

Reserve capacities of the small intestine for absorption of energy

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Weber, E., and H. J. Ehrlein. Reserve capacities of the small intestine for absorption of energy. *Am. J. Physiol.* 275 (Regulatory Integrative Comp. Physiol. 44): R300–R307, 1998.—Previous *in vitro* studies showed that the small intestine has reserve capacities for absorption of nutrients. However, the size of the reserve capacity is controversial. Therefore, we measured the intestinal capacity for absorption of energy in relation to the postprandial gastric delivery of energy into the gut. In minipigs, a 150-cm length of jejunum was perfused (1–8 kcal/min) with four nutrient solutions containing 60% of energy as carbohydrate, protein, and fat, respectively, or containing 33.3% of each nutrient. In separate experiments, gastric delivery of energy to the jejunum was measured after oral administration of four meals with the same nutrient composition as the perfusion solutions. With all nutrient solutions, intestinal absorption of energy demonstrated saturation kinetics. The jejunal capacity for absorption of energy ranged from 0.66 to 0.94 kcal·m⁻¹·min⁻¹. Despite large differences in nutrient composition of the four meals, equal amounts of energy (1.3 ± 0.41 kcal/min) were delivered from the stomach to the jejunum. The absorption rates of energy after meals ranged from 0.40 to 0.58 kcal·m⁻¹·min⁻¹. Therefore, only 58.8 ± 2.7% of the jejunal capacity for absorption of energy was used. Additionally, the length of small intestine that would have been required for complete absorption was 42.9 ± 3.7% of the total length. Results indicate that the feedback control of gastric emptying provides at least two types of intestinal reserve capacities: a reserve in absorption (1.7 fold) and a reserve in intestinal length (2.4 fold).

intestinal absorption; gastric emptying; feedback regulation

THE CAPACITY OF THE SMALL INTESTINE for absorption of nutrients has been investigated in several studies (5, 26, 27, 36). Results of these studies reveal large discrepancies. Some authors suppose a very large absorption capacity of the gut due to passive diffusion of nutrients (26). In contrast, other authors argue that passive diffusion of nutrients is negligible (8). *In vitro* studies have shown that the maximal transport capacity of brush-border glucose and several amino acid transporters exceeded daily substrate intakes by a factor of about two (6, 8). Furthermore, the daily energy uptake of cold-exposed mice rose by 2.5 times the previous intake, indicating a corresponding capacity for absorption (5, 36). *In vivo* intestinal absorption of energy depends on the gastric delivery of nutrients into the gut. Gastric emptying is regulated by a feedback control of the small intestine. Nutrients entering the duodenum and jejunum elicit an inhibition of gastric emptying. The degree of inhibition depends on the concentration of nutrients and the length of gut exposed to nutrients, i.e., on the intestinal load of nutrients (19, 20, 23). In recent years it was shown that the feedback control is not only limited to nutrients entering the duodenum and jeju-

num but is also induced by nutrients of the ileum, called the ileal brake (33, 35). It is supposed that the intestinal feedback control adjusts gastric emptying to the capacity of the small intestine required for digestion and absorption (14, 23, 32). However, relationships between gastric delivery of nutrients into the small intestine and the intestinal capacity for absorption have not yet been investigated.

The aim of the present study was to measure the intestinal capacity for absorption of energy and to determine relationships between the gastric delivery of energy into the gut and the absorption capacity of the small intestine under physiological conditions. In minipigs, two sets of experiments were performed. In the first set, the capacity for absorption of energy was determined by perfusing a 150-cm length of jejunum with different nutrient solutions. In the second set, gastric emptying of energy was measured after meals with the same composition of nutrients as the perfusion solutions. Based on data of these two sets of experiments, information can be obtained on the reserve capacities of the small intestine for absorption of energy.

METHODS

Four female "Troll" minipigs weighing 45–60 kg were used in this study. The animals were adapted to a diet containing 33.3% of energy from each nutrient. The diet was composed of 83.1 g/l maize starch, 64.2 g/l casein, and 35.3 g/l soy oil. Fiber (18 g/l) and a mixture of minerals and vitamins (3 g/l) were added in amounts sufficient to meet the daily requirement. The daily energy supply was 1,666 kcal/day (95.5 kcal/kg^{0.75}).

For chronic implantation of cannulas, the pigs were anesthetized intramuscularly with 5 mg/kg tiletamine and zolazepam (1:1) (Tilest; Parke-Davis, Berlin, Germany). Anesthesia was maintained with 0.8–1.5% halothane in O₂-N₂O. Three cannulas were implanted into the proximal jejunum, 1, 2, and 3.65 m distal to the ligament of Treitz, and were exteriorized through the right abdominal wall. The cannulas consisted of silicone rubber (Elastosil R401/70E; Wacker, Munich, Germany). The barrel of the T-shaped cannulas had an internal diameter of 13 mm and a length of 25–30 mm. The cannula base had a length of 60 mm and a diameter of 23 mm. It was positioned at the abdominal wall in a ventrodorsal direction. The upward flow of digesta facilitated outflow of chyme through the opened cannula.

Experiments were started 14 days after surgery. The pigs were fasted for 14 h before each experiment. During the experiments, the animals were positioned with a hammock.

Experiments

Two experiments were performed. In the first experiment, the intestinal capacity for absorption of energy was determined. The jejunal segment located between the middle and distal cannulas was temporarily isolated and perfused with

nutrient solutions of different composition. In the second experiment, gastric delivery of energy into the small intestine was measured by drainage of chyme from the proximal cannula after oral administration of different meals.

