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Consumption of a high glycemic index diet increases abdominal adiposity but does not influence adipose tissue pro-oxidant and antioxidant gene expression in C57BL/6 mice

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Abstract

The hypothesis of this study is that consumption of a high glycemic index (GI) starch will increase adiposity, increase expression of the pro-oxidant enzyme (nicotinamide adenine dinucleotide phosphate [NADPH] oxidase), and decrease expression of the antioxidant enzymes (catalase, glutathione peroxidase [GPx], and superoxide dismutase [SOD]) in adipose tissue of mice. C57BL/6 mice (n = 5-8/group) were fed a diet containing either high-GI starch (100% amylopectin) or low-GI starch (60% amylose/40% amylopectin) under low-fat (LF) or high-fat (HF) conditions for 16 weeks. Meal tolerance tests (MTTs) indicated that the postprandial blood glucose response over 120 minutes for the high-GI mice under LF and HF conditions was significantly greater than for mice fed low-GI diets. This result was not due to increased food consumption by the high-GI mice during the MTT. Although there was no difference in body weight between mice fed high-GI or low-GI starch, LF high-GI mice had significantly greater adiposity compared to LF low-GI mice. High-fat mice had a significant increase in NADPH oxidase expression compared to LF mice, but there was no significant effect of starch on NADPH oxidase expression. High-fat diet significantly decreased the expression of GPx and catalase, but there was no significant effect of starch on GPx and catalase expression. There was no difference in SOD expression among any of the diet groups. In conclusion, high GI diets increase adiposity under LF conditions but do not influence pro-oxidant or antioxidant enzyme gene expression in adipose tissue of C57BL/6 mice.

Keywords: Glycemic index; Adipose; Mouse; Nutrition; Oxidative stress
Abbreviations: ANOVA, analysis of variance; AUC, area under the curve; GI, glycemic index; GPx, glutathione peroxidase; HF, high-fat; LF, low-fat; MTT, meal tolerance test; NADPH, nicotinamide adenine dinucleotide phosphate; ROS, reactive oxygen species; SOD, superoxide dismutase.

1. Introduction

The dramatic increase in the incidence of obesity and diabetes in recent decades has prompted researchers to investigate potential dietary strategies to prevent the development and/or progression of these conditions [1]. Increased intake of refined carbohydrates has been reported to parallel the upward trend in the prevalence of obesity and type 2 diabetes in the United States, suggesting that the type of carbohydrate consumed may impact disease risk through

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alterations in postprandial blood glucose and insulin concentrations [2-4]. To account for these qualitative differences in carbohydrate type, the concept of glycemic index (GI) was developed by Jenkins et al [5] as a physiologic rather than a structural approach for classifying carbohydrates. The physiologic effect of a carbohydrate refers to the rate and magnitude in which dietary glucose enters the bloodstream after a meal, as well as the subsequent demand placed on the pancreas to secrete sufficient amounts of insulin to normalize blood glucose levels. Thus, postprandial plasma glucose and insulin concentrations following consumption of carbohydrate is highly governed by the quality and quantity of carbohydrate consumed [2,6,7].

Several cross-sectional and prospective cohort studies in humans have shed light on the potential usefulness of dietary GI in the determination and modification of metabolic disease. For example, a positive association was found between increased dietary GI and risk for coronary heart disease [8], whereas lower dietary GI was associated with a reduced risk for the development of type 2 diabetes in men and women [9,10]. While several interventional studies have also reported beneficial effects of consuming low-GI diets [11,12], several other studies have found no association with GI and risk for obesity [13-15]. Likewise, inconsistencies between studies have been seen when GI and risk for obesity were investigated [15-19]. In light of these equivocal findings, specific recommendations based on dietary GI have not been established.

In an attempt to circumvent some of the confounders observed in human studies, researchers have investigated the effects of dietary GI using animal models. Studies in rodents have linked high-GI diets with increased adiposity [20-24], decreased lean body mass [24], enhanced lipogenic gene expression [25], increased plasma triglyceride concentration [21], decreased plasma adiponectin concentration [24], and insulin resistance [22-24,26]. Taken together, these animal studies have provided insight into the potential influence of high-GI diets on body composition, gene expression, and glucose metabolism; however, the exact molecular mechanism(s) through which high-GI diets elicit their effects is currently unknown.

One common target shared among the animal studies was that altering dietary GI had specific effects on adipose tissue. Adipose tissue is now recognized as an active endocrine organ because it synthesizes and releases a group of biologically active molecules known as *adipocytokines* [27]. Interestingly, the normal balance of these adipocytokines is perturbed in obesity, and this alteration may influence the development of insulin resistance, diabetes, metabolic syndrome, and cardiovascular disease [28-32]. Attempts to identify a link between metabolic disease and altered adipose tissue metabolism have pointed to the potential role of oxidative stress. Oxidative stress is defined as an imbalance between the production of reactive oxygen species (ROS) and antioxidant defenses, in favor of pro-oxidants, leading to tissue damage [33]. ROS production has been shown to increase in parallel with fat accumulation in vitro and in vivo [28]. Also, cultured adipocytes exposed to hyperglycemic conditions display oxidative stress [34], and a direct link between postprandial hyperglycemia and oxidative stress production was identified by Ceriello et al [35,36]. Oxidative stress, in turn, could lead to activation of the transcription factor nuclear factor-κB that is an important mediator of proinflammatory gene expression resulting in whole-body inflammation [37]. A possible mechanism by which oxidative stress is generated is through up-regulation of the pro-oxidant enzyme nicotinamide adenine dinucleotide phosphate (NADPH) oxidase and down-regulation of antioxidant enzymes [28]. Altogether, these findings suggest that adipocytes may be susceptible to oxidative stress generated postprandially, or in accumulated fat, through long-term consumption of a high-GI diet.

Therefore, the hypothesis of this study is that mice consuming a high-GI diet will have increased adiposity, increased expression of the pro-oxidant enzyme NADPH oxidase, and decreased expression of the antioxidant enzymes catalase, glutathione peroxidase (GPx), and superoxide dismutase (SOD) in adipose tissue compared to mice consuming a low-GI diet.

2. Methods and materials

2.1. Animals and diets

Six- to 8-week-old male C57BL/6 mice were purchased from Harlan (Indianapolis, Ind) and adapted to the mouse facility for 1 week before initiation of study. All mice were housed in colony cages on a 12-hour light/dark cycle in a temperature and humidity controlled environment. The experimental diets used in this study were produced by Harlan-Teklad (Madison, Wis) and contained 1 of 2 different starches obtained from National Starch (Bridgewater, NJ) in low-fat (LF) and high-fat (HF) combinations, for a total of 4 experimental diets (n = 5-8 mice/group). The high-GI starch (Amioca; National Starch Inc., Bridgewater, NJ) was a waxy maize cornstarch composed of 100% amylopectin. The low-GI starch (Hi-Maize; National Starch Inc.) was a high amylose-resistant cornstarch composed of 60% amylose and 40% amylopectin. The macronutrient composition of the LF diet, expressed as a percentage by weight (g/kg) was 17.9% protein, 6.3% fat, and 62.1% carbohydrate. The macronutrient composition of the HF diet was 17.7% protein, 18.2% fat, and 50.9% carbohydrate. The amount of starch in the HF diet was reduced to increase the fat in the form of lard. The composition of the LF and HF diets are listed in Table 1. Mice were fed the experimental diets ad libitum for 16 weeks. Body weights were recorded weekly using an electronic balance. All animal experimental procedures were reviewed and performed with approval from the Institutional Animal Care and Usage Committee of Auburn University (Ala).