

Comparisons of the effects on satiety and eating behaviour of infusion of lipid into the different regions of the small intestine

I McL WELCH, C P SEPPLE, AND N W READ

From the Sub-Department of Gastrointestinal Physiology and Nutrition, The University of Sheffield, Royal Hallamshire Hospital, Sheffield

SUMMARY Food intake and feelings of hunger and fullness were monitored in paired studies carried out in two groups of six healthy non-obese male volunteers during infusion of isotonic solutions of either a 50% corn oil emulsion or saline into the jejunum or into the ileum. Infusion of the lipid emulsion at a rate of 1.2 ml/min (4.9 kcal/min) into either the ileum or the jejunum significantly reduced the period of eating ($p < 0.01$) and the quantity of food consumed ($p < 0.01$), but neither affected the rates of drinking or the amount of fluid consumed. Infusion of the lipid emulsion into the jejunum also significantly reduced the sensations of hunger before the meal ($p < 0.05$), and the rate of ingestion ($p < 0.01$). Ileal infusion did not influence these indices. The results suggest that jejunal and ileal infusion of lipid reduces the size of the meal that could be consumed possibly by inhibiting gastric emptying. The alleviation of hunger before ingestion and the slower rate of eating, however, suggests that jejunal lipid activates an additional mechanism that influences the appetite centre in the hypothalamus directly.

The mechanisms that regulate food intake and satiety in man are poorly understood, though on the basis of experiments carried out in rats, it has been suggested that food intake may be terminated by stimulation of nutrient receptors within the gastrointestinal tract.¹ In support of this hypothesis we have previously observed that infusion of lipid emulsion into the ileum reduced the amount of a meal consumed by normal volunteers² whereas intravenous infusion of a similar lipid emulsion did not influence eating behaviour.² The effect of ileal lipid on satiety is compatible with mediation by changes in gastric volume as it was associated with a delay in gastric emptying² and a reduction in the capacity for food with no change in the rate of eating. In support of this idea, studies in rats have shown suppression of food intake during distension of the stomach with a balloon.³ It is possible however, that satiety and

delayed gastric emptying after ileal infusion of lipid could be mediated by the central nervous system.

Experiments in animals, however, suggest that the interaction of nutrients with receptors in the upper small intestine may reduce food intake by an action that is independent of gastric distension. Instillation of nutrients into the duodenum inhibits food intake in rats and monkeys equipped with gastric fistulae and triggers behaviour identical to that which occurs after a meal even though there is no food in the stomach.^{4,5} The aim of the study was to investigate possible satiety mechanisms triggered by receptors in the upper small intestine, by comparing the effects of infusion of lipid into the jejunum and ileum of normal human subjects on eating behaviour feelings of hunger and fullness.

Methods

SUBJECTS

Studies were carried out on two groups of six healthy male volunteers, all of whom were non-smokers and

Address for correspondence: Dr N W Read, Sub-Department of Human Gastrointestinal Physiology and Nutrition, Royal Hallamshire Hospital, Sheffield, S10 2JF.

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within the normal range of body weight for their age and height. The two groups were matched for age, gender, and weight (jejunal experiments: age 20.5, range 19–23 years; weight 66.6, range 63.6–76.8 kg; ileal experiments: age 20.5, range 19–22 years; weight 64.4, range 61.8–74.5 kg). One group underwent infusion of lipid into the jejunum, the other group underwent infusion of lipid into the ileum (four of the six ileal infusion studies have been reported previously).² Each subject gave written informed consent for the studies to be carried out and the protocols were approved by the Southern District Ethical Sub-Committee of the Sheffield Area Health Authority (Teaching).

PROTOCOL

Each subject carried out two studies, separated by a period of 14 days. The studies were identical in design except that on one occasion, a lipid emulsion was infused into the small intestine and the other occasion a control solution of isotonic saline was infused at the same rate and site. An identical meal was presented to the subject on each occasion. The order of the studies was randomised.

