Assessment of endothelial function and blood metabolite status following acute ingestion of a fructose-containing beverage

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Abstract

Aim: Fructose intake has increased concurrent with sugar intake and this increase has been implicated in contributing to the development of metabolic syndrome risk factors. Recent evidence suggests a role for uric acid (UA) as a potential mediator via suppression of nitric oxide (NO) bioavailability. The aim of this study was to explore this hypothesis by measuring changes in UA concentration and systemic NO bioavailability as well as endothelial function in response to acute ingestion of a glucose-fructose beverage.

Methods: Ten young (26.80 ± 4.80 years), non-obese (body mass index: 25.1 ± 2.55 kg m⁻²; percent body fat: 13.5 ± 6.9%) male subjects ingested either a glucose (100 g dextrose in 300 mL) or isocaloric glucose-fructose (glucose : fructose; 45 : 55 g in 300 mL) beverage. Blood was sampled pre- and every 15-min post-ingestion per 90 min and assayed for glucose, lactate, fructose, total nitrate/nitrate, UA and blood lipids. Forearm blood flow and pulse-wave velocity were recorded prior to and at 30 and 45 min time intervals post-ingestion, respectively, while heart rate, systolic and diastolic blood pressure were recorded every 15 min.

Results: The glucose-fructose ingestion was associated with a significant (P < 0.05) increase in plasma lactate concentration and altered free fatty acid levels when compared with glucose-only ingestion. However, UA was not significantly different (P = 0.08) between conditions (AUC: 1018 ± 1675 vs. 2171 ± 1270 µmol L⁻¹ per 90 min for glucose and glucose-fructose conditions respectively). Consequently, no significant (P < 0.05) difference in endothelial function or systemic NO bioavailability was observed.

Conclusion: Acute consumption of a fructose-containing beverage was not associated with significantly altered UA concentration, endothelial function or systemic NO bioavailability.

Keywords: endothelial function, fructose, nitric oxide, reactive hyperaemia, uric acid.

Metabolic syndrome (MetSyn) describes a cluster of common pathologies including visceral obesity, dyslipidaemia, hyperglycaemia and hypertension (Eckel et al. 2005). Due to its strong association with premature morbidity and mortality, including a threefold increased risk for cardiovascular mortality (Miller & Adeli 2008), there is continued focus on prevention of the MetSyn (Vasudevan & Garber 2005) and thus, the identification of risk factors. One MetSyn risk factor that has gained renewed interest is hyperuricaemia (Havel 2005, Johnson et al. 2009). While hyperuricaemia was initially identified as a MetSyn indicator (hypertension,
hyperglycaemia and hyperuricaemia; Kylin 1923), subsequent research dismissed hyperuricaemia as an independent risk factor for MetSyn and attributed the elevated level of uric acid (UA) to reduced renal excretion as a result of hyperinsulinaemia (Facchinì et al. 1991). However, a number of papers have since re-investigated the association between hyperuricaemia and MetSyn, and have implicated hyperuricaemia as a direct and independent risk factor for the development of MetSyn and increased cardiovascular risk (Johnson et al. 2009). Indeed, hyperuricaemia often precedes the development of hyperinsulinaemia, obesity and diabetes (Nakagawa et al. 2005) and decreasing plasma UA levels have been shown to prevent or reverse features of the MetSyn (Nakagawa et al. 2006).

Although a number of mechanisms have been suggested to explain the relationship between hyperuricaemia and the development of MetSyn, it is likely that this relationship is mediated via a nitric oxide (NO)-dependent process (Nakagawa et al. 2005, Johnson et al. 2009). Indeed, UA has been shown to reduce NO bioavailability in various cell types (reviewed in Johnson et al. 2009) via mechanisms including changes in redox state (Sautin et al. 2007, Corry et al. 2008), stimulation of arginase (Zharikov et al. 2008), as well as directly and irreversibly reacting with NO leading to its deple-
tion (Nakagawa et al. 2005). Not surprisingly, hyperu-
ricaemia is associated with endothelial dysfunction in rats (Nakagawa et al. 2005), and lowering UA improves endothelial function in patients with diabetes (Butler et al. 2000).

While multiple causes for hyperuricaemia exist (Conover et al. 1992), fructose-induced hyperuricaemia (Choi et al. 2008) is gaining increasing attention given the link between excessive fructose intake and specific MetSyn risk factors (Miller & Adeli 2008). Indeed, while acute consumption of fructose is known to dose-dependently raise serum UA concentration (Akhavan & Anderson 2007), there is also a significant correlation between chronic fructose intake and serum UA concentration in males (Gao et al. 2007).

