Coffee Consumption Is Associated With Higher Plasma Adiponectin Concentrations in Women With or Without Type 2 Diabetes

A prospective cohort study

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To test whether the beneficial effects of coffee consumption in metabolism might be explained by changes in circulating levels of adiponectin, we evaluated self-reported habitual coffee and tea consumption and caffeine intake as predictors of plasma adiponectin concentrations among 982 diabetic and 1,058 nondiabetic women without cardiovascular disease from the Nurses' Health Study. Women with and without diabetes who drank ≥4 cups of coffee per day had significantly higher adiponectin concentrations than those who didn't drink coffee regularly (7.7 vs. 6.1 μg/ml, respectively, in diabetic women, $P = 0.004$; 15.0 vs. 13.2 μg/ml in nondiabetic women, $P = 0.04$). Similar associations were observed for caffeine intake. We confirm previously reported inverse associations of coffee consumption with inflammatory markers, C-reactive protein, and tumor necrosis factor-α receptor II. Adjustment for adiponectin did not weaken these associations, and adjustment for inflammatory markers did not attenuate the association between coffee consumption and adiponectin concentrations. High consumption of caffeine-containing coffee is associated with higher adiponectin and lower inflammatory marker concentrations.

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RESEARCH DESIGN AND METHODS — We studied 982 women with type 2 diabetes and 1,058 nondiabetic women from the Nurses' Health Study (which provided measures of plasma adiponectin concentration and data on usual coffee consumption) who were free of coronary heart disease, myocardial infarction, coronary artery bypass grafting, percutaneous transluminal coronary angioplasty, and stroke at blood draw in 1990. Disease status was confirmed as previously reported (1).

Data on exposures, outcomes, and covariates were collected from questionnaires, as previously reported (1–4). Food intake data in the Nurses' Health Study have been assessed using a semiquantitative food frequency questionnaire (SFFQ) (4), the validity and reliability of which have been previously described (5–7), with high correlations between responses to the SFFQ and four 1-week dietary records for coffee ($r = 0.78$), tea ($r = 0.94$), and caffeinated sodas ($r = 0.85$) (5). We also assessed total caffeine intake (8). Averages of coffee, tea, and caffeine intake from the 1984, 1986, and 1990 SFFQs were calculated to account for long-term dietary exposure and reduce within-person variability. Blood samples were taken in 1989 or 1990, and adiponectin was assayed (2,9).

Comparisons of descriptive measures were conducted using ANOVA for continuous variables and appropriate χ^2 tests for categorical variables across groups of caffeine-containing coffee consumers. Associations between beverage consumption and plasma adiponectin concentrations were evaluated using simple linear regression models for crude analysis and multiple linear regressions with logarithmic transformation of hormone values to achieve normal distribution. We adjusted for potential confounders in multivariate analyses. Tests for interaction were conducted using linear regression with multiplicative interaction terms. Analyses were conducted using SAS (version 9.1 for UNIX; SAS Institute, Cary, NC). *P* values are two sided.

RESULTS — Both diabetic and nondiabetic women who drank coffee on a daily basis had significantly higher total energy and caffeine intake and were more likely to be current smokers and less likely to be hypertensive or use thiazide diuretics. Diabetic women in the highest coffee consumption group also had a significantly lower BMI, higher alcohol intake, and were more likely to report a family history of diabetes, whereas nondiabetic women in the highest coffee group had significantly higher weekly physical activity and were more likely to be employed full-time. (Table 1)

Diabetic women who consumed four or more cups of caffeine-containing coffee per day had significantly higher adiponectin concentrations than those who drank lower amounts, even after full adjustment (Table 1). Nondiabetic women in the same group had higher adiponectin concentrations as well, with significant differences among coffee groups after ad-

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Abbreviations: SFFQ, semiquantitative food frequency questionnaire.

Table 1—*Baseline characteristics and adiponectin levels of diabetic and nondiabetic subjects categorized into quartiles of caffeine-containing coffee (cups) or caffeine (milligrams) consumption*

