Self-Stimulation in the Ventromedial Hypothalamus

Abstract. *Male Sprague-Dawley rats pressed a bar for electrical stimulation of the ventromedial hypothalamus. The threshold for such behavior correlated positively with the threshold to stop feeding and the threshold to escape from prolonged stimulation at the same electrode site. The results again open the question of the role that the ventromedial area is playing in positively reinforcing and punishment systems.*

When rats are stimulated in the ventromedial portion of the hypothalamus, they stop any ongoing feeding and learn to turn off the stimulation if given the opportunity (*1*). Some animals will learn to turn on the stimulation, although such self-stimulation behavior is usually regarded as ambivalent (*2*). From a theoretical point of view, the ventromedial hypothalamus and, especially, the ventromedial nucleus have been allocated at least two major functions. They have been included in a periventricular punishment system (*3*) and are believed to be part of a satiety mechanism involved in feeding behavior (*1*). Consequently, stimulation of the ventromedial area is generally regarded as being both aversive and satiating, and any self-stimulation behavior as probably due to spread of current into adjacent positively reinforcing areas.

In 1962, Krasne suggested that perhaps the stimulation of the ventromedial area was purely aversive, and that animals stopped feeding simply because the stimulation was painful (*4*). He went on to show that the threshold current to stop feeding or drinking correlated positively with the escape threshold. I repeated Krasne's study but also looked at self-stimulation behavior. I reasoned that if an animal stops feeding because of the activation of a punishment system, animals which stop feeding at low thresholds should be the least likely to show self-stimulation. Secondly, if the stimulation is ambivalent, because of the simultaneous stimulation of a punishment and a positively reinforcing system, there should be a negative correlation between escape thresholds and self-stimulation thresholds. I found that the electrode placements which stopped feeding the most readily also produced the best self-stimulation behavior, and that there was a high positive, not a negative, correlation between the threshold producing escape behavior and that producing self-stimulation.

I implanted male Sprague-Dawley rats with bipolar electrodes aimed at the ventromedial nucleus (*5*). Several days after the operation, I stimulated the area with a negatively going pulse, 1 msec in duration, delivered every 10 msec from a constant-current source. I ascertained whether a current of 150 μa or less would stop a rat deprived of food for 23 hours from eating wet mash. All animals requiring more than this amount of current were discarded from the experiment in order to minimize arguments about spread of current. I then determined the current threshold for eliciting each of three behaviors. (i) The threshold to stop feeding was measured by determining the current level necessary to stop an animal deprived of food for 23 hours from eating wet mash. (ii) The threshold to escape from continuous stimulation was measured by determining the current level necessary to make an animal press a bar that turned off the stimulation for a period of 5 seconds. (iii) I determined the current threshold necessary to sustain self-stimulation behavior for a period of 2 minutes. In all three determinations I used the psychophysical method of minimal changes. Each animal was tested for 20 minutes a day for at least 2 weeks on a particular measure. The order of testing was randomized among the animals. Altogether, 23 animals were tested for self-stimulation and stopping of feeding, and 12 of these were randomly chosen to be tested in the escape test.

Figure 1A shows the threshold of each animal for escaping from the stimulation plotted against its threshold to stop feeding. The results support Krasne's finding that both variables are positively correlated. The lowest thresholds recorded, in the order of 15 μa, are as low as any thresholds I have found in other areas of the brain for producing a behavioral effect. In Fig. 1B, the self-stimulation threshold is plotted against the escape threshold. Again, the correlation is positive. However, here there is the paradoxical positive correlation between an animal that approaches the stimulation under one condition but escapes from it under another. These results make sense if it is assumed that the current is basically rewarding at the beginning of the stimulation but becomes aversive if it is left on too long. Such a state is not uncommon in other self-stimulation areas where most animals that show self-stimulation will also learn to turn off the stimulation (*6*). In Fig. 1C, the self-stimulation threshold is plotted against the threshold to stop feeding. The correlation between the two is very high and obviously positive. Only one animal failed to show any self-stimulation (*7*).

