Decaffeinated Coffee and Glucose Metabolism in Young Men

James A. Greenberg, phd¹ David R. Owen, phd² Allan Geliebter, phd³

OBJECTIVE — The epidemiological association between coffee drinking and decreased risk of type 2 diabetes is strong. However, caffeinated coffee acutely impairs glucose metabolism. We assessed acute effects of decaffeinated coffee on glucose and insulin levels.

RESEARCH DESIGN AND METHODS — This was a randomized, cross-over, placebocontrolled trial of the effects of decaffeinated coffee, caffeinated coffee, and caffeine on glucose, insulin, and glucose-dependent insulinotropic polypeptide (GIP) levels during a 2-h oral glucose tolerance test (OGTT) in 11 young men.

RESULTS — Within the first hour of the OGTT, glucose and insulin were higher for decaffeinated coffee than for placebo (P < 0.05). During the whole OGTT, decaffeinated coffee yielded higher insulin than placebo and lower glucose and a higher insulin sensitivity index than caffeine. Changes in GIP could not explain any beverage effects on glucose and insulin.

CONCLUSIONS — Some types of decaffeinated coffee may acutely impair glucose metabolism but less than caffeine.

Diabetes Care 33:278-280, 2010

ineteen of 22 epidemiological studies concluded that long-term consumption of coffee, both caffeinated and decaffeinated, can reduce the risk of type 2 diabetes (1-3), but several investigators have warned that the caffeine in caffeinated coffee can impair glucose metabolism (e.g., 4,5). While decaffeinated coffee contains very little caffeine and may safely protect against diabetes, there have been conflicting reports on decaffeinated coffee's acute effects on glucose metabolism (6–9). Our objective was to assess whether ground decaffeinated coffee enhances glucose metabolism and whether glucosedependent insulinotropic polypeptide (GIP), an incretin hormone that stimulates insulin secretion (10), plays a causal role.

RESEARCH DESIGN AND

METHODS — Eleven healthy male nonsmokers signed an informed consent and participated. The following participation requirements were started 1 week prior to the first lab visit: keep diet, exercise, and alcohol intake stable; no caffeinated drinks, foods, or medications; no smoking; and no alcohol or exercise during the 48 h prior to each visit.

There were four visits separated by at least a week. Participants ingested one of four beverages assigned by researchers in a single-blinded randomized fashion at a temperature of $43-49^{\circ}$ C (caffeinated coffee, decaffeinated coffee, caffeine in warm water, or warm water [placebo]). An oral glucose tolerance test (OGTT) was initiated 1 h later (t = 0 min) with ingestion of 75 g of glucose in water. Blood was drawn

From the ¹Department of Health and Nutrition Sciences, Brooklyn College of the City, University of New York, New York, New York; the ²Department of Psychology, Brooklyn College of the City, University of New York, New York, New York; and the ³Department of Psychology, Columbia University and New York Obesity Research Center, St. Luke's Roosevelt Hospital Center, New York, New York.

Corresponding author: James Greenberg, jamesg@brooklyn.cuny.edu.

at time -90, -60, 0, 10, 30, 60, 90, and 120 min.

Participants drank 500-600 ml of drip-filtered ground coffee (Chock Full O'Nuts Original; Massimo Zanetti Beverage, Portsmouth, VA). The recipe was eight cups of water with 40 g of grounds for caffeinated and 57 g of grounds for decaffeinated coffee. For the caffeine and hot water (placebo) beverages, we ran eight cups of water through the machine with filter paper without coffee grounds. For the caffeine beverage, we added foodgrade caffeine powder (Spectrum Chemical Manufacturing, Gardena, CA). The volume ingested was the same for each beverage and differed by participant to yield 6 mg caffeine/kg of body wt in the caffeine and caffeinated coffee beverage. The caffeine content of the caffeinated coffee was measured as 0.73 mg/ml coffee, by high-performance liquid chromatography.

Glucose was assayed in plasma using the oxygen rate method (Beckman Glucose Analyzer 2; Beckman, Brea, CA). Insulin was assayed in plasma (human-specific radioimmunoassay kit no. M114886; Millipore, Billerica, MA). GIP (total) was measured in plasma (human GIP [total] enzyme-linked immunosorbent assay kit no. M116520; Millipore).

