Caffeinated Coffee Does Not Acutely Affect Energy Intake, Appetite, or Inflammation but Prevents Serum Cortisol Concentrations from Falling in Healthy Men1–4

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Abstract

Our aim in this crossover study was to investigate the acute effects of caffeinated and decaffeinated coffee consumption on appetite feelings, energy intake, and appetite-, inflammation-, stress-, and glucose metabolism-related markers. Sixteen healthy men (age range, 21–39 y; BMI range, 19.7–28.6 kg/m2) received in a random order on 3 separate occasions a standard breakfast snack with 200 mL of either caffeinated coffee (3 mg caffeine/kg body weight), decaffeinated coffee, or water (control). Before intervention (−15 min) and at standard time points following breakfast consumption (0, 15, 30, 60, 90, 120, 150, and 180 min), participants recorded their appetite feelings and we collected blood samples for measurements of circulating glucose, insulin, cortisol, and appetite- and inflammation-related markers. At 180 min, participants consumed a meal ad libitum. The appetite-related ratings, the appetite plasma hormonal responses as well as the plasma glucose, serum insulin, and plasma and serum inflammatory marker responses did not show an overall intervention effect or an intervention effect over time. Ad libitum energy intake did not differ among the 3 interventions. However, a significant intervention effect (P = 0.04) and a time × intervention interaction (Pinteraction = 0.02) were found for serum cortisol; cortisol concentrations were significantly higher following the caffeinated coffee intervention, compared to control, at 60 min and thereafter. In conclusion, the usually consumed amount of caffeinated coffee does not have short-term effects on appetite, energy intake, glucose metabolism, and inflammatory markers, but it increases circulating cortisol concentrations in healthy men. J. Nutr. 141: 703–707, 2011.

Introduction

Coffee is a pharmacologically active, widely consumed beverage. Scientific interest in relation to coffee consumption has remained very active during the last decade in light of new, mainly epidemiological, evidence indicating coffee’s potential health benefits. Both cross-sectional and prospective observational studies show that habitual coffee consumption is associated with a lower risk for type 2 diabetes in both normal-weight and obese individuals (1,2). Furthermore, an inverse association has been found between habitual coffee consumption and markers of inflammation in healthy and/or diabetic participants (3,4). The opposite effect has also been reported in apparently healthy participants (5). Epidemiological data suggest that increasing caffeine consumption is associated with lower mean weight gain and energy intake during a 12-y period in men and women without chronic disease (6).

Information from clinical studies is scarce. Battram et al. (7) showed that the consumption of 4.45 mg caffeine/kg body weight, either in capsule form or as coffee, increased glucose and insulin concentrations over a 3-h period in healthy males, whereas high coffee consumption for 4 wk increased fasting insulin concentrations compared with coffee abstinence in nondiabetic participants (8). Furthermore, in habitual coffee drinkers, adiponectin blood concentrations increased and IL-18 concentrations decreased following an 1-mo intervention including daily ingestion of 8 cups of coffee (9).

Westerterp-Plantenga et al. (10) studied overweight or obese individuals and reported a positive association between habitual caffeine intake and body weight loss achieved through a very low-energy diet. The ingestion of 300 mg of caffeine prior to
food intake, compared to placebo, was shown to significantly reduce energy intake by 21.7% in healthy men, but not in women (11). More recently, the consumption of caffeine and red pepper was found to positively affect energy expenditure and negatively affect energy intake (12).

Taking into consideration the limited clinical evidence, we undertook a randomized, crossover, controlled study to investigate the acute effects of regular doses of caffeinated or decaffeinated coffee on energy intake, appetite feelings, appetite hormones, inflammatory markers, and cortisol and glucose metabolism in apparently healthy men.

**Methods**

**Study population.** Sixteen apparently healthy, nonobese, young men who were habitual coffee drinkers were recruited by local advertisement to participate in this study (Table 1). Smokers, restrained eaters [assessed using the Dutch Eating Behavior Questionnaire (13)], those who reported being on a slimming or any other special diet, competitive athletes, and those with a diagnosis of hypertension, metabolic or endocrine disease, gastrointestinal disorders, or a recent history of medical or surgical events were excluded from participation. Also, individuals who were taking medications that may affect glucose metabolism, appetite, or sensory functioning were not included. Potential participants were informed that the purpose of the project was to investigate the effect of breakfast consumption on blood lipids; the true purpose of the study was not revealed to decrease participants’ response associated with preconceived cognitions regarding the effect of coffee on appetite. They reported a stable body weight for at least 1 mo prior to the beginning of the study. They gave informed consent and the experimental protocol was approved by the University Ethics Committee. The study was undertaken at the Metabolic Unit of the Department of Nutrition and Dietetics, Harokopio University, from February to May 2009.

