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Meeting abstract

Long-term depression-like effect of a single immune challenge in neuropeptide Y Y_2 and Y_4 receptor knockout mice

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Background and aims

Deletion of neuropeptide Y (NPY) Y_2 and Y_4 receptors reduces anxiety-like and depression-related behaviour [1]. We have previously found that Y_2 receptor knockout ($Y_2^{-/-}$) mice are particularly sensitive to the short-term anxiogenic effect of immune stress evoked by systemic lipopolysaccharide (LPS) [2]. In the present study we investigated whether LPS challenge has long-term effects on anxiety-like and depression-related behaviour and whether these effects are altered in $Y_2^{-/-}$ and $Y_4^{-/-}$ mice.

Materials and methods

Adult control and germline $Y_2^{-/-}$ and $Y_4^{-/-}$ mice were used. Anxiety-like behaviour was assessed on the elevated plus maze, and depression-related behaviour was estimated with the forced swim test. These tests were carried out 1 day or 4 weeks after a single intraperitoneal injection of LPS (0.83 mg/kg) or vehicle (sterile saline).

Results

Relative to control animals, vehicle-treated $Y_2^{-/-}$ and $Y_4^{-/-}$ mice were less anxious and displayed reduced depression-like behaviour. One day after LPS injection, anxiety-like behaviour remained unaltered in control animals but was markedly enhanced in $Y_2^{-/-}$ and $Y_4^{-/-}$ mice. Four weeks post-treatment, the anxiogenic effect of LPS was still seen in $Y_4^{-/-}$ mice but had gone in control and $Y_2^{-/-}$ mice. Depression-related behaviour was enhanced 1 day after LPS treatment in control and $Y_2^{-/-}$ mice, but not in $Y_4^{-/-}$ mice. Four weeks post-treatment, the effect of LPS challenge to increase depression-like behaviour had waned in control mice, but was still present in $Y_2^{-/-}$ mice and was first observed in $Y_4^{-/-}$ mice.

Conclusion

$Y_2^{-/-}$ and $Y_4^{-/-}$ mice are particularly susceptible to the effects of immune stress to cause a long-term enhancement of anxiety- and depression-like behaviour. With Y_2 and Y_4 receptors playing distinct roles in these persistent alterations of emotional-affective behaviour, it is emerging that endogenous NPY has an important bearing on immune signalling to the brain.

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