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Vagotomy: Effect on Electrically Elicited Eating and Self-Stimulation in the Lateral Hypothalamus

Abstract. *A subdiaphragmatic vagotomy markedly inhibits eating and self-stimulation produced in rats by lateral hypothalamic stimulation. The stomach is known to be affected by hypothalamic stimulation via the vagus, and afferents from the stomach can influence the hypothalamus via the same nerve. Consequently, this result suggests that eating and self-stimulation may be partly controlled by hypothalamic influences on the stomach which, in turn, affects hypothalamic sensitivity.*

Rats with electrodes implanted in the lateral hypothalamus exhibit self-stimulation behavior and will also eat during continuous stimulation (*1*). On the other hand, studies show that stimulation in, or close to, the lateral hypothalamus affects the stomach, increasing gastric motility and acidity, while prolonged stimulation may produce hemorrhaging and ulceration (*2*). It is tempting to look for a connection between these two sets of data since the stomach has been implicated in theories of eating for many years.

Since lateral hypothalamic stimulation produces stomach conditions which in some respects mimic those found in the hungry animal, electrically elicited eating may be partly a function of these hypothalamic influences on the stomach. If this is so, severing the neural connection between the lateral hypothalamus and the stomach should attenuate this behavior. The major connection between the central nervous system and the gastrointestinal tract is the vagus nerve. It is already known that severing this nerve prevents lateral hypothalamic stimulation from influencing the stomach (*3*). In this study I severed this nerve to see if it prevented lateral hypothalamic stimulation from eliciting eating as well as the closely related phenomenon, self-stimulation.

Eight male Sprague-Dawley rats from the Charles River Breeding Laboratories were implanted with electrodes in the lateral hypothalamus and the lateral septal area (*4*). These septal electrodes were to serve as a check on the condition of the animals after the vagotomy operation. As septal stimulation does not produce eating, I intended to use any decrement in performance on this electrode as an indicator of debilitation due to the vagotomy.

After the animals had recovered from the implant operation, I determined their thresholds for eating and self-stimulation. Using a constant current stimulator which delivered a 1-msec negatively going pulse every 10 msec, I determined the amount of current needed on the lateral hypothalamic electrode to produce consistent eating of wet mash in a 10-second stimulation period, presented every 30 seconds. Later in the day, I measured the threshold current necessary to sustain self-stimulation behavior for a period of 2 minutes on the same electrode. The animals were further tested for septal self-stimulation thresholds. In all these determinations I used the psychophysical method of minimal changes. Each animal was tested for 20 minutes a day on each test for at least 2 weeks. Because some of the electrodes failed to elicit consistent behavior, and because of deaths following the vagotomy operation, only five animals completed the study.

Once highly repeatable performances had been obtained on all the appropriate measures, the vagal nerves were cut below the diaphragm in each of the rats. A section of nerve, at least 5 mm long, was removed from the side of the esophagus immediately above the stomach. The esophagus was carefully cleared of all visible fibers, and the animal was allowed to recover for several days before retesting. As animals tend to overeat immediately after vagotomy, they were deprived of food for 24 hours. After this time, they became somewhat anorexic for the next few days, confirming earlier observations (*5*). They seemed to have difficulty swallowing, which may have been due to possible damage to the esophageal musculature during the operation. Some failed to recover from the anorexia and died. However, the majority eventually started eating and gaining weight normally.

Eight days after the vagotomy the threshold currents for eliciting eating and self-stimulation were rechecked. Each animal was retested for 50 days after the operation. Figure 1 shows the results of the experiment. Median threshold scores are plotted for the five animals, beginning just before and continuing for 50 days after vagotomy. The vagotomy had its largest effect on the threshold for feeding, raising it by 150 percent. It had a similar, but slightly smaller, effect on the lateral hypothalamic self-stimulation threshold,

raising it by over 100 percent. However, septal self-stimulation thresholds were not significantly affected. Over the 50 days of testing, the lateral hypothalamic thresholds continued to rise while the septal thresholds showed a small decrease. This rise in hypothalamic thresholds was due to some animals, in the early days after vagotomy, showing poorly organized eating and self-stimulation responses which eventually became extinguished with continued testing.

