Caffeine and coffee: their influence on metabolic rate and substrate utilization in normal weight and obese individuals[1]

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ABSTRACT A series of four trials was carried out to investigate the effects of caffeine and coffee on the metabolic rate and substrate utilization in normal weight and obese individuals. In the first trial 8 mg/kg caffeine was compared with a placebo in normal weight subjects. Metabolic rate increased significantly during the 3 hr after caffeine ingestion. While plasma glucose, insulin, and carbohydrate oxidation did not change significantly, plasma free fatty acid levels rose from 432 ± 31 to 848 ± 135 μEq/liter and were accompanied by significant increases in fat oxidation during the last hour of the test. In the second and third trials the effects of coffee providing 4 mg/kg caffeine were studied in control and obese subjects. Metabolic rate increased significantly in both groups; however, significant increases in fat oxidation were only observed in the control group. Plasma free fatty acids did not change in the obese. In the fourth trial, coffee was taken with a 3080 kJ meal. The thermic effect of the meal was significantly greater after coffee than after decaffeinated coffee and again fat oxidation was significantly greater after coffee. In conclusion caffeine/coffee stimulates the metabolic rate in both control and obese individuals; however, this is accompanied by greater oxidation of fat in normal weight subjects. *Am. J. Clin. Nutr.* 33: 989–997, 1980.

Methylxanthines are naturally occurring substances that are widely consumed in beverages such as coffee, tea, cocoa, and some cola drinks and their properties as stimulants, smooth muscle relaxants, diuretics, and analgesics (1) are exploited by the pharmaceutical industry. Of the methylxanthines, it has been suggested (2) that methylation in the 1-position is responsible for the enhanced pharmacological actions of caffeine and theophylline.

It has been known since 1915 that ingestion of caffeine provokes an increase in the metabolic rate (3) and subsequent investigations (4–8) have confirmed this original observation. Metabolic stimulation appears to be dose dependent (7) and in rats it has been found to be partly due to endogenous catecholamine release and partly to the intrinsic calorigenic effect of caffeine (9). Bellet et al. (10) observed an increase in both plasma free fatty acids (FFA) and urinary catecholamine excretion in man after caffeine ingestion and concluded that the FFA response was the result of catecholamine induced lipolysis.

In the light of this, Miller et al. (8) proposed caffeine as a thermogenic agent that in combination with slimming regimens could be of use in promoting the loss of body energy. Underlying this view is the fact that caffeine can be regarded as a noncaloric thermogenic agent that is habitually consumed in many beverages. While a mild fever, anorexia, insomnia, and a loss of weight have been reported in a woman who habitually consumed the equivalent of 1.5 to 1.8 g caffeine per day as coffee (11), it is usually well tolerated in human subjects. Although no fatalities have been reported as a result of its use, a toxic dose is believed to be about 10 g or more (1).

In the first of a series of four trials, we investigated the effect of a large, nonphysiological dose of caffeine (8 mg/kg equivalent to 5 to 6 cups coffee) on metabolic rate, substrate utilization and other clinical parameters in control subjects. In trials 2 and 3 the effects of ingesting normal quantities of caffeine in the form of standard instant coffee

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(equivalent to ingesting 4 mg/kg caffeine or 3 cups coffee) was studied in both control and obese subjects. In the last trial we investigated whether the effect of coffee on the metabolic rate in the fasting state, was still in evidence after a meal and whether such an effect was synergistic with the effect of the meal itself

Materials and methods

In each of the four trials the subjects consumed a caffeine free regimen for at least 24 hr before the test. After an overnight fast resting metabolic rate was measured continuously using indirect calorimetry (12) until stable base-line values were obtained. The test substance or placebo was then ingested by the subject and respiratory exchange measurements were continued for a further 2 ½ to 3 hr.

Trial 1. A single blind study to investigate the effects of pure caffeine (8 mg/kg body weight) on control subjects

Six subjects (Table 1) within 15% of their ideal weight (Metropolitan Life Insurance (13)), consumed a gelatin capsule containing either 8 mg/kg caffeine or 0.5 g glucose which served as a placebo. Blood samples were taken from a superior antecubital vein every 30 min from 0 to 120 min and also at 180 min. These samples were analyzed for glucose (14), FFA using the Dole and Meinertz (15) extraction and determination of Ho (16) as modified by Heindel et al. (17), insulin (18), and caffeine (19). Urine was collected at the end of the test and was analyzed for nitrogen using the Kjeldhal method.

