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Combined effects of red pepper and caffeine consumption on 24 h energy balance in subjects given free access to foods

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The effects of red pepper and caffeine ingestion on energy and macronutrient balances were examined in eight Caucasian male subjects. All subjects participated in two randomly assigned conditions: control and experimental (red pepper and caffeine). After ingesting a standardized breakfast, subjects ate three meals *ad libitum* (lunch, dinner and breakfast) and snacks which were served approximately 2 h after the lunch and dinner over a 24 h period. Two appetizers (2×322 kJ with or without 3 g red pepper) were given before lunch and dinner, and a drink (decaffeinated coffee with or without 200 mg caffeine) was served at all meals and snacks except for the after-dinner snack. It is also important to note that on the experimental day, 8·6 and 7·2 g red pepper were also added to lunch and dinner respectively. Red pepper and caffeine consumption significantly reduced the cumulative *ad libitum* energy intake and increased energy expenditure. The mean difference in energy balance between both conditions was 4000 kJ/d. Moreover, the power spectral analysis of heart rate suggested that this effect of red pepper was associated with an increase in sympathetic:parasympathetic nervous system activity ratio. These results indicate that the consumption of red pepper and caffeine can induce a considerable change in energy balance when individuals are given free access to foods.

Red pepper: Caffeine: Energy balance: Sympathetic nervous system activity

Obesity is an important cause of morbidity and increasingly imposes an important burden on health care systems in both industrialized and developing countries (Taubes, 1998; Wickelgren, 1998). Obesity can be simply described as the outcome of a prolonged positive energy balance, i.e. an excess energy intake over energy expenditure (EE). However, Flatt (1988) has demonstrated in animals, that carbohydrate, protein and fat balances have to be considered separately, since carbohydrate and protein balances are precisely regulated whereas fat balance is not. As the development of obesity is characterized by the inability to adequately oxidize the fat content of the diet (Tremblay, 1995), conditions which stimulate fat oxidation are important for achieving fat balance and therefore body weight maintenance. It is known that the sympathetic nervous system (SNS) plays an important role in stimulating fat oxidation (Acheson *et al.*1988; Tremblay *et al.* 1992). Moreover, an inverse relationship between SNS activity and food intake has been observed in experimental animals (Sakaguchi *et al.* 1988). Therefore, SNS is thought to play an important role in the regulation of energy and fat balance.

Capsaicin, which is the major pungent principle in hot red pepper (Watanabe *et al.* 1987*a*), has been reported to reduce adiposity (Kawada *et al.* 1986; Matsuo *et al.* 1996), which can be partly explained by its stimulating effects on energy and lipid metabolism via catecholamine secretion from the adrenal medulla through sympathetic activation of the central nervous system in rats (Kawada *et al.* 1986; Watanabe *et al.* 1987*a*, 1988). However, only few studies have investigated the effect of red pepper on EE and energy intake in human subjects. We have previously reported that an addition of red pepper to meals increased diet-induced thermogenesis (Yoshioka *et al.* 1995, 1998) and decreased subsequent energy intake (Yoshioka *et al.* 1999). This increase in the facultative phase of diet-induced thermogenesis was probably due to β-adrenergic stimulation (Yoshioka *et al.* 1995).

Coffee is one of the most popular beverages consumed in western industrialized societies. In North America, the

Abbreviations: EE, energy expenditure; HR, heart rate; HRV, heart rate variability; PNS, parasympathetic nervous system; SNS, sympathetic nervous system; VAS, visual analog scale.

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estimates of daily consumption per capita indicate that approximately 90 % of the adult population consume an average of approximately 200 mg caffeine/d (Gilbert *et al.* 1976). It has been reported that caffeine increases lipolysis and EE in human subjects, in part via sympathetic activation of the central nervous system (Acheson *et al.* 1980; Hollands *et al.* 1981; Jung *et al.* 1981; Astrup *et al.* 1990). Moreover, a decrease in energy intake caused by caffeine has been reported in both animals (Racotta *et al.* 1994) and human subjects (Tremblay *et al.* 1988). These results also indicate that a beverage containing caffeine can modify energy and fat balance through SNS stimulation. These observations emphasize the relevance of measuring the impact of naturally-occurring compounds which have the potential to influence SNS activity and thus daily energy balance. We thus investigated whether the combination of red pepper and caffeine could influence 24 h energy intake *ad libitum*, under conditions mimicking real life as closely as possible as our experimental set-up would allow. We also measured the effects of these compounds on daily EE and substrate oxidation.