Intestinal Capacity for Absorption of Energy: Experiment 1

Perfusion solutions. In experiment 1, four different nutrient solutions were used: one with 60% of energy as carbohydrate (*solution C*), one with 60% of energy as protein (*solution P*), one with 60% of energy as fat (*solution F*), and one with carbohydrate, protein, and fat (*solution E*) each comprising 33.3% of the energy. Each solution contained 60 mmol/l (1,400 mg/l) sodium and small amounts of other electrolytes. This concentration of sodium is commonly used in enteral diets. Results of a parallel study showed that absorption of nutrients was influenced neither by variations of the sodium content between 30 and 150 mmol/l nor by other electrolytes (unpublished data). The nutrient and electrolyte compositions of the solutions are summarized in Table 1. The carbohydrate consisted of maltodextrin (C-Pur 1934; Cerestar, Krefeld, Germany) and the protein consisted of oligopeptides (Hyprol 8080; Quest International, Zwijndrecht, The Netherlands). Both the maltodextrin and oligopeptide were absorbable after final hydrolysis by brush-border enzymes. An emulsion of triglycerides (Lipovenös 10%; Fresenius, Bad Homburg, Germany) was used as fat. Before intestinal perfusion, the fat emulsion was hydrolyzed in vitro by pancreatic enzymes (pancreatin P-1750; Sigma, St. Louis, MO) to free fatty acids and *sn*-2-monoglycerides. Bile salts B-8756 (Sigma) were added to produce a micellar solution. The energy density of the nutrient solutions was adjusted to 0.4 kcal/ml, corresponding to the energy density of the chyme entering the jejunal segment after meals. The solutions were nearly isotonic (Table 1). Cobalt-EDTA (5.0 mg/100 ml) was added as a nonabsorbable marker.

Experimental procedure. The three cannulas were opened, and a balloon catheter was inserted into the middle cannula. After intestinal contractions had carried the balloon 15 cm distally, the balloon catheter was fixed at the cannula and the balloon was inflated with air by a pump to occlude the intestinal lumen. The pressure in the balloon was kept constant. The corresponding volume of the balloon varied from 5 to 15 ml, resulting in a balloon diameter between 10 and 20 mm. One of the nutrient solutions was infused into the isolated jejunal segment over a period of 105 min. The effluent of the perfusion solution was collected at the distal cannula at 15-min intervals. The initial 45 min served as an equilibration period. Absorption of energy was measured under steady-state conditions during the subsequent 60-min period (test period). Afterward, saline was infused over an additional 30 min for marker recovery. The recoveries of the cobalt-EDTA marker during the whole experiment and during the test period were 95.9 ± 3.6 and $96.2 \pm 4.5\%$,

respectively. X-ray examination demonstrated that the jejunal loops aboral to the cannulas run downwards. This effect, combined with the inflated balloon, completely prevented backflow of luminal content.

The nutrient solutions were perfused into the isolated jejunal segment at different rates: *solutions C, P, and F* at 1, 2, 3, 4, 6, 8 kcal/min and *solution E* at 1.8, 3.6, 4.8, 6, 7.2 kcal/min. The different solutions and perfusion rates were selected in random order. The weights and volumes of the effluents were measured.

In all perfusion experiments, the animals were fed a test meal at the onset of the test period. The meal was eaten within 2 min. Thus postprandial conditions were induced simultaneously with the measurement of intestinal absorption. The test meal was composed of 33.3% of each nutrient. The volume was 1,000 ml; the energy density was 1 kcal/ml. The test meal was drained by the proximal cannula as it emptied from the stomach.

Measurement of absorption. The absorption of energy was measured by the difference between the infused and recovered energy according to the equation

$$\text{absorption}_{\text{energy}} = \text{energy}_{\text{infused}} - \text{energy}_{\text{effluent}} \cdot \frac{\text{marker}_{\text{infused}}}{\text{marker}_{\text{effluent}}}$$

Kinetics of intestinal absorption. With increasing perfusion rate of the nutrient solutions, the absorption of energy showed saturation kinetics. The Michaelis-Menten kinetic was used to calculate the K_m and V_{\max} values

$$\text{absorption} = \frac{V_{\max} \cdot S}{(K_m + S)}$$

where V_{\max} is the absorption capacity and K_m is the caloric load (S) (kcal/min) to use 50% of the V_{\max} .

Gastric Emptying and Jejunal Flow of Energy: Experiment 2

Meals. In experiment 2, four different meals were used: one rich (60%) in carbohydrate (*meal C*), one rich (60%) in protein (*meal P*), one rich (60%) in fat (*meal F*), and one with carbohydrate, protein, and fat each making up 33.3% of the energy (*meal E*). The nutrient and electrolyte compositions of the meals are summarized in Table 2. The meals had a volume of 1,000 ml and an energy density of 1 kcal/ml. The nutrients consisted of maize starch, lactalbumin, and soy oil. The consistency of the meal was like ketchup. Cobalt-EDTA (100 mg/1,000 ml) was added as a nonabsorbable marker.

Experimental procedure. The cannulas were opened, and the animals were fed with one of the test meals. The chyme drained from the proximal cannula was collected at 5-min intervals over a period of 90 min. The weight of the effluent was determined. Small samples were taken for analysis and replaced with a nutrient solution of corresponding composi-

Table 1. Composition of perfusion solutions

Solution	Amounts of Nutrients, g/l			Calories From Nutrients, kcal/l			Ratio of Nutrients, %Energy			Osmolality, mosmol/kg	Electrolytes, mg/l					
	Carb	Protein	Fat	Carb	Protein	Fat	Carb	Protein	Fat		Na ⁺	K ⁺	Ca ²⁺	Mg ²⁺	Cl ⁻	PO ₄ ³⁻
<i>C</i>	62.1	16.8	102.0	240.0	80.0	80.0	60.0	20.0	20.0	314	1,400	175	146	7	1,220	85
<i>P</i>	20.7	50.4	102.0	80.0	240.0	80.0	20.0	60.0	20.0	339	1,400	524	438	22	665	255
<i>F</i>	20.7	16.8	306.0	80.0	80.0	240.0	20.0	20.0	60.0	295	1,400	175	146	7	220	85
<i>E</i>	34.5	28.0	170.0	133.3	133.3	133.3	33.3	33.3	33.3	322	1,400	291	243	12	819	142

Caloric values used to convert amounts of nutrients (g/l) to calories (kcal/l): carbohydrate (carb), 3.86 kcal/g; protein, 4.76 kcal/g; hydrolyzed fat solution, 0.78 kcal/g; energy density of perfusion solutions, 0.4 kcal/ml. *Solution C*, 60% carb; *P*, 60% protein; *F*, 60% fat; *E*, equal amounts of nutrients.