Based on current research in animal models and findings from epidemiological surveys, a compelling case has been presented suggesting a role for UA and NO in the development of MetSyn risk factors associated with excessive fructose consumption (Nakagawa et al. 2006, Miller & Adeli 2008, Johnson et al. 2009). While the acute rise in plasma UA has previously been assessed in humans following the ingestion of fructose (Akhavan & Anderson 2007), the subsequent effect on NO bioavailability or endothelial function has not been investigated. Therefore, in line with previous research we hypothe-
sized that acute fructose consumption would acutely increase plasma UA levels and thus reduce total nitrate/nitrite concentration (surrogate marker of NO bioavail-
ability; Le et al. 2008), leading to deleterious changes in endothelial function. To test this hypothesis, changes in metabolic and cardiovascular markers related to endothelial function were assessed following ingestion of a glucose-fructose solution, and these changes were compared with those elicited following consumption of an isocaloric glucose solution in young healthy males.

Method

Study population

Ten young (18–35 years), non-obese [body mass index (BMI) < 30] males were recruited from the local University community by advertisement. This sample size is consistent with previous research (Akhavan & Anderson 2007), which found significant differences in UA concentration in young males following ingestion of either a 50 : 50 or 80 : 20 (glucose : fructose) solution (n = 7; repeated measures design). Participants came to the Human Performance Laboratory at Syracuse University on three occasions. On the first occasion, the subjects read and signed the informed consent which was previously approved by the Syracuse University Institutional Review Board, and were then familiarized with the equipment and procedures to be used in the study. During this visit, height (cm) and weight (kg) were measured and body composition was assessed using air-displacement plethysmography (Table 1; BODPOD

| Table 1 Physical and metabolic characteristics of study participants |
|------------------|------------------|
| Age (years) | 26.8 ± 4.8 |
| Height (cm) | 180.57 ± 8.14 |
| Weight (kg) | 82.05 ± 4.33 |
| BMI (kg m⁻²) | 25.1 ± 2.55 |
| Percent body fat (%) | 13.49 ± 6.86 |
| Resting systolic blood pressure (mmHg) | 124.1 ± 10.95 |
| Resting diastolic blood pressure (mmHg) | 67.4 ± 6.20 |
| Resting pulse wave velocity* (m s⁻¹) | CR 8.2 ± 0.90 |
| CF 5.6 ± 0.68 |
| Alanine aminotransferase (IU L⁻¹) | 26.3 ± 7.69 |
| Fasting plasma insulin (μU mL⁻¹) | 4.0 ± 1.9 (gl) |
| (μU/mL) | 3.60 ± 2.0 (fr) |
| Fasting FFA (mmol L⁻¹) | 0.73 ± 0.3 |
| Fasting TG (mmol L⁻¹) | 0.29 ± 0.2 |
| HOMA2 | 2.58 ± 2.9 |
| HOMA-%B | 113.8 ± 2.3 |
| HOMA-%S | 83.7 ± 3.9 |

BMI, body mass index; FFA, free fatty acid; TG, triglyceride. *CR indicates the pulse wave velocity between carotid and radial sites. CF indicates the pulse wave velocity between carotid and femoral sites.
system, Life Measurement, Concord, MA, USA). During the second and third visit, participants arrived in the laboratory at 07:00 hours following an overnight fast. Participants were required to complete a dietary food record for the 3 days prior to each testing session and instructed to maintain dietary consistency between trials.

**Experimental design**

Upon arrival, subjects were asked to relax in a supine position for a period of 30 min prior to attaining an initial blood sample via a Teflon catheter inserted in the right antecubital vein. Blood sampling and measurement of blood pressure and heart rate (SunTech Tango Stress test BP Monitor; SunTech, Raleigh, NC, USA) was conducted at baseline and 15, 30, 45, 60, 75 and 90 min post ingestion of either a glucose (100 g dextrose in 300 mL) or an isocaloric (400 calories) glucose-fructose (45:55 g in 300 mL) solution. The glucose-fructose beverage was prepared by addition of a crystalline fructose powder (Swanson Vitamins, Fargo, ND, USA) to a commercially available glucose solution (NERL Diagnostics, East Providence, RI, USA). The crystalline fructose powder was independently evaluated for purity (>98%) in our laboratory using the fructose assay described below. The solutions were chilled in the refrigerator and served to the participants who were blinded to the treatment condition using a counter-balanced design. During the entire experiment, the subject was placed in the supine position with both arms rested on custom-made triangular cushions, ensuring the passive return of blood in the arm to the heart. After collection, blood samples were immediately centrifuged and plasma stored at −80 °C until subsequent analysis.

