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# Self-Stimulation of the Brain

## Its Use To Study Local Effects of Hunger, Sex, and Drugs

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This article reviews experiments which have led to the discovery and analysis of localized systems in the brain where electric stimulation has positive and negative motivational effects (*1*). Basically, the experimental animal in these studies is rewarded or punished by a brain shock. The site of electric stimulation determines the motivational effect.

The studies are important primarily as a beginning step toward filling the large gap which has existed between neurophysiological techniques and an understanding of complex psychological processes. Among other things, they carry the enterprise of brain mapping into the realm of clearly defined motivational functions; this by itself correlates an orderly array of integrative psychological mechanisms with an orderly array of anatomical points in the brain. Furthermore, these studies perform a unification long considered technically impossible between electrophysiological, independent variables and standard, behavioral, dependent variables to produce smooth interaction curves relating the two.

For psychologists, these experiments help to clarify the basic notions of reward and punishment. Reward and punishment, it is agreed, determine which behaviors will predominate in an organism's repertory and which will be erased from it. Rewarded responses are repeated more frequently than would be expected by chance; punished ones are repeated with less frequency. This is obvious.

Less self-evident is the thesis of the classical theory of reward, according to which reward is interpreted as being the falling phase of the same massive stimulation which at high levels constitutes punishment. This thesis is greatly weakened by the work outlined in this article; however, it has held sway for such a long time in psychology and conditions so many basic attitudes that it will certainly form a foundation stone for the new theories which replace it.

Drive and punishment are synonymous, according to this theory, and a reward is held to be fundamentally nothing more than the reduction of a drive. Physiological conditions which are inimical to survival, such as food deficiencies or tissue damage, cause massive receptor discharge into the central nervous system. This discharge is held to be the drive, and it is held to be reflected in behavioral activation. The latter is a nonselective function of the massive drive stimulation, energizing adaptive and maladaptive responses equally. The drive stimulation, however, also has a selective function by which it combines with other cue stimuli to select those responses which have repaired this particular physiological deficit in the past.

The response actually selected by the combination of drive and cue stimuli is determined entirely by structural cue-response connections whose strength has been determined by prior learning. More specifically, a group of cues actually selects the response which was previously followed by drive reduction in their presence. The drive reduction, on previous occasions, caused a rewarding or positive reinforcing effect which somehow increased the causal connection between these stimuli and this particular response.

The hedonistic view that behavior is pulled forward by pleasure as well as pushed forward by pain is rejected in this classical theory for the more parsimonious notion that pain supplies the push and that learning based on pain reduction supplies the direction.

The work reported in this article clearly shows one implication of the drive-reduction theory to be incorrect, for massive inputs to certain parts of the central nervous system are shown to have rewarding effects. Further, by showing that there are anatomically separate mechanisms for reward and punishment in the brain, it points directly to a physiological basis for the motivational dualism suggested in the hedonistic theory.

In fact, it appears that the area producing rewarding effects, upon electric stimulation, is far larger than the area producing punishment. In one early experiment, 76 electrodes were implanted in the brains of rats in an attempt to get a random sampling of midbrain and forebrain points. It was found that stimulation at 47 of these points had motivational effects. Stimulation at 36 of these motivational points produced approach behavior—that is, the rats stimulated themselves repeatedly by means of the technique described below; at only 11 points did stimulation produce avoidance behavior (*2*).

### Basic Studies

*Method.* The method of self-stimulation (*3*) is modeled in part after the chronic implantation technique of W. R. Hess (*4*) and in part after the box technique of B. F. Skinner (*5*). The former developed a technique for implanting electrodes permanently in the brain; the

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technique allows stimulation in the freely behaving animal. The latter worked out a way to measure positive reinforcement—that is, reward—by arranging a situation in which the experimental animal could deliver the reward to itself by a very simple manipulation, and then counting the frequency of the manipulations. Self-stimulation combines these techniques by allowing animals to deliver shocks to specific points in their brains through chronically implanted electrodes.

Figure 1 shows the method used. When the rat stepped on a pedal, a shock was delivered to its brain. The rat

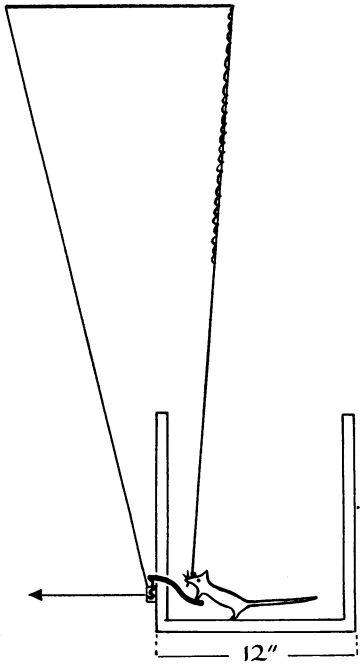


Fig. 1. Diagram of apparatus by means of which a rat delivers electric shocks to its own brain. When the rat steps on the pedal, the electric circuit is closed and current is transmitted to its brain by means of implanted electrodes.

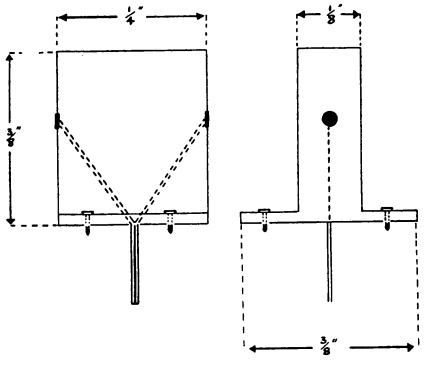

Fig. 2. Diagram of plastic electrode carrier, containing a pair of silver electrodes, which is screwed to skull of rat, with wires penetrating deep into the brain, as shown in Fig. 3.

never received any other reward for pressing the pedal, and the shock was never turned on except when the rat turned it on itself by stepping on the pedal.

In this box, animals invariably stepped on the pedal about 25 times during the first hour (although there was no rewarding electrical stimulation at all), because the pedal was so placed that it would be pressed when the animal looked out the only opening in the box. After the first hour there were about five responses or less per hour during hours in which no reward was produced. If the pedal-pressing produced a reward, the rate, even for the first hour, rose to 200 or more responses an hour; thus, "reward" was clearly discernible. If the pedal-pressing produced punishment, the rate dropped radically; there were only two or three responses during the total experimental procedure; thus, "punishment" was clearly discernible.

If the electrode was placed in the brain at a point at which maximum self-stimulation is produced, the rat, after its very first electric stimulation, began to search and pursue eagerly. Its response to the first shock was to sniff in all corners of the box and manipulate quickly the objects in its path until it stepped on the pedal a second time. After the rat had pressed the pedal a second or third time, it ceased to wander and began to respond at the rate of one or two pedal-presses per second. These animals learned to press the pedal within a minute or two.

Figure 2 shows, in schematic form, the plastic electrode carrier which was screwed to the skull and a pair of silver-wire electrodes implanted in the brain through a hole in the skull. The insulated wires, which were 0.01 inch in diameter, stimulated the brain only at their tips. The electrode apparently fired cells up to a distance of at least 0.5 millimeter from its tip. Figure 3 (top) is an x-ray photograph of an electrode in place in the brain of an intact animal; in Fig. 3 (bottom) the tip of the electrode track appears as a blackened area on the photomicrograph of a stained brain slice. In these experiments each brain was sectioned and stained after testing; all statements about localization are based on examination of this histological material.

