A MOTIVATIONAL ANALYSIS OF THE RETICULAR ACTIVATING SYSTEM [1]

J. OLDS, Ph.D. and B. PERETZ

Department of Psychology, The University of Michigan, Ann Arbor

(Received for publication: March 30, 1959)

INTRODUCTION

Work of Moruzzi and Magoun (1949) and more recent work (Magoun 1954) indicates that electrical stimulation at many points in the tegmentum of cats and monkeys causes electrical and behavioral signs of waking and attention in anesthetized or sleeping animals. These effects are grouped together and labeled arousal or activation, and the region which yields the effects has become known as the reticular activating system.

Work of Hess (1957) shows elicitation of some parasympathetic but many more sympathetic effects by stimulation of tegmental points in the awake cat. Work of our own (1954, 1956) indicates behavioral reward and behavioral punishment from stimulating tegmental points in the rat; Brady (1958) and Lilly (1958) report similar results for the monkey. These studies are closely related to earlier work by Delgado, Roberts and Miller (1954), who found negative reinforcement by stimulating certain points in posterior diencephalon of cats.

A question arises concerning the relation between arousal and the motivational effects: are there three anatomically discrete systems yielding, respectively, arousal, negative reinforcement, and positive reinforcement ? Or is there some anatomical overlap such that arousal is obtained only from points that yield the positive or the negative motivational effect; or such that positive and negative motivational effects are obtained from the same points by modifying some aspect of experimental technique ?

The present data suggest three separate anatomical regions very compactly related to one another. While we find very few points yielding arousal which do not also yield one of the two motivational effects, still the differences in the thresholds of the effects suggest that they are produced by stimulation of anatomically separate regions.

These problems were studied by means of an EEG test for arousal, a behavioral test for reward, and a different behavioral test for punishment; all three tests were carried out on each electrode in a grid of the tegmentum in the rat.

METHODS

The experiment was carried out on 51 rats. Each had two pairs of chronically implanted electrodes. One electrode pair was placed at a common point in the anterior cortex for the recording of electrocorticogram; the other electrode pair was placed to stimulate at a test point in the tegmentum, the test point differing systematically from rat to rat. The test area was a mesial region spanning much of the tegmentum and a small part of the posterior diencephalon. A grid of this region was formed by spacing test points 1 mm. apart from rat to rat.

The grid used is shown in figure 1. Placements were measured in mm. from the primary skull marking bregma and were denoted by three numbers, e.g., —5, 1, 9. The first number indicates mm. posterior from bregma, the second number indicates mm. away from the midline, and the third indicates mm. of depth measured from the upper surface of the skull. All implants were perpendicular to the skull at the point of entry. In the rat the upper surface of the skull approximates a plane.

[1] These studies were aided by grants to J. Olds from the Foundations Fund for Research in Psycriatry, the U. S. Public Health Service (National Institute of Mental Health), and the Ford Foundation.

Five anterior-posterior planes were used from —5 to —8, inclusive; 2 lateral planes, 1 and 2 mm. lateral to the midline; and 5 depths from 5 to 9 mm. inclusive. The depth of 9 mm. reaches the floor of the brain in several places and is out of the brain at most points. A plane at about —5 divides the diencephalon from the mesencephalon.

Electrode pairs consisted of insulated silver wires, 0.010 in. in diameter, placed side by side about 0.002 to 0.004 in. apart with only the cut cross section of the tips bared. The resistance of these pairs to alternating current ranges from 12,000 to 25,000 ohms, with 15,000 ohms as the most likely value, after a series of several hundred trains.

The stimulator produced a sine wave of 60 c/sec. Electric current was adjusted by measuring the voltage across a constant re-

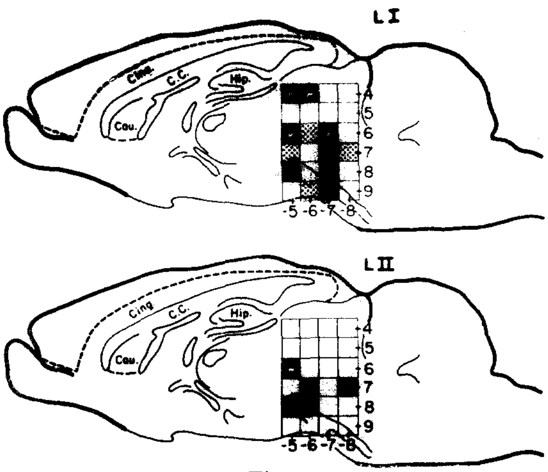

Fig. 1
Grid used in this study, with self-stimulation thresholds indicated. Black with white squares — thresholds of 10 μA.; black — thresholds of 20; grey — thresholds of 30, 40, or 50; white — no self-stimulation.

sistance in series with the electrodes on a cathode-ray oscilloscope. Current levels ranged from 0 to 50 μA rms.

