Consuming High-Fructose Corn Syrup- or Sucrose-Sweetened Beverages Increases Hepatic Lipid Content and Decreases Insulin Sensitivity in Young Adults

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Abstract: 5-LB

American Diabetes Association.

80TH SCIENTIFIC SESSIONS
A VIRTUAL EXPERIENCE • June 12-16, 2020

Financial Disclosure

Presenter: Desiree Sigala

No financial disclosures to report.

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No financial disclosures to report.

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No financial disclosures to report.

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No financial disclosures to report.

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No financial disclosures to report.

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No financial disclosures to report.

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No financial disclosures to report.

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No financial disclosures to report.

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No financial disclosures to report.

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No financial disclosures to report.

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Penguin Random House: book royalties for “Sugarproof”.

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No financial disclosures to report.

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No financial disclosures to report.

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No financial disclosures to report.

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No financial disclosures to report.

Background

- Over the past decade the prevalence of non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes (T2D) has dramatically increased worldwide, constituting both as global health concerns[1].

- While epidemiological research has linked sugar-sweetened beverage (SB) consumption to these adverse health outcomes, it has been reported that fructose consumption can directly alter hepatic lipid metabolism, insulin sensitivity and risk for metabolic disease[2-6].

- High fructose corn syrup (HFCS) and sucrose are the leading added sugars consumed in the U.S. and the main contributors of fructose in the diet, with HFCS being the main sweetener in sugar-SB[7].

- We have reported that insulin sensitivity decreases in overweight/obese adults consuming fructose-sweetened beverages for 10 weeks[2].

- Evidence from rodent studies suggest that compared to diets sweetened with sucrose, HFCS increases hepatic lipid content and decreases hepatic insulin sensitivity[8,9]. Clinical evidence from dietary intervention studies comparing the effects of HFCS and sucrose consumption is inadequate[10].

- Therefore, the objective of this study was to compare the consumption of sucrose- or HFCS-SB at 25% Ereq on hepatic lipid content and insulin sensitivity in young males and females.

Methods

- 75 healthy adults (18-40yr; BMI 18-35kg/m^2) were assigned to consume 3 SB/day containing either aspartame (n=23) or 25% of energy requirement (Ereq) as sucrose (n=24) or HFCS (n=28) for two weeks with their normal *ad-libitum* diet.

- Magnetic resonance imaging (MRI) for hepatic lipid content was conducted on the second day of both the baseline and intervention inpatient periods. Subjects were scanned at 3T using an advanced magnitude-based liver fat quantification MRI technique. To estimate liver proton density fat fraction (PDFF), gradient-recalled-echo technique using low flip angle and repetition time (TR) of ≥ 150 msec to minimize T1 bias and six gradient recalled echoes to calculate and correct to T2 signal decay was used [11].

- Standard 3-h OGTTs were performed at the end of a 3.5-d baseline inpatient period and 15 days later at the end of a 3.5-d intervention inpatient period. OGTT parameters were used to derive two separate indices of insulin sensitivity: Matsuda Insulin Sensitivity Index (ISI) and Oral Glucose Insulin Sensitivity (OGIS) index[12,13].

- During the baseline inpatient period all subjects consumed standardized eucaloric meals containing 55% Ereq as complex carbohydrate.

- During the intervention inpatient period subjects consuming sugar-SB consumed 25% Ereq as sucrose- or HFCS-SB and meals that provided 30% Ereq as complex carbohydrate.