Table 2. *Composition of meals*

Meal	Amounts of Nutrients, g/l			Calories From Nutrients, kcal/l			Ratio of Nutrients, %energy			Electrolytes, mg/l						
	Carb	Protein	Fat	Carb	Protein	Fat	Carb	Protein	Fat	Na ⁺	K ⁺	Ca ²⁺	Mg ²⁺	Cl ⁻	PO ₄ ³⁻	
<i>C</i>	142.8	36.9	21.9	600.0	200.0	200.0	60.0	20.0	20.0	170	63	59	7	30	11	
<i>P</i>	47.6	110.7	21.9	200.0	600.0	200.0	20.0	60.0	20.0	509	188	177	22	89	33	
<i>F</i>	47.6	36.9	65.7	200.0	200.0	600.0	20.0	20.0	60.0	170	63	59	7	30	11	
<i>E</i>	79.4	61.5	36.5	333.3	333.3	333.3	33.3	33.3	33.3	283	105	98	12	49	18	

Caloric values used to convert amounts of nutrients (g/l) to calories (kcal/l): carb, 4.20 kcal/g; protein, 5.42 kcal/g; fat, 9.14 kcal/g; energy density of meals, 1.0 kcal/ml.

tion. The chyme was returned into the jejunum via the distal cannula to maintain the feedback regulation of gastric emptying. In preliminary experiments, we tested whether gastric emptying differed when the chyme was returned via the middle or distal cannula. Because no difference was found, we returned the chyme via the distal cannula. The middle cannula was used to control possible aboral flow of chyme beyond the proximal cannula and backflow from the distal cannula.

For analysis of energy and marker in the effluent, samples of three 5-min periods were combined to obtain 15-min samples.

Measurement of gastric emptying and flow of energy to jejunum. Gastric emptying of energy was calculated by the formula

$$\text{gastric emptying of energy} = \frac{\text{marker}_{\text{effluent}}}{\text{marker}_{\text{meal}}} \cdot \text{energy}_{\text{meal}}$$

The flow of energy to jejunum was determined by multiplying the volume and energy density of the effluent of the proximal cannula.

During the initial 5 min after ingestion of the meal, gastric emptying was accelerated, then it declined and remained constant during the subsequent period. Both gastric emptying and jejunal flow of energy were determined as mean values over 90 min after ingestion of the meal.

Calculation of energy absorption and reserve capacity for absorption after meals. The energy delivered into the proximal jejunum after meals represented the jejunal caloric load. The absorption rate of energy per unit length of jejunum after meals was determined by the V_{max} and K_m values of the kinetics obtained by the perfusion values of *experiment 1*. The reserve capacity of absorption per unit length after meals was determined by subtracting the calculated amount of energy that was absorbed from the V_{max} . The reserve capacity for absorption is expressed as % V_{max} .

Calculation of intestinal length required for complete absorption and reserve of intestinal length. The kinetics determined during the perfusion experiments were further used to calculate the length of the small intestine that would be required for complete absorption of the energy delivered into the jejunum after the meals. At the proximal cannula, the energy flow (kcal/min) was measured, and both the absorption rate of energy along the subsequent meter of jejunum and the recovery of energy at the end of this segment were calculated according to the absorption kinetics. The energy recovered at the end of this jejunal segment represented the energy flow to the subsequent jejunal segment. Absorption and recovery of energy were calculated for each subsequent meter of jejunum. This procedure was repeated until the energy recovered at the end of a segment was <5% of the energy delivered into the jejunum after the meals. The exact length of jejunum required for complete absorption could be determined by extrapolation because the recovery of energy declined linearly.

The reserve of intestinal length was evaluated by subtracting the length of the small intestine required for complete absorption from the whole length of the small intestine. The reserve of length is expressed as percent of the total length of the small intestine. The total length of the small intestine was measured during surgery and confirmed at necropsy. The mean length of the small intestine between the pyloric and ileocecal sphincter was 9.7 ± 1.1 m. Perfusion studies performed in segments of the proximal and mid-jejunum showed that in minipigs the absorption rates of energy did not change within the proximal one-half of the jejunum. Absorption rates during perfusion of an enteral diet (Survived; Fresenius, Bad Homburg, Germany) were not significantly different between the proximal jejunum (0.57 ± 0.04 kcal·min⁻¹·m⁻¹) and the mid-jejunum (0.65 ± 0.09 kcal·min⁻¹·m⁻¹) (unpublished data).

Analysis of Marker and Energy

The concentrations of cobalt in the perfusion solutions, meals, or effluents from the proximal or distal cannulas were measured by an atomic absorption spectrometer (Perkin-Elmer, Überlingen, Germany). The energy contents were measured by an adiabatic electronic calorimeter (C7000 T; IKA-Analysentechnik, Heitersheim, Germany) after freeze drying of the samples (Lyovac GT2; Finn-Aqua, Tuusula, Finland).

Statistics

In each animal, two experiments were performed with each perfusion solution and perfusion rate (*experiment 1*) and with each meal (*experiment 2*). Data from the four pigs are presented as grand means \pm SD calculated from the mean values of the two experiments in each pig. Kinetics of intestinal absorption of energy were determined from mean values of the 60-min test period (*experiment 1*). Different parameters were compared using a variance analytical model (ANOVA, $n = 4$ pigs). Gastric emptying or jejunal flow of energy were evaluated from mean values over the 90-min period (*experiment 2*). Gastric emptying and jejunal flow of nutrients after the different meals were compared using ANOVA with linear contrasts. To validate how well the kinetics describe the data of intestinal absorption, the coefficients of determination (r^2) were estimated using the t -statistic. To detect differences among the kinetics of absorption, V_{max} values were compared using ANOVA with linear contrasts.