Two behavioral tests, one for approach, and one for escape, were used and compared with an EEG test for arousal.

For approach behavior, the self-stimulation test was used (Olds and Milner 1954). This test involved a circuit whereby the animal could turn on the stimulus to the brain by stepping on a pedal. Each response momentarily closed the stimulator circuit. If the animal let go of the pedal within half a second, his release terminated the stimulus train. If he held the pedal for more than a half second, the train was terminated by a cut-off device and the animal had to release and press again in order to receive a second stimulation (see fig. 2).

The behavioral rewarding effect was determined by the rate of self-stimulation. Animals were trained and tested in a box 5 in. wide 11 in. long and 10 in. high, with wires from the stimulator entering through a hole in the top. At one end of the box a lever 4 in. wide entered the 5-in. wall. The arrangement is shown in figure 2.

For training purposes, the electric current was set at 50 μA. Animals were placed in the box for an hour each day and allowed to become trained by their own exploratory behavior. They were never stimulated until they stepped on the pedal. The pedal re-

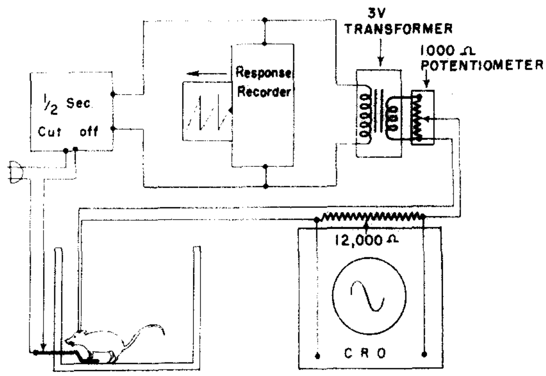

Fig. 2
Methods in self-stimulation experiments.

sponse occurred readily because of the large lever and because the only source of light from outside the box was the slit through which the lever entered. Animals exploring this source of light could not fail to press the pedal. With no reward at all, rats in this box responded at rates ranging from 10 to 50 responses per hour. Self-stimulation rates indicative of reward range from 500 to 7,000 per hour.

Animals were trained in this fashion for a two-week period for one hour every day. Then they were shifted to a second regime which permitted the determination of self-stimulation thresholds. The same self-stimulation boxes were used for this test. There were six 8-min. periods of testing every day for each animal. During the first interval, the current was set at 0. On successive intervals it was increased by steps of 10 μA. up to 50. Each time the current was set up, the animal was given, by the experimentor, three free trains of stimulation of half a second each; further stimulation was contingent on the self-stimulation response. At each level, the response frequency was counted as a measure of the positive reinforcing effect. In all cases where self-stimulation occurred at all, there was a marked threshold. That is, responding would occur at a chance level until the current was set above a certain point, and then purposive responding would begin. The

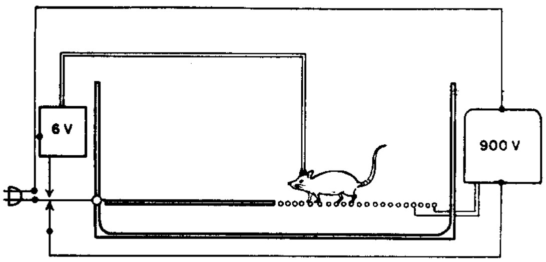

Fig. 3

Methods in escape experiments.

current setting which caused purposive responding to begin was recorded as the self-stimulation threshold.

This regime was continued daily for a period of four weeks; the range of scores for the final four days of this period forms the basis for the self-stimulation functions in figure 6.

Escape Test. The animal was placed in a box with the floor divided into two halves. One-half was a grid, the other was a large lever (see fig. 3). If the animal stayed on the lever, *no* shock was administered to the feet. If the animal was completely off the lever, an intermittent shock of 60 μA. *was* administered to the feet. While the animal stayed on the lever an intermittent stimulus was delivered via implanted electrodes. As in the approach test, this was a sine wave of 60 c/sec. varied from 0 to 50 μA. by steps of 10. In the case of intermittent shocks to head or feet, the current was on for half a second, then off for half a second and so forth.

Each animal was tested for six 8-min. periods. During the first interval, head current was set at 0; then in succeeding intervals it was increased by steps of 10 μA. up to 50 μA. The footshock remained at 60 μA., which was sufficient to cause all control animals (and all test animals with brain stimulus set at 0) to stay off the grid (on the large lever).

