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Consumption of artificial sweetened beverages associated with adiposity and increasing HbA1c in Hispanic youth

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Summary

Research examining the impact of artificial sweetened beverages (ASBs) on obesity and metabolic diseases in adolescents is limited. The overall goal is to examine the longitudinal effects of ASBs on changes in adiposity and metabolic parameters in Hispanic adolescents. Longitudinal cohort with 98 Hispanics (12–18 years) who were overweight or had obesity with the following data at baseline and 1-year later: anthropometrics, diet (24-h recalls), body composition (DXA), glucose and insulin dynamics (oral glucose tolerance and frequently sampled intravenous glucose tolerance test) and fasting lipids. Repeated measures analyses of covariance assessed changes over time between control (no ASBs at either visit), ASB initiators (no ASBs at baseline/ASBs at 1-year) and chronic ASB consumers (ASBs at both visits). ASB initiators (n = 14) and chronic ASB consumers (n = 9) compared to control (n = 75) had higher total body fat at baseline and 1-year (P = 0.05 for group effect). Chronic ASB consumers had a 6% increase in haemoglobin A1c, 34% increase in energy intake (kcal d^{-1}) and 39% increase in carbohydrate intake (g d^{-1}) over time, while control and ASB initiators maintained (P < 0.05 for group-by-time interactions). These results do not support promoting ASBs as a strategy for adiposity loss or to improve metabolic health.

Keywords: Adiposity, artificial sweeteners, HbA1c.

Introduction

Added sugars, particularly those from sugar-sweetened beverages (SSBs), have been consistently linked to adiposity and metabolic disease risks in both children and adults (1, 2). Given the increase in research linking sugar and SSBs to obesity and related diseases, artificial sweetened products and beverages have gained enormous popularity, particularly in youth populations. Studies in adults have shown that increased intake of artificial sweeteners are linked to increases in obesity and weight gain (3, 4).

There has been an increase in research studies investigating the impact of artificial sweeteners on health in children. A meta-analysis of six prospective observational cohort studies on artificial sweeteners in children with a minimum of 1-year follow-up data revealed that artificial sweeteners were linked with increased body mass index (BMI) and fat mass (5). However, the above studies included primarily non-Hispanic White populations and the outcomes did not include metabolic outcomes. A few experimental studies have been conducted and have yielded mixed results. One 18-month randomized controlled trial (RCT) with 641 children (7–10 years) found that subjects randomized to receive artificial sweetened beverages (ASBs) compared to those who received SSBs had less weight gain (+6.4 kg vs. +7.4 kg, P < 0.001) and less fat accumulation (+3.2 vs. +5.5, P = 0.02) (6). In contrast, an 8.5-month RCT found that participants randomized to receive ASBs compared to those receiving SSBs had a higher weight for age z-score (+0.07, 95% CI 0.14–0.002, P = 0.03) (7). To date, no study has assessed the impact of ASB intake on adiposity in an exclusively Hispanic population.

In addition, the literature is sparse on how ASBs impact metabolic health in youth. Several adult studies have shown that ASB intake is linked to the metabolic syndrome, glucose intolerance, type 2 diabetes (T2D) and cardiovascular disease (8, 9). Only a few cross-sectional studies have examined the impact of ASBs on metabolic health in youth and found no effect of ASB on blood pressure, or fasting glucose, insulin or lipids (10, 11). These studies all relied on fasting blood samples and, to our knowledge, no study has examined the impact of ASBs on glucose and insulin action using more sophisticated measures, such as oral and intravenous glucose tolerance tests. Nor any study has examined the longitudinal effects of ASBs on metabolic health in high-risk Hispanic adolescents.

Hispanic children are disproportionately impacted by obesity (12) and over 30% of Hispanic children who are overweight or have obesity (8–14 years) have pre-diabetes and the metabolic syndrome (13). Hispanic children who are overweight or have obesity have increased insulin resistance and greater risk for T2D compared to their counterparts who are overweight (13–15). In cross-sectional and longitudinal studies with over 500 Hispanic youth (2–18 years), diets high in added sugar and SSBs are linked to increased obesity prevalence (16, 17) and poor β-cell function (2, 18). To date, no study has examined how ASBs impact adiposity, metabolic health, and dietary intake in a high-risk Hispanic youth population, i.e., those who are overweight or have obesity and have a family history of T2D. Given that recent national consumption trends in the United States show the prevalence of low-calorie SSB consumption significantly increased from 2.3% in 2003–2004 to 4.8% in 2013–2014 among 12–19-year-old children, it is important to examine how changes in ASB can impact obesity and related disease risk, particularly in high-risk populations (19). Thus, the overall goal of this study is to examine the longitudinal changes in adiposity, metabolic parameters, and dietary intake within and between high-risk Hispanic adolescents who do not consume ASB, ASB initiators and chronic ASB consumers. The hypothesis is that ASB consumption will be linked to increases in adiposity and metabolic disease risk over time in this population.

