THE URINARY BLADDER

NEUROLOGY AND DYNAMICS

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Foreword

I am honored and greatly pleased to have been invited by the authors to make a few remarks regarding their book "The Urinary Bladder—Neurology and Dynamics." It is entirely fitting that an Uroneurologist and a Neurourologist combine efforts to update the state of our knowledge regarding the lower urinary tract. Their endeavor follows a pattern initiated by Kolb, Langworthy, and Lewis with the publication of their monograph "Physiology of Micturition" in 1940 and continued by Bors and Comarr with the printing of their text "Neurological Urology" in 1971. Drs. Bradley and Hald, in accord with their predecessors, are experienced investigators as well as clinicians—attributes which enable them to survey the literature in a critical fashion and draw valid conclusions.

The publication is quite timely in view of the marked increase over the past decade in research, acquisition of new knowledge, and interest of physicians in general in the relationship of vesicourethral function to urinary tract disease. It is particularly gratifying to note that the authors have emphasized the importance of a sound understanding of neurourology in diagnosing and treating the many disorders of the urinary tract found in the "normal" patient as well as in the spinal cord-injured and myelodysplastic individual.

This volume will serve as an excellent source of information for the medical student, resident, postgraduate, investigator, or clinician in almost any field of medicine.

Jack Lapides
Ann Arbor, MI

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The authors wish to thank all of the people who have contributed material to this book directly and indirectly. These especially include the sustained camaraderie and, often, the inspiration of Drs. Gerald W. Timm and F. Brantley Scott, as well as Robert Buuck. Their efforts and suggestions through the years have led to many of the newer therapeutic approaches as well as innovative diagnostic efforts described in this book. Dr. Thomas Fletcher of the Veterinary Science Facility at the University of Minnesota also has been a constant source of scientific information and validation.

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Special graphs were prepared by our colleagues in the Urological Laboratory, notably, Dr. J. Nordling, Dr. T. Gerstenberg, Dr. H.H. Meyhoff, Dr. S. Walter, and Dr. J.T. Andersen, and many other collaborators have given freely of their experience. Dr. Knud Mauritzen, Rigshospitalet, Copenhagen, Professor U. Ulmsten, Aarhus, Professor C. Constantinou, Stanford, Professor A. Ingelman-Sundberg, Stockholm, and Dr. H. Busch, Glostrup, also have been very helpful. Drs. John Oliver, Gaylen Rockswold, and Mark Rise, at the University of Minnesota also have provided continuous support through the years.

For excellent and patient secretarial assistance, our thanks go to Mrs. Ulla Hammerich, Mrs. Betty Beck, and Mrs. Barbara Gilman.

Many others have been involved in the process of the creation of this monograph—but none more than our nearest family and personal relations. We wish to thank them from our hearts.

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Introduction

Since World War II the interest in lower urinary tract dysfunction has been on the increase. Neuromuscular problems have always been a particularly difficult area and much has been written and spoken about this subject. This means that there are almost as many opinions on the pathophysiology and treatment as there are researchers and practicing physicians within the field. Neurological disorders are not always easy to distinguish from disorders of a purely urological or urodynamic nature and the issue is further clouded by the occurrence of a good number of psychoneurotic problems. It is the aim of this book to introduce the reader into the neurophysiology and urodynamics of incontinence and micturition and, at the same time, review the pertinent disease entities that may be either conceived as solely of a neurological nature or urological, but having a strong relation to the neurological control systems. This is not the time for a rigid classification of disorders of the function of the lower urinary tract. Some disorders are obviously true neuromuscular such as, e.g., voiding and continence problems in multiple sclerosis, but that very same situation becomes obviously urological in nature when we realize that infravesical obstruction may result and further modify the course of the condition. A disease like urethral valves is certainly conceived as truly urological, but some of its symptoms depend on changes in the neurological control system. The same holds true, e.g., for prostatic hyperplasia.

Therefore, rather than focus solely on neuropathic bladders in the strictest sense of the word, we have strived to include most functional lower urinary tract disorders in order that the reader may obtain a comprehensive impression of a dynamic organ system, where many different physiological processes interact, each of which is quite meaningless without taking the others into consideration.

Our aim is best illustrated by our personal conviction that a separation of the lower urinary tract from the nervous system is artificial and mainly due to tradition and our limited capacity and education to deal with too many factors at the same time.

