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Neuropeptide Y in the basolateral amygdala modulates the acquisition of conditioned fear

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Background

Neuropeptide Y (NPY), a highly conserved 36 amino acid peptide, is widely distributed in the central nervous system. Besides its functions in various metabolic processes NPY has attracted considerable attention in modulating emotional-affective behavior. NPY exerts a pronounced anxiolytic effect most likely mediated by Y_1 receptors, whereas stimulation of predominantly presynaptic Y_2 receptors results in increased anxiety. The role of NPY in the processing of fear, however, is still not conclusive. The current study aims to elucidate the role of NPY in Pavlovian fear conditioning, a simple form of associative learning.

Methods

NPY KO mice as well as KO mice for the different NPY receptors (Y_1, Y_2 and Y_4) were subjected to a delay fear-conditioning paradigm (5 tone/shock pairings), followed by an extinction session 24 h later (40 tone alone presentations).

Results

NPY KO mice revealed faster acquisition and excessive expression of conditioned fear. Baseline freezing was increased on retention/extinction day and the ability to distinguish an explicitly paired tone from an unpaired tone was limited, both indications for a generalization of conditioned fear. Moreover, NPY KO mice displayed a pronounced deficit in the extinction of fear memory. Within session, extinction as well as extinction recall were significantly impaired in NPY KO mice. Expression of NPY by an AAV-vector in the basolateral amygdala (BLA) partly ameliorated deficits seen in NPY KO mice. Y_1 KO mice showed increased acquisition and delayed extinction, whereas no obvious phenotype was seen in Y_2 KO mice. Y_4 KO mice exhibited a significant deficit in fear extinction.

Conclusions

Our data indicate that NPY in the BLA exerts a protective role in the acquisition of fear memories. In addition, it facilitates extinction of conditioned fear. Experiments performed in Y receptor KO mice suggest a prominent role of the Y_1 receptor in acquisition and extinction of conditioned fear, whereas Y_4 receptors seem to be involved in extinction learning.

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