Peripheral and central factors in the pathophysiology of irritable bowel syndrome

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Avhandlingen baseras på följande arbeten:

- I. Posserud I, Syrous A, Lindström L, Tack J, Abrahamsson H, Simrén M. Altered perception in irritable bowel syndrome is associated with symptom severity.
 Submitted for publication.
- **II.** Posserud I, Agerforz P, Ekman R, Björnsson ES, Abrahamsson H, Simrén M. Altered visceral perceptual and neuroendocrine response in patients with irritable bowel syndrome during acute mental stress.

Gut 2004; 53: 1102-8.

- **III.** Posserud I, Svedlund J, Wallin J, Simrén M. Hypervigilance in irritable bowel syndrome compared with organic bowel disorders. *Submitted for publication*.
- **IV.** Posserud I, Stotzer P-O, Björnsson ES, Abrahamsson H, Simrén M. Small intestinal bacterial overgrowth in patients with irritable bowel syndrome. *Gut 2007; 56: 802-808*



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Abstract

Irritable bowel syndrome (IBS) is a functional gastrointestinal (GI) disorder characterized by abdominal pain and/or discomfort together with abnormal bowel habits. The pathophysiology is complex and incompletely understood. Potential important factors are altered brain-gut interactions, visceral hypersensitivity, psychosocial factors, disturbed GI motility, inflammatory changes, and bacterial overgrowth. Our aim was to investigate some of the different pathophysiological factors in IBS.

Altered rectal perception was found in 62% of IBS patients. These subjects more frequently reported moderate or severe abdominal pain, bloating, diarrhea, satiety, and anxiety. Symptoms of abdominal pain and bloating were associated with altered rectal perception in a multivariate analysis. Moderate or severe symptoms overall were also associated with female gender and anxiety.

Stress decreased visceral sensory thresholds in controls, probably due to distraction. In IBS patients, sensory thresholds remained stable during stress, indicating a disability to suppress signals from the bowel during stress in these patients. Compared with controls, IBS patients had altered neuroendocrine hormones both in the basal state and in response to stress.

In an experimental setting, investigation of memory and attention showed that compared with patients with organic GI disease, IBS patients were faster at identifying words, especially words representing GI symptoms and negative affects. There were no group differences regarding levels of anxiety or depression, but in IBS patients these levels were correlated with memory processing of GI words.

Small intestinal bacterial overgrowth investigated with proximal jejunal cultures, was present in 4% of IBS subjects, which was not different from healthy controls. However, mildly elevated counts of bacteria were more common in IBS patients than in controls. Patients with bacterial overgrowth tended to have fewer phase IIIs, and enteric dysmotility was twice as common in these subjects. There was no relation between mildly elevated counts of bacteria and small bowel motility.

Conclusions: The pathophysiology of IBS is complex and multifactorial. Altered visceral perception is associated with symptom severity, and stress induces an altered visceral and neuroendocrine response in IBS patients, which could explain why stress is sometimes associated with the onset and worsening of symptoms. IBS patients seem to be hypervigilant regarding GI symptoms through memory processing connected to psychological state. Small intestinal bacterial overgrowth is not common in IBS, but of uncertain relevance, a proportion of IBS patients have elevated counts of bacteria in the proximal jejunum.

Keywords: irritable bowel syndrome; visceral perception; rectal perception; visceral hypersensitivity; gastrointestinal symptoms; hypervigilance; selective attention; stress; small bacterial overgrowth; rectal barostat; small bowel motility; gastrointestinal dysmotility.

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