Subjects and methods

Subjects

Eight healthy Caucasian men volunteered to participate in this study. They were aged 25 (SD 2·9) years old. Their physical characteristics were as follows: height 178 (SD 9·2) cm, body weight 79 (SD 12·3) kg, BMI 24·3 (SD 2·3) kg/m^2. None of the subjects were obese as their BMI ranged from 20·7 to 26·8 kg/m^2. The written consent of each subject was obtained prior to the admission into the study, whose procedures conformed to the Declaration of Helsinki.

Experimental protocol

On the day preceding each experimental condition, subjects were asked to maintain their regular dietary habits and to abstain from alcohol and caffeine intake. Strenuous physical activity was not allowed for 2 d before each experimental condition. All subjects participated in two testing conditions (the control condition as well as the red-pepper and caffeine condition) which were separated from each other by at least 1 week.

Food intake. The experimental protocol was designed to evaluate the effects of dietary red pepper and caffeine ingestion on energy balance. Each subject participated in two randomly assigned conditions which are summarized in Table 1. The subjects consumed a standardized breakfast (% energy: protein 18, fat 39, carbohydrate 43) and were fed by the laboratory supervisor who instructed subjects to eat *ad libitum* until satiety. They had to consume two appetizers providing 322 kJ (% energy: protein 15, fat 29, carbohydrate 56) at 11.45 and 17.45 hours as well as a cup of coffee at 12.30, 15.10, 18.30 and 08.00 hours on the next day. Powdered red pepper (*Saemaul Kongjang*) was used in order to distribute it thoroughly in each meal of the red pepper condition. The capsaicin content of dried hot red pepper used in the present study was 3 mg/g red pepper (Ku & Choi, 1990). Red pepper consumption by the subjects was 3 g for each appetizer (two appetizers for lunch and two at dinner to give a total of 12 g red pepper), 8·57 (SD 3·16) g for the meat-sauce spaghetti (% energy: protein 15, fat 38, carbohydrate 47) at lunch and 7·19 (SD 3·40) g for the enchiladas (% energy: protein 20, fat 37, carbohydrate 43) at dinner. Caffeine (200 mg) was added to a cup of decaffeinated coffee. Non-caffeine beverages were always available. Desserts after lunch and dinner and snacks at 15.10 and 21.00 hours were also offered, and the subjects were again instructed to eat *ad libitum*. All foods were previously weighed and remains were reweighed in order to determine the exact quantity of food spontaneously ingested. A detailed description of the meals is presented in the appendix. The Canadian Nutrient File 1991 software was used to calculate energy, protein, lipid and carbohydrate intakes from these measurements.

Table 1. Summary of the experimental protocol

Time (hours)			
08.00	Standardized breakfast at home		
11.00	Arrival at the lab followed by a resting period		
11.45	Appetizers*	↕EE1	↕HRV
12.00	Lunch *ad libitum* (meat-sauce spaghetti* and water)		
12.30	Dessert *ad libitum* (dessert and coffee†)		
14.30	Entry into the whole-body calorimeter	↕EE2	
15.00	Coffee†		
15.10	Snack 1 *ad libitum* (snacks and drinks)		
17.45	Appetizers*		
18.00	Dinner *ad libitum* (enchilladas* and water)		
18.30	Dessert *ad libitum* (dessert and coffee†)		EE3
21.00	Snack 2 *ad libitum* (snacks and drinks)		
08.00	Coffee†		
08.10	Breakfast *ad libitum* (cereals, bread and drinks)		
10.30	End of the whole-body calorimeter stay		
11.00	Finish	↕EE4	

EE, energy expenditure measurement; HRV, heart rate variability measurement; EE3 from 15.00 to 10.30 hours
* With or without red pepper.
† With or without 200 mg caffeine.

