Impact of Caffeine on Macronutrient Metabolism: A Review of Literature

Helen Cheung[1], Cara Feng[1], Karen Chan[1], Cassandra Nikolaus[2]

[1] **Department of Food Science and Human Nutrition;** [2] **Division of Nutritional Science; College of Agriculture, Consumer, and Environmental Sciences, University of Illinois at Urbana-Champaign**

Introduction

Inspired by the profound use of everyday caffeine consumption in the United States, our group is interested in the interaction between macronutrient metabolism and caffeine consumption. Further exploration of how macronutrient metabolism is impacted when caffeine is ingested with food was probed.

Aim

To investigate the benefits or risk or harm between caffeine and macronutrients consumption.

Method

- A review was conducted (Figure 1) using the guidelines published by the Centre for Reviews & Dissemination (CRD's Guidance for Undertaking Reviews in Health Care, 2009).
- Two databases were used:
  1. EBSCO Host Academic Search Complete
  2. Google Scholar
- Search terms (used in varying combinations): "the metabolic effects of caffeine", "carbohydrates", "proteins", "metabolism" and "insulin response to caffeine"
- Research databases were searched between July 2015 and April 2016
- Summarized based on specific research characteristics

Results

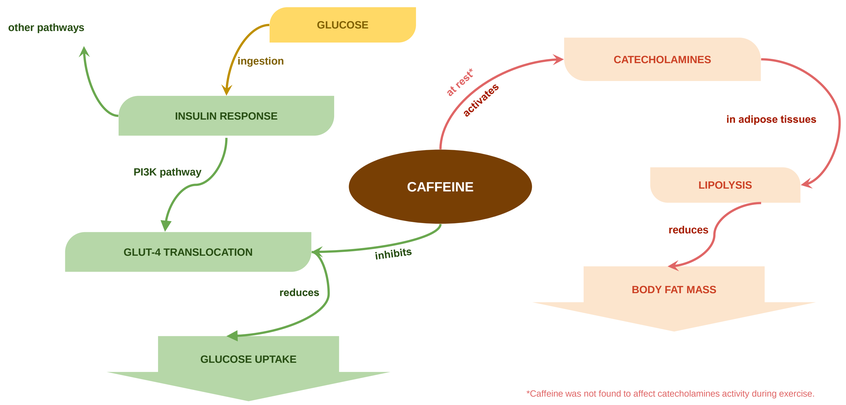
Figure 1. Characteristics table of Published Papers of Impact of Caffeine on Macronutrient Metabolism