The trapezoidal rule was used to calculate area under the curve (AUC). The insulin sensitivity index (ISI) was calculated using the formula of Belfiore et al. (11). All blood data were analyzed for time and beverage effects using two-way repeated-measures ANOVA. AUC and ISI data were analyzed using one-way repeated-measures ANOVA. All tests were adjusted for multiple comparisons by means of Tukey Studentized range adjustments. Two-sided P < 0.05 was considered significant. We used SPSS 11.5 for all statistical analyses.

RESULTS — The subjects had a mean $(\pm \text{ SD})$ age of 23.5 \pm 5.7 years, BMI 23.6 \pm 4.2 kg/m², fasting glucose 4.41 \pm 0.49 pmol/l, and fasting insulin 109.0 \pm 91.7 pmol/l. Participants reported no nonminor adverse reactions.

During the first 30 min of the OGTT, decaffeinated coffee yielded significantly higher glucose than placebo (Table 1).

Received 17 August 2009 and accepted 3 November 2009. Published ahead of print at http://care. diabetesjournals.org on 16 November 2009. DOI: 10.2337/dc09-1539. Clinical trial reg. no. NCT00950898, clinicaltrials.gov.

^{© 2010} by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. See http://creativecommons. org/licenses/by-nc-nd/3.0/ for details.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

	T = -90	T = -60	T = 0	T = 10	T = 30	T = 60	T = 90	T = 120	3-h AUC
Glucose (mmol/l)									
Placebo	4.50 ± 0.15	4.25 ± 0.14	4.35 ± 0.19	4.57 ± 0.20^{a}	6.66 ± 0.28^{a}	7.38 ± 0.70	6.95 ± 0.79	5.45 ± 0.57	$4.35 \pm 1.01^{a,b}$
Decaffeinated coffee	4.55 ± 0.17	4.34 ± 0.16	4.44 ± 0.18	$5.25 \pm 0.28^{\rm b}$	8.13 ± 0.41^{b}	6.86 ± 0.61	5.99 ± 0.48	5.09 ± 0.45	4.1 ± 0.67^{b}
Caffeinated coffee	4.29 ± 0.14	4.29 ± 0.09	4.62 ± 0.11	5.51 ± 0.26^{b}	$7.63 \pm 0.39^{\rm b}$	8.11 ± 0.43	7.14 ± 0.32	5.96 ± 0.35	$5.63 \pm 0.38^{a,b}$
Caffeine	4.33 ± 0.13	4.18 ± 0.14	4.31 ± 0.12	$5.04 \pm 0.18^{\rm b}$	7.44 ± 0.26^{b}	7.87 ± 0.75	7.00 ± 0.69	6.05 ± 0.64	5.39 ± 0.80^{a}
Insulin (Φ mol /l)									
Placebo	105.3 ± 33.3	85.1 ± 25.6	71.2 ± 17.4	124.8 ± 21.7^{a}	331.2 ± 51.8^{a}	421.4 ± 44.0^{a}	413.4 ± 51.2	296.4 ± 55.2	489.4 ± 75.8^{a}
Decaffeinated coffee	114.7 ± 28.4	80.2 ± 11.0	71.0 ± 9.9	$231.0 \pm 54.8^{\rm b}$	$537.4 \pm 97.1^{\rm b}$	$518.1 \pm 56.7^{\rm b}$	489.8 ± 99.7	316.3 ± 54.5	$705.5 \pm 109.8^{\rm b}$
Caffeinated coffee	102.7 ± 22.7	87.7 ± 10.7	75.7 ± 9.1	$238.4 \pm 59.1^{\rm b}$	$544.7 \pm 97.4^{\rm b}$	$626.2 \pm 109.6^{\rm b}$	692.3 ± 140.7	457.2 ± 110.0	$884.9 \pm 159.4^{\rm b}$
Caffeine	113.3 ± 29.0	103.7 ± 30.1	76.9 ± 10.8	$202.9 \pm 32.8^{\rm b}$	$555.8 \pm 85.6^{\rm b}$	$717.8 \pm 127.3^{\rm b}$	669.8 ± 140.1	480.8 ± 124.8	$882.0 \pm 185.9^{\rm b}$
GIP (pg/ml)									
Placebo	68.8 ± 15.3	65.0 ± 14.6	58.4 ± 16.9^{a}	106.7 ± 17.7	157.3 ± 18.2	164.6 ± 17.1	166.0 ± 18.4	143.2 ± 17.9	164.9 ± 23.0^{a}
Decaffeinated coffee	131.0 ± 31.9	91.3 ± 18.5	44.2 ± 7.1^{b}	130.4 ± 13.4	187.4 ± 24.7	173.8 ± 20.4	160.1 ± 19.0	136.9 ± 16.9	109.4 ± 35.6^{a}
Caffeinated coffee	83.5 ± 24.9	72.3 ± 14.0	$43.8 \pm 8.5^{a,b}$	120.2 ± 22.0	158.3 ± 23.2	148.1 ± 17.8	134.1 ± 12.9	124.0 ± 13.4	112.7 ± 30.2^{a}
Caffeine	88.0 ± 29.1	77.7 ± 19.6	67.2 ± 10.8^{a}	141.3 ± 28.3	174.6 ± 27.3	166.8 ± 20.5	159.3 ± 21.7	139.2 ± 21.7	150.8 ± 34.6^{a}
Data are means \pm SEM. $n = 11$. T denotes time point in minutes. Initial values ($T = -90$ min) are fasting values. Beverage ingested at $T = -60$ min. OGTT started at $T = 0$ min. ISI was based on the formula of Belfiore et al. (11). Three-hour AUC was calculated between $T = -60$ and $T = 120$. Means in a column with different letter superscripts differ significantly ($P < 0.05$), by two-way repeated-measures ANOVA for glucose and insulin and by one-way repeated-measures ANOVA for glucose adjusted for multiple comparisons by means of a Tukey test.	11. T denotes time p was calculated betw eated-measures ANC	oint in minutes. Ini een $T = -60$ and T DVA for 3-h AUC. 1	itial values ($T = -9$ = 120. Means in a Post-hoc tests adjus	0 min) are fasting valu 1 column with differer sted for multiple com	ues. Beverage ingeste nt letter superscripts o parisons by means o	d at <i>T</i> = -60 min. OG liffer significantly (<i>P</i> < f a Tukey test.	60 min. OGTT started at $T = 0$ min. ISI was based on the formula of Belfiore ficantly ($P < 0.05$), by two-way repeated-measures ANOVA for glucose and est.	in. ISI was based on th ppeated-measures ANt	ie formula of Belfiore OVA for glucose and
insulin and by one-way repe	eated-measures Aive	JVA IOT 3-N AUC. J	ost-noc tests adjus	sted for multiple com	parisons by means o	r a Tukey test.			

