Physical state of meal affects gastric emptying, cholecystokinin release and satiety

A. Santangelo[1]*, M. Peracchi[2], D. Conte[2], M. Fraquelli[2] and M. Porrini[1]

[1]*Department of Food Science and Technology, Nutrition Section, University of Milan, via Celoria 2, 20133 Milan, Italy*
[2]*Department of Gastroenterology, Institute of Medical Science, University of Milan, IRCCS Hospital, via F. Sforza 35, 20122 Milan, Italy*

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To verify the influence of food consistency on satiety mechanisms we evaluated the effects of the same meal in solid–liquid (SM) and homogenized (HM) form on satiety sensation, gastric emptying rate and plasma cholecystokinin (CCK) concentration. Eight healthy men, aged 21-28 (mean 24·5) years were given two meals (cooked vegetables 250 g, cheese 35 g, croutons 50 g and olive oil 25 g, total energy 2573 kJ, with water 300 ml) differing only in physical state: SM and HM. The subjects consumed the meals in randomized order on non-consecutive days. The sensations of fullness, satiety and desire to eat were evaluated by means of a questionnaire, gastric emptying was assessed by ultrasonographic measurement of antral area, and plasma CCK concentration was measured by radioimmunoassay. The vegetable-rich meal was significantly more satiating ($P < 0{\cdot}05$) when in the HM form than when eaten in a SM state. Furthermore, the overall gastric emptying time was significantly slowed (255 (SEM 11) min after HM *v.* 214 (SEM 12) min after SM; $P < 0{\cdot}05$) and CCK peak occurred later (94 (SEM 12) min after HM *v.* 62 (SEM 11) min after SM; NS) when the food was consumed in the HM form. Independently of the type of meal, antral area was significantly related to fullness sensations (r^2 0·46, $P = 0{\cdot}004$). These results demonstrate that meal consistency is an important physical food characteristic which influences both gastric emptying rate and satiety sensation. Moreover, the relationship observed between antral area and fullness sensation confirms that antral distension plays a part in the regulation of eating behaviour.

Food consistency: Gastric emptying: Cholecystokinin: Satiety

Food, according to Kissileff *et al.* (1984), is characterized by different sensorial, chemical and physical properties that contribute to the regulation of eating behaviour. Among the physical properties, the consistency of food seems to affect its satiating power. Some authors (Bolton *et al.* 1981; Tournier & Louis-Sylvestre, 1991; Hulshof *et al.* 1993) observed that solid foods suppressed appetite for a longer period of time than liquid foods, whereas other authors (Kissileff *et al.* 1984; Kissileff, 1985; Rolls *et al.* 1990) reported that the latter were more satiating than solid foods. Information on the possible roles of gastric emptying rate and gastrointestinal hormone secretion in mediating the effect of food consistency on satiety signals is still limited. It is well known that liquids empty from the stomach more rapidly than solids (Read & Houghton, 1989). However, meals contain discrete solid and liquid components that are mixed in the mouth and stomach producing, more or less, a viscous solution in which solid particles are suspended. An increase in the viscosity of the gastric contents reduces sedimentation of solids in liquids and thus impairs the ability of the antrum to preferentially empty liquids faster than solids (Vincent *et al.* 1995). Independently of the type of food consumed, a good correlation has been observed between the gastric emptying rate and satiety sensation (Bergmann *et al.* 1992). Neural mechanisms as well as the presence of digestion products in the duodenum, particularly fats and amino acids, stimulate the secretion of various gastrointestinal hormones such as cholecystokinin (CCK) which seems to play a role in the regulation of food intake (Kissileff *et al.* 1981; Pi-Sunyer *et al.* 1982; Smith & Gibbs, 1987; Moran & McHugh, 1988; Holt *et al.* 1992; Smith, 1992). To verify the influence of food consistency on satiety mechanisms, in the present study we evaluated the effects of the same meal in solid–liquid (SM) and in homogenized (HM) form on satiety sensation, gastric emptying rate and plasma CCK concentration. The relationships between these variables were also studied.

Abbreviations: AUC, area under curve; CCK, cholecystokinin; HM, homogenized form of meal; SM, solid–liquid form of meal.

