Nutritional Sciences 9(4), November, 2006, pp.280-287

Effect of Glucose-Sweetened Drinks on Blood Glucose, Energy, and Water Intake at a Meal 3h Later in Healthy Males*

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The aims of this study were to describe the effects of glucose-sweetened drinks on blood glucose, energy, and water intake at a meal 3 hours later. The effect of blood glucose on prandial energy intake and the relationship between water and energy intake during a meal were also determined. Twenty healthy normal-weight men were fed pizza test meals 3h after consuming four drinks of 0, 50g, 65g, and 75g glucose in random order, within-subjects design. Blood samples were measured at baseline and every 30 min after ingestion of drinks and 30min after the end of the test meal and the appetite was also assessed by visual analog test at the same interval. The results of this study showed that various glucose drinks altered blood glucose responses compared with that of water control($p<0.0001$). Blood glucose areas under the curve(AUC) for glucose-sweetened drinks were significantly($p<0.05$) higher than that for the control over 3 hours after a drink and 30 min after the test meal. Consumption of the glucose-sweetened drinks significantly increased($p<0.05$) energy and water intake at a test meal compared with the water control, except the drink containing 75g glucose. For all drinks combined, the energy intake was negatively correlated with the blood glucose and positively correlated with the volume of water consumed at a test meal at 3 hours later.

Key words: Sugar drink, Blood glucose, Water intake, Energy intake, Hunger

Received August 4, 2006; Revised September 27, 2006; Accepted October 11, 2006

INTRODUCTION

The current trends in consumption patterns have shown that a reduction of dietary fat tends to cause a compensatory increase in sugar and starch intakes.[1] Moreover, the consumption of sugar-containing beverages has become one of the major dietary causes of obesity in certain young age groups.[2] It has been hypothesized that sugar consumption is a causal factor in hypoglycemia. The rationale for this hypothesis begins with the assumption that simple carbohydrates are more rapidly digested and absorbed than complex carbohydrates and therefore cause greater increase in blood glucose concentration.[3,4] This rapid rise in blood glucose stimulates insulin secretion, which may increase peripheral glucose uptake to such an extent that blood glucose concentration nadir is lower than the fasting concentration in a short time later.[5,6]

Several previous studies showed that the blood glucose reached a peak at 30 min after the consumption of 50-75 g glucose containing drinks and then returned to the baseline by 90-180 min. It was also observed that blood glucose was below the baseline from 90 to 210 min after the ingestion of glucose drinks.[7-9] It has been repeatedly shown that a transient drop of blood glucose concentration, both insulin induced hypoglycemia and spontaneous falls within the normal range, stimulates hunger and food intake.[10,11] Thus, it can be assumed that the decreased blood glucose following the consumption of glucose-sweetened drink would play a certain role in triggering hunger, leading eventually to overeating at a test meal. However, it is still hardly anything known about the effects of decreased blood glucose induced glucose-sweetened drink on appetite and food intake in healthy subjects. Moreover, most of the published studies on sugar-sweetened drinks are short-term studies in which the interval between a preload and test meal lasts less than 2 hours. Generally, the interval between meals lasts longer than 3 hours because humans occasionally have a few meals per day. Therefore, in order to investigate the effect of sugar-sweetened drinks on the subsequent test meal, the interval between a preload and test meal might be more than 3 hours.

* This study was supported by the research funds of 2003 GSNU Professor Sabbatical Year Programme.
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People drink approximately two-thirds of their daily water intake around meal time.[12] In addition, a significant positive correlation has been found between the amount of fluid consumption and the size of meal in the natural environment.[13] Diabetics are characterized by not only hyperglycemia but also polydipsia and hyperphagia, and water consumption was elicited by insulin administration.[14-16] However, knowledge on the relation between blood glucose response, prandial water and food intake is limited.

Therefore, the purpose of this study is to investigate the effect of glucose-sweetened drinks on blood glucose, energy, and water intake. In addition, the effect of blood glucose at 3 hours later on prandial food intake and the relationship between water and food intake during a meal were also determined.

