during attempts to void in 5 (18%), during rest and filling in 2 (7%) patients, during filling and voiding in 6 (22%) patients, and throughout the study in 2 (7%) patients. Among the 23 patients with CRDs who reported any symptoms of incontinence, 19 (83%) had an incontinence disorder diagnosed by MCUD. 3 (11%) patients were unable to void during the study, and 10 (37%) patients voided with an interrupted urinary stream. Detrusor-sphincter-dyssynergia was present during attempts to void in 4 (15%) patients.

Conclusions

CRDs were recorded in 8% of our patients undergoing MCUD evaluation of their symptoms of urinary incontinence or retention. Slightly less than a quarter of this subgroup had a known relevant neurologic disorder. CRDs occur more commonly in patients with subjective voiding difficulty, but are not rare in women without voiding complaints. The relationship between these two entities remains to be explored. Based on the uncertain clinical relevance of the finding of CRDs, we believe it is premature to recommend alterations in the approach to patients with lower urinary tract dysfunction based on this finding.

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DIFFERENTIAL EFFECTS ON BLADDER AND EXTERNAL URETHRAL SPHINCTER OF CHEMICAL STIMULATION IN THE PERAQEDUCTAL GRAY OF THE ANESTHETIZED RAT

Aims of Study In rats, the pontine micturition center (PMC) is crucial for mediating coordinated micturition. It receives direct projections both from neurons in the sacral spinal cord [1] and from other areas of the brainstem including the periaqueductal gray (PAG)[2]. Because portions of the PAG receive direct projections from the spinal cord and contain cells that in turn project directly to the PMC, it has been proposed that the supraspinal portion of the micturition reflex path could have sequential connections in PAG and PMC [2, 3]. In urethane-anesthetized rats neurotransmission in the caudal part of the ventrolateral PAG was required to support micturition provoked by continuous cystometry [4]. We sought to determine whether discrete areas of the PAG, in addition to participating in the basic micturition pathway, had influences on bladder and urethra.

Methods Rats were anesthetized with urethane (1.2 mg/kg i.p.). A PE-60 tube was secured in the dome of the bladder for infusion and intravesical pressure measurements. Fine silver wire electromyography (EMG) electrodes were placed in the external urethral sphincter. The ureters were cannulated for urine drainage. With the rat's head secured in a stereotaxic apparatus, a minimal craniotomy was performed to expose the dorsal surface of the brain. Constant infusion saline cystometry (0.1 ml/min) was used to elicit repeated micturition contractions with bursting EMG activity and voiding. Measurements were also made under isovolumic

conditions with the bladder distended to 50% of the capacity determined from continuous cystometry. The following chemicals were applied to restricted areas of the brain by pressure ejection (15-20 nl) from double-barrel micropipettes: 2-4 mM CoCl2, a blocker of synaptic transmission; 0.1-0.5 M L-glutamate (GLU), an excitatory amino acid; 0.2% Fluoro-Gold, for marking injection sites. At the end of the experiments, rats were transcardially perfused with buffered saline and 10% formalin. Injection sites were identified using fluorescence microscopy in 40 um sections stained with thionin.

Results Micturition during continuous cystometry was blocked by microinjection of CoCl2 in 14 of 158 sites tested. The effective sites were in the PMC and in a very restricted region of the caudal ventrolateral PAG (bregma-8.3). Ineffective sites were found between the effective area and the PMC and also more rostrally (to bregma -5.8). Under isovolumic conditions, injection of GLU into the PMC and parts of the PAG induced bladder contraction with coordinated EMG activity and voiding (36 of 222 sites). The PAG sites were concentrated in the areas where CoCl2 was effective but extended both rostrally and caudally. In 6 rats micropipettes were placed both in the PMC and in caudal ventrolateral PAG. The coordinated bladder and sphincter EMG response elicited by GLU injection in the PAG could be blocked by injection of CoCl2 into the PMC on the same side. At 10 sites in the PAG, GLU injection evoked sphincter activity with little or no bladder response. These sites were located in the dorsal half of the PAG and approximately in the middle third of the structure (bregma -6.8 to -7.8).

Conclusions Blockade of synaptic transmission with CoCl2 interrupts micturition only in restricted regions of the PAG and the pons. These results confirm that the caudal ventrolateral PAG and the PMC are critically involved in the basic micturition reflex in anesthetized rats [4]. With the bladder partly filled, chemical stimulation in these regions evoked the coordinated bladder and sphincter pattern characteristic of micturition indicating that either region could coordinate micturition. As the micturition evoked by chemical stimulation in PAG was blocked by CoCl2 injected into the PMC, these two centers are probably organized "in series" in the micturition pathway. The PAG also contains other regions at which chemical stimulation elicited sphincter activity independent of bladder function or coordinated micturition. It was concluded that whereas these areas are probably connected to the brainstem micturition circuit, they are not an obligatory part of that circuit because injection of CoCl2 at these sites does not interfere with micturition. Thus, the PAG, in addition to being a crucial part of the basic micturition pathway in anesthetized rats, has other areas with a variety of influences on lower urinary tract function.

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