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Meeting abstract



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

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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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