***Corresponding author:** Alessandra Santangelo, fax +39 2 70 63 86 25, email Nutr_lab@imiucca.csi.unimi.it

Subjects and methods

Subjects

Eight healthy males of mean age 24·5 (SD 2·1) years and mean BMI 22·8 (SD 1·1) kg/m^2 entered the study. All subjects were non-smokers and none of them was taking medication, had gastrointestinal symptoms, or a history of gastrointestinal disease. Written informed consent was obtained from all participants and the protocol was approved by the local ethics committee.

Meal

The meal used consisted of 250 g cooked vegetables, 35 g cheese, 50 g croutons and 25 g olive oil; its nutrient composition, determined by chemical analysis (Association of Official Analytical Chemists, 1984), is shown in Table 1. This meal was either given in SM form with 300 ml water to drink during its consumption, or in HM form (Minipimer compact, MR 300; Braun) with the addition of the same amount of water.

The macroscopic appearance of the two meals was assessed after a preliminary destructive treatment for 1 min with a laboratory blender (Stomacher 400; PBI International) and acidification with 0·5 M-HCl to pH 4. After being left at room temperature for 30 min, the SM was clearly separated into solid and liquid components, whereas the HM formed an apparently uniform viscous phase. Samples of the two meals were also put on a 4 mm^2 aperture sieve for about 15 min. Only 15 % of the HM was retained on the sieve as compared with 75 % of the SM. The material released from the sieve was mainly water when the SM was analysed.

Experimental procedures

Subjects were studied twice on non-consecutive days during a period of about 2 weeks. They were instructed not to eat or drink from midnight before the test, which started between 08.30 and 09.30 hours with the consumption of the meals. The two meals were given in randomized order and subjects were asked to consume them in 15 min. Ultrasound examination of the gastric antral region was performed before the meal (time 0) and at 30 min intervals after the meal for 5 h. Blood samples were obtained from the forearm through a venous cannula (kept patent by slow saline (9 g NaCl/l) infusion) before the meal and 15, 30, 45, 60, 90, 120, 150 and 180 min afterwards. Samples were collected in ice-chilled polypropylene tubes containing EDTA (1 mg/ml) and aprotinin (500 kIU/ml), and plasma was immediately separated by centrifugation at 4° and stored in portions at −80° until assayed. The palatability of the meal, the estimated energy content and the perceived fat content were recorded on 100 mm fixed-point scales. Subjects were also asked to fill in a satiety-rating questionnaire each time blood was sampled. Three questions ('How satiated do you feel?', 'How full do you feel?' and 'How great is your desire to eat?') already used in previous investigations (Porrini *et al.* 1995*a*,*b*, 1997) provided useful information about the satiety condition. Subjects were instructed to rate each sensation by drawing a line, parallel to the baseline, across an isosceles triangle (height 150 mm, base 30 mm and area of 2250 mm^2) oriented horizontally on the paper with the base on the right-hand side. The triangle was unbroken and was marked with a word anchor at the apex to indicate the minimum (none) of the experienced sensation and at the baseline for the maximum (extreme). The ratings were expressed in mm^2 of area from the apex to the line drawn by the subjects.

Table 1. Nutrient composition of the meal per test portion (660 g)

Energy (kJ)	2573
Protein: g	20·5
% energy	13·3
Fat: g	40·9
% energy	60·0
Carbohydrate: g	41·3
% energy	26·7
Dietary fibre (g)	8·0
Water (g)	247+300

Gastric emptying

Ultrasound examination was performed with a Diagnostic Ultrasound System I model 3535 fitted with a high-resolution real-time scanner (model 8524; B&K Medical) with a 3·5 MHz linear array transducer. All subjects were studied in the upright position. The cross-sectional area of the gastric antrum was measured on the sagittal plane passing through the superior mesenteric vein. The longitudinal and antero-posterior diameters were measured twice at each time-point during inter-persistaltic gastric relaxation, the mean was obtained and the antral area was calculated assuming an elliptical shape (Bolondi *et al.* 1985). When the antral area returned to basal value and remained unchanged for at least 30 min, gastric emptying was considered ended. Half emptying time was calculated from the linear part of the emptying curve (Duan *et al.* 1993; Acalovschi *et al.* 1997). The same operator performed all the ultrasound studies and was unaware of the type of meal consumed.

