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Modulation of Viscero-Somatic H-reflex during Bladder Filling: A Possible Tool in the Differential Diagnosis of Neurogenic Voiding Dysfunctions

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Abstract

Objective: Despite evidence that the activation of visceral afferents modulates spinal motoneurone activity in humans, the circuits responsible for this modulation remain unclear. The aim of the present study was to assess the effect of urinary bladder filling on the excitability of somatic spinal motoneurones in patients affected by overactive bladder secondary to neurogenic and non-neurogenic causes in both patients with bladder underactivity and normal subjects by means of a urodynamic evaluation.

Methods: In order to evaluate the influence of bladder filling on somatic reflexes, we studied the H-reflex evoked by electrical stimuli applied to the tibial nerve at the popliteal fossa and recorded from the soleus muscle. The H-reflex was tested in the following conditions: (1) empty bladder; (2) medium bladder filling; (3) maximum bladder filling; (4) five minutes after bladder emptying. The H-reflex amplitude at empty bladder was considered as the control value.

Results: In healthy subjects, we observed a progressive reduction in the H-reflex amplitude during bladder filling. In spinal cord-injured patients affected by a neurogenic overactive bladder, bladder filling failed to inhibit the H-reflex amplitude; a decrease in the H-reflex amplitude similar to that displayed by normal subjects was observed in patients with a non-neurogenic overactive bladder. By contrast, H-reflex behavior was unmodified in neurogenic underactive bladder patients and was similar to normal subjects in psychogenic underactive patients.

Conclusions: As behavior of the H-reflex varies during bladder filling in neurogenic and non-neurogenic overactive bladder patients as well as in neurogenic and non-neurogenic underactive bladder patients, H-reflex modulation may be considered a useful tool in the differential diagnosis of voiding dysfunctions.

Keywords: Neurogenic bladder; Bladder proprioception; H-reflex

1. Introduction

The neurophysiological control of the bladder is particularly complex, involving both the peripheral and central nervous systems at different levels.

Many of the neuronal mechanisms involved during the filling and voiding phases are fairly well known. Bladder distension causes a gradual increase in pelvic nerve afferent firing; when the micturition threshold is reached, pelvic nerve afferent firing activates the efferent pathways which are switched on and burst for a short period, thereby determining bladder contraction and consequent micturition [1–3]. The micturition reflex is thought to be due to the activation of afferent unmyelinated C fibers and the finely myelinated A delta fibers of pelvic nerves connected to the slowly adapting mechano-receptors of the bladder wall [2,4,5].

Several studies have shown that neurons receiving input from the urinary bladder, such as spinal cord cells, are connected to supraspinal structures involved in the control of the micturition reflex. The spinal cell threshold is influenced by small rises in bladder pressure, the firing rate being increased by vesical pressure

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perceived as noxious by the subject [3,6,7]. Several studies performed on animals have shown that urinary bladder distension inhibits spino-thalamic tract cells in monkey and depresses the activity of the vast majority of interneurones in rats [8]. Moreover, some authors have demonstrated that bladder distension or contraction can inhibit respiratory activity in animals, probably by acting on the brainstem [9,10].

Recent researches [11], using the PET technique, have demonstrated a correlation between the act of micturition and a significant increase in blood flow in the right dorsal pontine tegmentum and right inferior frontal gyrus.

However, despite these important findings on the neurophysiological control in bladder function, the effect of the vesical afferent input, as activated by bladder distension, on spinal excitability remains unclear. The aim of the present study was to assess the effect of urinary bladder filling on the excitability of somatic spinal motoneurones in normal subjects, in patients affected by overactive bladder secondary to neurogenic and non-neurogenic causes and in patients with bladder underactivity, all diagnosed by means of a urodynamic evaluation. Moreover, the authors evaluated the possible role of the H-reflex recording in the diagnostic assessment of patients suffering from neurogenic voiding dysfunctions related to the location of the neurological lesion. For this purpose, the authors studied the excitability of the spinal cord by testing the influence of proprioceptive input on the soleus motoneurones by tibial nerve stimulation (H-reflex); the H-reflex, in fact, represents a quantitative estimation of the excitability of the motoneurone pool. The H-reflex is evoked by the stimulation of the peripheral nerve and the motorneurone evoked reflex discharge is recorded from the electromyogram of the muscle innervated by the nerve [12].