Therefore, we operate with the concept of *the neurourological axis* which extends from the cerebral cortex, via the spinal cord, the peripheral lower urinary tract innervation, the bladder with its detrusor, trigone and neck, the urethra with its sphincters and literally right to the urethral meatus.

To be extreme, one may say that disease processes in the cortex may lead to urethral problems and urethral problems will necessarily surface in the consciousness of the patients, that is, the sensation reaches the brain. Obviously, traditionalists may have some difficulty in accepting this concept, but there is little doubt that such an approach is essential to further progress in a discipline which is, admittedly, still in its infancy. Two different approaches may be used in dealing with continence and micturition. The urodynamic approach invites an understanding that fluid mechanics are important in a system which is designed to carry and hold the juice of urine. For example, pressure gradients are important in making urine flow and also being arrested in the bladder. The neurophysiological approach stresses the fact that the events causing urine storage and expulsion are ultimately occurring in an excitable neuromuscular system where the central coordinating mechanisms are all important. This book attempts to incorporate and integrate both approaches.

Contents

chapter 1

Historical Background

Our present knowledge of the function of the lower urinary tract has been gathered over centuries but with accelerating speed the last two decades. Galen gave an anatomical description and Thomas Vicary, in the 16th Century, described the bladder as "two nervous pannicles, in complexion colde and dry, whose neck is carnous and hath muscles to withholde and let go." Research of a more scientific nature started in the mid-19th Century when Budge described the parasympathetic motor innervation of the detrusor.[1] Physiological investigation of the nature of urine storage in the bladder dates back to Dubois.[2] The reflex nature of micturition was known already in the 1890's, but little was known about the central regulatory mechanisms. The sympathetic nervous system's influence on the base of the bladder and urethra was known at that time, but the work of Elliott[2] especially served to clarify this in different species. One of the milestones was reached by the works of Barrington.[4–6] During his years as a general surgeon at St. Peter's Hospital, London, with a special interest in urological surgery, he performed a series of experiments which still serve as a model of scholarly research. He discovered the brainstem centers for bladder function and described the reflexes combining the various anatomical structures of the lower urinary tract. F.J.F. Barrington (1884–1956) (Fig. 1.1) is described by D. Innes Williams[7] as a man with a remarkable facility for recalling the relevant case on every occasion. He kept copious notes which were legible only to himself. His operating technique was aggressive and without finesse. His operations on rabbits and cats were the most delightful exercises in gentle skill. He died in a famous London club, in the company of two physiologists, who failed to recognize that, in the absence of false teeth, he had inhaled a bolus of food which asphyxiated him.

Further anatomical studies helped to clarify the local structure of the lower urinary tract.[8] The concept of an external and internal sphincter was popular from the turn of the century. The work of Lapides[9] and Woodburne,[10] however, showed conclusively that there was no such structure as an internal sphincter, only the bladder neck which represented the direct distal continuation of the detrusor muscle fibers. The detailed knowledge of the corresponding histology is of more recent date. With the advent of specific staining methods for some of the important neurotransmitters (acetylcholine, noradrenaline),[11, 12] a better correlation of function and structure appeared.

At the same time, the understanding of pathophysiology developed. Head and Riddoch[13] described the reflex type of voiding in World War I paraplegics. Denny-Brown and Robertson[14] supplied us with knowledge of how the peripherally denervated bladder works. With increased understanding of the complexity of the organ system, the need for more precise diagnostic data became evident. Rose[15] developed the method of cystometry into a clinically useful tool which gained acceptance, especially with the construction of the Lewis cystometer. In the 1960's, a new generation of cystometers using electronic pressure registration entered the market, and gas was used more frequently as the filling medium.[16] The addition of electromyography (EMG) registration from periurethral striated muscle represented another great step.[17] The technique of evoking potentials in structures,

Figure 1.1. F.J.F. Barrington (1884–1956), English Surgeon and Physiologist. Barrington's work formed the core structure for the field of modern Neurourology. (Courtesy D. Innes Williams, M.D., M.Chir., F.R.C.S.)

connected by reflex arcs to the lower urinary tract is still relatively new, but is spreading rapidly, indicating that the need for neurophysiological data has become understood. Further development of this technique, resembling that occurring in other organ disciplines, can be forecasted.[18]