Visual analog scale. Prospective food consumption, desire to eat, hunger, fullness and satiety were rated immediately before and after each appetizer, meal, dessert, snack and drink by using a 150 mm visual analog scale (VAS) as previously described by Hill & Blundell (1986). All results obtained with the VAS were converted into scores ranging from 0 to 100 for statistical analysis. Since elemental conditions and the physical state of foods affect spontaneous energy intake in human subjects (Kissileff, 1985; Himaya & Louis-Sylvestre, 1998), precautions were taken to maximize the reliability of experimental conditions. Also of importance is the fact that VAS measurements were always performed in the same environment, i.e. at the same table with the same lighting in the same room which was kept free of odours and sounds as well as other factors which might contaminate this measurement (visual stimuli, individuals in the room, etc.). Under these conditions, VAS measurement in our laboratory was shown to be highly reliable both before and in response to a meal (Arvaniti *et al.* 2000).

Calorimetry. As shown in Table 1, subjects took a standardized breakfast at home at 08.00 hours and came to the laboratory at 11.00 hours. After resting on a reclined chair for 30 min, EE measurements (EE1) were performed with an open-circuit gas analysis system (Hartmann & Braun Uras 10E, Frankfurt, Germany; KL Engineering Volume Ventilation measuring system S-430 with a turbine flow transducer K520-C521, Ventura, CA, USA) from 11.30 to 11.45 hours. From 12.45 to 14.30 and from 10.30 to 11.00 hours on the next morning, EE measurements (EE2 and EE4 respectively) were also performed. At 14.30 hours, subjects entered a whole-body indirect calorimetry system, and EE (EE3) was measured for 20 h as previously described (White *et al.* 1996). Since total indirect calorimetric measurement time was 22.5 h (EE2 + EE3 + EE4), each value was multiplied by 1·067 to calculate the energy balance for 24 h. Fat, carbohydrate and protein oxidation were derived from O_2 consumption, CO_2 production and urinary N excretion according to the calculations described by Frayn (1983). Accordingly, 24 h urinary N excretion, which was measured for each subject during both experimental and control sessions, was used to derive protein oxidation. EE was not measured continuously throughout the 24 h period mainly because we wanted to measure acute changes in EE in response to the experimental meal and drinks and because measurements of heart rate variability (HRV), as performed in our laboratory are difficult to carry out once subjects have entered the chamber. Subjects were allowed to sleep at anytime in the chamber, and their sleeping time under both testing conditions was similar. There was no predetermined activity schedule in the chamber, however, subjects had to remain sedentary.

Spectral analysis of heart rate. Heart rate (HR) power spectral analysis was performed through the experiment using an electrocardiograph (Q4000 Quinton, Seattle, WA, USA). The electrocardiographic signals were digitized, stored on hard disk and sampled at a rate of 500 Hz, with twelve precision bits. The QRS complex (lead II) was automatically recognized by a classic derivative–threshold algorithm. Power spectra were calculated from a consecutive series of 512 R–R intervals. As previously reported (Pomeranz *et al.* 1985; Arai *et al.* 1989), the ratio low-frequency (0·04–0·15 Hz Eq):high-frequency (0·15–0·50 Hz Eq) components of spectra were used as an indicator of the SNS:parasympathetic nervous system (PNS) activity ratio. Hence, the low-frequency components of the power spectra are associated to SNS activity while high-frequency components are associated to PNS activity. The main limitation of this measurement is the fact that from a ratio, we cannot conclude with certainty whether a change depends on an increase of one component or the decrease of the other, or *vice versa*. Nonetheless, it has been reported that the intra-individual CV of HR spectral analysis measured four times over 27 d was 16·7 % (Hirsch *et al.* 1991). It has also been found that this method provides realistic information about changes in SNS activity in the context of experimental overfeeding and underfeeding (Aronne *et al.* 1995).

Statistics

A two-way ANOVA with repeated measurements was used to determine the effects of diet (red pepper and caffeine ingestion), time as well as their interaction on energy and macronutrient intakes, VAS variables, HR, RER, EE, substrate oxidation and HRV. When the ANOVA revealed a significant effect, a contrast analysis was applied to identify which conditions were different from each other. According to our *pre-hoc* hypothesis, we also used a paired *t* test to determine the effect of red pepper appetizer at lunch on HR, HRV and VAS, or caffeine at breakfast on HR, and of red pepper and caffeine on cumulative 24 h EE, substrate oxidation and energy and macronutrient balances. Pearson correlation coefficient was calculated to quantify the associations between changes in energy intake and those derived from the HRV. Differences were considered to be statistically significant at $P < 0{\cdot}05$.