Cholecystokinin assay

CCK was measured by radioimmunoassay in plasma extracted on SEP-PAK 18C cartridges (Shoelson *et al.* 1986). A commercially-available antibody (C2581, Lot 105H4852; Sigma Chemical, St Louis, MO, USA) raised in rabbits against synthetic sulfated CCK-8 was employed. This antibody binds all CCK peptides containing the sulfated tyrosine residue in position 7, shows a 26 % cross-reactivity with unsulfated CCK-8, less than 2 % cross-reactivity with human gastrin I, and does not bind to structurally-unrelated peptides. The working dilution was 1:25 000 (w/v) in RIA buffer (50 mM-phosphate, pH 7·4, containing 10 mM-EDTA and gelatin (2 g/l)). Synthetic sulfated CCK-8 (Sigma Chemical) was used as standard and sulfated CCK-8 ^{125}I-labelled with Bolton and Hunter reagent (Amersham International, Amersham, Bucks., UK) was used as tracer. Incubation was performed at 4° for 48 h. Separation of free and bound tracer was achieved by the

double-antibody technique. The 95 % confidence detection limit was 1·2 pg/tube and the intra- and inter-assay CV were 6·4 and 11·7 % respectively. To monitor the peptide loss during the extraction procedure ^{125}I-labelled CCK-8 (500 counts/min) was routinely added to the plasma samples and the mean recovery was 86 (SD 6) %. Plasma extracts tested at three different dilutions yielded constant final peptide values, after correction for the dilution factors.

Statistical analysis

Results are given as means with their standard errors of means. Postprandial data were computed at each time-point by subtracting basal values and the integrated areas under these curves (AUC) were calculated using the trapezoidal rule. Satiety sensation, gastric-emptying rate and plasma CCK concentration were evaluated using a one-way repeated-measures analysis of covariance with time as covariate and type of food (SM or HM) as dependent variable; means were compared using the least significant difference test. Student's paired *t* test was employed to evaluate the difference in cognitive perception and AUC values. Relationship between variables were assessed by linear regression analysis. A $P<0·05$ was considered statistically significant. The computer program STATISTICA for Windows (StatSoft Inc., Tulsa, OK, USA) was used for the analysis.

Results

Cognitive perception of meal

The subjects' perception of the palatability, energy content and fat content of the two meals did not differ significantly.

Satiety-rating questionnaire

The satiety ratings given as variation with time and as integrated AUC are shown in Fig. 1. After the HM the sensations of satiety and fullness were significantly greater ($F(1, 62)$ 9·237, $P = 0·003$ and $F(1, 62)$ 36·413, $P < 0·001$ respectively) and the desire to eat was significantly lower ($F(1, 62)$ 4·277, $P = 0·043$) than after the SM. Considering the integrated AUC, the fullness response was significantly greater after the HM (*t* 2·523, $P = 0·040$).

Gastric emptying

Fig. 2 reports the antral areas given as variation with time and as integrated AUC. For both meals the antral area reached its maximum between 30 and 60 min and then gradually decreased, returning to basal values. Dilation of the gastric antrum was always greater after the HM than after the SM ($F(1, 78)$ 21·679, $P < 0·001$). There was no significant difference in AUC values. The half and overall emptying times were significantly longer with the HM than with the SM (160 (SEM 9) min *v.* 131 (SEM 9) min, *t* 3·284, $P = 0·013$ and 255 (SEM 11) min *v.* 214 (SEM 12) min, *t* 3·667, $P = 0·008$ respectively). On ultrasound examination, 90 min after consumption of the SM the intraluminal antrum content appeared mainly hyperechoic, whereas after the HM it was less homogeneous with an unechoic part and a hyperechoic part which tended to stratify.

Plasma cholecystokinin response

No significant difference was observed in CCK release after the SM and the HM expressed both as variation with time and as integrated AUC (Fig. 3). However, the CCK peak occurred later after the HM compared with the SM (94 (SEM 12) min *v.* 62 (SEM 11) min; NS) and CCK values were still elevated 180 min after the HM.

Correlation

Independently of the type of meal, there was a positive correlation between fullness sensation AUC and antral area AUC (r^2 0·46; $P = 0·004$) and a negative correlation between desire to eat AUC and antral area AUC (r^2 0·29; $P = 0·031$); (Fig. 4). No correlation was found between plasma CCK concentration AUC and antral area AUC.

Discussion

Understanding the mechanisms involved in the relationship between food intake and satiety is important not only for the therapy but also for the prevention of over- and under-nutrition. In this regard, the influence of different foods on physiological variables such as gastric-emptying rate and the release of gastrointestinal hormones could play an important role in modulating satiety signals. We therefore performed the present study to investigate how the consistency of a meal, SM or HM, affects satiety sensations, rate of gastric emptying and plasma CCK concentration. We found that an HM vegetable-rich meal was more satiating than the same meal consumed in the SM state, and that homogenization delayed the gastric-emptying.

