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

Anna Gavrieli, Mary Yannakoulia, Elizabeth Fragopoulou, Dimitris Margaritopoulos, John P. Chamberland, Panagiota Kaisari, Stavros A. Kavouras, and Christos S. Mantzoros

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 study investigators (A.G.) was responsible for the randomization and the enrollment of the participants. Preliminary testing included a semi-structured interview to establish the study investigators’ awareness of the intervention assignment.

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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 were asked to select and eat similar foods, to abstain from caffeine and food intake data were analyzed for energy and macronutrient content

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 ghrelin 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 an 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 5.0–9.9% 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

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### TABLE 1 Baseline characteristics of the male participants, including caffeine intake during the CAF intervention

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Study population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>27.8 ± 5.2 (21.0–39.0)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>81.8 ± 7.5 (66.7–93.3)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>25.5 ± 2.3 (19.7–28.6)</td>
</tr>
<tr>
<td>Physical activity level</td>
<td>1.5 ± 0.3 (1.3–2.1)</td>
</tr>
<tr>
<td>Energy intake in previous day, MJ/d</td>
<td>10.9 ± 3.3 (6.1–20.8)</td>
</tr>
<tr>
<td>Habitual caffeine intake, mg/d</td>
<td>250 ± 170 (20–562)</td>
</tr>
<tr>
<td>Derived from noncoffee sources, %</td>
<td>32.4 ± 32.6</td>
</tr>
<tr>
<td>Habitual coffee intake, 2 servings/d</td>
<td>1.3 ± 1.0 (0.0–3.5)</td>
</tr>
<tr>
<td>Exclusive Greek-style coffee consumption, %</td>
<td>6.3</td>
</tr>
<tr>
<td>Exclusive espresso-style coffee consumption, %</td>
<td>12.5</td>
</tr>
<tr>
<td>Consumption of several types of coffee, %</td>
<td>81.8</td>
</tr>
<tr>
<td>Caffeine intake during CAF intervention, mg</td>
<td>247 ± 24 (201–279)</td>
</tr>
</tbody>
</table>

1 Values are means ± SD (range) or relative frequencies, n = 16.
2 One serving corresponds to 240 mL filtered instant coffee or 60 mL Greek-style espresso coffee.

9 Abbreviations used: AUC, area under the curve; CAF, caffeinated coffee; DECAF, decaffeinated coffee; GLP-1, glucagon-like peptide-1; IAUC, incremental area under the curve; PYY, peptide tyrosine-tyrosine; VAS, visual analog scale.
Ad libitum energy and macronutrient intakes from the test meal and energy and macronutrient intakes during the rest of the day and the total experimental day by men after the control, CAF, and DECAF interventions

<table>
<thead>
<tr>
<th>Dietary intake</th>
<th>CAF</th>
<th>DECAF</th>
<th>Control</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ad libitum test meal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy, MJ</td>
<td>7.3 ± 1.7</td>
<td>7.2 ± 1.7</td>
<td>7.3 ± 1.9</td>
<td>0.97</td>
</tr>
<tr>
<td>Carbohydrates, % E</td>
<td>55.4 ± 12.6</td>
<td>55.4 ± 13.0</td>
<td>56.5 ± 13.2</td>
<td>0.98</td>
</tr>
<tr>
<td>Proteins, % E</td>
<td>16.7 ± 3.7</td>
<td>16.5 ± 4.2</td>
<td>16.5 ± 4.0</td>
<td>0.98</td>
</tr>
<tr>
<td>Lipids, % E</td>
<td>28.3 ± 9.1</td>
<td>28.4 ± 9.1</td>
<td>27.5 ± 9.0</td>
<td>0.95</td>
</tr>
<tr>
<td>Total experimental day</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy, MJ</td>
<td>6.2 ± 3.3</td>
<td>7.2 ± 3.0</td>
<td>6.5 ± 2.9</td>
<td>0.63</td>
</tr>
<tr>
<td>Carbohydrates, % E</td>
<td>42.8 ± 12.5</td>
<td>45.6 ± 13.1</td>
<td>48.5 ± 11.7</td>
<td>0.44</td>
</tr>
<tr>
<td>Proteins, % E</td>
<td>15.9 ± 5.3</td>
<td>13.4 ± 5.0</td>
<td>14.0 ± 5.4</td>
<td>0.41</td>
</tr>
<tr>
<td>Lipids, % E</td>
<td>38.0 ± 9.2</td>
<td>39.2 ± 10.1</td>
<td>35.3 ± 10.9</td>
<td>0.55</td>
</tr>
</tbody>
</table>

1 Values are means ± SD, n = 16.

2 % E, percent energy.

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 unhealthy 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.

Acknowledgments
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References