Gut vagal afferent lesions increase meal size but do not block gastric preload-induced feeding suppression

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Gut vagal afferent lesions increase meal size but do not block gastric preload-induced feeding suppression. Am. J. Physiol. 276 (Regulatory Integrative Comp. Physiol. 45): R1623–R1629, 1999.—Subdiaphragmatic vagal afferent (SVA) signals arising from gut sites may provide critical feedback for the control of food intake within a meal. To evaluate the role of SVAs in both spontaneous and scheduled meals, food intake was assessed in two paradigms in male Sprague-Dawley rats. In the first study, control (Con) rats (n = 6) and rats with subdiaphragmatic vagal deafferentation (SDA) (n = 7) had 12-h nightly access to Ensure liquid diet (1 kcal/ml). SDA rats had larger and fewer meals and maintained initial rapid rates of licking, yet total numbers of licks were unaffected. In the second study, Con (n = 8) and SDA (n = 7) rats had scheduled access to 12.5% liquid glucose after overnight food deprivation. Glucose intake was assessed after 5-ml gastric preloads of 0.9% saline or glucose, peptone, and Intralipid solutions at three concentrations (0.5, 1, and 2 kcal/ml). Glucose and peptone preloads suppressed intake similarly in Con and SDA rats, whereas Intralipid was ineffective. These results suggest that meal-related SVA signals similarly in Con and SDA rats, whereas Intralipid was ineffective. These results suggest that meal-related SVA signals arising from gut sites contributes to the within-meal controls of food intake.

A VARIETY OF MEAL-RELATED stimuli, such as gastric-distending loads (19), duodenal nutrient infusions (11, 30, 31), and meal-induced gut-brain peptides, such as CCK (11), have all been shown to suppress ingestive behavior and food consumption. These findings support the suggestion that gut stimuli arising during a meal contribute to the negative feedback control of ingestion. The afferent vagus nerve provides the major neuroanatomical linkage between the gut sites that handle and deliver ingested nutrients and the central nervous system sites that mediate the control of food intake. Results from neurophysiological studies have revealed that vagal afferents arising from the stomach and/or duodenum are responsive to meal-related mechanical, nutrient, chemical, and gut-brain peptide stimuli that alter food intake (8, 15, 24, 25).

A significant role for vagal afferents in the feeding-suppressive actions of meal-related gut stimuli has been suggested by results of surgical and chemical vagal blockade. Acute hepatic vagotomy increases meal size during feeding (10). Total vagotomy or selective surgical transection of celiac and hepatic vagal branch afferents significantly attenuates or blocks the ability of small intestinal nutrient infusions to suppress food intake (30, 32). Finally, systemic application of the neurotoxin capsaicin, which damages a population of unmyelinated vagal afferents, reduces the ability of intestinal nutrients to suppress intake (31) and produces overconsumption of liquid sucrose (3) and a novel caloric diet in rats (2). Taken together, these results provide evidence that vagal afferent feedback from gut sites contributes to the within-meal controls of food intake.

The present studies were designed to further evaluate the specific contribution of subdiaphragmatic vagal afferents to the negative feedback control of ingestion. These experiments use the surgical vagal afferent disconnection technique designed by Norgren and Smith (18) to completely transect subdiaphragmatic vagal afferents while leaving some vagal efferent outflow and without affecting splanchnic innervation. We evaluated the effect of these disconnections in two paradigms: during dark-cycle spontaneous liquid diet consumption and during consumption of scheduled access to liquid diet after nutrient and nonnutrient gastric preloads.

METHODS

Male Sprague-Dawley rats (Charles River, 250–275 g at surgery) served as subjects in all experiments. Rats were housed individually in hanging wire cages in a temperature- and humidity-controlled room at 21°C on a 12:12-h dark-light cycle with lights on at 0900. Before surgery, rats were trained for 1–2 wk to consume liquid Ensure (Ross Laboratories, 1 kcal/ml) as their maintenance diet, available from 1900 to 0700, with tap water available ad libitum. Two sets of experiments were performed with different groups of rats: spontaneous feeding studies and gastric preload studies in conjunction with scheduled intake tests. In each study, rats were divided into two experimental groups: sham-surgery controls (Con) and subdiaphragmatic vagal deafferentation rats (SDA).

