M. A. Psychology

HEART-RATE REACTION TO REWARDING SEPTAL AND MIDBRAIN STIMULATION IN THE RAT

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Rats with electrodes in septal areas and midbrain were trained to self-stimulate. Phasic heart-rate (HR) changes were recorded during stimulation with parameters used to elicit self-stimulation. Subjects with rewarding placements in the lateral septum, diagonal bands of Broca, ventral tegmental nucleus (Tsai), medial lemniscus, and periventricular gray showed a phasic HR deceleration only in response to stimulation, while subjects with rewarding medial septal placements showed an initial brief acceleration preceding the main deceleratory component.

The locus-specific results in the septal areas confirmed conclusions from previous findings. The new HR findings with midbrain stimulation were considered in relation to behavioral observations (bar-pressing and stimulation-evoked movements) and in relation to neuroanatomy of the region. The main findings were discussed in relation to concepts of reinforcement.

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HEART-RATE REACTION TO REWARDING SEPTAL AND MIDBRAIN STIMULATION IN THE RAT

by

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The autonomic nervous system (ANS) plays a diverse and important role in adaptive mechanisms. It has been studied by many disciplines, each with its own orientation. This system interests psychologists because of its immense role in various behavioral adaptations and physiological-behavioral interactions such as psychosomatic illnesses. An example of the use of the ANS is evident in the work of Miller and DiCara (1967) who make extensive use of these responses by operantly conditioning them using brain stimulation as the reward. In addition, autonomic measures have been used to aid in the examination of ideas concerning sexual behavior (Singer, 1968), activity and other motor responses (Hyde, 1966; Nashold, Urbaniak, & Hatcher, 1965) as well as cognitive problems such as problem solving (Blatt, 1961; Hess & Polt, 1964). These recent studies are by no means the extent of the work done on the autonomic nervous system (see Woodworth & Schlosberg, 1954 for an historical review).

Recent technological advances have made it easier to record autonomic measures from freely moving subjects and has enabled both biological and behaviorally relevant stimuli to be combined with autonomic recording. This emphasis on an integrated systems' approach combines the

traditional approaches of physiological psychology and psychophysiology (Sternbach, 1966).

The present study uses heart rate (HR) as its autonomic measure. This is just one of many indicants of circulatory function that have been used to elucidate diverse problems in psychology. Such measures as blood flow (Folkow & Rubinstein, 1965), blood pressure (Reis & Oliphant, 1964) as well as HR as measured by the electrocardiogram (EKG) and electrocardiotachograph (ECTG) (Malmo, 1965) have been used to study the ANS. The present experiment uses the ECTG to analyse HR response to rewarding electrical brain stimulation.

Hess' early work (1957) established that many areas in the higher brain are autonomically active. He classified an area either ergotropic (sympathetic) or trophotropic (parasympathetic) (for a thorough discussion of these terms, see Gloor, 1954) and related these classifications to various behaviors that were observed. For example, it was found that the posterior hypothalamus was sympathetically active and when intracranial stimulation (ICS) was delivered to this part of the brain, sham rage occurred.

Soon after the discovery of the self-stimulation phenomenon by Olds and Milner (1954), Olds perceived a correspondence between rewarding brain loci and those that

produced parasympathetic affects when stimulated (see Olds, Travis & Schwing, 1960). However, his interpretation of these relationships became more cautious (Malmo, 1963; Olds & Olds, 1963).

Septal Stimulation

The earliest study using cardiac activity to measure autonomic response to brain self-stimulation was that of Malmo (1961). By contrasting the difference in HR immediately before and after septal stimulation, Malmo concluded that phasic deceleration of HR occurs in response to the ICS. This finding was supported by the work of Perez-Cruet, Black and Brady (1963) even though the interval analysed was considerably longer. Instead of analysing changes over seconds as Malmo did, Perez-Cruet et al. contrasted five-minute periods with and without septal stimulation. Malmo's (1961) results were also supported by additional data collected in his laboratory (Kasper, 1963; Malmo, 1963, 1964).

A study by Meyers, Valenstein and Lacey (1963) also measured HR change to septal ICS and extended this line of research to the hypothalamus. These investigators employing beat-by-beat measurement found HR deceleration as the main effect of spaced septal stimulation. However, during the first few beats following stimulation they noted a brief

acceleration which they assumed Malmo's method of measurement had obscured. This assumption proved to be incorrect. Malmo's (1964) beat-by-beat analysis revealed immediate deceleration of HR.

Malmo's electrode placements were different from those of Meyers et al., being more lateral. These differences in stimulation sites appeared to be the most probable reason for the minor discrepancy between the findings from the two laboratories. Additional data from Malmo's laboratory favored the view that lateral septal stimulation produced immediate HR deceleration, and that brief acceleratory phase followed by the main change (deceleration) was characteristic of medial septal stimulation.