Results

Energy and macronutrient intakes

Effects of red-pepper and caffeine ingestion on energy and macronutrient intakes are presented in Table 2. In both conditions, subjects ingested comparable total weights of food and liquid. However, the addition of red pepper and caffeine significantly decreased the cumulative energy and macronutrient (protein, lipid and carbohydrate) intakes. Significant differences in energy and carbohydrate intakes were observed especially at dinner and breakfast, whereas the difference in protein and lipid intakes were observed only at dinner. During the snacks, energy and macronutrient intakes were similar in both conditions (results not shown). It is also important to note that the difference between the total weight of each variable in Table 3 and the sum of lunch, dinner and breakfast is equivalent to the weight of foods and liquids eaten during snacks.

Hunger ratings

Prospective food consumption, desire to eat, hunger, fullness and satiety were measured immediately before

Table 2. Effect of red pepper and caffeine on daily energy and macronutrient intake†
(Mean values and standard deviations for eight subjects)

	Total		Lunch‡		Dinner‡		Breakfast	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Energy intake (kJ)								
Control	21 350	7140	5710	2500	6140	1470	5350	2510
Red pepper and caffeine	17 660*	5780	5390	2150	4510*	1640	4260*	1890
Food intake (g)§								
Control	5165	1330	1629	530	1376	349	1178	404
Red pepper and caffeine	5024	1100	1626	300	1410	325	1093	363
Liquid intake (g)								
Control	2991	819	809	309	705	289	773	231
Red pepper and caffeine	3140	974	871	143	883	305	720	338
Protein intake (g)								
Control	192·1	14·5	59·7	15·2	75·7	12·4	36·0	18·6
Red pepper and caffeine	160·4*	11·7	55·1	12·4	59·4*	14·1	29·5	16·8
Lipid intake (g)								
Control	191·2	22·6	56·2	29·1	60·5	19·1	36·4	17·1
Red pepper and caffeine	151·9*	17·3	53·4	25·0	41·0*	19·1	27·8	11·5
Carbohydrate intake (g)								
Control	649·0	78·8	153·7	70·7	153·7	36·4	200·6	99·5
Red pepper and caffeine	548·6*	65·5	145·7	62·4	116·5*	45·1	161·4	74·7*

Mean values were significantly different from those of the control group (two-way ANOVA): $*P < 0{\cdot}05$.
† For details of diets and procedures see appendix and p. 204.
‡ Including the appetizer and dessert.
§ Total weight of food and liquid ingested.

and after each appetizer, meal, dessert, snack and drink. No significant difference was found between the control and red pepper and caffeine condition by the two-way ANOVA. However, the hunger level immediately after the red pepper appetizer at lunch was significantly lower than in the control condition 32·9 (SD 28·0) and (51·2 (SD 31·9) mm respectively) and the desire to eat also tended to be lower in the experimental condition (red pepper + caffeine) compared with the control condition (53·7 (SD 26·3) and 64·4 (SD 27·6) mm respectively; $P < 0{\cdot}08$).

Energy expenditure and RER

The two-way ANOVA revealed that 24 h EE was significantly affected by time and tended to be modified by diet ($P = 0{\cdot}06$), while variations in 24 h RER under both conditions were significantly affected by the time and diet × time interaction (results not shown). The contrast analysis showed that RER in the red pepper and caffeine condition after lunch (at 13.00 and 14.00 hours) was significantly higher than that in the control condition whereas RER in the red pepper and caffeine condition during sleep (at 24.00, 01.00, 03.00, 04.00, 05.00, 06.00 and 08.00 hours) was significantly lower than that in the control condition. As for RER, carbohydrate oxidation in red pepper and caffeine condition after lunch (at 13.00 and 14.00 hours) was significantly higher whereas significantly lower values were found during sleep (at 24.00, 01.00, 04.00, 05.00, 06.00 and 07.00 hours). However, lipid oxidation in red pepper and caffeine condition after lunch (at 13.00 and 14.00 hours) was significantly lower whereas significantly higher values were found during sleep (at 24.00, 01.00, 03.00 and 04.00 hours). The cumulative EE and substrate oxidation are presented in Table 4. Total EE for 24 h under the red pepper and caffeine condition was significantly higher than under the control condition. However, there was no significant difference between the two conditions in the mean RER and total substrate (protein, lipid and carbohydrate) oxidation.