SDA surgical procedure. SDA was performed as previously described (16), according to the methods of Norgren and Smith (18). Rats were deprived of food, but not water, overnight before surgery. Deprived rats were anesthetized with a mixture of ketamine HCl, 100 mg/ml (Aveco), and xylazine (Rompun) (20 mg/ml; Mobay), 43, 0.1 ml/100 g body wt, and maintained at 36–37°C throughout surgery with a heating pad. The ventral muscles of the neck were exposed by a midline skin incision, and the omo- and sternohyoideus muscles were gently retracted, revealing the base of the left skull. Under microscopic observation, a hole was drilled into the base of the skull at the posterior lacerated foramen, revealing the brain stem and overlying dura. The dura was broken, permitting observation of left vagal afferent and...
efferent rootlets where they attach to the brain stem. The left dorsal vagal rootlets were severed by avulsing them with fine forceps, with no bleeding and no damage to the vagal efferent rootlets. The left rootlets were chosen because they contain not only afferents from the ventral gastric vagus and accessory celiac nerve but they also carry afferents from the hepatic vagus, which supplies the liver and proximal duodenum (1). Gel foam was placed in the skull hole, and the neck wound was closed with surgical clips. The ventricle was then exposed by a midline laparotomy incision, and the stomach and esophagus were gently retracted. The dorsal vagal subdiaphragmatic trunk was exposed using cotton swabs, and gently detached from the esophagus using fine forceps. Two 5–0 silk suture ties were used to isolate a 1-cm portion of the dorsal subdiaphragmatic vagal trunk orad to the celiac vagal branch, and the dorsal subdiaphragmatic trunk was cauterized, leaving no intact nerve bundles between the two silk sutures. The muscle and skin layers of the laparotomy incision were closed with suture and wound clips, respectively. Rats were treated with intramuscular penicillin (10,000 U) for 2 days after surgery. Control surgeries were performed without exposing but not drilling the skull and exposing but not ligation of the dorsal subdiaphragmatic vagus. Before behavioral testing, SDA rats were allowed to fully recover their presurgical body weight and rate of body weight gain by maintaining them on overnight access to Ensure liquid diet for a 2-wk period (SDA rats 356 ± 12 g, Con rats 363 ± 15 g when testing began). This recovery time is consistent with that demonstrated by Walls et al. (29) in vagally deafferented rats. Behavioral testing of all rats was completed within a 6- to 7-wk time frame postsurgery to minimize the possibility for functional regrowth (T. Powley, personal communication). Separate functional and anatomic tests (see below) confirmed the success of the vagal transections.

Spontaneous feeding tests. During spontaneous feeding procedures, rats had access to a surfeit of Ensure diet overnight (180 ml), with no food available during the day. Rats maintained on this liquid diet regimen show normal rates of weight gain. In spontaneous ingestion studies, the rate, pattern, and total number of licks of the Ensure milk diet during the first 6 h of the dark cycle were assessed for two consecutive 3-day periods: once in the week before SDA surgery and once in the 3rd wk after SDA surgery, when average postsurgical body weights and rates of body weight gain had reached their presurgical values. Spout diameters were identical for all rats for all tests, minimizing the variation in the amount of milk delivered per lick, and all rats always had milk remaining in their bottles after the overnight test periods, with minimal (<2 ml/12 h) spillage observed in the cages.

Gastric preload studies. For gastric preload studies, rats were maintained on 5-h daily access to Ensure diet (1200–1700), and diet, but not water, was removed overnight. Rats in the gastric preload study were also trained to consume a 12.5% (wt/vol) glucose solution during 30-min morning consumption tests after an overnight food deprivation. After adaptation to glucose drinking, all rats drank at least 10 ml in the 30-min test period. All rats in the gastric preload study were also adapted to a gastric gavage procedure, where an 8 Fr. tube was inserted orally and advanced 6 cm into the esophagus and stomach, left in place for 15 s, and then removed 5 min before 12.5% glucose access. Glucose consumption tests were performed each morning after an overnight food deprivation. During a gastric preload test, 5 ml of warmed (37°C) gastric load was infused. Five minutes later, rats were given access to 12.5% glucose in their home cages and glucose consumption (ml) was measured 30 min later.

