

Título: Growth hormone secretagogue receptor signaling in dopamine neurons mediates high fat diet intake in a binge-like eating protocol”.

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Ghrelin is a peptidic hormone that regulates a variety of biological processes, including energy homeostasis. Ghrelin induces food intake when administered to rodents and humans and this orexigenic effect is exerted through binding of the hormone to the growth hormone secretagogue receptor (GHSR), a G protein-coupled receptor mainly expressed in the brain. Ghrelin regulates both the homeostatic and the hedonic components of food intake, acting on hypothalamic and mesolimbic neuronal circuits, respectively. GHSR is present in different neuronal populations of these circuits and, particularly, GHSR-expressing dopamine neurons of the mesolimbic circuit are involved in ghrelin's regulation of food reward. In this study, we investigated the role of GHSR-expressing dopamine neurons in the regulation of the different ghrelin's biological effects. We utilized a genetically modified mouse model in which Cre recombinase is expressed exclusively in dopamine neurons (DAT-Cre mice). We crossed DAT-Cre mice to a mouse model in which GHSR expression is blocked by a LoxP-flanked transcription blocking cassette (GHSR-deficient mice) in order to generate mice expressing GHSR selectively in dopamine neurons (GHSR-deficient/DAT-Cre mice). We first tested if the GHSR-deficient/DAT-Cre mice were useful to study the effect of GHSR expression exclusively in dopamine neurons. Then, we studied the effect of peripheral ghrelin administration to GHSR-deficient/DAT-Cre mice. We also studied the effect of central ghrelin administration in the locomotor activity and food intake of GHSR-deficient/DAT-Cre mice. Finally, we used a binge-like eating and a conditioned place preference protocol in order to determine the role of GHSR-expressing dopamine neurons in the regulation of ingestive behaviors. Our results indicate that ghrelin receptor signaling in dopamine neurons mediates complex feeding behaviors while the selective expression of GHSR in dopamine neurons is not sufficient to restore ghrelin-induced food intake and locomotor activity