

## An Endogenous Pain Control System is Altered in Subjects with Interstitial Cystitis

Timothy J. Ness<sup>\*,†</sup>, L. Keith Lloyd<sup>‡</sup> and Roger B. Fillingim<sup>§</sup>

From the Department of Anesthesiology (TJN) and Department of Urology (LKL), University of Alabama at Birmingham, Birmingham, Alabama, and University of Florida College of Dentistry and Gainesville Veterans Affairs Medical Center, Gainesville, Florida (RBF)

### Abbreviations and Acronyms

BPS = bladder pain syndrome  
CPM = conditioned pain modulation  
HC = healthy control  
IC = interstitial cystitis

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\* Correspondence: Department of Anesthesiology, University of Alabama at Birmingham, 901 19th St. S, BMR2-236, Birmingham, Alabama 35205 (telephone: 205-975-9643; FAX: 205-934-7437; e-mail: [tjness@uab.edu](mailto:tjness@uab.edu)).

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**Purpose:** Multiple studies have demonstrated that in healthy subjects, painful stimuli applied to one part of the body inhibit pain sensation in other parts of the body, a phenomenon referred to as conditioned pain modulation. Conditioned pain modulation is related to the presence of endogenous pain control systems. Studies have demonstrated deficits in conditioned pain modulation associated inhibition in many but not all chronic pain disorders. In this study we determine whether conditioned pain modulation is altered in subjects with interstitial cystitis/bladder pain syndrome.

**Materials and Methods:** Female subjects with and without the diagnosis of interstitial cystitis/bladder pain syndrome were studied psychophysically using quantitative cutaneous thermal, forearm ischemia and ice water immersion tests. Conditioned pain modulation was assessed by quantifying the effects of immersion of the hand in ice water (conditioning stimulus) on threshold and tolerance of cutaneous heat pain (test stimulus) applied to the contralateral lower extremity.

**Results:** The conditioned pain modulation responses of the subjects with interstitial cystitis/bladder pain syndrome were statistically different from those of healthy control subjects for cutaneous thermal threshold and tolerance measures. Healthy control subjects demonstrated statistically significant increases in thermal pain tolerance whereas subjects with the diagnosis of interstitial cystitis/bladder pain syndrome demonstrated statistically significant reductions in thermal pain tolerance.

**Conclusions:** An endogenous pain inhibitory system normally observed with conditioned pain modulation was altered in subjects with interstitial cystitis/bladder pain syndrome. This finding identifies interstitial cystitis/bladder pain syndrome as similar to several other chronic pain disorders such as fibromyalgia and irritable bowel syndrome, and suggests that a deficit in endogenous pain inhibitory systems may contribute to such chronic pain disorders.

**Key Words:** diffuse noxious inhibitory control, urinary bladder, pain

MULTIPLE studies have demonstrated that in healthy subjects painful stimuli applied to one part of the body inhibit pain sensation in other parts of the body, a phenomenon referred to as conditioned pain modulation.<sup>1</sup>

We previously demonstrated that reduced CPM is associated with an increase in clinical pain in a community based sample.<sup>2</sup> Others have demonstrated that painful disorders such as fibromyalgia and irritable

bowel syndrome are associated with deficits in endogenous pain inhibitory systems,<sup>3-7</sup> which are reflected as alterations in CPM. Alterations in CPM have also been identified prospectively as predictors of difficult to control postoperative pain and with the development of chronic pain.<sup>8-10</sup> It is not known whether alterations in CPM are present in painful urological disorders such as interstitial cystitis/bladder pain syndrome.<sup>11</sup>

