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Meeting abstract

Increased novelty-induced motor activity and reduced depression-like behavior in NPY Y_4 receptor knockout mice

Ramon O Tasan*[1], Shu Lin[2], Alfred Hetzenauer[3], Nicolas Singewald[3], Herbert Herzog[2] and Günther Sperk[1]

Address: [1]Department of Pharmacology, Medical University of Innsbruck, 6020 Innsbruck, Austria, [2]Neuroscience Research Program, Garvan Institute of Medical Research, Sydney, New South Wales 2010, Australia and [3]Department of Pharmacology and Toxicology, Institute of Pharmacy and Center of Molecular Biosciences Innsbruck (CMBI), University of Innsbruck, 6020 Innsbruck, Austria

Email: Ramon O Tasan* - ramon.tasan@i-med.ac.at

* Corresponding author

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There is growing evidence that neuropeptide Y acting through Y_1 and Y_2 receptors has a prominent role in modulating anxiety- and depression-like behavior in rodents. However, a role of other Y receptors like that of Y_4 receptors in this process is poorly understood. We now investigated male Y_2, Y_4 single and Y_2/Y_4 double knockout mice in behavioral paradigms for changes in motor activity, anxiety and depression-like behavior. Y_4 and Y_2 knockout mice revealed an anxiolytic phenotype in the light/dark test, marble-burying test and motor-activity independent in stress-induced hyperthermia, and reduced depression-like behavior in the forced swim and tail suspension tests. In Y_2/Y_4 double knockout mice, the response in the light/dark test and in the forced swim test was further enhanced compared to Y_4 and Y_2 knockout mice, respectively. Motor activity was increased in Y_2, Y_4 and Y_2/Y_4 knockout mice under changing and stressful conditions, but not altered in a familiar environment. High levels of Y_4 binding sites were observed in brain stem nuclei including nucleus of solitary tract and area postrema. Lower levels were found in the medial amygdala and hypothalamus. Peripheral administration of PP induced Y_4 receptor-dependent c-Fos expression in brain stem, hypothalamus and amygdala. PP released peripherally from the pancreas in response to food intake, may act not only as a satiety signal but also modulate anxiety-related locomotion. Lack of central Y_4 receptors appears to be responsible for the alterations in behavior seen in Y_4 and Y_2/Y_4 knockout mice suggesting a potential new target to treat anxiety-related disorders.

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