Materials and methods

Subjects

Procedures and findings of the SOLAR (Study of Latino Adolescents at Risk for Diabetes) cohort have been previously described in detail (13). Participants were recruited from the greater Los Angeles County through community health clinics, health fairs and word of mouth. The present analyses included 98 adolescents with at least two annual visits, 1 year apart, with complete dietary data and adiposity/metabolic data collected between 2004 and 2013. Inclusion criteria for SOLAR were as follows: (i) 8–18 years; (ii) BMI ≥85th percentile for age and sex; (iii) Hispanic ancestry (all four grandparents of Hispanic origin as determined by parental self-report) and (iv) family history of T2D. Participants were excluded for taking any medication known to affect body composition or diagnosed with a disease(s) known to affect body composition. The Institutional Review Board of University of Southern California approved this study. Informed written consent and assent were obtained from both parents and children before testing commenced.

Anthropometrics and adiposity measures

A licensed paediatric health-care provider performed a detailed physical examination where Tanner staging was determined using established guidelines (20, 21). Height and weight were measured using a beam medical scale and wall-mounted stadiometer to the nearest 0.1 kg and 0.1 cm, respectively, and the average of the two measurements was used for analysis. BMI *z*-scores were determined by using the EPII 2000 software (version 1.1; Centers for Disease Control and Prevention, Atlanta, GA, USA) (22). Whole-body fat and soft lean tissue were measured by dual-energy X-ray absorptiometry with the use of a Hologic QDR-4500W (Hologic, Bedford, MA, USA).

Metabolic parameters

After an overnight fast, a 2-h oral glucose tolerance test (OGTT) was conducted with a dose of 1.75 g glucose per kilogram body weight. Blood was sampled and assayed for glucose and insulin at −5 min (fasting state) and at 120 min relative to glucose ingestion. Within 1 month, children without diabetes returned for an overnight visit when a frequently sampled intravenous glucose tolerance test (FSIVGTT) was performed. At time 0, glucose (25% dextrose, 0.3 g kg^{-}1 body weight) was administered intravenously and insulin (0.02 U kg^{-1} body weight; Humulin R; Eli Lilly, Indianapolis, IN, USA) was injected intravenously at 20 min. A total of 13 blood samples were collected. Glucose and insulin incremental area under the curve (IAUC) were calculated from the 13 blood samples. Using the MINMOD MILLENIUM 2003 computer program (version 5.16; Bergman, USC, Los Angeles, CA, USA), insulin sensitivity (SI), acute insulin response (AIR) and disposition index (DI – an index of β-cell function) were determined. Lipids and haemoglobin A1c (HbA1c) were obtained from the fasting blood draw at the FSIVGTT.

Assays

Blood samples were centrifuged immediately to obtain plasma, and aliquots were frozen at –70 °C until assayed. Glucose from the OGTT was analysed on a Dimension® Clinical Chemistry System with the use of an *in vitro* Hexokinase method (Dade Behring, Deerfield, IL, USA). Glucose from the FSIVGTT was assayed in duplicate on an analyser (model 2700; Yellow Springs Instrument, Yellow Springs, OH, USA) using the glucose oxidase method. Insulin was assayed in duplicate by using specific human insulin Enzyme-Linked Immunosorbent Assay (ELISA) Kit (Linco, St Charles, MO, USA). Fasting lipids, including triglycerides (TAG), low-density lipoprotein (LDL) cholesterol and high-density lipoprotein (HDL) cholesterol were assessed using Vitros Chemistry DT Slides (Johnson and Johnson Clinical Diagnostics Inc., Rochester, NY, USA). HbA1c was measured by high-pressure liquid chromatography (model 11c 2.2 HLC-723; Tosoh, Tokyo, Japan).