Trial 2. Effect of coffee (caffeine ingested equivalent to 4 mg/kg body weight) and decaffeinated coffee on control subjects

The metabolic rate of seven normal weight subjects (Table 1) was measured until stable base-line measurements had been obtained. The subject then consumed a solution of instant coffee which provided the equivalent of 4 mg/kg caffeine or an equivalent weight of decaffeinated coffee dissolved in 200 ml water. The respiratory exchange data of these subjects were used as control values for the obese group studied in trial 3.

Trial 3. Effect of coffee (caffeine consumption equivalent to 4 mg/kg body weight) and decaffeinated coffee on obese subjects

Six obese subjects (Table 1) were studied by indirect calorimetry. Four of the subjects were volunteers who were studied twice: once after consuming 200 ml of instant coffee (providing 4 mg caffeine per kilogram) and again after ingesting a similar quantity of decaffeinated coffee. Blood samples were taken and analyzed for glucose, insulin, and FFA using the methods cited above. The other two subjects were patients who volunteered only for the test with coffee.

Trial 4. Effect of coffee (caffeine consumption equivalent to 4 mg/kg body weight) and decaffeinated coffee when taken with a meal

A double-blind study was carried out to investigate the effects of caffeinated and decaffeinated coffee on the thermic effect of a meal. Again control subjects were studied using indirect calorimetry (Table 1). After 30 to 40 min of base-line measurements, the subject ate a breakfast, the composition of which is given in Table 2, within a 15-min period. During the breakfast the subject consumed either coffee (providing 4 mg caffeine per kilogram body weight) or an equivalent weight of decaffeinated coffee dissolved in 300 ml of water; respiratory exchange measurements were continued for a further 3 hr.

Substrate utilization was calculated from the nonprotein respiratory quotient according to the tables of Lusk (20) only during the last hour of each test. This convention has been used in trials 1 to 3 since caffeine/coffee ingestion in the fasting state has been found to have a short term effect on the respiratory quotient (7, 21) by its stimulatory action on the respiratory center. In trial 4, substrate utilization was calculated throughout the test to investigate the influence of the meal and coffee on substrate utilization.

Results

Trial 1

The mean resting metabolic rates, which were not significantly different from each other, were 176 ± 7 and 164 ± 5 kJ/(m^2·hr)

TABLE 1
Physical characteristics of the subjects

	Trial 1 (control subjects)	Trial 2 (control subjects)	Trial 3 (obese subjects)	Trial 4 (control subjects)
	8 mg caffeine/kg body weight	Coffee providing 4 mg caffeine/kg body weight	Coffee providing 4 mg caffeine/kg body weight	Coffee providing 4 mg caffeine/kg body weight taken with a breakfast
Age (yr)	30 ± 5[a]	25 ± 4	30 ± 5	23 ± 1
Height (cm)	171 ± 4	177 ± 6	177 ± 6	170 ± 7
Weight (kg)	67 ± 3	66 ± 3	105 ± 23	61 ± 5
Percentage ideal weight	10 ± 6	1 ± 6	60 ± 34	5 ± 8
Body surface (m^2)	1.79 ± 0.07	1.81 ± 0.04	2.20 ± 0.22	1.69 ± 0.09
n	6	7	6	8

[a] Mean ± SD.

during the placebo and caffeine experiments respectively. After caffeine the metabolic rate rose progressively reaching a plateau of 198 kJ/(m^2·hr) or an increase of 34 kJ(m^2·hr), (Fig. 1) at 105 min which continued to the end of the test. The mean value of metabolic rate (192 ± 9 kJ/(m^2·hr)) during the 180 min was significantly higher ($P < 0.02$) than the resting metabolic rate and it represented a 16% stimulation. There was, however, considerable individual variation (range 8 to 30%). During the placebo experiment, the metabolic rate decreased nonsignificantly by 3%.

