Even at temperatures near 600°C, where the KBr matrix itself started to sublime, the optical densities of the formate bands decreased only very slowly. In comparison, the decomposition temperature of pure sodium formate is reported to be about 310°C (*5*). We did not observe formaldehyde in our disks, and this is not surprising since we expected it to decompose readily into H_2 and CO under our experimental conditions. However, formaldehyde is reported to be formed in the pyrolysis of pure sodium formate powder (*5*).

We believe that the reduction mechanism observed in these disks involves the CO_2 anion free radical. This radical has already been identified by electron spin resonance spectroscopy in single crystals of sodium formate irradiated with x-rays (*6*). Evidence for the importance of this radical in our reaction is as follows. First, in KBr, isotopic formates were obtained during the thermal decomposition of oxalates hydrated with H_2O or D_2O. Second, formate appeared as a major product in the decomposition of acetate ion in KBr matrices. Third, we have observed what appears to be the reverse of the free-radical mechanism, namely, the formation of bicarbonate from formate. In thermal degradation studies of potassium formate in KBr matrices (*4*), we invariably observed bicarbonate as one of the minor products (see spectrum *A*, Fig. 1). This bicarbonate was not due solely to hydrolysis of the product carbonate by the atmospheric moisture, since decomposition of deuterium formate gave deuterium bicarbonate. Finally, the electron paramagnetic resonance spectra of our disks showed the presence of long-lived free radicals. The electron spin resonance signals decreased markedly if the disks were ground into fine powders and disappeared completely if the disks were dissolved in water. Details of these studies will be presented later (*4*).

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Interaction of Positive and Negative Reinforcing Neural Systems

Abstract. *Evidence is presented indicating that the repetitive turning on and off of reinforcing brain stimulation is not a special property of restricted hypothalamic and tegmental areas. Results from a sample of 22 diverse hypothalamic, septal, amygdala, and hippocampal sites suggest that such behavior can be obtained from most neural areas from which self-stimulation behavior may be elicited. Questions thus arise about the location of aversive neural systems when aversion is considered as being expressed by the act of terminating positively reinforcing brain stimulation.*

Reports that animals will repetitively initiate and terminate electrical stimulation of some brain areas (*1*) has led to speculation that an aversive or negative reinforcing system is activated by prolonged positive stimulation. It has been suggested that this aversive system is activated by a summation of subthreshold stimuli at the periphery of the influenced neural area (*2*). Because these reports have implicated either the hypothalamus or neighboring and functionally allied tegmental areas, interpreters of such data have concluded that aversive and positive neural systems are adjacent to each other in this relatively delimited area (*3*).

We have recently completed a study which suggests that animals will repetitively initiate and terminate reinforcing brain stimulation from most if not all neural areas from which self-stimulation behavior may be elicited. Eighteen rats were implanted with bipolar electrodes of a type previously described (*4*). As four of the animals had two electrodes implanted, a total of 22 neural sites were studied. Histological confirmation of these sites which included diverse hypothalamic, septal, amygdala, and hippocampal (dorsal and ventral) areas is illustrated in Fig. 1 (*5*).

Animals were first trained to press a lever for continuous reinforcement with 0.5-second trains of biphasic rectangular pulses (duration, 0.2 msec; frequency, 100 pulse-pairs per second). After this initial training animals were placed in a plexiglas testing chamber with two levers 10 cm apart, mounted on the front wall. Pressing the left (onset) lever initiated the stimulation train, and responses on the right (offset) lever terminated the train. Animals rapidly learned to turn the stimulation on and off, but in three instances the experimenter facilitated learning by turning off the stimulation when the animal approached the offset lever. This "two-lever" method of determining an animal's preferred duration of stimulation was favored over the "single-lever" method which requires that the lever be held down to receive stimulation. A comparative study of the two methods indicated that animals often terminated the stimulus with the "single-lever" method simply because motoric side effects or the general excitement resulting from the electrical stimulus made them unable to hold the lever down (*7*).