The stimulus was a sine-wave shock at 60 cycles per second; the current ranged from 5 to 100 microamperes; the animal received a shock lasting for a maximum of 0.5 second. If the animal held the pedal down for less than 0.5

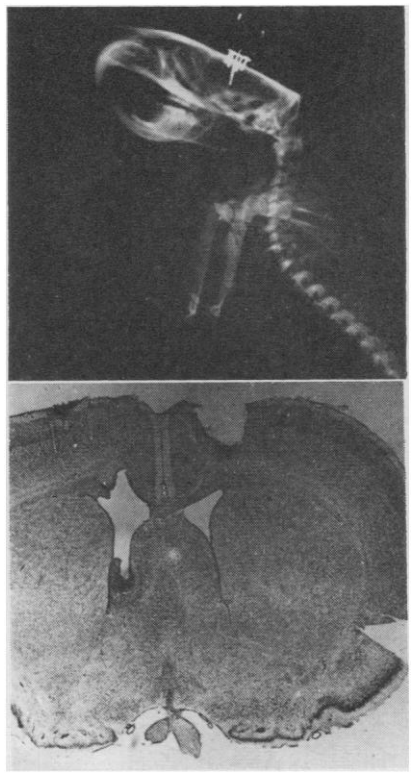

Fig. 3. (Top) X-ray photograph of an electrode (deepest shaft) in place in the brain of a rat. The four shorter shafts are screws which hold the electrode carrier to the skull. (Bottom) Photomicrograph of stained brain slice from a rat sacrificed at the end of a series of experiments. The tip of the electrode track appears as darkened area. Wires are insulated along their whole length and stimulate the brain only at the tip.

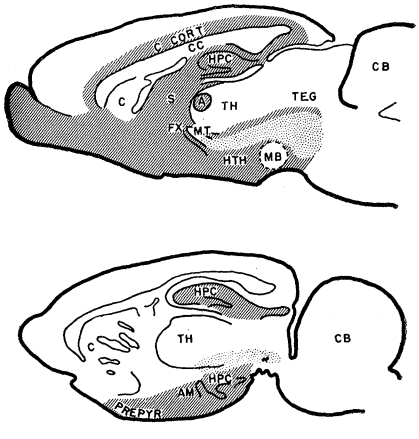


Fig. 4. Medial and lateral sagittal sections of the rat brain showing, by cross-hatching, the areas where electric stimulation causes approach behavior and, by stippling, the areas where electric stimulation causes avoidance. *A*, anterior thalamus; *AM*, amygdala; *C*, caudate nucleus; *CB*, cerebellum; *CC*, corpus callosum; *C CORT*, cingulate cortex; *FX*, fornix; *HPC*, hippocampus; *HTH*, hypothalamus; *MB*, mammillary bodies; *MT*, mammillothalamic tract; *PREPYR*, prepyriform cortex; *S*, septal area; *TEG*, tegmentum; *TH*, thalamus.

second, the current went off when it released the pedal. If it held the pedal down for longer than 0.5 second, the current went off automatically and the rat had to release the pedal and press it again to produce another shock.

*Locus.* Electric stimulation in most parts of the rhinencephalon, and in many parts of the hypothalamus and related structures (see cross-hatching, Fig. 4), produced the approach response (2). Stimulation in small areas in the midbrain and in certain adjacent parts of the thalamus and hypothalamus (see stippling, Fig. 4) produced the avoidance response. Such avoidance behavior was first demonstrated in the cat, by Delgado, Roberts, and Miller (6). In the rat, the area in which stimulation produced avoidance behavior was small compared with the area in which it produced approach behavior.

The rate of self-stimulation tended to diminish steadily as the site of stimulation was moved toward the cortex. Rates as high as 7000 per hour were achieved when electric stimulation was applied in the region of the interpeduncular nucleus of the tegmentum.

With electrodes placed in the posterior hypothalamus, just in front of the mammillary body, very high rates, in the range of 5000 per hour, occurred frequently. With electrodes placed in the anterior hypothalamus, rates ranged from 400 to 1100 per hour. With electrodes placed farther forward, in the preoptic and telencephalic areas, there was a second series of rates, ranging from quite high ones (about 3000 per hour) for the preoptic area to very low ones (about 200 per hour) for the anterior forebrain. The high rates obtained in the forebrain series were lower than the high ones of the hypothalamic series.

Thus, there was, for the hypothalamus, a decline of response rates as the electrode was moved forward. There was a similar trend for the telencephalic region, and the rates for the whole of the telencephalic region seemed to be lower than those for the whole of the hypothalamic region.

*Electric current.* Studies in which the level of electric current was varied (see Fig. 5) provide some basis for explaining these differences in rate of self-stimulation. The level of the shock was raised from 0 to 150 microamperes by steps of 10. Self-stimulation rates started at chance levels of about 4 to 40 responses per hour and remained at these chance levels at 0, and sometimes at 10, microamperes. Then, usually at 20 or 30 microamperes, but sometimes at 10 microamperes or less, a threshold was crossed and self-stimulation rates rose rapidly. As the current was raised further, the response rate showed a steady increase, undulated, or showed no further increase.

We assume that the cells and fibers excited by the electric stimulus obey the all-or-none principle and have relatively similar thresholds. If this is true, each increase in current brings cells at a greater radius from the tip of the electrode to threshold.

Thus, the steep asymptotic curves at the top of Fig. 5 indicate that stimula-

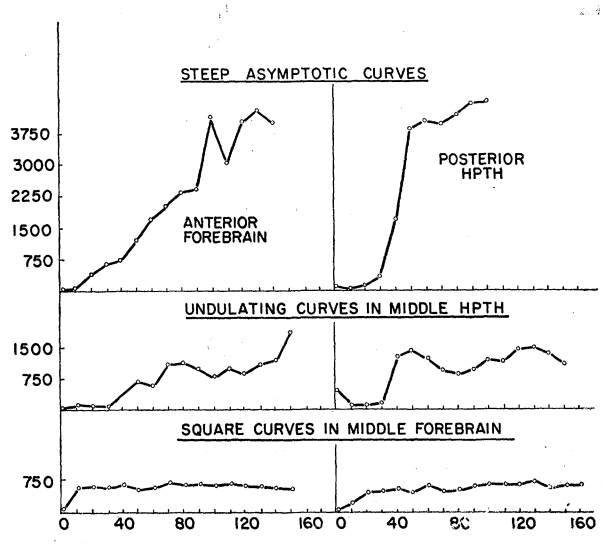


Fig. 5. Electric-current functions. The hourly self-stimulation rate (plotted along the ordinate) tends to rise as current (on the abscissa) increases from 0 to 160 microamperes in steps of 10. In the middle hypothalamus the curve shows a temporary decline when the electric field invades an area where electric stimulation has a negative motivational effect. In the middle forebrain there is an abrupt rise to 500 responses an hour and then no further increase, because there is a very small field in which positive motivational effects are obtained, surrounded by a larger neutral area.

