Visceral Sensory Neurons that Innervate Both Uterus and Colon Express Nociceptive TRPV1 and P2X3 Receptors in Rats

INTRODUCTION

The incidence of persistent, episodic, or chronic visceral pain disorders such as irritable bowel syndrome and other “functional” syndromes (fibromyalgia, interstitial cystitis, chronic pelvic pain, and others) are more prevalent in women. Indeed in most clinical studies, women report more severe pain levels, more frequent pain, and longer duration of pain than do men. Nociception is a balance of pro- and anti-nociceptive inputs that is subject to regulation depending on the normal state of the organism. The cell bodies of primary visceral afferent neurons are located in dorsal root ganglia (DRG). Direct activation of chemosensitive receptors and ion channels on their peripheral terminals and modulation of neuronal excitability activates extrinsic primary afferent nerves. Nociceptors belong predominantly to small- and medium-size DRG neurons whose peripheral processes detect potentially damaging physical and chemical stimuli.

Defining the sites and mechanisms of pain transmission in visceral nociception is an important step in understanding the pain perception and in designing appropriate therapies. One such mechanism may be the convergence of nociceptive stimuli in the primary afferent neurons that innervate different viscera. Visceral nociceptive C-fibers are activated by ATP released by noxious stimuli from cells in target organs and have been implicated as mediators of noxious stimulus intensities. Alteration in signal transduction of primary afferent neurons can result in enhanced perception of the visceral sensation, which is common in patients with different disorders, resulting in elevated pain perception. Irritable bowel syndrome is currently defined as a chronic functional syndrome characterized by recurring symptoms of abdominal discomfort or pain and alterations in bowel habits in the absence of detectable organic disease. In the context of visceral pain, the capsaicin-sensitive vanilloid (TRPV1) receptor is a sensory neuron-specific cation channel that belongs to the transient receptor potential subfamily 1 and plays an important role in transporting thermal and inflammatory pain signals. Evidence for TRPV1’s role in the pathogenesis of many diseases come from studies showing that mice lacking the TRP1 receptor gene have deficits in thermal- or inflammatory-induced hyperalgesia. Capsaicin-induced TRPV1 receptor-mediated changes in [Ca2+], may represent a level of DRG activation to noxious cutaneous stimulation, while ATP-induced changes in [Ca2+], may reflect the level of DRG neuron sensitization to noxious visceral stimuli, since ATP is released by noxious stimuli and tissue damage near the primary afferent nerve terminals. In this report, we investigated whether subsets of visceral DRG neurons that innervate both uterus and colon express nociceptive P2X3 and TRPV1 receptors in rats.

METHODS

Retrograde Labeling

Retrograde labeling was used to identify uterus-specific and colon-specific DRGs and sensory neurons innervating both visceral organs: uterus and colon. For colonic afferents, the descending colons of adult female ovariectomized Long-Evans rats (weighing...