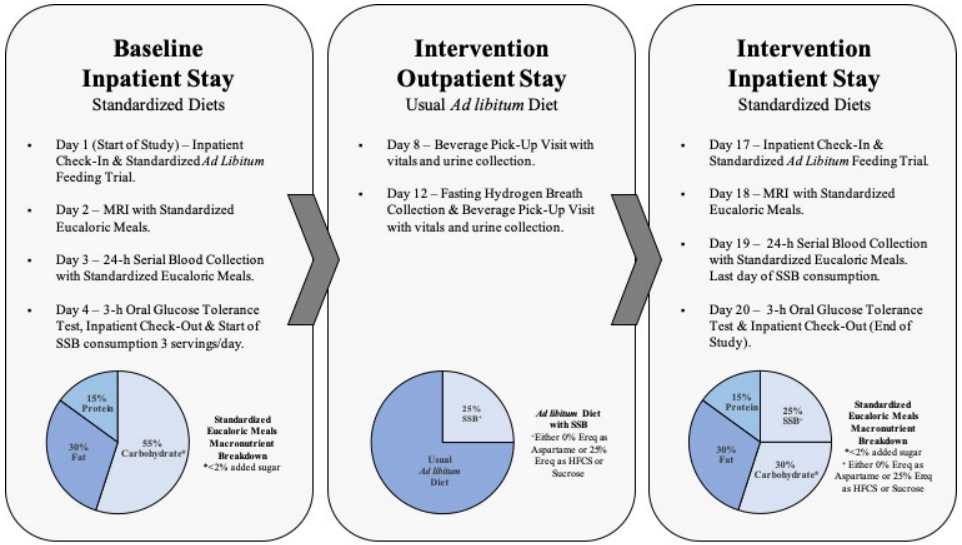

Figure 1. Study design, experimental testing days, and dietary protocol. MRI for hepatic lipid content was scheduled on Days 2 and 18; Oral glucose tolerance test was scheduled on Days 4 and 20.

Table 1. Participant characteristics at baseline, mean ± SD

Parameter	Aspartame	HFCS	Sucrose
Age (yr)	25.4 ± 6.2	26.8 ± 6.6	25.9 ± 6.3
Sex (M/F)	11/12	15/13	12/12
Weight (kg)	71.8 ± 10.6	72.9 ± 14.5	71.9 ± 12.1
BMI (kg/ m2)	24.8 ± 3.3	24.9 ± 4.0	25.3 ± 3.4
Waist circumference (cm)	75.2 ± 6.4	77.0 ± 10.1	75.4 ± 7.2
Body fat (%)	27.1 ± 9.6	26.0 ± 9.7	29.1 ± 11.5
Energy requirement (kcal/d)	2353.7 ± 322.4	2389.9 ± 349.9	2351.1 ± 334.5
Systolic blood pressure (mm Hg)	112.3 ± 11.5	117.1 ± 10.0	114.3 ± 8.4
Diastolic blood pressure (mm Hg)	69.2 ± 8.6	72.7 ± 7.2	72.2± 5.5
Fasting glucose (mg/dL)	90.5 ± 6.6	90.6 ± 6.3	89.9 ± 5.3
Fasting insulin (μU/mL)	12.7 ± 5.5	13.0 ± 5.2	13.0 ± 4.5
Fasting triglyceride (mg/dl)	100.5 ± 52.6	107.8 ± 50.1	113.6 ± 48.4
Total cholesterol (mg/dl)	148.9 ± 25.5	157.6 ± 34.3	159.1 ± 23.1
Fasting HDL cholesterol (mg/dl)	39.4 ± 7.4	45.6 ± 13.7	42.9 ± 6.6