The animals were given five practice tests in the two-lever situation at each of three stimulus intensities. During each 15-minute test only one intensity was presented. Different intensities were presented in a random sequence with an interval of at least 1 hour between tests. A 1-minute "warm-up" period during which time no data were collected preceded each 15-minute test. The intensities selected were derived from preliminary tests: the low intensity was judged to be slightly above reinforcement threshold; the intermediate intensity yielded maximum response rates; the high intensity, which was approximately 75 percent higher than the intermediate figure, resulted in great excitement and in some cases marked motoric side effects.

After the practice tests the animals were given an additional five tests at each of the three stimulus intensities, with all conditions as described for the practice tests. Two of the animals were tested at four intensities. The number of stimulus trains was recorded, along with the total time that the stimulus was left on (duration

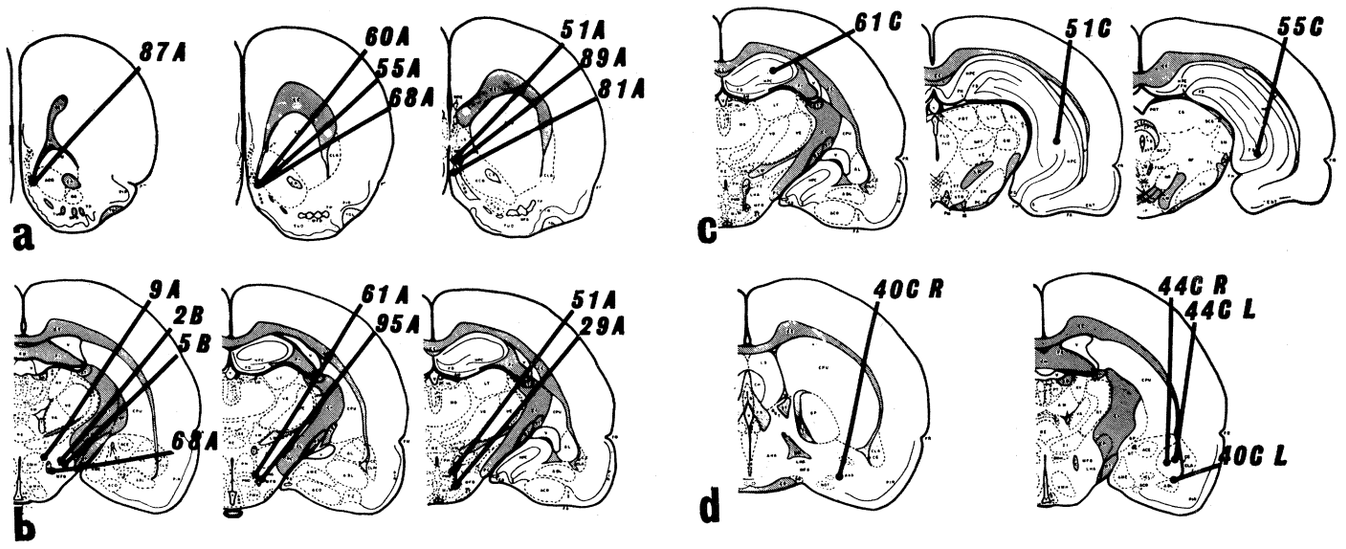

Fig. 1. Cross sections of the rat brain after de Groot (*6*), illustrating placement of the electrodes.

time) and off (reset time) (recorded in 0.1-second units) during each 15-minute test. Average duration and reset times were calculated by dividing the total duration and reset times by the number of stimulus trains initiated by the animal during a session. During a few tests, clonicotonic convulsions were induced in some animals, but with an observer always present it was possible to end such tests and repeat them later.

The results are summarized in Fig. 2. All the animals terminated the stimulus, and the slope of the curves indicates that animals terminated the stimulus more rapidly at the higher intensities. It is of considerable interest that, although the stimulus was terminated earlier at the higher intensities, it was also turned on again earlier.

