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Function of neuropeptide Y within the nucleus of the solitary tract in food intake

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Neuropeptide Y (NPY) is a highly conservative neuropeptide expressed in the central and peripheral nervous systems and is involved in the regulation of different physiological functions. NPY localised within the hypothalamus is well established to stimulate hunger[1,2,3]. The nucleus of solitary tract (NTS) is another key homeostatic brain region that integrates and modulates peripheral signals and originates a range of neuroactive substances orchestrating the metabolic state[4,5]. We hypothesised that NPY NTS neurons could also be involved in the regulation of the feeding behaviour.

The Cre-dependant chemogenetic technique Designer Receptors Exclusively Activated by Designer Drugs (DREADD) was used in adult male NPY-Cre mice to examine the effect of NPY in the NTS on feeding behaviour. NPY-Cre mice (n = 17) were stereotaxically injected with a viral construct consisted of an activating DREADD (DREADD-Gq) or inhibiting DREADD (DREADD-Gi) and a marker gene (mCherry) into the NTS. To manipulate the activity of the transducted receptors, designer drug clozapine-N-oxide (CNO) was used (1 mg/kg/10 ml, i.p.). Food intake and body weight was measured. All studies were conducted in accordance with The Animals (Scientific Procedures) Act 1986 and the principles of the 3Rs. The raw data were checked for outliers, which were removed from the further analysis. Two-tailed paired t-test or Wilcoxon sign-rank test were used to analyse the data statistically. The difference was considered significant at $p < 0.05$. The data are presented as Mean ± SEM.

The activation of NPY neurons with designer drug CNO in DREADD-Gq-mCherry group significantly stimulated differential and cumulative food intake at 1, 3 and 5 hours post-treatment as compared with control saline treatment using a within subjects design. This increase led to a rise in body weight change (−0.76 ± 0.14 vs −1.41 ± 0.05 g of body weight change for 5 h, n = 6, p = 0.0067). Conversely, the inhibition of NPY neurons with CNO in DREADD-Gi-mCherry group significantly reduced cumulative food intake at 1, 3 and 5 hours, which was associated with an alteration in body weight change (0.02 ± 0.10 vs 0.33 ± 0.07 g of body weight change for 5 h, n = 8, p = 0.0234).

To summarize, here we report the impact of the NPY NTS neurons on the appetite and body weight regulation. We found that the activation of the NPY NTS neurons stimulated hunger, caused a rise in food intake and body weight gain, whereas the inhibition of these cells decreased hunger, reduced food intake and decelerated body weight gain in the refeeding stage.

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