Dietary intakes

Dietary intake was assessed from two 24-h dietary recalls using the multiple pass method by Nutrition Data System for Research (NDS-R 2012 version 5.0_35). The multiple pass consists of the following: (i) a "Quick List" pass in which the respondent are asked to list everything eaten or drunk the previous day; (ii) a "Forgotten Foods" pass in which a standard list of food/beverages, often forgotten, is read to prompt recall; (iii) a "Time and Occasion" pass in which the time and name of the eating occasion are collected; (iv) a "Detail" pass in which detailed descriptions and portion sizes are collected and the time interval between meals is reviewed to check for additional foods and (v) the "Final" pass, which provides one last opportunity for the respondent to remember foods consumed. Dietary recalls (one in person and one via telephone) were performed within 1 week of the FSIVGTT testing visit by a bilingual trained technician with the use of three-dimensional food models. The NDS-R program calculates energy, macronutrients, and food/beverages, including ASBs (those found in sodas, coffees, energy drinks, teas, sports drinks, juices and flavoured waters) and SSBs. A serving size of ASB is eight fluid ounces.

Dietary data was screened for plausibility by performing a regression of caloric intake on body weight. All subjects were within two standard deviations from the mean; therefore, all subjects were included for this analysis. Average days between recalls at baseline were 6.7 ± 2.0 and 7.0 ± 4.0 for 1-year. Participants were divided into the following ASB groups: control (no ASBs at either baseline or 1-year; $n = 75$), ASB initiators (no ASBs at baseline but started drinking ASBs at 1-year; $n = 14$) and chronic ASB consumers (consumed ASBs at both time points; $n = 9$).

Statistical analyses

Data were examined for normality, and the following variables were non-normally distributed and were log-transformed: insulin IAUC, SI, AIR, total cholesterol, TAG, dietary carbohydrate, dietary fat, added sugar, dietary fibre and SSB. Repeated measures analyses of covariance (ANCOVA) were run to examine changes in adiposity and metabolic measures, and dietary intake within control, ASB initiators and chronic ASB groups (i.e., group effect) and between groups (i.e., interaction effect). The following *a prior* covariates were included: energy intake (kcal d^{-1}), sex, Tanner at baseline and 1-year and total body fat (for metabolic outcomes only). All analyses were performed by SPSS version 24.0 (SPSS, Chicago, IL, USA) and the significance was set at $P \leq 0.05$.

Table 1 Physical and metabolic characteristics of participants at baseline and 1-year follow-up ($n = 98$)*

Physical and adiposity measures	Baseline	1-Year follow-up
Sex (M/F)	55/43	
Age (years)	14.0 ± 1.8	15.1 ± 1.8
Tanner stage		
1 and 2	21 (20.6)	10 (9.8)
3–5	77 (78.6)	89 (90.8)
Height (cm)	162.0 ± 10.1	165.1 ± 9.3
Weight (kg)	84.4 ± 20.8	88.8 ± 20.3
BMI percentile	96.6 ± 4.6	95.7 ± 7.9
BMI *z*-score	2.1 ± 0.5	2.0 ± 0.6
Overweight prevalence (%)	17 (16.5)	24 (23.3)
Obese prevalence (%)	86 (83.5)	79 (76.7)
Total fat (kg)	30.6 ± 10.7	31.1 ± 11.5
Trunk fat (kg)	15.1 ± 5.8	15.8 ± 6.4
Percent fat (%)	36.7 ± 7.1	35.2 ± 8.1
Metabolic parameters		
Fasting glucose (mg dL^{-1})	91.8 ± 7.8	87.8 ± 8.5
Fasting insulin (μU mL^{-1})	14.2 ± 10.0	14.8 ± 13.6
2-h glucose (mg dL^{-1})	123.9 ± 22.0	119.0 ± 23.4
HbA1c	5.4 ± 0.4	5.5 ± 0.4
Glucose IAUC (nmol min^{-1} L^{-1})	79.1 ± 33.6	80.2 ± 34.1
Insulin IAUC (nmol min^{-1} L^{-1})	288.3 ± 202.3	258.0 ± 195.6
SI ($\times 10^{-4}$ min^{-1} μU mL^{-1})†	1.6 ± 1.0	1.7 ± 0.9
AIR (μU mL^{-1} × 10 min)†	1521.7 ± 1038.5	1492.0 ± 919.6
DI ($\times 10^{-4}$ min^{-1})†	1881.9 ± 820.5	2095.4 ± 969.1
Total cholesterol (mg dL^{-1})‡	145.8 ± 24.1	139.5 ± 26.7
Triglycerides (mg dL^{-1})‡	105.4 ± 53.0	95.8 ± 48.7
LDL cholesterol (mg dL^{-1})‡	87.5 ± 20.1	83.9 ± 23.9
HDL cholesterol (mg dL^{-1})‡	37.3 ± 7.8	36.4 ± 8.5

*Data are mean ± SD or *n* (%).
†$n = 55$.
‡$n = 66$.
AIR, acute insulin response; BMI, body mass index; DI, disposition index; HbA1C, haemoglobin A1c; HDL, high-density lipoprotein; IAUC, incremental area under the curve; LDL, low-density lipoprotein; SI, insulin sensitivity.