Focus of interest in these studies was on HR changes accompanying self-stimulation of the brain. Malmo's (1961, 1964) observations of HR change were made during times when the animals were self-stimulating, whereas Meyers et al. recorded HR while they administered medial septal stimulation outside the self-stimulation situation. Possibly as a result of these procedural differences there were differences in parameters of stimulation which may have favored the appearance of a prominent acceleratory component in the HR reactions reported by Meyers et al.

The first purpose of the present study was to obtain further data bearing on this problem.

Hypothalamic Stimulation

In reviewing their HR findings with spaced lateral hypothalamic stimulation, Meyers et al., (1963) stressed the polyphasic character of the HR changes. Actually, from their published graphs of HR change in the three rats they studied, it is clear that one rat showed marked slowing, and that the other two rats showed some slowing as well.

Malmo (personal communication) in beat-by-beat measurements had observed pronounced HR slowing following spaced stimulation of the lateral hypothalamus in the four rats he studied. Blevings (personal communication) noted HR slowing as the predominant effect of lateral hypothalamic self-stimulation in rats. Ross and Blevings have noted the same relationship with rewarding stimulation of the posterior hypothalamus as well as in the preoptic area, reticular formation and the ventral midbrain although their assessment procedure was not sensitive to the very transient changes seen by Meyers et al., (1963).

The second purpose of the present study was to extend (for the first time) the recording of autonomic responses during rewarding brain stimulation in the midbrain. There have been numerous studies of self-stimulation in the ventral tegmental area of the midbrain. This literature is summarized in Table 1.

Experiment 1: Septal Areas

This experiment attempted to obtain further data bearing on Malmo's (1964) suggestion that medial septal stimulation, unlike lateral septal stimulation, produced an initial acceleratory component. Previous experiments (Malmo, 1961, 1964; Meyers et al., 1963) employed different animals in relating the locus-specific effects observed while the present experiment employed lateral and medial stimulation in the same animal.

Method

Ten male hooded rats of the Royal Victoria Hospital strain were used as subjects. Each weighed approximately 250 gm. at the start of the experiment. Four bipolar platinum electrodes were implanted in the plane of DeGroot (1959) with the use of a Kopf stereotactic instrument. Separate electrodes were aimed at the lateral septum of one hemisphere and the medial septum of the other. There were also two midbrain placements in opposite hemispheres (one dorsal and the other ventral) which were not used in this experiment. Electrode implantation, generally following the procedure of Olds and Milner (1954), was carried out under Nembutal anesthesia (0.54 mg/kg) with additional local anesthesia of the scalp incision by xylocaine (0.2 cc). The electrode assembly

consisted of two strands of 0.01 in. diameter platinum wire, bared only at the tip, soldered to the poles of a 27-9 Amphenol plug. The assembly was held in place by Caulk NuWeld which was poured around it and the jeweler's screws fixed in the skull. Postoperatively each rat was given 0.09 cc/kg Ritalin (10 mg/cc) intraperitoneally and 0.2 cc Bicillin (300,000 IU/cc) intramuscularly.

At the time of electrode implantation, two permanent EKG electrodes were placed under the skin of each subject. The electrodes consisted of twisted lengths of No. 28 B & S Hoskins Chromel "A" resistance wire. One electrode was placed over the right shoulder blade, the other at the posterior end of the rib cage on the left side.

Recording. Beat-by-beat heart rate (HR) data were obtained by recording EKG and ECTG (see Mundl, 1965, 1966a). HR data were recorded continuously although stimulations were delivered at least 35 seconds apart. The data were divided so that the six second prestimulus and twenty-four second poststimulus periods were free of artifacts produced by signal disruption from contact with the HR electrodes during grooming, scratching, and similar activities. Since interest centered on HR change produced by brain stimulation, the prestimulation periods selected were relatively free from phasic fluctuations

and extreme rates. This procedure was followed in order to cut down on the variance and therefore increase the validity of the statements about the averaged curves.

The data were analysed by reading in the height of the ECTG tracings into a system containing a CAT 400B averaging computer (Mundl, 1967). This was accomplished with a manually operated ruler which converts the height of the ECTG tracing into voltage which is then averaged by the computer (Mundl, 1968).

Histology. The subjects were sacrificed with ether anesthesia. They were immediately perfused with physiological saline followed by 10% formol-saline. Following perfusion, the brains were fixed in 10% formol-saline for five days and then were sectioned at 40 micra on a freeze microtome. The brain sections were then stained with Neutral Red and Luxol Fast Blue.

Procedure. Approximately a week after the surgical procedure, HR was recorded. The recording occurred on two consecutive days, each septal placement being stimulated approximately 10 times each day. Fifteen stimulations were chosen for analysis according to the aforementioned criteria.

The recording procedure began at very low current levels. If the animal did not show signs of a stimulation-evoked HR reaction and if the stimulation did not seem

aversive, the current level was increased. Although the amperage varied, all stimulation consisted of 0.5 sec. trains of 100 Hz. biphasic rectangular pulses of 0.5 msec. pulse duration. Current was monitored with a Fairchild 704 oscilloscope after restoring the rectangular character of the stimulator output (Mundl, 1966b).

