The Journal of Nutrition
Ingestive Behavior and Neurosciences

Jejunal Infusion of Glucose Decreases Energy Intake to a Greater Extent than Fructose in Adult Male Rats[1,2]

Alexander A Moghadam,[3] Timothy H Moran,[3] and Megan J Dailey[4]*

[3]Department of Psychiatry and Behavioral Sciences, Johns Hopkins University, Baltimore MD; and [4]Department of Animal Sciences, University of Illinois at Urbana-Champaign, Urbana, IL

Abstract

Background: Intestinal nutrient infusions result in variable decreases in energy intake and body weight based on nutrient type and specific intestinal infusion site.

Objective: The objective was to test whether an intrajejunal fructose infusion (FRU) would lower energy intake and body weight and induce similar increases in gut hormones as those found after intrajejunal glucose infusions (GLU).

Methods: Male Sprague-Dawley rats received an intrajejunal infusion of either an equal kilocalorie load of glucose or fructose (11.4 kcal) or saline (SAL) for 5 d while intake of a standard rodent diet was continuously recorded; body weight was measured daily. Immediately after the infusion on the final day, rats were killed and plasma was collected to measure hormones.

Results: Daily energy intake was significantly lower in the GLU group than in the SAL group, but the FRU group did not differ from the GLU or SAL groups when the 11.4 kcal of the infusate was included as energy intake. Lower energy intake was due to smaller meal sizes during the infusion period in the GLU group than in the FRU and SAL groups; the FRU and SAL groups did not differ. The percentage of change in body weight was lower in the GLU group than in the FRU and SAL groups. Plasma glucagon-like-peptide 1 (GLP-1) concentrations were greater in the GLU group than in the SAL group; the FRU group did not differ from the GLU or SAL groups. The plasma insulin concentration was greater in the FRU group than in both the GLU and SAL groups.

Conclusion: These results demonstrate that glucose induces a greater decrease in energy intake and increase in GLP-1 at distal intestinal sites than fructose in rats, which may explain differential effects of these monosaccharides between studies when delivered orally or along the proximal to distal axis of the intestine. *J Nutr* 2016;146:2124–8.

Keywords: intestinal infusion, fructose, glucose, gut peptides, rats

Introduction

Much of the sugar in our diet is contributed from either sucrose, a disaccharide composed of fructose and glucose, or its commonly used substitute, high-fructose corn syrup, which primarily consists of mixtures of free glucose and fructose monomers (1–3). Glucose and fructose have varied physiologic and endocrine effects after different modes of delivery (i.e., oral, intragastric, or intraintestinal) in humans and other animals, leading to confusion about whether one monosaccharide is more effective at decreasing energy intake or body weight and the underlying mechanisms driving these dissimilar actions. It is often thought that monosaccharides are likely to be completely absorbed before reaching the mid-small intestine, and thus the effect of these nutrients on distal intestinal sites has been neglected. This is despite a number of studies that showed that oral ingestion or intragastric delivery of glucose or fructose can stimulate distal intestinal hormones (4, 5). In addition, the transporters for glucose and fructose, sodium-dependent glucose transporter 1 (SLGT1)[5] and glucose transporter 5 (GLUT5), respectively, are expressed in epithelial cells of the jejunum, ileum, and colon (6). Taken together, glucose and fructose may be present in the lumen beyond the duodenum and upper jejunum and could potentially directly affect these sites to alter energy intake and metabolism. Thus, we wanted to investigate if there is a differential action of glucose or fructose in the distal intestine on energy intake and/or body weight and if varied

[1] Supported by NIH grant DK 19302 (to THM).
[2] Author disclosures: AA Moghadam, TH Moran, and MD Dailey, no conflicts of interest.
*To whom correspondence should be addressed. E-mail: mdailey5@illinois.edu.

[5] Abbreviations used: FRU, intrajejunal fructose infusion; GLP-1, glucagon-like peptide 1; GLU, intrajejunal glucose infusion; GLUT5, glucose transporter 5; PYY, peptide YY; SAL, intrajejunal saline infusion; SGLT1, sodium-glucose transporter 1.

