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The Relationship between Leptin and Fatty Acid

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Abstract

Background: Leptin is important for the regulation of energy metabolism. Fatty acids are essential components of all biological membranes and represent an important form of energy storage in both animals and plants. In addition to leptin's central effects on appetite control and energy expenditure, it has been shown to have a strong influence on fatty acid metabolism.

Approach: This review summarizes recent knowledge on leptin and fatty acids and their roles in biochemistry and clinical chemistry.

Keywords: Leptin; Fatty acids

Introduction

Leptin, the product of the *ob* gene, is a recently discovered single-chain proteohormone with a molecular mass of 16 kDa that is thought to play a key role in the regulation of body weight [1]. Leptin acts on the central nervous system, in particular the hypothalamus, suppressing food intake and stimulating energy expenditure [2]. In addition to its central effects on appetite control and energy expenditure, leptin has been shown to have a strong influence on fatty acid (FA) metabolism and on thel endocrine axis (Figure 1) [3]. Leptin has also been demonstrated to have profound effects on skeletal muscle FA metabolism, resulting in an increase in the capacity to oxidize FA and a lowering of triacylglycerol stores [4,5]. Further demonstrated that leptin acutely alters skeletal muscle FA metabolism. Their results indicated that leptin stimulates FA oxidation while simultaneously decreases the incorporation of FA into the intramuscular triacylglycerol pool in incubated murine muscle. Several previous animal [6-8] and human studies [9] have reported the effects of leptin upon lipid metabolism. Leptin had profound effects on peripheral lipid metabolism, but the majority was explained by its effects on food intake. Leptin had additional centrally mediated effects to increase the expression of a limited number of genes concerned with FA oxidation, whereas we cannot exclude direct peripheral effects of leptin on certain aspects of lipid metabolism [10]. The study by Shimabukuro et al. [11] suggests the existence of a parallel but presumably distinct system through which leptin may regulate triglyceride synthesis and oxidation in tissues. That is a system by which leptin, perhaps acting in part directly on peripheral cells, simultaneously inhibits triglyceride synthesis and stimulates oxidation within the cell [12].

Leptin, adiponectin, and resistin are produced by the adipose tissue. The protein leptin, a satiety hormone, regulates appetite and energy balance of the body. These hormones have important roles in energy homeostasis, glucose and lipid metabolism, reproduction, cardiovascular function, and immunity. They directly influence other organ systems, including the brain, liver, and skeletal muscle, and are significantly regulated by nutritional status [3]. Across the groups, there were positive linear correlations between leptin concentrations, body mass index (BMI), versus subcutaneous (SC) fat mass and free fatty acid (FFA) levels. Leptin and FFA concentrations are higher and insulin levels lower in both groups of black women compared to the two groups of white women, despite a similar BMI and body fat mass [13]. Especially the omega-3 series, have antiinflammatory actions, which increase the concentrations of anandamides, enhance the levels of acetylcholine and nitric oxide. It modulate the concentrations and actions of various neurotransmitters, including leptin, in the brain [14]. Isomers of conjugated linoleic acid (CLA) are found in beef, lamb and dairy products. Diets containing CLA reduce adipose mass in various depots of experimental animals. In addition, CLA delays the onset of diabetes in the Zucker Diabetic Fatty (ZDF) rat model for obesity-linked type 2 diabetes mellitus. We hypothesize that there would be an inverse association of CLA with body weight and serum leptin in subjects with type 2 diabetes mellitus [15]. Leptin, the product of the *ob* gene, is a hormone mainly secreted by white adipocytes [16-19]. Binding of leptin to its hypothalamic receptors alters various messengers that regulate energy expenditure, food intake, and the activity of the sympathetic nervous system, at least in rodents [20]. Plasma leptin levels are tightly correlated with the total amount of white fat in the body. Leptin has therefore been considered as a "lipostatic factor" contributing to the regulation of body weight via a negative feedback loop [1]. Several hormones can modulate leptin transcription and secretion *in vivo* and *in vitro*, the most important being insulin and norepinephrine [21-23]. *In vivo*, starvation or food deprivation decreases plasma leptin concentrations and leptin transcription in adipose tissue. These changes are closely associated with decreased plasma insulin concentrations, activation of the sympathetic nervous system, increased lipolysis, and elevated plasma FFA levels. Receding or injection of insulin reverses the decrease of plasma leptin concentrations and leptin transcription in rodents and in humans [24]. Long-chain fatty acids may play an important metabolic role as messengers between the hormonal activation of lipolysis and the final inhibition of leptin secretion from white adipocytes [25]. The correlation among PUFA, obesity, and *Ob* gene has been previously investigated in *in vivo* and *in vitro* studies [26,27]. Although there is extensive experimental research exploring the putative role of FFAs in insulin resistance, glucose intolerance, and type 2 diabetes, there are surprisingly few prospective epidemiologic studies [28,29].