		Carbohydrate			Lipid			Protein	
Authors		4. Greer F, et al.	6. Johnston KL, et al.	1. Akiba T, et al.	8. Kobayashi-Hattori k, et al.	5. Jacobson TL, et al.	3. Graham TE, et al.	2. Eaton T, et al.	7. Kendall KL, et al.
Population Tested		Healthy, lean, sedentary males, non-smokers, not regular caffeine users, screened for type 2 diabetes	Healthy adults, BMI≤25, non-smokers, no heavy alcohol consumption	Mouse preadipocyte cells and mouse brown adipocytes	Animal Model (Rats)	healthy highly trained male cyclists and triathletes	healthy individules	Football players who regualarly competing and training	Healthy Individuals who exercise regularly
Final Sample Size		9	9	24 well plates/cell type	44	8	10	8	17
Participant Characteristics	Age	25 ± 0.5	26 ± 3.2	N/A	N/A	21.2±3	20-28	22 ± 2	21 ± 4
	Sex	Male	Male and female	N/A	Male Rats	Male	Male	Male	Males
Study Design		[Subjects were asked to abstain from all methylxanthine-containing products for 48 h before each trial. For each subject, two catheters are used to infuse nutrients (normal saline, insulin, glucose and potassium) and to draw blood samples. Insulin was infused at a rate of 40 mU/(m^2*min^1) for 180 min while 20% glucose was infused to keep plasma glucose concentration at 5.0-5.5 mmol/L. Upon receiving the treatment, a hyperinsulinemic-euglycemic clamp procedure was performed drawing blood sample every 30 min for the duration of the clamp.	Test beverages were selected and were reconstituted to a final CQA concentration of 2.50 mmol/L, with 25g glucose. The day before study the subjects were given a sample menu high in carbohydrates. After fasting overnight, they proceeded to consume 400ml treatment/control. Blood samples were taken at frequent intervals for the next 180 min. Insulin, glucose- dependent insulinotropic polypeptide (GIP) and glucagon-like peptide 1 (GLP-1) levels were analyzed.	Glucose Uptake: Primary cultured mouse brown adipocytes were incubated and were treated with caffeine (conc. 0.0, 0.1, 0.25, 0.5, 1.0 mM) or adenosine receptor antagonists with 1 hr incubation. Before being exposed (or not) to insulin, 2-deoxy-D-[1-^{3}H]glucose was added, the cells were incubated for another 5 min before extraction with 1N NaOH (later neutralized with 1N HCl). Liquid scintillation spectroscopy was performed to measure radioactivity incorporated into the cells. Immunoblotting: Mouse preadipocyte cells were incubated and treated with caffeine (conc. 0.1, 0.25, 0.5, 1.0 mM) and incubated for 1 hr. Insulin was added and the cultures were incubated for 5 min, then the cells were lysed for immunoblot analysis.	Experiment 1: 32 rats fed with a standard diet for 7 days were divided into 4 groups, pair-fed with a diet containing 20% lard and various amount of caffeine for 21 days. Blood samples, adipose tissues, and liver tissues were collected after a 7-hour fast to measure the serum, hapatic lipid and the total weight of the adipose tissues. Experiment 2: 12 rats fed with a standard diet for 7 days were divided into 2 groups. After a 7-hour fast, distilled water and caffeine were orally administered to the control group and test group, respectively. Blood samples were collected at 0, 30, 60, 120 and 180 minutes time point after the administration. The serum concentrations of catecholamines were then determined.	Four trials were performed on each subject in a random order, resting blood sample was obtained at the first trail. In each trial, subjects ingested one test meal and blood samples were obtained 30 and 55 minutes following ingestion; they then cycled at steady-state for 120 minutes on a cycle ergometer. More blood samples were obtained at 20, 40, 60, 80, 100 and 119 minutes during the cycling, and exhalation was collected for 60s at 19, 39, 59, 79 and 119 minutes during the cycling.	Two trials, one with treatment and one with placebo were administered with one week in between. Subject abstained from all caffeinated foods and beverages for 48 hours and fasted overnight before the tests. After 30 min of supine rest, an arterial blood sample was taken and the subject ingested gelatin capsules containing either caffeine (6 mg/kg body wt) or placebo (dextrose) with 250 ml water. After another 60 min rest the subjects exercised for 60 minutes on a Krogh cycle ergometer. Heart rate and blood pressure were recorded at 0, 10, 30, 45 and 60 minutes. Leg blood flow was determined, and arterial and venous blood samples were drawn.	Participants performed a repeat sprint running protocol on a nonmotorized treadmill in an extreme environment on 4 separate occasions. Participants were randomly assigned and ingested one of the 4 supplements: a double placebo, caffeine + placebo, essential amino acid (EAA) +placebo, or caffeine + EAA. Electromyography (EMG) activity, quadriceps evoked responses to magnetic stimulation, blood sample was assessed at regular intervals.	Participants were assigned to either the placebo or the supplement randomly. Participants were required to maintain their current diet throughout the duration of the study while treatment was ingested everyday for at least 28 days. Blood sample, resting heart rate, blood pressure, body composition assessment and percent fat were assessed in the study. Maximum volume of oxygen test was used to measure performance.