Energy and macronutrient balances

Effects of red pepper and caffeine ingestion on energy and macronutrient balances are presented in Table 4. Red

Table 3. Effect of red pepper and caffeine on daily energy expenditure, RER and substrate oxidation†
(Mean values and standard deviations for eight subjects)

	Control		Red pepper and caffeine	
	Mean	SD	Mean	SD
Energy expenditure (kJ)	9870	1550	10190*	1490
RER	0·911	0·018	0·908	0·033
Protein oxidation (g)	93·8	26·6	86·2	36·4
Lipid oxidation (g)	45·6	36·4	53·2	41·4
Carbohydrate oxidation (g)	391·0	56·4	401·2	55·9

Mean value was significantly different from that of the control group (paired *t* test): $*P < 0{\cdot}05$.
† For details of diets and procedures see appendix and p. 204.

Table 4. Effect of red pepper and caffeine on energy and macronutrient balances†
(Mean values and standard deviations for eight subjects)

	Control		Red pepper and caffeine	
	Mean	SD	Mean	SD
Energy balance (kJ/d)	11 480	6140	7480*	5210
Protein balance (kJ/d)	1650	870	1250	1000
Lipid balance (kJ/d)	5500	1690	3730*	2080
Carbohydrate balance (kJ/d)	4320	3970	2480*	3000

Mean values were significantly different from those of the control group (paired *t* test): *$P < 0{\cdot}05$.
† For details of diets and procedures see appendix and p. 204.

pepper and caffeine consumption did not affect protein balance. However, energy, lipid and carbohydrate balances under the red pepper and caffeine condition were significantly lower than in the control condition. Differences in energy balance between both conditions are presented in Fig. 1. As shown in this figure, a positive energy balance was observed under both conditions but to a significantly lesser extent under the red − pepper + caffeine condition.

Heart rate and heart rate variability

HR immediately after the red pepper appetizer ingestion at lunch and caffeine ingestion at breakfast was significantly higher than in the control condition (after the red pepper appetizer 79·9 (SD 6·7), after the control appetizer 70·4 (SD 17·9), after the caffeinated coffee 82·9 (SD 11·8), after the decaffeinated coffee 72·2 (SD 11·0). Red pepper appetizer (Fig. 2(A)), red pepper spaghetti and snack with caffeinated coffee significantly increased Δ HRV ratio (changes in low:high frequency ratio) compared with the control appetizer, control spaghetti and snack with decaffeinated coffee (3·85 (SD 3·13), 4·10 (SD 2·90) and 4·04 (SD 3·37) *v.* 1·94 (SD 2·46), 2·61 (SD 3·31) and 2·60 (SD 3·88) respectively). Fig. 2(B) presents the correlation between Δ HRV and energy intake at lunch (meat-sauce spaghetti). Δ SNS : PNS activity ratio as determined by HRV

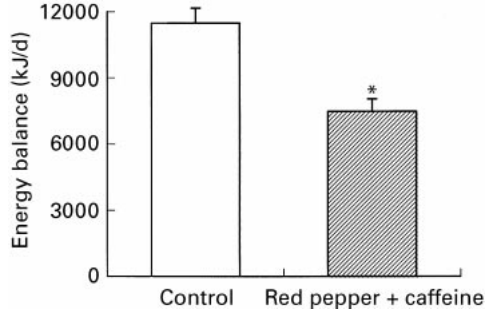

Fig. 1. Effect of red pepper and caffeine on 24 h energy balance. Values are means for eight subjects with standard errors of the means shown by vertical bars. For details of diets and procedures see appendix and p. 204. Mean value was significantly different from that of the control group: *$P < 0{\cdot}05$ (Δ 4·011 kJ/d).

immediately after the appetizer was negatively correlated with subsequent food intake.