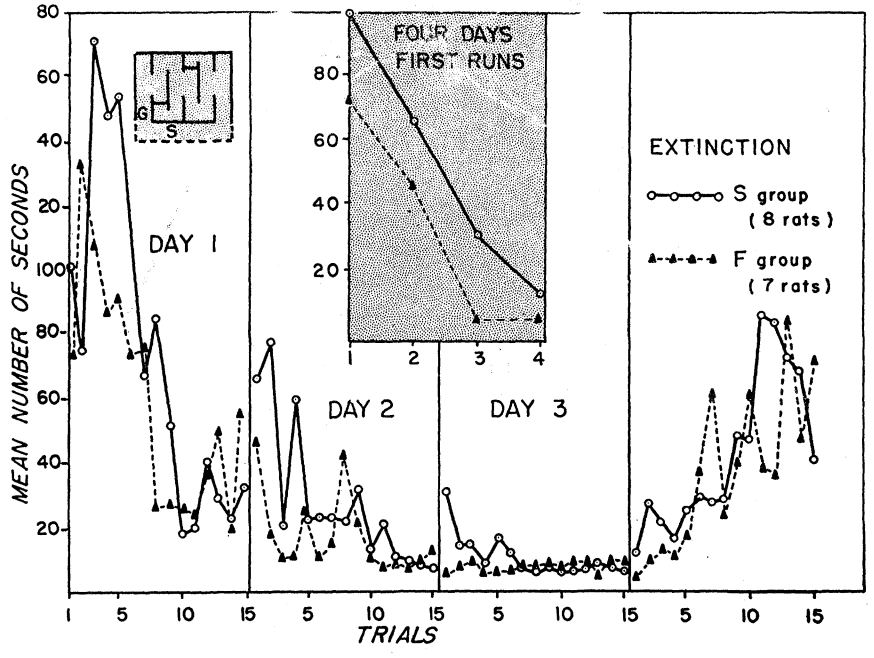


Fig. 6. Maze experiment. At the upper left is a maze. The animal runs from the start position *S*, through the maze, to the goal poistion *G*. At *G* it finds a pedal, steps on it, and stimulates its brain. After the stimulation, the pedal is swung back, and the goal box becomes the start box as the animal runs the maze again. The graphs show a comparison of a group running for food as the reward (broken line) with another group running for electric shock as the reward (solid line). Both groups were 24-hours-hungry. The shock-reward group ran as fast as the food-reward group, at the end of the test, and learned almost as fast. The marked day-to-day improvement shown in the first runs of the four days is especially important. The animals of the shock-group averaged over 100 seconds on the first run the first day. They took about 50 seconds on the first run the second day, 30 seconds on the first run the third day, and 12 seconds on the fourth day. This indicates that an animal runs directly to its goal on the first run of the day, having had no pretaste of the electric stimulus to whet its desire.

tion of several rings of cells around the electrode tip induced the rat to stimulate itself with progressively greater frequency. The undulating curves obtained by stimulation in the middle hypothalamus suggest that stimulation of some rings of cells decreases the rate of self-stimulation; from other evidence it is known (*2*) that "negative" or "punishing" areas infiltrate into the "reward" system in the part of the middle hypothalamus from which these curves were obtained. The "square" curves obtained for the dorsal septal area show that only one ring of cells around the electrode tip had any motivational function; the rest were neutral. Such "square" functions have always resulted when the electrodes were implanted in or near the diagonal band of Broca; the threshold increased as the distance of the electrode from the diagonal band increased. These data on electric current level permit an important inference to be drawn: the asymptotic self-stimulation rate of an area probably depends on the number of concentric rings of "reward" cells surrounding the tip of the electrode.

The square curves indicate several other important points. Since the full rate occurred at 10 microamperes, when the electrodes were in the diagonal band, it appears that cells outside the diagonal band are neutral (the diagonal band is, thus, the only active site in the septal area). The fact that current up to 150 microamperes does not slow the rate of self-stimulation indicates that the reward units of the diagonal band are affected equally by any current from 10 microamperes (threshold) to 150 microamperes (15 times threshold). Since this function was produced repeatedly by the same rat every day for 8 months, it may be assumed that the current of 15 times threshold did no damage to the nearby cells which produce self-stimulation.

Finally, because electrodes may be placed at varying distances from the diagonal band, it is possible to define the shape and size of the suprathreshold electric field produced by various levels of electric current.

*Summary.* (i) The areas in which the stimulation produces the approach or rewarding effect occupy a larger proportion of the brain than do the areas in which the avoidance or punishing effect is produced. Therefore, the brain cannot be thought of as tending mainly to produce behaviors which *decrease* its own excitation, for a large portion causes behaviors which *increase* excitation. (ii) There is some sort of orderly arrangement of the rewarding effect in the rhinencephalon and related structures, with the result that response rates tend to decline as stimulation is moved forward toward the cortex; this is true both within structures and from structure to structure. (iii) Finally, by gauging the way in which rates of self-stimulation increase as the strength of the brain-shock increases, it is possible to estimate the size of the sphere, surrounding a point of stimulation, in which electric stimulation is rewarding. When the size of this sphere is large, as in the ventral posterior hypothalamus, the rate of self-stimulation at high current levels is very high. When there is only a narrow ring, as in the dorsal septal area, the rate, even at high current levels, is low.

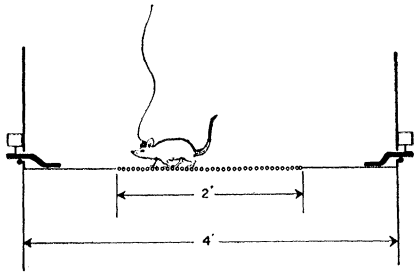


Fig. 7. Obstruction box. An animal receives electric stimulations on one side, then must cross the grid to get more. The animals withstood more foot-shock for the sake of electrical reward than they did when they were 24-hours-hungry and were running for food.

## Analytic Studies

Further studies indicate that the electrical brain-shock reward has the effect of a strong primary reward object in several different experimental situations. These studies suggest also that the electric brain shock excites cells which are normally involved in the mediation of the effects of conventional primary reinforcers such as food and sex objects.

*Maze running.* At first it seemed possible that the animal did not really seek the electric stimulus but pressed the pedal only as a result of some sort of compulsion in a small, confined box. Maze studies (*7*), however, indicated that animals show day-to-day learning of a complex problem in order to get the electric reward (see Fig. 6). Test animals certainly ran as fast as, if not faster than, others running for a food reward. In the case of a runway instead of a maze (*7*), animals ran much faster for the electric stimulus than for food.

*Obstruction box.* The next two studies

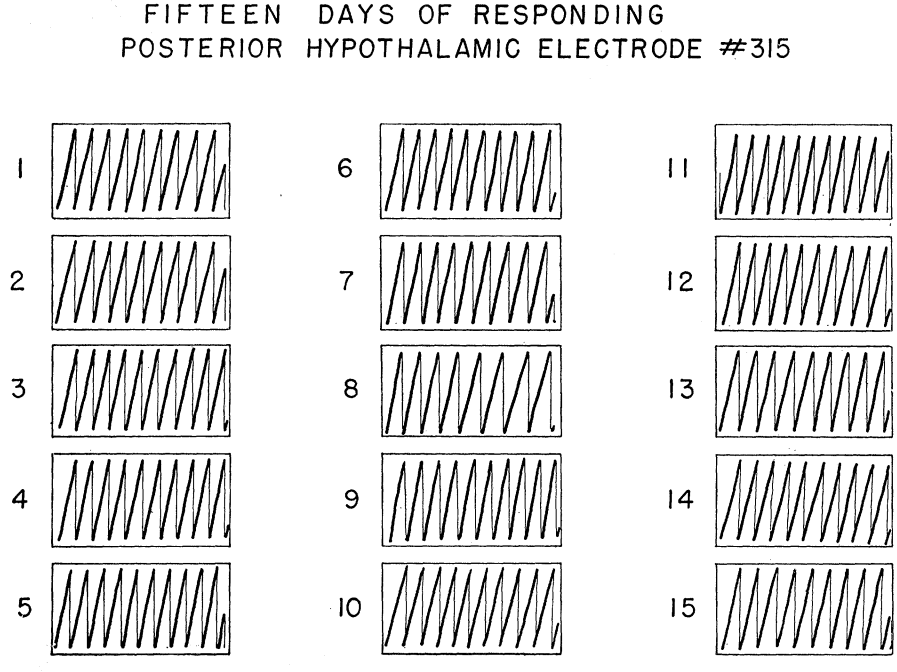


Fig. 8. Response rates in maze studies of one animal for 15 consecutive days. Each square indicates a 1-hour test period on a given day. Each time the record goes from the bottom to the top of a square, the animal has made 500 responses; thus, each peak represents 500 responses or self-stimulations (*9*). The slope of the rising edge of each "sawtooth" indicates the response rate. There are about ten peaks in each day's record; thus, the animal was responding at the rate of about 5000 responses an hour. The electrode in this case was implanted in the posterior hypothalamus. The same rate is maintained all through the hour, and it is also maintained on all 15 days. Such rates are maintained, in fact, for several months in a row—that is, for as long as we choose to run the animal.