After consumption of the HM meal the antral area, and also the half and overall gastric emptying times were significantly greater than after the SM meal. These findings contrast with those of Malagelada *et al*. (1979) who found that meals given in SM form were emptied at a slower rate than those in the HM form. The major difference between our study and the Malagelada *et al*. (1979) study was the inclusion in our meal of 250 g cooked vegetables, a good source of dietary fibre (8 g). We may suppose that homogenization of the meal increased the release of fibre from vegetables, resulting in higher viscosity of the HM compared with the SM, as suggested by the simulation analysis (see p. 522). Our HM, which retained both liquid and solid components, probably had greater inertia to propulsive contractions in the stomach (Vincent *et al*. 1995), thus accounting for the observed slow gastric emptying rate. The ultrasound examination also supported this theory: HM stratified in the antrum, and antral areas were always greater than after SM.

The ultrasonography technique however cannot differentiate between the emptying of liquid and solid components of a meal, but it is well known (Malagelada,

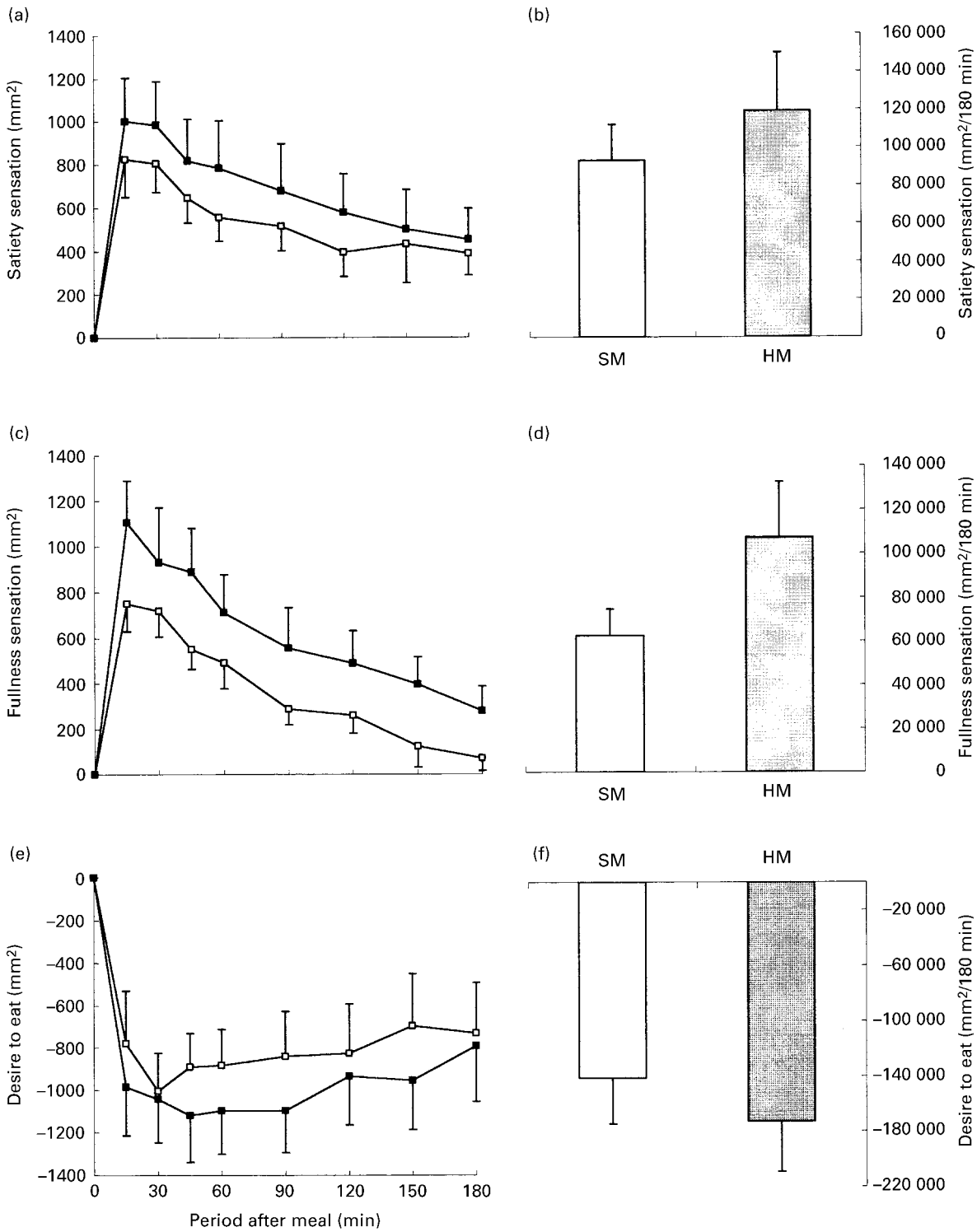

Fig. 1. (a,b) Satiety, (c,d) fullness and (e,f) desire to eat after the solid–liquid (SM; □) and the homogenized meal (HM; ■) in eight healthy adult male subjects. Results are shown as variation from baseline at different time-points (a,c,e) and as integrated areas under the curves (b,d,f). Values are means with their standard errors represented by vertical bars. For (a,c,e) mean values after SM were significantly different from those after HM: $P = 0{\cdot}003$, $P = 0{\cdot}001$, $P = 0{\cdot}043$ respectively; for (d) mean values for SM were significantly different from those after HM: $P = 0{\cdot}040$. For details of meals and procedures, see Table 1 and p. 522.

1977) that a meal in the mixed SM form separates in the stomach into different physical phases which empty independently, more rapidly in the case of the liquid component. Our findings after the SM are in agreement with this view, as indicated by the smaller antral areas observed in comparison with the HM.

