Description for the general public

The inflammation caused by bacterial infection disrupts the homeostasis of an organism and leads to changes in secretory activity of the endocrine system, including the pituitary gland. In experimental conditions, in order to induce systemic inflammation without introducing an active pathogen, the animals are injected with bacterial endotoxin – lipopolysaccharide (LPS), a part of the outer cell membrane of a Gram (−) bacteria. It was found, that inflammation caused by LPS, increases growth hormone (GH) secretion both in humans and ewes. It is worth noting that there is observed a high homology between human and sheep in interactions between immune system and somatotropic axis. So the sheep's role as a model animal for research on these interactions must be stressed, also because mainly and most commonly used animals, such as rodents, do not show this similarity. It was found, that the activation of immune system increases secretion of proinflammatory mediators ie., interleukin (IL)-1β, IL-6 and tumor necrosis factor α (TNFα). It is believed, that these pleiotropic in their action mediators play an important role as factor connecting immune and neuroendocrine systems. One of the endocrine axis, the activity of which is modulated during inflammation, is somatotropic axis, namely the axis of GH → insulin-like growth factor 1 (IGF1) → target tissue, that plays a key role in regulation of metabolic processes in mammals. It is believed, that aforementioned mediators of inflammation stimulate the secretion of GH. An interesting phenomenon is, that these cytokines actions omit the standard controlling pathway affecting the secretion of GH, which is associated with the activity of hypothalamic hormones: somatoliberin and somatostatin. It was found, that despite increased GH secretion, under the influence of inflammation, the transduction of GH signal was inhibited, which is caused by decrease expression of GH receptor. In conclusion, despite the increase of GH level, its action is inhibited, which is associated also with decrease in IGF1 level, which plays an intermediary role in GH signaling in the aforementioned axis GH→ IGF1→ target tissue. This state is described as a GH resistance (GHres). It has been shown, that decreased level of GH may cause among others growth disorders, negative changes in body mass composition, development of cardiovascular diseases, decrease of bone density or it may cause metabolic disorders and thus leads to obesity. Recent studies indicates an important role of fibroblast growth factor 21 (FGF21) in induction of GHres. Its blood level, like GH, also increases after immune system stimulation. Moreover, studies have shown, that administration of FGF21 inhibits the GH action in target tissue, also leading to GHres. It was found also, that FGF21 inhibits the immune system response, including secretion of inflammatory mediators, which may suggest its important role in GHres induction. However, the FGF21 role in GHres induction and progress has not yet been fully investigated. Research has shown mutual regulating mechanism between SIRT1 and FGF21. Similar to FGF21 action of SIRT1 was stated, but SIRT1 action is tissue dependent. In peripheral tissues (out of the central nervous system) the action of SIRT1 is similar to FGF21 action. However on the central nervous system level, SIRT1 stimulates the somatotropic axis activity, which seems to be inversed to its peripheral tissue action. Currently, most researches are focused on GHres mechanisms and its consequences on the peripheral level tissues and glands. The intended project is assumed to investigate the GHres state at the central nervous system level, and more precisely, in the hypothalamus and pituitary gland where the presence of GH and IGF1 receptors was stated. The obtained results can be valuable for both human and veterinary medicine.