afferents spread more in the suburothelium than in the muscle layer and can be found predominantly in the trigone [12].

It seems that myelinated axons are the most sensitive axons to sense distension; they not only sense bladder fullness but also reinforcing reflex control of the bladder by monitoring the contractile state of the detrusor [13]. These A δ bladder afferents are activated at pressure thresholds in the range of 5–15 mm Hg, which are similar

to pressures at which humans report the first sensation of bladder filling [14–16].

Most of the unmyelinated afferent axons seem to come from the urothelial layer and the lamina propria. It is believed that these afferents are activated only at larger filling levels by stretching of the urothelial cells [16]. Following transection of the spinal cord these afferents activate the so-called C-fiber micturition reflex [14]. Other unmyelinated afferents found in cats and rats do not respond to stretching but they get activated by chemical irritation like high osmolality or high potassium levels.

In humans, sensations arising from the lower urinary tract can be observed during filling cystometry. As an example, Wyndaele et al. [17] performed filling cystometries with 30 ml/min filling rate in 50 healthy volunteers and compared the results to subjects studied 5 years before in the same institution. In males, the first filling sensation occurred at 222 ± 151 ml, first desire to void at 325 ± 140 ml and strong desire to void at 453 ± 94 ml. In females, the first filling sensation was observed at 176 ± 96 ml, first desire to void 272 ± 106 ml and strong desire to void at 429 ± 153 ml. It was concluded that there is a normal pattern of sensations reported during cystometric bladder filling that corresponds to physiological mechanisms associated with increasing filling levels.

Even after spinal cord injury, presence or absence of bladder sensation can be studied in filling cystometries. In 1991, Wyndaele [18] studied 42 patients with complete spinal cord lesions. In 15 patients some degree of bladder sensation was preserved. The majority of these patients had a lower thoracic or a lumbar lesion, and it was hypothesized that these bladder sensation might be preserved through the hypogastric nerves. Ersoz and Akyuz [19] studied bladder filling sensation in 52 spinal cord-injured patients with complete lesions above T11 and below T10 as well as in 21 incomplete lesions. In patients with complete lesion some degree of bladder filling was preserved in 82% of patients with lesions below T10 and in 39% of patients with lesions above T11. The initially determined bladder sensation category was reproducible in 36 patients who had a second cystometry. Interestingly, in these patients first sensation of bladder filling was sensed, but first and strong desire to void sensations were not sensed. The authors argued that intravesical pressures in mostly hypercompliant bladders in these patients were too low to provoke a desire to void sensation. Furthermore, it was noted that also the quality of the sensation changed to a pain, tension or burning sensation in-

stead of a real desire to void sensation. In their discussion, the authors consider the hypogastric nerves as a possible conduction route of the bladder sensation to the spinal cord, and it was concluded that especially in incomplete lesions and lesions below T10 preserved bladder sensations can be useful to establish a sensation-dependent bladder emptying.

After spinal cord injury various changes of the afferent activity arising from the urinary bladder can be observed, e.g. changes in nerve morphology, neuropeptide expression, and function of C-fibers. Somal hypertrophy of pudendal and bladder afferent neurons was observed in cats [20] and rats [21]. On the level of the urothelium, the suburothelial layer, the density of vanilloid and purinergic receptors was found to be increased after injury [22–24]. The expression of various neuropeptides and the electrophysiological properties of sodium and potassium channels are changed after injury [for a review, see 14]. Nerve growth factor may contribute to neuronal plasticity of bladder afferents after spinal cord injury [25]. Formerly silent C-fibers become active after spinal injury and trigger bladder reflex activity and neurogenic detrusor overactivity [15]. Disruption of descending pathways to the lumbosacral segments result in denervation of sacral neurons that could lead to changes in the properties of afferent neurons, afferent nerve sprouting and remodeling of spinal synaptic connections [14]. Secondary, bladder outlet obstruction due to detrusor sphincter dyssynergia leads itself over time also to changes in the bladder wall, the afferent nerve morphology and protein expression like nerve growth factor levels [26].

This raises the question whether these changes influence the perception of bladder sensation in complete spinal cord injured humans. In the phase of the spinal shock, bladder sensation in complete lesions is usually absent. After recovery from the spinal shock, bladder sensation remains absent in patients with early stage and chronic complete spinal cord lesions at a thoracic level below T6 and above Th12. Involuntary detrusor contractions did not provoke any filling or desire to void sensation in this study. Even high-amplitude detrusor contractions were not noticed as such, at most unspecific symptoms like increased abdominal or lower limb spastics together with personal experience provided an indirect reference to bladder filling. This observation may indicate that the various changes of the afferent axis on urothelial, suburothelial and peripheral nervous level probably do not influence the sensation perceived by the patient.

However, in patients with a complete lesion of the cauda equina or a lower lesion of the conus medullaris, a certain sensory input from the bladder was preserved. From the neurophysiological point of view, these findings imply that the preserved filling sensation in complete cauda or lower conus lesions is possibly transferred through the intact hypogastric plexus to the thoracolumbar segments of the spinal cord. Compared to subjects without neurological lesion, this sensation is perceived at a similar pressure threshold but at a far higher volume threshold. It seems that more likely changes in volume than changes in pressure are perceived in cases with lower conus or cauda equina lesions. In neurologically healthy subjects bladder sensation is considered to be a mixed sensation coming from both tension and urothelial stretch receptors. For the qualitatively and quantitatively correct perception of the first filling sensation and the desire to void sensations, both sensory systems are mandatory. Accordingly, if pathways of one sensory system are disrupted in a complete cauda lesion (A δ fibers travelling in the pelvic nerve originating from tension receptors in the detrusor muscle), the bladder sensation will change in qualitative and quantitative terms. Ersoz

and Akyuz [19] already observed qualitative changes in bladder sensations and this was also noted in this study: the filling sensation was perceived and described by patients as something qualitatively different as that before the lesion. These sensations can be described according to Abrams et al. [2] as nonspecific bladder sensations during filling cystometry that may make the individual aware of bladder filling, for example, abdominal fullness or vegetative symptoms.

Conclusion

In patients with a complete lesion of the cauda equina or a lower lesion of the conus medullaris, a certain sensory input from the bladder is preserved. Compared to subjects without neurological lesion this sensation is perceived at a similar pressure threshold but at a far higher volume threshold. This residual filling sensation in complete cauda or lower conus lesions is possibly transferred through the intact hypogastric plexus to the thoracolumbar segments of the spinal cord.

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