

عنوان مقاله:

Intracerebroventricular injection of ghrelin receptor antagonist alleviated NAFLD via improving hypothalamic insulin resistance

محل انتشار:

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خلاصه مقاله:

Objective(s): Non-alcoholic fatty liver disease (NAFLD) is a hepatic manifestation of clinical metabolic syndrome. Insulin resistance is an important factor in the pathogenesis of NAFLD. Ghrelin, widely distributed in peripheral tissues and the central nervous system, plays a vital role in regulating food intake, energy balance, and substance metabolism. In this study, the effect of intracerebroventricular (ICV) injection of ghrelin receptor antagonist on NAFLD was explored.Materials and Methods: A rat model of NAFLD was established by feeding a high-fat diet, and a selective ghrelin receptor antagonist [D-Lys-\mathbf{P}]-GHRP-\mathbf{F} was injected via ventricular intubation implantation. The serum total cholesterol (TC), triglycerides (TGs), aspartate aminotransferase (AST), alanine aminotransferase (ALT), and hepatic TGs were measured using the colorimetric method. Fasting plasma glucose (FPG) and fasting plasma insulin (FPI) were determined to calculate homeostatic model assessment insulin resistance (HOMA-IR). Hematoxylin-eosin (HE) and Oil Red O staining were conducted to observe the pathological changes and lipid accumulation in the liver. Hosphatidylinositide\mathbf{P}-kinase (PI\mathbf{K})/protein kinase B (Akt)/mammalian target of rapamycin (mTOR) signaling pathway protein expressions were measured using western blot analysis.Results: ICV injection of [D-Lys-\mathbf{P}]-GHRP-\mathbf{F} significantly reduced serum lipids, transaminase, and HOMA-IR, improved liver injury, and inhibited lipid accumulation in the liver of NAFLD rats. Moreover, ICV injection of [D-Lys-w]-GHRP-۶ significantly up-regulated the phosphorylation levels of PIWK/Akt/mTOR signaling protein expressions in the hypothalamus, indicating a significant improvement in hypothalamic insulin resistance. Conclusion: Blockade of central ghrelin receptor can treat NAFLD possibly via the .hypothalamic PIWK/Akt/mTOR signaling pathway to improve insulin resistance

کلمات کلیدی: ghrelin, Hypothalamus, insulin resistance, NAFLD, PI۳K/Akt/mTOR

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