The visual observation of the urinary stream for the purpose of evaluating micturition must have been popular for ages. The first clinically useful method to study flow rate dates back to Drake,[19] who constructed a rotating flowmeter. However, the credit of being the true father of modern urodynamics should go to von Garrelts (Fig. 1.2).[20] He combined measurement of bladder pressure and flow rate using strain gauge manometers and a flowmeter measuring the weight of urine and continuously differentiating the resulting curve. Scott and his coworkers[21] used urodynamic methods on a larger scale, added simultaneous EMG-registration from the anal sphincter, and created a urodynamics laboratory. Credit should also be given to Earl Miller and coworkers[22] in San Francisco and Turner-Warwick and Whiteside[23] in London, who combined urodynamic measurements and radiology, setting a standard which is now widely respected. The suprapubic pressure measurement was first reported by Sandøe et al.[24] Analysis of micturition by drop spectrometry was invented by Zinner and coworkers.[25] This was the first approach towards a noninvasive comprehensive urodynamic test.

The measurement of sphincter pressure by a membrane catheter was performed by Simons[26] and by Bors[27] using retrograde urethral perfusion. Urethral pressure measurements were first reliably performed by Enhörning.[28] The current method of urethral profilometry was introduced by Brown and Wickham,[29] and later modified by Harrison and Constable,[30] who employed the automatic withdrawal of the recording catheter. This method is used now more often than

Figure 1.2. Bodo v. Garrelts (born 1914), Swedish urologist. Founder of modern Urodynamics.

any other urethral study. Further development is due to Ulmsten and Asmussen.[31] They used a microtip transducer in the so-called urethrocystometry. The gas urethral closure pressure profile also came into existence at this time. The micturition cystourethrography was introduced in the 1950's.[32–34] Many clinics use urodynamic methods in various combinations which are all, however, the result of fundamental studies done by a few persons.

In the 1960's, a surge of interest was seen in electrical stimulation of the bladder and urethra with the purpose of reestablishing voluntary control of continence and micturition. Although this approach turned out largely to be a failure, the shared interest made researchers, particularly in Europe and North America, form two new scientific societies: The International Continence Society and The Urodynamics Society. Within these organizations, a rapid spread of information took place, spurring research in many new centers. Also, the level of scientific communication improved, and a standardization of terminology was undertaken. The coming together of people with training in such diverse medical fields as urology, neurology, neurosurgery, gynecology, physical medicine and rehabilitation, pediatrics, radiology, anatomy, physiology and biochemistry, along with nonmedical specialists such as biomedical engineers and physicists, created an atmosphere of openness which fertilized the area for a rapid growth in research which is still in effect.

Along with increased diagnostic capability, the search for effective modalities of treatment has intensified. However, there is admittedly a scarcity of rational methods and this area seems backlocked in comparison to the diagnostic side. The various uses of the urethral catheter were known in ancient Egypt and although some sophistication has taken place, our inadequacies are clearly demonstrated by the fact that catheters are still necessary. Intraurethral surgery, developed especially since World War I, has been of great value in solving the problems of infravesical obstruction. The development of an implantable continence prothesis has been of special benefit to patients with neuromuscular lower urinary tract problems. Pharmacological manipulation had a tremendous upswing in the 1970's, but the lack of selectivity of the drugs still makes these methods unsatisfactory.

It is reasonable to conclude that progress in understanding neuromuscular bladder dysfunction has been reasonably good, but also that we are far from the truth. Further research and nontraditional ways of thinking are desperately needed and should be stimulated.

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chapter 2

Neuroanatomy

The lower urinary tract including the urinary bladder and urethra and its nervous connections, is a complex structure whose twin functions of storage and evacuation depend upon the integrated activity of many levels of the central nervous system. The location and organization of these levels is frequently obscure. Much of the information available is derived wholly or in part from studies in the experimental animal. Where these investigations contribute valuable insight, they are often discrepant from fewer and necessarily more limited studies in humans. Human studies, in turn, are confined in their aim almost wholly to the investigation of abnormal anatomy and physiology. Certain features of neural organization of the urinary reflexes, however, do appear. These include redundancy or duplication of neural circuitry, and the presence of neuroanatomical structures and reflex pathways providing for amplification of reflex responses.