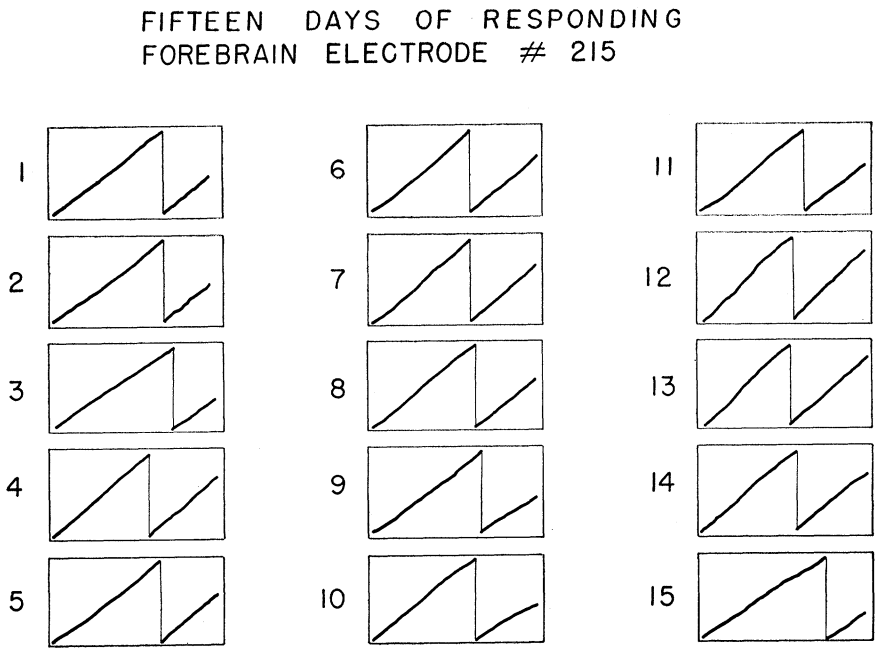


Fig. 9. Diagram similar to Fig. 8, showing response rates in maze studies of an animal with an electrode implanted below the septal region. Here the rate is about 750 self-stimulations an hour.

were concerned with the strength and duration of the drive for self-stimulation. To study the strength of the drive, the obstruction box shown schematically in Fig. 7 was used. In this study (*8*) the rat was permitted to stimulate itself three times at one lever. Then it had to cross a grid, which delivered an increasingly painful foot shock, to stimulate itself three more times at the opposite lever. It went back and forth until the foot shock became so great that it stopped the rat from crossing. Healthy, well-fed rats running for a brain-shock reward endured far more painful shock to the feet than did 24-hour-hungry rats running for food. The drive for self-stimulation appeared to be (in some cases) at least twice as strong as a 24-hour hunger drive.

*Satiation?* As for the endurance of the drive for self-stimulation, two questions may be asked: (i) How many days did the drive last if rats were allowed to stimulate themselves for an hour per day? (ii) How many minutes or hours did the drive last if rats were allowed to stimulate themselves continuously?

When animals were run for periods of an hour a day, they usually maintained the same rate of self-stimulation throughout the hour and for as many days or months as they were tested. Such stable rates (shown in Figs. 8 and 9) were obtained when high suprathreshold electric current (60 to 100 microamperes) was used.

If animals with electrodes implanted in the hypothalamus were run for 24 hours or 48 hours consecutively, they continued to respond as long as physiological endurance permitted. Rats with electrodes implanted in the telencephalon, on the other hand, seemed to slow down considerably when they were shifted from a 1- to a 24-hour self-stimulation schedule. Figure 10 shows the following pattern: a rate of 2000 self-stimulations per hour maintained for 24 consecutive hours, then sleep, and then further response at a rate of 2000 self-stimulations per hour; this is typical when electrodes are implanted in the hypothalamus. Figure 11 shows rates of self-stimulation for a series of animals on such a regime. All curves obtained from animals with electrodes in the telencephalon have early, sharp inflection points. An animal with an electrode in the telencephalic septal area, which responded 1000 times per hour if it was permitted to stimulate itself for only one hour per day, responded only 1000 times in 24 hours if it was permitted to stimulate itself for 24 hours per day. Thus, animals with electrodes in the telencephalon appeared to show some genuine satiation. No similar satiation appeared in animals with electrodes in the hypothalamus.

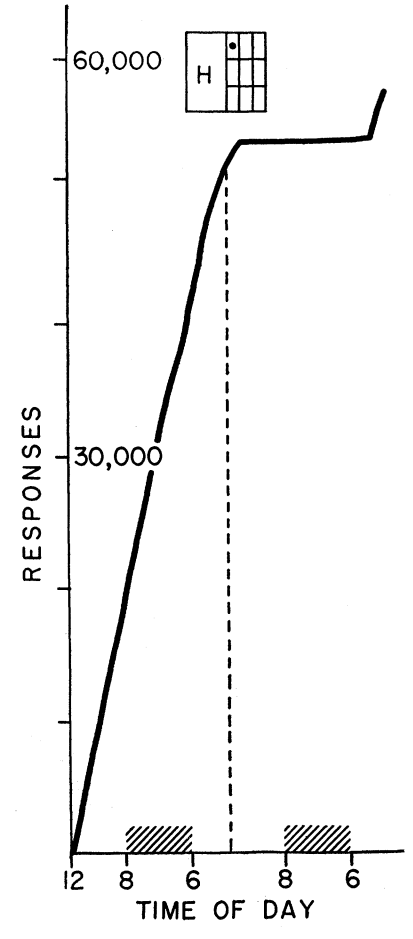


Fig. 10. Graph of continuous self-stimulation for a 48-hour period. Cumulative response totals are plotted along the ordinate, hours along the abscissa. The experiment started at noon; cross-hatching indicates darkness from 8 P.M. to 6 A.M. The animal (with an electrode implanted in the anterior medial hypothalamus) stimulated itself at a rate of more than 2000 responses an hour for 26 hours, then slept, and then resumed self-stimulation at the same rate.

*Effects of drives.* Further studies showed that the animal's taste for the electric reward is often sensitive to basic drives in the way that its taste for conventional rewards is. The extensive reward system appears to break down into subsystems subservient to the different basic drives; there appears to be a food-reward system, a sex-reward system, and so on.

If electric stimulation at some points fires cells that mediate food reward, the animal's appetite for self-stimulation at this point may go up and down with hunger as its appetite for food does. A large series of animals has been tested in order to compare their rates of self-stimulation when hungry with their rates when full. When tests were made at a constant current of 65 microamperes with a set of electrodes placed in the midline of the brain, in the ventromedial hypothalamus, and in the septal area,

hunger seemed to have an important positive effect, increasing self-stimulation rates (*9, 10*). When, however, animals were tested at *a series of current levels,* a somewhat different picture of the hunger system appeared.