Discussion

The most important finding of this present study is that when caffeine and red pepper are combined together a substantial difference in energy balance (about 4000 kJ/d) is observed when this condition is compared with a day during which these compounds were not given. This difference is mainly explained by a difference in energy intake between both conditions. This fits well with previous results from our group that have demonstrated that caffeine has the potential to reduce energy intake, particularly in men (Tremblay *et al.* 1988). We have also recently published results which demonstrate that adding red pepper to the diet acutely reduces energy intake (Yoshioka *et al.* 1999). In the present study, as in a previous study documenting the effect of red pepper on appetite and food intake (Yoshioka *et al.* 1999), we demonstrated that the reduction in energy intake might be mediated by an increased sympathetic tone induced by these compounds. Our observations are supported by other data, since increased SNS activity has been shown to lead to a decrease in energy intake (Bray, 1993; Raben *et al.* 1996). It is also possible that adding red pepper and caffeine decreased the palatability of foods which were served and that the decrease in energy intake under that condition might be partly due to this decrease in palatability. However, since no objective measurements of palatability were performed in the present study, this issue will need to be clarified. Another explanation for our results might be related to the potential decrease in energy density since the decrease in food intake under the red pepper and caffeine condition tended to be compensated for by an increase in fluid intake because the total weight of foods during both conditions was quite comparable. Although we cannot discard these potential explanations for our results, this study, by design, could not answer these questions since it was rather aimed at assessing whether the combination of these sympathomimetic compounds could influence energy balance under conditions mimicking real life as closely as possible. Hence, further results will be needed in order to assess whether the decrease of energy intake induced by these compounds is a result of increased sympathetic tone, decreased palatability, decreased energy density or a combination of these factors.

The observation that no consistent differences in VAS-related variables were observed between the two conditions might be due to the experimental design. Indeed, it has been shown that hunger and satiety ratings are less relevant when they are continuously corrected by *ad libitum* energy intake (Westerterp-Plantenga *et al.* 1999). In this sense, it is possible that no consistent differences in VAS-related variables were observed because of the experimental design.

It might be of some concern that power spectral analysis of HR was used to determine the influence of these compounds on SNS activity, since it could be argued that this measurement is rather a reflection of the ratio between

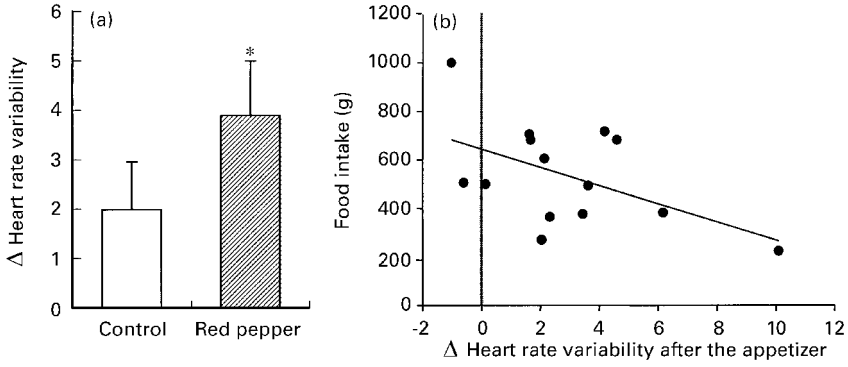

Fig. 2. Effect of red pepper appetizer on Δ heart rate variability (Δ SNS : PNS activity ratio). Values are means for eight subjects with standard errors of the means shown by vertical bars. For details of diets and procedures see appendix and p. 204. (a), Values were calculated by subtracting values measured after the ingestion of the appetizer from those measured before. Mean value was significantly different from that of the control group: $^{*}P = 0{\cdot}02$. (b), Correlation between Δ heart rate variability and following meal (spaghetti) at lunch: $y = -38{\cdot}1x + 646{\cdot}4$, $r = 0{\cdot}522$, $P = 0{\cdot}05$.

SNS : PNS activity or more precisely the ratio between low-frequency : high-frequency peaks as derived from the power spectrum of beat-to-beat variability. However, it should be noted that this procedure has been reported to have an intra-individual CV for HR spectral analysis measured four times over 27 d of 16·7 % (Hirsch *et al.* 1991). It has also been found that this method provides realistic information about changes in SNS activity in the context of experimental overfeeding and underfeeding (Aronne *et al.* 1995). Thus, in a study designed to mimic real life conditions, deriving an index of SNS : PNS balance from HRV provides a non-invasive tool to measure the influence of naturally occurring sympathomimetic compounds on SNS activity.