**Study design.** The experiment had a randomized crossover design. Each volunteer participated in 3 interventions on separate days, at least 1 wk apart, in a random order (using a random-number table). One of the 3 interventions was given to each participant on each separate day, with the sequence of the interventions being randomly determined by a random-number table. The first intervention was a control intervention (water); the second intervention was a breakfast snack consisting of common Greek diet foods (pasta, tomato sauce, beef, salad, cheese, yogurt, fruit, and chocolate); and the third intervention was one of the 3 interventions:

1. 200 mL of instant decaffeinated coffee (same amount of coffee as the previous intervention) (DECAF);
2. 200 mL of instant decaffeinated coffee at 900 kJ (same amount of coffee as the previous intervention) (DECAF);
3. 200 mL of water (control).

The breakfast snack was provided to imitate real-life settings in terms of time and context of coffee consumption and to supply some energy for the participants; the energy and nutrient content were, however, kept low to avoid any potential nutrient effects. Immediately after breakfast consumption, a second blood sample was obtained (0 min) and subsequently obtained at 15, 30, 60, 90, 120, 150, and 180 min. After each blood draw, the cannula was flushed with saline (0.9% NaCl). Approximately 90 mL of blood in total was collected from each participant. Along with each blood draw, participants had to complete three 10-point visual analog scales (VAS) to record their subjective feelings of hunger, satiety, and desire to eat.

Participants were not allowed to exercise or drink and eat anything for 3 h following the experiment and rested in a sitting position. Study investigators supervised them to ensure compliance. During this period, participants were interviewed about the previous day’s dietary intake using the 24-h recall method.

At the end of the 3-h period, participants consumed ad libitum a buffet-style lunch consisting of common Greek diet foods (pasta, tomato sauce, beef, salad, cheese, yogurt, fruit, and chocolate). They were instructed to eat until they were satiated, within 30 min. Foods were provided in excess amounts and participants had to serve themselves the quantities they wanted to eat. Food quantities were measured as well as any leftovers to estimate dietary intake in the ad libitum meal. One day after the experiment, participants were asked in a telephone interview to report their food intake for the rest of the experimental day.

**Analyses of biochemical markers.** Blood samples from all time points were analyzed for glucose, insulin, ghrelin, peptide tyrosine-tyrosine (PYY), and glucagon-like peptide-1 (GLP-1) concentrations. Because no immediate effect of a meal was hypothesized, analyses for cortisol, IL-6, IL-18, and adiponectin concentrations were conducted for the baseline samples and then for the 30- to 180-min samples.

Plasma glucose analysis was performed in an automated analyzer using standard reagents (ACE Schiapparelli, Biosystems). Serum insulin and adiponectin and plasma ghrelin concentrations were measured by RIA (Millipore) with sensitivities of 12 pmol/L, 27.5 pmol/L, and 1 pg/L and intra-assay CV of 2.2–4.4, 3.3–10.0, and 1.8–6.2%, respectively. Plasma PYY and active GLP-1 concentrations were determined by commercially available human ELISA kits (Millipore) with intra-assay CV of 0.9–5.8 and 6.0–9.0% and sensitivities of 2.5 and 2 pmol/L, respectively. Plasma IL-6 concentrations were measured by a chemiluminescent ELISA kit (R&D Systems) with intra-assay CV of 3.0–5.8% and a sensitivity of 0.16 pg/L, whereas serum IL-18 was determined by commercially available human ELISA kit (MBL) with an intra-assay CV of 0.8–9.9% and a sensitivity of 12.5 μg/L. Serum cortisol concentrations were determined using an automated immunoassay hormone analyzer (Immulite; Siemens), which had a sensitivity of 5.5 nmol/L and an intra-assay CV of 5.8–8.8%. All blood samples were analyzed in duplicate and laboratory staff was not aware of the intervention assignment.