Manuscript received February 23, 2016. Initial review completed March 15, 2016. Revision accepted August 4, 2016.
First published online August 31, 2016; doi:10.3945/jn.116.231860.

concentrations of distal intestinal or other hormones could account for such differences. We used adult male Sprague-Dawley rats to compare the effects of an intrajejeunal glucose infusion (GLU), an intrajejunal fructose infusion (FRU), or an intrajejunal saline infusion (SAL) on *1*) energy intake and meal variables and *2*) and plasma concentrations of glucagon-like peptide 1 (GLP-1), peptide YY (PYY), amylin, and insulin.

Methods

Animals. Two separate cohorts of 16 (n = 32 total) adult male Sprague-Dawley rats (Charles River Laboratories) were used. Rats were initially individually housed in conventional tub cages with access to water ad libitum and a standard, commercially available rodent diet in pellet form (Teklad Global 18% Protein Rodent Diet 2018; 18.6% protein, 6.2% fat, 44.2% carbohydrate; Envigo), which has been previously described (7). The composition of the diet (grams per kilogram of feed) was as follows: crude protein, 188 g; crude oil, 60 g (total saturated, 9.6 g; total monounsaturated, 12.8 g; and total polyunsaturated, 34.1 g); crude fiber, 38 g; carbohydrates, 500 g (starch, 450 g; and sugar, 50 g); mineral mix, 32 g; vitamin mix, 2.9 g; and energy, 13.7 kJ/g. The room was maintained on a 12-h light-dark cycle (lights off at 1000 h). The Institutional Animal Care and Use Committee of Johns Hopkins University approved all procedures.

Jejunal cannulations. Two days before surgery, rats were switched from the standard rodent diet to a liquid Ensure (Abbott Laboratories) diet to minimize the presence of food in the intestine at the time of surgery. The composition of the Ensure was 10% protein, 22% fat, and 68% carbohydrate. Cannula implantations were performed as described previously (8, 9). The rats were allowed to recover from surgery in their home cage for 5–7 d. They were fed the Ensure liquid diet for 2 d to facilitate weight regain after surgery followed by a standard rodent diet for the remaining days. Cannula placement and viability were assessed after death by ensuring that the cannula insertion was 50 cm from the ileocecal junction (no leakage of fluid in the tubing or at the insertion site) and traveling toward the distal part of the intestine. Two rats were excluded from analysis on the basis of these parameters, which resulted in the following groups sizes: FRU, n = 10; GLU, n = 9; and SAL, n = 11.