Table 1
Healthy subjects

Patient	Age (years)	Sex
1	50	M
2	52	F
3	54	M
4	52	M
5	56	M
6	57	M
7	60	F
8	63	F
Mean	57.8	
S.D.	9.2	

2. Materials and methods

Thirty-three subjects (22 males, 11 females), mean age 55.9 ± 13.1 years (mean ± S.D.) were enrolled in the study to evaluate the influence of bladder filling on somatic reflexes in patients suffering from neurogenic bladder dysfunction secondary to various neurogenic diseases as well as in normal subjects; the patients were divided in three groups as follows:

1. Eight healthy, neurologically intact subjects (mean age 57.8 ± 9.2 years) with no pathological urodynamic findings (Table 1).

Table 2
Overactive bladder patients

Patient	Age (years)	Sex	Etiology	Lesion level	Clinical features	Diagnosis
1	33	F	Spondilosys	D2 (incomplete)	Paraplegia	
2	57	M	Spondilosys	C5–C6 (incomplete)	Spastic tetraparesis	
3	76	M	Traumatic	C5–C6 (complete)	Spastic tetraplegia	
4	69	M	Traumatic	C5–C6 (complete)	Spastic tetraplegia	
5	48	F	Traumatic	D3 (complete)	Spastic tetraplegia	
6	58	M	Traumatic	C5–C7 (complete)	Spastic tetraplegia	
7	74	M	Traumatic	D1–D2 (complete)	Spastic tetraplegia	
8	61	M	Traumatic	D4 (complete)	Spastic tetraplegia	
Mean	59.5					
S.D.	14.23					
9	71	M	Non-neurogenic			Overactive bladder + BOO
10	45	M	Non-neurogenic			Idiopatic overactive bladder
11	66	M	Non-neurogenic			Idiopatic overactive bladder
12	57	F	Non-neurogenic			Urethral hypermobility + urge incontinence
13	68	M	Non-neurogenic			Overactive bladder + BOO
14	44	F	Non-neurogenic			Genital prolapse + urge incontinence
Mean	58.5					
S.D.	11.81					

Table 3
Underactive bladder patients

Patient	Age (years)	Sex	Etiology	Clinical features
1	48	M	Conus medullaris ischemia	S3–S4 hypoesthesia + incontinence
2	59	M	Conus medullaris ischemia	S3–S4 hypoesthesia + incontinence
3	36	M	Conus medullaris ischemia	S3–S4 hypoesthesia + incontinence
4	75	M	Conus medullaris ischemia	S3–S4 hypoesthesia + incontinence
5	43	F	Conus medullaris ischemia	S3–S4 hypoesthesia + incontinence + claw foot
6	64	M	Conus medullaris ischemia	S3–S4 hypoesthesia + incontinence + claw foot
7	65	F	Subacute combined degeneration	Pyramidal sign + lower limb paraesthesia
8	36	M	Post-surgical peripheral denervation	Incontinence + impotence
9	45	M	Diabethic neuropathy	Reduced pin-prick sensation in the feet + orthostatic hypotension
10	51	F	Psychiatric	
11	58	F	Psychiatric	
Mean	52.72			
S.D.	12.6			

2. Fourteen patients (mean age 59.07 ± 12.76 years) affected by overactive bladder secondary to (Table 2);
   - neurogenic lesions: 8 patients (chronic spinal cord lesions),
   - non-neurogenic lesions: 6 patients.
3. Eleven patients (mean age 52.72 ± 12.6 years) with underactive bladder due to (Table 3);
   - neurogenic lesions: 9 patients,
   - non-neurogenic lesions: 2 patients.

All the subjects gave their informed consent and the procedure was approved by the Local Ethical Committee.

