necessary for nitrate reductase induction (or synthesis) in leaves of tobacco because of its effect on the concentrations of one or more endogenous growth regulators. This effect may be due to either stimulation of synthesis or retardation of breakdown of those hormones required for nitrate reductase synthesis.

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Visceral and Behavioral Responses to Intraduodenal Fat

Abstract. *Introduction of milk or corn oil into the duodenum of the cat evokes an increase in superior mesenteric blood flow (blocked by atropine), an inhibition of gastric and duodenal motility, and sedation. Cholecystokinin-pancreozymin mimics the mesenteric vascular effect of intraduodenal fat and seems to have a sedating action.*

Increased blood flow in the mesenteric artery occurs in dogs after a meal (*1*). We now report that in cats this increased flow depends in part on stimuli arising in the duodenum, and that these stimuli elicit other characteristic autonomic and behavioral responses.

Under sterile conditions, the following devices were implanted in eight cats in a single-stage operation: (i) noncannulating electromagnetic flowmeter probes (Micron) around the superior mesenteric and external iliac arteries for recording of blood flow via Biotronex electromagnetic flowmeters, along with miniature hydraulic occluders for transient occlusion of the vessels to obtain zero-flow levels; (ii) polyvinyl cannulas in the inferior mesenteric artery and jugular vein for pressure recordings via Statham pressure transducers; (iii) polyvinyl cannulas inserted through the wall of the stomach and ending in the gastric antrum and at three levels in the duodenum, for recording motility (pressure) changes and for instillation of various substances; (iv) skull and deep, stereotaxically oriented, electrodes for electroencephalograms (EEG); and (v) neck and periorbital intramuscular electrodes for electromyograms. The cannulas and flowmeter cables were contained inside a small pack at the interscapular region, after having been tunneled along the skin of the back from the lumbar region. The head electrodes were connected to a miniature socket anchored to the skull with stainless steel wire and dental cement. Recordings were made on a Grass polygraph model VII and a Grass electroencephalograph model IV, with common time and signal marking.

At each recording session (9:30 a.m. to 5:00 p.m.) an animal was placed in a ventilated, lighted box, 40 by 60 by 80 cm, with a one-way window. Food and water were not available to the animal during this period. Generally, the animals had free access to food and water in their cages until placed in the recording box. Observations began 7 to 10 days after the surgery and could be continued for 1 to 4 months.

Introduction of milk (5 ml) into the duodenum produced (i) a 50 to 100 percent increase in superior mesenteric blood flow, starting in 3 to 6 minutes and lasting for 30 to 60 minutes, which was unaccompanied by any changes in heart rate, arterial pressure, or iliac

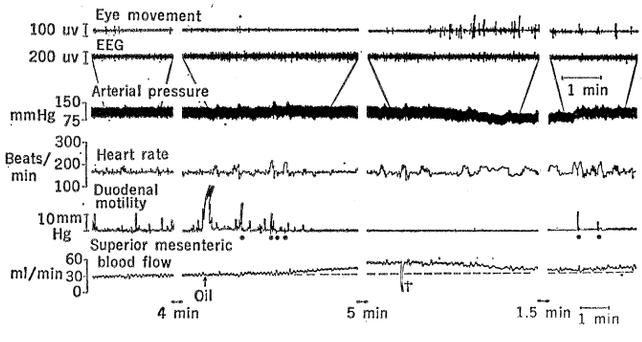

Fig. 1 (left). Response to injection of 1.0 ml of corn oil into the second part of the duodenum in an awake male cat. Diagonal lines connecting EEG and arterial pressure tracings indicate points of simultaneity between events recorded on electroencephalograph (eye movement and EEG) and polygraph (other parameters). Heart rate was recorded via Grass tachograph from pressure pulses. Dots beneath duodenal motility record indicate movement artifacts. Cross beneath lowest tracing indicates zero blood flow during arterial occlusion. Dashed line is drawn for convenience to indicate control level of blood flow. Time intervals between the selected segments of the continuous record are indicated at the bottom.

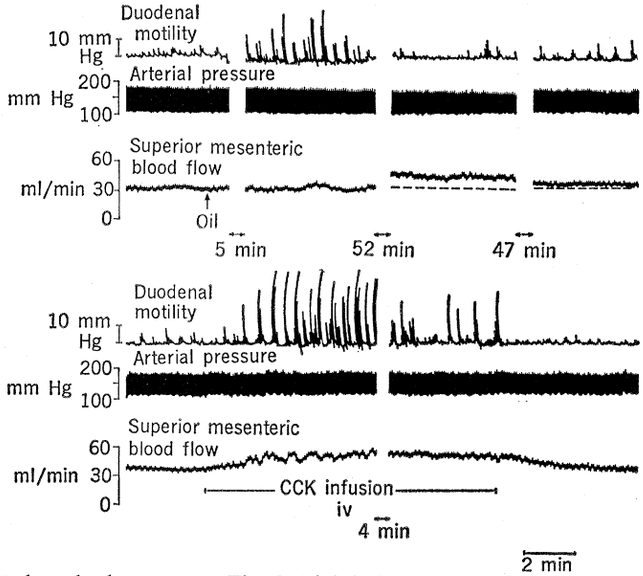

Fig. 2 (right). Response to intraduodenal injection of 1.5 ml of corn oil in a chloralose-anesthetized male cat (4.1 kg) (top). Response in the same cat to intravenous infusion of CCK-PZ (4.7 unit kg^{-1} $hour^{-1}$) (bottom). Dashed line and time interval notations as in Fig. 1.

blood flow; (ii) a transient increase in duodenal motility at the injection site, followed by inhibition for 30 to 90 minutes of spontaneous motor activity in the antrum and throughout the duodenum; (iii) a significant sedating effect characterized by curling up and drowsiness (EEG spindling) if the animal was active, or a transition to persistent slow-wave, high-voltage sleep if the cat was already drowsy; within the hour after intraduodenal injection of milk, the frequency or duration of rapid eye movement (REM) episodes was markedly augmented if the animal was already asleep. Injection of the same amount of milk directly into the stomach had no detectable effect.

