The organization of the central control of micturition in cats and humans
Blok, Bertil Feddo Maarten

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Summary

Incontinence in the elderly is a major problem. Urodynamic investigations have shown that the majority of incontinence in humans over 65 years is caused by lesions in the brain. Surprisingly little is known about the brain structures involved in the control of micturition. The goal of this thesis is to describe how the central nervous system controls micturition and continence in cats and humans. In cats the pathways involved in micturition have been visualized using neuroanatomical tracers. Electrical stimulation in the brain or spinal cord has also been used to identify the micturition related areas. The investigations in humans have been done with the so-called positron emission tomography (PET). The PET technique demonstrated differences in regional cerebral blood flow evoked by the performance of specific tasks, such as micturition and pelvic floor straining.

During micturition the bladder muscle contracts and the external urethral sphincter relaxes. The bladder and the bladder sphincter are innervated by respectively the sacral cord parasympathetic motoneurons and the motoneurons in the nucleus of Onuf. The coordination between these two motoneuronal cell groups during micturition does not take place in the spinal cord, but in an area in the pons, the so-called M-region, also called pontine micturition center (PMC) or Barrington’s nucleus. The contraction of the pelvic floor musculature is controlled by another group of neurons in the pons, the so-called L-region. In order to decide that micturition can take place, the central nervous has to be informed about the amount of urine in the bladder. This information is generated by slowly adapting mechanoceptors in the bladder wall, and enters, via the nervus pelvicus, the lumbosacral cord. Neurons in the lumbosacral cord, in turn, project to the caudal brainstem. The results of chapter 1 demonstrate that interneurons in the lumbosacral cord of the cat project to only a very limited extent to the PMC, but very strongly to the ventrolateral part of the midbrain periaqueductal gray (PAG). The PAG is part of the emotional motor system, and plays a central role in the control of emotional related behavior, such as cardiovascular control, respiration, and reproductive behavior. Also micturition is a component of emotional behavior. Chapter 2 and 3 describe how the PMC controls the bladder muscle and the external urethral sphincter. The PMC terminals on bladder motoneurons are excitatory and control the bladder contraction during micturition. The PMC terminals on the sacral dorsal gray commissure are also excitatory, and the majority makes contact with inhibitory g-aminobutyric acid (GABA) immunoreactive neurons, which in turn inhibit the motoneurons of the external urethral sphincter in the nucleus of Onuf. This corresponds with the observation that electrical stimulation of the sacral dorsal gray commissure results in a sharp decrease of the intraurethral pressure (chapter 4). Chapter 5 describes the location of the anal sphincter motoneurons of the female domestic pig. These motoneurons are located dorsolateral from the central canal in the sacral spinal cord. In other animals, including cat, monkey, but also in humans, the location of these sphincter motoneurons is in the sacral ventral horn. Chapter 6 demonstrates that the PMC and the L-region are not interconnected at the level of the pons. This suggests that micturition and continence are controlled by two separate systems, which have different pathways to the sacral motoneurons of the bladder and/or the external urethral sphincter. In chapter 7 it is demonstrated that the ventrolateral PAG of the cat, which receives bladder filling information, projects to the PMC, which completes the circuit of the micturition reflex. It also explains why stimulation of the PAG can evoke complete micturition. In chapters 8 and 10 the PET scan results
are described of the structures involved in human micturition. These structures differ between the healthy volunteers, who were able to micturate in the PET camera, and those who were not, because of emotional reasons. In the first group (performers), both in men as in women, the PMC was activated as well as the PAG and hypothalamus. In the second group (non-performers) the L-region was activated. The anterior cingulate gyrus and the lateral prefrontal cortex were activated in the performers as well as in the non-performers group. These cortical areas are important for attention mechanisms and response selection, and probably not specifically involved in micturition control. In the chapter 9 the voluntary motor control of the pelvic floor and abdominal musculature in humans has been investigated. The PET results showed that the primary and secondary motor cortex produce contraction of these muscles. The pelvic floor musculature is controlled by the superomedial part of the precentral gyrus and the abdominal musculature by the superolateral part. Parts of the thalamus and parts of the cerebellum were activated during these straining tasks. In the general discussion the scientific and clinical consequences of the results presented in the thesis are discussed.

Fig. 1  Schematic overview of the ascending and descending pathways involved in the central control of micturition and continence. (+) = excitatory pathways; (-) = inhibitory pathways.