Figure 2 represents the fasting substrate utilization and the changes observed during the last two 30-min periods. The base-line carbohydrate (CHO) utilization rates were the same in both experiments (117 ± 11 and 112 ± 12 mg/min for caffeine and the placebo, respectively) and although decreases were observed during the last hour of the test they were nonsignificant. Fat oxidation showed an increase in the last hour in both tests, however, this was greater after caffeine (50 ± 5 to 83 ± 9 mg/min $P < 0.02$) than after the placebo (56 ± 2 to 72 ± 4 mg/min $P < 0.02$).

The results of the blood analyses are presented in Table 3. Blood glucose and plasma insulin levels did not change significantly after either caffeine or the placebo. However, the FFA rose in both groups; the increase being greater after caffeine than the placebo. The mean increase in FFA was from 432 ± 31 to 807 ± 82 μEq/liter ($P < 0.01$) following caffeine and from 416 ± 28 to 500 ± 40 μEq/liter ($P < 0.025$) during the placebo experiment. Plasma caffeine concentration in-

TABLE 2
Composition of the meal

Food Item	Weight	Protein	Carbohydrate	Fat	Energy	value
		g			*kcal*	*Kj*
Bread roll	130	15.1	74.4	4.2	377	1578
Butter	20	0.1		16.4	148	619
Jam	50	0.2	35.0		130	544
Cream (single)	20	0.5	0.6	4.2	42	176
Sugar	7		7.4		28	117
Instant coffee	11	1.6		1.2	11	46
Total	238	17.5	121	22.4	736	3080
Percentage composition g		11	75	14		
Percentage energy composition		10	63	27		

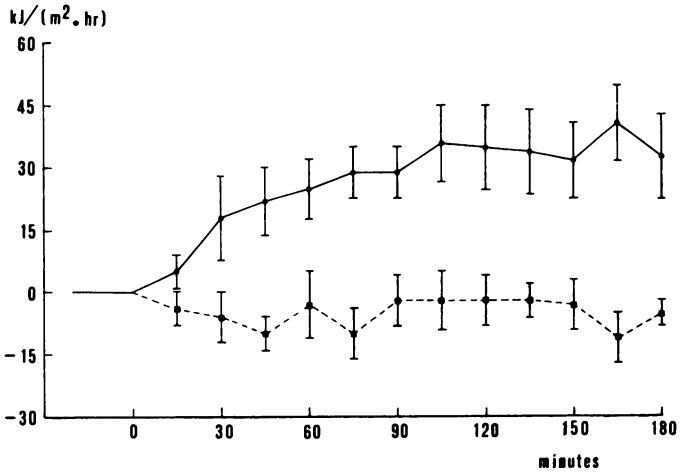

FIG. 1. Change in metabolic rate (kJ/(m^2·hr) after ingestion of either 8 mg/kg caffeine (●—●) or 500 mg glucose placebo (■----■). Mean ± SEM.

creased in all subjects after caffeine ingestion; however, the individual responses were considerably different (Table 4) with the result that no definite peak was observed from the mean values.

Trial 2 and 3

Figure 3 illustrates the time course of the change in metabolic rate after coffee and decaffeinated coffee. In the control group the base-line metabolic rates were not significantly different in the coffee and decaffeinated coffee tests (170 ± 8 kJ/(m^2·hr) and 176 ± 4 kJ/(m^2·hr), respectively). During both tests the metabolic rate rose significantly, however, the stimulation was greater after coffee (mean value for 150 min 190 ± 7 kJ/(m^2·hr) or an increase of 20 ± 5 kJ/(m^2·hr)) than decaffeinated coffee (mean value for 150 min 184 ± 6 kJ/m^2·hr) or an increase of 8 ± 3 kJ/(m^2·hr)). The mean metabolic stimulation during the 150 min test was 12 ± 3% $P < 0.01$ with coffee and 5 ± 2% $P < 0.05$ with decaffeinated coffee.