Of the components of milk, apparently only fat was able to evoke the response. Equal volumes of water or saline, or solutions of glucose, lactose, or casein had no effect, but 0.5 to 2.0 ml of corn oil elicited the typical response. The duration of the changes (approximately 30 to 90 minutes) was proportional to the amount of oil injected; the latency was shortened by administration of 0.3 to 0.5 ml of cat bile or detergent (approximately 0.5 mg Alconox) with the fat. The response was elicitable from any segment of the duodenum, but most readily from the second portion (Fig. 1).

Intravenous injection of atropine sulfate, at a dose (0.03 mg/kg) that does not seem to modify the EEG pattern of the awake cat, blocked completely the appearance of mesenteric vasodilatation after intraduodenal introduction of fat. Also, the spontaneous intraluminal pressure waves in the duodenum, which persisted after this low dose of atropine, were not inhibited after introduction of the oil. However, a sedating effect apparently remained. Mesenteric vasodilatation after instillation of oil into the duodenum could be elicited in animals under light chloralose anesthesia, but not under pentobarbital. In some cases, duodenal motility was apparently augmented by fat in the anesthetized animal (Fig. 2).

Because fat in the duodenum releases cholecystokinin-pancreozymin (CCK-PZ) (*2*), we tested the effect of intravenous infusion (4 unit kg^{-1} $hour^{-1}$) of a partially purified preparation of this hormone (*3*). This induced an increase in mesenteric blood flow and a variable increase in duodenal motility in anesthetized and awake cats (see Fig. 2). In two trials on an initially awake but drowsy cat, high-voltage sleep ensued during the CCK-PZ infusion.

The extent to which the increase in mesenteric blood flow is in pancreas or intestine remains to be determined; vasodilatation in the pancreas might accompany the increased metabolic activity in that organ induced by CCK-PZ. In any case, the facts that CCK-PZ induces mesenteric vasodilatation, and that atropine, which interferes with release of endogenous CCK-PZ (*4*), prevents the fat-induced vasodilatation, point to a role of CCK-PZ in the response.

The inhibition of duodenal motility by fat, comparable to that described in the dog (*5*), cannot be ascribed to CCK-PZ, because administration of that substance tended to increase motility, in consonance with the observations of Hedner *et al.* (*6*). It is unknown whether the mechanism is humoral, nervous (involving intrinsic or extrinsic innervation of the gut), or a combination of these.

The sedation induced by intraduodenal fat may be mediated by either (i) a direct central action of a released gastrointestinal hormone, perhaps comparable to the effect of gonadotrophins in promoting the appearance of high-voltage and REM sleep in the rabbit (*7*); or (ii) an indirect neurogenic mechanism through the stimulation of duodenal receptors by the released gastrointestinal hormone or by the food (fat), as described for glucose and amino acids (*8*). The observations suggest that the sedating effect of intraduodenal fat may be important in the correlation between the feeding and the sleep-waking cycles, and possibly also in short-term satiation.

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10. After this report was submitted, we saw the article by G. P. Burns and W. G. Shenk [*Arch. Surg.* **98**, 790 (1969)] who observed increased mesenteric blood flow in dogs after a meal or after intravenous injection of crude preparations of gastrin or secretin, the latter containing CCK-PZ.

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Surface Areas of the Cerebral Cortex of Mammals Determined by Stereological Methods

Abstract. *The surface areas of the cerebral cortex excluding archipallium of 20 human, 11 cetacean, 6 carnivore, and 5 marsupial brains were determined by stereological methods. There exist rather strict relationships between volume, length of superficially exposed gyri, and cortical surface area.*

The volumes of brains of 42 mammals pertaining to widely separated taxonomical groups, fixed in 20 percent formalin, were determined by suspension in water. By a median cut, the hemispheres were separated. One hemisphere of each brain was sliced by frontal sections; the other by horizontal sections of thickness *t*. This thickness was calculated by dividing the measured height or length of each hemisphere by the number of slices. The terms "horizontal" and "frontal" are defined as respectively parallel or per-

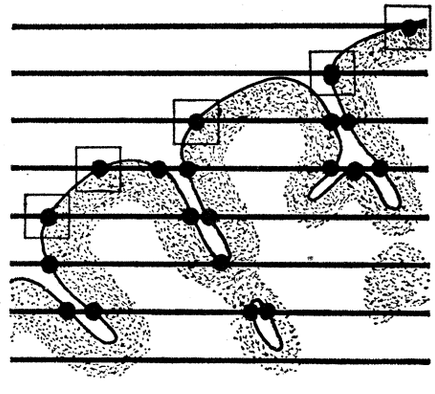

Fig. 1. Method of intersection counts for cerebro-cortical surface determination. The index of folding equals the number of all black dots divided by the number of squares.