SUBJECTS AND METHODS

1. Subjects

Subjects included in the study were 12 males between 18-35 years of age, healthy, non-smokers, with BMI between 20 and 25. They were recruited through advertising around the University of Toronto campus. Diabetics, breakfast skippers, and restrained eaters were excluded. Restraints were determined by a score of 11 or higher on the Eating Habits Questionnaire.[17] Characteristics of the subjects are shown in Table 1. Fasting blood glucoses were from 5.2 to 5.1 mmol/L which were in the normal range. They all gave their written informed consent before the session and were financially compensated for completing four sessions. This study was approved by the Medical Ethics Committee of the University of Toronto, Toronto.

Table 1. Subjects' characteristics and sensory ratings of preloads and the test meal

	Value[1]
Height(m)	1.79±0.01
Weight(kg)	74.5±1.8
Body mass index(kg/m^2)	23.3±0.4
Age(y)	22±1
Fasting blood glucose(mmol/L)	5.1±0.0
Restraint scores[2]	6.1±0.8
Pleasantness rating of preload(mm)[3]	
Control	57±6
50g glucose	57±6
65g glucose	63±7
75g glucose	59±5
Pleasantness rating of test meal(mm)	79±2

[1] Mean±SEM: n=12 men.
[2] See, literature number 17.
[3] Pleasantness were rated on 100-mm vertical visual analogue scales.

2. Design

Four drinks were given to each of the subjects weekly in random order within-subjects design. Subjects came to the laboratory on 4 separate days. Test days were separated by ≥1 wk.

3. Experimental Protocol

The subjects presented themselves at the same time for each of four sessions after a 12-14 h fast in order to test the effect of glucose-sweetened drinks on food intake. Four drinks were administered: a water control, 50 g glucose, 65 g glucose, and 75 g glucose. All preloads were given in the form of beverage and matched for sweetness using sucralose. Palatability of all preloads was improved using lemon juice. All drinks were made up to 400 mL using bottled spring water. An additional 100 mL spring water was consumed in a separate glass, which brought the total volume consumed to 500 mL. The energy content of drinks was ranged between 0 and 300 kcal and the temperature was kept at constant level(6-8 ℃). The composition of drinks is shown in Table 2.

During the test day, subjects arrived from 8:00 to 10:30, 2 hours after waking up in the morning. Upon arrival, subjects filled out a questionnaire to describe their sleep, stress, and activity levels in the past 24 hours, and they were measured baseline blood glucose. Then one of the drinks was served. Each of the drinks was consumed within five minutes. They spent the test days with one or two other volunteers in a quiet room and were allowed to read and rest, but had no verbal contact with other volunteers.

Subjects' subjective feelings of desire, hunger, fullness, and prospective consumption for food were regularly recorded on 100 mm vertical analog scales(VAS)

Table 2. Ingredients and energy contents of the preloads

	Control	50G	65G	75G
Sucralose[1](mg)	200	50	10	0
Glucose[2](g)	0	50	65	75
Water[3](g)	382	344	336	329
Lemon Juice[4](ml)	10	10	10	10
Energy(kcal)	0	200	260	300

Control : water only, 50G : 50g glucose, 65G : 65g glucose, 75G : 75g glucose
[1] Tate&Lyle Sucralose, The Science & Technology Centre, Reading, United Kingdom.
[2] Grain Process Enterprises Ltd. Scarborough, ON, Canada.
[3] Crystal Springs. Edan/Dwna Inc., Quebec, Canada.
[4] Realemon, Cadbury Beverages Canada Inc., Mississauga, ON, Canada.

at baseline and at t= 30, 60, 90, 120, 150, 180 min after the ingestion of drinks and at 30 min after the end of the test meal. Pleasantness of drinks and test meal eaten was rated after each consumption. Blood samples were also taken at baseline and every 30 min after the end of the drink and the test meal. Blood glucose was taken using a Lancet Device(Becton, Dickinson and Company, Franklin Lakes, NJ, USA) for the finger pricks, and a portable blood glucose monitor(Accu-Chek, Compact, Roche Diagnostics Division of Hoffmann-La Roche Limited 201, Boul. Armand Frappier, Laval, Québec, Canada).