The threshold of escape was defined as the lowest brain stimulus level which forced an animal off the lever onto the footshock grid during more than half of an 8-min. interval. Each animal was tested two times.

Arousal Tests. In arousal tests, animals were housed in a screened room until they went to sleep naturally. Potential differences were recorded between a pair of permanently implanted silver electrodes. These were 0.010-in. silver wires, 0.002 in. apart, penetrating about 0.5 mm. into the brain. They were insulated except at the cut cross section of their tips. The recording was made from an area in frontal cortex (area 10), about 2 mm. anterior to bregma, and 2 mm. lateral from the midline.

During sleep, potential differences of about 50 μV. occurred at frequencies ranging from 1 to 4 per sec.; these appeared to be the typical slow waves of sleep. During arousal, frequencies of about 40 c/sec. were observed, and amplitude was greatly diminished. When animals were observed to go to sleep, the taking of the sleeping position and closing of the eyes always preceded, by about a minute, the appearance of slow, high-amplitude activity. On waking, however, behavioral arousal (particularly opening of the eyes) always occurred simultaneously with the blocking of the slow activity, and the commencement of high-frequency, low-amplitude waves.

Tests for arousal thresholds were made during sleep, 10 min. or more after the onset of slow wave activity. For this purpose, a series of 2-sec. trains of stimulation was applied by means of the electrodes implanted in the midbrain. Trains were separated by about 15 sec., and the intensity was augmented until arousal occurred. Cortical recording continued at all times except during the actual period of stimulation, but amplifiers were blocked for about 4 sec. after each stimulation. The criterion of arousal was a lasting block of slow activity recorded from the cortex (i.e., fast activity persisting for 10 sec. or longer).

current reading for the first stimulation to cause arousal was recorded as the arousal threshold (see fig. 4 and 5).

RESULTS

Approach Test. Of 51 animals tested, 15 self-stimulated in a dependable fashion; 36 failed to self-stimulate. The self-stimulators

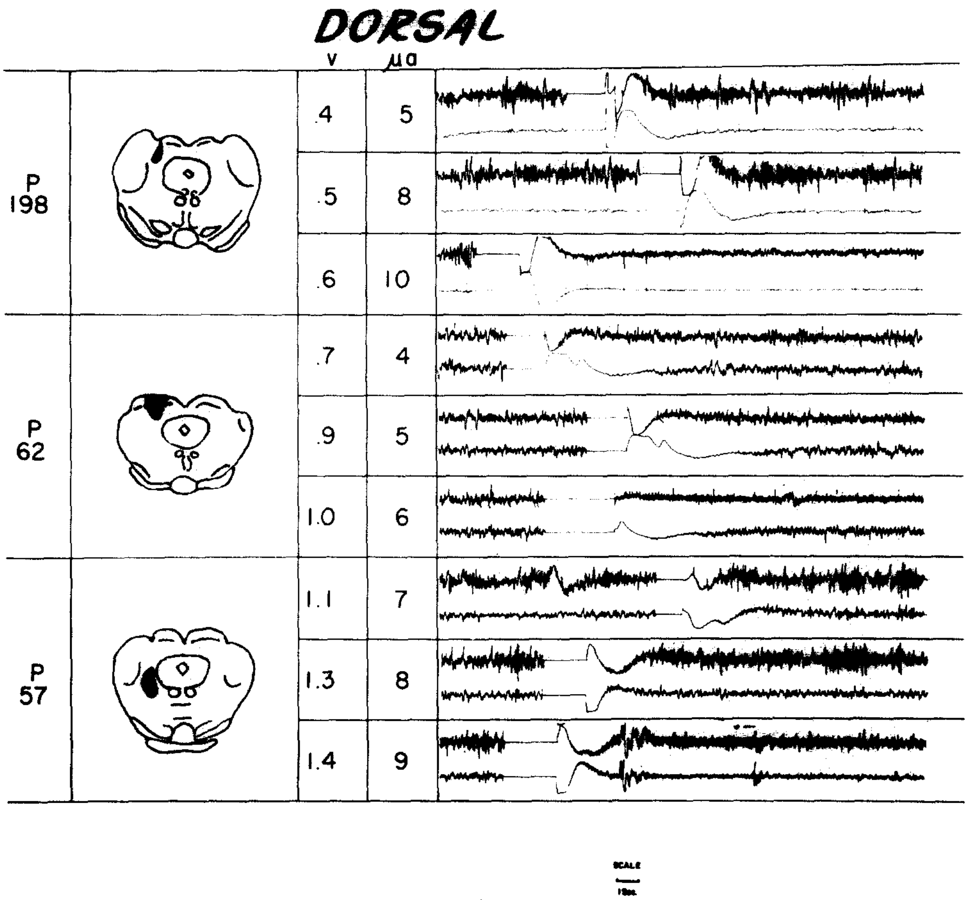

Fig. 4

Methods in EEG arousal test. Records are taken from anterior cortex (upper tracing of each pair) and from point of stimulation in the tegmentum (lower tracing). Voltage is set prior to stimulation, and current is read when stimulation is applied. The letter P above the indentification number indicates punishment from stimulation. The electrode track is shown in black on the drawing of the brainstem. On the right are 3 pairs of tracings for each animal with 2/sec. stimulus trains interposed during the flat part of the record.