Table 2 Mean (SD) physical and adiposity measures at baseline and 1-year in control (n = 75), ASB initiators (n = 14) and ASB chronic (n = 9) consumers

Physical and adiposity measures	Control		ASB initiators		Chronic ASB		Group (P-value)	Group × time (P-value)
	Baseline	1-Year	Baseline	1-Year	Baseline	1-Year		
BMI z-score	2.0 ± 0.5	2.0 ± 0.6	2.1 ± 0.4	2.1 ± 0.4	2.2 ± 0.3	2.2 ± 0.5	0.15	0.28
Total fat (kg)	28.3 ± 9.5	28.9 ± 10.7	34.1 ± 11.7	34.2 ± 10.2	34.9 ± 9.8	34.5 ± 12.2	0.05	0.96
Trunk fat (kg)	14.3 ± 5.4	15.1 ± 6.1	17.0 ± 6.9	17.2 ± 6.3	16.3 ± 4.2	17.0 ± 5.9	0.22	0.91
Fat (%)	35.8 ± 6.9	34.4 ± 8.3	37.4 ± 7.9	37.0 ± 7.4	37.2 ± 6.4	35.5 ± 7.8	0.34	0.72
Metabolic parameters								
Fasting glucose (mg dL^{-1})	92.5 ± 7.3	88.7 ± 9.0	91.9 ± 8.3	84.6 ± 8.1	91.9 ± 6.6	85.0 ± 4.3	0.67	0.47
Fasting insulin (μU mL^{-1})	13.6 ± 10.3	14.2 ± 10.0	15.6 ± 8.0	20.1 ± 23.6	16.3 ± 11.1	13.8 ± 10.3	0.36	0.51
2-h glucose (mg dL^{-1})	124.2 ± 21.5	118.4 ± 23.2	126.9 ± 28.8	127.9 ± 20.9	122.3 ± 19.8	110.1 ± 25.6	0.46	0.46
HbA1c	5.5 ± 0.4	5.5 ± 0.4	5.4 ± 0.3	5.5 ± 0.4	5.1 ± 0.2	5.4 ± 0.3	0.28	0.01
Glucose IAUC (nmol min^{-1} L^{-1})	79.9 ± 35.5	80.5 ± 34.9	77.5 ± 18.7	86.2 ± 25.3	76.0 ± 40.5	73.5 ± 35.8	0.89	0.93
Insulin IAUC (nmol min^{-1} L^{-1})	277.7 ± 199.9	243.4 ± 157.7	281.9 ± 192.6	256.7 ± 154.8	345.6 ± 262.5	316.4 ± 424.3	0.57	0.98
SI ($\times 10^{-4}$ min^{-1} μU^{-1} mL^{-1})*	1.7 ± 1.0	1.7 ± 0.8	1.8 ± 1.0	1.9 ± 1.4	1.6 ± 0.7	1.7 ± 0.9	0.95	0.99
AIR (μU mL^{-1} × 10 min)*	1580.2 ± 961.0	1497.8 ± 832.0	1126.8 ± 413.8	1058.2 ± 389.6	1103.3 ± 210.1	1566.8 ± 1258.0	0.44	0.43
DI ($\times 10^{-4}$ min^{-1})*	2101.2 ± 866.2	2168.6 ± 989.6	1789.0 ± 748.4	1622.8 ± 529.1	1817.0 ± 899.7	2041.4 ± 682.7	0.28	0.70
Total cholesterol (mg dL^{-1})†	148.6 ± 22.8	142.2 ± 23.7	129.6 ± 19.6	137.1 ± 29.8	143.3 ± 31.8	148.4 ± 39.4	0.30	0.30
Triglycerides (mg dL^{-1})†	107.9 ± 61.0	105.1 ± 55.4	78.8 ± 28.9	78.2 ± 28.1	115.6 ± 37.3	106.6 ± 44.4	0.24	0.90
LDL cholesterol (mg dL^{-1})†	88.8 ± 18.6	84.9 ± 20.6	77.3 ± 16.3	84.1 ± 19.2	83.5 ± 24.8	92.5 ± 39.7	0.58	0.25
HDL cholesterol (mg dL^{-1})†	37.9 ± 8.3	36.4 ± 8.2	36.6 ± 6.5	37.4 ± 13.4	36.7 ± 6.5	34.6 ± 7.4	0.70	0.53

Repeated measures ANCOVA, *a priori* covariates included energy (kcal d^{-1}), Tanner at baseline and 1-year f/u, sex and BMI z-scores (for metabolic measures).