Energy and water intakes were assessed at the test meal. Food was measured by weighing the pizza before and after baking and reweighed after subjects finished eating to obtain the net(grams) consumed. At mealtime, the subjects were served pizzas which were cooked according to manufacturer's instructions. A 1.5 L bottle of spring water(Crystal Springs, Québec, Canada) was also served. The subjects were instructed to eat and drink as much as desired but only until they felt comfortably full. They were given an unlimited amount of time to eat. Energy(kilocalories) consumed was calculated from information provided by McCain Foods, Florenceville, N.B.

4. Calculations and Statistical Analysis

SAS(version 7.1, Statistical Analysis Systems, SAS Institute Inc., Carey, NC) was used for the statistical analyses. All results were presented as mean± standard error of the mean(SEM). Area under the curves(AUCs) for blood glucose concentrations were calculated for the 3 h after a drink and 30 minutes after a meal according to the trapezoidal method.[18] Mean appetite was calculated using the average of four aspects of the motivation-to-eat VAS questionnaire, according to the following equation: {Desire+Hunger+(100-Fullness)+Prospective consumption}/4. Analysis of variance (ANOVA) for two-factors with repeated measures[19] was used to test VAS ratings and blood glucose concentration. ANOVA for one-factor with repeated measures was also used to investigate to test for the effect of the drinks on the outcome variables of AUCs, energy intake, water intake, and appetite. Duncan's or Tukeys' multiple range tests were performed when drink effects were statistically significant($p<0.05$). Correlation analyses were conducted between AUCs, appetite, and energy intake using the Pearson correlation coefficient.

RESULTS

1. Blood Glucose Response

Blood glucoses over 180 min after a glucose-sweetened drink and at 30 min after a test meal were affected by both drink($F=36.22$; $P<0.0001$, Fig. 1) and time ($F=63.93$; $P<0.0001$), and a time by drink was present ($F=15.89$; $P<0.0001$). The baseline concentrations of blood glucose was from 5.1 to 5.2 mmol/L, which were in the normal range. Peak blood glucose concentrations occurred at 30 min after the ingestion of glucose-sweetened drinks in all groups. The blood glucose concentrations after the consumption of 50 g and 65 g glucose were returned to baseline by 120 minutes, whereas the blood glucose concentration for the 75 g glucose returned to baseline by 150 minutes. The absolute blood glucose concentrations for the control were not different from baseline over 180 minutes.

The 75 g glucose-sweetened drink produced the largest AUC and the control produced the smallest AUC measurement($F=37.58$;$P<0.0001$, Fig. 2-a). However, blood glucose AUC over 180 min for the various glucose drinks were not different from each other. Similarly, the blood glucose AUCs over 180 min before and 30 minutes after the meal had the same trend($F=37.77$;$P<0.0001$, Fig. 2-b).

2. Energy and Water Intake

The overall effect of drinks on energy intake at 180 min was significantly different($F= 3.43$; $P<0.05$, Fig. 3-a). The 50 g glucose and 65 g glucose drinks increased

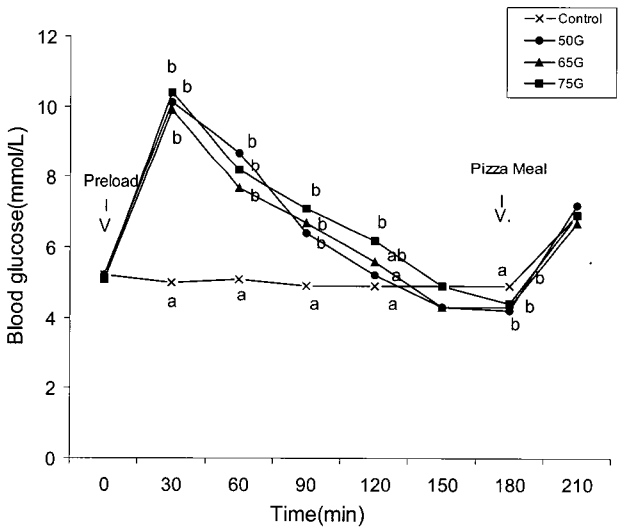

Fig. 1. Effect of treatments on blood glucose concentration(n=12)
Means with the same letter are not significantly different from each other($p<0.05$)