Bar-pressing training started the day after the recording procedure. After the lead to one electrode was attached, the rat was placed in a Skinner box 12 in. long, 8 in. wide, and 17 in. high. The box consisted of a grid floor and four opaque walls. A 1.125 in. wide lever was mounted 1 in. above the floor and projected 3.5 in. from one of the shorter sides of the chamber. After allowing a few minutes for the animal to habituate to the situation, electrical brain stimulation at current parameters which produced the HR response became available contingent on pressing the lever. If the rat did not continue to press after emitting the first few responses, the experimenter delivered stimulation manually when the subject approached the lever. When the rat stayed in the vicinity of the lever the criteria for delivering the stimulation was changed. At this point, the animal was rewarded with stimulation only for physical contact with the lever. When the rat started to press the lever, manual presentation of brain stimulation was discontinued.

After all subjects were tested for self-stimulation through one electrode for a 10 min. period, the above procedure was repeated for the other septal placement. This procedure was repeated for five days. On the day after this training, the subject was placed in the apparatus for an additional 10 minute session for each electrode in which no shaping occurred. These final self-stimulation data were used for rating the animal on self-stimulation.

Results

The electrode placements shown in Figure 1 are coded to indicate the rate of self-stimulation during the ten minute test period (the triangle represents less than 62 responses in the session, the star, from 62 to 166 responses, and the circle, more than 166 responses in the ten minute session). An animal was considered to have self-stimulated if the number of responses exceeded by two standard deviations ($s = 19.2$), the mean ($\bar{X} = 22.6$) operant rate of bar-pressing in the Skinner box obtained by noting the frequency of unrewarded bar-presses in 28 animals.

Table 2 presents a summary of the data with bar-pressing rate converted to an hourly rate. The data confirm previous findings: stimulation which was rewarding as measured by a bar-pressing task caused a phasic HR deceleration. In addition, prior results (Malmo, 1964) concerning the area-specific HR reactions were also replicated.

Medial vs. Lateral Septal Stimulation: Differential Effects on HR

Three of the four subjects which had electrodes in both the medial and lateral septal areas bar-pressed for stimulation at both sites (Rats 1, 4 & 9). Rat one's placements are shown in Figure 8. The rewarding medial placements exhibited an initial, brief acceleration followed by a much larger deceleration when stimulated. Figure 2 shows Rat one's medial HR curve as well as curves representative of other placements. The lateral placements in these animals showed only a deceleration in response to stimulation. Rat five, which did not self-stimulate for either lateral or medial stimulation, exhibited the same HR response to medial stimulation as those subjects which bar-pressed for stimulation of this locus. Subject five's lateral placement, which bordered the caudate nucleus, showed no response to stimulation.

HR Changes Associated with Rewarding Placements

In addition to those placements already mentioned, two rats with electrodes in the diagonal bands of Broca (2 & 7) and one with a placement in the medial preoptic area (6) bar-pressed for stimulation. The stimulation-evoked HR response for these loci resembled that for the lateral septum: phasic deceleration occurred in response to stimulation.

HR Changes Associated with Nonrewarding Placements

Other than that of Subject five, no medial placements failed to support self-stimulation. Five lateral placements which bordered on the caudate nucleus did not support self-stimulation (Rats 2, 3, 5, 7, & 10). Only Subject nine self-stimulated for stimulation at a similar site although this placement was the most posterior of those placements bordering the lateral septum and the caudate. The rats which did not self-stimulate showed varied HR reactions to stimulation (see Table 2 for a summary of these data and Figure 2 which includes some HR averages of nonrewarding placements among a sampling of these curves for the present experiment).

Experiment 2: Midbrain Areas

In order to further test the hypothesis that all rewarding brain stimulation is followed by HR deceleration, an unexplored brain region was sought in order to extend the scope of the existing data. The ventral midbrain was chosen due to the large amount of work already done with self-stimulation (see Table 1). Furthermore, if there were an area in which reinforcement and HR acceleration were associated, it seems likely that this area might be in the midbrain (Stein, 1962, 1966, 1970 personal communication).

Method

Seventeen male hooded rats of the Royal Victoria Hospital strain were used as subjects. The ventral midbrain electrode implanted for Experiment 1 was used for two animals (Rats 4 & 10 in Experiment 1 are numbered 23 & 25 respectively in this experiment). An additional 15 subjects were used. They were operated on as in the manner already described and were implanted with one electrode each, aimed at the anterior region of the ventral midbrain. The recording and testing procedures were identical to that in the first experiment.

Results

The electrode placements are shown in Figure 3 and are displayed in the same manner as in Experiment 1. A summary of the data is displayed in Table 3. Only Subject 12 bar-pressed above criteria. The tip of this animal's electrode extended into the substantia nigra. The heart rate change evoked by the stimulation showed a brief deceleration during stimulation followed by an acceleratory phase. Head movements were evoked by the stimulation of this animal and were often followed a few seconds later by grooming and rearing. None of the three other subjects with electrodes in this area exhibited self-stimulation. Two of these animals (13 & 14) had no HR reaction to stimulation while Rat 11 showed HR acceleration (see Figure 4).

