Satiety from fat? Adverse effects of intestinal infusion of sodium oleate

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Ramirez, Israel, Michael G. Tordoff, and Mark I. Friedman. Satiety from fat? Adverse effects of intestinal infusion of sodium oleate. Am. J. Physiol. 273 (Regulatory Integrative Comp. Physiol. 42): R1779–R1785, 1997.—To determine whether damage to the intestinal mucosa by oleic acid causes the suppression of food intake observed in response to intraintestinal infusion of the fatty acid, we measured lactate dehydrogenase (LDH) activity, a marker for cell damage, in the intestinal lumen after intestinal infusion of fatty acid under conditions similar to those employed in studies of eating behavior. Infusions of 25 or 51 mM sodium oleate (neutralized oleic acid) markedly and rapidly increased LDH activity, whereas infusions of saline had little or no effect. Infusion of octanoate, which has been reported to be ineffective in reducing eating behavior, did not increase intestinal LDH activity relative to saline infusion. Similarly, infusion of ethyl oleate or free (nonneutralized) oleic acid neither increased luminal LDH activity nor suppressed food intake. Infusion of sodium oleate also produced a strong conditioned aversion to sucrose. The results strongly suggest that the suppression of food intake induced by intraintestinal infusion of sodium oleate is due to the injurious effects of this unphysiological form of the fatty acid.

Intraintestinal infusions of carbohydrates, fats, and proteins suppress ingestive behavior in rats under a variety of conditions. The rapid and marked suppression of eating behavior in rats during intraintestinal infusion of triglyceride has been used as evidence that an intestinal mechanism underlies the satiety from fat (e.g., 5, 6, 16, 21, 23, 24). However, ingestion of triglyceride has little, if any, immediate effect on subsequent food intake of rats (see Ref. 7). This finding, together with measurements of gastric emptying of ingested fat (3), indicates that the suppression of intake observed in response to intraintestinal infusion of triglyceride may be due to an inappropriate rate of delivery of an unphysiological form of fat into the intestine (3).

Intraintestinal infusion of sodium oleate also reduces ingestive behavior of rats; however, it is possible that infusion of fatty acids, like that of triglycerides, suppresses eating behavior through an abnormal mechanism of satiety. Prolonged infusion of sodium oleate into the intestine of anesthetized rats, rabbits, and infant pigs damages the intestinal mucosa (4, 8, 18–20). Such injury is characterized by severe disruption of intestinal villi membranes and increased permeability of the intestine to large molecules (4, 8, 18–20). In the present experiments, we sought to determine whether adverse effects on the intestine account for the suppression of food intake produced by intraintestinal infusion of sodium oleate. To accomplish this, we examined the effects of oleic acid infusions on intestinal integrity in anesthetized and conscious rats using infusions rates, fatty acid concentrations, and a form of oleic acid (sodium oleate) typically employed in studies of the behavioral effects of oleic acid infusion. The relationship between intestinal damage and the suppression of eating behavior was also examined by manipulating the type or form of fatty acid infused and by determining whether infusion of sodium oleate, which reduces food intake, also produces a learned taste aversion. The results strongly suggest that the suppression of food intake in response to intraintestinal infusion of sodium oleate is due to adverse effects of the infusion on the intestine.

METHODS

Animals. Male CD rats (Crl:CDBR, Charles River Breeding Laboratories, Wilmington, MA), ~8 wk of age on arrival into the laboratory, were housed individually in hanging stainless steel cages, maintained on a 12:12-h light-dark cycle at 21–24°C, and given Purina Laboratory Chow (no. 5001) and water ad libitum except where indicated otherwise. Rats were maintained in the laboratory for at least 1 wk after arrival to acclimate them to their surroundings before surgery or testing.

Infusates. A peristaltic pump was used for perfusions and infusions. Sodium oleate was prepared by neutralizing oleic acid with NaOH and HCl to a pH of 7.2–7.4 and adjusting the osmotic pressure to 300 mosM with NaCl. No alkali was used in the preparation of free oleic acid. All other infusates were adjusted to an osmotic pressure of 300 mosM with NaCl and to a pH of 7.2–7.4 with NaOH and HCl. Infusates containing fatty acids were unstable and were therefore agitated continuously with a magnetic stir bar during infusion. Oleic acid, having a purity of 95%, from Sigma Chemical (St. Louis, MO) was used in all experiments except the first, which employed oleic acid from Fisher Scientific (Pittsburgh, PA). Intralipid (10%), a stable triglyceride emulsion, was diluted with 0.9% NaCl. All other chemicals were reagent grade and were obtained from Sigma.

