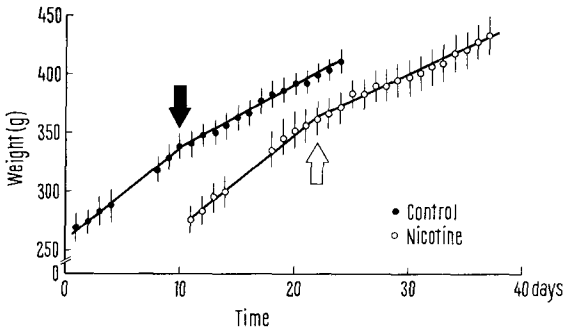
be further increased by ICI-50123; the slight fall in pepsin output may have resulted from volume changes. It is of interest that no ulcers were seen.

The reduced weight gain in control rats was probably due to the pH of the injectable. In the nicotine-treated rats the greater reduction in growth can be ascribed to the nicotine[16]. The mechanism of nicotine-induced gastric secretory stimulation with chronic exposure is not clear but may be due to enzyme induction[17,18], for example,



Body weight gain in control and nicotine-injected rats. Data are presented as mean values ± S.E.M. for 12 control (●) and 48 nicotine-injected (○) rats. The groups were run simultaneously but are separated for illustrative purposes. Day 1 for the saline (closed arrow) and nicotine injections (open arrow) are indicated. Control groups – pre-injection: r, +0.9973; $P<0.001$; Y, 299.8+7.8 (X, 5.3); post-injection: r, +0.9935; $P<0.001$; Y, 374.3+5.3 (X, 16.0). Nicotine-injected groups – pre-injection: r, +0.9954; $P<0.001$; Y, 328.2+7.9 (X, 7.3); post-injection: r, +0.9868; $P<0.001$; Y, 400.7 +4.2 (X, 19.0).

histamine[4] or other substances[19]. Results presented may explain why smoking is a contributory factor in the aetiology and healing of peptic ulcers in man[20].

Résumé. Après avoir reçu 300 µg de tartrate de nicotine-hydrogène pendant 15 jours il y eut des augmentations significatives dans le volume du suc gastrique et dans la production de pepsine. Des injections de nicotine on abaissé tous les paramètres, mais combinées avec de la gastrine synthétique (ICI-50123), elles n'ont aucun effet. Les résultats présentés peuvent expliquer pourquoi l'habitude de fumer est un facteur contribuant à la formation à la guérison des ulcères peptiques.

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Effect of Electrical Stimulation in VPM on Saccharin Preference and Water Intake in Cats[1]

Studies have shown that electrical or chemical stimulation of the tongue evokes responses in the medial part of the nucleus VPM of the thalamus[2-5]. Bilateral lesions in the same region produce an elevation of the rejection threshold for quinine solutions as well as decreases in volume intake of sucrose and sodium chloride solutions[6-8]. Studies on alimentary behavior have repeatedly pointed to the importance of taste in feeding and drinking reactions[9-15]. As a continuation of our studies on central mechanisms related to feeding behavior[16-19], we wished to gather more data concerning the role of the proposed thalamic taste relay nucleus in a preference behavioral situation[20].

Methods. The experiments were performed on 10 adult cats weighing between 3.0 and 3.6 kg. Bipolar strut electrodes were implanted bilaterally in the medial part of the VPM nucleus (A 8.5, L 3.5, H 0) in 8 cats (VPM cats) and in the region of n. lateralis posterior (A 7.5, L 5.0, H +5.5) in 2 cats (LP cats), according to the atlas by Jasper and Ajmone-Marsan[21]. Electrodes were constructed of stainless steel wires (0.2 mm in diameter) whose tips were bared.

Two weeks after surgery, the cats were water-deprived and then taken to the observation chamber. This chamber was provided with 2 feeders located on opposite sides of the cage. Each animal was trained to press the bar at the feeder and for each press 0.1 cm³ of water was automatically delivered. Every day the animal remained in the experimental cage about $^1/_2$ h until it no longer pressed the bar.

