now been fully confirmed anatomically and electrophysiologically. These receptors send information to the brain regarding the extent and duration of peristalsis in the foregut, which is also a measure of the fullness of the crop as the crop contents pass through the foregut on the way to the midgut for digestion (*6*). On the basis of behavioral experiments, the action in the brain of the stretch receptor input is hypothesized to be inhibition of external chemoreceptor input (*1*). If the fly is deprived of the input from the foregut receptors by cutting of the recurrent nerve, feeding behavior is not inhibited in the normal manner, and hyperphagia results (*3*).

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Enterogastrone Inhibits Eating by Fasted Mice

Abstract. *In mice fasted for 17 hours, administration of enterogastrone purified from hog duodenum reduced the food intake. This effect was greatest during the first 30 minutes, but the cumulative reduction continued for at least 4 hours. Other peptides prepared from hog duodenum or colon, as well as glucagon, secretin, glucose, and bovine serum albumin, were ineffective.*

The mechanisms controlling food intake are many and their interrelations are complex (*1–4*). Among the factors suggested are sensations from the digestive tract associated with eating and the presence of food in the stomach and the intestines (*3, 4*). Gastric contractions appear to be a common element of the hunger complex (*2*). The hormone enterogastrone, derived from the small intestine, is known to reduce gastric secretion and gastric motility (*5*), and so could be associated with inhibition of eating (*4*). Grossman (*4*) and Janowitz and Grossman (*6*) tried to elicit release of enterogastrone, and thus inhibit gastric contractions, by prefeeding dogs with sucrose or cream. Small amounts of these nutrients did not reduce the subsequent consumption of food, but larger amounts did. They concluded that enterogastrone may not play a role in regulation of food intake.

Availability of purified enterogastrone (*7*) prompted us to reexamine the role of enterogastrone in the regulation of food intake. Enterogastrone and other peptides were prepared from extracts of hog duodenum. The purification of enterogastrone and its effects on gastric secretion will be detailed elsewhere (*7*).

We trained female mice of the White Swiss strain (25 to 30 g in body weight) to eat a liquid diet consisting of 7.4 percent protein, 11.6 percent carbohydrate, and 2.1 percent fat. They were fasted for 17 hours, but water was always provided before and during the test period to eliminate the effects of thirst and dehydration. The mice were then injected intravenously or subcutaneously with the test substances; control mice were injected with saline or carrier vehicle. Ten to 15 minutes later, food, in a special volumetric feeder, was placed in their cages and food consumption was measured after 30, 60, 120, and 240 minutes. The results are presented as cumulative intake by volume for each period in comparison with those of control groups of mice. At least three experiments were carried out with each of the substances tested, with ten mice per group in each experiment.

The results (Table 1) indicate that a

Table 1. Effects of enterogastrone and other substances on food consumption by fasted mice. Each value is the mean for three experiments; each experiment used ten mice. The carrier contained 16 percent gelatin and 0.5 percent phenol. Abbreviations: i.v., intravenous; Ent 1, enterogastrone batch 1; NS, not significant; Ent 2, enterogastrone batch 2; s.c., subcutaneous; Duod 1, duodenal peptide batch 1; Duod 2, duodenal peptide batch 2; Colo, colonic fraction; Secr, secretin; Gla, glucagon; Bov, bovine serum albumin; Glo, glucose; i.p., intraperitoneal.

