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MEETING ABSTRACT

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Transient receptor potential ankyrin 1 channels participate in somatic pain hypersensitivity in experimental colitis

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Background: Gastrointestinal disorders such as inflammatory bowel disease (IBD) are associated with pain symptoms also described in rodent models of IBD such as that induced by dextran sulfate sodium (DSS). Central sensitization has been proposed to contribute to the somatic pain symptoms in IBD and related rodent models. The transient receptor potential ankyrin 1 (TRPA1) channel expressed by a subpopulation of primary sensory neurons of the dorsal root ganglion (DRG) and trigeminal ganglion (TG) is a major transducer of nociceptive signals produced by inflammation and tissue injury and is involved in hypersensitivity conditions. There is indication that TRPA1 contributes to visceral pain-like behavior in DSS-evoked colitis. The present study was designed to investigate the role of TRPA1 channels in the colitis-evoked mechanical and thermal hypersensitivity at the somatic level.

Methods: Colitis was induced in C57BL/6 male mice by adding 2% DSS to the drinking water for 7 days. Following this treatment, on day 8, control and DSS-treated mice were tested for various parameters of colitis as well as mechanical sensitivity in the abdominal and facial skin and thermal sensitivity in the plantar skin. Pharmacological blockade of TRPA1 by the selective antagonist HC-030031 (100 mg/kg, i.p.) and genetic deletion of TRPA1 were used to investigate the role of TRPA1 in DSS-induced colitis. The pain sensitivity to mechanical stimuli was evaluated with von Frey hairs (facial and abdominal region) and to thermal stimuli with the hot- and cold-plate method (plantar skin). Colitis-associated parameters, such as body weight, disease activity score, colon length, colon weight and colonic myeloperoxidase (MPO) activity, were measured. The expression of mRNA of various TRP channels (TRPA1, TRPV1 and TRPV4) was quantified in isolated DRGs and TGs of control and DSS-treated mice. On day 8, control and DSS-treated mice were also tested for behavioural (freezing, locomotion, rearing) and molecular changes (c-Fos in spinal cord) in response to a chemical pain stimulus (intrarectal instillation of 2% allylisothiocyanate; AITC) in the presence or absence of HC-030031 (100 mg/kg, i.p.).

Results: Induction of colitis was confirmed by a decrease in body weight and colon length and an increase in colon weight, disease activity score and MPO activity. DSS increased the mechanical (abdominal and facial) and thermal (hot) sensitivity in mice. The TRPA1 antagonist reduced mechanical sensitivity of both the abdominal and facial region. DSS treatment caused an increase in TRPA1 mRNA expression in the DRG. Intrarectal AITC evoked freezing behaviour which was reduced in the presence of the TRPA1 antagonist.

Discussion: Taken together, the current findings indicate that the TRPA1 channel participates in colitis-associated pain hypersensitivity at the somatic level.

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