When the cat had learned to bar-press and its water intake had reached a constant level, a saccharin solution was introduced into one feeder. The animal then drank distilled water or saccharin solution according to its preference. The bottles were exchanged every few days to prevent the establishment of a habit of drinking from one feeder only. After 10 days, a control series of 20 sessions was performed on the 8 VPM animals. During these sessions the saccharin concentration was increased 0.1% daily, beginning at 0.1% and continuing until a concentration of 2% was reached. A 1-week interval followed during which the animals received water ad libitum.

In a second series of sessions, the VPM cats were divided into 2 groups. With the first group of 4 cats (CW1, CW2, CW3 and CW4), sessions similar to the above control series were repeated except that unilateral bipolar electrical stimulation was administered through the implanted electrodes. Monophasic, square-wave pulses were delivered from a Grass stimulator. The usual stimulation parameters were 0.5–1.0 V, 20 cps and 1 msec pulse duration. Each stimulation epoch consisted of 15 sec stimulation followed by a 15 sec interstimulation interval. 20 stimulation epochs were tested daily and started 30 sec after the animal was brought into the observation chamber. Following stimulation, the cat was allowed to continue to press and drink ad libitum.

The second group of 4 VPM cats was used as a 'special' control in which no stimulation was applied. After 1 week, these 4 control cats were also used for electrical stimulation studies of the VPM area. The procedure was some-

what different in these cats: one bottle contained distilled water while the second contained saccharin solution of the most preferred concentration (individually defined for each cat). These were offered to the cats in the experimental cage for 10 days and interchanged as described above. After 1 week, the same procedure was repeated with electrical stimulation applied to the thalamus. The remaining 2 LP cats were similarly tested. The sites of electrode insertion in the diencephalon were determined anatomically by serial sections of the brains stained with the thionin method.

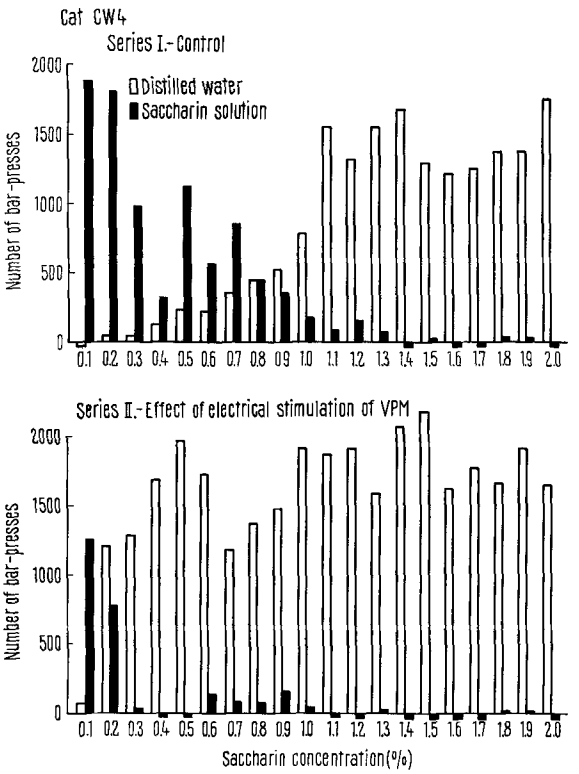
Results. Controls. The first control series of sessions in a cat of the VPM series (Cat CW4) is graphically shown in the top of the Figure. This graph serves as an example of results obtained in the control sessions of all 10 cats. Initially the animal drank more saccharin solution than distilled water. When the concentration of saccharin became higher than 0.7%, the cat drank more distilled water than saccharin. As the saccharin solution reached concentrations stronger than 1.3%, this cat preferred water almost completely. There were certain individual differences in rejection thresholds, but generally the cats in our study refused to drink saccharin stronger than 2%.

