Activation of human enteric neurons by supernatants of colonic biopsy specimens from patients with irritable bowel syndrome.

BACKGROUND & AIMS: Pathological features in irritable bowel syndrome (IBS) include alterations in mucosal cell content and mediator release that might alter signaling to nearby submucosal neurons. METHODS: Voltage sensitive dye imaging was used to record the effects of mediators, released from mucosal biopsies of IBS patients, on cell bodies of 1207 submucosal neurons from 76 human colonic tissue specimens. Supernatants, containing these mediators, were collected following incubation with colonic mucosal biopsies from 7 patients with diarrhea-predominant IBS (D-IBS), 4 with constipation-predominant IBS (C-IBS), and 4 healthy controls. Serotonin, histamine and tryptase concentrations in supernatants and lamina propria mast cell density were determined. RESULTS: In contrast to controls, IBS supernatants significantly increased the rate of spike discharge in 58% of human submucosal neurons. Neurons that responded to IBS supernatant had a median spike frequency of 2.4 Hz compared to 0 Hz for control supernatants. Supernatants from C-IBS and D-IBS evoked similar spike discharge. The activation induced by IBS supernatants was inhibited by histamine receptor (H1-H3) antagonists, 5-HT3 receptor antagonist, and protease inhibition. Serotonin, histamine and tryptase
levels in supernatants correlated with the spike discharge induced by the supernatants. Mast cells density as well as histamine and tryptase levels in supernatants were higher in IBS than in controls. CONCLUSIONS: Mediators released from mucosal biopsies of IBS patients can activate human submucosal neurons. The activation required histamine, serotonin and proteases but was not associated with IBS subtype. Altered signaling between mucosa and the enteric nervous system might be involved in IBS pathogenesis.