Methods: Our approach involves a histological examination of the gastrointestinal tract, organ bath experiments, oesophageal manometry and behavioural testing.

Results: Expression of Foxp1 was detected in all segments of the gastrointestinal tract, and was reduced in *Foxp1*$^{+/-}$ mice. *Foxp1*$^{+/-}$ tissue showed a marked atrophy of the tunica muscularis in the oesophagus and colon. Moreover *Foxp1*$^{+/-}$ animals have a lower body weight than wild type mice and display altered feeding behaviour with decreased food and water intake. We detected a pronounced defect in nitric oxide-induced relaxation of the lower oesophagus sphincter which was subsequently confirmed by manometry. In addition to achalasia, total gut transit was significantly prolonged most likely due to impaired colonic contractility and peristalsis.

Conclusions: Overall, our findings indicate for the first time that the observed gastrointestinal disturbances in patients with FOXP1 syndrome may be caused by impaired motility, specifically in the oesophagus and colon. Furthermore, this is the first report of achalasia attributed to a heterozygous gene deletion.

196 | Impact of high-fat diet and toll-like receptor 4 signaling on the integrity of mouse enteric and central nervous systems

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Objective: Toll-like receptor 4 (TLR4) is involved in controlling neuroplasticity of both enteric and central nervous systems (ENS and CNS). Our aim was to investigate the role of TLR4 in the neuroglial rearrangements of ENS and CNS in a mouse model of high-fat diet-induced obesity.

Methods: TLR4$^{-/-}$ (N = 16) and wild-type (WT; N = 16) C57BL/6J male mice (age = 6 ± 2 weeks) were fed with standard-diet (SD; fat: 18% kcal) or high-fat diet (HFD, fat: 60% kcal) for 8 weeks. Ileal longitudinal muscle-myenteric plexus whole-mounts and hippocampus frozen-sections were analyzed to evaluate the distribution of neuronal marker HuC/D, astroglial markers S100β and GFAP, and macrophage/microglia marker Iba1.

Results: In the ENS of TLR4$^{-/-}$ mice, SD determined a reduction of the total number of HuC/D$^+$ neurons (−11%, N = 4, $P < 0.05$) together with increased S100β immunoreactivity (+80%, N = 4, $P < 0.01$) and higher number of Iba1$^+$ muscularis macrophages (+33%, N = 4, $P < 0.05$), with no changes in GFAP$^+$ gliofilament length. In both genotypes, HFD determined a significant increase in the total number of myenteric HuC/D$^+$ neurons (+13% in WT mice and + 27% in TLR4$^{-/-}$ mice, N = 4, $P < 0.05$) and enteric gliosis together with a marked reduction of Iba1 immunofluorescence (−50% in WT mice, −68% in TLR4$^{-/-}$ mice, N = 4, $P < 0.05$).

In the hippocampus of TLR4$^{-/-}$ mice fed with SD, a marked loss of HuC/D$^+$ neurons (−30%, N = 4, $P < 0.01$) was accompanied with a significant GFAP$^+$ density index enhancement (+27%, N = 4, $P < 0.05$) and GFAP$^+$ gliofilament length (+70%, N = 4, $P < 0.05$) with no difference in S100β density index. In WT hippocampus, HFD caused a marked reduction in the total number of HuC/D$^+$ neurons (−34%, N = 4, $P < 0.05$) and microglia activation, evidenced by increased Iba1 immunofluorescence (+33%, N = 4, $P < 0.05$).

Conclusions: These findings highlight that TLR4 is involved in high-fat diet neuro-glial plasticity in both ENS and CNS.

197 | Comparison of MRI assessed small bowel dysmotility in irritable bowel syndrome (IBS) and healthy controls

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Objective: Irritable bowel syndrome (IBS) is characterised by gastrointestinal symptoms, subclassified into constipation-predominant IBS (IBS-C), diarrhoea-predominant IBS (IBS-D) and mixed IBS (IBS-M) [Drossman, D. A., 2016]. Abnormal motility patterns have been hypothesised as a key cause of symptoms. Quantitative measures of motility can be derived from routine clinical small bowel Magnetic Resonance Enterography (MRE) using advances in medical imaging post-processing [Odille, F. et al., 2012]. In this study, we investigate whether there are differences in motility patterns between IBS subgroups and healthy controls.

Methods: 34 IBS patients and 20 healthy controls (HCs) underwent MRE at SUS, Sweden, after ingesting 1 L of macrogol 3350 solution 45 minutes prior the scan. The MRE protocol included a free breathing (minimum 50 seconds) cine motility sequence, repeated to encompass the whole small bowel volume. Visual Analogue Scale for IBS (VAS-IBS) to assess current abdominal symptoms was available [Bengtsson M, Hammar O, Mandl T, Ohlsson B., 2011]. A total of 5 motility analysis metrics were developed to assess 1) mean motility, 2) spatial motility variability, 3) temporal motility variability, 4) area of active bowel and 5) distension (figure 1A). For each metric, Kruskal-Wallis was performed to see if there were differences between IBS subgroups (IBS-M, IBS-C, IBS-D) and HCs, followed by Mann-Whitney U to determine which 2 groups showed differences.

Results: Differences were found between IBS-M and IBS-C for mean motility, temporal variation and area of active bowel (all $P < 0.005$) (figure 1B). Specifically, values were significantly lower in IBS-C. No significant differences were found between IBS overall or IBS subgroups and HCs (figure 1B).

Conclusions: This preliminary study suggests that there are potential small bowel motility differences between IBS-C patients, and other subtypes, notably IBS-M. Motility metrics are highly variable in health and not significantly different to IBS patients overall. However this normal variability appears to be reduced in IBS-M and IBS-C subtypes.