Before studying the effects of electrical stimulation on changes in saccharin preference, controls were performed in order to observe simply the behavioral effects of electrical stimulation at the sites where the electrodes were implanted. Bipolar stimulation (2–3 V, 50 c/sec, 1 msec duration) evoked licking movements of jaw and tongue (a type of slow chewing) and searching of the floor. A consistent effect of stimulation was licking, which became more pronounced when the intensity of stimulation was increased. In 2 cats, electrical stimulation of the VPL nucleus evoked orienting reactions and generalized excitation with increasing voltage. We chose that side of the thalamus where the licking behavior was evoked at the lowest intensities. Stimulation parameters were then lowered even further to the point where stimulation did not evoke any visible effects.

Electrical stimulation. Following the control sessions, the effects of electrical stimulation of VPM applied daily tor 10 min during each session were studied. These results are illustrated in the bottom graph of the Figure. The cat preferred distilled water over saccharin solution at a much lower concentration than in the control series. This specific animal (CW4) refused to drink saccharin solution stronger than 0.2% concentration. It was consistently found that all animals switched to distilled water at lower saccharin concentrations upon electrical stimulation. Cat CW2 still accepted 1.9% saccharin solution in the control series but refused to drink saccharin solution stronger than 0.4% upon VPM stimulation and cat CW3 accepted 1.4% saccharin in the first series but left the saccharin feeder at 0.4% concentration upon electrical stimulation.

The results of stimulation in 3 VPM cats of the second group (CW6, CW10 and CW14) in which only a single concentration of saccharin solution was used throughout all sessions were as follows: 2 cats (CW6 and CW10) after a few days switched to distilled water and only drank saccharin solution occasionally, while the third cat (CW14) showed no clear differences.

Discussion. Electrical stimulation of the VPM area in the thalamus results in effects which generally are in accord with observations of other investigators. HESS[22] reported that licking and chewing were observed when similar loci were stimulated in the medial thalamus in cats. ANDERSSON and JEWELL[7] localized the sites of similar reactions in the medial part of the VPM area in goats.



These graphs show the number of bar presses which one cat in our series made in order to get saccharin solution (black bars) or water (white bars). The top graph shows that in the control situation the animal prefers saccharin to water until the concentration of saccharin solution reaches 0.8. However, when the VPM nucleus is electrically stimulated (bottom), the animal prefers saccharin solutions only at much lower concentrations (0.1–0.2%).

[1] Supported by a grant from the U.S. Public Health Service, No. MH13958.

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They observed not only licking and chewing, but also ejection movements from the mouth resembling those induced when quinine solution is tasted. They concluded that the stimulated area must be a sensory and not a motor structure, which later received support by the fact that projections from the tongue were obtained at this same site[2]. Weak stimulation of the VPM did not induce ejection movements in our cats. Daily stimulation in this area, however, resulted in a comparable effect. Stimulated animals rejected concentrations of saccharin solutions 5 times more dilute than controls. This suggests that stimulation produced certain sensations which, when added to the taste sensations of the saccharin solutions, became undesirable to the animal. Lower concentrations of saccharin solution coupled with stimulation had the same effect as that produced by higher concentrations of saccharin without stimulation.

Zusammenfassung. Elektrische Reizung im VPM-Nukleus der Katze setzt die Schwellenkonzentration bei denjenigen Tieren, die Saccharinlösung reinem Wasser vorzogen, auffallend herab.

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Synapses in the Rat Stomach and Small Intestine

In several accounts of the ultrastructure of the myenteric plexus (Auerbach's plexus), synaptic junctions have occasionally been seen[1-3]. In the present research we intend to study the distribution and relative frequency of synapses of the myenteric plexus in the rat stomach (glandular portion) and small intestine (penultimate loop).

Specimens were fixed in 5% glutaraldehyde, post-fixed in osmium tetroxide, then dehydrated with ethanol and embedded in araldite (CIBA). Sections, stained with uranyl acetate and lead citrate, were observed at a Siemens 1 A electron microscope.