The stimulus was the same as described earlier, a sine wave of 60 c/sec. Voltage was increased from 0.1 V. by steps of 0.1 and a measure of actual current flow was made for each stimulation. Resistance of electrodes to the a-c stimulus was about 15,000 ohms. The

divide into two groups: those with ventral electrodes, just below and lateral to the medial lemniscus, form the main group; those with dorsal electrodes, placed mesially half-way up from the ventral floor of the midbrain, form the second group. The locus of stimulation for the main group appears to be a posterior extension of the system formed by the medial forebrain bundle in the hypothalamus (see fig. 6-8). It curves upward and appears to cross the midline in the very posterior part of tion, arousal thresholds were consistently high and most of these animals failed to escape from the electric stimulation when it was applied in the escape tests. The very high self-stimulation rates in this main group were not,

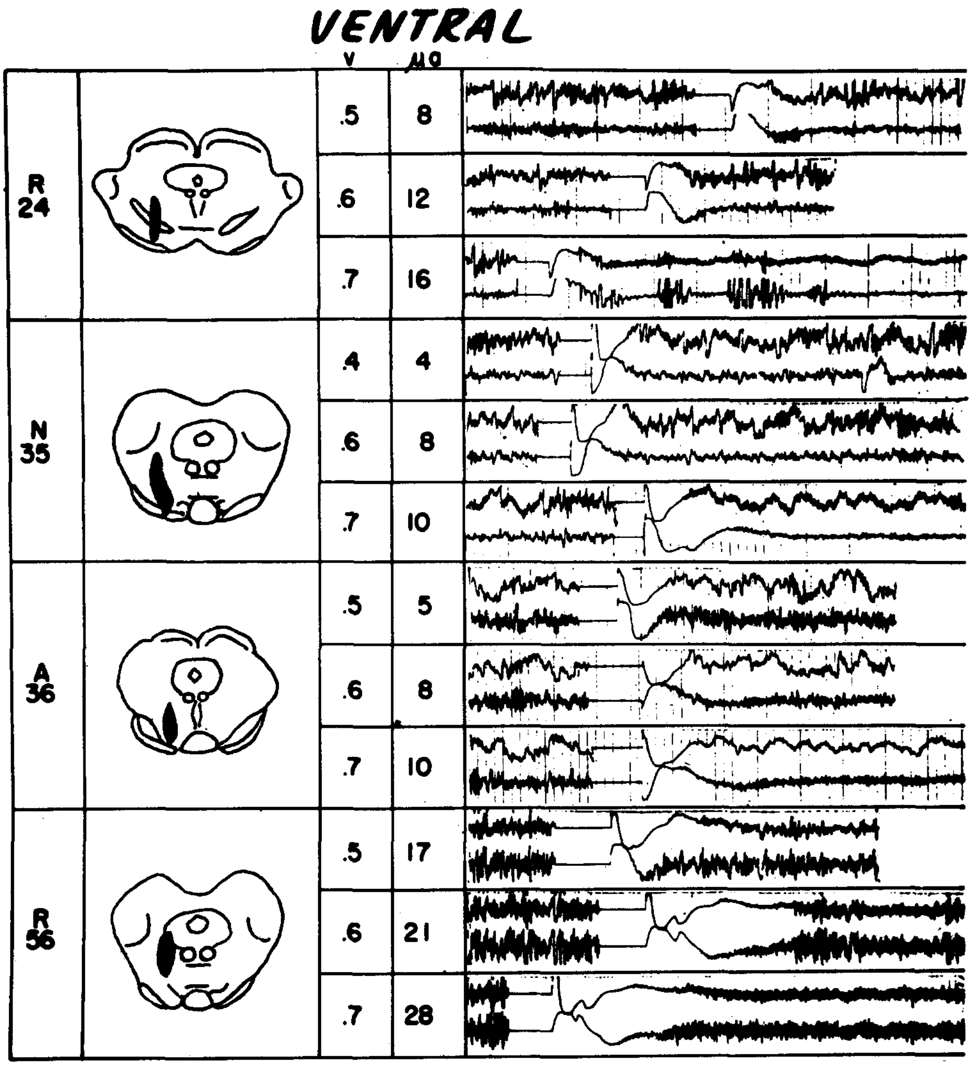

Fig. 5

Same as figure 4 but with more ventral electrode placements. R indicates reward from electric stimulation, N indicates neutral effects of stimulation (no motivational effect). A indicates ambivalence — animal self-stimulates but also escapes from stimulation at this point.