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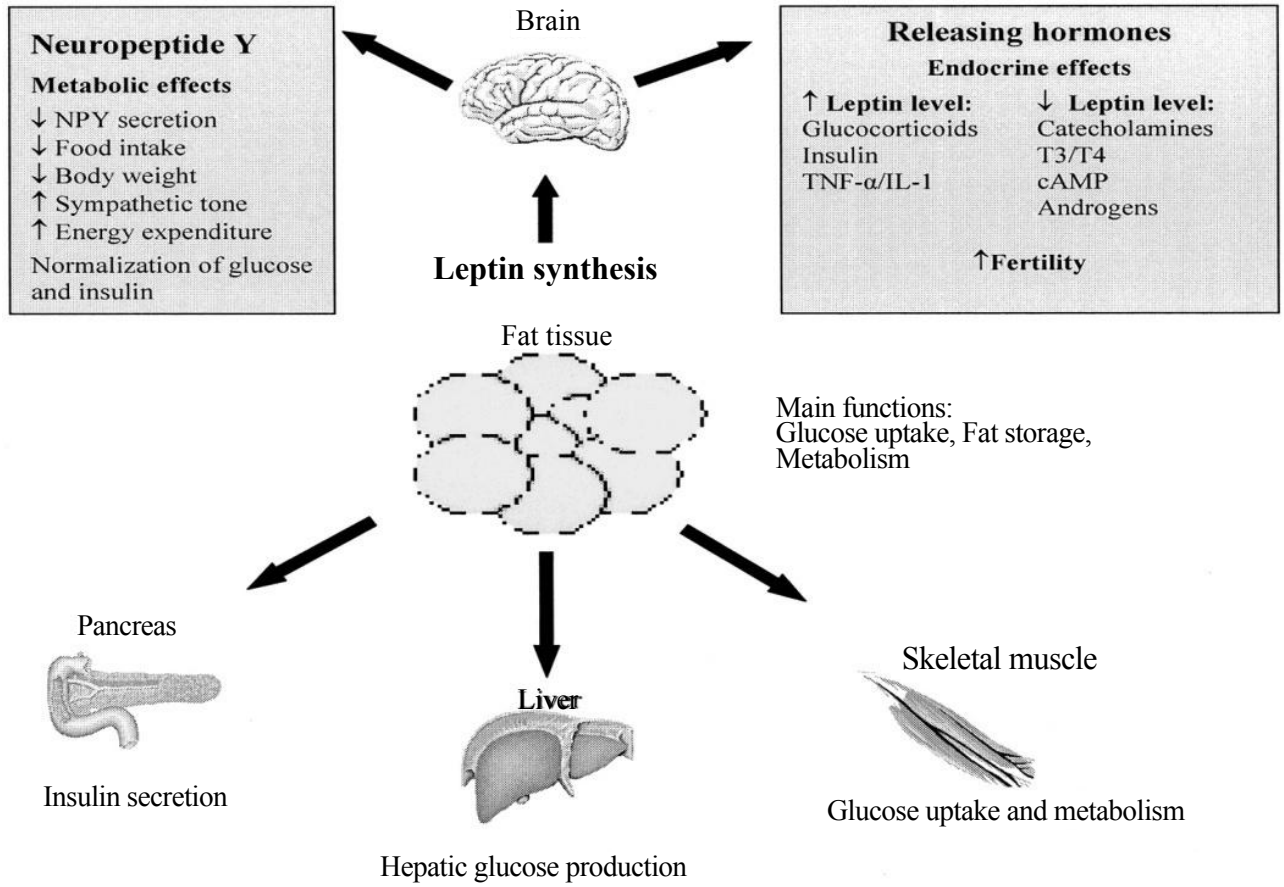