The physical state of food (liquid *v.* solid) can also influence satiety signals (Bolton *et al.* 1981; Rolls *et al.* 1990; Tournier & Louis-Sylvestre, 1991; Hulshof *et al.* 1993). However, in some studies on this topic, food differed not only in physical state but also in macronutrient content (Rolls *et al.* 1990) or volume (Bolton *et al.* 1981). In addition, when Kissileff (1984) measured food intake by means of two different procedures (concurrent evaluation and preloading paradigm) he found that liquefied foods were more satiating than solid ones, although he underlined that the results obtained depended also on the procedure adopted. In our study we used two isoenergetic isovolumic meals which differed only in physical state (SM *v.* HM). These meals were served on plates and eaten with cutlery to avoid any cognitive or psychological variables. To minimize any personal bias related to subjective evaluation of satiety sensations, our study included the objective measurement of antral distension. A relationship has been suggested already between variations in antral area and satiety. Jones *et al.* (1997), using a D-glucose solution, found a positive linear relationship between antral distension and postprandial fullness. Bergmann *et al.* (1992) showed that the antral diameter, as measured at sonography, correlated well with sensations of hunger and satiety in overweight subjects who had received psyllium or placebo before a standard meal. They therefore proposed ultrasonography as a simple and non-invasive method, useful in clinical pharmacology, to study the effect of bulk agents in reducing hunger and food intake. Using this method we found that, independently of the type of meals, fullness and desire to eat correlated significantly with antral area. Moreover, at each time-point, antral distension was greater after HM, which was also more satiating than the same meal in the SM form. After HM the delay in gastric emptying determined a greater sensation of fullness, which was still evident at 180 min. At this time, when SM was almost completely emptied from the

