Ghrelin

The etymology of the word is an acronym: GHR (“growth hormone-releasing peptide”) + -lin (“a common hormone suffix”), with an incidental pun on both Proto-Indo-European *g^{h}reh$_{1}$- (“to grow”) and English growling.

It is often referred to as “the hunger hormone”. Also known as lenomorelin (INN), it is a peptide hormone produced by ghrelinergic cells in the gastrointestinal tract which functions as a neuropeptide in the central nervous system.

Besides regulating appetite, ghrelin also plays a significant role in regulating the distribution and rate of use of energy.

When the stomach is empty, ghrelin is secreted. When the stomach is stretched, secretion stops.a It acts on hypothalamic brain cells both to increase hunger, and to increase gastric acid secretion and gastrointestinal motility to prepare the body for food intake.

Ghrelin receptor

The receptor for ghrelin, the ghrelin/growth hormone secretagogue receptor (GHS-R), is found on the same cells in the brain as the receptor for leptin, the satiety hormone that has opposite effects from ghrelin.

Ghrelin also plays an important role in regulating reward perception in dopamine neurons that link the ventral tegmental area to the nucleus accumbens (a site that plays a role in processing sexual desire, reward, and reinforcement, and in developing addictions) through its colocalized receptors and interaction with dopamine and acetylcholine.

Ghrelin is encoded by the GHRL gene and is presumably produced from the cleavage of the prepropeptide ghrelin/obestatin. Full-length preproghrelin is homologous to promotilin and both are members of the motilin family.

Ghrelin, a brain-gut peptide, has been proven to exert neuroprotection in different kinds of neurological diseases; however, its role and the potential molecular mechanisms in secondary brain injury (SBI) after intracerebral hemorrhage (ICH) are still unknown. In this study, we investigate whether treatment with ghrelin may attenuate SBI in a murine ICH model, and if so, whether the neuroprotective effects are due to the inhibition of nucleotide-binding oligomerization domain-like receptor pyrin domain-containing 3 (NLRP3) inflammasome activation and promotion of nuclear factor-E2-related factor 2 (Nrf2)/antioxidative response element (ARE) signaling pathway. Stereotactically intrastriatal infusion of autologous blood was performed to mimic ICH. Ghrelin was given intraperitoneally immediately following ICH and again 1 h later. Results showed that ghrelin attenuated neurobehavioral deficits, brain edema, hematoma volume, and perihematomal cell death post-ICH. Ghrelin inhibited the NLRP3 inflammasome activation and subsequently suppressed the neuroinflammatory response as evidenced by reduced microglia activation, neutrophil infiltration, and pro-inflammatory mediators release after ICH. Additionally, ghrelin alleviated ICH-induced oxidative stress according to the chemiluminescence of luminol and lucigenin, malondialdehyde (MDA) content,

and total superoxide dismutase (SOD) activity assays. These changes were accompanied by upregulation of Nrf2 expression, Nrf2 nuclear accumulation, and enhanced Nrf2 DNA binding activity, as well as by increased expressions of Nrf2 downstream target antioxidative genes, including NAD(P)H quinine oxidoreductase-1 (NQO1), glutathione cysteine ligase regulatory subunit (GCLC), and glutathione cysteine ligase modulatory subunit (GCLM). Together, our data suggested that ghrelin protected against ICH-induced SBI by inhibiting NLRP3 inflammasome activation and promoting Nrf2/ARE signaling pathway [1)].

Continuous infusion of ghrelin increased body mass and food intake, but did not increase muscle mass nor improve muscle function, in a long-term critical illness recovery model. Further studies with pulsatile ghrelin delivery or additional anabolic stimuli may further clarify the utility of ghrelin in survivors of critical illness [2)].

Unclassified

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