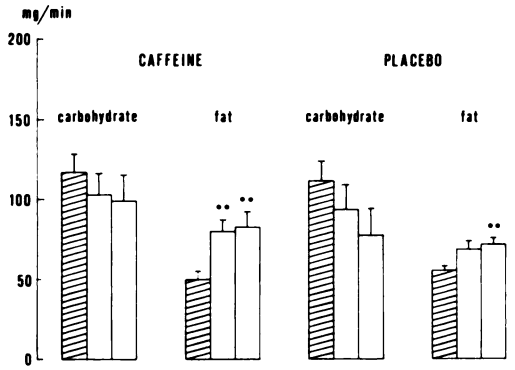

FIG. 2. Substrate utilization (mg/min) during the base-line ▨ and the last two 30 min periods of the test □ after ingestion of either 8 mg/kg caffeine or 500 mg glucose placebo. Mean ± SEM, n = 6, ** $P < 0.02$.

In the obese group the base-line measurements in the coffee and decaffeinated coffee experiments were not significantly different to each other (174 ± 6 kJ(m^2·hr) and 177 ± 9 kJ/(m^2·hr), respectively) nor to the control group. With coffee the metabolic rate increased to a similar extent to that of the control group, resulting in a metabolic stimulation of 10 ± 2% $P < 0.05$. While a slight rise in metabolic rate was observed after decaffeinated coffee, it was not significantly different to the base-line measurement.

Substrate utilization for the control group

TABLE 3
Blood parameters obtained in trial 1

Time	8 mg caffeine/kg body weight			Placebo (500 mg glucose)		
	Glucose	Insulin	FFA	Glucose	Insulin	FFA
min	*mg/100 ml*	*μU/ml*	*μEq/liter*	*mg/100 ml*	*μU/ml*	*μEq/liter*
0	97 ± 4[a]	5.6 ± 1.0	432 ± 31	93 ± 3	5.4 ± 1.1	416 ± 28
30	97 ± 2	7.8 ± 1.1	790 ± 122	94 ± 2	5.4 ± 1.5	431 ± 38
60	97 ± 2	6.4 ± 0.9	724 ± 102	93 ± 1	4.5 ± 1.2	511 ± 45
90	97 ± 1	6.0 ± 1.4	816 ± 93	93 ± 3	4.1 ± 0.9	548 ± 64
120	97 ± 4	5.1 ± 1.1	854 ± 191	92 ± 2	4.3 ± 1.2	534 ± 56
180	96 ± 2	4.7 ± 1.2	848 ± 135	91 ± 2	5.0 ± 1.1	546 ± 62

[a] Mean ± SEM.

TABLE 4
Plasma caffeine concentration mg/liter in trial 1

Subject	Min					
	0	30	60	90	120	180
1	0	2.0	9.2	12.4	18.5	13.9
2	0	20.1	16.8	12.4	11.6	10.7
3	0	11.7	17.1	11.1	10.6	10.0
4	0	10.9	12.6	13.0	18.8	9.8
5	0	7.5	8.7	9.0	7.4	5.8
6	0	25.0	16.4	13.2	12.9	9.7
Mean	0	12.9	13.5	11.9	12.0	10.0
SEM		3.4	1.6	1.6	1.5	1.1