Beyond the impact of combining these two compounds on energy intake, it would have also been expected that an increase in EE and possibly fat oxidation would have been observed. Indeed, it has been previously demonstrated that adding spices such as chilli sauce and mustard sauce to a meal increases dietary induced thermogenesis (Henry & Emery, 1985). This fits well with recent results from our laboratory that demonstrated that adding red pepper to breakfast increases diet-induced thermogenesis and fat oxidation (Yoshioka *et al.* 1998). Moreover, there are numerous studies which support the fact that caffeine ingestion has the potential to increase metabolic rate (Acheson *et al.* 1980; Hollands *et al.* 1981; Dulloo *et al.* 1989; Astrup *et al.* 1990; Bracco *et al.* 1995). However, we cannot derive strong conclusions regarding EE from the present results for one main reason. Indeed, in order to have a valid comparison of dietary induced thermogenesis between two conditions, subjects would have had to be in energy balance otherwise RER and hence substrate oxidation mainly represent the effect of overfeeding. This is especially relevant in the present case where positive energy balance was observed under both conditions but to a much greater extent during the control day. Nevertheless, it might still be important to emphasize that total EE was greater under the experimental session although energy intake was about 4000 kJ lower during that day. Studies specifically designed to address the question as to whether the combination of caffeine and red pepper increases daily EE will be needed to clarify this issue.

This present study was designed to investigate the impact of combining widely consumed sympathomimetic compounds on daily energy balance under conditions mimicking real life. For this reason, it is hard to determine whether the impact of these two compounds on energy balance is additive considering that this study was not designed to answer this question. However, since both these compounds influence SNS activity by either stimulating the sympathoadrenal system (Bellet *et al.* 1969; Berkowitz & Spector, 1971; Watanabe *et al.* 1987*a*,*b*; Kawada *et al.* 1988) or by antagonizing adenosine action and/or inhibiting phosphodiesterase (Jung *et al.* 1981) some degree of interaction might have been at play. Results demonstrating an additive effect on EE between such compounds are available. Indeed, it was demonstrated that when nicotine (Perkins *et al.* 1994) or adrenaline (Astrup *et al.* 1991) are combined with caffeine, their effects on EE are additive. From these observations, it could be speculated that such an effect also took place in the present study since the effects of capsaicin on SNS activity are similar to what is observed in response to either adrenaline and/or nicotine administration. However, since this present study was rather designed to address a clinical question, we cannot conclude on an interaction effect between these two compounds based on our results.

It is intriguing to observe the spontaneous overfeeding which occurred in the respiratory chamber under both conditions, since a positive energy balance (7 and 11 MJ for the caffeine + capsaicin and control days respectively) was observed under both conditions. These results suggest that, when given free access to food, individuals tend to spontaneously overconsume energy in the confined environment of the chamber. However, this phenomenon seems to be considerably attenuated when subjects concomitantly consume caffeine and red pepper. Since conditions of high

food availability do occur quite often in our societies, it would be useful to employ strategies that permit reduction of energy intake under such conditions. Hence, it could be speculated that employing both of these compounds under real-life conditions might also result in a substantial difference in daily energy balance.

Another question which might be important is whether subjects would acclimate to red pepper and caffeine ingestion over time. We can only partly answer this question by looking at the two first papers from our group which addressed this question. Indeed, in Japanese women who were accustomed to eating spicy foods, we still observed an increase in fat oxidation (Yoshioka *et al.* 1998) and a decrease in appetite as well as in energy intake (Yoshioka *et al.* 1999) following red pepper ingestion. Moreover, it has also been demonstrated that in mild to moderate (250–500 mg/d) methylxanthines consumers, relatively low doses of caffeine (100 mg) managed to increase resting metabolic rate by 3–4 % over 2.5 h (Dulloo *et al.* 1989). These results thus tend to show that regular consumption of these compounds does not necessarily abolish their impact on energy balance.

In order to exert an optimal control on energy balance, a number of dietetic manipulations have to be performed, such as, for example, lowering fat, maximizing low-glycaemic-index carbohydrates, increasing unsaturated fatty acid and fibre intake. Some of these manipulations have more impact than others, however, it is the combination of all these manipulations which should favour optimal results. Consequently, we do not pretend that increasing caffeine and red pepper consumption by itself constitutes a solution to reverse obesity prevalence. However, it should be noted that the present study was conducted with dosages of these compounds that are within normal consumption and that were agreeable to subjects. In this context, we think that such manipulations might be performed not as a front running approach but rather as a complementary strategy to help reduce spontaneous food intake under free-living conditions.

In summary, these results demonstrate that the combination of caffeine and red pepper has the potential to considerably reduce energy intake when this condition is compared with a control day without these compounds. Our results also suggest that these effects are mediated by an increase in the SNS : PNS activity ratio as measured by power spectral analysis of HR.