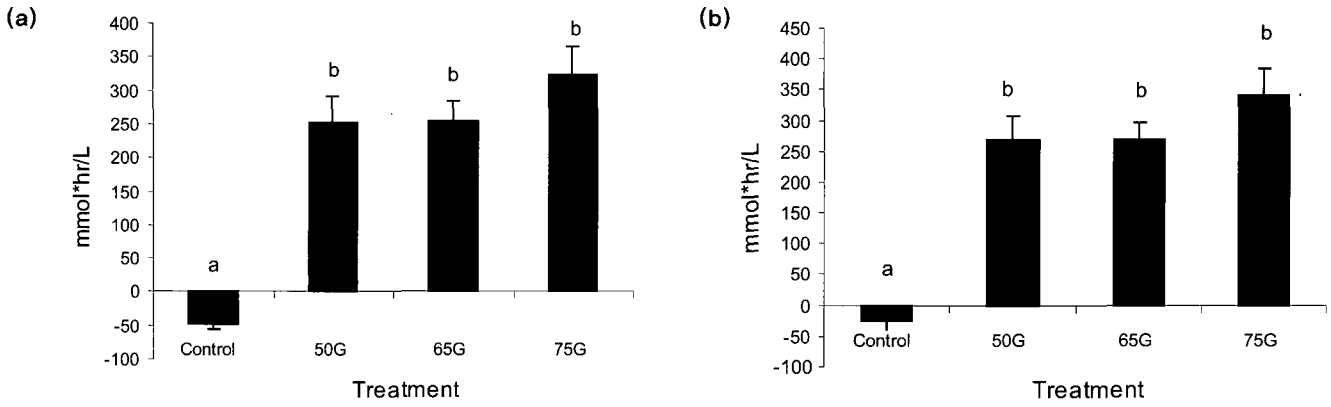

Fig. 2. (a) Mean(±SEM)areas under the curves(AUC) for blood glucose concentrations during 3 hours after consumption of preloads. (b) Mean(±SEM)areas under the curves(AUC) for blood glucose concentrations during 3 hours after consumption of preloads and 30min after the test meal

n=12, Means with the same letter are not significantly different from each other(p<0.05).

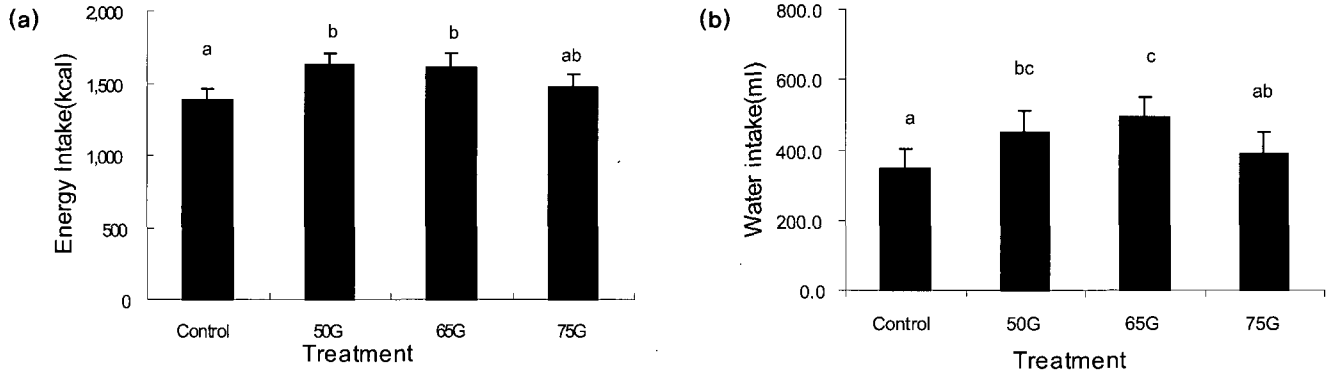

Fig. 3. (a) Energy intake at the test meal 3 hours after consumption of the preloads. (b) Water intake at the test meal 3 hours after consumption of the preloads

Mean±SEM, n=12, Means with the same letter are not significantly different from each other (p<0.05).