Feeding tests. After recovery from surgery, the rats were housed separately in 16 AccuDiet energy-intake monitoring cages (33 × 23 cm; Accuscan Instruments). A powdered form of the standard rodent diet (3.1 kcal/g, Teklad Global Diet 2018C; 18.6% protein, 6.2% fat, 44.2% carbohydrate; Envigo) and water was available ad libitum through the feeding tests unless otherwise specified. Polyurethane tubing (~0.3 m in length, MRE –065; Braintree Scientific) was connected to syringes on a multi-syringe pump (BS-9000; Braintree Scientific), as previously described (8, 9). All rats received a jejunal infusion of 0.9% saline at a rate of 0.2 mL/h for 7 h at the beginning of the daily dark period for 3 d. The rats were allowed to move freely within the chamber during the delivery of the infusate. Energy intake was monitored continuously by the AccuDiet system for 22 h (2 h with no food access to collect data and to prepare for the next infusion cycle). This 3-d period of SAL allowed the rats to habituate to the test chamber and the infusion cycle. The rats were then divided into 3 groups to ensure an equal average body weight and SEM per group (GLU = 384 ± 11.7 g, FRU = 394 ± 12.9 g, and SAL = 392 ± 9.8 g). Each group received either an equal kilocalorie load of GLU or FRU (11.4 kcal; Sigma-Aldrich), or SAL at a rate of 0.2 mL/h for 7 h at the beginning of the daily dark period for 5 d. An isotonic saline solution has been used previously as a control solution in human (10, 11) and nonhuman animal (12, 13) intestinal infusion studies. The parameters were chosen on the basis of previous research that showed a reduction in energy intake over a multiday infusion of an equal caloric load and duration of infusion of glucose and other nutrients, which we have used previously (8) and that have been used by others (13). Energy intake was monitored continuously as described above. With the use of custom-designed software, energy-intake data were analyzed to determine meal patterns. The initiation of a "meal" was defined as ≥200 mg food consumed. The end of the meal was registered when there was >10 min without energy intake. These criteria are based on previous research by others (14), and we have tested them under a variety of feeding conditions (8, 15). These criteria include those reported to be most effective in separating the log-survivorship curve for interbout intervals into within-meal and between-meal intervals. Castonguay et al. (14) found that a 10-min intermeal interval was shown to be the mean interval time between feeding episodes for rats that had >400 feeding intervals over a 7-d period (a similar time frame was used in our present study). In addition, we chose a 10-min intermeal interval because Castonguay et al. (14) also found that the statistical relation between the intermeal interval and meal size is strengthened with longer end-of-the-meal definitions. With the use of the 10-min intermeal interval, we previously analyzed the energy-intake data on rats fed the powered rodent diet in our Accuscan energy-intake monitoring system (8, 9, 16). We found that the mean intake of a feeding bout is 0.2 g and, by using these parameters, accounts for ~95% of the feeding data in the current study.

Plasma hormone assays. Rats were decapitated immediately after the last 7-h monosaccharide or saline infusion. Trunk blood was collected from each rat into an EDTA-coated tube kept on ice until centrifuged at 2000 × g for 15 min. A multiplex rat gut hormone panel (RMHMAG-84K; Millipore) was used to determine concentrations of plasma PYY, insulin, and amylin according to the manufacturer's protocol. Plasma GLP-1 (active) was determined by using an ELISA kit (EGLP-35K; Millipore) and processed according to the manufacturer's instructions.

Data analysis. Data are presented as means ± SEMs. The 24-h energy intake and meal patterns and daily body weight measures were analyzed by using separate 2-factor repeated-measures ANOVAs with infusate (saline, glucose, or fructose) as the between-subjects factor and time as the within-subject factor with the use of Statistica software (Statsoft, 2000). Plasma hormone measures were compared by using 1-factor ANOVA with infusate as the between-subjects factor. Bonferroni post hoc tests were used, when appropriate, and corrected for multiple comparisons. Differences between groups were considered significant if $P \leq 0.05$.

Results

Energy intake. There was a main effect of infusion type on energy intake across the experimental days (**Figure 1**A; $P \leq 0.05$). Energy intakes were significantly lower in the GLU group on days 4–7 and in the FRU group on days 4, 6, and 7 than in the SAL group, but the GLU and FRU groups did not differ from one another (Figure 1A; $P \leq 0.05$). Energy intake was reduced by more than the 11.4 kcal energy value of the infusate in the GLU group on days 4–6 compared with the SAL group, but the FRU group did not differ from the GLU or SAL groups (Figure 1B; $P \leq 0.05$).

During the 7-h infusion period, there was a main effect of infusion type on energy intake (Figure 1C; $P \leq 0.05$). Energy intakes were lower in the GLU group on days 4–7 than in the SAL group, but the FRU group did not differ from either the GLU or SAL groups (Figure 1C; $P \leq 0.05$). During the 15 h after the infusion period, there was a significant main effect of infusion type ($P \leq 0.05$). Energy intakes were lower in the GLU group on day 4 and in the FRU group on days 6 and 7 than in the SAL group, but there were no differences between the GLU and FRU groups (Figure 1D; $P \leq 0.05$).