the region studied (see brain for R56 in fig. 5). Self-stimulation rates were consistently very high with electrodes in this region (see table I), most of them ranging above 3000 responses per hour. In the case of electrodes yielding these very high rates of self-stimulation, however, associated with low self-stimulation thresholds (see table I); thresholds ranged from 10 to 40 with a mode at 20 μA.

The locus of stimulation for the dorsal group of self-stimulators was mesial, and halfway up from the floor of the tegmentum; it appears to be the posterior extension of a system in the mid-thalamus where self-stimulation occurs (see light shading in fig. 8). It curves downward and appears to meet the ventral system in the posterior part of the region studied.

Self-stimulation rates were consistently very low with electrodes in this region (see table I), all of them below 1500 responses per hour. In these cases *arousal* thresholds were often low and animals ordinarily indicated ambivalence, by escaping excessive amounts of the same electric stimulus in the escape tests. As has previously been reported for dorsal self-stimulators in the diencephalon, the low rates of self-stimulation were associated with anomalously low self-stimulation thresholds; almost all animals had self-stimulation thresholds of 10 μA. (see table I).

Escape Test. Of 51 animals tested, 22 did escape; 29 failed to escape in a dependable fashion (see table II). The escapers may also be divided into two groups: those with dorsal electrodes, just lateral to the central gray and on the boundary between tegmentum and tectum, form the main group; those with more ventral electrodes reaching down toward the medial lemniscus form a second group. Escape thresholds were consistently very low with electrodes in the dorsal region; there were four thresholds of 10 μA., and two more with thresholds of 20. Except for one case with electrodes in the cortex, there was never any self-stimulation via these electrodes, and the arousal thresholds were consistently low, all of them falling from 6 to 12 μA. Escape thresholds were ordinarily high with electrodes in the ventral region; 11 of 12 cases tested had thresholds of 30 or more. In five of these cases, there was self-stimulation via the same electrodes, and the arousal thresholds had very wide range, from 8 to 28 μA.

TABLE I

POSITIVE REINFORCEMENT

Self-stimulators											
15											Non S-S 36
Ventral					Dorsal						
Animal No.	SS Rate [1]	SS ⊖	Arousal ⊖	Escape ⊖	Animal No.	SS Rate [1]	SS ⊖	Arousal ⊖	Escape ⊖		
197	700	20	18	—						Very Good	
11	600	20	14	—							
24	600	10	18	—							
56	500	20	28	40							
200	400	40	27	—							
37	200	20	15	45	16	200	10	10	55	Good	
36	150	10	10	40	15	200	10	?	40		
					19	200	10	?	25		
33	100	30	16	—	26	100	10	10	30	Poor	
					31	100	10	20	35		
					40	50	10	22	—		
					13	100	50	?	—		

[1] Response output for 8-min. test period.
⊖ Thresholds given in μA.
— No escape.

Arousal Test. The 48 cases tested divided into three distributions: (1) those with arousal thresholds in the 10 μA. range, (2) those with arousal thresholds in the 18 μA. range, and (3) those with arousal thresholds above 30 μA. (see fig. 9). The very low arousal thresholds of group 1 appeared to be produced by electrodes in the mesial tegmentum, reaching from the medial lemniscus up to the boundary of the tectum. Except for medial extensions at the top, this effect was largely confined to