RESULTS

Intestinal Capacity for Absorption of Energy

During perfusion of the jejunal segment with the four nutrient solutions, the absorption of energy increased with increasing energy load (Fig. 1). The patterns of

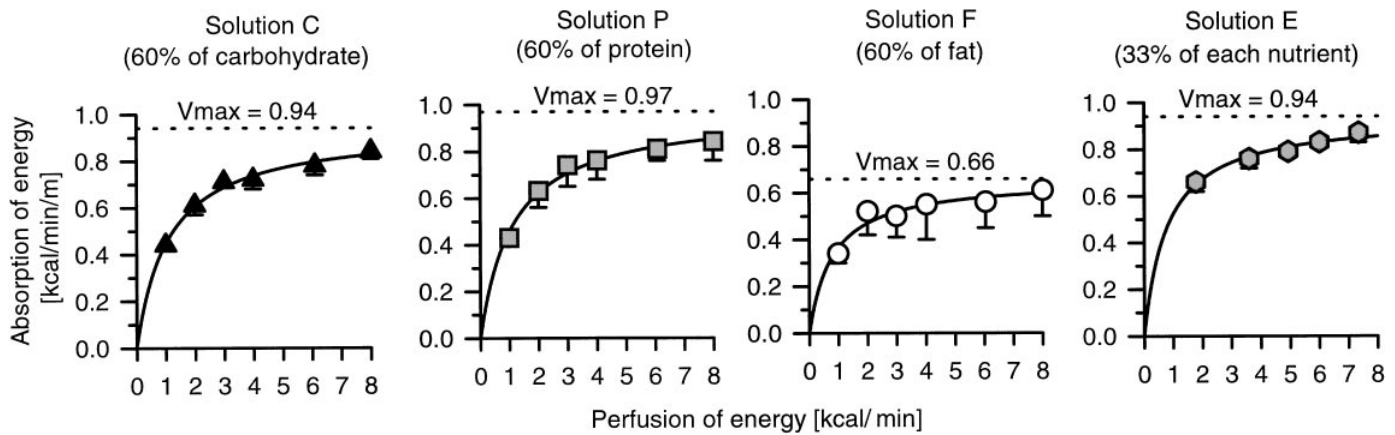


Fig. 1. Saturation kinetics of energy absorption determined by perfusing a 150-cm jejunal segment with 4 nutrient solutions. Despite large differences in nutrient composition, maximal absorption (V_{\max}) of energy per unit length was identical in solutions C, P, and E. Only with solution F was absorption of energy significantly reduced.

energy absorption exhibited saturation kinetics (Table 3). Despite large differences in the nutrient composition of the perfusion solutions, V_{\max} of energy per unit length of jejunum did not differ among the nutrient solutions with the exception of solution F (60% fat), at which maximal absorption was reduced (Fig. 1). Only the solution rich (60%) in fat resulted in a significantly lower jejunal capacity for absorption of energy. Due to the saturation kinetics, the amounts of energy remaining unabsorbed during the transit along the jejunal segment increased markedly with increasing energy load. Figure 2 illustrates the large amounts of energy remaining unabsorbed during perfusion of the jejunal segment with solution E.

Gastric Emptying and Jejunal Flow of Energy

After administration of the different meals containing 60% of energy either as carbohydrate, protein, fat, or equal amounts of each nutrient, the gastric emptying rates of energy were 1.75 ± 0.38 , 1.80 ± 0.62 , 1.63 ± 0.30 , and 1.56 ± 0.60 kcal/min, respectively (Table 4). Despite large differences in meal composition, the gastric emptying rates of energy were not significantly different. The mean gastric emptying rate of energy was 1.7 ± 0.48 kcal/min. Additionally, the flow of

energy into the proximal jejunum was also not significantly different among the four meals (Table 4). The mean energy flow to the proximal jejunum was 1.3 ± 0.41 kcal/min.

Intestinal Absorption of Energy After Meals

Experiment 1 provided data on the kinetics of jejunal absorption of energy, and experiment 2 provided data on the physiological jejunal flow of energy after meals. Based on these data, the amounts of energy that would be absorbed per unit length of jejunum and the amounts of energy that would remain unabsorbed per unit length were calculated after oral administration of the four meals. Additionally, the lengths of the small intestine that would be required for complete absorption of energy were also calculated (Table 4). Figure 3 illustrates that the amounts of energy entering the proximal jejunum after the four meals provided for only

Table 3. Parameters of Michaelis-Menten kinetics determined during perfusion of jejunal segment with different nutrient solutions

Solution	Kinetics of Energy Absorption = $V_{\max} \cdot S / (K_m + S)$			Statistics of V_{\max}	
	V_{\max} , kcal· min ⁻¹ ·m ⁻¹	K_m , kcal/min	r^2	P of curve fit	Solution P of V_{\max}
C	0.94 ± 0.03	1.10 ± 0.11	0.987	<0.001*	C vs. P 0.532
P	0.97 ± 0.06	1.13 ± 0.11	0.982	<0.001*	C vs. F 0.005†
F	0.66 ± 0.13	0.80 ± 0.12	0.907	<0.010*	P vs. F 0.003†
E	0.94 ± 0.02	0.79 ± 0.13	0.958	<0.010*	E vs. C 0.926 E vs. P 0.234 E vs. F 0.001†

Values for maximal absorption (V_{\max}) and Michaelis-Menten constant (K_m) are means \pm SE. S, caloric load. *Significant curve fit (*t*-statistic); † significant differences between solutions (ANOVA).

