CORRESPONDENCE

Readers are encouraged to write letters to the editor concerning articles that have been published in GASTROENTEROLOGY. Letters that include original, unpublished data will not be considered. Letters should be typewritten and submitted electronically to http://www.editorialmanager.com/gastro/

Visceral Hypersensitivity in Irritable Bowel Syndrome: Does It Really Normalize Over Time?

Dear Sir:

We would like to comment on the article by Naliboff et al[1] published in the August 2006 issue of GASTROENTEROLOGY. Hypersensitivity of the colon is often considered as a biological marker of irritable bowel syndrome (IBS) in many of these patients.[2–4] The causes and consequences of this process are still debated, and data are obviously lacking on the natural history of this hypersensitivity. Naliboff et al[1] realized a *tour de force* when they studied the pain threshold to rectal balloon distention in IBS patients every 4 months during 1 year. The information provided here is unique and essential. The authors observed that:

1. IBS symptoms remained stable over 12 months, whereas visceral hypersensitivity improved, suggesting an absence of direct relationship between both phenomena, and confirming the notion extrapolated from other studies where clinical improvement could be obtained by psychological[5] or pharmacologic[6,7] treatments, without modification of intestinal sensitivity.
2. The measure of visceral sensitivity remained stable over 4 months, an important confirmation of other studies,[5–7] often using a 10- to 14-week comparison period.
3. At the 3rd and 4th barostat testing, done at 8 and 12 months, respectively), the pain threshold of the 20 IBS patients increased significantly (real values not given in the text but were extrapolated from figures) from ≈30 mm Hg to ≈36 mm Hg (the normal range being ≈34–44 mm Hg).

We absolutely agree with the authors that this increase in the pain threshold probably reflects a process of habituation (although definitive proof is indeed still lacking). However, we believe that this habituation process is not restricted to IBS. As the authors mention, a definite trend ($P > .1$) was noted; the mean discomfort threshold in their 12 healthy control subjects increased over time from ≈35–36 mm Hg to ≈42–43 mm Hg. It is striking to see in Figure 2 in the article that the longitudinal changes in discomfort thresholds revealed absolute parallel curves for IBS patients and for healthy controls, clearly suggesting that both groups had a similar evolution. Such an increase in visceral pain thresholds has been already described in healthy controls submitted to repeated distentions of the esophagus.[8] Consequently, if we can appreciate the increase in the measured pain threshold with repeated testing, we are not convinced that "visceral hypersensitivity normalized over time" as the authors said. In Figure 2, the distribution of normal controls cannot follow the hatched area extrapolated from the initial test, but must be adjusted for the control values obtained at 0, 4, 8, and 12 months specifically. The manuscript report did not allow us to perform statistical analyses, but the discomfort thresholds at each time point seem always lower in IBS patients than in the control subjects, the difference between IBS patients and controls being thus stable over time.

In our opinion, this most interesting paper therefore shows that visceral hypersensitivity is (1) present in IBS patients, (2) stable over a 4-month period, and (3) persistent over a longer period of 8–12 months (although the discomfort thresholds can vary over time).

CHRISTOPHE FAURE
Division of Gastroenterology
Department of Pediatrics
Université de Montréal
Montréal, Canada

MICKAEL BOUIN
PIERRE POITRAS
Division of Gastroenterology
Hôpital Saint-Luc
Université de Montréal
Montréal, Canada

1. Naliboff BD, Berman S, Suyenobu B, Labus JS, Chang L, Stains J, Mandelkern MA, Mayer EA. Longitudinal change in perceptual and brain activation response to visceral stimuli in irritable bowel syndrome patients. Gastroenterology 2006;131:352–365.
2. Mertz H, Naliboff B, Munakata J, Niazi N, Mayer EA. Altered rectal perception is a biological marker of patients with irritable bowel syndrome. Gastroenterology 1995;109:40–52.
3. Bouin M, Plourde V, Boivin M, Riberdy M, Lupien F, Laganiere M, Verrier P, Poitras P. Rectal distention testing in patients with irritable bowel syndrome: sensitivity, specificity, and predictive values of pain sensory thresholds. Gastroenterology 2002;122:1771–1777.
4. Faure C, Wieckowska A. Somatic referral of visceral sensations and rectal sensory threshold for pain in children with functional gastrointestinal disorders. J Pediatr (in press).
5. Poitras P, Riberdy Poitras M, Plourde V, Boivin M, Verrier P. Evolution of visceral sensitivity in patients with irritable bowel syndrome. Dig Dis Sci 2002;47:914–920.
6. Kuiken SD, Tytgat GN, Boeckxstaens GE. The selective serotonin reuptake inhibitor fluoxetine does not change rectal sensitivity and symptoms in patients with irritable bowel syndrome: a double blind, randomized, placebo-controlled study. Clin Gastroenterol Hepatol 2003;1:219–228.
7. Tack J, Broekaert D, Fischler B, Van Oudenhove L, Gevers A, Janssens J. A controlled cross-over study of the selective seroto-