The patients were first submitted to a urodynamic evaluation which included flowmetry, cystometry and a pressure/flow study with simultaneous EMG recording. With the patients lying in the gynecological position, a Dantec Duet urodynamic apparatus was used to record bladder pressure by means of a Porges double lumen 6 Fr catheter and abdominal pressure by means of a rectal balloon; EMG activity was recorded using concentric needle electrodes. Bladder filling was performed using NaCl solution 0.9% at 37 °C at a filling rate of 30 ml/min.

Electrical stimuli were delivered to the tibial nerve at the popliteal fossa to evoke an H-reflex in the soleus muscle. The recording of electromyogram signals was performed using Ag–AgCl surface electrodes (bandwidth 20 Hz–10 kHz) and analyzed by means of a Mystro Vickers apparatus. Ten trials were executed and averaged in each bladder filling condition, at 30 s intervals. Stimuli intensity was chosen in order to obtain an H-reflex amplitude of approximately 50% of the maximum. The H-reflex was tested in different conditions: (1) empty bladder; (2) medium bladder filling; (3) maximum bladder filling and (4) five minutes after bladder emptying. Bladder capacity values were calculated in each subject on the basis of the first cystometric evaluation.

The H-reflex amplitude at empty bladder was considered as the control value.

Statistical analysis of the data was performed using the paired *t*-test, and the R^2 value was calculated to evaluate the correlation between bladder filling and H-reflex amplitude.

Table 4
Results

Patients	Mean age ± S.D. (years)	H-reflex amplitude medium filling (percentage of control value at empty bladder) mean ± S.D.	H-reflex amplitude maximum filling (percentage of control value at empty bladder) mean and S.D.
Healthy subjects (8)	57.8 ± 9.2	74.9 ± 30	50.9 ± 29
Neurogenic overactive bladder patients (8)	59.5 ± 14.23	113 ± 23	125.9 ± 25.6
Non-neurogenic overactive bladder patients (6)	58.5 ± 11.81	84.6 ± 13.7	72.5 ± 24.8
Neurogenic underactive bladder patients secondary to spinal cord injury (6)	54.16 ± 14.47	135.19 ± 65.1	127.5 ± 29.2
Underactive bladder patients secondary to peripheral nerve lesion (3)	48.7 ± 14.8	86.6 ± 17.3	92.11 ± 8
Underactive bladder patients secondary to psychiatric condition (2)	54.5 ± 4.95	70.8 ± 11	43.0 ± 10.3