In the latter experiments (as shown in Fig. 12) animals were tested every day at a series of shock levels; accordingly, they yielded a series of response rates (usually of increasing magnitude). Each shock level was maintained for 8 minutes, response output was recorded, and then the shock was shifted to the next higher level. Zero microamperes (no reward) was usually maintained for the first interval, and then the shock level was raised to 5 microamperes, 10 microamperes, and so on. Response rates started at very low (chance) levels during the first interval and gradually rose to an asymptote characteristic of the area of stimulation.

Animals were run alternately—one day hungry and the next day full—to see whether this would change the rate of self-stimulation during the various intervals. Many animals responded faster when hungry and slower when sated, but this difference appeared only at a limited range of electric shock levels. The shock level at which the hunger difference appeared is called the "threshold of the hunger effect."

Before discussing these thresholds I shall mention the gross findings of this recent hunger study. When electrodes were in the hypothalamus, all large hunger effects on self-stimulation were obtained with those electrodes which were clustered in the posterior sector. No hunger effects were found when electrodes were in the portion of the anterior hypothalamus that was explored. With electrodes in the telencephalon, however, strong hunger effects appeared again in a rather unclear pattern. With electrodes in the posterior hypothalamus, the interesting and orderly picture shown in Fig. 13 was obtained.

Thresholds for the hunger effect declined as the location of the electrodes approached a point about 1.25 millimeters lateral to the midline at a point just in front of the mammillary body. If we assume that a hunger-reward center is located at this point, we find that it can be reached by 10 microamperes of current from electrodes at points about 0.25 millimeter away and by 20 microamperes from electrodes at points about 0.5 millimeter away. From these data we may surmise (see Fig. 14) that a 50-microampere stimulus has a suprathreshold field with a diameter of about 1 millimeter.

Electric stimulation in the whole posterior hypothalamus has rewarding effects, for stimulation through electrodes anywhere in this area produces very high rates of response even at the lowest current levels. Only stimulation of areas shown schematically at the lower left of Fig. 14, however, seems related to hunger; the other areas must be controlled by other drives.

A hunger differential appears, we may surmise, whenever an electric field is increased to the point where there is a hunger-sensitive area on the boundary between the supra- and subthreshold parts. If this is true, our data suggest a

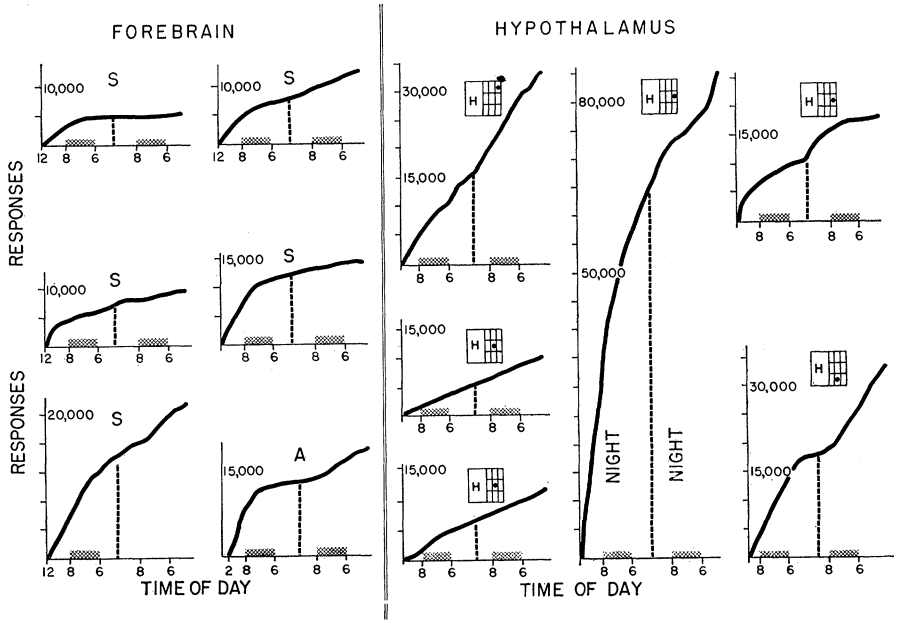


Fig. 11. Graphs of comparative responses of animals with electrodes implanted in forebrain and of others that had electrodes in hypothalamus, in a continuous 48-hour experiment. Animals with electrodes in the forebrain show a point of satiation which does not appear in animals with electrodes in the hypothalamus.

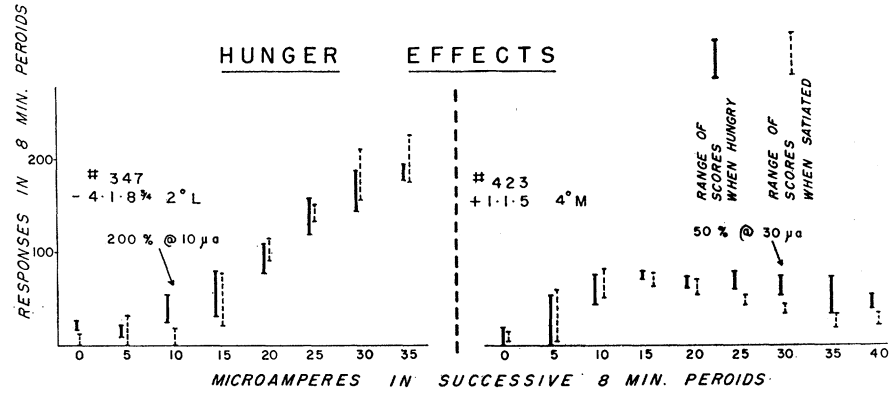


Fig. 12. Hunger effects. Response output is plotted against electric current; each bar or dotted line represents a range of scores obtained on several days. The testing started with current at zero. Current was increased after 8 minutes to 5 microamperes, then to 10 microamperes, and so forth, being maintained for 8 minutes at each level up to 35 or 40 microamperes. Response rates gradually increased, approaching an asymptote characteristic of the area of stimulation. The heavy black lines represent response ranges for three different days when animals were 24-hours-hungry; the broken lines represent ranges for three days when the animals were full. At the left, a sharp hunger differentiation at 10 microamperes is indicated. There is no overlap of scores at this point. The animal averaged 200 percent more responses when it was hungry. However, at all other levels of current this difference disappears. At the right are scores for a different animal with a different electrode placement. Here there is a marked separation of scores at the higher current levels of 25, 30, and 35 microamperes. But at the lower levels, where the animal had quite high response rates, there is no difference between scores while it is hungry and scores while it is full.

sharp localization of a hunger reward center in the hypothalamus and a very compact relation between it and the other drive-reward centers in the hypothalamus—a relation so compact that different effects will be achieved at different current levels.

### Androgen-Level Studies

In androgen-level studies (*11*), animals were castrated after they had been trained to press the lever for brain shock. After castration, rates of self-stimulation were measured for 14 days of declining androgen level. Then testosterone propionate was injected, in doses of from 1 to 5 milligrams per animal, and rates were measured over a period of days while androgen levels rose and fell again. A series of testosterone injections was also given to see how rates of self-stimulation were maintained under androgen replacement therapy.