Meal patterns. There were no main effects of infusions on 24-h meal size or meal number (data not shown), but there were significant main effects of the infusions when data were analyzed

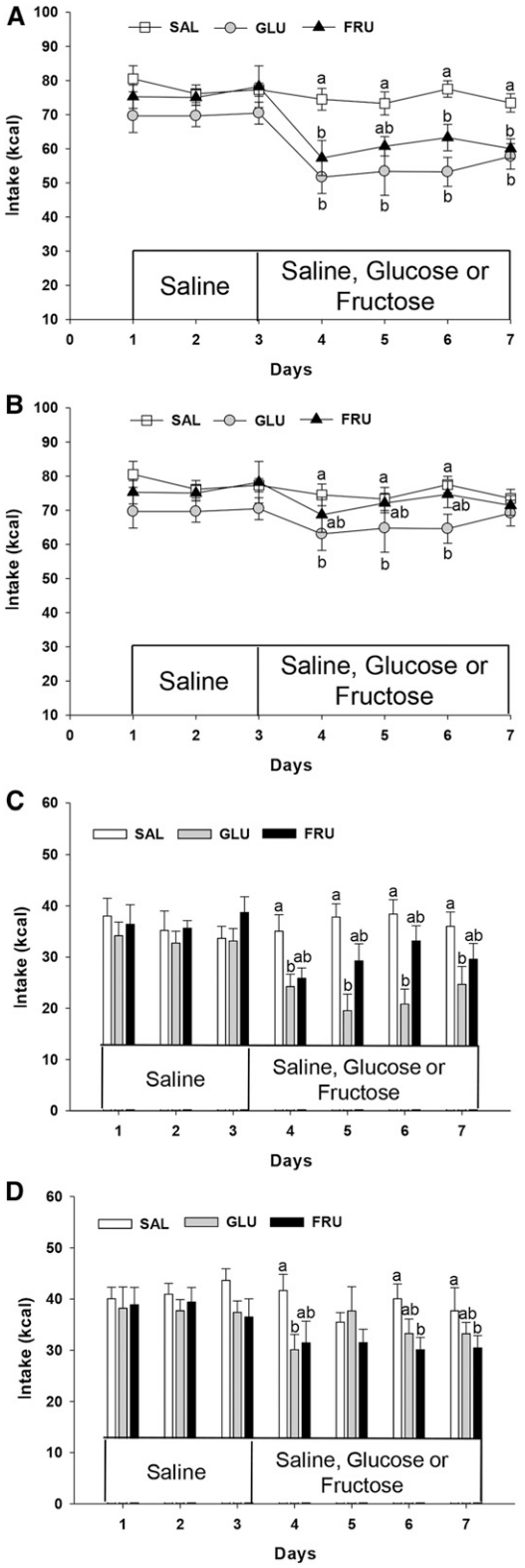

FIGURE 1 Energy intakes of adult male rats in FRU, GLU, or SAL groups without the caloric value of the infusates added (A), with the caloric value of the infusates added (B), during the 7-h infusion (C), and after the infusion period (D). After 3 d of acclimation to a jejunal infusion of saline, rats were divided into 3 groups and equal kilocalorie loads (11.4 kcal) of either fructose (n = 10), glucose (n = 9), or saline (n = 11) were infused into the jejunum for 7 h at the beginning of the daily dark period while computerized feeding monitors recorded intakes of a standard rodent diet during and after (17 h) the infusion cycle. Values are means ± SEMs. Labeled means at a time without a common letter differ, $P \leq 0.05$. The absence of letters for a given day indicates no differences between group means. FRU, intrajejunal fructose infusion; GLU, intrajejunal glucose infusion; SAL, intrajejunal saline infusion.

during and after the infusion period. During the infusion period, meal size was lower in the GLU group than in the SAL group on days 6 and 7 and was lower than in the FRU group on days 5 and 7; the FRU group did not differ from the SAL group on any day (**Figure 2**A; $P \leq 0.05$). After the infusion period, meal size was lower in the GLU group than in the SAL group on day 4; the FRU group did not differ from the GLU or SAL groups on any day (Figure 2B; $P \leq 0.05$). There were no effects on meal number during the infusion period (Figure 2C). After the infusion period, the meal number was lower in the GLU group on day 6 and in the FRU group on days 4 and 7 than in the SAL group, but there were no differences between the GLU and FRU groups (Figure 2D; $P \leq 0.05$).