Electrode placements for animals that failed to self-stimulate were as follows: the ventral tegmental nucleus of Tsai (15), between substantia nigra and the ventral tegmental nucleus (16, 17, & 18), between the substantia nigra and the cerebral peduncle (19 & 20), in the cerebral peduncle (21, 22, & 23), the pons (24 & 25), interpeduncular nucleus (26), and the lateral tegmental nucleus (27). All but Rats 15, 19, 20, 22, 24, and 27 showed a change in HR after stimulation. Rats 17, 18 and 21 showed a brief acceleration followed by a deceleration. Subject 16 showed only a deceleration and Rats 23, 38, and 26 showed only a HR acceleration in response to stimulation.

Experiment 3: Midbrain Areas

Since only one animal self-stimulated in Experiment 2, a meaningful test of the hypothesis was not possible. In order to obtain a sufficiently large sample of rewarding placements, all the electrodes in this experiment were aimed at a specific area (the one that seemed most favorable) instead of sampling diverse parts of the midbrain as in Experiment 2.

Method

Ten male hooded rats of the Royal Victoria Hospital strain were used as subjects. At the start of the experiment they weighed approximately 250 gm. each. The electrode assembly

and implantation procedure were identical to those described in the first experiment. Each rat was implanted with bilateral electrodes which were aimed at the ventral tegmental nucleus (Tsai). The co-ordinates were: 3.0 mm. posterior to bregma, 1.0 mm. lateral to the midline and from 7.6 to 7.8 mm. below dura. Metrazol (100 mg/cc) was given intraperitoneally in place of Ritalin, each rat receiving 0.15 cc.

The recording and testing procedures were almost identical to those in the first two experiments although the order in which they occurred was reversed. The stimulation parameters were identical to those described in the first experiment. Only the current was varied. Initial bar-press training occurred at low current levels. If the subject did not self-stimulate and the stimulation did not seem aversive, the current was increased.

After all subjects were tested for self-stimulation through their right electrode for a ten-minute period, the above procedure was repeated for the left electrode. This procedure was repeated for three days. If during this period, the desired bar-pressing occurred, HR was recorded at the current level which elicited the self-stimulation. Although self-stimulation and HR recording occurred at a specific electrode, testing was continued for at least three days. If after three days, the animal did not exhibit self-stimulation,

HR was recorded at current levels which caused phasic deceleration at moderate tonic levels of HR. Immediately after these recordings were taken, the subject was given the opportunity to bar-press for these current parameters for ten minutes. For some animals where self-stimulation occurred after this procedure, the current was reset to the level at which bar-press training had been given and HR was recorded again. Often, another self-stimulation session was given at these parameters.

Movement during HR recording was noted visually and recorded during the pre- and poststimulus intervals with the use of a manual trigger which controlled a pen on the HR record. If the animal did not move very often, observation was suspended unless the HR record showed movement artifacts (phasic and often tonic acceleration). If this occurred, the rat was not stimulated again until the HR resumed normal levels. Observation was also suspended if the subject exhibited stereotyped stimulus-bound movement after each stimulation which did not affect the HR recordings for more than a few beats. The switch which was used to record movement was closed during the initiation of motor activity rather than throughout the movement. This procedure was followed because in this situation rats usually move in quick jerks and it was therefore impossible to get an accurate measure of duration. A hash-mark on the

record represents one of these events so that a number of them, closely spaced, stand for continuous motor activity. Often, the type of movement (exploration, grooming, or rearing) was noted either on the moving record or on another sheet of paper.

Results

The electrode placements are shown in Figure 5 and are displayed as in the previous experiments. A summary of the data is presented in Table 4. It is evident that phasic deceleration occurred for all positive placements except one in the ventral tegmental area (Tsai) and another situated between the medial lemniscus and the parafascicular thalamic nucleus. A section of the later animal's (32 left) HR record is shown in Figure 6. Both of the above mentioned animals often moved violently in response to the stimulation. Motor activity of the remaining subjects was not correlated with HR reaction to the brain stimulation. Although all animals made similar movements, the resulting phasic acceleration did not occur in the period immediately following stimulation. Most rats showed stimulus-bound motor activity, in response to stimulation, consisting of the elevation of the anterior part of the body with a concomitant movement back and to the side. These responses were time-locked to the onset of the current and did not disrupt the HR recordings for more than a beat or two.