On the day preceding the experiment, each subject swallowed a radiopaque polyvinyl tube (external diameter = 2 mm), which had a distal side opening and terminated in a latex bag containing 1 ml elemental mercury. After the bag had been swallowed, the tube was rerouted through the nose. This procedure was important because it allowed the tube to be retained for long periods of time and allowed subjects to eat with minimum discomfort from the tube. The tube was allowed to progress down the gut until the distal port was located fluoroscopically either in the jejunum, 100 cm distal to the teeth or the ileum, 205 cm distal to the teeth, whereupon the terminal mercury bag plus a small length (1 cm) of tubing was detached by a rapid injection of 20 ml air.⁶ This prevented progression of the tube during the test.

On the day of the experiment, each subject ate

breakfast, if this was his usual custom, but mid-morning snacks were not permitted. At 12.30 pm a solution of either isotonic saline (containing 3% w/v albumen) or lipid (50% corn oil + 50% saline emulsified with 3% w/v albumen) was infused into the small intestine at a rate of 1.2 ml/min for a total of 75 minutes. The lipid infusion corresponded to 41 g lipid (370 kcal), and the delivery of calories to the small intestine was 4.9 kcal/min. Subjects were unaware of the nature of the intestinal infusion, as the tubing was opaque and the pump was concealed behind a screen. Thirty minutes after the start of the infusion each subject was presented with an appetising meal, that he had selected from a menu at least a week before the start of the experiment. The meal was prepared in quantities in excess of what he would normally be expected to consume, and the subject was then invited to eat and drink as much as he wished for the remaining 45 minutes. At 15 minute intervals throughout the studies, each subject scored a range of subjective feelings including hunger, fullness and drowsiness on visual analogue scales. The quantity of food eaten and the volume of fluid drunk were assessed by weighing the food containers before and after eating. The time taken for each subject to complete the meal was also measured. The average rates of drinking and eating and the calorie intake were calculated from these measurements.

Studies were carried out in a relaxed unstressed atmosphere, while subjects read or listened to audiocassettes of 'fictional or non-fictional material'. If experiments were carried out on more than one subject on the same day, the subjects were isolated and screened from each other to prevent factors other than hunger and satiety from influencing eating behaviour.

STATISTICAL ANALYSIS

The statistical significance of the difference in results obtained during the lipid versus the saline infusions were assessed by Student's paired *t* test.

Table Effect of jejunal or ileal infusion of lipid emulsion on feeding behaviour and satiety

	Jejunal infusion			Ileal infusion		
	Saline	Lipid	<i>p</i>	Saline	Lipid	<i>p</i>
Amount eaten (g)	1143 (103)	557 (76)	<0.01	957 (87)	734 (44)	<0.05
Amount drunk (ml)	423 (62)	367 (88)	NS	448 (48)	479 (52)	NS
Total energy intake (Kcal)	2157 (196)	1076 (202)	<0.01	2026 (194)	1377 (79)	<0.02
Time for eating (min)	25 (1)	18 (2)	<0.01	29 (3)	22 (1)	<0.05
Eating rate (g/min)	51 (6)	33 (3)	<0.01	33 (3)	34 (4)	NS
Drinking rate (ml/min)	16 (3)	19 (4)	NS	11 (2)	13 (2)	NS

Results are expressed as mean (SE) (n=6 in each case); NS=not significant.