Time (min)	Cumulative intake per mouse (ml, ± S.E.)		*P*	Cumulative intake per mouse (ml, ± S.E.)		*P*
	Control	Injected		Control	Injected	
	Saline i.v.	*Ent 1 i.v. (0.1 mg)*		*Saline i.v.*	*Ent 1 i.v. (1 mg)*	
30	1.5 ± 0.1	0.7 ± 0.15	.01	2.5 ± 0.1	0.2 ± 0.0	.001
60	2.4 ± 0.06	1.6 ± 0.2	.02	3.1 ± 0.06	.9 ± 0.2	.001
120	3.4 ± 0.1	2.7 ± 0.26	NS	3.8 ± 0.12	2.4 ± 0.04	.001
180	4.3 ± 0.07	3.6 ± 0.2	NS	5.0 ± 0.12	3.7 ± 0.16	.001
240	4.9 ± 0.22	4.2 ± 0.2	NS	5.9 ± 0.2	5.0 ± 0.14	.05
	Saline i.v.	*Ent 2 i.v. (1 mg)*		*Carrier s.c.*	*Ent 1 s.c., carrier (1 mg)*	
30	1.3 ± 0.1	0.00 ± 0	.001	1.6 ± 0.2	0.7 ± 0.1	.02
60	1.7 ± 0.04	.4 ± 0.0	.001	2.2 ± 0.3	1.0 ± 0.2	.05
120	2.8 ± 0.1	1.6 ± 0.3	.001	2.9 ± 0.3	1.6 ± 0.2	.05
180	3.7 ± 0.2	2.7 ± 0.04	.01	4.0 ± 0.3	2.5 ± 0.3	.05
240	5.0 ± 0.3	3.6 ± 0.1	.01	5.0 ± 0.3	3.5 ± 0.4	.05
	Saline i.v.	*Duod 1 i.v. (1 mg)*		*Saline i.v.*	*Duod 2 i.v. (1 mg)*	
30	2.4 ± 0.1	1.0 ± 0.3	.005	1.7 ± 0.11	1.3 ± 0.04	.05
60	2.7 ± 0.2	1.8 ± 0.4	NS	2.1 ± 0.1	1.8 ± 0.1	NS
120	3.3 ± 0.3	2.4 ± 0.6	NS	3.1 ± 0.15	2.6 ± 0.2	NS
180	3.8 ± 0.5	2.8 ± 0.4	NS	3.9 ± 0.13	3.8 ± 0.15	NS
240	5.2 ± 0.4	4.4 ± 0.7	NS	5.1 ± 0.1	5.2 ± 0.2	NS
	Saline i.v.	*Colo i.v. (1 mg)*		*Saline i.v.*	*Secr i.v. (10 μg)*	
30	2.6 ± 0.2	2.0 ± 0.15	NS	2.1 ± 0.2	2.2 ± 0.1	NS
60	3.2 ± 0.15	2.7 ± 0.15	NS	3.2 ± 0.3	3.5 ± 0.1	NS
120	4.2 ± 0.1	4.3 ± 0.1	NS	4.8 ± 0.3	5.0 ± 0.1	NS
180	5.2 ± 0.15	5.4 ± 0.3	NS	5.8 ± 0.3	5.9 ± 0.1	NS
240	6.1 ± 0.3	6.4 ± 0.3	NS	6.5 ± 0.3	6.6 ± 0.1	NS
	Saline i.v.	*Gla i.v. (1 mg)*		*Saline i.v.*	*Bov i.v. (1 mg)*	
30	1.9 ± 0.2	1.8 ± 0.3	NS	2.2 ± 0.2	2.2 ± 0.2	NS
60	2.5 ± 0.3	2.5 ± 0.4	NS	2.9 ± 0.3	2.8 ± 0.2	NS
120	3.6 ± 0.5	3.8 ± 0.6	NS	4.1 ± 0.3	3.9 ± 0.4	NS
180	4.9 ± 0.2	5.4 ± 0.5	NS	4.8 ± 0.3	5.1 ± 0.4	NS
240	5.7 ± 0.3	6.7 ± 0.5	NS	6.1 ± 0.3	6.2 ± 0.3	1.3
	Saline i.p.	*Glo i.p. (75 mg)*		*Saline i.v.*	*Pre-Sate i.v. (300 μg)*	
30	1.4 ± 0.1	1.3 ± 0.1	NS	1.9 ± 0.1	0.6 ± 0.1	.001
60	2.3 ± 0.2	2.1 ± 0.1	NS	2.6 ± 0.2	1.3 ± 0.2	.005
120	3.4 ± 0.2	3.7 ± 0.1	NS	3.7 ± 0.3	2.6 ± 0.2	.05
180	4.2 ± 0.2	4.7 ± 0.2	NS	5.2 ± 0.3	4.3 ± 0.3	NS
240	5.0 ± 0.1	5.6 ± 0.3	NS	6.3 ± 0.4	5.6 ± 0.2	NS

