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COMMENTARY

Irritable bowel syndrome, inflammatory bowel disease and TRPV1: How to disentangle the bundle

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In this issue, you will find a paper by Keszthelyi et al. entitled 'Alterations in mucosal neuropeptides in patients with irritable bowel syndrome and ulcerative colitis (UC) in remission: a role in pain symptom generation?' (Keszthelyi et al., 2013). The authors hypothesized that since transient receptor potential channel V1 (TRPV1) channel has been demonstrated to be up-regulated in irritable bowel syndrome (IBS) (Akbar et al., 2010), TRPV1 transcription might be increased in the sigmoid colonic mucosa of patients harbouring this condition; concentrations of neuropeptides that are oppositely regulated by TRPV1 would also be altered, thus giving evidence to a peripheral explanation of hypersensitivity in IBS. They compared sigmoid mucosal biopsies from IBS patients, UC in remission and healthy subjects, and correlated mucosal peptide concentrations with pain intensity measured by a questionnaire. TRPV1 transcription, substance P and somatostatin were all significantly increased in the colonic mucosa of IBS, but only TRPV1 correlated with pain intensity. A potential role of TRPV1 in pain generation was further vindicated by the observation that when UC patients with abdominal pain were analysed separately, TRPV1 transcription showed significant correlation with the composite score for pain.

TRPV1, the receptor responsible for the pain elicited by capsaicin application to viscera in several experimental and clinical models (Gonlachanvit et al., 2009; Brock et al., 2010; Bortolotti and Porta, 2011), is a polymodal nocisensor that can be sensitized by several pro-algogenic and inflammatory mediators, and the observation made in the present study on increased transcription in a condition lacking overt inflammation as IBS should not be surprising. In fact, several studies have demonstrated that IBS can follow acute bacterial gastroenteritis in a significant proportion of patients, symptoms may persist for years, and this is associated with persistent ongoing chronic inflammation (Spiller and Garsed, 2009). Others have reported greater numbers of intraepithelial lymphocytes in the colonic mucosa of IBS patients even when history of previous gastrointestinal infections is absent (Chadwick et al., 2002; Cremon et al., 2009), and, finally, Akbar et al. (2008) showed that increased TRPV1 nerve fibres in patients with IBS are associated with a low-grade inflammatory infiltrate also when the distal colonic mucosa was histologically normal. In this context, studies on visceral sensitivity involving inflammation-sensitive patterns like TRPV1 in PI-IBS as opposed to non PI-IBS are lacking and careful dissection of patients populations based on this assumption would be welcome. In addition, TRPV1 immunoreactive fibres are increased in the colon of inflammatory bowel disease (IBD) patients with IBS-like symptoms and correlate with pain (Akbar et al., 2010), and a recent meta-analysis showed that 39% (CI: 30–48%) of all IBD patients and 31% (CI: 21–43%) of UC patients in remission have symptoms of IBS (Halpin and Ford, 2012), among which pain and discomfort are the most frequent. Thus, the results of the present study are relevant to IBS as much as they are to UC and IBD in general, since such symptoms might be confusing to the clinician and might hinder the achievement of well-being in this subgroup of IBD patients. Moreover, drug treatments aiming at TRPV1 as a potential therapeutic target are therefore justified.

In this study, the questionnaire used to measure pain was derived from one developed for UC (Hamer et al., 2010) and a composite pain score was created, which includes an assessment of both intensity and frequency. The same authors (Keszthelyi et al., 2012), in a recent review, have discussed the heterogeneity of IBS pain rating scales in the experimental setting. These include thresholds of sensation and pain/discomfort, intensity of the perceived stimulus, elicitation of sensation in referral areas and their extension. This underlines the lack and, consequently, the need of instruments capable of measuring visceral pain based on uniform criteria, and possibly able at extricating the multi-modal components (physiological and psychological) of pain thresholds, both in the laboratory and in the clinical setting.

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Conflicts of interest
None declared.

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