The lower urinary tract includes the lower one-third of the ureter, the ureterovesical junction, the urinary detrusor muscle, the prostate gland, and the urethra with its smooth and striated muscle investments. These anatomical structures include the appropriate autonomic and somatic innervation and vascular supply in order to maintain viability and contractility of the neuromuscular structures.

Although there is always the temptation to directly relate structure to function, this must be resisted until functional observations are confirmed by physiological experimentation or clinical observation. The innervation of the lower urinary tract can be conceived as a central and peripheral organization. The components of the central nervous system innervation include the brain and spinal cord.

Cerebral Cortex

The cerebro-cortical control of the urinary bladder resides in two areas of the cerebral cortex. They are bilaterally represented in the two hemispheres. The first area concerned with innervation of the urinary detrusor muscle has been delineated in man by correlation of frontal lobe lesions with bladder dysfunction (Fig. 2.1).[1] Similarly, stimulation of the pelvic detrusor nerve in the experimental animal evokes a bilateral diphasic response in the frontal lobe (Fig. 2.2).[2] Similar responses

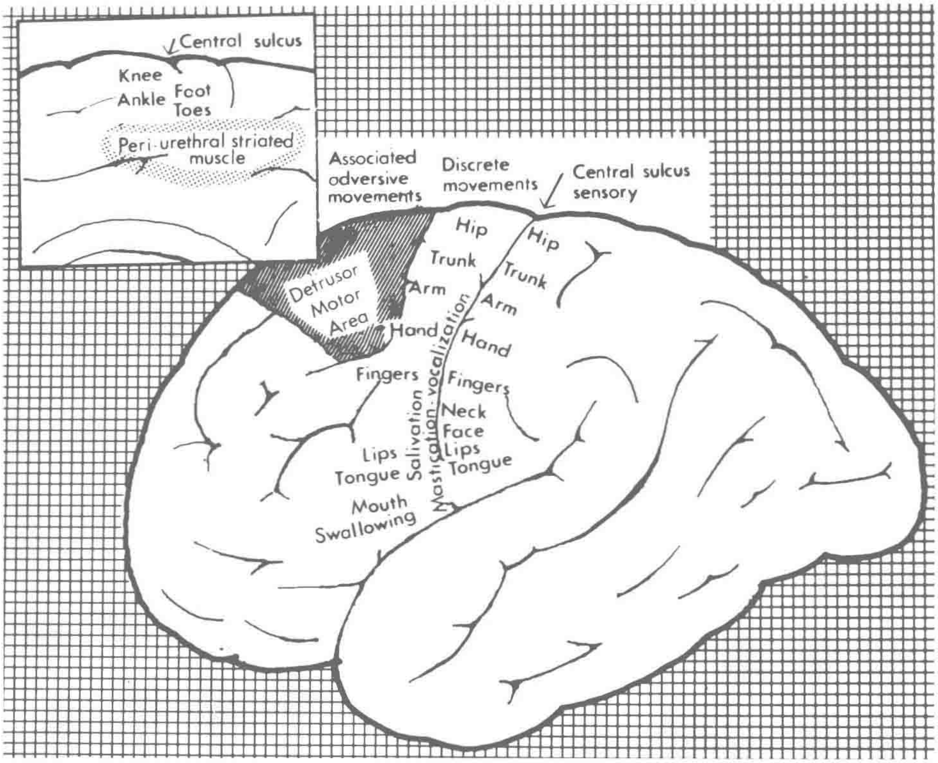

Figure 2.1. Representation of detrusor muscle control and the periurethral striated muscle in the cerebral cortex.