nin reuptake inhibitor citalopram in irritable bowel syndrome. Gut 2006;55:1095–1103.
8. Worthen SF, Hanisen J, Aziz Q, Hobson AR. Effect of anxiety on the sensory and perceptual characteristics of visceral and somatic sensation. Gut 2005;54:A19.

doi:10.1053/j.gastro.2006.11.037

Reply. We appreciate the comments of Dr Faure and colleagues on our manuscript entitled "Longitudinal change in perceptual and brain activation response to visceral stimuli in irritable bowel syndrome patients."[1] They point out that the change in visceral perception over the course of the multiple testings observed in the patients with irritable bowel syndrome (IBS) may also occur in the control subjects, suggesting that the group differences in perceptual sensitivity would therefore remain constant despite the changes for both groups. The control subjects in our study did in fact show an increased discomfort threshold from the first to the fourth testing (39.6–43.5 mm Hg), which was not significant. The controls also showed a small but nonsignificant (11.7–10.9 cm) decline in ratings of the 50-mm Hg distention, which we did not report in the original paper. This measure decreased by about 1.4 cm in the IBS patients (see Figure 1*C* in the original article). Although we would argue that for both these measures the changes for the control subjects were somewhat smaller than that for the IBS subjects due to less vigilance, given the small sample of controls it is not really possible (nor was it a primary purpose of this study) to test directly group differences in the amount or temporal pattern of perceptual change. In any event, we do agree with Dr Faure and colleagues that, in a larger sample, one would expect to see significant changes in perception in the control subjects with repeated exposure, and that this is an important consideration for barostat studies.

We have also argued that cognitive and attentional factors such as vigilance, although very significant components of the perceptual response in IBS, are not exclusive mechanisms and in fact some degree of hypersensitivity may come from multiple other sources.[2–4] The primary purpose of the paper, however, was to test whether the perceptual response in IBS patients was to a significant extent modifiable by experience, and with experience, would the behavioral response move to within the range usually associated with normal perception? We also wanted to examine the central circuits associated with this modifiable part of the perceptual response we hypothesized was associated with hypervigilance. Hopefully, future studies will be able to more carefully examine the separate mechanisms of afferent input, attention, cognition, and pain modulation in both IBS and control subjects to better clarify these issues of visceral hypersensitivity.[5]

BRUCE D. NALIBOFF
EMERAN A. MAYER
Center for Neurovisceral Sciences and Women's Health
Departments of Medicine, Physiology, Psychiatry & Biobehavioral Sciences
Division of Digestive Diseases, and Brain Research Institute
David Geffen School of Medicine at the University of California
Los Angeles
and VA Greater Los Angeles Healthcare System
Los Angeles, California

1. Naliboff BD, Berman S, Suyenobu B, Labus JS, Chang L, Stains J, Mandelkern MA, Mayer EA. Longitudinal change in perceptual and brain activation response to visceral stimuli in irritable bowel syndrome patients. Gastroenterology 2006;131:352–365.
2. Naliboff BD, Munakata J, Fullerton S, Gracely RH, Kodner A, Harraf F, Mayer EA. Evidence for two distinct perceptual alterations in irritable bowel syndrome. Gut 1997;41:505–512.
3. Mayer EA, Collins SM. Evolving pathophysiologic models of functional gastrointestinal disorders. Gastroenterology 2002;122:2032–2048.
4. Mayer EA, Berman S, Suyenobu B, Labus J, Mandelkern MA, Naliboff BD, Chang L. Differences in brain responses to visceral pain between patients with irritable bowel syndrome and ulcerative colitis. Pain 2005;115:398–409.
5. Mayer EA, Naliboff BD, Craig AD. Neuroimaging of the brain-gut axis: from basic understanding to treatment of functional GI disorders. Gastroenterology 2006;131:1925–1942.

doi:10.1053/j.gastro.2006.11.036