Greenberg, Owen, and Geliebter

Glucose AUC for decaffeinated coffee was significantly lower than for caffeine. Insulin was significantly higher after caffeine and decaffeinated coffee than after placebo during the first hour of the OGTT. Insulin AUC was significantly higher for caffeine and decaffeinated coffee than for placebo.

ISI (means \pm SE) was 1.22 ± 0.07 for placebo, 0.98 ± 0.09 for caffeine, $1.09 \pm$ 0.08 for decaffeinated coffee, and $0.97 \pm$ 0.09 for caffeinated coffee. ISI for decaffeinated coffee was significantly higher than for caffeine and showed a trend toward being lower than for placebo (*P* = 0.052). Caffeinated coffee induced effects on glucose and insulin that were similar to those for caffeine. GIP decreased after ingestion of all beverages and became significantly lower for decaffeinated coffee than for caffeine and placebo 60 min after beverage ingestion.

CONCLUSIONS — Decaffeinated coffee acutely impaired glucose metabolism in healthy young men. Within the first 60 min of the OGTT, both glucose and insulin were significantly higher after decaffeinated coffee than after placebo. During the whole OGTT, insulin AUC was significantly higher for decaffeinated coffee than placebo. Decaffeinated coffee did not impair glucose metabolism as severely as caffeine. During the whole OGTT, decaffeinated coffee yielded lower glucose AUC and higher ISI than caffeine. Our findings require confirmation in future studies. However, they do suggest that caution is needed in the quest to harness coffee's potential to reduce the risk of diabetes, demonstrated in epidemiological studies.