Treatment		Caffeine at 5mg/kg body wt in gelatin capsules. Control: placebo gelatin capsules.	Decaffeinated coffee 400 ml, CQA 2.50 mmol/L, 25g glucose. Caffeinated coffee 400 ml, CQA 2.50 mmol/L, 25g glucose. Control: water 400 ml, 25g glucose.	Glucose Uptake: Caffeine/adenosine receptor antagonists/no treatment; insulin/no insulin Immunoblotting: Caffeine/no treatment; insulin	Experiment 1: An experimental diet with 0% or 0.025% or 0.05% or 0.1% caffeine and 20% lard. Experiment 2: A normale diet with distilled water or caffeine.	Four test meals: 1. 2.6g(kg BM) -1 of high glycaemic index carbohydrate 2. 2.6g(kg BM) -1 of high glycaemic index carbohydrate plus 6mg caffeine 3. 1.2g (kg BM) -1 saturated fat 4. 1.2g (kg BM) -1 saturated fat plus 6mg caffeine	Two treatments, a gelatin capsules containing either caffeine (6 mg (kg body wt)) or placebo (dextrose) with approximately 250 ml water.	a double placebo, 3 mg.kg-1 body mass of caffeine + placebo, 2x1 g essential amino acid (EAA) (Musashi Create)+placebo, or caffeine + EAA	The supplement is marketed as Assault, (Denver, CO, USA) contained BCAAs (6 g), creatine (5 g), β -alanine (4 g), citrulline malate (1.5 g), and caffeine (300 mg). The placebo was flavored maltodextrin, similar color and taste as the supplement.
Outcomes	Test Results	Glucose disposal after caffeine ingestion was 24% less than after placebo. Plasma C-peptide concentrations were also similar in both trials throughout the 180 min clamp, they both decreased over time with the influx of exogenous insulin (C-peptite concentration is positively correlated with a body's insulin secretion)	Plasma glucose concentration was higher after consumption of caffeinated coffee than other two beverages, and plasma insulin concentration was found higher after caffeinated coffee than decaffeinated coffee.	Glucose Uptake: Caffeine inhibited insulin-induced 2-deoxy-D-[1-^{3}H]glucose uptake in a concentration-dependent manner, but no effect without insulin. Immunoblotting: Analysis with anti-GLUT4 antibody indicated that caffeine inhibited the insulin-induced GLUT4 translocation to plasma membrane. GLUT4 translocation from intracellular space to the plasma membrane is primarily responsible for insulin-induced glucose uptake by muscle and adipocytes.	Experiment 1: The intake of caffeine at 0.025, 0.05 or 0.1% for 21 day progressively reduced the body fat mass and body fat percentage in rats fed on a high-fat diet with increasing administration level. Experiment 2: Caffeine increased the serum concentration of catecholamines and free fatty acids in rats orally administered with 5mg/kg caffeine while at rest.	The overall respiratory exchange ratio, carbohydrate oxidation, fat oxidation, heart rate and blood samples suggest that caffeine co-ingestion with carbohydrate had little effect on exercise metabolism or performance compared to the ingestion of carbohydrate alone; caffeine did not increase FA oxidation in exercising subjects, even when fat availability was optimized via fat ingestion.	Caffeine enhanced lipolysis in adipose tissues; blood pressure, resting heart rate, serum fatty acid and glycerol concentration were found to increase after caffeine ingestion. The circulating adrenaline concentration also increased at rest following caffeine ingestion. However, muscle biopsy shows no differences in respiratory exchange ratio, leg glucose uptake, net muscle glycogenolysis, leg lactate release muscle lactate, or glucose 6-phosphate concentration during exercises. The treatments did not affect leg fatty acid uptake, glycerol release or muscle acetyl CoA concentration while exercising.	Coingestion of caffeine and EAA appears to maintain muscle activation and central drive with a small improvement in running performance. The improvement is appeared to be associated with the central drive and muscle activation.	Supplements that contain similar ingredients and doses should be safe for taking up to 28 days in healthy, physically active adolescents. Caffeine, creatine, β -alanine, BCAA, etc can be responsible for the improvements in performance. The researcher hypothesize that the caffeine and creatine played a primary role.

Discussion

Carbohydrate and Fat

Figure 2. Flowchart of impact of caffeine on carbohydrate and fat



Protein

Few studies focused on the relationship between caffeine and protein, and the main focus of those studies were exercise or muscle performance instead of nutritional impacts. A study that reported co-ingestion of essential amino acid and caffeine has small improvement in running performance compared to a placebo, only caffeine or only essential amino acid (Kendall, Moon, Fairman 2014). Having both amino acid and caffeine might be beneficial for sport performance. However, here is a clear gap in the literature, and studies investigating the effects of caffeine on protein metabolism are needed.

Conclusion

All but one human-subject experiments reviewed in this study recruited only healthy (screened for medical history and BMI>25), young (age 18-28) males for their experiments. Previous medical conditions, high BMI or age variations can introduce significant variation in overall metabolism. The largest age range in the studies we examined was 8 years (age 20-28). Males were preferred over female subjects in the studies for consistency; even with an all-female population it is difficult to achieve homogeneity, due to individual menstrual positions, oral contraceptive use, possible pregnancy and other conditions that may affect metabolism on top of caffeine metabolism.

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