*n = 55 (control: n = 39, ASB initiators: n = 9 and chronic ASB consumers: n = 7).

†n = 66 (control: n = 48, ASB initiators: n = 11 and chronic ASB consumers: n = 7).

AIR, acute insulin response; BMI, body mass index; DI, disposition index; FSIVGTT, frequently sampled intravenous glucose tolerance test; HbA1c, haemoglobin A1c; HDL, high-density lipoprotein; IAUC, incremental area under the curve; LDL, low-density lipoprotein; OGTT, oral glucose tolerance test; SI, insulin sensitivity.

Results

Physical and metabolic characteristics of participants (n = 98) at baseline and 1-year follow-up are displayed in Table 1. The sample size was smaller for the FSIVGTT data (total n = 55; control n = 39, ASB initiators n = 9 and chronic ASB consumers n = 7) and the lipid data (total n = 66; control n = 48, ASB initiators n = 11 and chronic ASB consumers n = 7). Fourteen percent of the population were ASB initiators; average intake at 1-year was 1.75 ± 0.5 servings a day. Nine percent of participants were chronic ASB consumers with an average intake of 1.4 ± 0.8 servings per day at baseline and 1.6 ± 1.0 servings per day at 1-year.

Changes in adiposity and metabolic measures within and between control, ASB initiators, and chronic ASB consumers are shown in Table 2. Repeated measures ANCOVA showed ASB initiators and chronic ASB consumers compared to control had 20% and 23% higher total body fat at baseline and 18% and 19% higher total body fat at 1-year (P = 0.05 for group effect). Figure 1 shows these changes in total body fat over time in control and ASB groups. There was a significant interaction effect (group × time) with chronic ASB consumers having increases in HbA1c while ASB initiators and controls maintained HbA1c levels (P = 0.01 for interaction, Fig. 1b). No other significant difference (group or time by group interactions) in metabolic parameters existed between control and ASB groups.

Table 3 displays the changes in dietary intake variables within and between ASB and control groups over time. Chronic ASB consumers compared to control and ASB initiators had 5% and 15% higher protein intake at baseline and 31% and 40% higher protein intake at 1-year (P = 0.01 for group effect). Over time, chronic ASB consumers had a 34% increase in energy intake from baseline to 1-year, while energy intake remained relatively constant in ASB initiators and controls (P = 0.03 for interaction, Fig. 2a). Over time, chronic ASB consumers also had a 39% increase in carbohydrate intake (g d^{-1}) from baseline to 1-year, while carbohydrate intake remained relatively constant in ASB initiators and controls (P = 0.04 for interaction, Fig. 2b). There were no other significant differences in nutrients or foods and beverage servings per day within or between ASB groups and control.