**Vasodilatory measurements**

Forearm blood flow (FBF) measurement was conducted prior to as well as 30, 60 and 90 min following drink consumption as described previously (Higashi et al. 2001). Briefly, resting FBF was measured using a mercury-filled strain-gauge plethysmograph (EC-6; D.E. Hokanson, Bellevue, WA, USA) placed around the widest part of the subject’s left forearm. One inflatable cuff was placed around the subject’s upper arm, while another inflatable cuff was placed around the subject’s wrist to occlude hand circulation. FBF was determined by inflating the upper arm cuff to 50 mmHg, to allow for arterial inflow without venous outflow, for 7 s, followed by an 8-s deflation, creating 15 s cycles for 1.5 min. The plethysmographic signal was transmitted to a Biopac digital recorder for further analysis (Biopac Systems, Santa Barbara, CA, USA). FBF was expressed as mL per min per 100 mL of forearm tissue (mL min⁻¹ per 100 mL tissue). All the plethysmography readings were analysed by one single investigator (A.B.) blinded to the condition and averaged over a minimum of six recordings for baseline FBF.

To obtain measures of vasodilatory capacity, reactive hyperaemia (RH) was induced by occluding arm blood flow with an additional cuff placed over the existing upper arm cuff and inflated to 100 mmHg above resting systolic blood pressure (SBP) for a period of 5 min. After rapid release of the inflated upper arm cuff, FBF was measured as described above.

**Pulse wave velocity**

Pulse wave velocity (PWV) was measured prior to and at 45 and 75 min following drink consumption. Simultaneous waves were recorded on the right side of the body by applying mechanotransducers directly on the skin above the carotid, radial, femoral and dorsalis pedis arteries using the Complior® SP Doppler (Colson, Les Lilas, France). The PWV was then calculated by means of a correlation algorithm using the foot-to-foot transit time of each wave form and the measured distance between the carotid and brachial site (C-B PWV) and the carotid and femoral site (C-F PWV) in accordance with specified guidelines (Laurent et al. 2006).

**Metabolite assays**

Total nitrate/nitrite plasma concentrations were used as surrogate markers of systemic NO production using a commercially available calorimetric assay kit (Cayman Chemicals, Ann Arbor, MI, USA; intra-assay coefficient of variation <3%; sensitivity 2.5 μM), while UA concentration was measured using the Amplex® Red UA Kit (Molecular Probes, Carlsbad, CA, USA; intra-assay coefficient of variation <5%; sensitivity <1 μM). Plasma free fatty acids (FFA) were assayed using the Wako NEFA C Kit (Code 990-75401; Wako Diagnostics, Richmond, VA, USA; intra-assay coefficient of variation <4%) while plasma triglycerides (TG) were assayed using the Randox Triglycerides GPO-PAP Method (Cat no. TR 212; Randox Laboratories, Crumlin, UK; intra-assay coefficient of variation <5%; sensitivity <1 μM). All kits were used in accordance with manufacturer specifications. Alanine aminotransferase (ALT) was measured using an automated analytical bench-top system (Cholestech, Hayward, CA, USA). Plasma glucose and lactate was measured on a calibrated YSI2300 STAT analyser. Plasma fructose concentration was analysed using coupled hexokinase (HK), phosphoglucoisomerase (PGI), and glucose-6-phosphate dehydrogenase (G6PDH) reaction steps.
modified from Kunst et al. (1984). Briefly, plasma glucose was initially converted to gluconate 6-phosphate by the addition of HK and G6PDH and the absorbance at 340 nm read upon cessation of reaction. The fructose concentration was then assessed by the addition of PGI and reading the new absorption value at 340 nm (inter-assay coefficient of variation <4%).

Insulin assay and homeostatic model assessment (HOMA) modelling

Plasma insulin concentration was measured from two separate fasting blood samples using a commercially available Enzyme-linked ImmunoSorbent Assay kit (Phoenix Pharmaceuticals, Burlingame, CA, USA; intra-assay coefficient of variation <10%, inter-assay coefficient of variation <15%; sensitivity = 4.39 mIU mL\(^{-1}\)). Insulin resistance was then estimated from basal glucose and insulin concentrations measured on two separate days using the homeostatic model assessment (Levy et al. 1998) using the HOMA Calculator (available at: http://www.dtu.ox.ac.uk/index.php?maindoc=hma/model, accessed 1 February 2009). HOMA2 estimates of β-cell function (HOMA-%β) and insulin sensitivity (HOMA-%S) were not normally distributed and therefore reported as geometric means (SD).