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Appendix

Table 1. Composition of the red pepper and control appetizers

Food	Weight (g)	Protein (g)	Fat (g)	Carbohydrate (g)
Red pepper appetizer*				
White bread	18	1·51	0·68	8·64
Tomatoes	10	0·07	0·01	0·33
Pimentos	5	0·05	0·01	0·21
Cream cheese (regular)	8	0·85	1·33	0·32
Red pepper	3	0·33	0·46	1·39
Total: g	44·0	2·8	2·5	10·9
kJ	323·0	46·9	93·7	182·4
% energy	100·0	14·6	29·0	56·4
Control appetizer*				
White bread	20·5	1·71	0·78	9·84
Tomatoes	10	0·07	0·01	0·33
Pimentos	5	0·05	0·01	0·21
Cream cheese (regular)	10	1·07	1·67	0·40
Total; g	45·5	2·9	2·5	10·8
kJ	322·2	48·5	92·9	180·3
% energy	100·0	15·1	28·9	56·0

* Two appetizers were served before lunch and two before dinner.

Table 2. Composition of the red pepper and control lunch*

Food	Weight (g)	Protein (g)	Fat (g)	Carbohydrate (g)
Red pepper–meat-sauce spaghetti				
Meat sauce	248	17·33	10·40	13·61
Garlic	15	0·00	1·50	3·00
Cheddar cheese	105	26·15	34·76	1·37
Beef	150	0·00	35·85	33·90
Spaghettini	285	33·52	6·70	197·82
Red pepper	15	1·65	2·30	6·95
Total: g	818	78·6	91·50	256·60
kJ	9091	1321·1	3458·60	4311·60
% energy	100	14·5	38·0	47·40
Control–meat-sauce spaghetti				
Meat sauce	255	17·85	10·71	14·03
Garlic	15	0·00	1·50	3·00
Cheddar cheese	105	26·13	34·76	1·37
Beef	150	0·00	35·85	33·90
Spaghettini	300	35·28	7·05	208·23
Total: g	825	79·3	89·90	260·50
kJ	9105	1331·8	3396·90	4376·70
% energy	100	14·6	37·30	48·10

* Portion served.

Table 3. Composition of the red pepper and control dinner*

Food	Weight (g)	Protein (g)	Fat (g)	Carbohydrate (g)
Red pepper–meat-sauce enchilladas				
Garlic	8	0·00	0·75	1·50
Onions	75	0·90	0·15	6·45
Pimentos	75	0·68	0·15	4·80
Tomatoes	90	0·81	0·18	5·76
Mayonnaise	15	0·20	12·00	0·10
Cream cheese	60	5·58	3·60	2·22
Cheddar cheese	63	15·69	20·85	0·82
Chicken	98	30·23	3·51	0·00
Tortillas	255	22·49	22·49	149·99
Red pepper	15	1·65	2·30	6·95
Total: g	753	78·20	66·0	178·60
kJ	6809	1314·10	2494·20	3000·30
% energy	100	19·30	36·60	44·10
Control–meat-sauce enchilladas				
Garlic	8	0·00	0·75	1·50
Onions	75	0·90	0·15	6·45
Pimentos	75	0·68	0·15	4·80
Tomatoes	90	0·81	0·18	5·76
Mayonnaise	15	0·20	12·00	0·10
Cream cheese	45	4·19	2·70	1·67
Cheddar cheese	75	18·68	24·83	0·98
Chicken	113	34·88	4·05	0·00
Tortillas	255	22·49	22·49	149·99
Total: g	750	82·8	67·30	171·20
kJ	6812	1391·2	2543·80	2876·90
% energy	100	20·4	37·30	42·20

* Portion served.

Table 4. List of foods served (in large amounts) at breakfast

Croissants	Butter
Bagels	Peanut butter
Rice Crisps Bars ®	Strawberry jam
Nutri Grain Bars ®	Cream cheese
Oranges	Yoghurt
Apples	Milk (1, 2 and 3·3 % fat)
Bananas	Orange juice

Table 5. List of foods served during the snacks

Oranges	Milk chocolate
Apples	Yoghurt
Bananas	Cola
Potato chips	7-up®
Popcorn	Milk (1, 2 and 3·3 % fat)
Bread sticks	Orange juice
Chocolate bars	