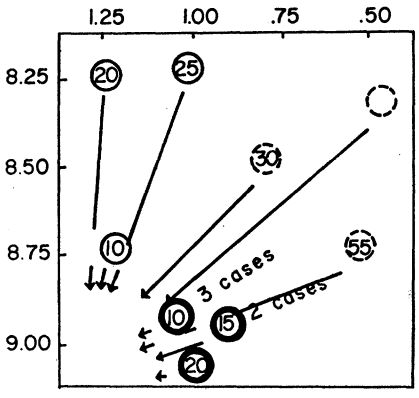


Fig. 13. Hunger map. This is a schematic map of the region of the posterior hypothalamus. (Electrodes 8 to 9 mm long are implanted 4 mm behind the primary skull marking bregma.) The ordinate gives distance (in millimeters) from the top of the skull. The abscissa gives distance (in millimeters) from the midline. Thus, the right side of the drawing represents the medial portion of the hypothalamus. The very dark circles indicate electrode implantations accompanied by very large hunger effects; plain circles indicate those accompanied by moderate effects; broken circles indicate those accompanied by very small effects. The broken circle without a numeral indicates no hunger effect at all. The numerals inside the other circles indicate the level of current (in microamperes) at which the hunger effect could be detected. In the case of the electrodes represented by the cluster of circles at the lower left-hand corner of the map, levels of current of about 10 microamperes produced the hunger effect. With electrodes represented by circles above this point, current levels of 20 and 25 microamperes gave the hunger effect. With electrodes nearer the midline, currents of 30, then of 55, microamperes were required to get hunger differentiation, and even then it was small. With the electrodes represented by circles in the top medial part of the square, no hunger effect is detected at any of the levels of stimulation used. It is almost, but not quite, true that the distance from a point 9 mm deep and 1.25 mm lateral determines the amount of current needed to get the hunger effect.

The second point is that there is an inverse relation between androgen effects and hunger effects on the rate of self-stimulation (see Fig. 16). Hunger effects and androgen effects on rate of self-stimulation were measured in 16 animals, with electrodes in different parts of the hypothalamus and telencephalon, on 1-hour self-stimulation runs with a stimulus of 1 volt (about 60 to 80 microamperes). Animals which showed a strong increase in rate of self-stimulation in response to androgen showed a decline in rate of self-stimulation in response to hunger, and vice versa. In other words, if hunger raised the response rate, androgen lowered it; if androgen raised the response rate, hunger lowered it. If we presume that the placement of the electrode determines the degree of sensitivity to hunger or to androgens, this study gives a firm basis for expecting to find anatomical differentiation between the hunger-reward system and the androgen-reward system.

Other experiments showed the effect of forced electric stimulation on food consumption (consummatory behavior). In these experiments (*12*), electrodes were implanted and were used first to test the effect of stimulation on food consumption. The animals were maintained on an *ad libitum* diet. Eating, under stimulation, in stimulation boxes, was measured for 1 hour per day with current of about 80 microamperes applied for 0.5 second every 10 seconds. Other groups were stimulated with current of 25 microamperes applied for 0.5 second every second. Measures of food intake under stimulation were matched against food intake during control weeks during which there was no stimulation. As has been reported by others (*13*), stimulation in the ventral posterior hypothalamus at points about 1.5 millimeters lateral to the midline caused an increase in eating; stimulation medial to these points sometimes, but not always, caused a decrease in eating. After these tests were completed, the same animals were subjected to self-stimulation tests with the same levels of current. The lateral electrode placements, in areas where stimulation seemed to increase hunger drive, were the ones that usually produced extremely high rates of self-stimulation. The medial placements, in areas where stimulation seemed to reduce the

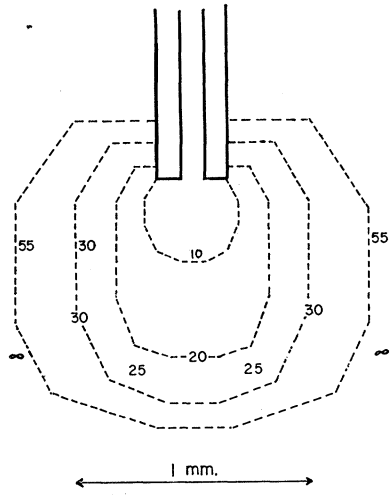


Fig. 14. Electric fields for different levels of current. A current of 10 microamperes seems to produce a suprathreshold electric field which extends more than 0.25 mm downward but a much shorter distance out to the sides and a still shorter distance upward; 20 microamperes seems to reach about 0.75 mm downward; 55 microamperes, about 1 mm. If reference is made to this schematic drawing of the field in connection with each point on the diagram of hunger effects (Fig. 13), it may be seen that the boundary of the suprathreshold field cuts through the supposed hunger point at the shock level where the hunger difference appears. This drawing is intended to suggest orders of magnitude but not exact relationships.

hunger drive, ordinarily produced much slower rates of self-stimulation.

To avoid the notion that there is a food-reward "center" in the posterior hypothalamus, it should be mentioned that a similar relationship between hunger and electric stimulation seems to exist in several more anterior parts of the brain. Figure 17 shows the effect from a rewarding electrode placement in the telencephalon. Electric stimulation at this point increased eating behavior by almost 50 percent, and the animal stimulated itself at a rate of over 1000 responses per hour with no change in level of current.

There is a superficial anachronism in these data correlating drive increase (measured by eating behavior) and reward (measured by self-stimulation); reward has classically been thought to be correlated with drive reduction. There is, of course, the possibility that some conflicting drive is reduced by the stimulation, thereby permitting the animal to eat. There may also be neighboring drive and reward areas, both activated by the same electric field. However, the correlation of rewarding properties with a stimulus which produces consummatory behavior need not be surprising. If we think, for example, of a stimulus to a sexual consummatory response, we might expect some rewarding properties. Why not expect a similar result in the case of hunger?

Thus, our analysis permits the following generalizations: (i) the electrical reward is effective where more conventional rewards are effective—in a Skinner box, runway, complicated maze, and obstruction box; (ii) the reward has the same effect from day to day over long periods of time; (iii) with stimulation through electrodes in some brain areas, hunger augments the rate of self-stimulation, and with stimulation through electrodes in other brain areas, androgens augment the rate; (iv) the rewarding stimulus often appears to produce a temporary increment in some consummatory behavior.

## Drug Studies

The last part of this article deals with more practical considerations. It seems that certain behavior disorders might be benefited if "reward" or "pleasure" systems of the brain could be selectively controlled by use of pharmacological agents. It might be important to control one of the drive-reward systems without affecting the other systems, or to control the forward or cortical reward systems without affecting the posterior, hypothalamic systems.

For these reasons we have hoped to find differential sensitivity of different reward placements to different drugs with known emotional or psychological effects. In recent drug studies (*14*), series of levels of current were used, as in the drive studies. Animals were allowed to stimulate themselves for eight minutes at each level of current, starting at zero and working up to 40 or 50 microamperes. As was indicated previously, the animals did not respond at zero and 5 microamperes. At 10, 15, or 20 microamperes, the animals began to respond. The eight-minute interval in which they began to respond was called the threshold interval. A drug was injected, to become effective at the beginning of the threshold interval (which had been determined by several weeks of previous control testing).

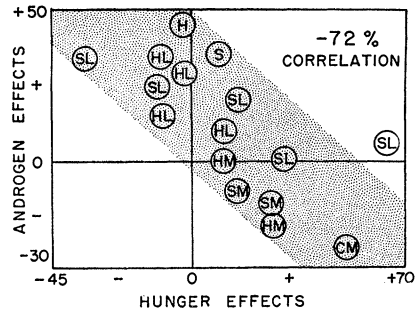


Fig. 16. Relation of hunger effects and androgen effects. Along the abscissa, differences from control rates caused by 24 hours of hunger are plotted as percentages of control rates. Along the ordinate are plotted similar differences caused by administration of 2 milligrams of testosterone to castrated animals. Each point represents one electrode. *SL,* lateral septal area; *SM,* medial septal area; *HL,* lateral hypothalamic area; *HM,* medial hypothalamic area; *CM,* medial caudate area. Animals were run at high, constant levels of electric current. Stimulation points positively affected by hunger tend to be negatively affected by androgens, and vice versa.