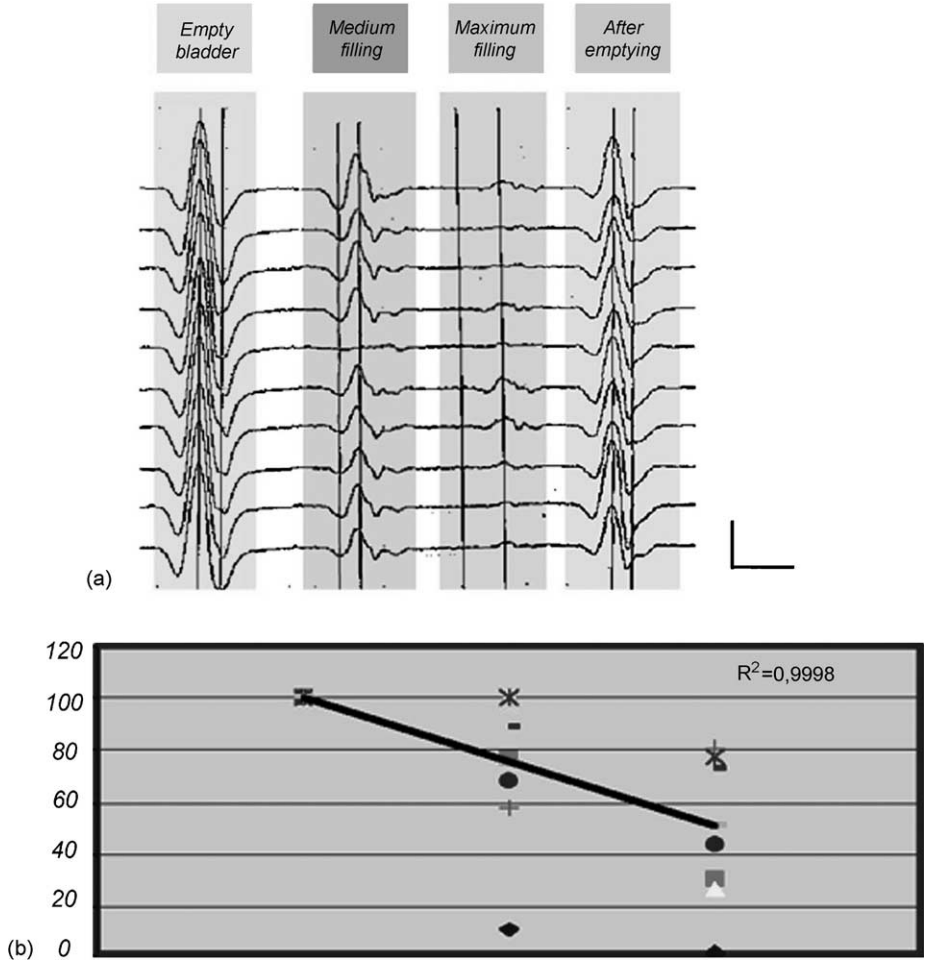

Fig. 1. (a) H-reflex in normal subjects, showing reduction in H-reflex amplitude during bladder filling (calibration: *Y*-axis 2 mV, *X*-axis 15 ms). The three columns of traces, in different colours, represent the series of 10 trials of H-reflex determination in each bladder filling condition; (b) shows, through a linear regression line, H-reflex behavior in healthy subjects during bladder filling; the R^2 value demonstrates the correlation between these data.

3. Results

The results are summarized in Table 4.

In healthy subjects, we observed a progressive reduction in the H-reflex amplitude during bladder filling. The H-reflex amplitude returned to the control value after bladder voiding (Fig. 1(a) and (b)):

1. H-reflex amplitude at medium filling: $74.9 \pm 30.2\%$ of the control value (p is non-significant).
2. H-reflex amplitude at maximum filling: $50.9 \pm 29.6\%$ of the control value ($p = 0,001$).
3. H-reflex amplitude after voiding: $97.6 \pm 31\%$ of the control value (Fig. 1(a) and (b)).

The R^2 value reveals the correlation between the reduction in H-reflex amplitude and bladder filling (Fig. 1(b)).

In the spinal cord-injured patients affected by neurogenic overactive bladder, bladder filling failed to inhibit the H-reflex amplitude; by contrast, in the same group of patients we observed a significant increase in the H-reflex amplitude at maximum filling ($125.9 \pm 25.6\%$ of the control value $p = 0.029$ (Fig. 2a and b).

The patients with a non-neurogenic overactive bladder presented a decrease in the H-reflex amplitude similar to that displayed by normal subjects (H-reflex amplitude at maximum filling: $72.5 \pm 24.8\%$ of the control value, $p = 0.013$) (Fig. 3).

In the underactive bladder patients, H-reflex behavior was not homogeneous (Fig. 4a and b): in six patients, bladder filling failed to inhibit the H-reflex amplitude (H-reflex amplitude at maximum filling: $127.5 \pm 29.2\%$ of the control value, $p = 0.124$); further neurophysiological and morphoradiological investigations identified a spinal cord injury at the conus level. In three patients, we failed to record any modification in the H-reflex amplitude during

