

275 | Small intestine neuromuscular dysfunction in a mouse model of dextran sulfate sodium-induced colitis: Involvement of toll-like receptor-4

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Objective: Enteric commensal bacteria play a crucial role in the pathogenesis of inflammatory bowel disease (IBD), a group of recurring debilitating inflammatory conditions, triggered by inappropriate activation of the immune system by gut microbiota. IBD-associated specific mutations include genes involved in microbial recognition, such as mutations in the Toll-like receptor 4 (TLR4). In this study, we aimed to assess the impact of TLR4 signaling on the structural and functional integrity of enteric nervous system (ENS) in a model of dextran sulfate sodium (DSS)-induced colitis.

Methods: Male TLR4^{-/-} mice (8 ± 1 weeks old; N = 32 mice) received 1.5% DSS in their drinking water for 5 days, then switched to regular drinking water for 3 days. Inflammation was measured using the disease activity index and by histologic analysis of intestinal tissues. Changes in ileal muscle tension were isometrically recorded following: i) electric field stimulation (EFS, 10 Hz); ii) addition of 30 μM serotonin (5-HT) with or without 0.1 μM ondansetron (5-HT3R antagonist). Plasma levels of 5-HT were measured by HPLC with fluorescence detection. Distribution of neuronal (HuCD and nNOS), glial (GFAP) and 5-HT3R markers was determined by immunofluorescence in longitudinal-muscle-myenteric plexus whole-mounts (LMMPs).

Results: In vitro contractility studies in TLR4^{-/-} mice showed a significant reduction in 5-HT-induced excitatory response (-50%, N = 8, P < 0.001), sensitive to ondansetron (N = 8, P < 0.001), and a 1.9-fold increase of neuronal cholinergic transmission (at 10 Hz; N = 8, P < 0.01) after DSS treatment. Changes in ENS neurochemical coding were evidenced by the reduction of nNOS⁺ neurons (-32%, N = 5; P < 0.05) with a proportional increase of HuCD⁺ neurons, together with a slight but not significant reduction of 5-HT3R and GFAP immunofluorescence in DSS-treated TLR4^{-/-} LMMPs. A marked increase in 5-HT plasma levels (15 ± 5%, N = 5; P < 0.05) was found after DSS treatment.

Conclusions: In mice, TLR4 signaling influences the severity of small intestine inflammation as well as ENS structure and neurochemical coding, affecting cholinergic- and serotonergic-mediated neuromuscular function.

276 | Intraintestinal delivery of tastants using a naso-duodenal-ileal catheter does not influence food intake or satiety

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Objective: Intra-duodenal activation of taste receptors has been shown to increase satiety and reduce food intake. Taste receptors are expressed throughout the whole gastrointestinal (GI) tract. Currently it is unknown, whether the effect of taste receptor activation to influence satiety and food intake is more pronounced in the proximal or distal GI tract.

The aim of the present study was to investigate the effects of intra-duodenal- vs intra-ileal infusion of a tastant mixture (sweet, bitter, and umami) on food intake and satiety feelings.

Methods: Fourteen healthy volunteers (11 female, age 25.6 ± 10.5 years, mean BMI 22.3 ± 1.7 Kg/m²) were intubated with a naso-duodenal-ileal catheter. In a single-blind randomized controlled trial, participants received four regimens on consecutive test days: duodenal placebo and ileal placebo (DPIP), duodenal tastants and ileal placebo (DTIP), duodenal placebo and ileal tastants (DPIT), duodenal tastants and ileal tastants (DTIT). On test days, 150 minutes after a standardized breakfast, mixtures were infused for 60 minutes. Fifteen min after cessation of infusion, participants received an *ad libitum* pasta meal and food intake was measured. Visual analogue scales (VAS) scores for satiety feelings and GI symptoms were collected over the course of the test day.

Results: Intraintestinal infusion of the tastant mixture did not alter food intake compared with intraintestinal infusion of placebo (DPIP: 786.6 ± 79.2 kcal, DTIP: 803.3 ± 69.0 kcal, DPIT: 814.7 ± 77.3 kcal, DTIT: 834.8 ± 59.2 kcal, P 0.59). No differences in VAS scores for satiety feelings and GI symptoms were observed.

Conclusions: Within the setting of the present study, infusion of a tastant mixture into the duodenum and/or the ileum using a naso-duodenal-ileal catheter did not influence food intake or satiety feelings. It is possible that the burden of the four-day naso-duodenal-ileal intubation masked a small effect that tastants might have on food intake and satiety.

278 | Prevalence and impact of self-reported constipation in the general population

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Objective: Chronic constipation (CC), as defined by the Rome IV criteria, is a highly prevalent functional bowel disorder. However, as the criteria impose strict diagnostic thresholds, the prevalence of self-reported constipation is considerably higher, and there is major overlap