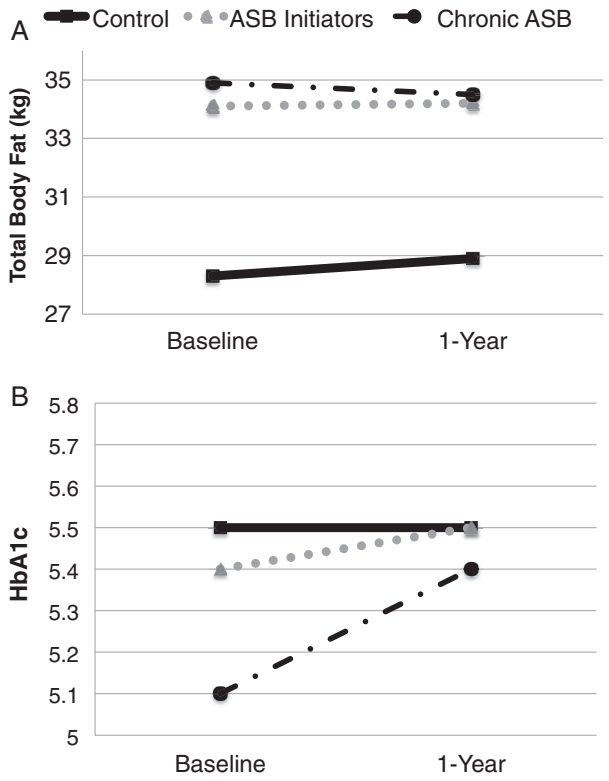

Figure 1 Baseline and 1-year total body fat (a), and HbA1c (b) within and between control (n = 75), ASB initiators (n = 14) and chronic ASB consumers (n = 9). Repeated measures ANCOVAs were run with energy, sex and Tanner as covariates. Total body fat (kg) was higher at both time points in ASB initiators and chronic ASB consumers compared to control (P = 0.05 for group effect). Chronic ASB consumers compared to ASB initiators and control had increase in HbA1c over time (P = 0.01 for group × time effect).

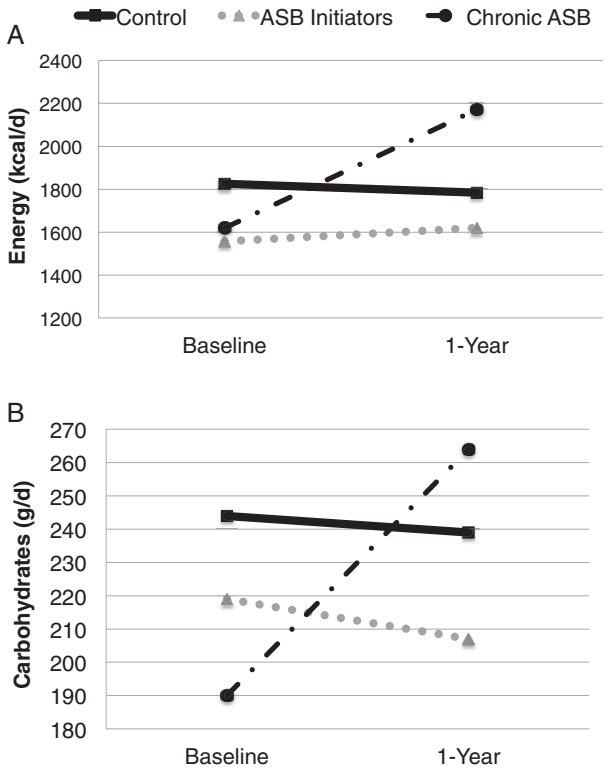

Figure 2 Baseline and 1-year energy (a) and carbohydrates (b) within and between control (n = 75), ASB initiators (n = 14) and chronic ASB consumers (n = 9). Repeated measures ANCOVA were run with sex, Tanner and energy intake (kcal d^{-1}) as covariates. Chronic ASB consumers compared to control and ASB initiators had an increase in energy intake (kcal d^{-1}) and carbohydrates (g d^{-1}) over time (P = 0.03, P = 0.04 for group × time effect).

Table 3 Mean (SD) dietary intake at baseline and 1-year in control (n = 75), ASB initiators (n = 14) and ASB chronic (n = 9) consumers

	Control		ASB initiators		ASB chronic			
Dietary intake	Baseline	1-Year	Baseline	1-Year	Baseline	1-Year	Group (P-value)	Group × time (P-value)
Energy (kcal d^{-1})	1825.7 ± 546.1	1783.8 ± 538.6	1556.9 ± 465.7	1619.2 ± 447.5	1619.2 ± 515.6	2170.9 ± 424.1	0.36	0.03
Total fat (g d^{-1})	66.4 ± 24.3	64.0 ± 24.0	52.2 ± 19.7	57.6 ± 19.8	65.5 ± 23.9	86.8 ± 19.7	0.06	0.43
Total CHO (g d^{-1})	243.7 ± 75.9	238.9 ± 94.3	218.9 ± 76.6	206.5 ± 72.2	189.8 ± 76.1	264.5 ± 67.4	0.88	**0.04**
Total protein (g d^{-1})	68.6 ± 21.5	68.6 ± 26.1	62.4 ± 18.7	64.1 ± 16.7	71.7 ± 23.5	90.0 ± 28.5	**0.01**	0.33
Total sugars (g d^{-1})	109.2 ± 43.2	105.9 ± 57.0	112.3 ± 47.6	85.1 ± 41.3	73.7 ± 34.9	110.6 ± 30.4	0.07	0.22
Added sugars (g d^{-1})	68.4 ± 40.7	62.7 ± 52.6	72.1 ± 39.6	54.5 ± 36.0	45.5 ± 28.7	71.4 ± 28.1	0.33	0.69
Dietary fibre (g d^{-1})	14.9 ± 5.8	15.4 ± 7.0	12.6 ± 4.5	12.5 ± 4.2	14.1 ± 5.6	17.8 ± 6.9	0.30	0.53
Saturated fat (g d^{-1})	23.0 ± 8.2	21.7 ± 12.0	18.1 ± 7.4	20.4 ± 8.4	22.9 ± 9.3	25.5 ± 7.4	0.69	0.18
SSB (serv d^{-1})*	1.2 ± 1.0	1.4 ± 1.6	1.7 ± 1.7	1.5 ± 1.7	0.8 ± 0.8	1.7 ± 1.6	0.09	0.77
Fried foods (serv d^{-1})	0.8 ± 1.2	0.5 ± 0.9	0.6 ± 1.0	0.5 ± 0.6	1.0 ± 1.2	0.9 ± 1.6	0.39	0.81
Fruit (serv d^{-1})	0.9 ± 0.7	1.0 ± 1.0	0.7 ± 0.8	0.7 ± 0.7	0.4 ± 0.4	1.1 ± 1.4	0.51	0.29
Vegetable (serv d^{-1})	1.3 ± 1.2	1.6 ± 1.3	1.2 ± 0.9	1.8 ± 1.2	1.3 ± 1.1	2.4 ± 1.9	0.54	0.60