Results

JEJUNAL EXPERIMENTS

Food intake

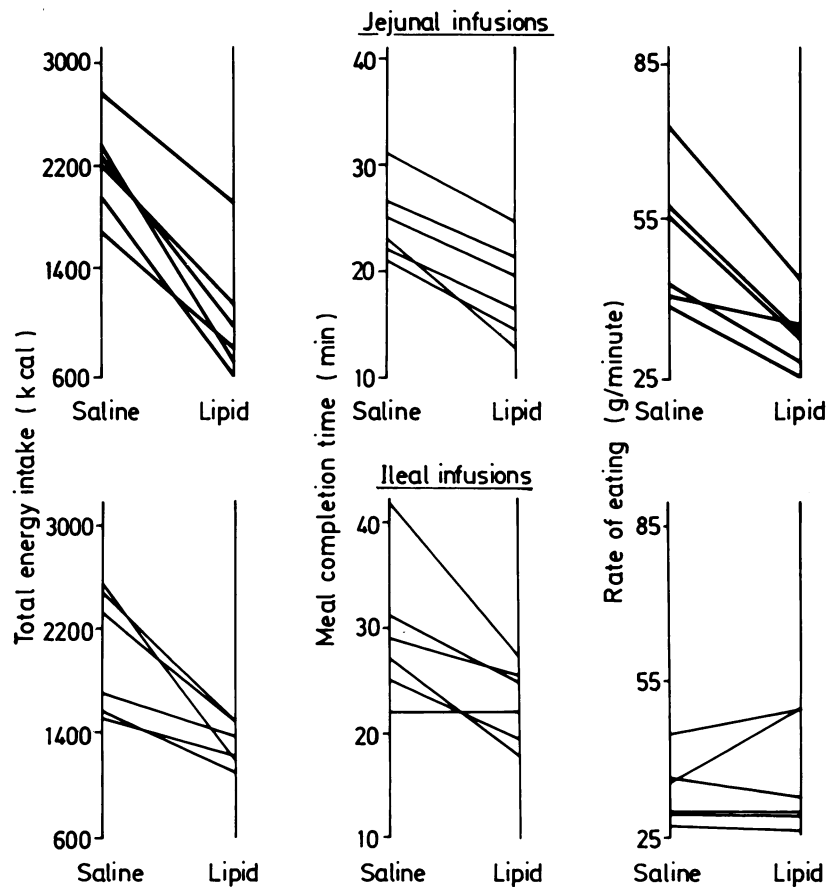
The amount of food eaten and the total energy intake were significantly reduced during jejunal infusion of corn oil emulsion, compared with infusion of isotonic saline ($p < 0.01$) (Table). This effect was associated with significant reductions in the time taken for subjects to complete a meal ($p < 0.01$) as well as in the rate of eating ($p < 0.01$), which was observed in all six subjects (Fig. 1). None of the subjects appeared to ingest particular components of the meals in preference to others during either infusion. The amount of fluid drunk and the rate of drinking were similar during jejunal infusion of lipid compared with saline. The reduction in energy intake from the meal during infusion of lipid compared with the saline (1080 (154)kcal, mean (SEM) $n=6$) was greater than the energy supplied by the corn oil emulsion (370 kcal) in all six subjects.

Subjective feelings

Similar degrees of hunger were experienced at the start of the lipid and saline infusions. Thirty minutes later, however, just before presentation of the meal, all six subjects felt significantly less hungry during lipid infusion into the jejunum than they did during saline infusion ($p < 0.05$) (Fig. 2). Ingestion of the meal was associated with reductions in the scores for hunger during jejunal infusion of both lipid and saline, but the hunger ratings were significantly lower 15 minutes after commencing the meal during lipid infusion compared with saline infusion ($p < 0.01$) (Fig. 2).

The scores for fullness were very low before the meal during jejunal infusion of lipid and saline, but upon commencing the meal these values rose at similar rates and subjects ate to similar levels of fullness (Fig. 2). There were no significant differences in the scores for any of the other subjective feelings during either infusion. None of the subjects experienced any discomfort during either infusion.

Fig. 1 Effects of jejunal (top) and ileal infusions of lipid (bottom) and saline on total energy intake from the meal (left), time taken for meal completion (centre) and the rate of ingestion (right), in six healthy volunteers.



