Available online at www.sciencedirect.com

SciVerse ScienceDirect

www.nrjournal.com

Change in postprandial substrate oxidation after a high-fructose meal is related to body mass index in healthy men

Anne C. Smeraglio[a], *Emily K. Kennedy*[b], *Angela Horgan*[c], *Jonathan Q. Purnell*[d], *Melanie B. Gillingham*[c,e,*]

[a] *School of Medicine, Portland, OR 97239, USA*
[b] *Graduate Programs in Human Nutrition, Portland, OR 97239, USA*
[c] *Oregon Clinical and Translational Research Institute, Portland, OR 97239, USA*
[d] *Department of Medicine, Portland, OR 97239, USA*
[e] *Department of Molecular and Medical Genetics, Oregon Health and Science University, Portland, OR 97239, USA*

ARTICLE INFO

Article history:
Received 19 October 2012
Revised 25 March 2013
Accepted 28 March 2013

Keywords:
Fructose
Glucose
Fat oxidation
Carbohydrate oxidation
RQ
NPRQ
BMI
Obesity
Energy expenditure
Indirect calorimetry

ABSTRACT

Oral fructose decreases fat oxidation and increases carbohydrate oxidation in obese subjects, but the metabolic response to fructose in lean individuals is less well understood. The purpose of this study was to assess the effects of a single fructose-rich mixed meal on substrate oxidation in young healthy nonobese men. We hypothesized that a decrease in fat oxidation and an increase in carbohydrate oxidation would be observed after a fructose-rich mixed meal compared with a glucose-rich mixed meal. Twelve healthy, normal weight to overweight, aged 23 to 31 years participated in a double-blind, crossover study. Each participant completed 2 study visits, eating a mixed meal containing 30% of the calories from either fructose or glucose. Blood samples for glucose, insulin, triglycerides, and leptin as well as gas exchange by indirect calorimetry were measured intermittently for 7 hours. Serum insulin was higher after a fructose mixed meal, but plasma glucose, plasma leptin, and serum triglycerides were not different. Mean postprandial respiratory quotient and estimated fat oxidation did not differ between the fructose and glucose meals. The change in fat oxidation between the fructose- and glucose-rich meals negatively correlated with body mass index (BMI; $r = -0.59$ [$P = .04$] and $r = -0.59$ [$P = .04$] at the 4- and 7-hour time points, respectively). In healthy nonobese men, BMI correlates with altered postprandial fat oxidation after a high-fructose mixed meal. The metabolic response to a high-fructose meal may be modulated by BMI.

1. Introduction

The prevalence of obesity in the United States has more than doubled since 1980 and is now estimated to be 33.8% of the adult population [1,2]. This dramatic increase in obesity has corresponded to a rise in consumption of fructose containing sweeteners in the United States [3]. From 1970 until 2008, the average daily US household fructose intake increased from 37 to 54.7 g/d, with the main sources of fructose being sucrose and high-fructose corn syrup sweetened beverages and grains

Abbreviations: ANOVA, analysis of variance; AUC, area under the curve; BMI, body mass index; CHO, carbohydrate; Fru, fructose; Glu, glucose; HOMA-IR, homoeostatic model assessment of insulin resistance; NPRQ, nonprotein respiratory quotient; OCTRI, Oregon Clinical and Translational Research Institute; OHSU, Oregon Health and Science University; RQ, respiratory quotient.

* *Corresponding author*. Oregon Health and Science University, Portland, OR 97239, USA. Tel.: +1 503 4941682; fax: +1 503 4946886.
E-mail address: gillingm@ohsu.edu (M.B. Gillingham).

0271-5317/$ – see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.nutres.2013.03.007

[4]. Although these data are correlative, the association has led some researchers to suggest a causative relationship between increased fructose consumption and societal weight gain [5,6]. Still other researchers suggest that the observed increase in obesity is more likely related to an increase in total energy consumption, which also increased 18% from 1977 to 2004 and total carbohydrate (CHO) intake, which increased 41% over the same period [3].

Although both fructose and glucose are 6-carbon sugars, they have different metabolic fates in the liver. The liver efficiently takes fructose up from the portal vein on first pass metabolism. It is converted to fructose-1-phosphate and without further regulation immediately enters glycolysis [7-9]. In contrast, glucose enters glycolysis via the enzyme 6-phosphofructo-1-kinase, a highly regulated enzyme that is sensitive to energy needs [10,11]. The ability of fructose to bypass this enzymatic control allows glycolysis to proceed independent of energy demand. This leads to a hepatic surplus of energy production and glycolytic intermediates that are shunted to other metabolic pathways, including fatty acid synthesis and glucose production [12].

