

MEETING ABSTRACT

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Reduced fear conditioning after viral vector mediated neuropeptide Y administration into the basolateral amygdala

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Background

Neuropeptide Y (NPY) is a 36-amino-acid peptide that is abundantly expressed in the central nervous system. It is involved in various physiological and pathophysiological processes, including energy homeostasis, pain and epilepsy, but also in anxiety and depression. Consistent findings have demonstrated an anxiolytic effect of NPY. The presence of different NPY receptors in the amygdala and the effects of NPY on anxiety raise the question, whether NPY and its receptors may influence acquisition and extinction of conditioned fear. Therefore, we investigated NPY and NPY receptor knockout mice in Pavlovian fear conditioning.

Methods

Pavlovian fear conditioning is a simple form of associative learning. NPY knockout (NPY-KO) mice as well as Y receptor knockout mice (Y₁, Y₂, Y₄ and Y₁/Y₂ double KO) were subjected to a discriminative delay fear-conditioning paradigm. Extinction learning was performed the following day by repetitive exposure to the tone in the absence of a foot shock.

Results

In cued fear conditioning NPY-KO mice acquire higher freezing levels and show increased expression and impaired extinction of conditioned fear. Y₁-KO mice show faster conditioning and delayed extinction, whereas Y₂-KO mice are similar to wildtype mice. Compared to Y₁-KO mice, however, Y₁/Y₂ double KO mice exhibited

enhanced fear acquisition and impaired between session extinction, indicating an important role of Y₂ receptors in these processes. Interestingly, Y₄-KO mice show normal fear conditioning but impaired extinction. Adeno-associated viral (AAV) vector-mediated over-expression of NPY in the basolateral amygdala (BLA) of NPY-KO mice significantly reduced the increased fear acquisition of NPY-KO mice. In addition, extinction was significantly improved after AAV-induced over-expression of recombinant NPY (rNPY) in the BLA of NPY-KO mice. No change was observed, however, after over-expression of rNPY in the central amygdala.

Conclusions

Our data indicate that NPY has an inhibitory role in the acquisition and facilitates extinction of conditioned fear. These effects seem to be mediated predominantly in the BLA. In particular, the Y₁ receptor may modulate the acquisition of fear, whereas for extinction a concerted action of Y₁ and Y₄ receptors seems to be conceivable.

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