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Mini Review

The Endocannabinoid System in the Control of Glucose Homeostasis

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Abstract

The endogenous cannabinoid system participates in the regulation of energy homeostasis, regulation also of glucose homeostasis. It appears to play a very important regulatory role in the secretion of hormones. The important elements of this system are endocannabinoid receptors (types CB1 and CB2). The endocannabinoid receptors are distributed both in the central and peripheral nervous system, in multiple peripheral tissues. They are also localized on islets of Langerhans. Endocannabinoid system plays role in regulation of endocrine secretion in the human pancreas. The endocannabinoid system regulates not only the central and peripheral mechanisms of food intake, but also lipids synthesis and turnover in the liver and adipose tissue as well as glucose metabolism in muscle cells.

Keywords: Endocannabinoid system; Endocannabinoid receptors; Glucose metabolism endocrine secretion pancreas

Introduction

The Endocannabinoid System (ECS) regulates multiple physiological processes in the human body. Endocannabinoids and cannabinoid receptors are known to play a generalized role in energy homeostasis - they control energetic balance mechanisms [1-5]. The endocannabinoid system consists of central and peripheral receptors (CB1 and CB2), egzogenic agonists as well as endogenic: cannabinoids and endocanabinoids as well as enzymes, which regulates its system endogenic ligands synthesis and degradation. Endocannabinoids are immunosupressive active factors, so their role in autoimmune diseases (like diabetes) is important. These mechanisms act in apoptosis, preventing proliferation, cytokines supression, chemokines synthesis as well as regulatory T lymphocytes (T-reg) induction [6]. ECS takes part in hungry and energetic homeostasis control and glucose and lipids (metabolism [7-11]).

Experimental clinical research are conducted over the influence of genetic or pharmacological inactivation of CB1 in reduced body weight and increased energy expenditure in rodents [12].

Increased activity of the endocannabinoid system has emerged as a pathogenic factor in visceral obesity, which is a risk factor for Type 2 Diabetes Mellitus (T2DM) [13].

Cannabinoid system plays an important role in endocrine functions regulation. Recently, much attention is paid to the role of cannabinoids in the regulation of alpha and beta islet cell function. The presence of cannabinoid receptors CB1 and CB2 found in isolated islets of Langerhans. In the experimental research cannabinoid receptors (CB1, CB2) and their agonists as well as their impact on the secretion of insulin, glucagon and somatostatin was observed [14,15]. Also, other authors pointed out the participation of cannabinoid receptors and their agonists in the regulation of endocrine function of the pancreas [16,17].

Since insulin is a major mediator of glucose homeostasis, the number of beta cells is tightly regulated for the purpose of maintaining blood glucose levels within the narrow normal limits. Insulin regulates beta cell proliferation in an autocrine manner by the Insulin Receptor (IR). Also other studies are conducted to determine the effect of endogenous cannabinoids (EC: Endogenous Cannabinoids) on the proliferation of beta cells [18,19].

The biological effects of Endogenous Cannabinoids (ECs) are mediated by two receptors coupled to the G protein (CB1R and CB2R). Receptors CB1R role in insulin-regulated beta cells proliferation is under wide discussion. The presence of CB2R receptors on beta cells is also discussed [14,20].

British author studies demonstrated the active role of both receptors (CB1, CB2) in the stimulation of insulin secretion [2].

ECs also affect insulin action in insulin-dependent tissues such as the liver, muscle and fat [22].

Cannabinoids through their receptors CB1 and CB2 also exert an immunosuppressive effect, may inhibit proliferation of leukocytes, induce apoptosis of cells and reduce secretion of proinflammatory cytokines. Thus, research are carried out on their use as immunosuppressive agents in autoimmune diseases, including type 1 diabetes [23].

Currently studies are mainly conducted in animal models. The application in humans requires further investigation. The results of the research over endocannabinoid system participation in modulating the secretion of insulin and glucagon confirm that these observations have practical significance, may in fact be used in the regulation of glucose homeostasis [15].

An extensive discussion of the role of endocannabinoids and the CB1 receptor in the regulation of energy homeostasis of the organism, regulation of glucose homeostasis and endocrine function of the pancreas has recently presented a group of Spanish and French authors [24].

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These authors pointed out that the knowledge of these mechanisms may be important for the development of new therapeutic approaches. Recently the results of experimental research on CB1R role in the regulation of the viability and growth of beta cells, which may be important in the design of therapies diabetes, were presented [25]. Also appeared some publications discussing the participation of endocannabinoids in the induction of insulin resistance, which leads to the occurrence of type 2 diabetes [26,27] Observations regarding the participation endocannabinoid system in insulin resistance were also presented by other authors [28,29].

Lipina et al in experimental trials indicate a key role for CB1R in aging-related insulin resistance and metabolic dysfunction and highlight CB1R blockade as a potential strategy for combating metabolic disorders associated with aging [28].

The relationship of the endocannabinoid system activation and expression of CB1 receptor with insulin resistance in the women with in women with Polycystic Ovary Syndrome (PCOS) was presented by Juan et al. [30].

Extensive discussion over the role of ECS in diabetes appearance and its long distance complications was presented by Horvath at al. [31]. According to the authors ECS modulation can have significant meaning in diabetes prevention and treatment as well as in its long term complications..

Summary

More and more evidence suggests that hyperactivity Endocanabinoinoid System (ECS), may contribute to the development of diabetes adversely affecting glucose and lipid metabolism, as well as to run apoptosis and inflammation in the islet cells of the pancreas [32]. Preclinical data indicate the involvement of hyperactivity of the system in the pathogenesis of chronic complications. Modulation of hyperactivity may therefore have therapeutic relevance. Also, other authors take the view that reducing the activity of the cannabinoid receptor type 1 (CB1) may play a role in the management of obesity and obesity-related metabolic disorders Including type 2 diabetes [13].

The role of modification activity CB1R in regulation of β-cell functions can indicate the therapeutic potential of this class of compounds [26].

Endocannabinoids control lipid and glucose metabolism in several peripheral organs, particularly the liver and adipose tissue. Direct actions in skeletal muscle and pancreas are also emerging. This knowledge may help in the design of future therapies for the metabolic syndrome [5]. There are signs that these various biological effects of cannabinoids create hope for the introduction of treatment, including for the treatment of diabetes and its consequences, a new group of drugs [33-35].

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