Intestinal perfusion. Rats were food deprived overnight and anesthetized with ketamine (90 mg/kg) and acepromazine (1 mg/kg). Through a midline abdominal incision, a silicone catheter (2 mm OD) was inserted from the stomach through the pylorus into the duodenum and fastened with silk thread. Another catheter was inserted into the jejunum 7 cm beyond the ligament of Treitz and fastened with silk thread. Rats were kept on a warm (36°C) surface during the experiment, and exposed intestine was covered with a paper towel soaked in isotonic saline.

In four groups of rats (n = 7) intestines were perfused for 12 min (0.5 ml/min) via the pyloric catheter with isotonic saline, 51 mM sodium oleate, an equal weight of triglyceride in the form of Intralipid (1.4%), or a mixture of 51 mM sodium oleate and 1.4% Intralipid. Immediately afterward, all groups were perfused with isotonic saline for an additional 6 min. Samples of the perfusate were collected from the jejunal catheter every 3 min from the start of perfusion and assayed for lactate dehydrogenase (LDH). After the last sample was
collected (at 18 min), the perfusion was terminated, the jejunal catheter was closed, and 1 ml of 3% Evans blue was rapidly injected into the intestine via the pyloric catheter. Blood samples were taken from the tail 10 and 20 min after injection of dye, and plasma was assayed for Evans blue.

Intestinal catheterization. Chronically implanted intraduodenal catheters were used for infusion and for sampling intestinal contents. Catheters, made of silicone rubber (1 mm OD), were inserted into the duodenum through a small hole placed in the stomach ~1 cm from the pylorus and threaded ~4 cm into the intestine. Catheters were sutured to both the stomach and abdominal wall, but not to the duodenum, and were threaded under the skin to exit through an incision in the back of the neck. During surgery, rats were anesthetized with ketamine (90 mg/kg) and acepromazine (1 mg/kg), supplemented with ether as needed. After surgery, the animals were allowed to recover for at least 8 days after surgery before they were tested. Catheter placement was verified at the end of each experiment.

Sampling of intestinal contents. Rats with chronically implanted intestinal catheters were deprived of food overnight and then confined to a plastic cylinder that allowed freedom of movement. Rats were connected to the infusion pump, infused via the intestinal catheter for 10 min at 1 ml/min, and then disconnected. At various time points thereafter, rats were gently held by hand while a syringe was inserted into the catheter, and 0.1–0.4 ml was withdrawn after, rats were gently held by hand while a syringe was inserted into the catheter, and 0.1–0.4 ml was withdrawn from the intestine. For experiments using a within-subject design in which rats were tested more than once, infusions were made no more often than twice weekly.

Food intake tests. Two experiments examined the effects of fatty acid infusions on food intake after an overnight fast. Rats were habituated to the food deprivation schedule by depriving them of food overnight on Sunday, Tuesday, and Thursday and refeeding them the following day. Food intake tests began after four to six such habituation trials and were separated by 3- to 4-day rest periods. In each test, the rats were infused in their home cage for 10 min at a rate of 1 ml/min and then offered food. Food intakes were measured to the nearest 0.1 g (corrected for spillage) at various intervals thereafter.

Learned taste aversion test. To ascertain whether sodium oleate infusions induce malaise, a learned taste aversion test was conducted using intestinal infusion of sodium oleate as the unconditioned stimulus. In this test, rats were given a novel fluid to drink, infused with either saline or sodium oleate, and then offered a choice of the novel and a familiar fluid to drink. Rats were first familiarized with 10% maltodextrin (Maltin M200, Grain Products, Muscatine, IA) by providing it ad libitum on two occasions before the intestinal catheters were implanted. Ten days after surgery, rats were deprived of food for 24 h, allowed to drink 10% maltodextrin for 30 min at the beginning of the dark period, and then refed overnight beginning 90 min later. This procedure was repeated on three subsequent occasions except that access to maltodextrin was gradually reduced to 15 min. On the training day, all rats were offered 10% sucrose solution instead of maltodextrin to drink for 15 min and were then infused with either isotonie saline (n = 8) or 51 mM sodium oleate (n = 7). Rats were then given three more trials with maltodextrin and, on the final trial, were given a choice of 10% sucrose vs. 10% maltodextrin for 15 min. Intakes of the two solutions were measured at the end of the 15-min access period.