Gastric infuses included glucose, peptone (Sigma; Primate, from meat), and Intralipid (10 and 20% stock, diluted as needed with physiological saline; Baxter) delivered at each of three caloric concentrations: 0.5, 1.0, and 2.0 kcal/ml. Thus the total calories in the gastric preload were 2.5, 5, and 10 kcal. On any given test day, each rat received the same gastric infuse, and gastric infuses were delivered in random order across days. Glucose intake after no tubing, sham gavage using an empty tube, and 5-ml nonnutrient physiological saline preload was also assessed.

Functional verification of SDA procedure. To verify the completeness of the SDA, 30-min consumption of a 12.5% glucose solution was assessed when intraperitoneal saline and 2 µg/kg injections of CCK were given 5 min before 30-min access to 12.5% glucose solution after a 6-h daytime deprivation. We (16) and Smith et al. (27) previously demonstrated that anatomically successful SDA blocks the ability of low doses of intraperitoneal CCK to suppress food intake. All Con rats significantly suppressed their glucose consumption by an average of 35 ± 4.2% compared with saline vehicle injections [F(1,13) = 14.2, P < 0.01], whereas CCK failed to significantly suppress glucose consumption in SDA rats [mean 10 ± 7.1%, F(1,13) = 1.2, P > 0.3].

Anatomic verification of SDA procedure. After functional verification of the SDA, rats underwent a standard protocol to evaluate the surgical completeness of the SDA procedure. At the end of all behavioral testing, rats were injected with 2 mg/kg−1 ml−1 ip fluorogold tracer (Fluorochrome). Three days later, rats were euthanized with an overdose of pentobarbital sodium (Euthasol) and perfused transcardially with phosphate-buffered saline followed by 4% paraformaldehyde. After perfusion, the brain stem was exposed under a dissecting microscope at ×40, and the integrity of the vagal afferent and efferent rootlets on each side of the brain stem was assessed by visual inspection. In all SDA rats, all left vagal afferent rootlets were interrupted, with no damage to any other vagal or adjacent innervation. In all control rats, no damage to any brain stem vagal or other cranial nerve innervation was observed. After visual inspection of vagal rootlets, brains were removed, sectioned at 40 µm, mounted on subbed slides, dried overnight, cleared with alcohol and xylene, and placed under a coverlip with nonfluorescent DPX mounting medium. With the use of fluorescence microscopy, slides were checked for the presence of label throughout the full extent of the left dorsal motor vagal nucleus, consistent with an intact ventral vagal efferent trunk, and the absence of fluorogold label in the right dorsal motor vagal nuclei (normally supplied by the transected dorsal subdiaphragmatic vagal trunk). The dorsal subdiaphragmatic vagal nerve transection was also verified in each SDA rat at death by microscopic observation of the absence of vagal nerve fibers in the two silk sutures that had been placed along the trunk at the time of transection.