IL-1: Interleukin-1; T3: Triiodothyronine; T4: Thyroxin [3]

Figure 1: Action of leptin on the hypothalamus and peripheral organs (pancreas, liver and skeletal muscle).

Recently there has been increasing interest in the active role of adipose tissue in the regulation of metabolism. Adipocytes secrete signaling molecules such as leptin, adiponectin, and proinflammatory cytokines that have important effects on lipid and carbohydrate metabolism [30,31].

Discussion

Leptin, is the protein product of brain which regulates body weight [32]. Furthermore, leptin appears to be the signal indicating the size of the fat deposited in the body [19]. When injected into rodents, leptin reduces food intake and increases energy expenditure, resulting in the loss of body weight [33,34]. It has been shown recently that treatment of mice with FA synthase inhibitors lead to the inhibition of feeding and body weight loss. This suggests that FA synthase may also play an important role in the control of feeding behaviour [35]. Furthermore, it has been found that leptin suppresses the FA synthase gene transcription in primary cultured adipocytes [36]. The results presented in this paper indicate that there are two distinct phases of changes in perirenal white adipose tissue's leptin mRNA level and serum leptin concentration. The first phase, between 1 and 3 months, is characterized by a strong positive correlation between adiposity index and perirenal white adipose tissue's leptin mRNA level as well as between adiposity index and serum leptin concentration. The second phase is characterized by no significant change in perirenal white adipose tissue *ob* gene expression. The increase in *ob* gene expression at the first phase (between 1 and 3 month old rats) could be related, at least in part, to the increase in food intake by the rats [37]. However, these changes might also be related to the development or simply be secondary to differences in the amount of fat pads appearing in rats at different ages, since the size of fat cells and fat content of adipocytes are important determinants of lipid metabolism [38]. Leptin, FA and triglyceride synthesize by increasing the intracellular lipid concentration, reducing or directly inhibiting lipid oxidation. Leptin is the effect of lipid metabolism, FA synthesis, acetyl-CoA carboxylase activity, and the rate of limiting enzyme inhibition. This enzyme is blocked by inhibiting fatty acid synthesis and reduction in the intracellular concentration of fatty acids and triglycerides. In some studies, it has been claimed that lipid accumulation in many tissues of leptin reverses insulin resistance and improves glucose homeostasis through beneficial effects on cell function [39,40]. FAs released from white adipose tissue provide important energy substrates during fasting. However, uncontrolled FA release from white adipose tissue during non-fasting states causes lipotoxicity and promotes inflammation and insulin resistance, which can lead to and worsen type 2 diabetes. White adipose tissue is also a source for insulin sensitizing FAs such as palmitoleate produced during *de novo* lipogenesis. Insulin and leptin are two major hormonal adiposity signals that control energy homeostasis through signaling in the central nervous system [41]. Another study of leptin shows that an obese individual has the stimulating effect on fat oxidation [42]. Leptin

has also been suggested in some cases, as it can modulate fatty acids [43]. Adipokines have important roles in FA and lipid metabolisms [3,44-46] and determine the relationships of serum leptin, adiponectin and resistin concentrations to serum levels of non-esterified fatty acids (NEFA) and phospholipids [47].

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