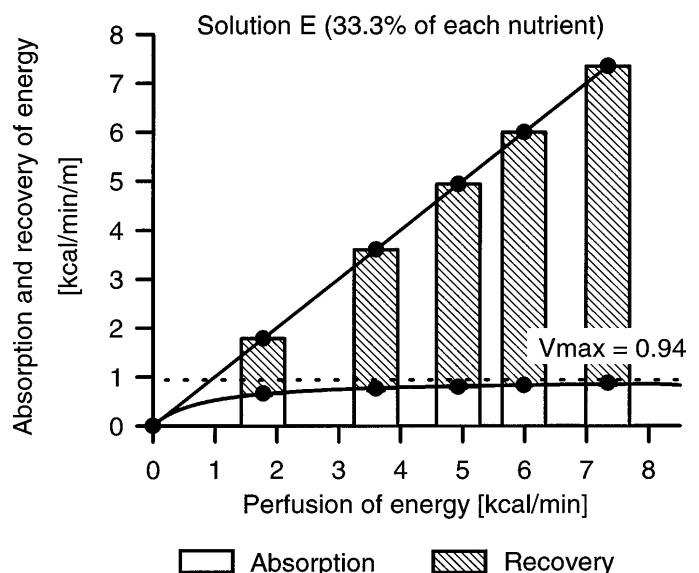


Fig. 2. With increasing energy load of jejunal segment, amounts of energy remaining unabsorbed increased markedly due to saturation kinetics of absorption.

Table 4. Gastric emptying, energy flow, and absorption of energy in proximal jejunum after different meals

Meal	Gastric Emptying, kcal/min	Energy Flow to Jejunum, kcal/min	Absorption of Energy/m Jejunum			Length of Small Intestine Required for Complete Absorption		
			kcal · min ⁻¹ · m ⁻¹	% of V _{max}	Reserve capacity, fc	m	% of Gut length	Reserve capacity, fl
C	1.75 ± 0.38	1.35 ± 0.33	0.55 ± 0.04	58.1	1.7	4.3 ± 0.3	43.8	2.3
P	1.80 ± 0.62	1.37 ± 0.39	0.53 ± 0.09	54.8	1.8	4.2 ± 0.3	43.5	2.3
F	1.63 ± 0.30	1.21 ± 0.38	0.40 ± 0.08	60.6	1.7	4.6 ± 0.4	47.3	2.1
E	1.56 ± 0.60	1.38 ± 0.54	0.58 ± 0.10	61.7	1.6	3.6 ± 0.5	37.0	2.7
Mean	1.69 ± 0.48	1.33 ± 0.41	0.52 ± 0.08	58.8	1.7	4.2 ± 0.4	42.9	2.4

Values for gastric emptying, energy flow to jejunum, absorption of energy/m jejunum in kcal · min⁻¹ · m⁻¹, and length of small intestine in m are means ± SD. fc, V_{max}/absorption of energy; fl, total length/required length.

submaximal absorption rates. The absorption of energy after meals C, P, F, and E reached only 58.1, 54.8, 60.6, and 61.7% of the jejunal capacity for absorption per unit length, respectively (Table 4). Therefore, in relation to the postprandial energy load, the jejunum had a 1.7-fold reserve capacity for absorption of energy. Furthermore, the calculated length of the small intestine that would be required for complete absorption of energy after meals C, P, F, and E were 4.3, 4.2, 4.6, and 3.6 m, respectively. In relation to the whole length of the small intestine of 9.7 ± 1.1 m, the intestinal lengths that would be required for complete absorption of energy were only 43.8, 43.5, 47.3, and 37.0%, respectively; i.e., there was a 2.4-fold reserve in intestinal length (Table 4). These results indicate that the small intestine has at least two types of reserve capacities: a reserve capacity for absorption and a reserve in intestinal length.

DISCUSSION

Results of the present study show four major findings. 1) Gastric emptying of energy and the energy flow into the proximal jejunum are independent of meal composition, 2) jejunal absorption of energy demonstrates saturation kinetics despite large variations in luminal composition of nutrients, 3) the jejunal capacity for absorption per unit length is larger than the postprandial energy load, and 4) only parts of the small intestine are required for complete absorption; i.e., the feedback regulation of gastric emptying provides reserve capacities for both absorption and intestinal length.

Gastric emptying is regulated by a feedback mechanism. It is evoked from all parts of the small intestine and by all kinds of nutrients. It was recently shown that the feedback inhibition depends on the intestinal load of nutrients and, additionally, on the intestinal length (19, 20). Hunt (12) and Hunt and Stubbs (13) were the first to postulate that the delivery of energy is the major determinant in the feedback control of gastric emptying. This hypothesis was confirmed by several investigations (22, 23, 37). Our present results show that the delivery of calories into the gut remains constant despite large variations in the nutrient composition of the meals. The nutrient composition of the jejunal chyme corresponded to that of the meal (39). Therefore, it could be excluded that in the stomach a separation of the nutrients occurred and that the nutrients emptied at different rates. The chyme delivered from the stomach into the small intestine was drained from the proximal cannula and returned via the distal cannula. Thus a length of 2.65 m was bypassed. It is unlikely that this procedure affected the feedback mechanism for several reasons. First, Lin and co-workers (19, 20) demonstrated in dogs that maximal feedback inhibition of gastric emptying occurred when the chyme was in contact with at least 50% of the small intestine. In minipigs, the small intestine is extremely long. In the present study, >70% of the small intestine remained in contact with the postprandial chyme. Second, there were no differences in gastric emptying when the length of the bypassed segment varied between 1 m and 2.65 m. Third, a previous study in minipigs showed that infusion of nutrients into the

