Afferent Neurourology: A Novel Paradigm

J. Quentin Clemens*
Department of Urology, University of Michigan Medical Center, Ann Arbor, Michigan

The term “afferent neurourology” is introduced to describe the study of sensory processing related to the genitourinary tract. Urologic disorders that are characterized by abnormal sensory processing are reviewed, and unique challenges to our understanding of these disorders are described. A paradigm which separates afferent urologic disorders from efferent disorders and structural abnormalities is presented. Neurourol. Urodynam. 29:S29–S31, 2010.

© 2010 Wiley-Liss, Inc.

Key words: chronic prostatitis; interstitial cystitis; orchalgia; overactive bladder

INTRODUCTION

The field of neurourology may be succinctly defined as the study of normal lower urinary tract neurophysiology, as well as functional urologic abnormalities resulting from neurologic disease or injury. Many neurologic disorders can adversely affect urinary tract function, including congenital disorders (spina bifida), systemic diseases (multiple sclerosis), and localized injuries (cerebrovascular accident, traumatic spinal cord injury). The urologic management of these patients focuses on improving continence and preventing upper urinary tract complications. Management principles are well established, and include a variety of non-surgical and surgical techniques to reduce reflex detrusor activity and maintain low bladder storage pressures. These techniques are primarily focused on identifying and modulating motor (efferent) neurologic activity.

There exists an entirely different group of “urologic” abnormalities which are characterized by pain and/or urinary urgency. A variety of diagnoses can be assigned to these symptoms (Table I). However, these diagnostic labels are largely based on clinical criteria rather than on objective criteria. Therefore, such diagnoses are likely to have poor reliability and validity. Many of these disorders are characterized as infectious or inflammatory conditions, even though current evidence suggests that neither infection nor inflammation is involved in the etiology of the symptoms. Instead, it may be more appropriate to consider these conditions as urologic manifestations of sensory neurologic dysfunction.

PROPOSED TERMINOLOGY

The term afferent neurourology is proposed. This term refers to the field of study concerned with the processing of sensory information related to the genitourinary (GU) tract. This includes sensory processing within the GU tract as well as sensory data from the GU tract which is processed elsewhere within the peripheral and central nervous system. Furthermore, it is acknowledged that many afferent signals are not perceived at the conscious level but they still play a vital role in afferent neurourology as it relates to lower urinary tract physiology. Inclusive in this concept is that abnormal processing of sensory information related to the GU tract results in distressing symptoms and healthcare seeking. The term afferent urologic disorders is used to describe the various clinical terms that are often employed to categorize these symptoms (Table I). Certain clinical disorders (e.g., vulvodynia, endometriosis) are excluded, as they are typically not managed by urologists. However, such disorders could potentially be included in a broader term such as “Afferent Pelvic Disorders.”

AFFERENT NEUROUROLOGY—SYMPTOMS

Abnormal processing of sensory information related to the GU tract results in pain and/or urgency. The International Association for the Study of Pain (IASP) defines pain as an “unpleasant sensory or emotional experience associated with actual or potential tissue damage, or described in terms of such damage.” From a urologic standpoint, pain can be from bladder or non-bladder sources. This categorization is relevant because bladder pain is significantly more difficult to describe and characterize than non-bladder pain (see below). The International Continence Society defines urgency as the “sudden compelling desire to pass urine, which is difficult to defer.” It could potentially be argued that this commonly accepted definition of urgency may in fact meet the IASP criteria for pain presented above. However that interpretation is certainly open to debate, and the inclusion of urgency as a separate symptom component within the afferent neurourology paradigm seems to be appropriate at this time.

Conflicts of interest: Dr. Clemens-Equity interest: Merck; Consultant: Wiley, Pfizer, Proctor. Medtronic.
Roger Dmochowski led the review process.
Correspondence to: J. Quentin Clemens, MD, MSCI, Department of Urology, University of Michigan Medical Center, 1500 East Medical Center Drive, Ann Arbor, MI 48109-5330. E-mail: gclemens@umich.edu
Received 13 May 2009, Accepted 23 June 2009
Published online 15 April 2010 in Wiley InterScience
(www.interscience.wiley.com)
DOI 10.1002/nau.20792
Nocturia and urinary frequency are additional bothersome symptoms that are a frequent cause of urology clinic visits. However, these two symptoms are actually behaviors that are driven by urinary urgency, bladder pain, and/or many other factors. For instance, frequency and nocturia may occur in individuals with completely normal urinary tracts who drink excessive amounts of fluid. For this reason, nocturia and frequency are not included as symptom components within the afferent neurourology paradigm.