Statistical analysis

Descriptive statistics (means and SD) were generated using SPSS 16.0 (Chicago, IL, USA). The Kolmogorov–Smirnov Z-test (exact tests) was applied to each data set to assess whether the distribution was not significantly different from normal while Levene’s statistic was adopted to test homogeneity of variances. Plasma concentrations of metabolites as well as PWV and FBF were analysed using a two-way ANOVA with repeated measures. Differences between time points were analysed using a paired t-test with a Bonferroni correction factor, while correlations between FBF and PWV against HOMA2 scores were analysed using Pearson’s correlation coefficients. The area under the curve (AUC) for metabolic and cardiovascular parameters was calculated using the trapezoidal method (GraphPad Software, San Diego, CA, USA) using baseline values. A priori significance level of 0.05 was set.

Results

Metabolite responses to carbohydrate ingestion

The time-series curve shows that the plasma fructose concentration was significantly (\(P = 0.03\)) elevated within 15 min of consuming the glucose-fructose solution (12.94 ± 2.40 mmol L\(^{-1}\)) solution compared with glucose (2.84 ± 0.62 mmol L\(^{-1}\)) and remained significantly higher during the glucose-fructose condition at each time point for the duration of the 90 min study (Fig. 1a). In line with this, the area under the fructose curve was significantly (\(P = 0.002\)) higher in the glucose-fructose condition (1339.0 ± 124.0 mmol L\(^{-1}\) per 90 min) than in the glucose condition (126.2 ± 59.6 mmol L\(^{-1}\) per 90 min; Fig. 1a). Blood glucose concentrations were elevated in both conditions, although the blood glucose concentration was significantly (\(P = 0.038\)) higher at 60 min for the glucose condition (6.795 ± 0.68 mmol L\(^{-1}\)) compared with the glucose-fructose condition (5.657 ± 0.684 mmol L\(^{-1}\)). There were no significant changes in AUC for glucose between conditions (glucose = 560.9 ± 43.2 mmol L\(^{-1}\) per 90 min; glucose-fructose = 541.6 ± 41.7 mmol L\(^{-1}\) per 90 min; Fig. 1b). Lactate AUC was significantly (\(P = 0.0001\)) different between conditions (glucose = 30.3 ± 4.0 mmol L\(^{-1}\) per 90 min; glucose-fructose = 116.8 ± 10.6 mmol L\(^{-1}\) per 90 min) and plasma lactate concentrations were significantly higher at 30, 45, 60, 75 and 90 min during the glucose-fructose condition when compared with the glucose condition (\(P < 0.001\); Fig. 1c).

The AUC for UA tended to be higher in the glucose-fructose condition (−1018 ± 1675 vs. 2171 ± 1270 mmol L\(^{-1}\) per 90 min), but this did not reach significance (\(P = 0.08\); Fig. 2a). Total nitrate/nitrite concentrations as well as AUC for total nitrates and nitrites showed no significant differences (\(P = 0.35\)) between conditions over time (Fig. 2b). The percent change for FFA was significantly (\(P < 0.0001\)) lower at 60 min in the glucose condition compared with the glucose-fructose condition and remained lower at 90 min (Fig. 3a). Moreover, AUC for FFA concentrations was significantly (\(P = 0.0014\)) lower for the glucose condition (−0.883 ± 0.01610 mmol L\(^{-1}\) per 90 min) than for the fructose condition (−0.20430 ± 0.0630 mmol L\(^{-1}\) per 90 min; Fig. 3a). TG AUC and concentrations across time points showed no significant differences between conditions (\(P = 0.225\); Fig. 3b).

Cardiovascular responses and endothelial function

Net heart rate AUC was significantly (\(P = 0.004\)) higher in the glucose-fructose condition (363.8 ± 16.3 beats \(\text{min}^{-1}\) for 1.5 h) than in the glucose condition (198.7 ± 24.9 beats \(\text{min}^{-1}\) for 1.5 h). The net AUC for SBP and DBP however did not differ significantly between conditions (\(P = 0.09\) and 0.10 for glucose and glucose-fructose conditions respectively). There were no significant differences between conditions over time and AUC for peak FBF (\(P = 0.82\); Fig. 4a). Moreover, C-R
PWV and C-F PWV were not significantly different across conditions ($P = 0.19$ and 0.13 respectively; Fig. 4b).