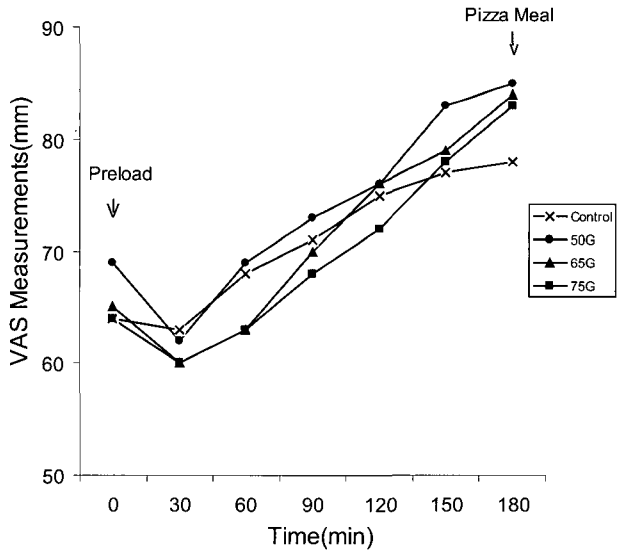

Fig. 4. Effect of the treatments on appetite(n=12)

All values are not significantly different from each other(p<0.05).

energy intake at the test meal compared to the control. However, the energy intake after the consumption of 75 g glucose drink was not different from that after the control.

Water intake was affected by drinks(F=4.22; P<0.05, Fig. 3-b). After the consumption of 65 g glucose and 50 g glucose drinks, the water intakes at the meal were higher than that after the control. However, water intakes following 75 g glucose and control were similar to each other.

3. Ratings

Average appetite was initially decreased and then increased with time(F=19.18; P<0.0001, Fig. 4) However, the ratings during the 180 min after the consumption of drinks were not different among the drinks.

4. Relations Among Dependent Measures

The blood glucose concentration at 3 hours was negatively correlated with the energy intake at test meal

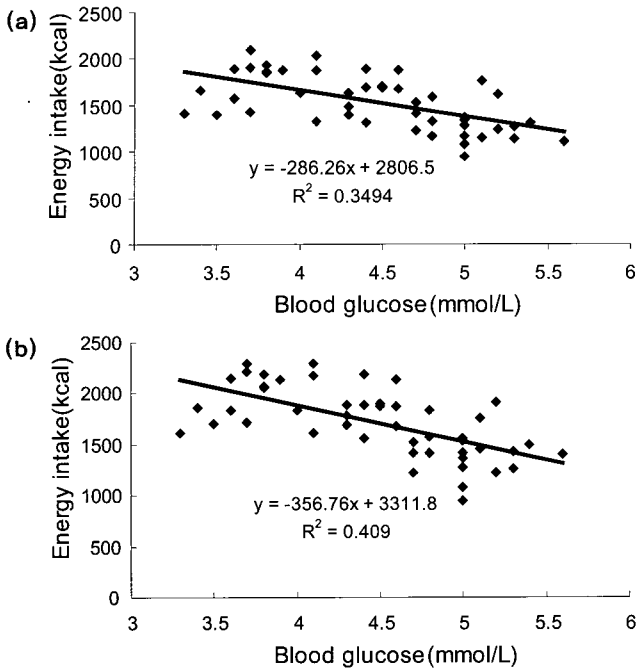

Fig. 5. (a) Relationship between the blood glucose and the energy intake at the test meal 3 hours after consumption of preloads. (b) Relationship between the blood glucose and the energy intake from preloads plus the test meal 3 hours after consumption of preloads.