Once it occurred, self-stimulation continued until the last training session in all but one subject. The left electrode of Rat 32 did not support self-stimulation until the next to last session. Prior to this time, no responses occurred. When the animal was tested with current parameters which caused a reliable HR reaction, self-stimulation occurred in the first four and last minutes of the testing period. Due to the inconsistent responding noted, this rat was given an additional ten-minute session at these parameters during which no responses occurred. An example of the typical data is that of Rat 37's right electrode. On the second day of training 101 responses were recorded while the number of bar-presses on the third day amounted to 110. Data relevant to this point are not available for those subjects which did not respond above the operant rate until the last day although it must be noted that the rate of responding for these animals was much higher than that from Rat 32's left electrode.

Because of these structures' part in Stein's "punishment" system (1962, 1966, 1970 personal communication), it is perhaps surprising to note that high rates of responding occurred with stimulation of sites in the medial lemniscus and periventricular gray (32 right and 34 respectively). HR records of these placements showed phasic deceleration in response to stimulation.

Of the four subjects tested for HR reaction to stimulation at current parameters below that which supported self-stimulation, only one showed the decelerative response. This placement (Rat 30's right electrode) showed a decreased response rather than the elimination of the deceleration. (See Figure 7). A photomicrograph of this subject's placements is shown in Figure 9.

Discussion

The results indicate that rewarding placements in the septal area and the midbrain are autonomically active. The locus-specific findings of Malmo (1964) are supported by the data in this experiment. Three subjects had rewarding placements in both the medial and lateral septum. In each of the three medial septal placements that were rewarding, a brief HR acceleration occurred followed by a longer deceleratory phase. In the lateral septum, rewarding placements showed only the phasic deceleration. These results suggest that one should hesitate in generalizing findings in one area into other adjacent areas. Meyers et al., (1963) after only considering medial placements concluded that "septal ICS is accelerative, but the late effect is pronouncedly decelerative." In pointing out Meyers' et al.'s overgeneralization, Malmo suggested that the different HR reactions were consistent with Guillery's (1957) anatomical data which showed that the medial forebrain bundle sends different tracts to the two septal areas.

Visual inspection of the septal HR curves from Meyers' laboratory shows that two subjects had a brief but pronounced HR acceleration preceding the major deceleratory component. The difference between these curves and those from

the medial septum in Experiment 1 can be accounted for by the way the curves are plotted and the initial baseline HR of the animals prior to stimulation. Meyers and his co-workers use an ordinal scale of beats per minute while the curves in the present study are plotted on a logarithmic scale of beats per second. Because of this, both the acceleratory and deceleratory components in the present study appear smaller when compared with those of Meyers and his co-workers. In their animals, the baseline HR probably accounts for the relatively larger acceleration. These subjects had a slower basal HR level than the rats in the present study and therefore, according to the Law of Initial Values, one would expect any HR acceleration in Meyers et al.'s animals to be larger than that seen in Experiment 1.

The present data suggest that it may be inappropriate to divide the HR responses on a medial-lateral basis alone. The similarity of the diagonal band stimulation-evoked HR to that found with stimulation of rewarding lateral septal placements points to the necessity of specifying anatomical loci according to the dorsal-ventral dimension as well. The diagonal bands receive fibers from the medial forebrain bundle by way of the mammillary peduncle (Morest, 1961) as do the septal nuclei. Afferent fibers from the diagonal bands radiate to the hippocampus as well as the septal area. From the

septum, diagonal band and septal efferents return to the medial forebrain bundle by way of the fornical system and the preoptic area (Knook, 1965). Although fibers from the medial septum merge with the more ventral diagonal band fibers (Cragie, 1925; Daitz & Powell, 1954) the fiber connections from these areas are not identical. For example, all diagonal band fibers go to the inferior thalamic peduncle while only a limited number of septal fibers go to this structure. Rather than considering the diagonal bands as being continuous with the medial septum, it is perhaps better to conceptualize this structure as connecting the septum with the medial parolfactory area, preoptic area, hippocampus, amygdala, lateral olfactory nucleus, and piriform cortex (Kappers, Huber, & Crosby, 1961). With its diverse connections, it is not surprising that the diagonal bands display a HR response to reinforcing brain stimulation similar to that in the lateral septum.

In the second experiment, only Subject 12 self-stimulated. This subject showed a stimulation-evoked HR response which was the opposite of that found in the rats with rewarding placements in the medial septum. The phasic acceleration which followed the initial deceleration in this animal was probably due to movement artifacts. After each stimulation, a stereotyped head movement occurred and this

was often followed a few seconds later by grooming and rearing. It is not possible to assert that if the movement had not occurred the deceleration would have continued but the obvious change in HR when movement did occur suggests that at the least, only the deceleratory component would have been evident had the movement been eliminated.

Although other subjects had electrodes at similar brain loci, self-stimulation did not occur. This inconsistency in the data is unfortunate but not surprising as a great number of conflicting reports have been published concerning self-stimulation in the structures in the ventral midbrain (see Wetzel, 1968). The results in the third experiment clearly indicate that rewarding placements in the midbrain are autonomically active. Almost all of the loci which supported self-stimulation produced a phasic HR deceleration when stimulated. The parasympathetic character of the HR change supports and extends Malmo's (1961) suggestion that the "quieting" effect of rewarding septal stimulation on HR had "reinforcing properties." It should be stressed that Malmo did not conclude this from his data. In fact, his suggestion was cautiously stated. The present data in addition to replicating earlier findings from Malmo's laboratory (Kasper, 1963; Malmo, 1961, 1963, 1964, & 1966 personal communication) extend the findings into the midbrain and strengthen the earlier suggestion.