Data analysis. For spontaneous feeding studies, lick data were collected by an automated lick measurement system (DiLog Instruments, Tallahassee, FL), and meal size and lick variables (burst size, burst number, meal size, meal frequency, and intermeal interval) were computed using TongueTwister lick analysis software (Thomas Houpt, University of Florida, Tallahassee). The time of each individual lick was recorded, and the data were summed over 1-min intervals throughout the 6-h period. The average for each lick variable was computed for each rat for the 3-day presurgical and postsurgical periods described above. Criteria for the end of a burst was an interlick interval >0.23 s but <0.5 s. Licks were divided into meals using the criteria of three licks with interlick intervals of <0.25 s to initiate a meal. This criterion...
was adopted to identify licks that were occurring during a burst of licking (5). The intermeal interval was defined as 5 min without licking, an interval that has been validated for spontaneous liquid diet meals (22). Lick rate data for each individual animal were fit to a Weibull function, \( y = A e^{-Bt^C} \) by the least-squares method to quantify changes in the rate of licking during the spontaneous feeding tests. The \( r^2 \) values (goodness of fit) for the Weibull functions for these data all ranged from 0.62 to 0.94, indicating significant fits. The three critical Weibull parameters, \( A \) (initial rate of licking), \( B \) (rate of decay in lick rate), and \( C \) (relating to the duration of maintained initial rates of licking) were averaged across meals for each rat for the 3-day pre- and postsurgical periods. The \( C \) parameter provides a shape parameter that indicates how the function deviates from an exponential. When \( C = 1 \), the Weibull function degenerates to a simple exponential curve. A value of \( C > 1 \) indicates that the initial rate of decline is less rapid than it would be for an exponential. One the basis of the pre- and postsurgical averages for each rat, two-way repeated measures ANOVAs were used to determine changes in all lick variables as a function of surgical treatment (Con vs. SDA) and surgical time (pre- vs. postsurgery). When significant overall effects were identified, planned \( t \)-comparisons were used to assess significant differences among individual treatment \( \times \) time conditions using the overall error terms from the ANOVA.

For gastric-preload studies, 30-min glucose intake was analyzed by repeated measures ANOVAs for each macronutrient tested, across concentration and between surgical groups. Planned \( t \)-comparisons were used to assess significant differences between the effects of individual concentrations within and between surgical groups.

**RESULTS**

Spontaneous feeding. SDA produced a variety of changes in meal patterns and licking behavior. An example of the overall difference in meal pattern over the 6-h measurement period for a single SDA rat before and after SDA surgery is shown in Fig. 1. Results for meal size and licking parameters pre- and postvagal deafferentation are summarized in Table 1. Before SDA surgery, there were no differences in any of the meal or lick parameters between SDA and Con rats (\( P \) values > 0.4). Control surgery produced no significant changes in any of the meal parameters measured. In contrast, SDA significantly increased meal size \( [F(1,11) = 14.3, P < 0.02, \text{planned } t, P < 0.01] \), intermeal interval \( [F(1,11) = 25.6, P < 0.01, \text{planned } t, P < 0.01] \), and burst size \( [F(1,11) = 23.4, P < 0.05, \text{planned } t, P < 0.01] \). SDA significantly reduced meal frequency \( [F(1,11) = 52.8, P < 0.01, \text{planned } t, P < 0.01] \), satiety ratio \( [F(1,11) = 15.5, P < 0.01, \text{planned } t, P < 0.01] \), and the number of bursts \( [F(1,11) = 11.2, P < 0.02] \). In Weibull analyses of the rate of licking during meals, the rate of decay of licking, \( B \), was significantly reduced by SDA \( [F(1,11) = 10.2, P < 0.05] \), and the shape factor, \( C \) (reflecting the maintained initial rate of licking), was significantly increased by SDA \( [F(1,11) = 18.4, P < 0.01, \text{post hoc } t, P < 0.01; \text{Table } 1] \).

Sustained meals after gastric preloads. Higher concentrations of peptone and glucose gastric preloads significantly suppressed subsequent scheduled glucose intake in both Con and SDA rats [glucose – overall \( F(2,13) = 25.4, P < 0.001 \); peptone – overall \( F(2,13) = 32.5, P < 0.001 \) relative to levels produced by physiological saline preloads (Fig. 2), and there was no significant treatment \( \times \) group interaction for either macronutrient [glucose \( F(2,26) = 0.454, P > 0.6 \); peptone \( F(2,26) = 0.536, P > 0.5 \)]. Thus, within each macronutrient category for glucose and peptone preloads, the two groups did not significantly differ in the degree to which gastric preloads suppressed subsequent glucose intake. A 5-kcal load was the threshold for a significant suppression in both SDA and Con rats, and planned \( t \)-tests revealed that 10-kcal loads did not significantly suppress intake below levels produced by 5-kcal loads in both groups (\( P \) values > 0.2). Intralipid preloads equicaloric to the protein and glucose loads failed to suppress subsequent glucose intake at any of the three concentrations tested in either the Con or SDA groups \( [F(2,13) = 0.462, P > 0.3] \). Physiological saline preloads failed to suppress subsequent glucose intake in either of the
surgical groups compared with either control (no pre- load) or gavage using an empty tube [F(2,13) = 0.425, P > 0.2 (data not shown)].