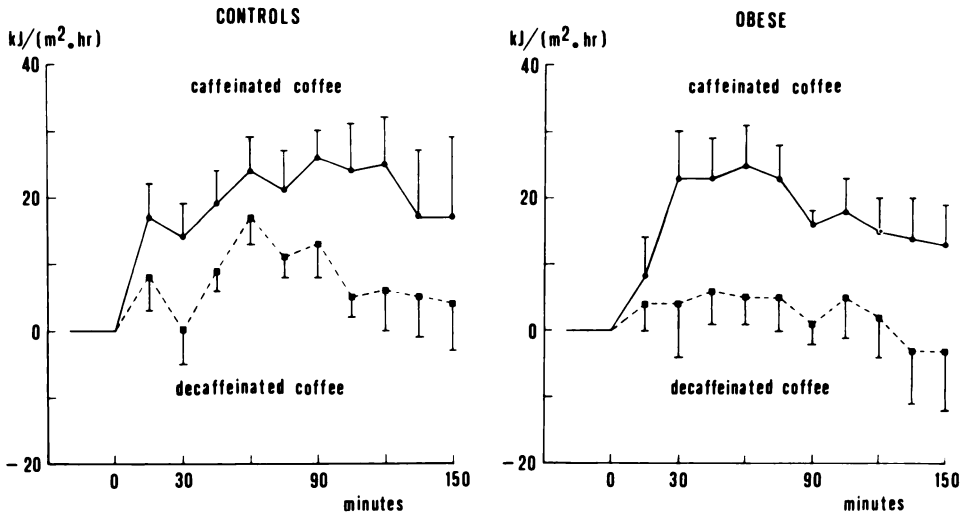

FIG. 3. Evolution of the change in metabolic rate (kJ/(m^2·hr)) in control (n = 7) and obese (n = 6) subjects after coffee (providing 4 mg caffeine per kilogram) (●—●) and decaffeinated (■----■) coffee. Mean ± SEM.

is presented in Figure 4. Baseline values were the same in both the coffee and decaffeinated coffee experiments (122 ± 8 and 122 ± 12 mg/min respectively for CHO utilization and 53 ± 3 and 51 ± 4 mg/min respectively for fat oxidation). During the last hour of the test CHO utilization had decreased to 100 mg/min after coffee and was almost the same as the baseline after decaffeinated coffee. Fat oxidation increased after coffee and during the last hour had reached 75 ± 4 mg/min $P < 0.02$ (period 1) and 79 ± 9 mg/min, not significant (period 2). Decaffeinated coffee had very little effect on this parameter.

Base-line CHO utilization was slightly lower in the obese group 110 ± 17 mg/min (Fig. 5) than in controls but not significantly so. However, basal fat oxidation rates were significantly higher in the obese group than in the controls (mean of base-line values in caffeinated and decaffeinated coffee experiments 78 ± 7 mg/min in the obese and 52 ± 3 mg/min in controls $P < 0.001$). During the last two periods of the test slight increases in CHO utilization (112 ± 18 and 125 ± 17 mg/min) and fat oxidation (100 ± 10 and 94 ± 10 mg/min) were apparent after caffeinated coffee but these were not significant. Similarly the changes observed after decaffeinated coffee were not significant.

The blood parameters for the obese group are presented in Table 5. No change was

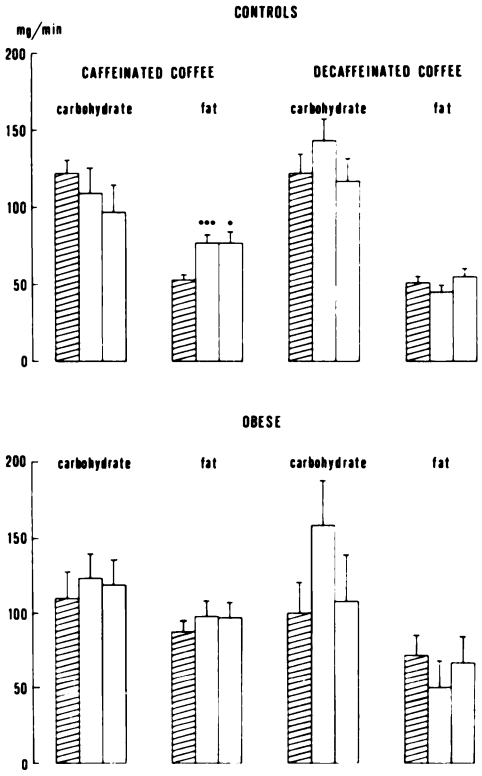

FIG. 4. Substrate utilization (milligrams per minute) during the base-line ▨ and the last two 30-min periods □ of the test after ingestion of either coffee (providing 4 mg caffeine per kilogram) or decaffeinated coffee in control (n = 7) and obese (n = 6) subjects. Mean ± SEM, * $P < 0.05$, *** $P < 0.01$.