Body weight. There was a main effect of the percentage change in body weight across the experimental days (data not shown; $P \leq 0.05$). The percentage change in body weight was lower in the GLU group on day 6 (−0.05% ± 0.85%) and day 7 (0.2% ± 0.85%) than in both the FRU (day 6 = 1.88% ± 0.39%, day 7 = 2.22% ± 0.45%; $P \leq 0.05$) and SAL (day 6 = 2.53% ± 0.37%, day 7 = 3.12% ± 0.51%; $P \leq 0.05$) groups, but the FRU group did not differ from the SAL group on any day.

Plasma hormones. There was a significant main effect of infusion type on plasma GLP-1 concentrations (**Table 1**; $P \leq 0.05$). GLP-1 concentrations were greater in the GLU group than in the SAL group, but the FRU group was not different from the GLU or SAL groups (Table 1; $P \leq 0.05$). There was also a significant main effect of infusion type on plasma insulin concentrations (Table 1; $P \leq 0.05$). Plasma insulin was greater in the FRU group than in the GLU and SAL groups, which did not differ from one another. There were no significant differences between groups in plasma amylin and plasma PYY concentrations (Table 1).

Discussion

The effect of GLU to decrease energy intake was greater than that of FRU. Similar to what we showed previously (8), GLU reduced intakes significantly beyond the calories infused. Although FRU did decrease energy intake compared with SAL, the magnitude of the reduction was equal to the infused calories. The effect on intake also differed in terms of how and when feeding was affected. GLU primarily resulted in reductions in meal size, which were evident during the infusion period. In contrast, the decreases in intake due to the FRU were expressed as reductions in meal number and were evident only during the postinfusion period. This delayed effect of FRU on energy intake is comparable to what has been previously reported. Fructose and glucose reduce energy intake similarly when given 30 min before a meal (17), whereas fructose inhibits energy intake to a greater extent than glucose when both are given 1.5 or 2 h before a test meal (10). Thus, glucose and fructose may both have the ability to decrease energy intake, but the magnitude and dynamics of each differ.

The expression of SGLT1 and GLUT5 along the intestinal axis and in select epithelial cell types may help to explain the