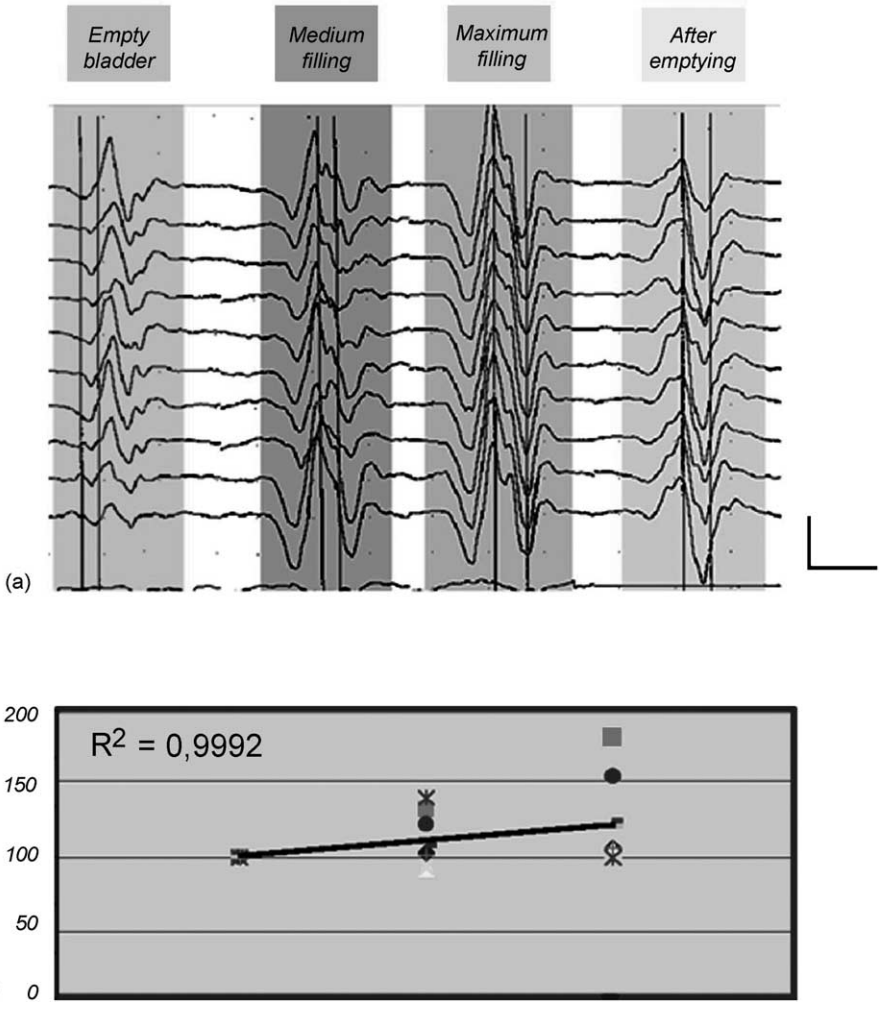

Fig. 2. (a and b) H-reflex in neurogenic overactive bladder patients, showing the absence of H-reflex amplitude inhibition during bladder filling ((a) calibration: *Y*-axis 2 mV, *X*-axis 15 ms) and its increase at maximum filling (b); the R^2 value demonstrates the correlation between these data.

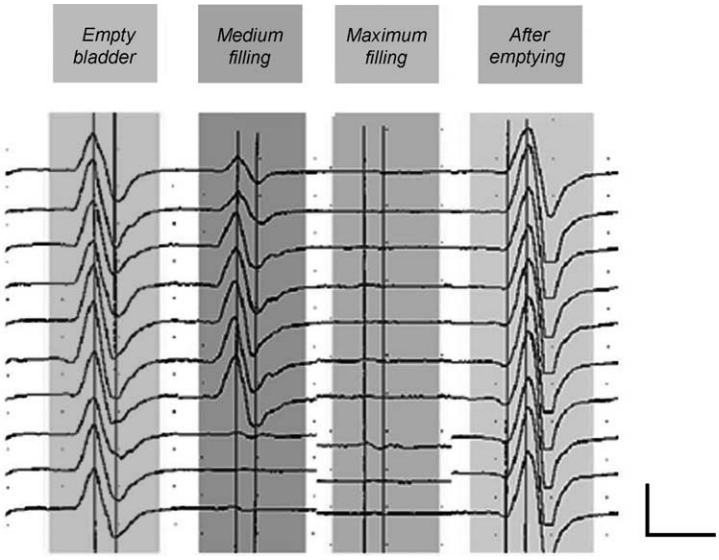

Fig. 3. H-reflex in non-neurogenic overactive bladder patients; in these patients we have a progressive reduction in the H-reflex amplitude during bladder filling comparable to that observed in healthy subjects (Fig. 1a) (calibration: *Y*-axis 2 mV, *X*-axis 15 ms).