**BLADDER PAIN VERSUS URGENCY**

The distinction between various afferent urologic disorders is not always clear. For instance, the criteria used to differentiate interstitial cystitis/painful bladder syndrome (IC/PBS) from overactive bladder (OAB) have received considerable attention. The hallmark symptom of IC/PBS is pain that is referable to the bladder, while the hallmark symptom of OAB is urgency. However, some individuals with a diagnosis of IC/PBS deny the presence of pain, and instead refer to their symptoms as "pressure" or "discomfort" or "urgency." This observation has caused some to differentiate between "urgency" (which would identify OAB), and "persistent urge to void" (which would be more consistent with IC/PBS symptoms). Others have stated that the urgency in OAB is characterized by fear of leakage, while the urgency of IC/PBS is due to pain, pressure, or discomfort. The problem with these categorization efforts is that there will invariably be individuals who defy categorization, regardless of the category that is chosen. For example, in a study of 180 women with incident IC/PBS diagnoses, nearly 21% reported urinary urgency due to a fear of leakage, and an additional 9% indicated no urgency at all.

**AFFERENT, EFFERENT, AND STRUCTURAL ABNORMALITIES**

Conceptually, afferent urologic disorders can be differentiated from efferent and structural abnormalities (Table II). Examples of **afferent** (motor) abnormalities include detrusor overactivity/ure incontinence, detrusor sphincter dyssynergia, diminished bladder compliance (due to increased detrusor muscle tone), detrusor failure, and dysfunctional voiding (pseudodyssynergia). Examples of structural abnormalities include stress urinary incontinence, pelvic prolapse, dimin-ished bladder compliance (due to bladder wall fibrosis), urinary fistulas, and anatomic bladder outlet obstruction. There is clearly a relationship between the afferent symptom of urgency and the efferent condition of urge incontinence/detrusor instability, but this relationship is not well understood. For instance, urge incontinence/detrusor overactivity does appear to include dysfunction of the prefrontal cortex and/or abnormal afferent signaling in at least some patients. The condition OAB is often subcategorized into "OAB dry" (urgency without urge incontinence) and "OAB wet" (urgency with urge incontinence). These two subgroups are considered part of an OAB disease spectrum, but it is not known if they in fact share the same underlying pathophysiolog y. It is also unclear to what extent those with "OAB dry" progress to "OAB wet." Furthermore, the mechanism respon-
sible for converting the afferent symptom of urgency to the efferent symptom of urge incontinence is not well understood.

It is notable that each of the efferent and structural abnormalities has an objective diagnostic test which can be used to confirm the diagnosis and quantify its severity. Conversely, the afferent urologic disorders currently have no objective tests which can confirm the diagnosis, identify specific subgroups of patients, or provide prognostic information. This may be one reason why these disorders have received little attention in the literature (Table III). Urgency and pain could theoretically be caused by abnormal sensory processing within the GU tract or by abnormal processing of sensory data from the GU tract, or a combination of both.

OVERLAP OF AFFERENT, EFFERENT, AND STRUCTURAL ABNORMALITIES

Clinicians will quickly recognize that multiple afferent, efferent, and structural disorders may be present in an individual patient (Fig. 1). For example, certain women may present with stress incontinence (structural), poor detrusor contractility (afferent), and bladder pressure/pain (afferent). Men may present with anatomic bladder outlet obstruction due to prostatic hyperplasia (structural), detrusor overactivity (afferent), and perineal pain (afferent). The clinical management is fairly straightforward in patients with symptoms in a single category (afferent, efferent, or structural), but becomes increasingly complex as they manifest symptoms in additional categories. It seems reasonable to conclude that effective patient management requires recognition of this overlap when it occurs.

CONCLUSION

The term “afferent neurourology” can be used to describe the processing of sensory information related to the GU tract. Abnormal sensory processing (within the GU tract or centrally) causes symptoms of pain and urinary urgency. Patients with these symptoms are often diagnosed with “interstitial cystitis,” “prostatitis,” or “overactive bladder” although these diagnoses are fraught with problems. These afferent urologic symptoms often overlap with efferent symptoms and structural abnormalities, and effective patient management requires an awareness of this.

REFERENCES