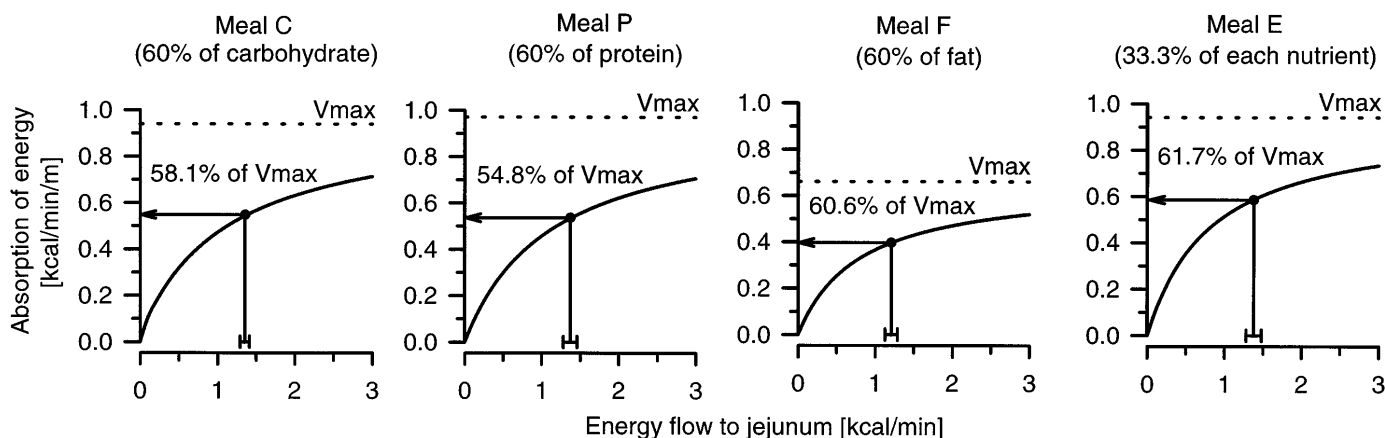


Fig. 3. Only 55–62% jejunal capacity for absorption of energy after 4 different meals was used.

midgut induced a pronounced feedback regulation (11). Therefore, it is likely that the intestinal length beyond the distal cannula was sufficient to induce a normal feedback control of gastric emptying.

Previous studies already investigated kinetics of intestinal absorption (9, 10, 24, 30). However, in most of these studies, isotonic solutions of glucose or amino acids were used. In the present study, we investigated for the first time absorption kinetics during perfusion of complex enteral diets containing carbohydrate, protein, and fat in various compositions. Saturation in energy absorption was found with all the nutrient solutions. Even during perfusion of a solution containing 60% of energy as fat, absorption of energy exhibited saturation kinetics.

The jejunal capacity for absorption of energy per unit length was not significantly different among solutions containing 60% of energy either as carbohydrate or protein or containing 33.3% of each nutrient. Only with the solution containing 60% of energy as fat was the jejunal capacity for absorption per unit length significantly less in comparison with the other solutions.

The postprandial flow of energy after the different meals provided a mean absorption rate of only 59% of the intestinal capacity for absorption. This result showed that intestinal feedback control did not adjust gastric emptying and the jejunal flow of energy to the absorption capacity of the small intestine. Several observations in our study indicated why it might be necessary for the gastric delivery of energy to be less than the jejunal capacity for absorption. Maximal absorption of energy occurred only at large caloric loads of the intestinal segment. Under this condition, large amounts of energy remained unabsorbed at the end of the jejunal segment due to the saturation kinetics of absorption. Consequently, considerable amounts of energy would be delivered distally and would not be absorbed up to the ileum. Furthermore, the absorption at a submaximal level of the kinetic contributes to a constant absorption of energy independent of the nutrient composition of meals in that an increase of a single nutrient would inevitably result in an enhanced absorption of this nutrient.

Besides the reserves in jejunal capacity for absorption per unit length, the feedback control of gastric emptying provided reserves in total length available for absorption. This finding is in agreement with results of previous studies (1, 14). However, it must be mentioned that in all these studies, the meals consisted of nutrients that could be easily digested and absorbed. In contrast to these observations, studies on both human (18, 21, 25, 34) and animal nutrition (3, 17) showed that under normal feeding conditions considerable amounts of nutrients enter the ileum, depending on the digestibility. Therefore, reserves in length of the small intestine are an essential feature to secure digestion and absorption of nutrients even of low digestibility.

The question arises as to whether the reserve capacities for absorption and in intestinal length are available to enhance energy uptake. Studies on enteral nutrition in dogs showed that an increased energy

infusion into the jejunum (1.5-fold of the physiological energy flow) caused a marked inhibition of intestinal motility and produced retrograde power contractions and vomiting after a period of 3.6 h (32). Although the energy load was in the range of the absorption capacity of the small intestine, it was not tolerated. These findings indicate that a balance between the delivery of energy, digestion, the resulting osmolality, and the absorption of nutrients is required to avoid intestinal sequelae. If the rate of digestion of nutrients exceeds the rate of absorption, luminal osmolality will increase, and, consequently, an enhanced secretion of water might result in symptoms referred to as the dumping syndrome. It is likely that the feedback inhibition of gastric emptying is adjusted to the complex events that are associated with intestinal digestion and absorption. Therefore, during enteral nutrition, the reserve capacities of intestinal absorption are not available to enhance energy uptake.

A further reserve capacity to provide increase in the daily energy uptake under normal conditions exists in time. Calculations based on the emptying rate of energy indicated that, in pigs, the digestive period required for the daily energy supply lasted ~18 h. In dogs, the digestive period lasts ~12 h (4). In humans, data on the emptying rate of energy (2, 29, 38) and on the occurrence of interdigestive motor cycles during 24 h (15) indicate that digestion of nutrients requires between 12 and 18 h per day. Therefore, the energy uptake can be increased by a prolongation of the digestive period at the expense of the interdigestive period. This reserve in time provides a 1.5- to 2-fold increase in the intestinal capacities for digestion and absorption that are always and immediately available. The interdigestive period is usually used to clean the stomach and small intestine and to avoid bacterial overgrowth. However, a prolongation of the digestive period might not produce sequelae. First, during a continuous energy supply, the migrating motor complexes will recur in dogs (7) and humans (40), as in pigs (16, 28, 31), despite a digestive period. Second, an enhanced energy uptake will increase absorption within a few days due to adaptive mechanisms (36).

