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EVIDENCE FOR CENTRAL HYPEREXITABILITY IN PATIENTS WITH INTERSTITIAL CYSTITIS

Hypothesis / aims of study
Pain in interstitial cystitis (IC) appears to have significant central and neuropathic components, as well as involvement of central modulatory pathways including those involving the limbic system. The startle blink reflex (SBR) is a defensive, involuntary eye-blink in response to sudden intense stimuli. This reflex is modulated the amygdala, a component of the limbic system involved in modulation of emotional states and physical sensations. Increases in SBR magnitude represent an objective index of affective response to stimuli, such as threat of pain. To test the hypothesis that IC patients have an upregulation of central pain modulation pathways, we compared the SBRs of healthy controls with that of IC patients.

Study design, materials and methods
SBRs were examined for 6 female IC patients and 19 healthy females under threat and safe periods. During threat periods, subjects would possibly receive aversive electrical stimulation to their bladder region. Each threat period consisted of an early and late phase. If stimulation was to occur, it would occur during the late phase. No stimulation was given during safe periods. SBRs were measured during all phases. Mixed-effects analysis for repeated measures was applied to determine the influence of diagnosis (IC, Control), threat (Danger, Safe) and phase (Early, Late) on the square-root transformed SBRs.

Results
Significant main effects were observed for diagnosis ($p=.008$), threat ($p<.001$), and phase, ($p<.001$) as well as an interaction between all 3 parameters ($p=.045$). Patients with IC had significantly greater estimated mean SBRs than controls during early and late safe periods (mean$\pm$SE SBR 12.4 ± 1.1 vs. 8.5 ± 0.6, $p=0.003$, and 12.7 ± 1.1 vs. 9.3 ± 0.6, $p=0.01$, respectively) and during the early danger period (13.9 ± 1.1 vs. 9.7 ± 0.6, $p=0.001$, respectively). During the late danger period the SBRs of IC patients and controls were similar (15.1 ± 1.1 vs. 14.1 ± 0.6, $p=0.46$, respectively).

Interpretation of results
This initial data indicates that IC patients have significantly greater SBRs than controls during baseline and during the non-imminent threat periods of the study. A similar alteration of the startle reflex is observed in humans with anxiety disorders and post-traumatic stress disorder. This is objective evidence that IC patients may have upregulation of limbic responses involved in anxiety and stress leading to altered pain perception and abnormal modulation of afferent pain signals. Further investigation is needed to determine if this upregulation is a causative agent or a secondary effect of the IC disease process.

Concluding message
This study provides objective evidence of upregulation within the limbic system of patients with interstitial cystitis. These results suggest that central alteration of pain perception may be involved in the IC disease process.

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