Repeated measures ANCOVA were run. *A priori* covariates included sex, Tanner at baseline and 1-year f/u and energy intake (kcal d^{-1}).
*SSB excludes flavoured milks.
ASB, artificial sweetened beverages; CHO, carbohydrates; SSB, sugar sweetened beverages; serv d^{-1}, servings per day.

Discussion

To date, this is the first study to show that consumption of ASBs is associated with higher adiposity in high-risk Hispanic adolescents. Chronic ASB consumers and ASB initiators compared to control had 20%–23% and 18%–19% higher total body fat levels at baseline and 1-year follow-up. Also, chronic ASB consumers had increased energy intake, carbohydrate intake and HbA1c levels over time, although the HbA1c levels for chronic consumers converged at 1-year for all groups. In addition, consumption of ASB was not linked to any other metabolic outcomes, such as glucose and insulin indices and fasting lipids profiles.

Beverages have been identified as the major sources of artificial sweeteners in the diet. National data found that ASBs were higher among female adolescents with 17% of girls consuming ASBs on a given day compared to 9.5% of boys of the same age (23). In our study, ASB consumption rates were lower at baseline, with only 9% consuming ASBs on any given day and higher at 1-year follow-up with 23% consuming ASB on any given day. Of note, there were no differences in ASB consumption between boys and girls at baseline or 1-year in the current study.

Another longitudinal study with over 13 000 children from the United Kingdom found that daily ASB consumption was associated with greater increase in body fat percentages, as measured by bioelectrical impedance, between ages 7 and 11 (24). In another longitudinal cohort with over 500 children from the United Kingdom, ASB consumption at 5–7 years of age was associated with increased fat mass, as measured by DXA, at 9 years of age (25). In contrast, increased diet soda consumption over a 19-month time period was associated with decreased incidence of obesity, whereas each additional serving of SSB was linked to a 60% increase in obesity (1). In a prospective study with over 1300 children (2–5 years), ASB consumption was not associated with changes in weight or BMI (26). While the current study had a much smaller sample size, our findings showed ASB consumption was linked to higher body fat levels at baseline and year 1, but did not show an affect of ASB consumption on changes in body fat levels across time. However, our study is the first to examine this in an exclusive Hispanic population and extended the analyses to examine the effects of ASB on metabolic factors, such as glucose and insulin dynamics using oral and intravenous glucose tolerance tests.

Several adult studies have shown that artificial sweeteners adversely impact metabolic health. Daily diet soft drink intake compared to no intake was linked to a 44% increase in a vascular event in 2564 multi-ethnic adults (8). In a study with 381 adults without diabetes, artificial sweeteners were linked to higher fasting blood glucose, HbA1c and impaired glucose tolerance (9). Fewer studies have examined how ASBs impact metabolic health in youth. In a double-blind RCT conducted with teenagers, encapsulated aspartame consumption for 13 weeks compared to placebo did not result in significant differences between groups in blood pressure, glucose, insulin or lipids (10). Similarly, in a 12-week RCT, teenage girls permitted to drink diet sodas vs. regular soda showed no significant differences between groups in weight loss, blood pressure or lipid profiles (11). In the current study, chronic ASB consumers compared ASB initiators and control had an increase in HbA1c; however, the HbA1c levels for all groups converged at 1-year follow-up. ASB consumption had no other effects on metabolic parameters.