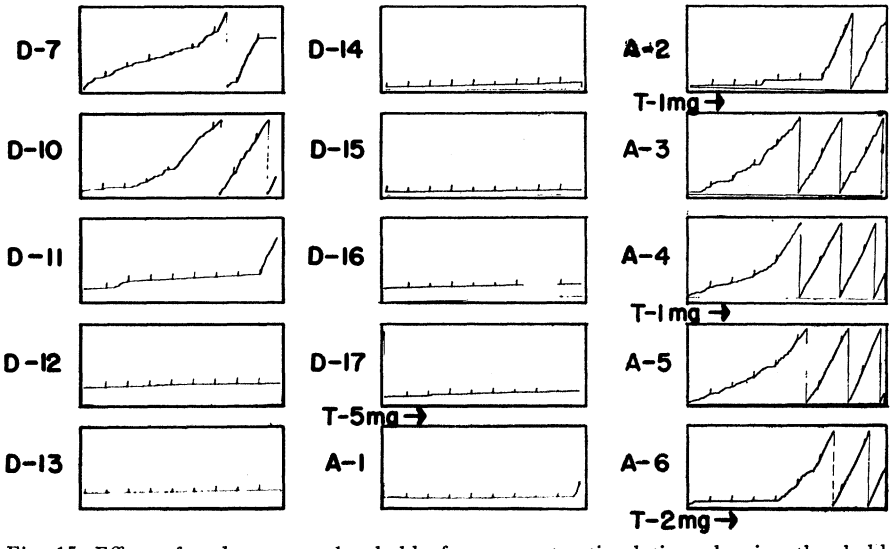


Fig. 15. Effect of androgen on threshold of response to stimulation, showing threshold changes from day 7 after castration to day 17 after castration and reversal of these changes by injection of 5 mg of testosterone propionate in oil. Animals are tested each day at levels of current that increase from 15 to 55 microamperes by steps of 5 microamperes.

*Tranquilizers.* In the bar graphs of Fig. 18 the rate of self-stimulation is shown for successive levels of current after threshold has been reached (these graphs start, that is, with the threshold interval). Restangular outlines show the average rate of response for the day before, and the day after, the drug test. The dark bars indicate the rate of self-stimulation when the animal was under the influence of the drug. The dotted lines show the degree of the effect of the drug. In Fig. 18 the data are for chlorpromazine injected intraperitoneally at 2 milligrams per kilogram. In the case illustrated at the left of Fig. 18, in which the electrode was in the middle hypothalamus, none of the self-stimulating response was eliminated at threshold, only 25 percent of the response was eliminated at the next level, and 21 percent was eliminated at the third level, after which all inhibitory effect of chlorpromazine was over, in this case. In the case illustrated at the right, in which the electrode was placed in the ventral posterior hypothalamus, the effect was much more pronounced; self-stimulation

is totally eliminated in all six of the intervals shown.

A map of the effects of chlorpromazine obtained with 31 cases has been made. It shows that the effects of chlorpromazine are strongly inhibitory on self-stimulation when electrodes are placed in the ventral posterior hypothalamus. With electrodes in the middle hypothalamus, there is a somewhat less marked effect, and with electrodes in the anterior hypothalamus, there is very little effect. The effects are small with electrodes in the anterior preoptic region but seem to become quite strong again with electrodes in parts of the septal region.

With electrodes in the posterior hypothalamus and in the anterior hypothalamus, the same drug has strikingly different effects on the rate of self-stimulation. Since the drug does not greatly slow self-stimulation via electrodes implanted in the anterior hypothalamus, there is some assurance that the drug does not impede behavior as such. Since the drug does greatly slow self-stimulation via electrodes implanted in the ventral posterior hypothalamus, there is some assurance that the drug acts selectively, either on this part of the brain or on some of the areas to which it projects, to produce its rewarding effect. Furthermore, it is reasonable to assume that the areas sensitive to the drug are not essential to all rewarding effects, because anterior hypothalamic stimulation has its rewarding effect in spite of the drug.

*Psychotomimetics.* Another example of a differential drug effect is the interaction of serotonin and lysergic acid diethylamide. Serotonin is supposedly a transmitter substance in the brain, and lysergic acid diethylamide is a psychotomimetic (producing effects somewhat similar to psychotic hallucinations). Studies by other workers (*15*) have suggested that in some cases serotonin might be antagonistic to the effects of lysergic acid diethylamide. When lysergic acid diethylamide was injected intraperitoneally just prior to the threshold interval, there was usually an inhibitory effect on self-stimulation. In most cases the drug was effective in both the first and second intervals after injection. The effect of the drug appeared most dependably in the second eight-minute interval after injection; therefore, we studied the inhibitory effect on self-stimulation in this second interval in further analysis. We found two types of interaction between lysergic acid diethylamide and serotonin. In the first, lysergic acid diethylamide alone had a strong inhibitory effect on self-stimulation; when serotonin was administered half an hour before the lysergic acid diethylamide injection, however, there was no effect of the latter at all. Finally, bromo-lysergic acid diethylamide, which is like lysergic acid diethylamide but is supposed not to cross easily from the blood into the brain, had no inhibitory effect on self-

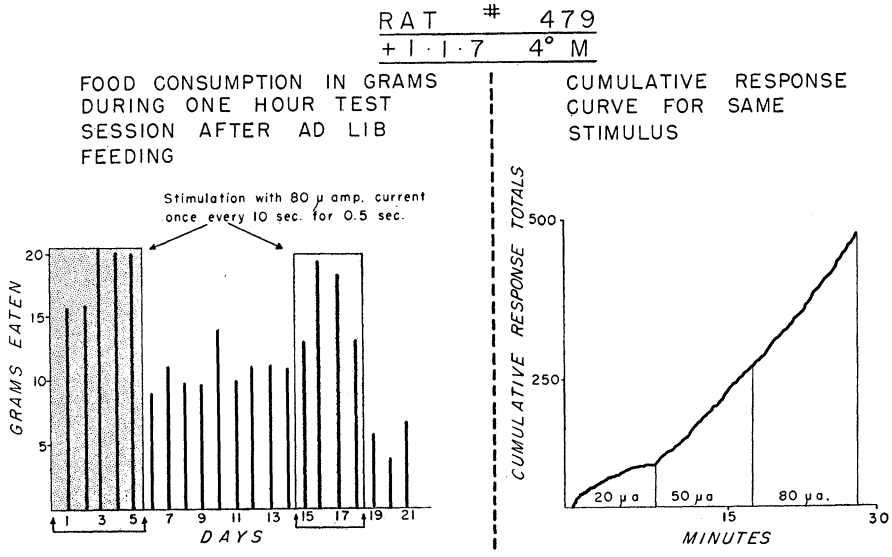


Fig. 17. Eating behavior produced by "rewarding" stimulus.