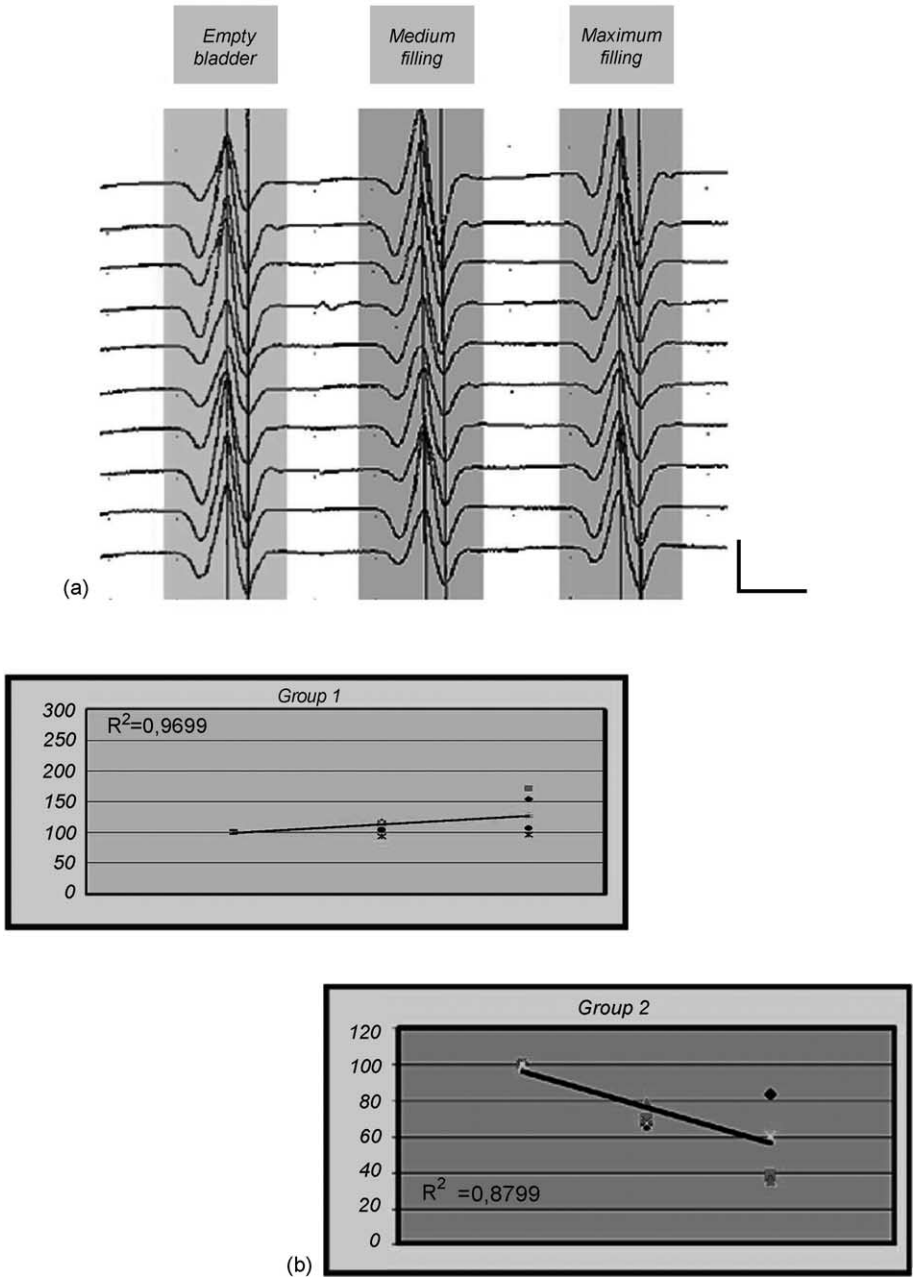

Fig. 4. (a and b) H-reflex in underactive bladder patients; the H-reflex traces during bladder filling ((a) calibration: *Y*-axis 2 mV, *X*-axis 15 ms) and linear regression lines; (b) both show the heterogenous behavior of the H-reflex amplitude in these patients.

bladder filling; further investigations in these three cases identified a peripheral nerve lesion. Two patients showed an inhibition of the H-reflex amplitude similar to that obtained in normal subjects; in these two cases we did not detect any clinical or instrumental evidence of organic neurogenic lesions at any level; a subsequent psychometric evaluation allowed us to confirm a presumptive diagnosis of hysterical neurosis, the bladder underactivity being related to the patients' primary psychiatric condition.

