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Gender and body mass index modify the effect of increasing amounts of caffeinated coffee on postprandial glucose and insulin concentrations; a randomized, controlled, clinical trial

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ABSTRACT

Objective. To examine the effects of different coffee amounts on blood glucose and insulin concentrations of healthy volunteers, and to assess potential effect modification by sex and body mass index category.

Materials/Methods. Thirty-three volunteers [16♀/17♂, 16 normal-weight and 17 overweight/obese, 27.3 ± 7.2 (19–44) y] took part in this randomized, crossover study. In the morning of each experimental day volunteers received a standardized meal along with 200 mL of water or instant coffee containing either 3 or 6 mg of caffeine/kg body weight. Blood samples were obtained and analyzed for glucose and insulin concentrations in the fasting state, immediately after meal/drink consumption and at standard time points for the next 3 h thereafter.

Results. Coffee delayed the rise of insulin in response to the standardized meal and the fall of glucose concentrations from its maximum levels in the entire study sample. Glucose incremental area under the curve (IAUC) was significantly different between interventions ($P = .009$) with both coffee amounts inducing a greater area compared to water. Secondary, subgroup analysis at the nominal level showed that this might be more evident among females ($P_{IAUC} = .05$) and overweight/obese participants ($P_{IAUC} = .03$). Furthermore, coffee, mainly the 6 mg dose, could be lowering insulin concentrations the first 30 min after its consumption compared to water in men and overweight/obese participants.

Conclusions. Coffee exerts an acute effect on postprandial glucose and insulin concentrations. This effect may be modified by sex and overweight/obese status. Future research is necessary to elucidate underlying mechanisms.

Abbreviations: DM2, type 2 diabetes mellitus; BMI, body mass index; FFQ, food frequency questionnaire; ELISA, enzyme-linked immunosorbent assay; CV, coefficient of variation; AUC, area under the curve; IAUC, incremental area under the curve; ANCOVA, analysis of covariance; SD, standard deviation; SEM, standard error of the mean.

Trial Registration: clinicaltrials.gov Identifier: NCT01495754.

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1. Introduction

Coffee, one of the most frequently consumed beverages, has gained special attention regarding its effects on several disease states [1]. For example, although in cardiovascular disease its effect has not been fully elucidated [2,3], its role in DM2 is more clear. Research has focused on the effect of coffee on glucose metabolism markers and the risk of DM2. Early epidemiological evidence indicated that coffee consumption is positively associated with insulin sensitivity and lowers the risk for DM2 in the long-term [4,5]. The results of a more recent meta-analysis confirmed previous findings and showed that for every additional cup of coffee consumed in a day the excess risk for DM2 is reduced by 7% [6]. Potential mechanisms include the hypoglycemic effects of non-caffeine coffee compounds [7–9], the anti-inflammatory [10,11] and antioxidant action of coffee [12,13] and a potential beneficial effect of coffee/caffeine on body weight management [14]. The positive association between coffee consumption and blood concentrations of sex hormone-binging globulin (SHBG) has also been proposed as a possible mediator [15]. However, a recent intervention study found no effect of coffee on SHBG after 8 weeks of consumption, putting under question this mechanism [16]. Finally, the protective effect of coffee on DM2 and insulin sensitivity has been proposed to partly explain the beneficial effect of coffee on other diseases, i.e. endometrial cancer [17].

Clinical research, however, does not confirm evidence from observational studies, as it presents an unfavorable effect of caffeine or caffeinated coffee on glucose metabolism markers either acutely, after 3–5 h of ingestion in the postprandial period, or after several days of consumption, in the fasted state [7,18,19]. Caffeinated coffee results in a less pronounced acute postprandial adverse effect on glucose tolerance and insulin sensitivity compared to pure caffeine, whereas decaffeinated coffee exerts no or a beneficial effect during a 2 h oral glucose tolerance test [20]. The discrepancy between epidemiological and clinical research could be attributed to the tolerance to caffeine's action that may be developed following chronic consumption and/or to potential interactions between caffeine and other non-caffeine coffee components that may reduce or antagonize the adverse effects of caffeine [21,22]. Alternatively, results from epidemiology may reflect uncontrolled confounding by beneficial factors that tend to coexist with higher coffee consumption i.e. higher anti-inflammatory status [10,11].

In a previous study by our group, coffee containing 3 mg caffeine/kg body weight induced acutely only minor changes in plasma glucose and no changes in serum insulin concentrations during a 3-h postprandial period in healthy, non obese men, compared to decaffeinated coffee and water [23]. In another study, coffee containing 5 mg caffeine/kg body weight resulted in greater postprandial increases of glucose and insulin levels compared to either decaffeinated coffee or water in male, normal-weight volunteers [18]. It remains unknown whether the administration of increasing amounts of coffee and caffeine affect glucose and insulin concentrations in a dose–response manner in the postprandial period after a standardized mixed meal and/or whether such effects of coffee are modified by sex or obesity status. Thus, the aim of the present study was to examine a potential dose effect of caffeinated coffee on glucose and insulin concentrations in the postprandial state of males and females, as well as of normal-weight and overweight/obese individuals utilizing a randomized, crossover, controlled, study design.

2. Methods

The study was originally designed to evaluate the effects of coffee on appetite. The present paper presents only the results of the trial on glucose and insulin concentrations.

2.1. *Participants*

Participants were recruited through local advertisements in the university campus. Thirty-four volunteers [17♂ and 17♀; 17 normal-weight (9 females) and 17 overweight/obese (8 females)] participated in this crossover, randomized, controlled study. However, one normal-weight female volunteer dropped out after participating at her first experimental trial without giving a reason. The characteristics of the 33 participants who completed the study are presented in Table 1. Participants were apparently healthy and reported habitual coffee intake (≥ 1 cup of coffee/d). For the assessment of their health status and their caffeine intake over the previous year, volunteers completed a medical history questionnaire and a semi-quantitative FFQ (including several types of caffeinated and decaffeinated coffee, tea, caffeinated soft drinks, energy drinks and chocolate) before participation in the study. Smokers, special population groups, i.e. athletes, pregnant women etc., those having a chronic or acute disease and those on medication were excluded from the study. Participants' body weight and height were measured on a levelled platform scale and a wall-mounted stadiometer and BMI was calculated as weight (kg)/height^2 (m^2). The cut-off point of BMI 25 kg/m^2 was taken to categorize participants as normal-weight (< 25 kg/m^2) and overweight/obese (≥25 kg/m^2) [24]. All participants provided written informed consent and the experimental protocol was approved by the Harokopio University Ethics Committee. The study was undertaken at the Metabolic Unit of the Department of Nutrition and Dietetics of Harokopio University, from February to June 2011. The biochemical analyses of fasting and postprandial glucose and insulin concentrations were completed in 2012.

2.2. *Experimental protocol*

Each volunteer took part in 3 trials with at least one week time interval between them and in a random order (using a random-number table). Female participants were on the follicular phase of their menstrual cycle during the experiments to avoid variability in the responses of the glucose and insulin concentrations [25,26]. The day preceding each experimental day participants were instructed to abstain from any caffeine and alcohol source and physical exercise, to get enough sleep (~7 h) and to come to the lab after an overnight fast of 10 h. Furthermore, the days before the three