The reason why such excellent self-stimulation behavior has not been seen by earlier investigators is probably because a large percentage of animals fail to show any substantial rates of bar pressing in the first few hours of testing and especially in the first few minutes of each daily session. Earlier mapping studies for self-stimulation typically looked at each electrode point for only relatively short periods of time (*2*). On the first day of testing, many animals are hyperactive and try to escape from the testing apparatus. Most animals will only show self-stimulation at high current levels. Their behavior is certainly ambivalent, as reported by

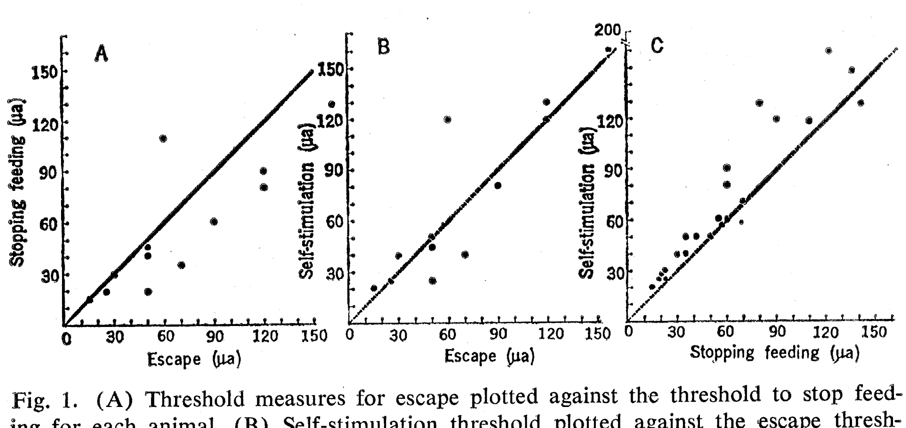

Fig. 1. (A) Threshold measures for escape plotted against the threshold to stop feeding for each animal. (B) Self-stimulation threshold plotted against the escape threshold for each animal. (C) Self-stimulation threshold plotted against the threshold to stop feeding for each animal. The dotted lines are lines of equal threshold.

Olds (*2*). However, with continued testing, the animals eventually settle down to low, stable thresholds with lever-pressing rates of several thousand responses per hour.

Also worth mentioning is how an animal behaves when the current reaches the level that stops it from feeding. The animal stops feeding abruptly and then exhibits searching behavior around the box, sniffing and rearing on its hind legs. The behavior is not that of an animal satiated for food (which normally goes to sleep) but of an animal actively searching for something. The stimulation appears to distract the animal from feeding rather than reducing its hunger.

At the end of testing, the animals were perfused and their brains were sectioned in order to determine the location of the electrode tips. All electrodes were medial to the fornix with the majority located in the ventromedial nucleus. Some were located in the dorsomedial nucleus of the hypothalamus and others fell in between these locations. Three animals had electrodes in the arcuate nucleus. An analysis of threshold levels with respect to location failed to reveal any relation between these specific nuclear groups and the effectiveness of stimulation.

The most significant aspect of these data is that the self-stimulation thresholds in the ventromedial area are positively correlated with both the escape and the stopping of feeding thresholds. This has three important implications.

1) This positive correlation shows that the self-stimulation behavior observed is not a result of the current spreading (presumably laterally) to other areas in the brain which are known to produce self-stimulation. It indicates that the electrode site which stops feeding behavior when stimulated also has rewarding properties, and that continued stimulation eventually becomes aversive.

2) The data question the concept of a major punishment system coursing through this area. Stimulation certainly produces escape behavior that is in keeping with the ambivalent results found in the earlier studies. However, stimulation is at least as rewarding as stimulation of the medial forebrain bundle, as far as threshold measures are concerned. This is incompatible with the idea that the ventromedial area is primarily part of a punishment system.