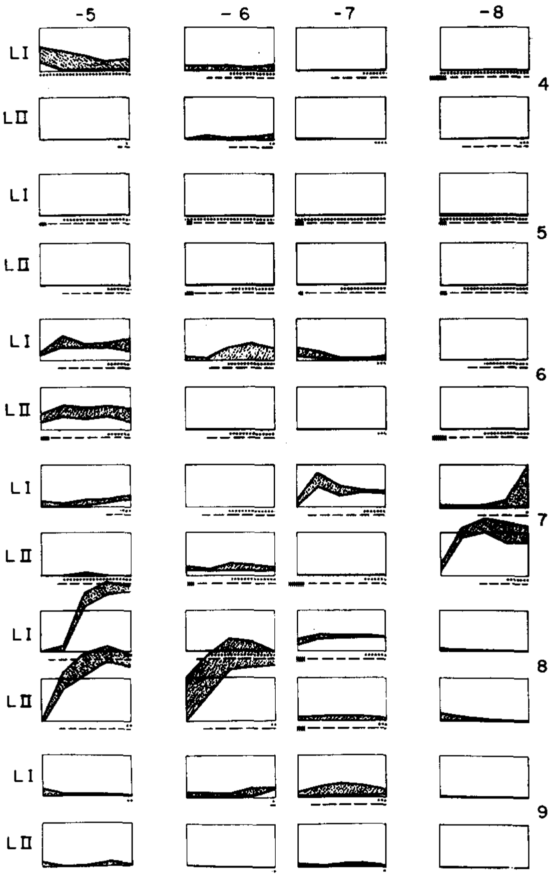

Fig. 6
Results. In each case, the abscissa indicates μA. from 10 to 50, inclusive. Arousal thresholds are indicated by the stopping point of the lower dashed line, escape thresholds by the stopping point of the upper dotted line. Above these lines is the self-stimulation function plotted as follows: in each rectangle, the ordinate indicates self-stimulation rate from 0 to 3000 responses per hour (or higher if the function extends above the box); the range of self-stimulation rates for a 4-day period is plotted for each of the 5 electric-current levels. The array of squares represents the grid studied with the LI plane as the top rectangle and the LII plane as the lower rectangle in each square. Each rectangle represents one animal.

the LII plane. The medium thresholds of group 2 appeared to be produced by all other electrodes in the tegmentum; and thresholds above 30 μA. occurred only with electrodes outside the tegmentum altogether (often outside the brain).

All the low-threshold escapers with dorsal electrodes had low arousal thresholds of the

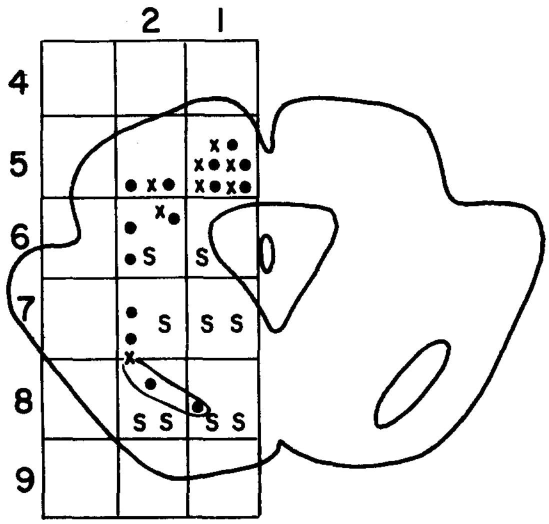

Fig. 7
Projection of extreme effects onto a transverse plane of the tegmentum. S stands for self-stimulation with threshold of 20 or less. X indicates escape at threshold of 20 or less. Blacks dots indicate arousal thresholds below 13.

10-μA. group; all the self-stimulators with very high response rates (ventral electrodes) had high arousal thresholds of the 18-μA. group.

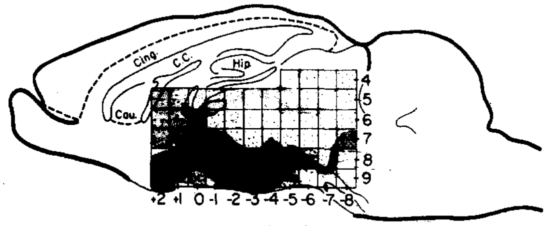

Fig. 8
Schematic map of self-stimulation results for brainstem. A ventral system (dark shading) gives strong self-stimulation. A thalamic system (light shading) gives mild self-stimulation. Many points in the strippled region produce escape behavior.

However, there were cases of arousal without any other motivational effect: three of 13 very low arousal thresholds were totally dissociated with escape and 6 more were associated with high escape thresholds. Three

TABLE II

NEGATIVE REINFORCEMENT

Escapers 22									Non-escapers 29
Dorsal				Ventral					
Animal No.	Escape ⊖'s[1]	Ar ⊖	SS ⊖	Animal No.	Escape ⊖'s[1]	Ar ⊖	SS ⊖		
62	20; 10	6	—					Very Good	
204	10; 20	12	—						
198	10; 20	10	—						
19	40; 10[c]	sz	10						
60	20; 30	10	—	14	20; 20	18	—		
95	30; 20	11	—						
29	40; 30	10	—	98	60; 30	10	—	Good	
42	50; 30	13	—	25	30; 30	18	—		
31	30; 40[c]	20	10	195	30; 40	20	—		
				202	30; 40	23	—		
				26	30; 30	10	10		
				57	50; 30	8	—		
				97	30; 30	21	—		
96	40; 40	20	—	56	40; 40	28	20	Poor	
				15	40	?	10		
				36	40; 40	10	10		
				37	40; 50	15	20		

[1] Each animal was tested two times for escape thresholds; the two scores are given in chronological order.