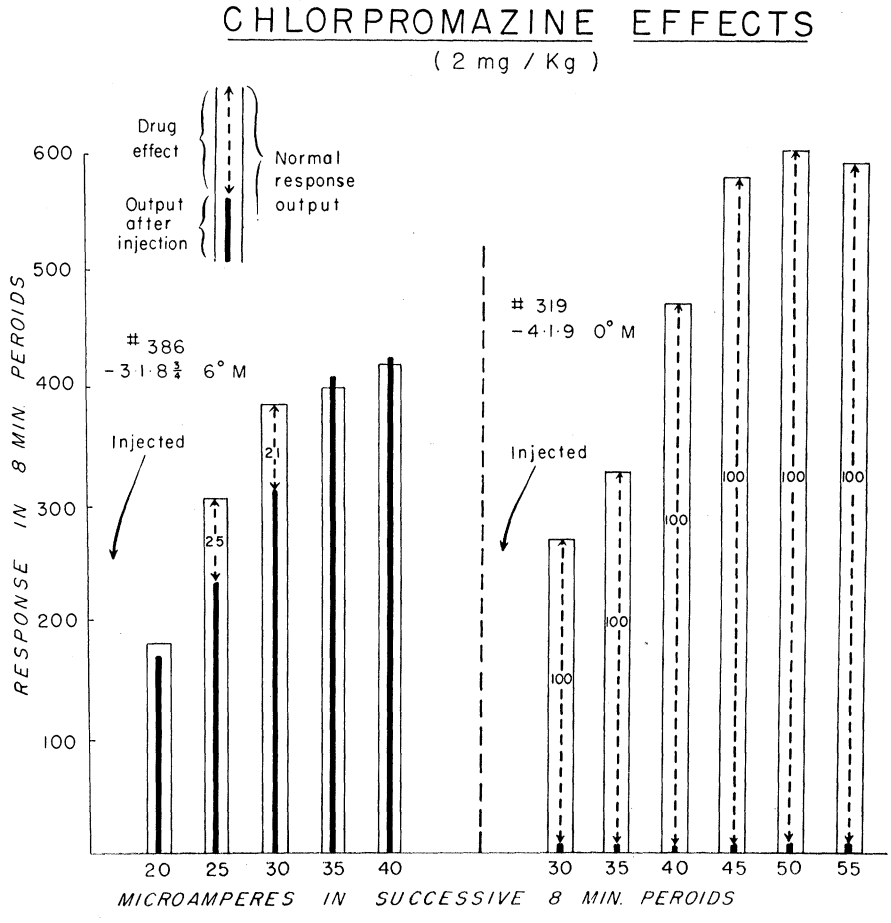


Fig. 18. Differential effects of chlorpromazine. Rectangles show normal response output. Black bars show output under influence of chlorpromazine. The animal for which data are given at left was almost unaffected by the drug. The animal for which data are given at right was almost totally inhibited; the difference is attributed to the more posterior position of the electrode in the latter case.

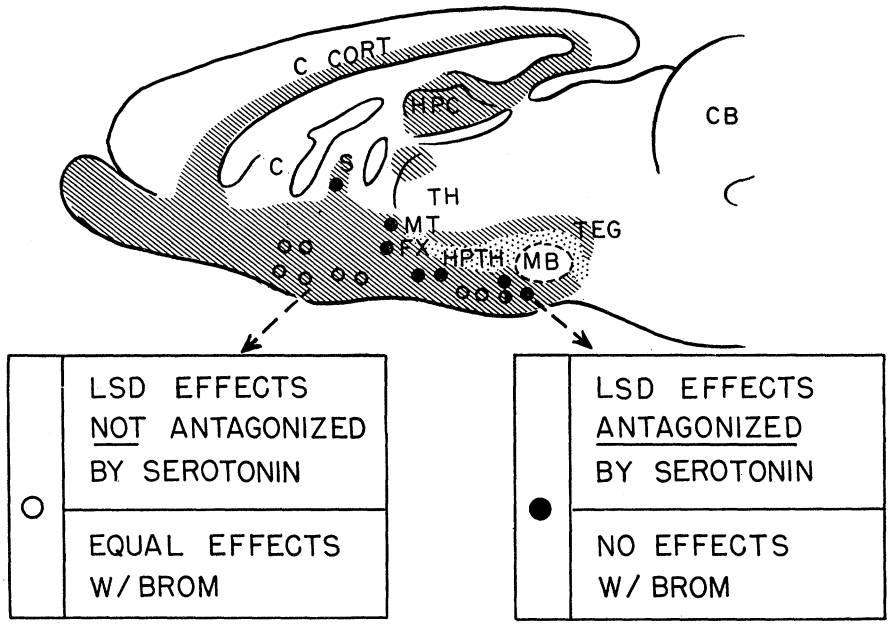


Fig. 19. Map showing points where effects of lysergic acid diethylamide on self-stimulation are antagonized by serotonin and other points where the effects are not antagonized. At the points where serotonin fails to protect againt lysergic acid diethylamide, bromo-lysergic acid diethylamide has the same effects as lysergic acid diethylamide itself.

stimulation. In the second case, lysergic acid diethylamide had a strong effect again. This time, however, serotonin did not antagonize the effect, and bromo-lysergic acid diethylamide had the same effect as lysergic acid diethylamide itself.

The two effects on self-stimulation are mapped in Fig. 19. We see that when electrodes are in certain delimited parts of the hypothalamus and telencephalon, serotonin fails to antagonize the effects of lysergic acid diethylamide, and in these cases bromo-lysergic acid diethylamide has the same effects as lysergic acid diethylamide. With electrodes implanted in other clear-cut regions, serotonin does antagonize the effects of lysergic acid diethylamide, and these are the cases in which bromo-lysergic acid diethylamide has no inhibitory effects on self-stimulation. Here, again, we have evidence of chemical differentiation between different parts of the reward system.

In some earlier tests on chlorpromazine and reserpine, a constant and quite high voltage level was maintained (*16*). Striking inhibition of response tendencies by reserpine was found when electrodes were implanted in the posterior hypothalamus, but no effects were found when electrodes were in the telencephalic region. Later work with graduated levels of electric current did not show such a sharp differentiation. The inhibitory effects of reserpine on self-stimulation in the hypothalamus do not appear at low voltages but only at very high ones. These data indicate that reserpine may selectively lower seizure thresholds for stimulation via the posterior hypothalamus. Petit mal states, elicited by stimulation at high voltages plus the reserpine, seem to account for the seeming inhibitory effect of reserpine on self-stimulation via the hypothalamus.

## Summary

My conclusions are these: (i) The cells which mediate primary rewarding effects are located in a midline system running from the midbrain through the hypothalamus and midline thalamus and into the subcortical and cortical groups of the rhinencephalon. (ii) The cell groups which mediate primary rewarding effects are different from those which mediate primary punishing effects. (iii) Despite this relative independence, there are, undoubtedly, relationships of mutual inhibition existing between these two systems. Rewards do, among other things, tend to reduce sensitivity to pain, and punishments do tend to reduce rewarding effects. (iv) These primary reward systems of the brain are subdivided into specific drive-reward subsystems mediating the specific drives such as hunger and sex. (v) Because there are also subsystems of this set of rewarding structures sensitive to different chemical effects, it is reasonable to hope that eventually it will be possible to control the reward systems pharmacologically in cases where behavior disorders seem to result from deficits or surfeits of positive motivation.

### References and Notes

1. These studies were aided by a grant from the Foundations Fund for Research in Psychiatry ("Brain Mechanisms and Motivation") to H. W. Magoun and J. Olds, by contract NR 144-102 [Nonr-233 (32)] between the Office of Naval Research, U.S. Department of the Navy, and the University of California, and by a grant from the Carnegie Corporation of New York ("Brain Organization and Behavior") to R. B. Livingston and D. B. Lindsley.
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