TABLE 5
Blood parameters obtained in the obese subjects (trial 3)

Time	Coffee providing 4 mg caffeine per kg body weight			Decaffeinated coffee		
	Glucose	Insulin	FFA	Glucose	Insulin	FFA
min	*mg/100*	*μU/ml*	*μEq/liter*	*mg/100*	*μU/ml*	*μEq/liter*
0	91 ± 6[a]	17.3 ± 2	819 ± 142	89 ± 4	17.5 ± 2	749 ± 105
30	90 ± 6	18.2 ± 4	797 ± 118	87 ± 4	16.5 ± 3	712 ± 91
60	90 ± 5	17.2 ± 3	793 ± 103	87 ± 4	21.8 ± 6	665 ± 93
120	90 ± 5	15.8 ± 3	804 ± 144	88 ± 3	18.4 ± 5	578 ± 83
180	90 ± 6	15.4 ± 2	775 ± 163	86 ± 4	15.3 ± 3	620 ± 119

[a] Mean ± SEM.

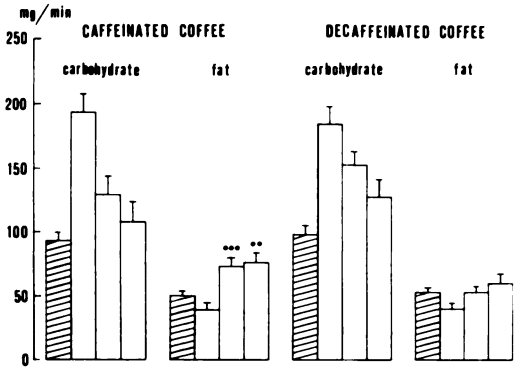

FIG. 5. Substrate utilization (milligrams per minute) during the base-line ▨ and for each hour □ after ingestion of a 3080 kJ (736 kcal) meal with either coffee (providing 4 mg caffeine per kilogram) or decaffeinated coffee. Mean ± SEM, n = 8.

observed in blood glucose, plasma insulin or FFA after either coffee or decaffeinated coffee.

Trial 4

In this trial, the base-line metabolic rates were not significantly different (Table 6) in the test and control experiments. After the breakfast which provided 3080 kJ (736 kcal) in the ratio 63, 27, and 10% for CHO, fat, and protein, the metabolic rate rose to a maximum of 212 ± 5 kJ/(m^2·hr) at 60 min and 231 ± 7 kJ/(m^2·hr) at 75 min after decaffeinated and caffeinated coffee, respectively. The mean increase in metabolic rate during the test was 33% after the breakfast with caffeinated coffee and 23% with decaffeinated coffee. These increases resulted in a thermic effect or "SDA" of the meal of 9 ± 0.8% and 6 ± 0.3%, respectively (Table 6). When the two tests were compared a significant difference was found ($P < 0.005$) using Student's paired *t* test.

CHO utilization increased in the first hour in both groups (Fig. 5) from 93 ± 6 to 193 ± 14 mg/min after caffeinated coffee and from 98 ± 7 to 185 ± 13 mg/min after decaffeinated coffee. It then decreased in both groups: falling more rapidly after the caffeinated coffee.

Fat oxidation initially decreased in the 60 min after the meal in both tests. It then rose above the base-line value of 50 ± 3 mg/min in the test with caffeinated coffee during the second (73 ± 6 mg/min $P < 0.01$) and third (76 ± 7 mg/min $P < 0.02$) hours. After decaffeinated coffee the rise in fat oxidation was slower and was at no time significantly different to the base-line value. When the two tests were compared, a level of significance was only obtained during the second hour after the meal for both CHO utilization ($P < 0.05$) and fat oxidation ($P < 0.005$) (Fig. 5).

Discussion

In all the experiments in which either caffeine (8 mg/kg) or caffeinated coffee (equivalent to 4 mg/kg caffeine) was consumed, a significant increase in metabolic rate was observed during the 3 hr after its ingestion. While 8 mg/kg of the pure alkaloid caused a mean increase of 16%, caffeinated coffee providing half the amount of caffeine stimulated the metabolic rate by 12% in the controls and 10% in the obese group. However, a wide range of individual variation was observed.

