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Decaffeinated coffee and glucose metabolism in young men.

Short title: Decaf and glucose metabolism in young men

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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: Randomized cross-over placebo-controlled trial of the effects of decaffeinated coffee, caffeinated coffee and caffeine on glucose, insulin and glucose-dependent insulinotropic polypeptide (GIP) levels during a two-hour oral glucose tolerance test (OGTT) in eleven 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.

Nineteen 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 Glucose-dependent 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. Participation requirements started one week prior to the first lab visit, and were: keep diet, exercise and alcohol intake stable; no caffeinated drinks foods or medications; no smoking; and no alcohol or exercise during the 48 hours 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 ^{o}C: caffeinated coffee, decaffeinated coffee, caffeine in warm water or warm water (placebo). An oral glucose tolerance test (OGTT) was initiated one hour later (t=0 min) with ingestion of 75 gm of glucose in water. Blood was drawn 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 USA, Portsmouth, VA). The recipe was eight cups of water with 40 gm of grounds for caffeinated and 57 gms 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 food-grade caffeine powder (Spectrum Chemical Manufacturing Corp, Gardena, CA). The volume ingested was the same for each beverage, and differed by participant to yield 6 mg of caffeine per kg of body weight 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, Brea, CA). Insulin was assayed in plasma (Human Specific RIA kit #M114886, Millipore Corp, Billerica, MA). GIP (Total) was measured in plasma (Human GIP (Total) ELISA Kit #M116520, Millipore Corp, Billerica, MA).

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 mean (SD) age 23.5 years (5.7), BMI 23.6 kg/m^2 (4.2), fasting glucose 4.41 pmol/L (0.49) and fasting insulin 109.0

pmol/L (91.7). Participants reported no non-minor adverse reactions.

During the first 30 minutes of the OGTT, decaffeinated coffee yielded significantly higher glucose than placebo (Table 1). 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 (mean (SE) was 1.22 (.07) for placebo, 0.98 (.09) for caffeine, 1.09 (.08) for decaffeinated coffee and 0.97 (.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 minutes 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.

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 non-caffeine compounds which acutely enhance glucose metabolism.

It seems unlikely that GIP played a role in our observed beverage effects. For example, 60 minutes after beverage ingestion decaffeinated coffee yielded significantly lower GIP than placebo and caffeine, but no significant changes in insulin or glucose.

Our study has several limitations. We only had eleven 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 minutes 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.

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Table 1. Glucose, insulin and glucose-dependent insulinotropic polypeptide (GIP) concentrations and Area Under the Curve (AUC) during an oral glucose tolerance test following ingestion of placebo, decaffeinated coffee, caffeinated coffee and caffeine in 11 healthy young men.

	T=-90	T=-60	T=0	T=10	T=30	T=60	T=90	T=120	3-hr 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 (1.01) [a, b]
Decaffeinated Coffee	4.55 (0.17)	4.34 (0.16)	4.44 (0.18)	5.25 (0.28) [b]	8.13 (0.41) [b]	6.86 (0.61)	5.99 (0.48)	5.09 (0.45)	4.13 (0.67) [b]
Caffeinated Coffee	4.29 (0.14)	4.29 (0.09)	4.62 (0.11)	5.51 (0.26) [b]	7.63 (0.39) [b]	8.11 (0.43)	7.14 (0.32)	5.96 (0.35)	5.63 (0.38) [a, b]
Caffeine	4.33 (0.13)	4.18 (0.14	4.31 (0.12)	5.04 (0.18) [b]	7.44 (0.26) [b]	7.87 (0.75)	7.00 (0.69)	6.05 (0.64)	5.39 (0.80) [a]
INSULIN (Φmol /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 (54.8) [b]	537.4 (97.1) [b]	518.1 (56.7) [b]	489.8 (99.7)	316.3 (54.5)	705.5 (109.8) [b]
Caffeinated Coffee	102.7 (22.7)	87.7 (10.7)	75.7 (9.1)	238.4 (59.1) [b]	544.7 (97.4) [b]	626.2 (109.6) [b]	692.3 (140.7)	457.2 (110.0)	884.9 (159.4) [b]
Caffeine	113.3 (29.0)	103.7 (30.1)	76.9 (10.8)	202.9 (32.8) [b]	555.8 (85.6) [b]	717.8 (127.3) [b]	669.8 (140.1)	480.8 (124.8)	882.0 (185.9) [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 (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 (SE, n=11). T denotes time point in min. Initial values (T=-90 min) are fasting values. Beverage ingested at T=-60 min. OGTT started at T=0 min. ISI based on the formula of Belfiore et al (2001).Three-hour Area Under the Curve (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, & by one-way repeated-measures ANOVA for 3-hr AUC. Post-hoc tests adjusted for multiple comparisons by means of a Tukey test.