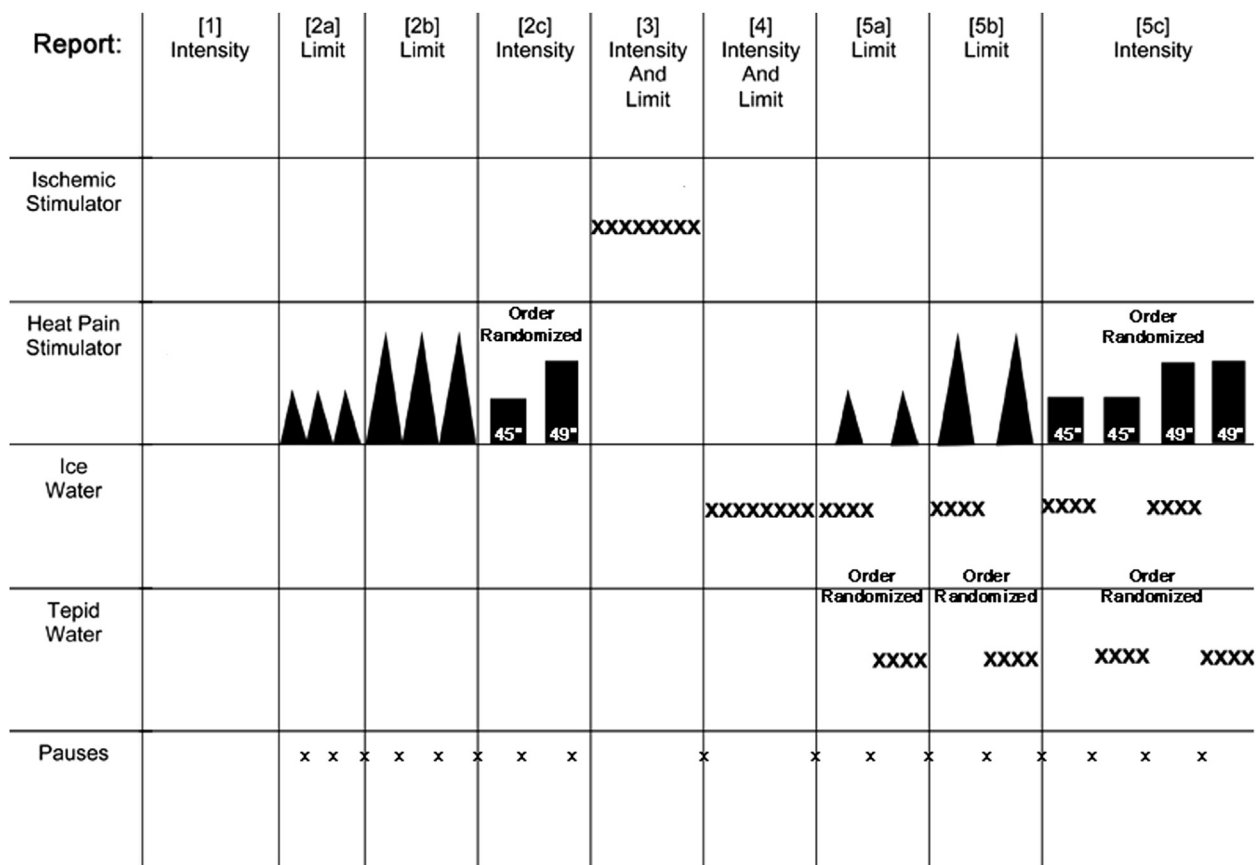
We previously demonstrated that subjects with IC/BPS are hypersensitive to bladder and other deep tissue sensations.<sup>12</sup> Therefore, it is notable that most chronic pain disorders that have demonstrated alterations in CPM (eg chronic joint pain, fibromyalgia, headache, temporomandibular disorder, irritable bowel syndrome) have also displayed increased pain sensitivity on psychophysical testing.<sup>5,6</sup> However, other chronic pain disorders such as classic trigeminal neuralgia,<sup>13</sup> vulvodynia<sup>14,15</sup> and rheumatoid arthritis,<sup>16</sup> which also have clear evidence of local hypersensitivity, have apparently normal CPM mechanisms. This finding suggests that alterations in CPM may reflect some underlying difference in

central nervous system function associated with the development or maintenance of particular pathological processes. Since it is not known whether subjects with IC/BPS have alterations in CPM, we quantitatively compared the effects of a heterosegmental conditioning noxious stimulus (immersion of hand in ice water) on responses evoked by a noxious hot thermal test stimulus applied to the lower extremity in subjects with the diagnosis of IC/BPS with responses of healthy control subjects.

## METHODS AND MATERIALS

### Study Summary

These studies were approved by the University of Alabama at Birmingham Institutional Review Board for Human Studies. A total of 29 female subjects (15 meeting the American Urological Association criteria for IC<sup>11</sup> and the more stringent National Institute of Diabetes and Digestive and Kidney Diseases consensus panel criteria for IC,<sup>17</sup> and 14 age matched, healthy controls) were recruited, and underwent a single session of testing as summarized in figure 1. Sequential measures consisted of 1) initial



**Figure 1.** Schematic diagram summarizing testing protocol. Different segments were performed in sequential order with some randomization of order within segments indicated. Segments included measures of 1) void report, 2a) heat threshold, 2b) heat tolerance, 2c) heat intensity, 3) ischemic tolerance, 4) ice water tolerance, 5a) CPM of heat threshold, 5b) CPM of heat tolerance and 5c) CPM of heat intensity. Pauses of 2 to 5 minutes between stimuli presentation allowed recovery of sensations to baseline.

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