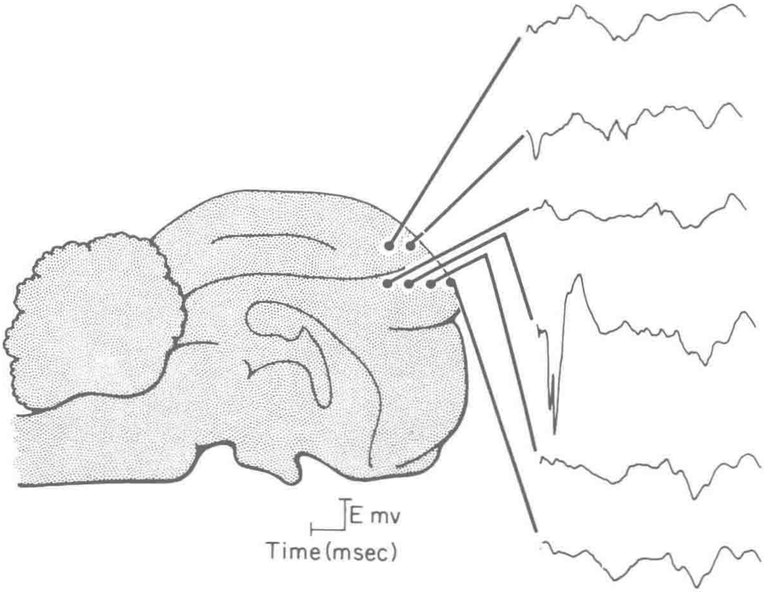

Figure 2.2. Responses evoked in the sensorimotor cortex of the experimental animal by electrical stimulation of the pelvic detrusor nerve. E = 50 mV, T = 25 msec.

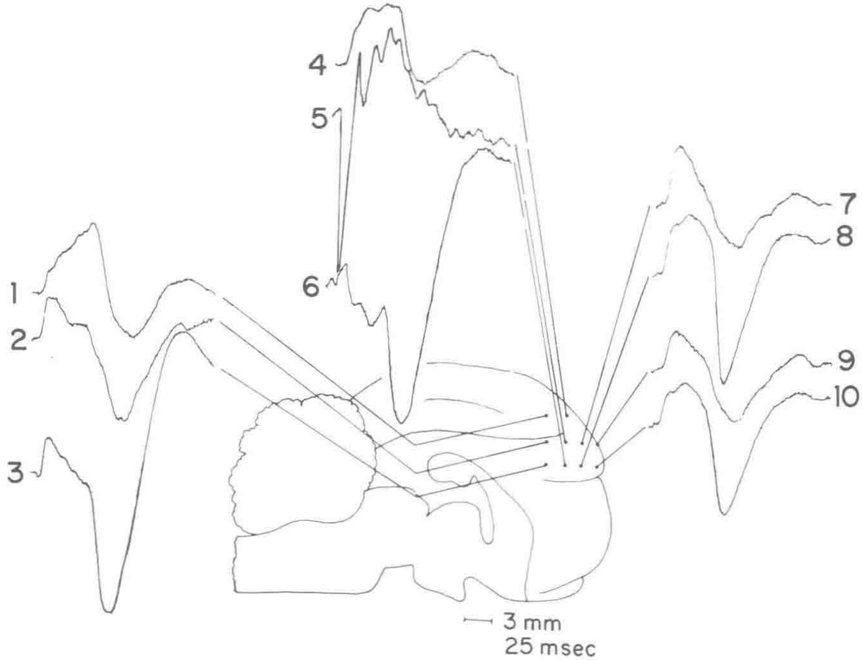

Figure 2.3. Responses evoked in the sensorimotor cortex of the experimental animal by electrical stimulation of the pudendal urethral nerve. Tracing 5 shows a diphasic positive-negative response consistent with the primary receiving area.

and locations are observed with stimulation of the pudendal urethral nerve (Fig. 2.3). However, the pudendal nerve area concerned with innervation of the periurethral striated muscle is assumed to be distinct and geographically separate from innervation of the urinary detrusor in humans. The clear documentation of these areas in humans and their interrelationships to one another present an exciting vista of future research.

Thalamus

The thalamus contains a collection of nuclei in which ascending sensory pathways relay before continuing to synapse on neurons in the cerebral cortex. Only the dorsomedial nucleus of the thalamus has been implicated in stimulation of splanchnic afferent axons.[3] The precise routing and location of afferents from the pelvic detrusor nerve await further investigation. Presumably afferent axons from the periurethral striated muscle synapse in nucleus ventralis posterolateralis before proceeding to synapse in the medial aspect of the sensorimotor cortex.

Basal Ganglia

The nuclei comprising the basal ganglia include the putamen and globus pallidus, the caudate nuclei, and the cells of the substantia nigra located in the mid-brain. The effect of stimulation of these nuclei has been investigated in the experimental animal.[4, 5] Suppression of spontaneous detrusor reflex contractions has been demonstrated. Accordingly, patients with Parkinson's disease with resultant loss of function of the basal ganglia report detrusor hyperreflexia with attendant symptomatology.[6] Stereotactic placement of lesions in nucleus ventralis lateralis of the thalamus in Parkinsonian patients resulted in increased reflex activity.[7] No definitive studies of the effect of basal ganglia input to the periurethral striated muscle in the experimental animal have been reported.