[c] Cortical electrodes.

⊖ Thresholds given in μA.

sz Seizure before arousal.

— No self-stimulation.

cases of slow self-stimulation were found in the group with low arousal thresholds. In the group with arousal threshold of about 18 μA., there were all the rapid self-stimulators, several moderate self-stimulators, quite a few high threshold escapers, and several cases with no motivational effects at all. These data are shown in figure 9.

Of the 14 cases with arousal thresholds above 30 μA., there were no motivational effects at all.

DISCUSSION

Self-Stimulation. The self-stimulation systems of the tegmentum appear to be direct extensions of their diencephalic counterparts. The self-stimulation system of the midthalamus with its low rates and low thresholds appears to extend through the middle tegmentum, passing downward toward the nucleus of Gudden. The main self-stimulation system of the medial forebrain bundle of the hypothalamus, with its higher thresholds and very

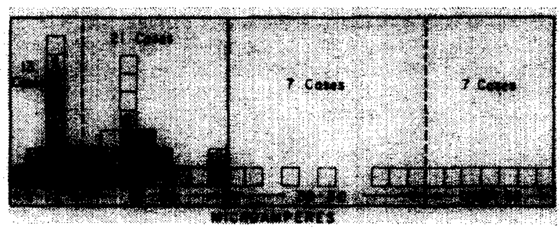

Fig. 9

Frequency distribution of arousal scores. Each square indicate one case. Its place on the abscissa indicates the arousal threshold. Dark shading indicates extreme escape, light shading indicates moderate escape. S indicates self-stimulation, and circled S indicated extreme self-stimulation. Empty boxes are devoid of positive or negative effects.

high response rates, appears to pass around the mammillary bodies into the ventral tegmentum where it works up toward the Gudden nucleus.

Escape. There appear to be two escape systems of the tegmentum. The main one has its focal point around the dorso-medial boundary of the tegmentum, just above and lateral to the central grey. The second seems to be focussed on the medial lemniscus.

Arousal. The main arousal system of the tegmentum appears to be more lateral than the positive and negative motivational systems, and about halfway between them on the dorso-ventral axis. However, the main escape system also yields consistently low arousal thresholds. An interesting sidelight on the arousal test is that resistance (see fig. 4 and 5) of the ventral points which yield self-stimulation is consistently lower than that of the dorsal points which yield escape. At present we surmise that this is due to the larger overall amount of stimulation applied via the ventral electrodes in self-stimulation *and* escape tests.

Overlap. Perhaps the most striking pattern is the grouping of negative effects at the top of the tegmentum, positive effects at the bottom, with overlapping effects and neutral arousal effects in between. In 7 out of 51 cases, both escape and self-stimulation were obtained from the same electrode; such results have been reported earlier for diencephalic electrodes between the positive and negative systems (Roberts 1958). The largest number of these cases in our study occurred at a depth of 7 where the medial lemniscus runs just above the self-stimulation system.

SUMMARY

In 51 rats electrode pairs were chronically implanted with spacing 1 mm. apart from rat to rat to make a grid of the tegmentum. In each case three tests were made: a self-stimulation test for positive reinforcement; an escape test for negative reinforcement; and an EEG test for cortical arousal. The main results were these: all points yielding escape at very low thresholds were clustered in the dorso-medial tegmentum just below the tectum and just lateral to the central grey; all points yielding self-stimulation at high rates were clustered ventrally, usually below and lateral to the medial lemniscus; and points yielding arousal at very low thresholds were clustered in the lateral tegmentum, half-way up from the ventral surface.

As for interactions between the three effects, all points yielding escape at low thresholds also yielded arousal at low thresholds; all points yielding self-stimulation at high rates yielded arousal at moderately high thresholds; and some points yielded both moderate escape and moderate self-stimulation. Finally, there definitely were points which yielded arousal at low thresholds and which yielded no other motivational effects.

RÉSUMÉ

Des paires d'électrodes étaient implantées de façon chronique chez 51 rats, avec un espace de 1 mm. de rat en rat, afin de faire un tamis du tegmentum. Trois tests furent pratiqués chez chaque cas: un test d'auto-stimulation pour du renforcissement positif; un test de fuite pour du renforcissement négatif; et un test EEG pour l'éveil cortical. Les principaux résultats étaient les suivants: tous les points donnant lieu à la fuite à des seuils très bas étaient groupés dans le tegmentum dorso-médian, immédiatement en bas du tectum et latéral à la substance grise centrale; tous les points donnant lieu à l'auto-stimulation à des taux élevés étaient groupés ventralement, généralement en bas de, et latéral au lemniscus médian; et les points donnant lieu à l'éveil à des seuils très bas étaient groupés dans le tegmentum latéral, à mi-distance de la surface ventrale.

