Open Access Meeting abstract The role of NPY in expression and extinction of conditioned fear Dilip Verma¹, Ramon O Tasan^{*1}, Herbert Herzog² and Günther Sperk¹

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from 15th Scientific Symposium of the Austrian Pharmacological Society (APHAR) Joint meeting with the Hungarian Society of Experimental and Clinical Pharmacology (MFT) and the Slovenian Pharmacological Society (SDF) Graz, Austria. 19-21 November 2009

Published: 12 November 2009

BMC Pharmacology 2009, 9(Suppl 2):A33 doi:10.1186/1471-2210-9-S2-A33

This abstract is available from: http://www.biomedcentral.com/1471-2210/9/S2/A33

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Background

Neuropeptide Y is a highly conserved 36 amino acid peptide that is widely distributed in the peripheral and central nervous systems. Besides its functions in various metabolic processes, NPY has attracted considerable attention in modulating emotional-affective behavior. NPY exerts a solid anxiolytic effect most likely mediated by Y₁ receptors, whereas stimulation of predominantly pre-synaptic Y₂ receptors results in increased anxiety. However, little is known about an involvement of NPY in processing of fear.

Methods

The current study aims to elucidate the role of NPY in Pavlovian fear conditioning, a simple form of associative learning. NPY knockout (NPY KO) mice as well as knockout mice for the different NPY receptors $(Y_1, Y_2, Y_4 \text{ and } Y_1/$ Y₂ double KO) were subjected to a delay fear-conditioning paradigm (5 presentations of a tone co-terminating with a mild electric foot shock, 0.7 mA). Extinction learning was performed the following day by repetitive exposure to the tone (40 presentations) in the absence of a foot shock.

Results

Compared to wild-type controls, NPY KO mice revealed faster acquisition and augmented expression of conditioned fear. Baseline freezing was increased on retention/ extinction day, indicating a generalization of conditioned fear. Moreover, NPY KO mice displayed a pronounced deficit in the extinction of fear memory. Within sessions,

extinction as well as extinction recall were significantly impaired in NPY KO mice. Conversely, acquisition of fear was reduced in Y₂ KO mice. Interestingly, no corresponding changes in extinction of conditioned fear were seen in Y₂ KO mice. However, Y₄ KO mice exhibited an impairment in fear extinction, similar to the one seen in NPY KO mice.

Conclusion

Our data indicate that NPY has a protective role in the acquisition of fear memories. In addition, it facilitates extinction of conditioned fear. Results from Y receptor KO mice suggest that Y₁ and Y₂ receptors are the most likely candidates for modulating the acquisition of fear, whereas for extinction a concerted action of Y1 and Y4 receptors seems to be conceivable.