The question arises, whether it is valid to calculate substrate utilization from the non-protein respiratory quotient after caffeine ingestion. Haldi et al. (7, 21) concluded from their results, that changes in respiratory quotient after caffeine or coffee ingestion were entirely due to the effect of caffeine on the

TABLE 6
Thermic effect of a 3080 kJ high-carbohydrate meal consumed with either caffeinated or decaffeinated coffee (mean ± SEM)

Subject	Resting metabolic rate/180 min (a)	Metabolic rate/180 min (b)	Increase in energy expenditure (b-a)	Thermic effect (b-a)/3080[a] × 100
		kJ		%
Coffee providing 4 mg caffeine/kg body weight				
CD	816	1023	207	6.7
SB	833	1200	367	11.9
FR	840	1181	341	11.1
YP	741	1011	270	8.8
J-JT	840	1152	312	10.1
AB	865	1088	223	7.3
P-AU	816	980	164	5.3
PC	908	1235	327	10.6
Mean ± SEM	832 ± 17	1108 ± 34	276 ± 26[b]	9.0 ± 0.8[b]
Decaffeinated coffee				
CD	796	1000	204	6.6
SB	824	1066	242	7.9
FR	873	1128	255	8.3
YP	755	954	199	6.4
J-JT	922	1047	124	4.1
AB	882	1036	154	5.0
P-AU	803	946	143	4.7
PC	954	1154	200	6.5
Mean ± SEM	851 ± 24	1041 ± 26	190 ± 16[b]	6.0 ± 0.5[b]

[a] 3080 is the energy content (kJ) of the meal. [b] $P < 0.005$, caffeinated versus decaffeinated values.

respiratory center (lasting 1½ hr) and that it did not reflect changes in substrate metabolism. However, it is difficult to conclude that caffeine has no effect on substrate utilization, particularly since other studies have observed increases in urinary catecholamine excretion (22, 23) after caffeine ingestion, the release of which is responsible for lipolysis and increased plasma FFA levels (10, 24). Avagaro et al. (25) and Daubresse et al. (26) have also reported increased plasma FFA after caffeine ingestion.

Thus caffeine not only causes respiratory modifications, due to its action on the respiratory center, but also increases the amount of available energy, in the form of circulating FFA via lipolysis. In the present study increases in FFA were observed 30 min after ingesting 8 mg caffeine/kg body weight. Since correlations exist between plasma FFA levels and lipid turnover rates (27, 28), fat oxidation must be increased during the initial phase when caffeine causes hyperventilation and alteration of the respiratory quotient. Hence, in the postabsorptive state, substrate utilization calculated from the respiratory exchange data, during the 1½ hr after caffeine ingestion, may not reflect the true substrate utilization. For this reason CHO and fat oxidation rates were only calculated during the last hour of each test in which caffeine or coffee was ingested in the fasting state (trials 1, 2, and 3).

Thus in control subjects consuming caffeine or coffee, not only is there an increase in metabolic rate but also an increased oxidation of lipid. Lipid oxidation has also been shown to increase in subjects performing exercise after caffeine ingestion (29). The results presented in this paper and those of Costill et al. (29) support the suggestion of Avogaro et al. (25) that caffeine/coffee seems to provide a transient supply of additional substrate energy. In the obese group however no significant change was observed in either plasma FFA or fat oxidation. This lack of increase of plasma FFA levels in obese subjects after coffee has been observed before (26) and is in agreement with a decreased sensitivity of obese patients to other lipolytic stimuli (30–34).

In the final trial in which coffee was consumed with a meal, caffeinated coffee had a synergistic effect on the "specific dynamic

action" of the meal when compared with the effect of decaffeinated coffee. As in the trials without a meal, CHO utilization decreased more rapidly after ingestion of coffee with a concomitant rise in fat oxidation.

Thus in conclusion it would seem that the consumption of caffeine or coffee, in reasonable quantities, would be a supplementary advantage to those following a weight reducing regime. However, if our short-term results are extrapolated, the effect of caffeine on normal, slightly overweight individuals would be a loss of weight due to an increased energy expenditure associated with a change in body composition, i.e., a decrease in fat stores, whereas the obese would lose body energy due to an increased metabolic rate with less mobilization and utilization of their fat stores.

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