But caution is again urged: it is not concluded that HR slowing is a necessary condition for reinforcement of bar-pressing. The absence of contradictory data however, suggests that generalizing these results to reinforcing electrical ICS as a whole may provide a tenable hypothesis. Even the report of Meyers and his co-workers (1963), which on first reading appears contradictory, supports this suggestion. The biphasic HR response to rewarding septal and hypothalamic stimulation that these investigators noted had conspicuous decelerative components after stimulation. This conclusion is also supported by some unpublished data collected by Ross and Blevings. These investigators found that one of their subjects, with an electrode aimed at the posterior hypothalamus, showed HR deceleration to stimulation and self-stimulated at this site for identical stimulus parameters.

These and other findings reviewed point up the dangers in assuming, on the basis of Hess' work (1957), that stimulation of the posterior hypothalamus will invariably produce sympathetic or "ergotropic" responses. Clearly it is important to employ unanesthetized animals and to use again, in the experiments on autonomic changes, precisely the same parameters of stimulation that were found to have a reinforcing effect on the same animals. This in no way casts any doubt on the validity of Hess' findings. Rather, it is an indication that

it is dangerous to assume that certain diencephalic areas are necessarily sympathetic in function under all conditions. In short, the findings suggest that this kind of view over-simplifies the problem.

On the behavioral side, it is dangerous to assume that a given brain locus is certain not to have reinforcing properties. For instance, present results show that with electrode placements near the medial lemniscus and the periventricular gray there was self-stimulation and HR deceleration.

These findings are meaningful in relation to anatomical evidence which shows that these supposedly negative loci (Kestenbaum, Deutsch, & Coons, 1970; Nashold & Wilson, 1966) have connections to the medial forebrain bundle. The periventricular system, which includes the periventricular gray, contains afferents which pass to the hypothalamus (diVirgilio, 1954; Papez & Freeman, 1930). Russell (1961) has concluded on the basis of early anatomical work (Papez, 1932; Roussy & Mosinger, 1934) that the medial lemniscus has collaterals to the hypothalamus which go through the mammillary peduncle and/or the periventricular system. Matzke (1951) found that a descending fiber tract ran through the hypothalamus to the medial lemniscus on its way to the ventrolateral posterior nucleus. These data suggest that electrical stimulation of

parts of the periventricular system and the medial lemnisci may be exhibiting rewarding effects due to involvement in the hypothalamic section of the medial forebrain bundle. In addition more attention should be given to the diverse connections of fiber systems such as the medial forebrain bundle which are implicated in the reinforcement process.

The critical conditions for reinforcement in self-stimulation are undoubtedly complex. At this stage of our knowledge, it is important to determine what there is in common between concomitants of reinforcement between one brain area and another. For instance, Olds (Olds & Olds, 1964) has argued effectively that various reinforcing brain loci have in common connections with the medial forebrain bundle.

In the same vein it is important to ask whether the autonomic concomitants of stimulation are similar in the various areas of the brain that support self-stimulation. Evidence for similar HR changes has been reviewed. In following up this point it is important to inquire whether the critical stimulation intensities are almost identical for autonomic and reinforcement effects. Although a strict psychophysical procedure was not followed in the third experiment, an approximate threshold for the phasic HR reaction and the self-stimulation behavior was recorded for a number of subjects. Four animals which exhibited self-stimulation and phasic HR

deceleration, did not self-stimulate at current levels which did not cause HR slowing. Only one animal showed the HR deceleration after self-stimulation was abolished by lowering the current, although the HR deceleration was not as great as that in response to current levels which did support self-stimulation.

These data when added to that of Ross' and Blevings' findings suggest that HR deceleration may be a necessary but not sufficient component of reward. Ross and Blevings, after testing HR reaction to electrical stimulation of many areas of the brain, selected those animals which exhibited a HR deceleration and then tested them to see if they would bar-press for these stimulus parameters. Five rats had an electrode which yielded this HR response. The placements sampled five different brain areas: anterior and posterior reticular formation, preoptic area, posterior hypothalamus and the ventral tegmental area. Only the subject with the posterior reticular formation electrode failed to self-stimulate for the current parameters which caused a HR deceleration.

This study when added to the data reported here leads one to the generalization that rewarding brain stimulation is followed by a phasic HR deceleration. The 53 placements included in the present data are ample evidence to support such an hypothesis. All rewarding placements which had artifact-

free HR recordings showed the stimulation-evoked HR slowing. Since no placements were found that were rewarding and did not show this HR response, it is probable that the HR reaction is necessary for electrical stimulation of the brain to be rewarding. Since five septal placements and nine midbrain placements, which were not rewarding as measured by the bar-pressing task, caused the same deceleratory HR reaction when stimulated; it must be concluded that the HR slowing response is not a sufficient condition for brain stimulation to be reinforcing.