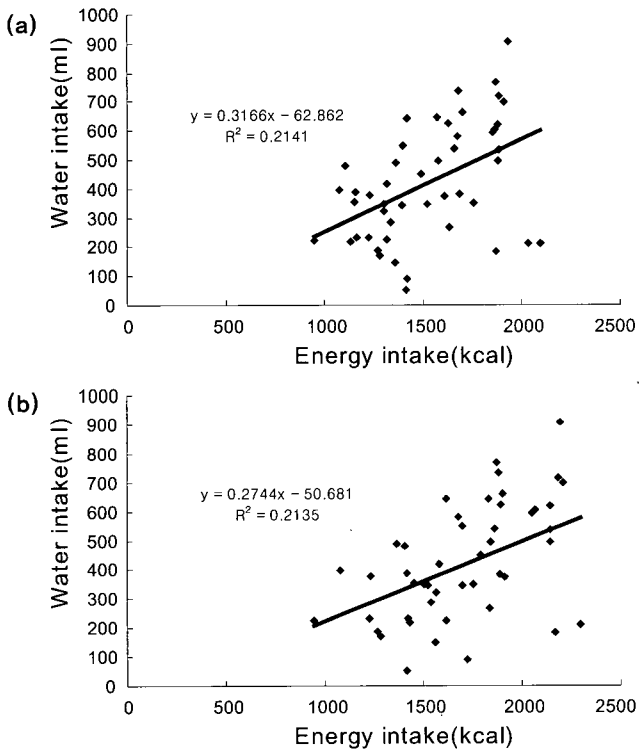

Fig. 6. (a) Relationship between energy intake and water intake at the test meal. (b) Relationship between energy intake from prloads plus the test meal and water intake at the test meal

in the pooled data from all drinks(Fig. 5-a). There was also a negative correlation between the blood glucose concentration at 3 hours and the energy intake from the test meal plus the preload(Fig. 5-b). A positive correlation was found between the volume of water consumed at the test meal and the mealtime energy intake in the pooled data from all preloads(Fig. 6-a). There was also a positive correlation between the water intake at the test meal and the energy intake from the test meal plus the preload(Fig. 6-b).

DISCUSSION

The present results showed that the consumption of 50 g and 65 g glucose-sweetened drinks increased energy intake at a test meal 3 h later compared with the water control, however, the energy intake after 75 g glucose was not significantly different from that after the control. It is well established that high-sugar diets, compared to polysaccharide based diets, promote overeating and obesity in laboratory animals.[20] Furthermore, sugar containing diets have been shown to increase energy intake and body weight in epidemiological studies or studies lasting for weeks.[2,21,22]

However, the short-term effect of sugar-sweetened drink on human appetite or food intake is still unclear. A few studies have reported that the ingestion of various amount of sugar preloads in the form of beverages suppressed food intake and appetite in healthy subjects,[23-25] whereas most of the other studies did not find this effect.[26-28] Moreover, the total energy intake was larger after sugar-sweetened drink compared with the water control when the energy from sugar-sweetened drink was included in those studies.[28,29] The differences in experimental design may account for some of the discrepant results, such as the length of interval between the preload and the test meal, the concentration, and the temperature of sugar-sweetened beverages.

The timing of preload consumption may be one of the critical factors on the subsequent energy intake. In the 20-60 min delayed condition, subjects compensated for the calories in the sugar drinks compared with the water control, but as the interval increased, the compensation was less precise. In a study comparing sugar or fat containing preload with three different intermeal intervals, it was found that subjects consumed less at 30 min after a sugar preload. However, energy intake was not different from that after 90 min or 180 min compared with a no-preload condition.[30] Energy intakes at test