Quant aux interactions entre les trois effets, tous les points donnant lieu à la fuite à des seuils bas donnaient lieu également à l'éveil à des seuils bas; tous les points donnant lieu à l'auto-stimulation à des taux élevés donnaient lieu à l'éveil à des seuils modérément élevés; et quelques points donnaient lieu et à une fuite modérée et à une auto-stimulation modérée. Enfin, il y avait, en définitif, des points qui donnaient lieu à l'éveil à des seuils bas, et qui ne donnaient lieu à aucun autre effet de motivation.

ZUSAMMENFASSUNG

Bei 51 Ratten wurden Dauerelektroden im Tegmentum implantiert. In jedem Falle wurden drei Reaktionen getestet: Selbstreizungstest für positive Verstärkung, ein Fluchttest für negative Verstärkung und ein EEG-Test um eine allfällige Weckreaktion der Hirnrinde zu registrieren. Die wichtigsten Befunde waren wie folgt: Sämtliche Punkte die eine Fluchtreaktion bei sehr niedriger Reizschwelle ergaben, lagen in der dorso-medialen Haubengegend, unmittelbar unter dem Tectum und lateral zum zentralen Höhlengrau. Sämtliche Punkte, die eine Selbstreizung mit hoher Wiederholungszahl ergaben, lagen in der ventralen Gegend, gewöhnlich unter, und lateral zur medialen Schleife. Punkte, welche eine Weckreaktion bei sehr niedriger Reizschwelle ergaben, waren im lateralen Tegmentum konzentriert, halbwegs aufwärts von der Ventralfläche. Die gegenseitige Beeinflussung der verschiedenen Testreaktionen wurde geprüft. Sämtliche Punkte die eine Flucht bei niedriger Reizschwelle ergaben, ergaben gleichfalls bei niedriger Reizschwelle eine Weckreaktion im EEG, und sämtliche Punkte die eine Selbstreizung mit hoher Wiederholungszahl ergaben, ergaben bei relativ hoher Reizschwelle eine Weckreaktion im EEG. Verschiedene Punkte ergaben gleichzeitig eine mittelmässige Fluchtreaktion und einen mittelmässigen Selbstreizungseffekt. Schliesslich gab es Punkte, von welchen eine Weckreaktion im EEG bei niedriger Reizschwelle erzeugt werden konnte und von denen keine Motivierungseffekte erhalten wurden.

REFERENCES

BRADY, J. V. Temporal and emotional factors related to electrical self-stimulation of the limbic system. In: H. H. Jasper *et al.* (eds.) *Reticular Formation of the Brain,* Boston, **1958**, pp. 689-703.

DELGADO, J. M. R., ROBERTS, W. W. and MILLER, N. E. Learning motivated by electrical stimulation of the brain. *Amer. J. Physiol.,* **1954**, *179*: 587-593.

HESS, W. R. *The Functional Organization of the Diencephalon.* New York, **1957**.

LILLY, J. C. Learning motivated by subcortical stimulation: the start and stop patterns of behavior. In: H. H. Jasper *et al.* (eds.) *Reticular Formation of the Brain,* Boston, **1958**, pp. 705-721.

MAGOUN, H. W. The ascending reticular formation and wakefulness. In: J. F. Delafresnaye (ed.) *Brain Mechanisms and Consciousness,* Oxford, **1954**, pp. 1-20.

MORUZZI, G. and MAGOUN, H. W. Brain stem reticular formation and activation of the EEG. *EEG Clin. Neurophysiol.,* **1949**, *1*: 455-473.

OLDS, J. and MILNER, P. Positive reinforcement produced by electrical stimulation of septal area and other regions of rat brain. *J. comp. physiol. Psychol.,* **1954**, *47*: 419-427.

OLDS, J. A preliminary mapping of electrical reinforcing effects in the rat brain. *J. comp. physiol. Psychol.,* **1956**, *49*: 281-285.

ROBERTS, W. W. Both rewarding and punishing effects from stimulation of posterior hypothalamus of cat with same electrode at same intensity. *J. comp. physiol. Psychol.,* **1958**, *51*: 400-407.

Reference: OLDS, J. and PERETZ, B. A motivational analysis of the reticular activating system. *EEG Clin. Neurophysiol.,* **1960**, *12*: 445-454.