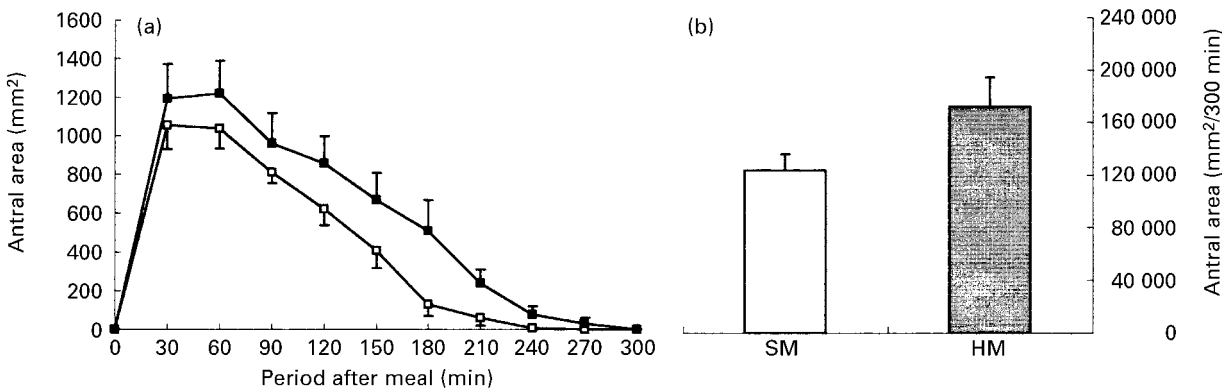

Fig. 2. Antral cross-sectional areas after the solid–liquid (SM; □) and the homogenized meal (HM; ■) in eight adult male subjects. Results are shown as variation from baseline at different time-points (a) and as integrated areas under the curves (b). Values are means with their standard errors represented by vertical bars. For (a) mean values after SM were significantly different from those after HM: $P = 0{\cdot}001$. For details of meals and procedures see Table 1 and p. 522.

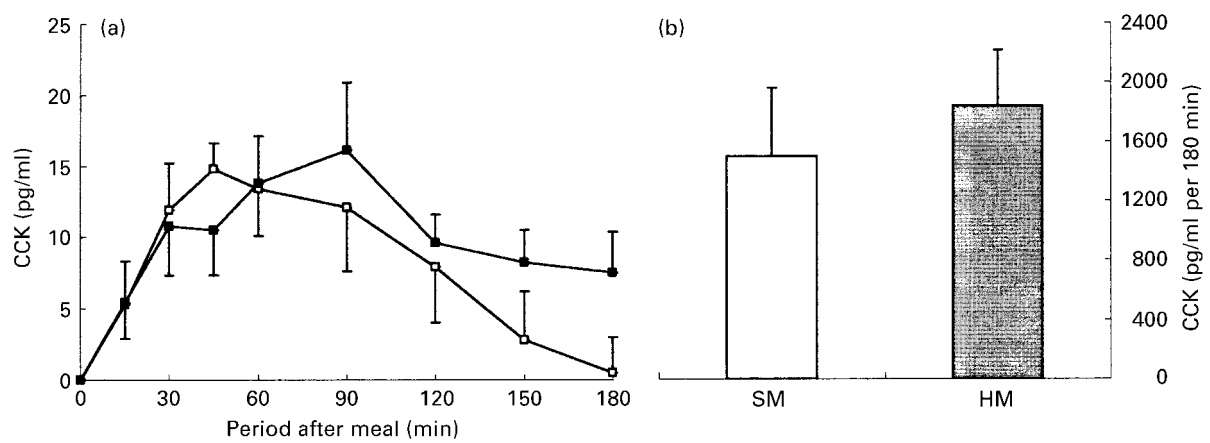

Fig. 3. Plasma cholecystokinin (CCK) concentration after the solid–liquid (SM; □) and the homogenized meal (HM; ■) in eight healthy adult male subjects. Results are shown as variation from baseline at different time-points (a) and as integrated areas under the curves (b). Values are means with their standard errors represented by vertical bars. For details of meals and procedures, see Table 1 and pp. 522–523.

stomach, the fullness sensation returned to the fasting level.

These results underline the importance of studying the effect of food consistency on food intake. This variable, together with other food characteristics, such as energy density, palatability and nutrient composition, could in fact be carefully considered in preparing dietary guidelines for the prevention and treatment of specific eating disorders like obesity and anorexia. The satiating properties of our HM rich in vegetables were higher than those of the SM, even 180 min after consumption. The fullness sensation 180 min after the HM was in fact comparable with that expressed 120 min after the SM, indicating a 1 h delay in returning to the basal sensation.

A further interesting finding of the present study was the different CCK profile after the two meals. CCK is a well-known endocrine peptide and neurotransmitter involved in several physiological and behavioural functions (Smith, 1992). It has been shown to reduce food intake in both normal and obese subjects (Kissileff *et al*. 1981; Pi-Sunyer *et al*. 1982), and postprandial CCK release has been found to correlate with satiety (Holt *et al*. 1992). Smith & Gibbs (1987) demonstrated that endogenous CCK released by one meal can alter the time and size of the following meal. Moran & McHugh (1988) found that endogenous CCK affects food intake through both inhibition of gastric and non-gastric vagal signals. Based on our results we can hypothesize a relationship between gastric emptying and CCK release, and a possible role of CCK in determining the higher satiating properties of an HM meal compared with an SM meal. In fact, during the first 60 min, with the stomach still in the distension phase, plasma CCK concentration was similar after both the meals. Subsequently, when the emptying phase started, the longer time necessary for the HM to empty completely from the stomach (1-2 h more than the SM) always determined higher plasma CCK concentrations and greater fullness sensations.