Assays. LDH activity was measured enzymatically using a commercial kit (Sigma) to assess mucosal cell damage (2, 11, 13, 14). Samples (10 µl) of perfusate or intestinal contents were assayed immediately after collection because pilot tests indicated that activity declined with storage. Evans blue in plasma was assayed fluorometrically according to a previously published method (9, 12).

Statistics. All group data are given as means ± SE. Group comparisons were made using analysis of variance. Individual t-tests were computed and reported here only if the overall analysis of variance produced a P < 0.05 (this is equivalent to a Fisher’s least-significant difference test except that variances were not pooled). All probability values are two-tailed.

**RESULTS**

Intestinal perfusion of sodium oleate and Intralipid. Previous studies (4, 8, 18–20) have shown that prolonged infusion of sodium oleate or oleic acid into the intestine of anesthetized rats and other animals produces damage to the intestinal mucosa. In this experiment, we examined the immediate effects of a short-term infusion of sodium oleate at a concentration and pH commonly used in experiments on feeding behavior.

Intestinal perfusion of sodium oleate (51 mM) in anesthetized rats increased LDH activity in the intestinal lumen within 3 min above levels seen during perfusion of saline ($t(12) = 2.8, P = 0.02; Fig. 1$). This was the earliest that the perfusate was sampled and was only slightly longer than the time it took for the perfusate to travel from the pylorus to the outflow catheter in the jejunum (2–2.75 min). LDH activity in the perfusate of rats given sodium oleate remained elevated throughout the test, even during the final 6 min when saline was infused. The opacity of the Intralipid solution interfered with measurement of LDH. When the Intralipid had been flushed out during saline infusion, LDH activity in the intestinal perfus-
ate from rats given Intralipid alone was identical to that from controls at 15 min (P = 0.19) and was slightly, but significantly, higher than that from saline controls at 18 min (t(12) = 2.5, P = 0.03). LDH activity in the perfusate of rats infused with a mixture of sodium oleate and Intralipid was comparable with that seen in rats infused with sodium oleate alone, suggesting that Intralipid neither interfered with nor prevented the detection of a change in LDH activity.

Both groups of rats infused with sodium oleate had substantially more Evans blue in their plasma 10 and 20 min after the dye was injected into the intestinal lumen than did the control group or the group infused with Intralipid only (P ≤ 0.005; Fig. 2).

Intestinal infusion of sodium oleate in conscious rats. This experiment investigated the effects of intraintestinal infusion of sodium oleate on intestinal LDH activity in conscious rats under conditions similar to those used to assess the effects of sodium oleate on eating behavior. Three groups of rats (n = 6–7) with previously implanted intestinal catheters were infused with isotonic saline or 25 or 51 mM sodium oleate. Samples of intestinal contents were collected at 0–1, 3–4, and 6–7 min after the end of the 10-min infusion and analyzed for LDH activity.

LDH activity in intestinal contents was significantly higher in rats infused with either concentration of sodium oleate than in rats infused with saline 0.5, 3.5, and 6.5 min after infusion (all P = 0.02; Fig. 3). LDH activity was similar in rats infused with 25 and 51 mM sodium oleate at 0.5 and 3.5 min (P = 0.08) but was greater in rats infused with 51 mM sodium oleate at 6.5 min (t(11) = 2.7, P = 0.02).

Comparison of oleate and octanoate acid. Yox and Ritter (23) found that intraintestinal infusion of octanoate, unlike oleate, does not reduce food intake of rats. In this experiment, we compared the effects of these two fatty acids on intestinal LDH activity. Each of nine rats with intestinal catheters was infused with isotonic saline, 51 mM sodium oleate, or an equicaloric concentration of sodium octanoate (58 mM) in a random order with at least 3 days between tests. Intestinal contents were sampled 5 and 10 min after the end of infusion for analysis of LDH activity.

Infusion of sodium oleate, compared with saline, greatly increased LDH activity in the intestinal lumen 5 min after infusion stopped (t(8) = 4.6, P = 0.002; Fig. 4), although this effect had largely dissipated by 10 min after the end of infusion (t(8) = 1.9, P = 0.09). When rats were infused with an equicaloric concentration of octanoic acid, LDH activity in the intestine was similar to that seen after saline infusion (P > 0.2 for 5 and 10 min) and significantly lower than that after sodium oleate infusion (t(8) = 5.8, P < 0.001 at 5 min; t(8) = 5.3, P < 0.001 at 10 min).