**DISCUSSION**

Different sets of results were obtained for the two experiments. In the first, SDA significantly altered patterns of food intake both within and between meals. In the second, SDA failed to alter rats’ responses to intragastric nutrients in scheduled meals.

The data from the first experiment demonstrate that rats lacking subdiaphragmatic vagal afferent feedback significantly alter their pattern of spontaneous liquid diet intake in ways consistent with a reduction in meal-related satiety signals. SDA rats showed longer, fewer meals and a reduced satiety ratio relative to their presurgical levels or those shown by a group of sham-operated controls. The pattern of liquid diet intake within a meal in SDA rats, as revealed by Weibull analysis, also corroborates an interpretation of reduced satiety. The initial rates of licking, although not different among SDA and control rats, were maintained for longer periods of time (i.e., the C shape factor was significantly greater in SDA rats compared with controls), and the rate of licking within a meal declined more slowly in SDA rats, suggesting that a reduction in gut vagal afferent negative feedback permitted a maintenance of ingestion at higher rates throughout the meal. Furthermore, SDA rats demonstrated longer bursts of licking. Increases in burst size have been interpreted as reflecting increased palatability (6), and the increase in burst size in SDA rats suggests that reduced gut feedback may increase the palatability of the consumed diet.

These overall findings parallel results from studies of another rat model of reduced satiety, the OLETF rat, an outbred strain of Long-Evans rats lacking CCK-A receptors (16). OLETF rats also show larger meal size, fewer meals, decreased satiety ratios, maintained initial rates of licking, and reduced decay in the rate of licking, but unlike SDA rats, OLETF rats are hyperphagic and become obese. In contrast, SDA rats produced equivalent total numbers of licks over the 6-h measurement period compared with controls, suggesting that their overall daily food intake does not differ. This suggestion is supported by the present finding that SDA rats recover and gain weight at the same rate as sham controls. Walls et al. (29) also reported that SDA rats have daily total food intake and body weight gain comparable to sham-operated controls. Thus, whereas SDA produces significant alterations in meal pattern consistent with satiety deficits, SDA rats maintain their ability to regulate their overall daily food intake and body weight.

Our results after selective gut vagal deafferentation can be compared with those from previous studies using other forms of surgical or chemical vagal blockade. Consistent with our results, total subdiaphragmatic vagotomy alters the microstructure of licking by increasing burst size and decreasing burst number (7). Furthermore, complete subdiaphragmatic vagotomy acutely increases liquid diet intake during the first 30 min and during the subsequent 16.5 h (20). These data are consistent with the interpretation that removal of vagal afferents blocks the gut negative feedback signals arising from meals. However, this effect was transient: in more chronic studies, total subdiaphragmatic vagotomy reduces body weight gain and food intake of dry food and liquid diets in rats (4, 7, 13, 20, 28). Total vagotomies include transection of all gastric vagal branch afferent and efferent fibers, and we previously demonstrated that gastric branch vagotomy dramatically increases liquid gastric emptying (23). Such dumping of liquid nutrients may prevent the efficient absorption and utilization of ingested calories and contribute to the maintained weight loss and reduction in food intake seen in total vagotomized rats.

Capsaicin treatment has also been used to selectively destroy unmyelinated visceral afferents, including vagal afferents, that may mediate the negative feedback control of ingestion. Curtis and Stricker (3) showed that systemic capsaicin pretreatment increases 10% liquid sucrose intake in overnight fasted rats compared with vehicle-treated controls. In studies of Chavez et al. (2), capsaicin treatment produced no changes in the overall daily consumption of a familiar diet. However, capsaicin-treated rats did significantly overconsume a novel high-fat diet on first, but not subsequent, exposure.