**Plasma insulin response to carbohydrate ingestion**

The plasma insulin AUC was higher following the glucose condition than the glucose-fructose condition, although this did not reach statistical significance ($P = 0.44$). HOMA2 scores ranged from 0.4 to 6.7 (2.3 ± 2.8; mean ± SD) while HOMA-%B and HOMA-%S were 105.5 ± 2.3 and 94.0 ± 3.8 respectively (Table 1). There were no significant correlations between resting FBF and HOMA2 scores ($r = 0.1915$) or resting PWV and HOMA2 scores (C-R PWV: $r = 0.3906$; C-F PWV: $r = 0.638$).

**Discussion**

Total carbohydrate intake and specifically, consumption of added sugars have increased considerably over the last 30 years which has resulted in a concomitant rise in fructose consumption (Bray et al. 2004, Marriott et al. 2009). This increase in fructose consumption correlates well with the increased prevalence rates of MetSyn risk factors (Bray et al. 2004, Havel 2005, White 2009) and for this reason has become a topic of intense investigation and debate (Johnson et al. 2009, Stanhope & Havel 2009, White 2009). Although short-to medium-term intervention studies have demonstrated inconsistency in results, it is apparent that those studies providing the highest doses of fructose result in the greatest deleterious health outcomes (Johnson et al. 2009). Indeed, a recent study investigating the effects of fructose intake on adipose distribution, lipid metabolism and insulin sensitivity in humans (Stanhope & Havel 2009) has provided additional support for a deleterious role of sustained fructose intake at high levels (25% of energy requirement). Research into chronic fructose consumption is now targeting the rise in UA as the likely candidate for these adverse metabolic and cardiovascular changes, via the ability of UA to
decrease NO bioavailability (Nakagawa et al. 2005, Johnson et al. 2009). However, direct experimental support for this hypothesis comes predominantly from studies utilizing either animal (Nakagawa et al. 2005, 2006) or in vitro (Sautin et al. 2007, Gersch et al. 2008, Zharikov et al. 2008) models and there is currently a dearth of studies investigating the concomitant response in the proposed metabolic initiators, specifically UA and NO, to fructose ingestion in humans. Moreover, endothelial function has not previously been investigated in response to fructose ingestion. Therefore, it was the purpose of this study to investigate changes in specific metabolic and cardiovascular markers following ingestion of a fructose-containing solution and compare these changes with an isocaloric glucose solution.

Figure 2 Time course and net area under the curve (AUC) for uric acid (a) and total nitrate/nitrite (b) following ingestion of the glucose-fructose (solid triangles) and glucose (solid square) solutions.

Figure 3 Percent change and net area under the curve (AUC) for free fatty acids (a) and triglycerides (b) following ingestion of the glucose-fructose (solid triangles) and glucose (solid square) solutions. *Significant (P < 0.05) difference between conditions over time. †Significant (P < 0.05) difference between conditions.
Following the ingestion of the glucose-fructose solution, there was a significantly greater increase in lactate concentration than following the ingestion of the glucose solution (Fig. 1c), indicating rapid metabolism of fructose by cells expressing Glut 2 or Glut 5 transporters. Hepatic clearance has previously been identified as the predominant path of blood-borne fructose disposal (>50%; Mayes 1993) which accounts for the correspondingly low concentration of systemic fructose observed in the current study and that of others (Daly 2003). Due to the unique metabolism of fructose, there is a net hepatic production of UA and release of UA into the systemic circulation (see review by Johnson et al. 2009). Indeed, the current study identified only a modest, non-significant ($P = 0.08$) rise in UA (Fig. 2a).

Interestingly, when compared with a previous study (Akhavan & Anderson 2007) the change score and AUC for UA concentration were similar to a comparable dose (50 g glucose and 50 g fructose condition) in healthy individuals ($n = 7$), although the study of Akhaven & Anderson (2007) demonstrated significant differences in AUC for UA when compared with a water-only condition (glucose-only condition not evaluated). The lack of significance in UA concentration between conditions in our current study may be explained on the basis of the large inter-individual variation obtained. While the study of Akhaven and Anderson recruited participants from a similar demographic to the current study, Akhaven and Anderson adopted 26 kg m$^{-2}$ as the BMI cut-off as opposed to the 30 kg m$^{-2}$ BMI cut-off adopted herein. Whether this difference in BMI could account for the difference in postprandial UA response remains to be established. However, BMI is known to be significantly correlated (positively) with fasting serum UA (Alatalo et al. 2009) even in non-clinical populations, but whether this relationship remains in the postprandial state has not previously been investigated.