Related Observations Bearing on Various Kinds of Reinforcement and Accompanying Autonomic Changes

It is admittedly speculative to go beyond the self-stimulation situation in looking for phenomena that appear to resemble the ones under discussion in the preceding section. However, such speculation may be useful in attempting to view reinforcement as well as the accompanying autonomic changes in broader perspective.

The notion that apparently reinforcing events are accompanied by a decrease in HR is encouraged by rather wide ranging observations. Blatt (1961) found, for instance, that HR increased during a difficult problem-solving task and decreased immediately before the solution. Additional evidence is supplied by work done in Malmo's laboratory (Ehrlich &

Malmo, 1967; MacNeilage, 1966; Malmo, Boag, & Smith, 1957; Malmo & Davis, 1956). Ehrlich and Malmo found that in the rat, HR increased for about three seconds before a bar-press response occurred and then decreased in the three seconds after the response. Malmo et al., (1957) recorded HR from the therapist and client during a psychiatric interview. When the interviewer was in a "good mood" HR of the patient increased significantly less than when the interviewer was having a "bad day." When the interviewer criticized the client's story about a TAT picture, HR increased, and when the therapist praised the story, HR decreased. An unexpected finding in the Malmo and Davis study also bears on this point. A group of subjects were given instructions to repeat a mirror tracing task four times. HR increased until the fourth tracing was begun at which time it either decreased or remained at the same level. This finding was considered to be artifactual since the subjects were given instructions to count their traversals and to stop after the fourth one. It is probable that the HR deceleration was accompanying the reward of being finished with the task. MacNeilage found that the HR of his human subjects increased in the beginning of various tasks and then decreased until the task was completed.

Berlyne, in an extensive review of the role of the concept of arousal in reinforcement (1967), supplied an

interesting description of changes in arousal due to biological reinforcement which bears on the support given in this paper to Malmo's suggestion concerning reinforcement and "quieting" of HR.

> many familiar rewards, like the opportunities to eat, drink, or mate, are followed relatively soon by quiescence and the cessation of the restlessness that commonly precedes them, ... Second, termination of some conditions ... --e.g., pain, fear, extremely intense stimulation of any kind--can be rewarding (p. 28).

It seems quite clear that the HR deceleration produced by brain stimulation is not an artifact of movement or of respiration (see Malmo, 1963, 1965). However, in the studies referred to in the immediately preceding section, movement or anticipatory "stop" or "go" mechanisms may well have influenced the HR changes. In the next section, skeletal-motor reactions will be considered in their own right.

Skeletal-Motor Mechanisms and Reinforcement

Motor responses to rewarding electrical brain stimulation have played a large role in theoretical positions taken by some authors (Glickman & Schiff, 1967; Milner, 1970; Schnierla, 1959, 1965; Valenstein, 1964). Valenstein reported that with rewarding ICS, rats "move forward and appear to be actively investigating the environment," that "negative brain

stimulation ... appears to activate a 'freezing' or backward movement" and that these motor activities are "directly triggered by the stimulation (p. 433)." This generalization would fit in very well with Schnierla's theoretical position. Schnierla postulates two opposing systems, one for approach (positive) and another for withdrawal (negative). Rewarding stimulation of the brain would come under the positive system and one would therefore predict from Schnierla's theory that appropriate approach movements would occur.

In the present study as well as in the study by Ross and Blevings, animals with midbrain electrodes made what seemed to be withdrawal movements (similar to those which Valenstein noted with negative stimulation) when rewarding electrical stimulation was delivered by the experimenter and when the animal was self-stimulating. In the third experiment, the aversive appearance of the behavior triggered by the stimulation caused the investigator to wait a long time before hesitantly raising the current in order to try to get the subject to self-stimulate. The subsequent self-stimulation shows that the stimulation-evoked motor effects bothered the experimenter more than the subject.

It is possible that Valenstein's (1964) observations (see p. 30) concerning motor patterns differed from those reported here due to the different loci being stimulated.

Valenstein based his conclusion on animals with electrodes in the limbic system where exploratory behavior may have occurred as a response to some internal disposition caused by the stimulation. If this were so, it would appear relatively more "voluntary" than the backing up observed when the ventral tegmentum was stimulated. Exploratory behavior implies that the animal does not exhibit a fixed motor pattern as the animals in Experiment 3 did. It is not probable that the sniffing and other responses Valenstein noted occurred in the same sequence every time the rat was stimulated. Stimulation of the brain areas which caused the exploratory behaviors are highly implicated in stimulus-bound consummatory behaviors. It is not unreasonable to assume that stimulation at these points might cause other appetitive or motivation-related responses to occur.

