Control of murine affective behaviour in health and intestinal inflammation by the gut hormone peptide YY

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Purpose of the study

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 central and peripheral neurons. While PYY is involved in the regulation of gut function and satiety, NPY controls emotional-affective behaviour, cognition, seizure activity, pain and appetite. 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 NPY alters emotional-affective behaviour in mice and whether the effect of gene deletion is modified by experimental colitis.

Methods

Male wildtype (WT), PYY (PYY-/-), NPY (NPY-/-) 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 evaluated with the elevated plus maze (EPM) test, and depression-like behaviour estimated with the forced swim test (FST). The circulating levels of corticosterone were determined with a sensitive enzyme immunoassay.

Results

In the absence of colitis, anxiety (reduction of open arm time) and locomotion on the EPM were increased in NPY-/- mice, but not in PYY-/- and PYY+NPY-/- mice.

Depression-like behaviour (time of immobility) in the FST was enhanced in PYY-/-, NPY-/- and PYY+NPY-/- mice.

In PYY-/- mice, plasma corticosterone at baseline was higher than in the other genotypes. FST increased corticosterone in all genotypes, particularly in NPY-/- mice.

DSS-induced colitis enhanced the colonic content of myeloperoxidase in all genotypes, this effect being smallest in NPY-/- mice.

Colitis had genotype-dependent effects on emotional-affective behaviour. It increased anxiety in WT and NPY-/- mice, but not in PYY-/- and PYY+NPY-/- mice.

In the FST, colitis reduced the time of immobility in PYY-/- mice but not in the other genotypes. The FST-induced rise of plasma corticosterone was amplified by colitis in all genotypes except in NPY-/- mice.

Conclusions

- Knockout of both NPY and PYY increases depression-like behaviour, whereas anxiety-like behaviour is enhanced only in NPY-/- mice, this anxiogenic effect of NPY deletion being cancelled by additional knockout of PYY.
- The anxiogenic action of DSS-induced colitis seen in WT mice is retained in NPY-/- mice but blunted by knockout of PYY or PYY plus NPY.
- Colitis does not affect depression-like behaviour, except in PYY-/- mice in which it has an antidepressant action.
- These genotype-dependent changes in emotional-affective behaviour are accompanied by distinct alterations in the activity of the hypothalamic-pituitary-adrenal axis.
- The current data attest to a novel role of the gut hormone PYY in regulating affective behaviour in health and intestinal disease.