Typical synaptic junctions are observed in both segments of the alimentary canal: synapses are morphologically recognized (and indicated as 'conventional synapses') on the basis of the following characteristics: a) thickening of the 2 apposed membranes (pre- and post-synaptic membranes); this may vary from a prominent to a minimal synaptic thickening. b) Pre-synaptic knobs contain vesicles, which may form aggregations near the synaptic cleft; although vesiculated nerve processes in the myenteric plexus have been tentatively grouped in 4 classes on the basis of different vesicular content[4], no clear correlation between structure and position of synapses and kind of nerve process has yet been observed. c) Pre- and post-synaptic membranes appear quite parallel, with an intervening cleft of about 200 Å. In some cases electron-dense material occurs between pre- and post-synaptic membranes.

However, it should be mentioned that symmetrical membrane thickenings (in nerve processes devoid of vesicles) at inter-neuronal or glia-neuronal contacts, are observed and are provisionally interpreted as attachment zones. Moreover many vesicle-containing nerve processes run in contact with other nervous structures but do not show membrane thickenings suggesting a typical synaptic junction.

In the majority of cases, synapses are formed between a vesiculated nerve process and the pericarion or a dendrite of intramural neurons, and are thus identified as axo-somatic (Figure 1) and axo-dendritic (Figure 2) junctions. A small number of junctions could not be classified.

We tried to obtain quantitative data on the distribution of synapses in the myenteric plexus; for this photographic montages were made to get overall pictures of intramural ganglia, and the number of synapses per unit section surface or per nerve cell counted. We have so far observed over 300 synapses. On this basis, we conclude that there are more than 6 times as many typical synapses in the stomach as in the small intestine. This highly significant difference in the number of synaptic junctions seems to be mostly due to synapses between axons and short dendrites (Figure 3); these synapses are a common occurrence in the stomach.

In conclusion, if in the small intestine synapses are indeed so scanty, other interneuronal connections at present not morphologically detectable, or other transmission mechanisms, such as diffusion of transmitter over long distances, may be admitted. Close contacts between nerve cells at sites other than the morphologically differentiated regions commonly recognized as synaptic junctions, have

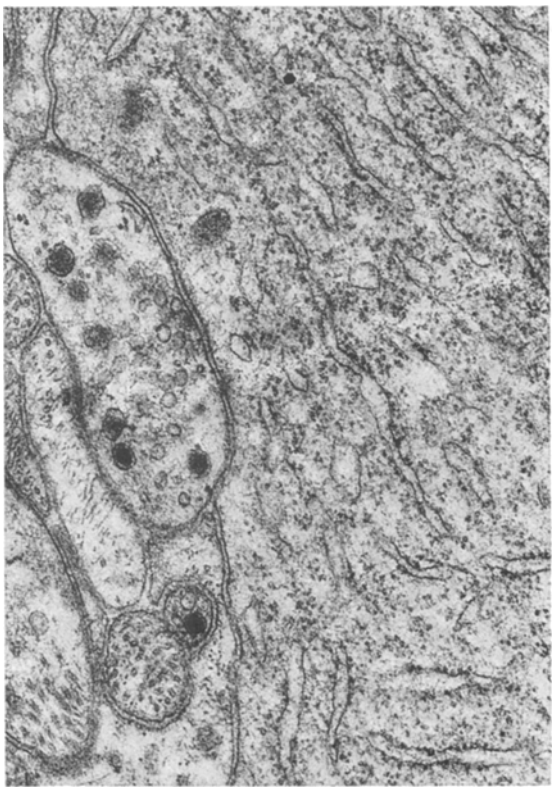

Fig. 1. Rat stomach. Myenteric plexus. Synaptic junction between a nerve fibre and the pericarion of an intramural neuron. The nerve process contains many agranular round vesicles partly aggregated near the presynaptic membrane, and a few large dense-core vesicles. × 40,000.