Fig. 2. Concentration of Evans blue in plasma after intestinal perfusion of fat. An intestinal segment in anesthetized rats was perfused for 12 min with saline, 51 mM sodium oleate, 1.4% Intralipid, or sodium oleate + Intralipid. Isotonic saline was perfused for an additional 6 min, and Evans blue was injected into intestine. Plasma was sampled 10 and 20 min later. Values are means ± SE of 7 rats/group.

Fig. 3. LDH activity in intestinal lumen of conscious rats after intraintestinal infusion of sodium oleate. Saline or 25 or 51 mM sodium oleate was infused for 10 min (1 ml/min) before start of sample collection. Values are means ± SE of 6–7 rats/group.

Fig. 4. LDH activity in intestinal lumen of conscious rats after intraintestinal infusion of sodium oleate or sodium octanoate. Saline, 51 mM sodium oleate, or equicaloric (58 mM) sodium octanoate was infused for 10 min (1 ml/min) before start of sample collection. Values are means ± SE of 9 rats.
Effect of ethyl oleate on luminal LDH activity and food intake. Valasquez et al. (19) showed that intraintestinal infusion of ethyl oleate, which is absorbed and metabolized like oleic acid, does not injure the intestinal mucosa in anesthetized piglets. Two experiments were performed to determine whether intraintestinal infusion of sodium oleate and its ethyl ester have differential effects on mucosal integrity and food intake in conscious rats.

Luminal LDH activity was measured in 10 rats after infusion with saline, 51 mM sodium oleate, or 51 mM ethyl oleate using a within-subject design. Infusion of sodium oleate increased luminal LDH activity both 1 and 4 min after the end of the infusion compared with infusion of saline [Fig. 5; \( t(9) = 3.8, P = 0.004 \) at 1 min; \( t(9) = 3.9, P = 0.004 \) at 4 min] or infusion of ethyl oleate \( [t(9) = 3.7, P = 0.005 \) at 1 min; \( t(9) = 3.9, P = 0.003 \) at 4 min]. LDH activity in intestinal contents was similar at both times after infusion of saline and ethyl oleate (Fig. 5).

Another seven rats were infused with saline, 51 mM sodium oleate, or 51 mM ethyl oleate in the middle of the light period after an overnight fast. Food intake was measured 15, 30, 60, and 120 min after refeeding. Rats ate less food after sodium oleate infusion than after saline infusion at 15, 30, 60, and 240 min \( [t(6) = 3.9, P = 0.008 \); Fig. 6] but not at 120 min \( [t(6) = 1.8, P = 0.12] \). Infusion of sodium oleate also reduced food intake compared with infusion of ethyl oleate at 15, 30, and 60 min \( [t(6) = 3.3, P = 0.02] \) but not at subsequent times \( [t(6) = 2.2, P = 0.07] \). Food intakes after infusion of ethyl oleate and saline were similar at all time points \( (P = 0.12) \).

Effects of free oleic acid on luminal LDH activity and food intake. When oleic acid is used in studies of mucosal injury or food intake, it is usually neutralized with NaOH, forming sodium oleate. This saponification of oleic acid greatly increases its hydrophilic-lipophilic balance value (1) and water solubility. Perfusion of intestinal segments from rats with surfactants has been shown to increase release of LDH and enhance intestinal permeability (14). To determine whether mucosal injury and suppression of food intake in response to intraintestinal infusion of oleic acid results because the fatty acid is neutralized to the sodium salt, we compared the effects of sodium oleate and free (nonneutralized) oleic acid on luminal LDH activity and food intake.

LDH activity was measured in samples of intestinal contents from 10 rats after intraintestinal infusion with either sodium oleate or free oleic acid. This experiment had been used previously to examine the effects of ethyl oleate on luminal LDH activity (see above). Luminal samples from rats infused with sodium oleate \( (n = 5) \) showed substantially higher LDH activity (Fig. 7) than did samples from rats infused with...
infusion of saline (Fig. 8) in the first 30 min of refeeding compared with later. Infusion of sodium oleate suppressed food intake on refeeding was measured 30, 60, and 120 min of the dark period after an overnight fast, and food saline, sodium oleate, or the free acid at the beginning of the dark period. Values are means ± SE of 12 rats.

Free oleic acid (n = 5) at both 1 and 4 min [t(9) = 2.6, P = 0.03 and t(9) = 3.6, P = 0.006, respectively].