Table 1—Glucose, insulin, and GIP concentrations and AUC during an OGTT following ingestion of placebo, decaffeinated coffee, caffeinated coffee, and caffeine in 11 healthy young men

Battram et al. (6) found an acute enhancement of glucose metabolism by ground decaffeinated coffee, and Johnston et al. (7), Thom (8), and van Dijk et al. (9) found no acute effect on glucose metabolism by instant decaffeinated coffee. It is possible that our decaffeinated coffee had a higher concentration of caffeine (12) than the decaffeinated coffees of these investigators, or that our decaffeinated coffee had lower concentrations of noncaffeine compounds, which acutely enhance glucose metabolism. It seems unlikely that GIP played a role in our observed beverage effects. For example, 60 min after beverage ingestion, decaffeinated coffee yielded significantly lower GIP than placebo and caffeine but no significant changes in insulin or glucose.

Decafinated coffee and glucose metabolism

Our study has several limitations. We only had 11 volunteers. More volunteers would have yielded more statistical power. Our study also has some strengths. Our protocol allowed us to convincingly separate the effects of each beverage from the effects of the OGTT glucose because ingestion of the beverages was separated by 60 min from ingestion of the glucose.

In conclusion, our human trial appears to be the first to find that decaffeinated coffee can acutely impair glucose metabolism, but less than caffeine, in healthy young men.

Acknowledgments — This work was supported by the Professional Staff Congress, City University of New York Research Award Program.

No potential conflicts of interest relevant to this article were reported.

References

1. Greenberg JA, Geliebter A, Boozer CN. Coffee and diabetes: a review of the literature. Am J Clin Nutrition 2006;84:682–693

- 2. Pereira MA, Parker ED, Folsom AR. Coffee consumption and risk of type 2 diabetes mellitus: an 11-year prospective study of 28 812 postmenopausal women. Arch Intern Med 2006;166:1311–1316
- Paynter NP, Yeh HC, Voutilainen S, Schmidt MI, Heiss G, Folsom AR, Brancati FL, Kao WH. Coffee and sweetened beverage consumption and the risk of type 2 diabetes mellitus: the Atherosclerosis Risk in Communities Study. Am J Epidemiol 2006;164:1075–1084
- Moisey LL, Kacker S, Bickerton AC, Robinson LE, Graham TE. Caffeinated coffee consumption impairs blood glucose homeostasis in response to high and low glycemic index meals in healthy men. Am J Clin Nutr 2008;87:1254–1261
- Lane JD, Feinglos MN, Surwit RS. Caffeine increases ambulatory glucose and postprandial responses in coffee drinkers with type 2 diabetes. Diabetes Care 2008; 31:221–222
- Battram DS, Arthur R, Weekes A, Graham TE. The glucose intolerance induced by caffeinated coffee ingestion is less pronounced than that due to alkaloid caffeine in men. J Nutr 2006;136:1276–1280

- Johnston KL, Clifford MN, Morgan LM. Coffee acutely modifies gastrointestinal hormone secretion and glucose tolerance in humans: glycemic effects of chlorogenic acid and caffeine. Am J Clin Nutr 2003;78:728–733
- Thom E. The effect of chlorogenic acid enriched coffee on glucose absorption in healthy volunteers and its effect on body mass. J Int Med Res 2007;35:900–908
- 9. van Dijk AE, Olthof MR, Meeuse JC, Seebus E, Heine RJ, van Dam RM. Acute effects of decaffeinated coffee and the major coffee components chlorogenic acid and trigonelline on glucose tolerance. Diabetes Care 2009;32:1023–1025
- 10. Gautier JF, Choukem SP, Girard J. Physiology of incretins (GIP and GLP-1) and abnormalities in type 2 diabetes. Diabetes Metab 2008;34(Suppl. 2):S65–S72
- 11. Belfiore F, Iannello S, Camuto M, Fagone S, Cavaleri A. Insulin sensitivity of blood glucose versus insulin sensitivity of blood free fatty acids in normal, obese, and obese-diabetic subjects. Metabolism 2001;50:573–582
- McCusker RR, Fuehrlein B, Goldberger BA, Gold MS, Cone EJ. Caffeine content of decaffeinated coffee. J Anal Toxicol 2006; 30:611–613