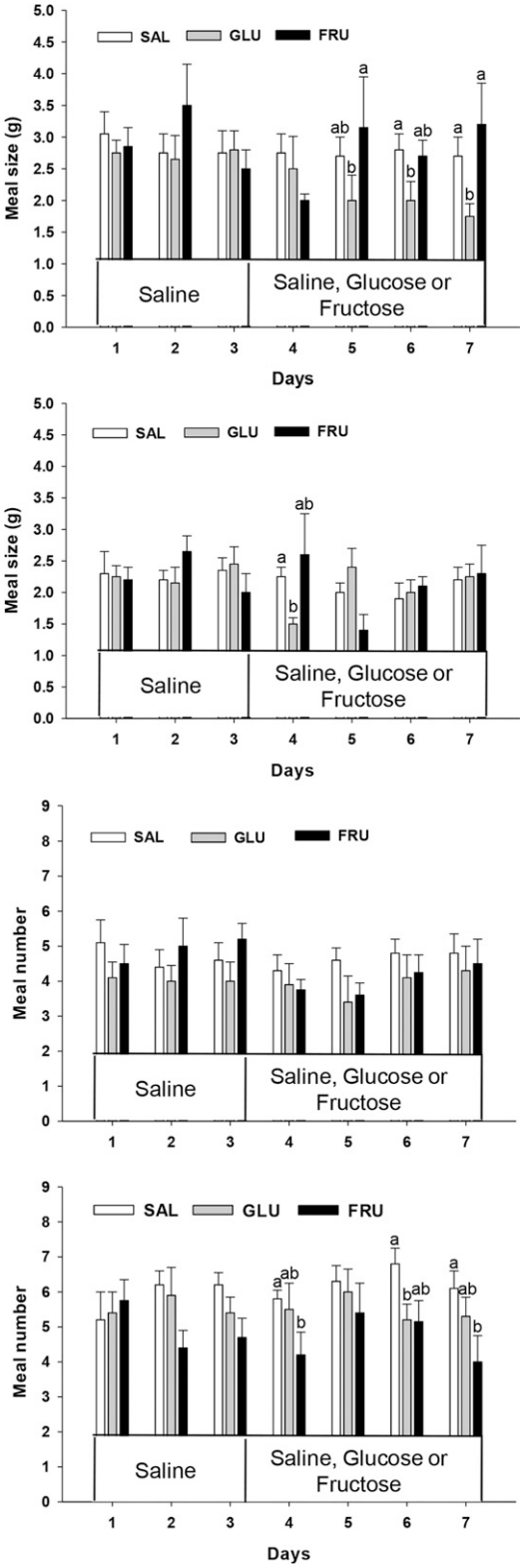

FIGURE 2 Daily meal patterns of adult male rats in FRU, GLU, or SAL groups. Mean meal size during the 7-h infusion (A) and after the infusion period (B) and mean meal number during the 7-h infusion (C) and after the infusion period (D). After 3 d of acclimation to a jejunal infusion of saline, rats were divided into 3 groups and equal kilocalorie loads (11.4 kcal) of either fructose (n = 10), glucose (n = 9), or saline (n = 11) were infused into the jejunum for 7 h at the beginning of the daily dark period while computerized feeding monitors recorded intakes of a standard rodent diet continuously. Values are means ± SEMs. Labeled means at a time without a common letter differ, $P \leq 0.05$. The absence of letters for a given day indicates no differences between group means. FRU, intrajejunal fructose infusion; GLU, intrajejunal glucose infusion; SAL, intrajejunal saline infusion.

distinct physiologic and behavioral phenomena between the 2 sugars. Although both SGLT1 and GLUT5 are expressed in epithelial cells along the intestinal axis, GLUT5 is expressed to a greater extent in more proximal instead of distal intestinal sites when laboratory mice are maintained on a standard rodent diet (18, 19). Because GLP-1 is a satiety hormone produced in L cells primarily located in more distal sites of the intestine (20–22), the lower expression of GLUT5 than of SGLT1 at more distal sites would significantly impact the effect of the 2 monosaccharides on GLP-1 release and energy intake. SGLT1 has been found to play a crucial role in glucose-dependent GLP-1 secretion (23, 24). The current findings, along with data showing that oral ingestion or intragastric loads of glucose are more effective than fructose in stimulating GLP-1 secretion (4, 5), may indicate a greater role of SGLT1 in distal intestinal sites. Consistent with this differential effect of GLP-1 secretion is the effect of GLU on meal size. We and others previously showed that GLP-1 or a GLP-1 receptor agonist affects energy intake by reducing meal size (22, 25, 26). Thus, the more pronounced effect of GLU on decreasing energy intake compared with FRU may be the result of SGLT1-stimulated GLP-1 release.

The methods used between studies testing the effect of glucose and fructose on intake may highlight other important aspects of the 2 monosaccharides. Rayner et al. (10) showed that intraduodenal fructose produces greater intake suppression and increases in blood GLP-1 concentrations than does glucose. This is in contrast to what we found in the current study. Rayner et al. (10), however, infused the monosaccharides before a meal, whereas we infused the monosaccharides during an ongoing feeding period. The use of each of these methods tests different effects of fructose and glucose. Rayner et al. (10) investigated the effect of the monosaccharides on later meal intake, whereas we tested the effect of the monosaccharides on ongoing intake. In fact, we observed that glucose suppresses intake to a greater extent during the infusion, but fructose suppresses intake to a greater extent after it has been infused. This is similar to the results of Rayner et al. (10) in that they infused the monosaccharides and measured the effect on later intake of a meal and found fructose to be more effective at decreasing intake. The differential GLP-1 measures between the 2 studies may also be the result of when the blood samples were collected. Blood was collected in our study after the infusion and ongoing intake and does not solely reflect the effect of glucose or fructose alone as in Rayner et al. (10) in which GLP-1 was measured after the infusion before the buffet meal.

