

Does Central Sensitization Help Explain Idiopathic Overactive Bladder? Reynolds, et al. *Nat Rev Urol.* 2016 August; 13(8):481-491.

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Abstract: The concept of central sensitization might be relevant to understanding the mechanisms and clinical manifestations of overactive bladder syndrome (OAB). An understanding of the pathophysiology and clinical manifestations of central sensitization and the evidence that supports a role of central sensitization in OAB, including the potential implications of mechanisms of central sensitization for the treatment of patients with OAB could provide a novel approach to the treatment of patients with this disease.

Overactive Bladder (OAB):

- Affects 1 in 7 people in the USA
- Defined by the presence of urinary urgency which is often accompanied by increased urinary frequency, nocturia and, in some cases, urgency-related incontinence.
- Pathophysiology integrates mechanisms involving input from within the bladder as well as the peripheral and central nervous systems.
 - Several potential mechanisms might contribute to OAB pathophysiology which are broadly characterized as abnormally increased afferent signals from the bladder or decreased capacity to modulate afferent signals in the CNS.
 - The CNS is responsible for modulating signals to suppress unnecessary and/or unconscious bladder sensations and to facilitate afferent signals necessary for homeostasis; evidence shows the CNS plays a prominent role in the development of OAB

Central Sensitization:

- Defined as “increased responsiveness of nociceptive neurons in the CNS to their normal or sub-threshold afferent input”; induced spinal hypersensitivity.
- In the pathogenesis of central sensitization, the peripheral nerves generally function normally, but changes in function occur in central neurons.
- Stimuli that generally do not provoke pain can produce pain (such as allodynia) and stimuli that normally provoke pain can produce pain of a higher intensity.
 - These effects on perception of nonpainful sensations might be particularly relevant to understanding the role of central sensitization in conditions such as OAB.
- Clinically, central sensitization is thought to contribute to the pathophysiology of a number of chronic pain and somatic conditions (including endometriosis, fibromyalgia, IBS, primary

dysmenorrhea, IC, painful bladder syndrome, vulvodynia/vulvar vestibulitis, chronic male pelvic pain, PTSD)

- Multiple conditions that arise from central sensitization can co-occur in the same individual
- Psychosocial comorbidities are common among individuals with central sensitivity syndromes and overlap with a variety of psychiatric disorders.
 - Psychological stress can frequently exacerbate the symptoms
- Clinical manifestation of central sensitization can be indexed using a group of psychophysical laboratory techniques known as quantitative sensory testing (QST)
 - Few other established objective measures of central sensitization are available

Central Sensitization and OAB:

- Data indicates that central sensitization can lead to hypersensitivity of afferent pathways which are involved in the generation of OAB-related sensations in the bladder.
- Both central sensitization and OAB are mediated or induced by activation of C-fibre afferent nerves.
- It is possible that the primary dysfunction may arise from the bowel (via pelvic organ cross-sensitization), but the bladder becomes affected secondarily owing to the ability of central sensitization syndromes to spread to different organs.
- The absence of obvious bladder pathology or injury in OAB also fits with the concept of central sensitization.

Current Evidence:

- Despite the potential overlap in mechanisms between central sensitization and OAB, current experimental data provide only indirect evidence for this association.
- Evidence of urinary biomarkers of bladder dysfunction might support a role of central sensitization in OAB but research is limited and lacking specificity.
- CNS imaging has increasingly been employed for research but the presence of common findings is certainly not conclusive or specific to the presence of central sensitization and OAB.
- Clustering of central sensitization syndromes in individuals with OAB has rarely been systematically examined and all studies are limited regarding the specificity of diagnoses or in the generalizability of the findings.
- Evidence published in 2014 on temporal relationships in women with IC/BPS also suggests that urinary symptoms such as those associated with OAB might predate the onset of IC/BPS.
 - If this is indeed the case, early identification and treatment of OAB might help prevent worsening of the condition and progression to IC/BPS.

Discussion:

- Few therapies exist that have demonstrated direct effects on any aspects of central sensitization
- A number of widely-used treatments of OAB also have effects on other organ systems and, as such, many treatments commonly employed for OAB might also be effective as treatments of comorbid central sensitization syndromes.
 - Antimuscarinic agents
 - Antidepressants
 - Sacral neuromodulation

- A role of central sensitization in OAB might explain the comorbid occurrence of this syndrome with many central-sensitization-related syndromes.

Discussion questions:

- 1) What common patterns of symptoms do you observe in your patients who have OAB symptoms?
- 2) How do you address the multiple organ and whole-body symptoms seen in patients with OAB and central sensitization?
- 3) What other health care providers do you rely on to help treat patients with complex symptoms?
- 4) What are your treatment techniques for calming the CNS?