In the literature, a discrepancy exists as to the physiological reserve capacities of the gut. Pappenheimer (26, 27) supposed that glucose and amino acids are mainly absorbed by passive diffusion and that the reserve capacities for absorption are therefore 20–30 times larger than the daily requirement. In contrast, Diamond and Hammond (5) and Ferraris et al. (8) postulated that absorption of glucose and amino acids is mainly caused by carrier-mediated active transport. Therefore, the intestinal uptake of these nutrients is limited. *In vitro* studies (6, 8) showed that the calculated capacity for intestinal brush-border uptake was about two times that of the daily requirement. *In vivo* studies in mice showed that the energy uptake increased 2.5-fold under stress conditions induced by cold exposure (5, 36). Therefore, the authors conclude that the intestinal capacity for absorption exceeds the dietary load by a factor of two. This relatively small reserve capacity serves as a safety margin and is

economical compared with the enormously large reserve capacity assumed by other authors. These studies, however, did not differentiate between the several types of intestinal reserve capacities. The experimental conditions of the previous study (36) indicate that the short-term increase in the uptake of nutrients by cold exposure might be caused mainly by a prolongation of the digestive period.

The present results show that there are at least three types of intestinal reserve capacities: a reserve in absorption, a reserve in intestinal length, and a reserve in time. All these reserve capacities have a factor of about two. Although the reserves in absorption and intestinal length are not disposable, energy uptake can be enhanced by the reserves in time because digestion and absorption of the normal daily requirements only need 12–18 h.

Perspectives

Since the fundamental studies on gastric emptying of Hunt and Stubbs (13) in the seventies, a large number of papers were published and the knowledge on the control of gastric emptying has increased greatly. Studies on intestinal feedback regulation showed that luminal nutrients elicit not only a duodenal brake, as emphasized by the earlier investigators, but also a jejunal and an ileal brake. Additionally, studies on intestinal absorption of single nutrients revealed a participation of carrier-mediated events. There is evidence that the regulation of gastric emptying provides a constant delivery of energy into the gut, although no “energy receptors” have been found. The question arises as to whether there is a link between the energy-related feedback inhibition and the intestinal absorption of nutrients. However, despite detailed information on intestinal epithelial transport mechanisms, little is known about the interrelationship between the control of gastric emptying and intestinal absorption. Previous studies have postulated that the energy metabolism of enterocytes might limit intestinal absorption of nutrients. Further investigations should focus on the role of the energy metabolism of enterocytes in regulating intestinal absorption and intestinal feedback control. It should also be considered that the metabolism of the liver and of other tissues might be a limiting factor for the daily energy intake and therefore might be involved in the regulation of intestinal absorption. Detailed information on the multiple factors involved in absorption and in metabolic processes and their limits will offer a more complex picture of intestinal and metabolic control mechanisms.

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REFERENCES

1. **Borgström, B., A. Dahlqvist, G. Lundh, and J. Sjövall.** Studies of intestinal digestion and absorption in the human. *J. Clin. Invest.* 36: 1521–1536, 1957.
2. **Collins, P. J., M. Horowitz, A. Maddox, J. C. Myers, and B. E. Chatterton.** Effects of increasing solid component size of a mixed solid/liquid meal on solid and liquid gastric emptying. *Am. J. Physiol.* 271 (*Gastrointest. Liver Physiol.* 34): G549–G554, 1996.
3. **Darcy, B., J. P. Laplace, and P. A. Villiers.** Digestion in the pig small intestine. 4. Kinetics of the passage of digesta at the ileo-caeco-colic junction and digestion balances according to the dietary starch and protein. *Ann. Zootech. (Paris)* 30: 31–62, 1981.
4. **De Wever, I., C. Eeckhout, G. Vantrappen, and J. Hellems.** Disruptive effect of test meals on interdigestive motor complex in dogs. *Am. J. Physiol.* 235 (*Endocrinol. Metab. Gastrointest. Physiol.* 4): E661–E665, 1978.
5. **Diamond, J., and K. Hammond.** The matches, achieved by natural selection, between biological capacities and their natural loads. *Experientia* 48: 551–557, 1992.
6. **Diamond, J. M., and W. H. Karasov.** Effect of dietary carbohydrate on monosaccharide uptake by mouse small intestine in vitro. *J. Physiol. (Lond.)* 349: 419–440, 1984.
7. **Felder, G., F. Crenner, and J.-F. Grenier.** Motricité intestinale et nutrition entérale continue: étude électromyographique chez le chien. *Gastroenterol. Clin. Biol.* 8: 599–603, 1984.
8. **Ferraris, R. P., and J. M. Diamond.** Specific regulation of intestinal nutrient transporters by their dietary substrates. *Annu. Rev. Physiol.* 51: 125–141, 1989.
9. **Hegarty, J. E., P. D. Fairclough, K. J. Moriarty, M. J. Kelly, and M. L. Clark.** Effects of concentration on in vivo absorption of a peptide containing protein hydrolysate. *Gut* 23: 304–309, 1982.
10. **Holdsworth, C. D., and A. M. Dawson.** The absorption of monosaccharides in man. *Clin. Sci. (Colch.)* 27: 371–379, 1964.
11. **Huge, A., E. Weber, and H. J. Ehrlein.** Effects of enteral feedback inhibition on motility, luminal flow, and absorption of nutrients in proximal gut of minipigs. *Dig. Dis. Sci.* 40: 1024–1034, 1995.
12. **Hunt, J. N.** Mechanisms and disorders of gastric emptying. *Annu. Rev. Med.* 34: 219–230, 1983.
13. **Hunt, J. N., and D. F. Stubbs.** The volume and energy content of meals as determinants of gastric emptying. *J. Physiol. (Lond.)* 245: 209–226, 1975.
14. **Johansson, C.** Studies of gastrointestinal interactions. *Scand. J. Gastroenterol.* 9, Suppl. 28: 1–60, 1974.
15. **Kellow, J. E., R. C. Gill, and D. L. Wingate.** Prolonged ambulant recordings of small bowel motility demonstrate abnormalities in the irritable bowel syndrome. *Gastroenterology* 98: 1208–1218, 1990.
16. **Laplace, J. P.** Organisation de la motricité de l'intestin grêle chez le porc et influence de l'alimentation. *Ann. Zootech. (Paris)* 27: 377–408, 1978.
17. **Laplace, J. P., B. Darcy, and O. Pons.** Digestion in the pig small-intestine. 5. Importance of the uncontrolled sources of variance—modelization of mean curves of passage at the ileo-ceco-colic junction using polynomial. *Ann. Zootech. (Paris)* 32: 201–213, 1983.
18. **Levitt, M. D.** Malabsorption of starch: a normal phenomenon. *Gastroenterology* 85: 769–770, 1983.
19. **Lin, H. C., J. E. Doty, T. J. Reedy, and J. H. Meyer.** Inhibition of gastric emptying by glucose depends on length of intestine. *Am. J. Physiol.* 256 (*Gastrointest. Liver Physiol.* 19): G404–G412, 1989.
20. **Lin, H. C., J. E. Doty, T. J. Reedy, and J. H. Meyer.** Inhibition of gastric emptying by sodium oleate depends on length of intestine exposed to nutrient. *Am. J. Physiol.* 259 (*Gastrointest. Liver Physiol.* 22): G1031–G1036, 1990.
21. **Livesey, G., J. A. Wilkinson, M. Roe, R. Faulks, S. Clark, J. C. Brown, H. Kennedy, and M. Elia.** Influence of the physical form of barley grain on the digestion of its starch in the human small intestine and implications for health. *Am. J. Clin. Nutr.* 61: 75–81, 1995.