Figure 4 Percent change in peak forearm blood flow (FBF) and total area under the curve (AUC) for FBF following reactive hyperaemia (a), time course and AUC for peripheral (b) and central (c) pulse wave velocity (PWV) following ingestion of the glucose-fructose (solid triangles) and glucose (solid squares) solutions.
Additionally, increased sensitivity to fructose ingestion has been observed in the hyperinsulinaemic population, possibly as a result of the underlying endothelial dysfunction in this population (Johnson et al. 2009). Moreover, given the important role of the liver in the disposal of fructose, it would come as no surprise that liver cirrhosis has also previously been recognized as a condition altering blood fructose handling in the postprandial state (Kruszynska et al. 1993). The participants recruited in the current study were apparently healthy young males, with ALT levels in the normal range (>40), BMI of less than 30, low body fat percentage and a C-F PWV of less than 12 m s⁻¹ (2007 European Society of Hypertension guidelines) (Table 1). Moreover, HOMA-%β (a measure of β-cell activity) and HOMA-%S (a measure of insulin sensitivity) scores are indicative of normal glucose tolerance and despite a large range in HOMA2 scores (0.4–6.7), no significant correlations between HOMA2 and markers of deleterious events (elevated TG, FFA, PWV or reduced RH) were observed. The apparent health of this cohort may therefore have blunted the increase in UA levels following fructose ingestion, and may in part also have contributed to the lack of significance observed in some of the study variables investigated. Investigating the metabolic and cardiovascular markers in response to fructose ingestion in a clinical population is an area that needs to be explored further.

As increases in UA following fructose ingestion are dose dependent (Akhavan & Anderson 2007), a greater fructose load is likely to have resulted in a greater UA response. However, the quantity of fructose provided in this study (55 g) was based on previous literature (Akhavan & Anderson 2007) and current data which indicate that an estimated 9.1% of Americans’ daily calories are derived from fructose (approx. 49 g day⁻¹) (Marriott et al. 2009). Hence the quantity of fructose adopted for the current study was considered to be realistic, albeit an upper extreme of fructose consumption in a single sitting, and providing a greater fructose load than was provided in the current study would become impractical. The proportion of fructose and glucose used was based on the relative proportion found in HFCS-55, the most common (~60%) of the HFCSs used in the food supply (Havel 2005).

In consequence of the lack of significant change in UA concentration, there was no associated change in systemic total nitrate/nitrite concentration (Fig. 2b), a marker of systemic NO bioavailability (Khosla et al. 2005). In line with the systemic NO bioavailability data, there were no significant differences in peak FBF between conditions, or in the AUC for peak FBF following RH (Fig. 4a). The RH protocol adopted in this study has previously been established as a valid technique for assessing resistance vessel endothelial function, which is dependent on local endothelial NO bioavailability (Higashi et al. 2001). Moreover, haemodynamic responses (SBP and DBP) as well as arterial compliance, which has received great interest in the development of cardiovascular disease (Laurent et al. 2006), were not different between conditions at either the central (C-F PWV) or peripheral (C-R PWV) sites (Fig. 4b,c).

Considering that increased TG levels are known to affect endothelial function (Vogel et al. 1997) and given that TG levels increase by 120 min after fructose ingestion (el-Sayed et al. 1997), this study was designed to avoid this elevation in TG. Thus, the absence of a significant difference in the period following either the glucose or glucose-fructose condition was an anticipated event. Plasma FFA concentration (Fig. 3a) was significantly lowered in the glucose condition which may have resulted from an insulin-dependent inhibition of lipolysis (Carmen & Victor 2006); however, this was not evaluated in the current study.

In conclusion, the acute ingestion of a glucose-fructose solution was associated with a significantly greater elevation in plasma lactate concentration than the glucose ingestion, indicating a rapid activation of the ATP-dependent fructokinase reaction. This was however associated with only a modest, non-significant increase in UA and consequently, endothelial function and systemic NO bioavailability were unaffected following the ingestion of the glucose-fructose solution in this cohort of young, non-obese males. The longer-term ramifications associated with even modestly elevated UA in response to chronic fructose consumption remain to be established and present as an important future line of research, as this may be a more important determinant of future cardiovascular risk. Finally, the interindividual variability in metabolite responses to a fructose load remains to be explored.

Conflicts of interest

There are no conflicts of interest to disclose.

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References