**Analysis of dietary intake and physical activity information.** All food intake data were analyzed for energy and macronutrient content.
using the Nutritionist Pro, version 2.2 software (Axxya Systems-Nutritionist Pro). The software food database was expanded by the analyses of traditional Greek foods and recipes as well as information provided by food companies. Caffeine intake from the various foods and beverages included in the FFQ was calculated using information from the USDA National Nutrient Database for Standard Reference (15) and the food industry. The information collected through the physical activity questionnaire (14) was analyzed using the metabolic equivalents of all activities of the previous week as reported by the study participants. A physical activity level, i.e. the ratio of total energy expenditure:basal metabolic rate, was then calculated for each participant.

**Statistical analysis.** Variables are presented as means ± SD, unless otherwise stated. For the determination of sample size, changes in blood glucose concentrations were used. To detect an increase of 0.5 SD with a 2-sided 5% significance level and a power of 80%, a sample size of 15 patients was necessary. We recruited 16 participants, because we anticipated a dropout rate of 5–10%.

Comparisons of the response curves of glucose, insulin, ghrelin, GLP-1, PYY, cortisol, adiponectin, IL-6, IL-18, and the VAS ratings after the 3 interventions were performed using the repeated-measures ANCOVA (participant as a covariate) by testing for intervention effect and time × intervention interaction. Bonferroni post hoc test was used to compare one intervention to another. Total and incremental areas under the curve (AUC and IAUC, respectively) for the above-mentioned biochemical markers as well as for the VAS ratings were calculated. Total AUC was defined as the sum of the areas under and over the baseline, whereas IAUC was defined as AUC = (baseline × 3.25 h)/2. AUC and IAUC were compared by 1-way ANOVA and they were further analyzed using the metabolic equivalents of all traditional Greek foods and recipes as well as information from the USDA National Nutrient Database for Standard Reference (15) and the Nutritionist Pro, version 18 was used for all statistical calculations. All reported P-values compared with a significance level of 5%.

**Results**

Ad libitum energy and macronutrient intakes from the test meal and during the rest of the day or the total day did not differ among the 3 interventions (Table 2) even after adjustment for the previous day’s energy intake. Ratings in the hunger and desire to eat VAS scales decreased immediately after breakfast snack consumption compared to the prebreakfast levels and started to increase again at 30 min, reaching maximum levels at 180 min in all 3 interventions. Satiety ratings were similar. The ratings in these 3 scales over time did not differ among the 3 interventions and there was no time × intervention interaction. However, at 180 min in the CAF intervention, participants reported lower desire to eat compared to the DECAF intervention (P = 0.03) and the control (P = 0.06) (Supplemental Fig. 1). Comparison of the AUC and IAUC did not differ among the 3 interventions, except in the IAUC for the desire to eat (P = 0.05) (data not shown). Post hoc analysis revealed that the CAF tended to result in a lower IAUC compared to the control intervention (P = 0.07) (data not shown).

Among the appetite-related hormones, plasma ghrelin started to increase 60 min after breakfast consumption, reaching the highest concentrations at 150–180 min (~23% increase from prebreakfast concentrations), plasma PYY values fell around 60–90 min after breakfast ingestion (~15% decrease at 180 min compared to prebreakfast concentrations), and plasma GLP-1 concentrations remained stable during the entire study period in all interventions. Ghrelin, PYY, and GLP-1 responses did not show an overall intervention effect or a time × intervention interaction and the comparison of the corresponding AUC and IAUC did not reveal differences among the 3 interventions (Supplemental Fig. 1).

Plasma glucose and insulin concentrations peaked at 30 min following all interventions. Neither glucose nor insulin responses presented an overall intervention effect or a time × intervention interaction (Fig. 1; Supplemental Fig. 2). Similarly, the corresponding AUC and IAUC did not differ. However, the glucose concentration was higher at 60 min (P = 0.03) and tended to be higher at 120 and 180 min (P = 0.08) of the CAF intervention compared to the control intervention.

Serum cortisol concentrations fell throughout the study period, reaching the lowest values at the end, 180 min (Fig. 1). Cortisol concentrations over time differed among the 3 interventions (P = 0.04); furthermore, there was a time × intervention interaction (P-interaction = 0.02). The AUC and IAUC also differed among the 3 interventions (P = 0.02 and P = 0.01, respectively). Post hoc analysis revealed a greater AUC and IAUC for the CAF compared to the control intervention (data not shown).

Plasma IL-6 concentrations started to increase 60 min after breakfast consumption and they were ~40% higher at the end of the experiment compared to the prebreakfast concentrations in all interventions (Supplemental Fig. 2). IL-6 concentrations presented a significant time × intervention interaction (P-interaction = 0.01). There was no effect of intervention and the AUC or IAUC did not differ among the 3 treatments. Serum IL-18 and adiponectin remained stable throughout the study course.

