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⁻²·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⁻²·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).

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/kg⁰.⁷⁵).

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; Ceres, 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 (Lipoveno ¨s 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 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:

\[
\text{absorption}_{\text{energy}} = \frac{\text{energy}_{\text{infused}} - \text{energy}_{\text{effluent}}}{\text{marker}_{\text{infused}}} - \frac{\text{marker}_{\text{effluent}}}{\text{absorption}}
\]

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

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/l,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>
<thead>
<tr>
<th>Table 1. Composition of perfusion solutions</th>
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<tbody>
<tr>
<td>Solution</td>
</tr>
<tr>
<td>----------</td>
</tr>
<tr>
<td>C</td>
</tr>
<tr>
<td>P</td>
</tr>
<tr>
<td>F</td>
</tr>
<tr>
<td>E</td>
</tr>
</tbody>
</table>

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.
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Table 2. Composition of meals

<table>
<thead>
<tr>
<th>Meal</th>
<th>Amounts of Nutrients, g/l</th>
<th>Calories From Nutrients, kcal/l</th>
<th>Ratio of Nutrients, %</th>
<th>Electrolytes, mg/l</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Carb</td>
<td>Protein</td>
<td>Fat</td>
<td>Carb</td>
</tr>
<tr>
<td>C</td>
<td>142.8</td>
<td>36.9</td>
<td>21.9</td>
<td>600.0</td>
</tr>
<tr>
<td>P</td>
<td>47.6</td>
<td>110.7</td>
<td>21.9</td>
<td>600.0</td>
</tr>
<tr>
<td>F</td>
<td>47.6</td>
<td>36.9</td>
<td>65.7</td>
<td>200.0</td>
</tr>
<tr>
<td>E</td>
<td>79.4</td>
<td>61.5</td>
<td>36.5</td>
<td>333.3</td>
</tr>
</tbody>
</table>

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.

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energy absorption exhibited saturation kinetics (Table 3). Despite large differences in the nutrient composition of the perfusion solutions, $V_{\text{max}}$ 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 $1.75 \pm 0.38, 1.80 \pm 0.62, 1.63 \pm 0.30,$ and $1.56 \pm 0.60 \text{ kcal/min},$ 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 $1.7 \pm 0.48 \text{ kcal/min}.$ 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 $1.3 \pm 0.41 \text{ kcal/min}.$

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

<table>
<thead>
<tr>
<th>Solution</th>
<th>$V_{\text{max}}$</th>
<th>$K_m$</th>
<th>$r^2$</th>
<th>$t$-statistic</th>
<th>$P$-value</th>
<th>$V_{\text{max}}$</th>
<th>$K_m$</th>
<th>$r^2$</th>
<th>$t$-statistic</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>0.94 $\pm$ 0.03</td>
<td>1.10 $\pm$ 0.11</td>
<td>0.987</td>
<td>$&lt;0.001^*$</td>
<td>C vs. P</td>
<td>0.532</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P</td>
<td>0.97 $\pm$ 0.06</td>
<td>1.13 $\pm$ 0.11</td>
<td>0.982</td>
<td>$&lt;0.001^*$</td>
<td>C vs. F</td>
<td>0.005†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>0.66 $\pm$ 0.13</td>
<td>0.80 $\pm$ 0.12</td>
<td>0.907</td>
<td>$&lt;0.010^*$</td>
<td>P vs. F</td>
<td>0.003†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>0.94 $\pm$ 0.02</td>
<td>0.79 $\pm$ 0.13</td>
<td>0.958</td>
<td>$&lt;0.010^*$</td>
<td>E vs. C</td>
<td>0.926</td>
<td></td>
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</tr>
</tbody>
</table>

Values for maximal absorption ($V_{\text{max}}$) and Michaelis-Menten constant ($K_m$) are means $\pm$ SE. $S,$ caloric load. *Significant curve fit ($t$-statistic); †significant differences between solutions (ANOVA).
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 were 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 proximal jejunum increased gastric emptying at a rate proportional to the amount of nutrients infused (39).
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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