For individual animals, there was a high positive correlation between the percentage changes in the lateral self-stimulation and eating thresholds. By the end of testing, two animals failed to eat or self-stimulate on the lateral hypothalamic electrode at current levels even three times higher than their control levels. The other three animals ate at current levels 150, 50, and 140 percent greater than their control levels, and self-stimulated at levels 100, 30, and 110 percent greater than controls. These threshold changes were highly significant for four of the animals, and relatively significant for the animal with the smallest change (*6*). No significant threshold changes were observed on any of the septal electrodes.

It is unlikely that these effects were due to sickness caused by the vagotomy, because the rats continued to self-stimulate on the septal electrode at the prevagotomy threshold level, while their thresholds on the lateral hypothalamic electrodes increased to higher levels. Also, the vagotomy did not drastically affect the animals' overall eating behavior, inasmuch as the rats gained weight once they had recovered from the initial effects of the vagotomy. This agrees with the present literature, which shows that vagotomized animals can quite adequately regulate long-term body weight, although their meal size tends to change (*7*). The rise in thresholds is also unlikely to be due to deterioration of responding at the lateral hypothalamic site, because we have run nonvagotomized animals with similar electrodes for at least 6 months with no substantial change in threshold.

At the end of testing, the animals were perfused and the brains sectioned. All electrodes were found to be in either the lateral hypothalamus or the lateral septum. Also, the esophagus and stomach were carefully examined for possible regrowth of vagal fibers. In all cases the vagus showed signs of regeneration, but I could not find any

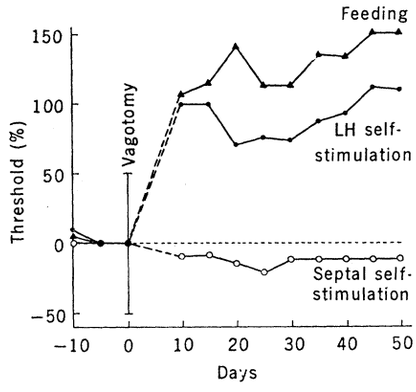

Fig. 1. Median threshold scores for feeding and self-stimulation, expressed as a percentage of prevagotomy levels. *LH*, lateral hypothalamus.

significant bundle of fibers that had grown back as far as the stomach. Overall, during the 50 days after the vagotomy, it appeared that the vagus remained severed in the animals that completed the experiment.

It would appear that electrically elicited eating and self-stimulation, produced through lateral hypothalamic electrodes, is partly dependent on an intact vagus nerve. Lesioning of the vagus is one of the most discrete lesions yet found in the nervous system which can disrupt these two behaviors. The septal area, presumably not involved in the motivational mechanisms of eating, is not affected by this manipulation. This argues for the existence of different motivational systems being located in different self-stimulation areas.

In most animals, the electrically elicited eating and self-stimulation behavior can still be seen at higher current levels. Obviously, the whole phenomenon cannot be explained in terms of the integrity of the vagus nerve. Other mechanisms must be involved: the connection between the central nervous system and the stomach is only part of the picture. In fact, somewhat similar effects are found in another centrally elicited motivational state, attack behavior. Flynn showed that sectioning the sensory branches of the trigeminal nerve drastically reduced the attack behavior elicited from hypothalamic electrodes in cats (*8*). Most cats failed to attack during stimulation and the remainder attacked less frequently.

Another possible interpretation of these results is that the lateral hypothalamic stimulation may be affecting liver glycogen and pancreatic insulin, as these two organs are also innervated via the subdiaphragmatic vagus. Both compounds have been shown to have a significant effect on lateral hypothalamic self-stimulation rates (*9*). However, both produce opposite effects, so that the net result is likely to be small. Also, following vagotomy, blood glucose and insulin levels remain normal (*10*). Although these arguments do not rule out that glucose and insulin may be part of the reason for the threshold changes, it seems unlikely that they are contributing more than a minor portion of the effect.

Electrically elicited eating and self-stimulation behavior is generally regarded as the result of stimulation of centrally organized rewarding and motivating systems (*1*). This report shows that at least part of the phenomenon is not so directly organized. It emphasizes that lateral hypothalamic stimulation affects at least one peripheral organ, the stomach, which in turn affects the responsiveness of the electrically elicited behaviors. The increased stomach activity affects the central nervous system via the vagus, altering the sensitivity of the lateral hypothalamus, either directly or indirectly. This feedback loop, between the hypothalamus, the periphery, and back to the central nervous system, needs to be incorporated into present theories.

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