Limbic System

The limbic system consists of areas principally in the temporal lobe and associated subcortical nuclei which are the rostral extension of the autonomic nervous system. This system represents an intermixing of the input from the somatic nervous system and efferents from the viscera including the urinary bladder. Electrical stimulation of areas of the cerebral cortex related to the limbic system of the cat has been demonstrated to result in alteration of detrusor muscle reflex function.[8] No clinical reports of bladder dysfunction, however, have been reported in patients or animals with bilateral temporal lobectomies, the Kluver-Bucy syndrome.

Hypothalamus

The hypothalamus consists of a collection of nuclei better known for control of neuroendocrine function and body water regulation than urinary bladder function. However, animal experimentation has demonstrated that the hypothalamic neurons have an effect upon detrusor muscle contractility.[9] Further, unit responses have been recorded in the hypothalamus of the cat in response to bladder distension.[10]

Cerebellum

The cerebellum is a neural structure which is concerned with control of motor activities and muscle contraction in four ways:[11] 1) maintenance of tone in skeletal muscle including the periurethral striated muscle and pelvic floor musculature; 2) control of rate, range, and force of striated muscle movement including the periurethral striated muscle; 3) interacts with the brain stem nuclei to suppress detrusor reflex contractions; 4) possibly the cerebellum provides for coordination between detrusor reflex muscle contraction and relaxation of the periurethral striated muscle.

The cerebellum is a midline structure located in the posterior cranial fossa. The histological structure of the gray matter of the cerebellum has a well-defined geometry with clear relation of cortical areas to underlying nuclei. Stimulation of the pelvic detrusor and pudendal urethral nerves has been demonstrated in the experimental animal to evoke a diphasic surface positive, surface negative response in the anterior vermis (Fig. 2.4).[12] The cortical neurons of the anterior vermis project to the underlying fastigial nucleus.

Brain Stem

The brain stem, specifically the neurons of the pontine-mesencephalic gray matter contain the nuclei which have been indicated as

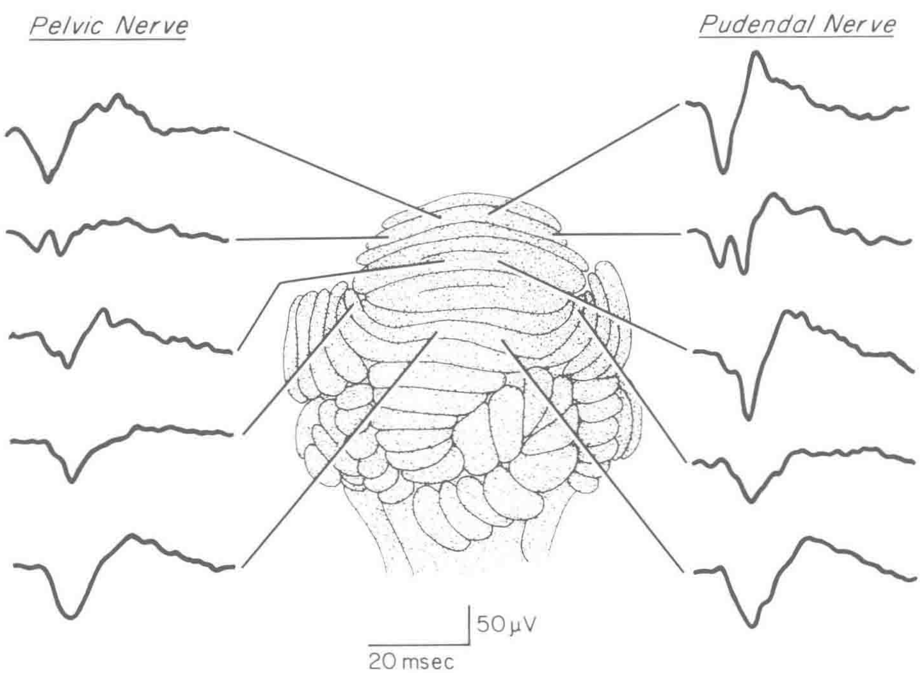

Figure 2.4. Responses evoked in the cerebellar cortex by electrical stimulation of the pelvic detrusor and pudendal urethral nerves.