4. Discussion

Our data suggest that vesical afferent pathways induce a viscero-somatic reflex which is similar to that reported in the literature by other authors: Deshpande and Devandan [13] (1970) and Anand and Paintal [14] investigated the inhibitory effect induced on spinal motoneurones by C pulmonary fibers; Schondorf and Polosa [9] and Gdovin et al. [10] demonstrated the depression of respiratory function secondary to bladder filling and bladder contraction in animals. Brennan

et al. [15] studied spino-thalamic tract cell inhibition induced by bladder distension in monkeys; Cadden and Morris [8] showed inhibition of convergent neurones in rats induced by bladder filling.

The effect of bladder filling on spinal motoneurones appears to be differ markedly in normal subjects, spinal injured patients with secondary overactive neurogenic bladder and in patients with underactive bladder due to neurogenic denervation. Bladder filling depresses the H-reflex amplitude in normal subjects, but not in patients with chronic suprasacral spinal lesions. Similar findings have been described by Koley et al. [16] in animals; he reported that the inhibitory responses of the viscero-somatic reflexes after bladder distension in healthy animals were normal, whereas those in spinal cord-injured animals were reduced.

The H-reflex modulation exerted by bladder filling in normal subjects may originate from the activation of spinal interneurones; these interneurones, activated by the vesical afferent input, may change the level of spinal motoneurone excitability through a post-synaptic mechanism (Inghilleri et al. [17]). Since maximum H-reflex inhibition coincides with maximum filling, the vesical afferent fibers involved in this phenomenon are those that convey nociceptive inputs normally relayed by unmyelinated and thinly myelinated fibers.

We believe that the modulation of the H-reflex amplitude in normal subjects during bladder filling is mediated by the propriospinal system (Inghilleri et al. [17]). This concept is supported by studies in cats that suggest that the propriospinal system is involved in the intersegmental transmission of input from bladder afferents to upper thoracic sympathetic pre-ganglionic neurones [18,19].

The increase in the H-reflex amplitude during bladder filling in spinal cord-injured patients may be due to the absence of descending modulation relayed by reticulospinal pathways which acts on propriospinal interneurones (De Groat et al. [3], Mc Mahon and Morrison [6], Blok and Holstege [7]).

Our data, which need to be confirmed by other authors' experiences and studies on larger numbers of patients, indicate that the absence of sensitive inputs from bladder receptors in patients with afferent fiber denervation may abolish H-reflex modulation during bladder filling. For this reason, it may be possible to use the modulation of the H-reflex during bladder filling as a tool to differentiate patients with bladder underactivity due to neurogenic causes (afferent denervation, parasympathetic nuclear lesion) from those with a myogenic or psychogenic underactive bladder [20].

Patterns of H-reflex modulation differ significantly in healthy, spinal injured and neurological peripherally damaged patients; these differences could, therefore, be used to identify the exact site of lesions in the differential diagnosis of neurogenic voiding dysfunctions.

5. Conclusions

Our findings confirm data in the literature on the inhibition of the somatic H-reflex induced by bladder distension in normal subjects. Our study also highlights the normal behavior of the H-reflex in non-neurogenic overactive bladder patients, which significantly differs from the abnormal increase in the H-reflex amplitude during bladder filling in patients with a neurogenic overactive bladder secondary to a spinal cord lesion. Moreover, the lack of H-reflex modulation in patients suffering from neurogenic underactive bladder, indicates that this technique may be a useful tool to investigate the vesical afferent in patients with a neurogenic bladder. This model may provide additional information on the integrity of the afferent pathways, thereby contributing to a better understanding of the anatomical site of the lesion in the spinal cord. It can, therefore, be considered as an interesting technique which may serve to differentiate between voiding dysfunctions and identify their pathogenesis.

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