Differential effects of the monosaccharides along the proximal to distal axis of the intestine have been highlighted across studies. Intraduodenal fructose, but not glucose, infusions in humans resulted in decreases in energy intake compared with saline infusions (10, 11). Intraileal glucose infusions have been found to suppress energy intake to a greater extent than intraduodenal infusions in rats (12). We found that intrajejunal infusions of glucose are more effective at decreasing energy intake and body weight than fructose. Thus, the effect of monosaccharides to suppress energy intake may be dependent on the morphology and physiology of the proximal to distal intestine that results in segmental differences in absorption, nutrient sensing, and hormonal release.

TABLE 1 Plasma concentrations of gut hormones in adult male rats after GLU, FRU, or SAL[1]

	FRU (n = 10)	GLU (n = 9)	SAL (n = 11)
GLP-1, pM	5.99 ± 0.58[a,b]	8.97 ± 1.36[a]	5.66 ± 0.55[b]
PYY, pg/mL	130 ± 19.5	95.2 ± 14.1	109 ± 9.2
Amylin, pg/mL	77.6 ± 8.8	67.7 ± 18.5	81.3 ± 11.2
Insulin, ng/mL	4.44 ± 0.43[a]	2.91 ± 0.48[b]	3.05 ± 0.41[b]

[1] Values are means ± SEMs. Labeled means in a row without a common superscript letter differ, $P \leq 0.05$. The absence of letters for a given gut hormone indicates no differences between group means. FRU, intrajejunal fructose infusion; GLP-1, glucagon-like peptide 1; GLU, intrajejunal glucose infusion; PYY, peptide YY; SAL, intrajejunal saline infusion.

Acknowledgments

AAM, THM, and MJD contributed to the design of the research, critically reviewed the manuscript for important intellectual content, and edited the manuscript; AAM conducted the analysis; and AAM and MJD interpreted the data and wrote the manuscript. All authors read and approved the final manuscript.