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**Table 1. Meal parameters during 6-h spontaneous liquid diet consumption**

<table>
<thead>
<tr>
<th></th>
<th>Control (n = 6)</th>
<th>Postsurgery</th>
<th>SDA (n = 7)</th>
<th>Postsurgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meal size, no. of licks</td>
<td>1,570 ± 113</td>
<td>1,657 ± 109</td>
<td>1,674 ± 90</td>
<td>2,309 ± 102*</td>
</tr>
<tr>
<td>Meal frequency, no. of meals</td>
<td>6.3 ± 0.32</td>
<td>5.7 ± 0.25</td>
<td>5.5 ± 0.22</td>
<td>4.2 ± 0.19*</td>
</tr>
<tr>
<td>Intermear interval, min</td>
<td>73.7 ± 4</td>
<td>77.9 ± 5.5</td>
<td>75.2 ± 2.9</td>
<td>92 ± 5.3*</td>
</tr>
<tr>
<td>Satiety ratio</td>
<td>4.79 ± 0.32</td>
<td>4.75 ± 0.36</td>
<td>4.57 ± 0.31</td>
<td>2.76 ± 0.23*</td>
</tr>
<tr>
<td>Burst size, no. of licks</td>
<td>42.6 ± 5.5</td>
<td>44.2 ± 4.2</td>
<td>42.5 ± 4.5</td>
<td>60.5 ± 6.02*</td>
</tr>
<tr>
<td>Burst no.</td>
<td>73.3 ± 8.4</td>
<td>78.2 ± 8.4</td>
<td>75.8 ± 6.8</td>
<td>59.5 ± 4*</td>
</tr>
<tr>
<td>Total no. of licks</td>
<td>9,482 ± 257</td>
<td>9,591 ± 440</td>
<td>9,381 ± 267</td>
<td>9,490 ± 258</td>
</tr>
<tr>
<td>Weibull parameters</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>235.5 ± 23.5</td>
<td>254 ± 22.1</td>
<td>258 ± 34</td>
<td>228 ± 35.2</td>
</tr>
<tr>
<td>B</td>
<td>0.0034 ± 0.0003</td>
<td>0.0041 ± 0.0005</td>
<td>0.0038 ± 0.0004</td>
<td>0.0021 ± 0.0005*</td>
</tr>
<tr>
<td>C</td>
<td>32.1 ± 4.5</td>
<td>38.4 ± 5.1</td>
<td>31.2 ± 6.1</td>
<td>57.2 ± 7.4*</td>
</tr>
</tbody>
</table>

Values are means ± SE. Satiety ratio is intermeal interval (min)/meal size (licks)·100. Weibull parameters: A, initial rate; B, slope; C, shape. SDA, subdiaphragmatic deafferentation. *Significant differences from corresponding presurgical value (P < 0.05).
These data suggest that capsaicin-sensitive vagal afferents may contribute to meal size but that this contribution is transient, unlike the present results that reveal a chronic increase in meal size. Because the SDA procedure transects both capsaicin-sensitive and capsaicin-insensitive vagal afferents, noncapsaicin-sensitive vagal afferents may be critical for the chronic increase in meal size and related lick rate parameters.

The second set of studies in this manuscript was designed to evaluate the role of gut vagal afferents in the feeding-suppressive action of gastric nutrient preloads during a scheduled, short-term feeding test. Five milliliters of noncaloric gastric saline preloads or sham gavage tubing failed to suppress subsequent feeding in both controls and SDA rats. This is consistent with the lack of feeding suppressive actions of 5, but not 10, ml gastric saline preloads found by Phillips and Powley (19). In contrast, nutrient gastric preloads had differential effects on subsequent intake, depending on nutrient type and caloric concentration. In both control and SDA rats, 5- and 10-kcal glucose and peptone loads inhibited intake, whereas 2.5-kcal loads did not. Gastric caloric loads over comparable ranges have often been demonstrated to suppress food intake in intact rats. The 5-kcal load was the lowest caloric load examined that suppressed food intake for both peptone and glucose solutions. Previous studies with slower infusions and indwelling gastric cannulas showed that 2-kcal loads can also suppress feeding (19). Neither peptone nor glucose preloads increased the magnitude of feeding suppression between 5- and 10-calorie doses. This lack of a dose-dependent suppression is also consistent with work of Phillips and Powley (19), demonstrating that 4- and 8-kcal gastric glucose loads do not differ in the magnitude of suppression they produce.