In another experiment, 12 rats were infused with saline, sodium oleate, or the free acid at the beginning of the dark period after an overnight fast, and food intake on refeeding was measured 30, 60, and 120 min later. Infusion of sodium oleate suppressed food intake (Fig. 8) in the first 30 min of refeeding compared with infusion of saline [t(11) = 3.8, P = 0.003] or free oleic acid [t(11) = 4.5, P < 0.001]. Food intakes at later time points did not differ as a function of infusate.

Learned taste aversion test. Intraintestinal infusion of sodium oleate conditioned a strong aversion to sucrose (Fig. 9). Rats that had been infused with saline when first given sucrose to drink preferred sucrose over maltodextrin when given a choice (69 ± 5% of total intake from sucrose), whereas rats that had been infused with sodium oleate avoided the sucrose, consuming only 27 ± 7% of their total intake as sucrose [t(13) = 5.1, P < 0.001]. Mean total intakes of rats given saline or sodium oleate were, respectively, 15.6 ± 0.6 and 12.8 ± 1.8 ml of fluid and did not differ statistically.

**DISCUSSION**

The results show that intraintestinal infusion of sodium oleate into rats, in concentrations and at rates commonly used to examine the satiating effect of the fatty acid, damages the intestine. The present experiments also indicate that these adverse effects probably underlie the reduction in ingestive behavior seen in response to intestinal infusion of sodium oleate. Infusion of different forms of oleic acid, which did not produce signs of intestinal damage, did not reduce food intake. Furthermore, intraintestinal administration of sodium oleate produced a learned taste aversion, suggesting that the suppression of ingestive behavior in response to infusion of this fatty acid may be due to its untoward effects on the intestine.

Previous studies have shown that prolonged infusion of sodium oleate into the intestine of anesthetized animals damages the intestinal mucosa. Morphological examination of the mucosa showed that the epithelial lining of the villous tips was severely disrupted (8). Measurement of Cr-EDTA transport from blood to intestinal lumen also indicated a breakdown in the permeability of the mucosal barrier (8, 18–20). The present experiments indicate that, even with shorter duration infusion of oleate, such mucosal damage occurs rapidly in both anesthetized and conscious rats. Oleate infusion produced a marked increase in luminal LDH activity, which is indicative of cell membrane disruption. This finding is consistent with observations showing that oleate damages intestinal villi and causes release of LDH from isolated enterocytes (4, 8, 11, 13). Transport of Evans blue from lumen to blood was also observed after infusion of sodium oleate. This observation is consistent with earlier findings using Cr-EDTA and suggests that the breakdown in intestinal permeability resulting from intraintestinal infusion of oleate increases leakage of large molecules both into and out of the intestine.

Infusion of ethyl oleate or free oleic acid, which did not produce any sign of intestinal damage (see also Ref. 19), did not suppress food intake. Also, intraintestinal infusion of octanoate, which apparently does not suppress ingestive behavior (23), did not produce any change in luminal LDH activity. LDH activity increased within 1–3 min during perfusion of sodium oleate (Fig. 1) and returned to baseline levels by 10 min after infusions ended (see Fig. 4). These rapid changes in LDH activity roughly parallel the transient effects of sodium oleate on food intake (Figs. 6 and 8) and may reflect the capacity for rapid reconstitution of villi membranes after damage from sodium oleate (8). Damage to the intestine is seen after a longer delay when sodium oleate emulsified in taurocholate is infused over a longer period (8). Similarly, the decrease in food intake observed after infusion of buffered oleic acid in

![Fig. 8. Food intake of rats after intraintestinal infusion of sodium oleate or free oleic acid. Fasted rats were infused with saline, 51 mM sodium oleate, or 51 mM oleic acid for 10 min (1 ml/min) before refeeding. Values are means ± SE of 12 rats.](image)

![Fig. 9. Learned taste aversion in rats to a sucrose solution paired with intraintestinal infusion of sodium oleate. Rats adapted to drinking a 10% maltodextrin solution consumed a 10% sucrose solution followed by intraintestinal infusion of either saline or 51 mM sodium oleate. Data shown are intakes on a subsequent test day when rats were given a choice of the 2 solutions. Values are means ± SE of 7-8 rats/group.](image)
the same vehicle is also delayed (22). Taken together, these results strongly suggest a relationship between the adverse effects of oleate infusion on the intestine and its effect on ingestive behavior.