In conclusion, the present findings confirm that antral

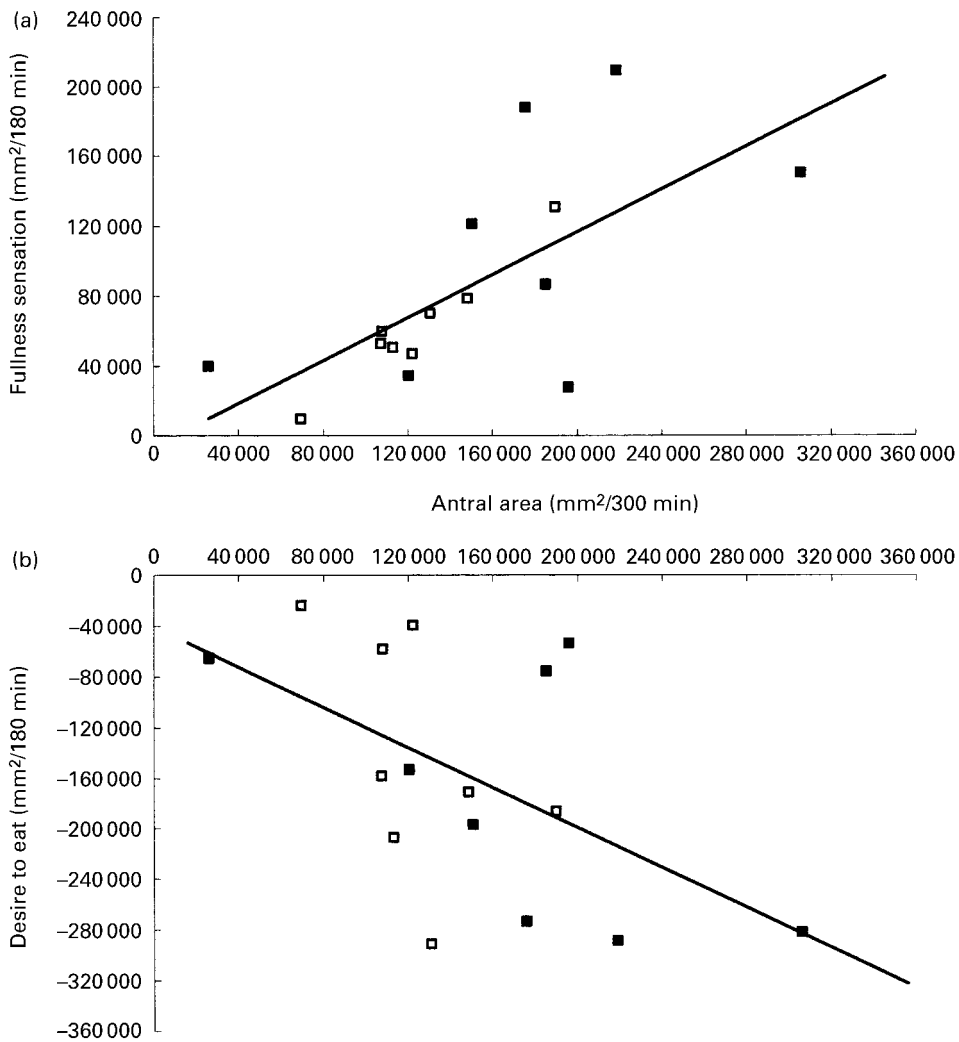

Fig. 4. Correlation between (a) fullness sensation (y) as a function of antral area (x): $y = 0{\cdot}61x - 59$, SE of estimate 447; $r^2 0{\cdot}46$, $P = 0{\cdot}004$) and (b) desire to eat (y) as a function of antral area (x): $y = -0{\cdot}79x - 407$, SE of estimate 831; $r^2 0{\cdot}29$, $P = 0{\cdot}031$) in eight healthy adult male subjects. Each point represents the value for area under the curve for each subject after the solid–liquid (□) and the homogenized (■) meal. For details of meals and procedures, see Table 1 and p. 522.

distension plays an important role in modulating eating behaviour. The area of the antral region was closely correlated with the subjective sensation of fullness, and the physical state of the meal represented an important food characteristic, influencing both gastric emptying and satiety sensation.

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