Fructose consumption has been shown to lower postprandial glucose response; increase serum triglyceride levels, visceral adiposity, and insulin resistance; and reduce leptin levels in humans in some but not all studies [6,13-17]. The variable results observed in research studies of fructose consumption may be related to the dose and form of fructose used in the study with beneficial effects on glycemic control at lower doses and more pronounced adverse triglyceride effects at higher doses [18,19]. Recently, fructose consumption has also been shown to decrease fat oxidation in obese subjects fed a high-fructose diet over a 10-week period [20]. This change in substrate oxidation has been hypothesized to occur as a result of increased de novo lipogenesis and increased gluconeogenesis when fructose is metabolized in the liver [7,21]. Fat oxidation is suppressed during lipogenesis via the control of malonyl-CoA levels and inhibition of carnitine-palmitoyltransferase-1, the rate-limiting step in fatty acid oxidation [22,23]. Gluconeogenesis stimulated by fructose intake provides a constant supply of glucose to skeletal muscles, thus encouraging glucose oxidation preferentially over fat oxidation [13]. Both mechanisms could contribute to the decreased fat oxidation reported with fructose consumption and, in the context of excess total energy, potentially lead to increased lipid storage and weight gain.

Based on these mechanisms, fructose might be expected to decrease fat oxidation in both lean and obese individuals. However, most prior fructose research has focused on obese or diabetic populations. In healthy normal-weight populations, the data remain sparse, with mixed results regarding the metabolic effects of fructose [24-27]. Thus, we hypothesized that fructose would have the same metabolic effects in a normal-weight to mildly overweight population as those observed in obese populations. Furthermore, these changes in metabolism with a high-fructose meal would alter postprandial substrate oxidation causing increased lipogenesis, decreased fat oxidation, and increased CHO oxidation. This hypothesis was evaluated in a double-blind, crossover trial where 12 healthy men with body mass indices (BMIs) of 20 to 30 kg/m^2 were given single meals rich in either fructose or the control substance, glucose. Metabolic parameters were then followed using indirect calorimetry and blood markers at hours 0, 1, 4, and 7 to evaluate for acute metabolic differences after glucose vs fructose-rich meals.

2. Methods and materials

2.1. Subjects

Twelve healthy men without diabetes, with a mean age of 25 (23-31) years and a BMI less than 30 kg/m^2, were recruited from Oregon Health and Science University (OHSU) through campus advertisements. Participants were at their lifetime maximal body weight and had been weight stable for at least 1 month. Those with any acute or chronic medical conditions that could affect metabolic rate were excluded from the study, as were smokers and individuals who consumed more than 2 drinks of alcohol daily. This protocol was approved by the OHSU institutional review board, and all subjects gave written consent before participation in the study.

2.2. Experimental design

Study visits were conducted at the Clinical and Translational Research Center of the Oregon Clinical and Translational Research Institute (OCTRI). Participants were evaluated on 2 separate occasions, greater than 1 week but less than 1 month apart, in a double-blind, crossover design. All participants were assigned to consume a single meal high in glucose or fructose in random order. The Bionutritionists and kitchen staff of the Clinical and Translational Research Center Bionutrition Unit maintained the randomization assignments and prepared the study meals, accordingly. Study staff and participants were blinded to beverage type during participant visits and during data analysis.

2.3. Study visit protocol

Participants arrived early in the morning after fasting from food, drink (except water), caffeine, and alcohol for more than 12 hours. A research nurse or study staff obtained vital signs, height, and weight measurements. Fasting blood markers including serum leptin, triglycerides, glucose, and insulin were obtained as well as baseline indirect calorimetry. Participants were fed a standardized breakfast as described below containing either glucose or fructose. After breakfast, participants again fasted from food and drink except water for another 7 hours while testing was conducted. Repeated blood markers and metabolic activity by indirect calorimetry were measured at 1, 4, and 7 hours postprandial.

2.4. Diet composition

Participants were fed an egg omelet, bagel with cream cheese, and sweetened beverage breakfast consisting of one-third of their estimated daily caloric needs as calculated from the average of the Harris Benedict and Mifflin–St Jeor equations multiplied by an activity factor of 1.4 [28-30]. The meal consisted of 30% of energy from fat, 15% from protein, and 55%