To further test the hypothesis that the suppression of ingestive behavior during sodium oleate infusion was due to its untoward effects in the intestine, we used sodium oleate as an unconditioned stimulus in a learned taste aversion test. The result was clear-cut: rats avoided the solution that was paired with intestinal infusion of sodium oleate after only one trial. This suggests that sodium oleate infusion has extremely negative consequences, although the nature of the apparent discomfort is unknown. From consideration of the transient nature of the suppression in food intake, it seems more likely that infusion of sodium oleate causes an acute bout of pain rather than a prolonged bout of nausea. Intraintestinal infusion of capsaicin, which produces painful chemical irritation, reduces food intake to a similar degree as does infusion of sodium oleate under the same test conditions (16). It is therefore possible that infusion of sodium oleate also causes pain or irritation. In this regard, desensitization seen after capsaicin treatment (15) may account for the transiently reduced behavioral effect of sodium oleate infusion after intraintestinal infusion of capsaicin (16).

Ethyl oleate is taken up by intestinal mucosal cells and, after cleavage of the ethyl group, is transported into the circulation and metabolized like oleic acid (19). This suggests that the damaging effects of sodium oleate infusion on the intestine does not depend on its intestinal uptake. It seems more likely that the adverse effects of sodium oleate are due to its surfactant properties. Octanoate, a less potent surfactant, did not damage the intestine, a finding consistent with those made in piglets (20) and isolated cells (11). Because infusion of the free oleic acid also did not cause damage, it appears that the saponification of oleic acid is critical to the toxic actions of sodium oleate. Presumably, as one would expect from a soap, the neutralized sodium salt of oleic acid is more hydrophilic and would have more surfactant actions than the polar, hydrophobic free acid. This is reflected by the differences in the hydrophilic-lipophilic balance values of oleic acid and its sodium salt (1 vs. 18). Attempts to ameliorate potential negative consequences of infusing the free form of oleic acid by neutralization with NaOH apparently have had the opposite effect by actually increasing the potential for damage to the intestinal mucosa.

Kvietys et al. (8) suggested that reversible damage to intestinal mucosa may be a normal consequence of fat ingestion. If this is the case, then it is possible that the adverse effects of sodium oleate infusion are simply correlates and not the cause of the suppression of ingestive behavior produced by intraintestinal sodium oleate infusion. The present findings indicate that it is the sodium salt of oleic acid that produces the damage to the intestinal mucosa. Fatty acids emptied from the stomach or released by hydrolysis in the intestine probably would not form sodium salts (i.e., soaps) but would instead form calcium soaps (see Ref. 17) if any.

Such calcium soaps are insoluble and would therefore have little surfactant action, which would apparently minimize their injurious effect on the intestine. During digestion, fatty acids are also incorporated in micelles and therefore may not interact with cell membranes to the same degree as a soap. Furthermore, normally ingested fats are emptied slowly from the stomach. It therefore seems unlikely that, under normal conditions, fatty acid concentrations in the intestine reach a high enough level in a saponified form to cause harm to the mucosa. Further experiments are needed to determine whether intestinal infusion of a physiological form of fatty acid causes intestinal injury and reduces eating behavior.

Although the present experiments focused on the effects of intraintestinal infusion of fatty acids, they also provide evidence that infusion of the triglyceride emulsion, Intralipid, may cause damage to the intestinal mucosa. Although the opacity of the Intralipid precluded measurement of LDH activity during Intralipid perfusion, intestinal perfusion with this emulsion increased LDH activity in the perfusate during the saline-washout period. This effect was much less pronounced than that observed during perfusion with sodium oleate but nevertheless raises the possibility that intestinal infusion of Intralipid may suppress food intake because of its adverse effects. This conclusion is consistent with recent results indicating that 1) gastrointestinal administration of triglycerides suppresses food intake because, under these conditions, fats are delivered into the intestine at an unusually fast rate and/or in an unphysiological form (3) and 2) normally ingested triglycerides produce little if any immediate effect on subsequent food intake in rats (see Ref. 7).

The present experiments strongly suggest that the suppression of ingestive behavior induced by intraintestinal infusion of fatty acids is due to the adverse effects of the form of fatty acids commonly used in behavioral studies. The results also raise concern about possible harmful effects of intestinal infusion of triglycerides. Intraintestinal infusion of glucose produces an unusually large decrease in food intake compared with that seen after glucose empties normally from the stomach (10). This observation and the present findings raise caution about the use of intraintestinal infusion of nutrients to study normal mechanisms of satiety.

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