Chronic ASB consumers compared to ASB initiators and control had large increases in energy intake over time (~550 kcal d^{-1}) and in carbohydrate intake (~75 g d^{-1}). There was also a trend for chronic ASB compared to ASB initiators and control to have higher total sugar intake ($P = 0.07$) and SSB (servings/day; $P = 0.09$) at 1-year follow-up. These findings support the possible mechanism that the dissociation of the sensation of sweet taste from caloric intake may stimulate appetite, which leads to greater food intake, and promotes weight gain in chronic ASB consumers. Another possible explanation is that consumption of artificial sweeteners alters taste preferences toward sweetened foods and beverages. A study with young children (3–5 years) found that after either artificial sweetened or sugar sweetened preloads, children consistently showed complete caloric compensation during an *ad libitum* snack 20 min after either preload (27).

Human and animal research have shown that artificial sweeteners play a role in activating the gastrointestinal tract to release glucagon-like peptide-1 (28, 29), which may lead to more rapid absorption of sugars from the intestine into the bloodstream, and alters both gastric emptying and insulin secretion. Thus, ASB intake in conjunction with sugar-containing food/drink could lead to rapid sugar absorption and increased insulin secretion, potentially impacting weight, satiety and glycaemic responses. Growing evidence exists that consumption of sweet foods/beverages impacts neural reward pathways and stimulates appetite (30). Another possible explanation is that people who consume ASBs may consciously overcompensate by indulging in other foods/beverages, particularly ones that may be higher in energy (31).

It is also possible that subjects who have obesity underestimated dietary intake to a greater extent, and that other macronutrients and foods/beverage servings were actually higher in chronic ASB consumers and ASB initiators. Given that adiposity was higher in ASB groups compared to control, it is also plausible that these adolescents were consuming ASBs as a way to lose weight and/or 'diet.' Another possible mechanism that has been recently explored is that artificial sweeteners induce gut microbial dysbiosis, or an

impaired gut microbiota, which may cause weight gain and metabolic disturbances (9).

There are several limitations to mention in the present study. The main limitation is the relatively small number of subjects in the study, particularly those who were chronic ASB consumers. Using G*power, *post hoc* ANOVA tests, with the sample of 98 and 3 groups (n = 75, n = 14 and n = 9), effect size at an α-level of 0.05 and with a 0.2–0.8 correlations between repeated measures, and with a moderate effect size of at 0.3, we have at least 80% power (1-b) to detect differences in total body fat, HbA1c and energy. However, the sample size is still small and longitudinal studies with larger sample sizes particularly with more ASB consumers are warranted. Additional longitudinal studies with larger sample sizes are warranted to replicate the results. Another limitation is that, dietary intake may have been underreported, especially among subjects who have obesity. However, 84% of the population had obesity at baseline and prevalence of overweight and obesity did not differ between ASB groups at baseline or at 1-year, thus underreporting would be expected to be consistent throughout.

Given this study, and numerous other studies consistently showing that ASBs are linked to obesity and the growing evidence that ASBs are also linked to metabolic disease risk, interventions should not encourage ASB intake as a replacement for SSBs. Other alternatives, such as water or water infused with fruit, herbs and/or vegetables (e.g., lemon and cucumber water) may be more effective strategies to use for interventions aimed at reducing or preventing childhood obesity. In addition, the beverage industry has begun producing and selling more flavoured sparkling waters (32), that are naturally flavoured and do not contain artificial sweeteners, and this may be a better alternative to ASBs, however, no research has been conducted examining the impact of such products on health.

In summary, ASB intake was linked to higher body fat at baseline and 1 year in Hispanic adolescents. These findings replicate others and further support that encouraging youth to consume ASBs may not result in lower adiposity. In fact, these findings indicate that ASB use may be associated with other negative aspects such as higher energy, carbohydrate intake and a rise in HbA1c levels indicating development of poor glucose control.

Conflict of Interest Statement

The authors declare they have no competing interests.

Author contributions

JND and MIG designed and supervised the research study used in this analyses; MIG obtained the funding; JND analysed the data; JND, FMA, MJL, SV, EK and RG all assisted with data interpretation; JND wrote the paper; all authors contributed to editing the manuscript; JND had primary responsibility for the final content presented. All authors read and approved the final manuscript.

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