Gastric preloads of fat completely failed to suppress subsequent liquid diet intake in both Con and SDA rats. This appears surprising in light of data from several studies demonstrating that intraduodenal infusion of fat potently suppressed sham and real feeding (12, 14, 31, 32). However, the current studies evaluated the feeding-suppressive effects of fats delivered into the stomach, not the duodenum. Friedman et al. (9) showed that orally ingested 5 and 10% Intralipid failed to suppress subsequent solid food intake in rats. The relatively slow emptying of fat may contribute to the complete lack of a feeding suppression during the intake test. Once in the stomach, ingested fat emulsions, including Intralipid, separate into aqueous and lipid phases, and in the rat, the aqueous phase appears to empty quite rapidly, reducing gastric volume but leaving the lipid phase for much slower emptying (9).

Perhaps the most surprising finding in the present study is the fact the SDA completely failed to attenuate the ability of glucose and peptone gastric preloads to suppress food intake. This finding appears to contrast with those of Walls and colleagues (30) and Phillips and Powley (20), evaluating the effects of various vagotomies to block the intake suppression of duodenal nutrients or gastric loads. Walls et al. (30) showed that celiac vagal deafferentation attenuated or completely blocked the ability of duodenal infusions of carbohydrates, fats, and proteins to suppress subsequent liquid intake. Also, Phillips and Powley (20) demonstrated that subdiaphragmatic vagotomy blocked the ability of gastric loads confined to the stomach to inhibit intake. Thus interruption of vagal afferent signaling appears to block the suppressions arising from stimulation of the gastric and duodenal compartments individually, but the suppression produced by combined stimulation is apparently unaffected. Our data are consistent with results from an earlier study of Ritter and Ladenheim

Fig. 2. Effects of 5-ml gastric preloads of glucose (Glu; A), peptone (Pep; B), and Intralipid (FAT; C) on 30-min daytime scheduled 12.5% glucose intake plotted as a function of caloric concentration in both control (Con; n = 8) and SDA (n = 7) rats. Preloads were delivered 5 min before glucose access. Higher caloric concentrations of glucose and peptone suppressed subsequent glucose intake similarly in both Con and SDA rats. Intralipid preloads were completely ineffective in suppressing subsequent intake. *Significant differences from physiological saline (SAL) preload condition (P < 0.01).
(21) in which capsaicin lesions blocked the satiety actions of CCK but did not affect the ability of gastric nutrients to inhibit intake. It may be that, in the present case of combined gastric and duodenal stimulation, splanchnic afferents mediate the ability of gastric peptone and glucose preloads to suppress feeding in the SDA rat. Alternatively, postabsorptive nutrient signals that remain after SDA may also mediate the persistent ability of gastric nutrient preloads to suppress feeding. We have demonstrated that SDA accelerates the initial rapid phase of gastric emptying (23), presenting two possibilities: 1) increased splanchnic signaling in SDA rats due to increased duodenal volume relative to controls and 2) increased numbers of calories in the duodenum compared with controls, leading to increased postabsorptive negative feedback via nonvagal humoral or splanchnic pathways. Because SDA accelerates gastric emptying, the duodenal loads resulting from our gastric bolus infusions would likely be greater than would occur in intact rats, and thus the maintained suppression of food intake in SDA rats after such loads may be under different controls from those operating in intact rats.

Perspectives

The present results showing that SDA rats have longer and fewer meals, maintain initial rates of licking, and show slower rates of decay of licking within a liquid meal are all consistent with a significant role for gut vagal signals in the negative feedback control of meal size, meal pattern, and satiety. However, in the absence of subdiaphragmatic vagal afferent feedback, some feedback controls are still active and intake in scheduled meals is equally affected by preloads in intact and SDA rats. The reduced satiety and increased meal size data from the first experiment do not prevent SDA rats from maintaining normal rates of body weight gain across days. The maintenance of body weight in the absence of some meal-related negative feedback signals suggests that compensations for alterations in the size and patterning of individual meals do not depend on vagal afferent signaling.

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