3) The data warrant the suggestion that the ventromedial system stops feeding, not because it activates some satiety mechanism, but because the stimulation in this area elicits searching behavior which is incompatible with feeding. It appears that the ventromedial area of the hypothalamus may be organized similarly to, and parallel with, the lateral hypothalamus and medial forebrain bundle. Both areas are rewarding and drive producing, although the exact nature of the drives elicited in the ventromedial nucleus are as yet undetermined.

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References and Notes

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3. D. L. Margules and L. Stein, *Amer. J. Physiol.* **217**, 475 (1969).
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5. The electrodes were made from stainless-steel wire, 0.008 in. in diameter, insulated with enamel. Two wires were twisted together and then cut so that the tips were next to each other with only the cross-sectioned area exposed.
6. G. H. Bower and N. E. Miller, *J. Comp. Physiol. Psychol.* **51**, 669 (1958).
7. The Spearman rank correlation coefficient between stopping of feeding and escape is .86; between self-stimulation and escape, .88; and between self-stimulation and feeding, .84. All are significant ($P < .01$).
8. Supported by NIH grants MH 13189 and GM 01789.

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Taste Stimuli: Time Course of Peripheral Nerve Response and Theoretical Models

Abstract. *The responses of a taste nerve in rats to sodium chloride were integrated over successive 10-millisecond intervals and averaged. The time course of the mean responses consisted of a 30-millisecond latency, a rapid rise to a maximum, and a slower decline to a sustained level. The chemoreceptor theories of Beidler and Paton failed to predict the relation between phasic response and time or concentration.*

The neural response of sensory systems often consists of initial, rapidly changing (phasic) components, which are followed by prolonged, relatively stable (tonic) activity (*1*). The biophysical bases for these components as well as their information content have received a variety of interpretations. In systems such as vision, audition, and somesthesis, the phasic activity is believed to be an important, if not predominant, representation of environmental events. Such designations of the primary importance of phasic response components are often based on observations of rapid behavioral re-

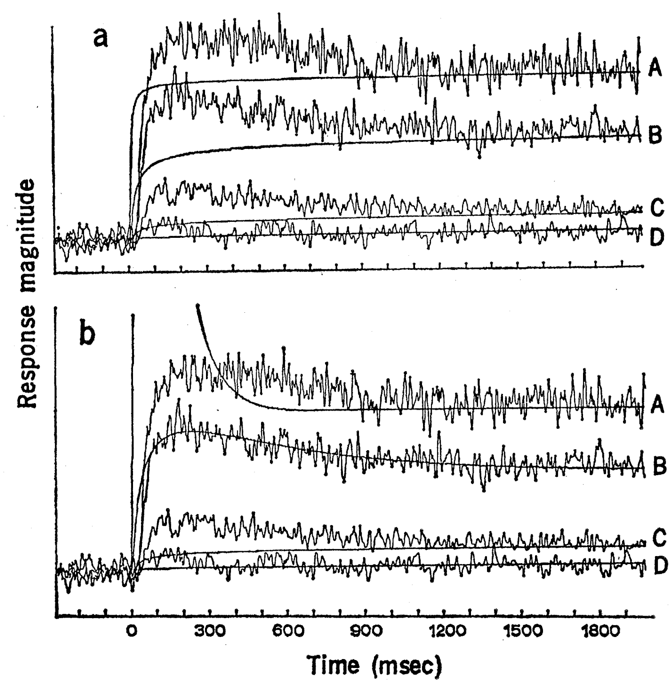

Fig. 1. Comparisons of observed responses (uneven lines) and responses predicted by theoretical models (smooth lines) for four concentrations of NaCl: (*A*) 1.0*M*, (*B*) 0.1*M*, (*C*) 0.01*M*, and (*D*) 0.001*M*. Zero time is the time of stimulus arrival at the tongue. (a) Predictions based on Beidler's theory (*4*). (b) Predictions based on Paton's theory (*6*).