meal were not reduced in response to the sugar-containing beverages compared to the water control as the length of time was increased longer than 2h. Thus the total energy intake, including food and beverage, was higher than that observed for water control.[31] Generally, food intake in humans is episodic. That is, the interval between meals lasts more than 3 hours. Therefore, in order to investigate the effect of sugar-sweetened drinks on a subsequent meal, test meals might be delayed more than 3 hours following a preload, which is rarely observed in the short-term study of human appetite. As far as it is concerned, this is the first time to show evidence that sugar-sweetened drinks stimulate subsequent energy intake 3 hours later in healthy subjects. Why should the consumption of glucose-sweetened drinks enhance the energy intake in the meal 3 hours later? Transient declines in blood glucose were first described by Louis-Sylvestre and Le Magnen,[32] who showed that a fall in blood glucose was correlated with meal initiation. After that, many studies have shown that dynamic declines or transient declines were related to meal request[33,34] and hunger[11] under various conditions. The rapid drop after a drink-induced rise in blood glucose is particularly a strong signal for meal initiation[33] Therefore, in order to investigate increased hunger represented by energy intake at test meal, the initiation of the teat meal must occur at a proper point in time point between preload and test meal consumption according to the concentration of glucose-sweetened drinks and subject conditions.[34] It might be very difficult to arrange such complicated experimental conditions, so that there are many studies with preloads ranging from 80 to 300 kcal and intermeal intervals ranging from 20 to 180 min have shown contrasting results.[24,26,27,30]

The temperature of drink might be another factor to influence subsequent energy intake. In previous studies, the temperature of beverage affected skin temperature and autonomic nervous system activation,[35] and it also affected gastric emptying[36] and food intake in male subjects.[37] The temperature of all drinks were kept at 6-8 ℃ in this study. Rolls[28] also reported that the temperature of preloads was 7 ℃. However, the temperature of preloads was not represented[23,2426] or at room temperature[25] in most of the short-term food intake studies. Therefore the uncontrolled or different temperature of preloads among studies may have been a contributing factor to the conflict results in those studies. Collectively, the postprandial decline in blood glucose following a 50 g or 65 g glucose in chilled beverage might act as one of the physiological signals for hunger, at least under this experimental condition.

In the present study, for all drinks combined, the energy intake in the test meal was negatively correlated with the blood glucose at 3 hours later. There was also a negative correlation between blood glucose concentration at 3 hours and the total energy intake including the meal and preload intake. The negative correlations between blood glucose and energy intake support the hypothesis that blood glucose patterns are involved in the physiological regulation of eating.[38]

This study also allowed an investigation of the promoting effect of glucose-sweetened drink on the water intake at a test meal. Consumption of glucose-sweetened drinks increased water intake at a test meal 180 min later compared with a water preload, except for the 75 g glucose drink, which was not significantly different. A significant positive correlation has been found between the amount of fluid consumption and the size of meal in the natural environment.[13] Although most drinking happens around meal time[12,39] very little is known about what controls this pattern of drinking or what factors influence prandial drinking.

Several studies reported that insulin is a dipsogenic substance in humans, and it significantly increases the sensation of thirst.[14] Since plasma insulin was not measured in the present study, the assumptions about how it may have responded to glucose-sweetened drinks can not be made. However, the rapid rise in blood glucose after the ingestion of sugar-sweetened drink may stimulate insulin secretion, which may promote water intake more than a water preload at test meal.

The energy intake in the pooled data from all preloads (Fig. 6-a) was positively correlated with the volume of water consumed at the test meal. The results implied that higher energy intake at the meal had a stimulating effect on the volume of water consumption. Currently, there are no data reported with which the present observations can be compared. Whereas, some studies have examined whether or not increasing volume of foods by adding water to food or drinking a beverage can lead to the reduction in energy intake. Results have shown that drinking water as a beverage or increasing soup volume by adding water does not affect energy intake at meal.[40,41] In those studies, water intake was an independent variable, and in the present study, the independent variable was energy intake at meals. From these findings, and considering the results of the above studies, drinking water as a beverage at meals could be affected by food intake, rather than influencing energy intake at meals.

In conclusion, the results of this study demonstrated

that the consumption of 50 g or 65 g glucose-sweetened drinks increased energy and water intakes at a test meal 3 hours later compared with the water preload, For all drinks combined, the energy intake in the test meal was negatively correlated with the blood glucose and positively correlated with the volume of water consumed at a test meal at 3 hours later.

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