Variable	Caffeine-containing coffee consumption (cups)				*P*
	<1 per week	1–6 per week	1–3 per day	≥4 per day	
Baseline characteristics					
Diabetic subjects					
n	269	224	387	102	
Adiponectin (μg/ml)	5.7 (3.4–8.6)	5.7 (3.6–8.5)	5.2 (3.5–8.7)	6.6 (4.2–12.1)	0.002
Demographic					
Age (years)	58.6 ± 6.7	59.2 ± 6.7	59 ± 6.7	58.1 ± 5.9	0.44
BMI (kg/m^2)	30.4 ± 6.5	30.8 ± 6.4	29.5 ± 5.9	28.5 ± 6.8	0.005
Waist-to-hip ratio	0.85 ± 0.13	0.84 ± 0.07	0.83 ± 0.07	0.83 ± 0.1	0.41
Physical activity (METs/week)	12.7 ± 17.6	12.4 ± 14.8	11.1 ± 14.4	10.2 ± 14	0.39
Total energy intake (kcal)	1713 ± 496	1762 ± 465	1833 ± 438	1842 ± 495	0.006
Alcohol (g/day)	2.2 ± 7.3	2.7 ± 5.8	4.7 ± 9.0	4.4 ± 9.1	0.0002
Caffeine (mg/day)	83 ± 69	185 ± 97	336 ± 114	630 ± 141	<0.0001
Current smoker	19 (7)	21 (9)	58 (15)	38 (34)	<0.0001
Married	221 (87)	175 (81)	294 (80)	86 (77)	0.07
Bachelor's degree or higher	66 (26)	54 (25)	82 (22)	26 (23)	0.71
Full-time employment	64 (25)	58 (27)	103 (28)	33 (29)	0.82
Medical history					
Hypertension	127 (47)	89 (40)	157 (41)	38 (33)	0.06
Hypercholesterolemia	113 (42)	95 (42)	151 (40)	37 (32)	0.30
Family history of diabetes	124 (46)	104 (46)	208 (55)	66 (58)	0.03
Nondiabetic Subjects					
n	276	232	444	106	
Adiponectin (μg/ml)	18.3 (12.6–23.6)	17.8 (13.3–22.7)	17.4 (12.8–22.5)	20.1 (15.1–23.1)	0.06
Demographic					
Age (years)	56.6 ± 7.4	57.1 ± 6.7	56.2 ± 6.8	55.0 ± 6.4	0.06
BMI (kg/m^2)	25.7 ± 5.9	26.6 ± 6.0	26.4 ± 6.1	25.8 ± 5.7	0.32
Waist-to-hip ratio	0.77 ± 0.06	0.79 ± 0.08	0.77 ± 0.06	0.77 ± 0.06	0.11
Physical activity (METs/week)	13.2 ± 16.1	15.7 ± 18.4	12.9 ± 14.4	19.7 ± 35.2	0.006
Total energy intake (kcal)	1746 ± 435	1739 ± 434	1750 ± 455	1897 ± 482	0.01
Alcohol (g/day)	5.1 ± 9.2	6.2 ± 9.0	6.9 ± 9.7	6.2 ± 9.6	0.09
Caffeine (mg/day)	90 ± 84	200 ± 99	354 ± 108	645 ± 142	<0.0001
Current smoker	17 (6)	24 (10)	55 (12)	26 (25)	<0.0001
Married	223 (82)	183 (81)	375 (86)	80 (82)	0.30
Bachelor's degree or higher	94 (35)	70 (31)	140 (32)	27 (28)	0.63
Full-time employment	88 (33)	60 (27)	163 (37)	43 (44)	0.007
Medical history					
Hypertension	31 (11)	49 (21)	84 (19)	19 (18)	0.02
Hypercholesterolemia	75 (27)	79 (34)	127 (29)	27 (25)	0.26
Family history of diabetes	56 (20)	44 (19)	101 (23)	17 (16)	0.40
Adiponectin (μg/ml)					
Diabetic subjects					
n	269	224	387	102	
Unadjusted	5.7 (1.0–41.8)	5.8 (1.2–35.9)	5.5 (1.1–30.2)	7.3 (1.3–31.7)	0.002
Model 1	5.4	5.5	5.1	6.5	0.01
Model 2	5.0	5.2	4.8	6.4	0.002
Model 3	6.1	6.3	5.9	7.7	0.004
Nondiabetic subjects					
n	276	232	444	106	
Unadjusted	16.9 (12.6–23.6)	16.8 (13.3–22.7)	16.5 (23.8–22.5)	19.0 (15.1–23.14)	0.06
Model 1	14.5	14.7	14.3	16.3	0.06
Model 2	14.0	13.9	13.6	15.9	0.04
Model 3	13.2	13.2	12.9	15.0	0.04

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Table 1—*Continued*

	Caffeine Q1	Caffeine Q2	Caffeine Q3	Caffeine Q4	*P*
Diabetic subjects					
n	243	244	245	245	
Unadjusted	5.6 (3.5–8.0)	5.4 (6.4–8.2)	5.6 (3.5–8.9)	6.4 (3.8–10.8)	0.02
Model 1	4.6	4.6	4.6	5.6	0.04
Model 2	4.8	4.8	4.8	5.8	0.003
Model 3	6.0	5.8	5.9	7.0	0.004
Nondiabetic subjects					
n	255	247	284	272	
Unadjusted	16.9 (12.7–24.2)	16.6 (12.9–22.2)	16.4 (12.7–22.9)	17.6 (13.9–23.4)	0.36
Model 1	14.6	14.3	14.3	15.3	0.29
Model 2	14.3	13.6	13.6	14.7	0.17
Model 3	13.5	12.9	12.9	13.9	0.18