Results

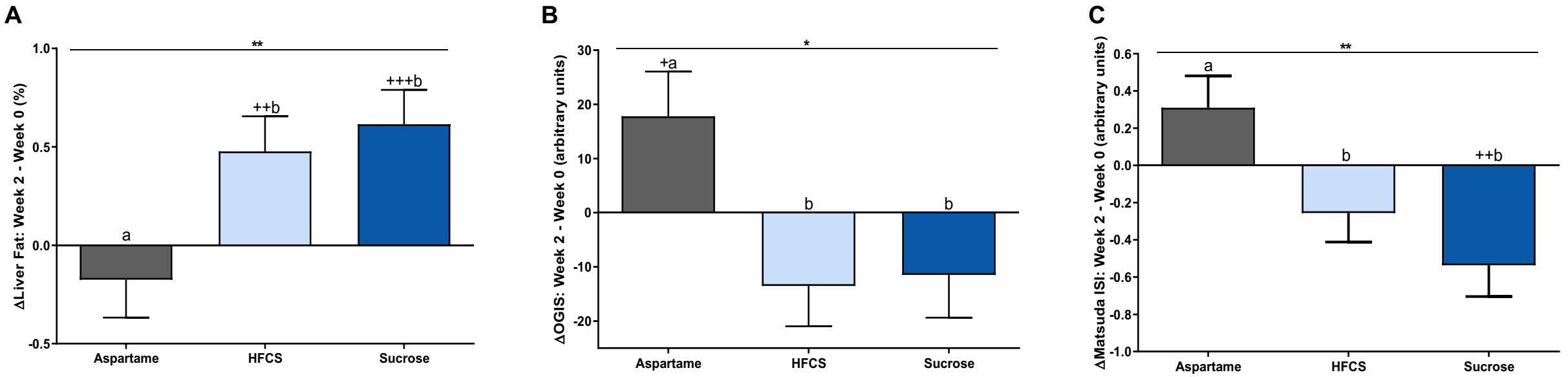

Figure 2 A-C. Change in Hepatic Lipid Content, Oral Glucose Insulin Sensitivity (OGIS) Index and Matsuda Insulin Sensitivity (ISI) Index; The least square (LS) mean ± SEM of the absolute change (Week 2 – Week 0) in hepatic lipid content (A) OGIS (B) and Matsuda ISI (C) in subjects consuming either HFCS-, sucrose, or aspartame-sweetened beverages for 2 weeks. 2-factor (sugar group, sex) analysis of covariance with adjustment for % body fat, sex, sex*sugar group (A), BMI and outcome at baseline(B) and sex and outcome at baseline (C) ; +P < 0.05, ++P < 0.001, +++P < 0.0001, LS means different from zero; a different from b, Tukey's. Effect of sugar, *P < 0.05, **P < 0.001.

Conclusion

- Hepatic lipid content was increased by consumption of HFCS-SB (LS means of absolute Δ±SEM: 0.5% ± 0.2, $P < 0.05$) and sucrose-SB (Δ: 0.5% ± 0.2, $P<0.01$) compared with baseline levels and compared with aspartame-SB (Δ: -0.2% ± 0.2, $P < 0.05$ vs HFCS- or sucrose-SB).

- The 3-hr Matsuda insulin sensitivity index was decreased by consumption of HFCS-SB (Δ: -0.3 ± 0.2) and sucrose-SB (Δ: -0.5 ± 0.2, $P < 0.01$ vs baseline) compared with aspartame-SB (Δ: 0.3 ± 0.2, $P < 0.05$ vs HFCS- or sucrose-SB).

- The 2-hr Oral Glucose Insulin Sensitivity index was also decreased by consumption of HFCS-SB (Δ: -13.6 ± 7.5) and sucrose-SB (Δ:-11.5 ± 7.9) compared with aspartame-SB (Δ: +17.9 ± 8.3, $P < 0.05$ vs HFCS- or sucrose-SB).

- This study demonstrates that consumption of HFCS- and sucrose-SB provided at 25% Ereq for 2 weeks increased hepatic lipid content and decreased insulin sensitivity compared to aspartame-SB in healthy adults.

- Our results, in which both the consumption of HFCS and sucrose-SB significantly increased risk factors for NAFLD and T2D compared to aspartame-SB consumption, do not support the rodent data that suggest that HFCS causes greater metabolic dysregulation than sucrose.

- These data are important for shaping public health policy and consumer choices as many consumers appear to believe that HFCS and aspartame are more detrimental to their health compared to sucrose[14].

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Acknowledgments

- Funded by the National Heart, Lung and Blood Institute
- Also supported by the National Center for Research Resources
- This study is registered at ClinicalTrails.gov (NCT01103921).