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# Intracolonic infusion of faecal supernatant fraction from patients with diarrhoea-predominant irritable bowel syndrome evokes visceral hyperalgaesia in mice: reversal by a probiotic treatment

A. Ait-Belgnaoui[1], H. Eutamene[1], L. Ferrier[1], H. Durand[2], J. Fioramonti[1], L. Bueno[1] and V. Theodorou-Bayle[1]

[1]*UMR 1054 INRA/EI-Purpan, Toulouse, France and* [2]*LALLEMAND, Toulouse, France*

Irritable bowel syndrome (IBS), a functional gastrointestinal disorder affecting 5–20% of the population worldwide, is characterized by abdominal pain, altered bowel habits, 'low-grade' mucosal inflammation, impaired intestinal permeability and quantitative alterations in commensal microbiota. Faecal supernatant fractions from patients with diarrhoea-predominant IBS (IBS-D) have three to four times higher protease activity, and mucosal application of these supernatant fractions in mice induces visceral hyperalgaesia that is prevented by serine protease inhibitors(1). Despite an improvement in IBS symptoms by some probiotics, their mechanism of action remains poorly understood. Consequently, the aim was to evaluate in mice whether (a) a probiotic (*Lactobacillus farciminis*; *Lf*) prevents visceral hypersensitivity induced by intracolonic infusion of an IBS-D faecal supernatant fraction and (b) this effect is linked to the ability of *Lf* to reduce serine protease activity.

Four groups of ten mice received orally for 15 d either $10^9$ CFU *Lf*/d (groups 1 and 2) or saline (9 g NaCl/l); groups 3 and 4). Mice were equipped with NiCr electrodes in the abdominal muscle, and electromyographic (EMG) activity was recorded as an index of visceral pain. Noxious colo-rectal distensions (CRD) were performed using an embolectomy probe inserted into the rectum and inflated from 0 ml to 0.12 ml, in 0.02 ml steps, each lasting 10 s. A faecal supernatant fraction from IBS-D faecal materials (groups 2 and 4) or vehicle (groups 1 and 3) was infused intracolonically (300 µl), and CRD was performed 1 h after the infusion. Serine protease activity of an IBS-D faecal supernatant fraction was assessed *in vitro* in the presence of *Lf* growth and *Lf*-free culture medium.

Intracolonic administration of IBS-D faecal supernatant fractions significantly increased the abdominal EMG response at 0.08 ml and 0.1 ml CRD volumes when compared with the control. *Lf* treatment prevented the hypersensitivity induced by infusion of an IBS-D faecal supernatant fraction (amplitude of contraction (mV/s) at 0.08 ml CRD volume; 139 (SE 6) *v*. 94 (SE 10); $P<0.05$). Serine protease activity of an IBS-D faecal supernatant fraction was inhibited by *Lf* fresh growth medium (LGM) or filtered LGM to obtain bacteria-free culture medium (−69% and −71% respectively; $P<0.01$).

*Lf* or its metabolites reduce the serine protease activity of IBS-D faecal supernatant fractions, and *Lf* treatment prevents protease-mediated visceral hyperalgaesia induced by IBS-D faecal supernatant fraction. These results suggest the involvement of a protease inhibitory factor released by this strain in the beneficial effect observed.

1. Gecse C, Roka R, Ferrier L *et al*. (2008) *Gut* (In the Press).