**Discussion**

We studied the acute effects of caffeinated and decaffeinated coffee consumption on energy and macronutrient intakes, subjective feelings, and biochemical markers of appetite, as well as on biochemical markers related to inflammation. The caffeine dose used in this study was estimated on the basis of body weight (240 mg for a 80-kg person). This corresponds to the usual intake of the study participants based on their dietary assessment and represents a usual intake for this population at large (5).
Moreover, this dose has been previously shown to produce metabolic effects in the long term (16,17). Our findings, however, indicate that this level of coffee consumption has no major acute effect on the subjective feelings of appetite or on molecules related to appetite, glucose metabolism, or inflammation, but does affect cortisol concentrations. In healthy men, acute administration of approximately similar doses (i.e. 3.3 mg caffeine/kg body weight) increased cortisol concentrations 1 h following administration (18), whereas administration of 200 mg of caffeine twice per day had no effect on cortisol levels after 7 d (19). In the present study, caffeinated coffee consumption prevented cortisol concentrations from falling rather than causing an absolute increase. This “awakening” profile would be expected on the basis of the known circadian rhythm of cortisol; despite the great intra-individual variability, cortisol’s main secretory phase is during the sixth to eighth hours of sleep and the first hour of awakening (20).

In addition to serum cortisol, we focused on appetite feelings and the concentrations of selected molecules with either orexigenic or anorexigenic effects. The blood concentrations of ghrelin, the only known gut hormone that stimulates appetite and food intake (21,22), paralleled the subjective feelings of hunger and desire to eat, as expected. However, there was no significant intervention effect for any of the hormones or the subjective ratings. Furthermore, concentrations of PYY, a gut anorexigenic peptide, paralleled the satiety ratings reported by the study participants. There is some recent evidence in relation to the effect of dietary factors on PYY blood concentrations: specifically, it has been shown that dietary lipid and protein intakes induce greater increases compared to carbohydrate intake (23,24). This is the first study to our knowledge to examine the effects of coffee, as another dietary factor, on PYY and ghrelin concentrations.

Changes in glucose metabolism markers following coffee or caffeine consumption have been investigated in a number of studies; 4.45 or 5 mg caffeine/kg body weight resulted in elevated insulin concentrations, but the effects on glucose responses over a 3- to 4-h period are not consistent across studies (7,25,26). The findings of the present study indicate no intervention effect on the glucose or insulin concentrations, but the caffeine dose was much less than that used in previous investigations. This may also explain why we did not find a treatment effect for the inflammation markers we measured. Although Kempf et al. (9) reported a decrease in IL-18 and an increase in serum adiponectin concentrations, a much higher dose was used for an extended period of time.

Our study has several strengths and limitations. The sample size was selected according to the power calculations performed for blood glucose concentrations and it is among the largest in the relevant literature comprising metabolic studies of acute interventions (23,27–29). Only men were included in order to eliminate potential sex-specific effects. The experimental conditions were similar to those of everyday life, because coffee was given early in the morning, accompanied by a small standardized breakfast snack. The study was performed with the use of state-of-the-art techniques for blood collection, separation, and analysis. Among the limitations is the fact that the participants were healthy males, nonsmokers, and moderate coffee consumers; thus, the results cannot be generalized to other populations. In particular, we think that a background of lower caffeine consumption (i.e. irregular coffee intake or coffee abstinence) might have resulted in more pronounced effects on the biomarkers studied, as a tolerance to the effects of caffeine probably would not have already developed. Moreover, the results would be different if nonhealthy participants were included in the study, such as people with disturbed glucose metabolism or inflammatory markers, including obese and/or diabetic patients. However, the evidence in this area is very scarce and we may only speculate on these outcomes; studying healthy participants is a starting point for future research. Finally, the energy content of the breakfast snack was not calculated on the basis of energy requirements of the participants and the caffeine dose was moderate; although higher doses may be needed to induce significant changes in the measured markers, the dose used corresponds to a commonly consumed dose.

In conclusion, coffee, providing 3 mg of caffeine/kg body weight, was found to prevent morning cortisol concentrations from falling; no significant acute or immediate effects on energy intake, appetite, or inflammatory markers were observed. Further research is needed to replicate and extend these findings to women or to no coffee/caffeine consumers and to explore potential outcomes using higher doses.

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Literature Cited