single injection of 0.1 to 1 mg of purified enterogastrone significantly reduced food-intake during the first 30 to 60 minutes, when some mice ate almost nothing. There was no decrease in intake during later periods, but the cumulative changes remained evident after 4 hours. Two different batches of enterogastrone showed this effect; it reduced intake whether it was injected intravenously, subcutaneously without carrier, or subcutaneously in a vehicle containing 16 percent gelatin and 0.5 percent phenol. Two peptide preparations from hog duodenum each had a slight effect when it was measured at 30 minutes, but the cumulative reduction was not observed between 1 and 4 hours later; their minor effects may be attributable to slight contamination with enterogastrone. Similarly, a material purified from the pig colonic mucosa, by the concentration procedure used for enterogastrone, had no effect on intake. Administration of other substances such as glucagon, secretin, glucose, and bovine serum albumin had no effects under the conditions employed. The anorexigen chlorphentermine-HCl (Pre-Sate), administered intravenously at 300 μg per mouse, significantly reduced intake during the first 30 minutes, and its cumulative effects were significant for as long as 2 hours.

The activity of duodenal enterogastrone fractions was apparently not due to toxicity or pyrogen-like properties; they did not elicit abnormal behavior in the mice or cause fever; mice injected with enterogastrone appeared to be active, healthy, and quite normal except for failure to eat after 17 hours of fasting. While it is still possible that the anorexic effect of our preparations is due to nonspecific toxic effects of enterogastrone or a contaminant present in these preparations, our studies suggest that enterogastrone may be involved in inhibition of feeding. Inhibition may be in some way related to elimination of gastric hunger contractions, since it is known that, when given to dogs in doses of 0.5 mg/kg, these enterogastrone preparations inhibit gastric motility and histamine-induced augmentation of secretion of pepsin and hydrochloric acid (*5, 7*) for as long as 1 hour. About 0.1 mg of enterogastrone was needed to inhibit significantly appetite in mice, or about seven times more (expressed per unit body weight) than the dose required to affect gastric secretion in dogs. However, many hormones able to exert more than one biologic effect show greatly different activities with respect to different responses; for example, doses of vasopressin required to obtain an effect on blood pressure in rats are at least 100 times larger than those necessary for an antidiuretic effect.

It is not clear, regarding all factors involved in control of food-intake, how the reflexes are signaled to the hypothalamic portion of the brain (*1, 2, 4*) to produce cessation of eating. The mechanisms of regulation of intake are most likely interrelated, and many various factors such as glucose utilization and energy balance (*1, 2*) and distention of the stomach (*4*) could be involved in inhibition of feeding or apparent satiety (*1–4*). It is also interesting that intraperitoneal administration of large amounts of glucose had no effect on food-intake in fasted mice; this finding is in agreement with those of Grossman and Janowitz (*4, 6*). Glucagon also was ineffective. It has been reported that administration of glucose or glucagon inhibits gastric hunger contractions in men and rats (*2, 8*). This problem is complex, since it is the rate of glucose utilization, and not the level of glucose, that is associated with cessation of gastric contractions (*2*). Moreover, under certain conditions gastric contractions may not be indicative of or necessary for the hunger state (*2*). It is possible therefore that enterogastrone did not exert all its effects through inhibition of gastric contractions, and that it acted, at least in part, humorally on the central nervous system. Although our studies suggest a role for enterogastrone in the overall complex relations of appetite control, they do not prove that secretion of enterogastrone under physiologic conditions affects food intake; much further work will be necessary to assess the importance of these preliminary findings.

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Resistance Shifts Accompanying the Evoked Cortical Response in the Cat

Abstract. *Clicks and flashes that evoke an electrical response from the auditory or visual cortex also evoke a resistance shift in the tissue. The resistance shift, a drop followed by a rise in resistance, closely follows the temporal pattern of the electrical response recorded simultaneously through the same electrodes. While several experimental manipulations produce corresponding changes in the amplitudes of both electrical response and resistance shift, the resistance shift is more sensitive to alterations in cortical temperature and anesthetic level. The two responses behave distinctly differently as a function of the depth of the electrode in the cortex.*

Since Cole and Curtis first measured impedance changes during activity of nerve cells (*1*), numerous authors have studied the impedance of brain tissue and the changes induced in it by electrical stimulation, spreading depression, asphyxia, ischemia, and even by normal activities such as sleep and learning (*2*). Resistive and capacitive changes of the order of several percent of the resting value with a time course of seconds or minutes have been reported. The measurements to be presented here show resistance changes sev-