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The gut–mood axis: a novel role of the gut hormone peptide YY on emotional-affective behaviour in mice

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Background

Peptide YY (PYY) and neuropeptide Y (NPY) are members of the PP-fold peptide family. PYY is expressed by endocrine cells of the gut, whereas NPY occurs in enteric, sensory, cerebral and autonomic neurons. While PYY is involved in the regulation of gut function and satiety, NPY is known to contribute to the regulation of emotional-affective behaviour, cognition, seizure activity, pain and satiety. Since we have previously found that the NPY system plays a role in the gut–brain axis, we explored in which way knockout of PYY and PYY plus NPY alters the emotional-affective behaviour in mice and how this phenotype is altered by experimental colitis.

Methods

Male wildtype (WT), PYY (PYY^{-/-}) and PYY plus NPY (PYY+NPY^{-/-}) knockout mice, all with a mixed C57BL/6:129/SvJ (1:1) background, were used. Mild colitis was induced by adding dextran sulphate sodium (DSS, 2%) to the drinking water for 7 days. Inflammation was assessed by the colonic myeloperoxidase content, anxiety-related behaviour was evaluated with the elevated plus maze (EPM) and open field (OF) tests, and depression-like behaviour was estimated with the forced swim test (FST).

Results

When the animals were phenotyped in the absence of colitis, anxiety-like behaviour in the EPM (reduction of open arm time) was increased in both PYY^{-/-} and PYY+NPY^{-/-} mice, whereas locomotion remained unaltered. The results obtained in the OF test were largely similar. The depression-like behaviour (immobility) in the FST was markedly enhanced in both PYY^{-/-} and PYY+NPY^{-/-} mice. DSS-induced colitis was associated with an increase in the colonic myeloperoxidase content. On the behavioural level, colitis had genotype-dependent effects on emotional-affective behaviour. Most conspicuous was that colitis increased anxiety primarily in WT mice so that in the EPM test WT mice spent less time on the open arms than the knockout animals. Similar changes were observed in the OF test. In contrast, colitis did not alter depression-like behaviour in WT and PYY+NPY^{-/-} mice but reduced immobility in PYY^{-/-} mice.

Conclusions

These data show for the first time that the gut hormone PYY has a significant impact on emotional-affective behaviour, because its deletion enhances anxiety- and depression-related behaviour. Colitis enforces anxiety-like behaviour only in the presence of PYY, whereas in the absence of PYY depression is less pronounced in animals with colitis. These data attest to an important role of PYY in the gut–mood axis.