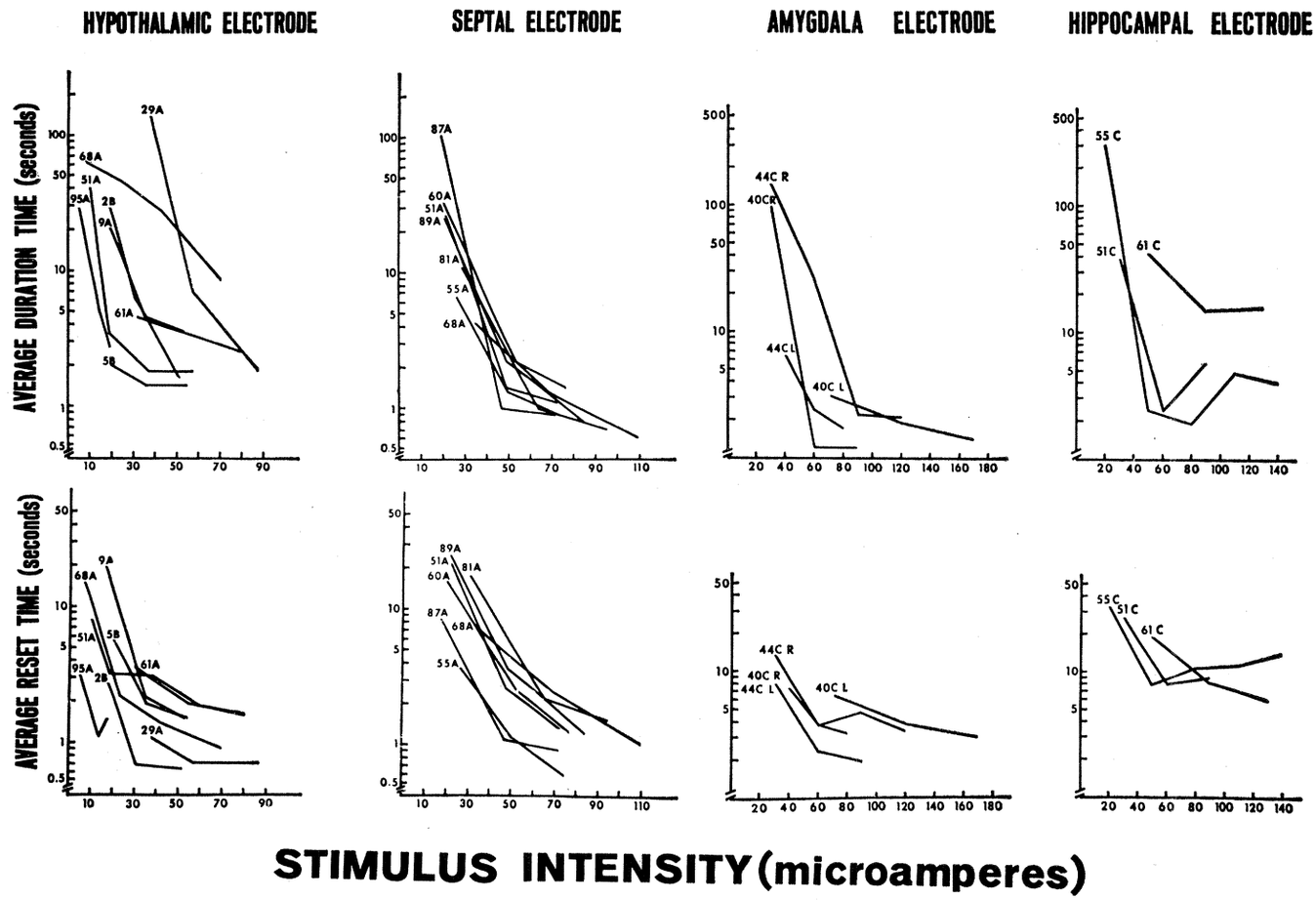

Fig. 2. Average time animals left the stimulus on (duration time), and average time the stimulus was left off (reset time). Data obtained from five tests at each intensity.

Some appreciation of the quality of the response pattern can be gained from inspection of the quantitative data. At the intermediate intensities the average duration of stimulation for all sites was 4.3 seconds, and the average reset time was 3.2 seconds. Thus, during the 15-minute tests animals were oscillating back and forth between the onset and offset levers. At the higher stimulus intensities this oscillation rate tended to be considerably faster (average duration, 2.8 seconds; average reset time, 2.6 seconds).