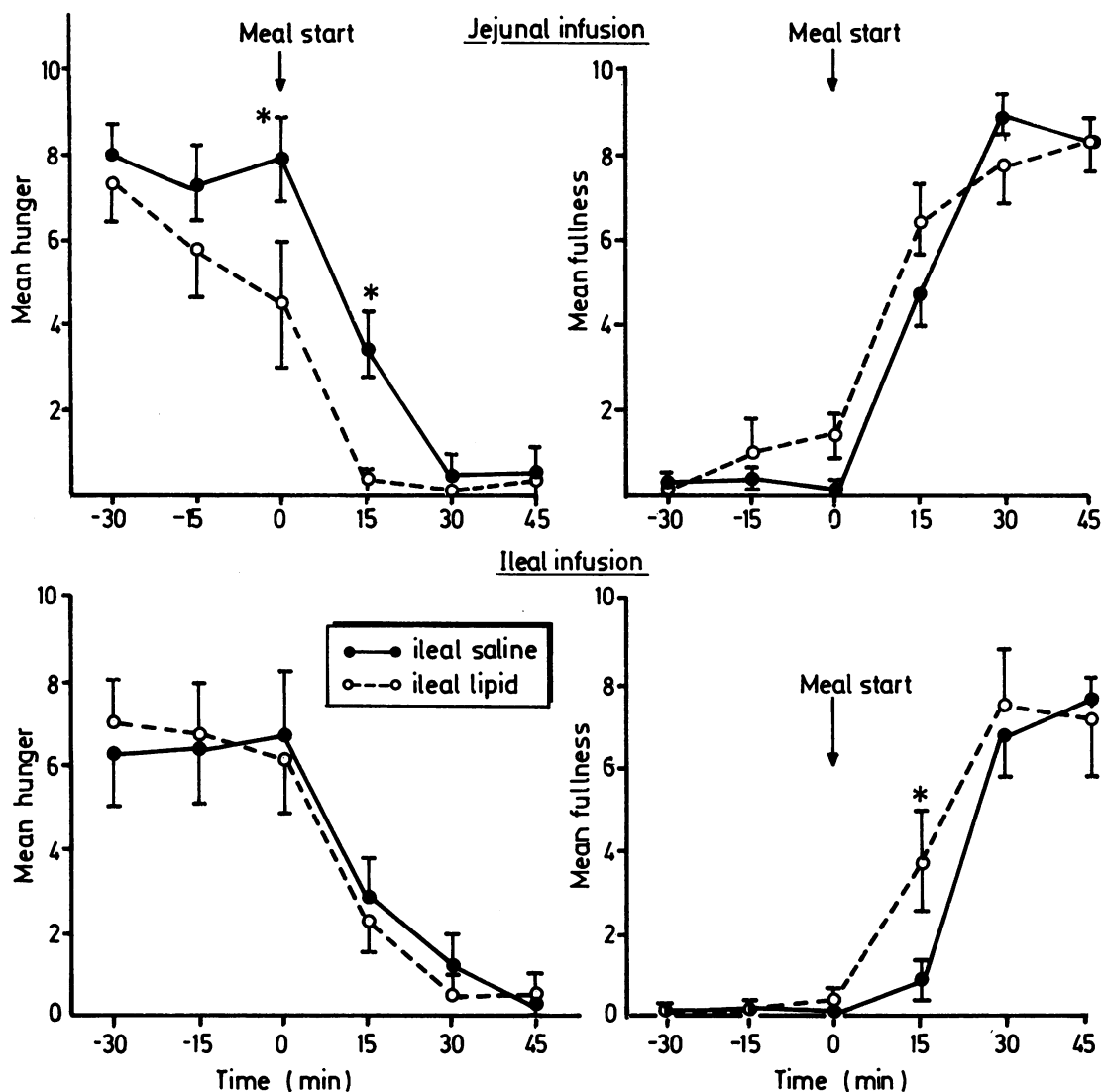


Fig. 2 Subjective sensations of hunger (left) and fullness (right), experienced by healthy volunteers before and after ingestion of the meal during infusion of lipid (dotted line) and saline (solid line) into the jejunum (top) or ileum (bottom). The infusion started 30 minutes before the meal and continued for 45 minutes. Results are expressed as mean (SEM) (n=6). Asterisks indicate significant difference between data pairs (p<0.05)

ILEAL EXPERIMENTS

Food intake

Ileal infusion of corn oil emulsion significantly reduced the amount eaten (p<0.05) and the total energy intake from the food (p<0.02) compared with ileal infusion of isotonic saline (Table, Fig. 1). These results were associated with significant reductions in the time taken to eat the meal, but unlike the effect of

jejunal infusion of lipid, there was no significant reduction in the rate of eating; only two of six subjects showed any reduction in eating rate and this was small. The amount of fluid drunk and the rate of drinking were similar during ileal infusion of lipid emulsion and saline. In contrast with the jejunal infusions, the reductions in energy intake and the time taken to eat the meal observed during lipid were greater if the control values were initially high (Fig.