22. **McHugh, P. R., and T. H. Moran.** Calories and gastric emptying: a regulatory capacity with implications for feeding. *Am. J. Physiol.* 236 (*Regulatory Integrative Comp. Physiol.* 5): R254–R260, 1979.
23. **Miller, L. J., J. R. Malagelada, W. F. Taylor, and V. L. W. Go.** Intestinal control of human postprandial gastric function. The role of components of jejunoileal chyme in regulating gastric secretion and gastric emptying. *Gastroenterology* 80: 763–769, 1981.
24. **Modigliani, R., and J. J. Bernier.** Absorption of glucose, sodium and water by the human jejunum studied by intestinal perfusion with a proximal occluding balloon and at variable flow rates. *Gut* 12: 184–193, 1971.
25. **Muir, J. G., A. Birkett, I. Brown, G. Jones, and K. O'Dea.** Food processing and maize variety affects amounts of starch escaping digestion in the small intestine. *Am. J. Clin. Nutr.* 61: 82–89, 1995.
26. **Pappenheimer, J. R.** Paracellular intestinal absorption of glucose, creatinine, and mannitol in normal animals: relation to body size. *Am. J. Physiol.* 259 (*Gastrointest. Liver Physiol.* 22): G290–G299, 1990.
27. **Pappenheimer, J. R.** On the coupling of membrane digestion with intestinal absorption of sugars and amino acids. *Am. J. Physiol.* 265 (*Gastrointest. Liver Physiol.* 28): G409–G417, 1993.
28. **Rayner, V., and G. Wenham.** Small intestinal motility and transit by electromyography and radiology in the fasted and fed pig. *J. Physiol. (Lond.)* 379: 245–256, 1986.
29. **Read, N. W., M. N. Al-Janabi, A. M. Holgate, D. C. Barber, and C. A. Edwards.** Simultaneous measurement of gastric emptying, small bowel residence and colonic filling of a solid meal by the use of the gamma camera. *Gut* 27: 300–308, 1986.
30. **Rey, F., F. Drillet, J. Schmitz, and J. Rey.** Influence of the flow rate on the kinetics of intestinal absorption of glucose and lysine in children. *Gastroenterology* 66: 79–85, 1974.
31. **Ruckebusch, Y., and L. Bueno.** The effect of feeding on the motility of the stomach and small intestine in the pig. *Br. J. Nutr.* 35: 397–405, 1976.
32. **Schmid, H. R., H. J. Ehrlein, and C. Feinle.** Effects of enteral infusion of nutrients on canine intestinal motor-patterns. *J. Gastrointest. Motil.* 4: 279–292, 1992.
33. **Siegle, M. L., H. R. Schmid, and H. J. Ehrlein.** Effects of ileal infusions of nutrients on motor patterns of canine small intestine. *Am. J. Physiol.* 259 (*Gastrointest. Liver Physiol.* 22): G78–G85, 1990.
34. **Silvester, K. R., H. N. Englyst, and J. H. Cummings.** Ileal recovery of starch from whole diets containing resistant starch measured in vitro and fermentation of ileal effluent. *Am. J. Clin. Nutr.* 62: 403–411, 1995.
35. **Spiller, R. C., I. F. Trotman, B. E. Higgins, M. A. Ghatei, G. K. Grimble, Y. C. Lee, and S. R. Bloom.** The ileal brake-inhibition of jejunal motility after ileal fat perfusion in man. *Gut* 25: 365–374, 1984.
36. **Toloza, E. M., M. Lam, and J. Diamond.** Nutrient extraction by cold-exposed mice: a test of digestive safety margins. *Am. J. Physiol.* 261 (*Gastrointest. Liver Physiol.* 24): G608–G620, 1991.
37. **Velchik, M. G., J. C. Reynolds, and A. Alavi.** The effect of meal energy content on gastric emptying. *J. Nucl. Med.* 30: 1106–1110, 1989.
38. **Vidon, N., P. Sogni, S. Chaussade, B. Huchet, and J. J. Bernier.** Gastrointestinal and biliopancreatic response to continuous nasogastric feeding in man: effect of increasing nutrient infusion rate. *Clin. Nutr. (Edinb.)* 13: 307–313, 1994.
39. **Weber, E.** *Beziehungen zwischen der Magenentleerung von Nährstoffen und der Resorptionskapazität des Dünndarms beim Schwein* (PhD dissertation). Marburg, Germany: Tectum, 1996, p. 1–140.
40. **Wienbeck, M.** Influence of enteral nutrition on gastrointestinal motility. In: *Enteral Nutrition in Surgery—Fashion or Progress?*, edited by B. Viell, K. H. Vestweber, and H. Troidl. Cologne, Germany: Eul, 1987, p. 119–124.