Some additional qualitative observations were made. For a few animals the reset time increased at the highest intensities. In some of these cases it was noted that a motoric response (for example, jumping), associated with the offset of the stimulus, appeared to interfere with the animals' ability to turn the stimulus on again. With ventral hippocampal electrode placements there was a significantly longer reset time. These animals tended to press the offset lever repeatedly before turning the stimulus on again. We could not determine with certainty whether some effects persisted after termination of the stimulus, so that experience of an abrupt offset was lacking; or whether after hippocampal stimulation the animals were confused and did not know which lever to press.

It was suggested (*2*) that animals receiving hypothalamic stimulation terminate the stimulus earlier at higher intensities as a consequence of more rapid activation of an aversive system. In contrast, it was also hypothesized that animals with septal electrodes may not exhibit this tendency because stimulation in this area does not activate an aversive system; in such animals the stimulus would be terminated only as a result of a loss of its effectiveness resulting from adaptation. It would be expected that adaptation would occur more slowly at higher intensities. The data from the present experiment directly oppose this hypothesis. The differences in duration and reset times attributable to these two neural areas seem to indicate that animals with septal electrodes terminate the stimulus faster at higher intensities than do animals with electrodes located in the hypothalamus. For the eight hypothalamic sites studied, the average duration and reset times were 7.1 and 1.6 seconds (intermediate intensity) and 3.0 and 1.2 seconds (highest intensity), respectively; for the seven septal placements the comparable averages were 1.5 and 2.3 seconds (intermediate intensity) and 0.9 and 1.1 seconds (highest intensity), respectively.

Several conclusions may be drawn from data which suggest that most, if not all, self-stimulating animals will repetitively turn a stimulus on and off when enabled to control duration. The position that these positive reinforcing areas have neighboring aversive areas would be difficult to maintain, however, in the absence of supporting evidence. In the past, when applied only to hypothalamic areas, this argument could be justified in view of the claims that medial hypothalamic stimulation produced ambivalent or avoidance reactions (*8*). According to another, perhaps more defensible conclusion, it is assumed that most positive systems have the potential to activate an aversive system or systems located at some unknown distance from the stimulation site. If this is true it is evident that any conclusion about the location of such an assumed aversive system(s) cannot be based solely upon the act of terminating positive brain stimulation. In fact, it would not be unreasonable to postulate that aversive consequences of prolonged stimulation may result from afferent feedback from systemic effects. Animals may terminate stimulation to obtain a respite from shifts in heart rate, body temperature, respiratory rhythm, and numerous other changes in bodily states known to be produced by central stimulation.

From another vantage point it may be asked whether termination of a stimulus should be considered sufficient evidence of the existence of an aversive system. It has been reported (*9*) that animals repeatedly turn on and off any appropriate stimulus placed under their control. With respect to reinforcing brain stimulation, more recent data raise some questions about interpretations in which an activation of an aversive system is assumed. From the present experiment it is evident that, although animals terminate the stimulus sooner at high intensities, there is no resistance to turning the stimulus on again. In fact, the stimulus is reset faster at the higher intensities. We have also fixed stimulation trains many times longer than the preferred durations, but even under these conditions there was no hesitancy in turning the stimulus on again (*10*). Similarly, it has been reported that when stimulus trains longer than the preferred duration are offered as a reward, animals respond at higher rates on a variable-interval reinforcement schedule (*11*), and at higher ratios on a progressive ratio test (*12*). This strong evidence that stimulus durations longer than those determined by the animals themselves have high reinforcement value raises a critical question about the nature of the presumed aversion which results from prolonged positive stimulation.

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Gravitational Stress: Changes in Cortical Excitability

Abstract. *Evoked responses, recorded from the visual cortex, are enhanced during positive (head to tail) acceleration, and during cerebral hypotension induced by hemorrhage. The phenomenon observed during positive acceleration may therefore be due, at least in part, to its hypotensive effect, but the increased somatic stimulation must also be considered.*

Electrical activity, recorded from the visual cortex and evoked by photic stimulation, is enhanced during mild positive acceleration. This effect is in marked contrast to the electrocortical depression which is produced by more severe acceleration.

Five cats were prepared with permanently implanted extradural electrodes,