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MEETING ABSTRACT

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The effect of intranasal neuropeptide Y on high-fat diet-induced anhedonia

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Background: Western diet contains a high percentage of saturated fatty acids and is dense in energy, which leads to overeating and the development of diet-induced obesity. There is growing evidence about the role of obesity in the development of mental health disorders such as major depression. Metabolic disturbances implicated in the development of depressive mood due to diet-induced obesity include dysregulation of the hypothalamic–pituitary–adrenal axis, release of proinflammatory cytokines, leptin and insulin resistance. In addition, both patients with mild depressive disorder and mouse models of high-fat diet (HFD)-induced depression show lower expression of neuropeptide Y (NPY), a peptide with antidepressant, anxiolytic and orexigenic properties. Therefore, the aim of this study was to evaluate the effect of intranasal NPY on HFD-induced anhedonia and its potential as a new therapeutic approach.

Methods: In this study, we fed 48 male mice a HFD containing 48 kJ% of fat or a control diet containing 12 kJ% of fat for a period of 8 weeks. Mice were housed in cages of two under standard laboratory conditions. Subsequently, the mice were placed in single cages in order to perform the sucrose preference test (SPT) to evaluate anhedonia. On day 2 and day 4 of SPT either NPY or sterile distilled water was applied intranasally at a dose of 100 µg per mouse. Mice were sacrificed 3 hours after the second NPY application. The same experiment was repeated in Y_2 receptor knockout mice.

Results: HFD reduced NPY gene expression and protein levels in the hypothalamus. Intranasal NPY reduced sucrose preference in the HFD group 3 hours after application, which is indicative of anhedonia. This effect was accompanied by lower food intake, greater weight loss and increased corticosterone levels in plasma. Sucrose preference, food intake and body weight remained unchanged in the experiment with Y_2 knockout mice.

Discussion: Our results are contrary to current knowledge about NPY as an orexigenic and antidepressant peptide. The fact that NPY inhibited food intake and induced anhedonia in the SPT may be due to the sedative effect of NPY, which occurs at higher doses. Another possible explanation might be a desensitization to NPY by HFD. Since no effect was seen in the Y_2 knockout group, the Y_2 receptor may also play a role in our observations.

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Keywords: depression-like behaviour – hypothalamus – sucrose preference – neuropeptide Y

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