1) and the scatter of results was smaller during lipid infusion than during saline infusion.

Energy intake from the meal was similar during infusion of saline into the jejunum and the ileum. There was a trend, however, for the reduction in energy intake to be greater when lipid was infused into the jejunum compared with the ileum (1080 (154) v 649 (165)kcal; mean (SEM) n=6, $p < 0.01$). The reduction in energy intake from the meal caused by ileal infusion of lipid was only exceeded by the energy supplied by the infusion of lipid (370 kcal) in those subjects whose intake was very high during saline infusion.

Subjective feelings

Unlike the results from the jejunal studies, ileal infusion of lipid did not reduce the degree of hunger just prior to eating the meal (Fig. 2). Subjects ate to the same level of fullness during ileal infusion of both lipid and saline, but during lipid scores for fullness were significantly higher 15 minutes after commencing the meal ($p < 0.05$) (Fig. 2). Scores for the other symptoms were not affected by the nature of the ileal infusion. None of the subjects felt any physical discomfort during either infusion.

Discussion

The data from this study show that infusion of lipid emulsion into the proximal small intestine as well as the distal small intestine induces early satiety and reduces food intake in normal volunteers. Our previous observation that intravenous infusion of lipid emulsion did not effect food intake² suggests that the effect of intestinal infusion of lipid is mediated by interaction of nutrients with intestinal receptors and is not a postabsorptive phenomenon. The rate of infusion of calories exceeds the entry of nutrients into the small intestine^{7,9} measured in most gastric emptying experiments in man and should therefore be regarded as a supramaximal stimulus, akin perhaps to what might happen in normal subjects after eating a heavy meal or in patients with abnormally rapid gastric emptying. Infusion of lipid into the jejunum reduced the duration of food intake. This is compatible with an earlier attainment of a critical level of gastric distension, caused possibly by the delay in gastric emptying that is known to occur during infusion of lipid into the jejunum.⁸ A similar effect was observed during infusion of the same amount of lipid into the ileum,² which also delays gastric emptying.¹ It is possible that the lipid infused into the jejunum could run down the small intestine and interact with ileal receptors, although we have previously observed that during jejunal infusion of 20% intralipid, insufficient lipid reached the ileum to

activate the receptors that delay small bowel transit.⁶ Unlike ileal infusion of lipid, however, jejunal lipid infusion also slowed the rate of ingestion and reduced feelings of hunger before starting the meal. These additional actions may explain why the reduction in food intake was greater during infusion of lipid into the jejunum than it was during infusion of lipid into the ileum,² and suggests that jejunal infusion of lipid, unlike ileal lipid infusion, may be able to influence hunger by a mechanism that is independent of gastric distension. This result therefore is compatible with the observations, that instillation of nutrients into the duodenum inhibits food intake of animals equipped with chronic gastric fistulae.^{4,5}

It is possible that the suppression of hunger and reduction in eating rate during infusion of lipid into the jejunum are caused by release of CCK. Early satiety can be induced by intravenous infusion of cholecystokinin (CCK), CCK is normally released from the duodenal and jejunal mucosae^{10,11} in response to the presence of lipid in the intestinal lumen.³ CCK can inhibit food intake in experimental animals equipped with a continuously draining gastric fistula,^{12,13} indicating that the effect of this peptide is not purely mediated by distension of the stomach. Finally, CCK also elicits a number of behaviour patterns such as grooming and drowsiness, commonly observed when experimental animals have completed a meal.¹⁴

In conclusion, the observation that infusion of lipid into the jejunum influences eating behaviour and sensations of hunger in different ways than infusion of lipid into the ileum, suggests that jejunal mechanisms may be more concerned with control of appetite. Thus the desire for food may be suppressed as long as lipid (and presumably other nutrients) is present in the upper small intestine, but that the presence of lipid in the lower as well as the upper small intestine, suppresses the delivery of food from the stomach and may influence the capacity for food possibly by allowing the earlier attainment of a critical level of gastric distension.

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