Data are median (interquartile range), means ± SD, and *n* (%) for baseline characteristics and modeled median (interquartile range) and geometric mean % for adiponectin data. *P* values determined by ANOVA for continuous measures with logarithmic transformation of biomarkers and χ^2 tests for categorical variables. Model 1: adjusted for age and BMI; model 2: adjusted additionally for physical activity (METs/week), total energy intake, alcohol intake (g/day), and smoking status (never, former, or current); model 3: adjusted additionally for hypertension, hypercholesterolemia, A1C, family history of diabetes, aspirin, postmenopausal hormone use, use of ACE inhibitors and other blood pressure medication, and oral diabetes medication use (A1C, insulin and oral diabetes medication not adjusted for in healthy women). Dichotomous (yes/no) variables and continuous measures categorized into quintiles and modeled using indicator variables. *P* values for differences between categories determined from multivariate linear regression models. For women with diabetes, data were missing for caffeine intake ($n = 5$), so the numbers will be less than the total sample size ($n = 982$). Q1, quartile 1 (0–100 mg); Q2, quartile 2 (101–237 mg); Q3, quartile 3 (237–378 mg); Q4, quartile 4 (379–967 mg).

justment. Also presented are analyses by quartile of caffeine intake, which were very similar to results for caffeine-containing coffee. We found no evidence of interaction by age, obesity, alcohol consumption, or smoking status on the association of caffeine-containing coffee with adiponectin. Additional adjustment for the dietary factors of glycemic load, dietary fiber intake, and Mediterranean diet pattern adherence did not significantly change the results.

No association between consumption of decaffeinated coffee and adiponectin concentration was found in either group. Intake of two or more cups of tea per day tended to be associated with higher adiponectin concentrations among diabetic women, and the association remained marginal after adjusting for lifestyle and medical history covariates ($P = 0.07$) (data not shown).

We confirm previously reported inverse associations of coffee consumption with inflammatory markers (4) among diabetic women, specifically C-reactive protein ($P = 0.001$) and tumor necrosis factor-α receptor II ($P = 0.03$). Adjustment for adiponectin did not weaken these associations, and adjustment for inflammatory markers did not attenuate the association between coffee consumption and adiponectin concentrations ($P < 0.05$ for all).

CONCLUSIONS — Regular consumption of coffee may have beneficial effects including decreased insulin resistance, decreased incidence of type 2 diabetes, and lower levels of markers of inflammation; however, the exact underlying mechanisms are not completely understood (4,8,10–17). Our study suggests that favorable metabolic effects of caffeine-containing coffee may partly operate through associations with serum adiponectin concentrations. We found that habitual consumption of four or more cups of caffeine-containing coffee per day was associated with ~20% higher serum adiponectin concentrations than those associated with habitual consumption of less than four cups of coffee daily, indicating that increased adiponectin may play a role in the beneficial effects of coffee on insulin sensitivity. Our data are consistent with several previous prospective studies that demonstrated a decreased risk of type 2 diabetes with higher coffee consumption, with observed benefits starting at three to six cups per day (8,12,15). Our data extend recent findings that coffee consumption is associated with lower levels of E-selectin and C-reactive protein among women with diabetes (4) and suggest that coffee and/or caffeine may have unique effects on inflammatory processes, insulin sensitivity, and metabolism. Decaffeinated coffee and tea consumption was not associated with high adiponectin concentrations, but only a small number of women consumed four or less cups of decaffeinated coffee per day.

In addition to genetic factors, several modifiable lifestyle factors, including diet (2,18) and increased physical activity (19), may at least partially determine circulating levels of the endogenous insulin sensitizer adiponectin (20–23). However, unlike high levels of physical activity and maintaining a healthy diet, which commonly cluster with an overall healthy lifestyle, coffee consumption has been linked to poorer health habits, such as cigarette smoking and physical inactivity (24).

Phenolic compounds found in coffee may slow intestinal glucose absorption postprandially and improve GLP-1 secretion and glucose metabolism (25,26), and coffee may have antioxidant activities (27). Mechanistic and interventional studies are necessary to determine whether the association between coffee intake and high adiponectin concentrations is causal and what bioactive components might underlie this relationship.

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