References

1. Ackroff K, Sclafani A. Rats' preferences for high fructose corn syrup vs. sucrose and sugar mixtures. Physiol Behav 2011;102:548–52.
2. Tappy L, Lê KA, Tran C, Paquot N. Fructose and metabolic diseases: new findings, new questions. Nutrition 2010;26:1044–9.
3. White JS. Straight talk about high-fructose corn syrup: what it is and what it ain't. Am J Clin Nutr 2008;88:1716S–21S.
4. Kuhre RE, Gribble FM, Hartmann B, Reimann F, Windelov JA, Rehfeld JF, Holst JJ. Fructose stimulates GLP-1 but not GIP secretion in mice, rats, and humans. Am J Physiol Gastrointest Liver Physiol 2014;306: G622–30.
5. Steinert RE, Frey F, Töpfer A, Drewe J, Beglinger C. Effects of carbohydrate sugars and artificial sweeteners on appetite and the secretion of gastrointestinal satiety peptides. Br J Nutr 2011;105:1320–8.
6. Drozdowski LA, Thomson ABR. Intestinal sugar transport. World J Gastroenterol 2006;12:1657–70.
7. Manolescu D-C, Sima A, Bhat PV. All-trans retinoic acid lowers serum retinol-binding protein 4 concentrations and increases insulin sensitivity in diabetic mice. J Nutr 2010;140:311–6.
8. Dailey MJ, Tamashiro KLK, Terrillion CE, Moran TH. Nutrient specific feeding and endocrine effects of jejunal infusions. Obesity 2010;18: 904–10.
9. Dailey MJ, Moghadam AA, Moran TH. Jejunal linoleic acid infusions require GLP-1 receptor signaling to inhibit food intake: implications for the effectiveness of Roux-en-Y gastric bypass. Am J Physiol Endocrinol Metab 2011;301:E1184–90.
10. Rayner CK, Park HS, Wishart JM, Kong MF, Doran SM, Horowitz M. Effects of intraduodenal glucose and fructose on antropyloric motility and appetite in healthy humans. Am J Physiol Regul Integr Comp Physiol 2000;278:R360–6.
11. Chapman IM, Goble EA, Wittert GA, Horowitz M. Effects of small-intestinal fat and carbohydrate infusions on appetite and food intake in obese and nonobese men. Am J Clin Nutr 1999;69:6–12.
12. Woltman T, Reidelberger R. Effects of duodenal and distal ileal infusions of glucose and oleic acid on meal patterns in rats. Am J Physiol 1995;269: R7–14.
13. Cox JE, Tyler WJ, Randich A, Kelm GR, Bharaj SS, Jandacek RJ, Meller ST. Suppression of food intake, body weight, and body fat by jejunal fatty acid infusions. Am J Physiol Regul Integr Comp Physiol 2000;278: R604–10.
14. Castonguay TW, Kaiser LL, Stern JS. Meal pattern analysis: artifacts, assumptions and implications. Brain Res Bull 1986;17:439–43.
15. Treesukosol Y, Moran TH. Analyses of meal patterns across dietary shifts. Appetite 2014;75:21–9.
16. Dailey MJ, Moghadam AA, Moran TH. Nutrient-specific feeding and endocrine effects of jejunal infusions in obese animals. Am J Physiol 2014;306:R420–8.
17. Guss JL, Kissileff HR, Pi-Sunyer FX. Effects of glucose and fructose solutions on food intake and gastric emptying in nonobese women. Am J Physiol 1994;267:R1537–44.
18. Yoshikawa T, Inoue R, Matsumoto M, Yajima T, Ushida K, Iwanaga T. Comparative expression of hexose transporters (SGLT1, GLUT1, GLUT2 and GLUT5) throughout the mouse gastrointestinal tract. Histochem Cell Biol 2011;135:183–94.
19. Zhao FQ, Glimm DR, Kennelly JJ. Distribution of mammalian facilitative glucose transporter messenger rna in bovine tissues. Int J Biochem 1993;25:1897–903.
20. Chelikani PK. Intravenous infusion of glucagon-like peptide-1 potently inhibits food intake, sham feeding, and gastric emptying in rats. Am J Physiol 2005;288:R1695–706.
21. Larsen PJ, Fledelius C, Knudsen LB, Tang-Christensen M. Systemic administration of the long-acting GLP-1 derivative NN2211 induces lasting and reversible weight loss in both normal and obese rats. Diabetes 2001;50:2530–9.
22. Williams DL, Baskin DG, Schwartz MW. Evidence that intestinal glucagon-like peptide-1 plays a physiological role in satiety. Endocrinology 2009;150:1680–7.
23. Gorboulev V, Schürmann A, Vallon V, Kipp H, Jaschke A, Klessen D, Friedrich A, Scherneck S, Rieg T, Cunard R, et al. Na+-d-glucose cotransporter SGLT1 is pivotal for intestinal glucose absorption and glucose-dependent incretin secretion. Diabetes 2012;61:187–96.
24. Röder PV, Geillinger KE, Zietek TS, Thorens B, Koepsell H, Daniel H. The role of SGLT1 and GLUT2 in intestinal glucose transport and sensing. PLoS ONE 2014;9:e89977.
25. Bello NT, Kemm MH, Ofeldt EM, Moran TH. Dose combinations of exendin-4 and salmon calcitonin produce additive and synergistic reductions in food intake in nonhuman primates. Am J Physiol 2010;299:R945–52.
26. Scott KA, Moran TH. The GLP-1 agonist exendin-4 reduces food intake in nonhuman primates through changes in meal size. Am J Physiol 2007;293:R983–7.