Functional Brain Imaging and the Neural Basis for Voiding Dysfunction in Older Adults

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KEYWORDS

• Urinary incontinence • Aging • Elderly • Frailty • Bladder • Lower urinary tract

KEY POINTS

- Brain abnormalities may contribute to the increased prevalence of urinary dysfunction such as overactive bladder and urge incontinence in older individuals.
- Functional brain imaging suggests that 3 independent neural circuits (frontal, midcingulate, and subcortical) control voiding by suppressing the voiding reflex in the brainstem periaqueductal gray.
- Damage to the connecting pathways subserving these circuits (white matter hyperintensities) increases with age and is associated both with severity of urge incontinence and changes in brain function.
- The pathway between the medial frontal cortex (circuit 1) and the periaqueductal gray seems particularly sensitive to the effects of white matter hyperintensities.
- These types of neurologic deficits may also contribute to declines in the ability of many older adults to sense, process, and execute appropriate decisions if there is urgency, thus rendering them more vulnerable to becoming incontinent.
- All of these considerations suggest that multicomponent therapies targeting these structural and functional neural abnormalities may be more effective than any single treatment focused on the bladder.

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INTRODUCTION

Disorders related to urinary control become increasingly prevalent and troublesome with age.[1–4] Symptoms of urgency, frequency, nocturia, and incontinence increase with age, even in the absence of an obvious genitourinary cause.[5] In contrast, many older adults with noticeable urodynamic abnormalities manage to remain dry and/or symptom free.[5] Unlike younger adults, the cause of incontinence in older adults becomes increasingly multifactorial, with nongenitourinary factors assuming important roles as both predisposing and precipitating risk factors. Thus this clinical problem assumes the mantle of a geriatric syndrome in elderly patients.[6] An association of storage, voiding, and incontinence symptoms with conditions increasingly common in older adults, including diabetes, hypertension, depression, and constipation,[7] further influences clinical presentation and outcomes, compounding the impact of urinary symptoms on life quality in older adults.

The standard approach to voiding symptoms and incontinence generally links symptoms to measurable function at the level of urodynamic studies, and function directly to the bladder and urethra; this is the bladder-centric model. This model is formalized by the terms overactive bladder and underactive bladder as descriptions of common storage and voiding symptom complexes, which are close to the terms describing urodynamic observations of detrusor performance during filling and voiding: detrusor overactivity and detrusor underactivity. The standard parsing of urinary incontinence symptoms into stress versus urge suggests a simplistic causal dichotomy of sphincteric insufficiency (urodynamic stress incontinence) or detrusor misbehavior (detrusor overactivity incontinence). Such bladder-focused associations have proved to be therapeutically useful in younger populations, thus reinforcing their apparent value. It has long been recognized that lower urinary tract symptoms are poorly predictive of observed (urodynamic) function.[8] Nevertheless, the presumption that incontinence, overactive bladder, and underactive bladder symptoms have something to do with the capabilities of the detrusor smooth muscle and urethral sphincteric mechanism has persisted.

Any presumed linkage of symptoms to dysfunction therefore hinges on an understanding of the impact of aging on lower urinary tract function and, by extension, structure and organ physiology. In contrast with a universal functional decline, aging is better characterized as a downward broadening of the spectrum of function; median levels of functionality trend downwards, the distribution widens, with many individuals retaining high levels of cognitive, visceral, and somatic performance.[9] Furthermore, at times, it can be difficult to disentangle the impact of aging per se from disease-induced changes. A growing body of knowledge suggests that aging and chronic diseases for which advanced age is a major risk factor may share common biological pathways.[10,11] These concerns are reflected in the sometimes contradictory reports regarding the impact of aging on lower urinary tract function. A consistent finding is a loss of sensitivity. The Pittsburgh group reported on urodynamics performed in a small number of healthy and asymptomatic women.[12] The threshold volume for strong desire to void increased, and urethral closure pressures and detrusor pressures at maximum flow decreased with increasing age and achievement of menopausal status. Animal models provide supportive evidence for a loss of system sensitivity to bladder volume.[13–15] Ultrastructural studies have shown evidence of depleted caveolae and slightly widened muscle intercellular spaces (so-called dense band pattern) in otherwise asymptomatic patients who did not strain to void or have a large postvoid residual volume.[16] Similar changes have been observed in an animal model.[17] Moreover, given the known role of caveolae in calcium signaling, the deletion of the caveolin