Additional studies are necessary to fully understand the connections between ANS responses, skeletal-motor activity and reinforcement. The use of autonomic responses produced by ICS in learning experiments (Kaplan, 1969; Malmo, 1965; Miller & DiCara, 1967) and the general use of rewarding brain stimulation, necessitates further investigation into the part the ANS plays in reward. In addition to other autonomic responses being used (see Malmo, 1965), additional brain areas should be explored. These studies and replications of past work might be done with an emphasis on threshold determination

for the autonomic, motor and self-stimulation responses. Comparing these data for diverse brain areas would possibly provide valuable information about brain function and organization.

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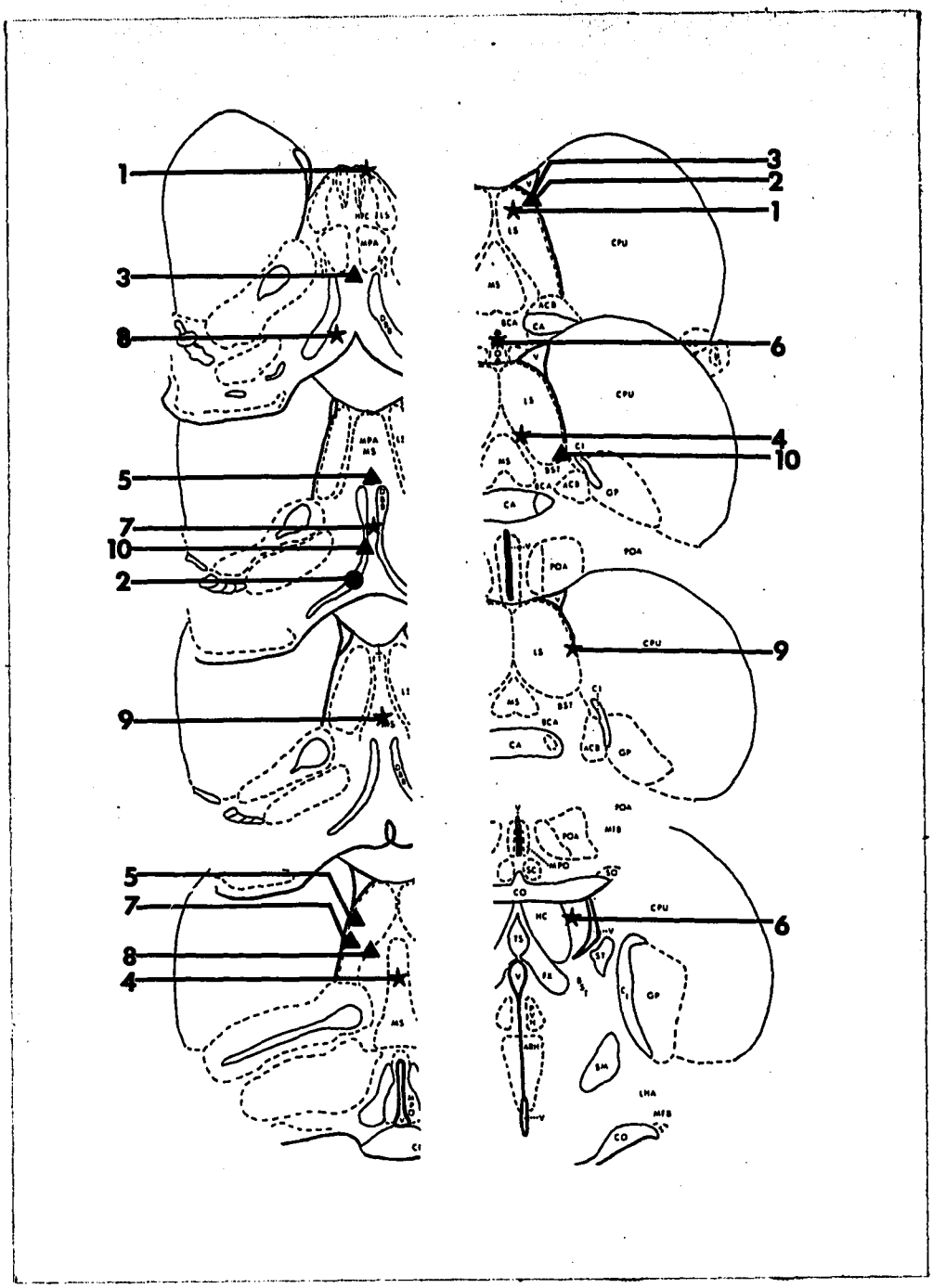

Fig. 1. Histological and self-stimulation findings in the septal area (Triangles: self-stimulation rate of less than 62 responses/ 10 minute session; Stars: more than 62 but less than 166 responses/ session; Circles: more than 166 responses/session). Brain sections have been modified from the Pellegrino and Cushman Atlas (1967). The section (top to bottom and left to right) are 3.0, 2.8, 2.6, 2.2, 2.0, 1.6, 1.4, and 1.0 mm. anterior to bregma.

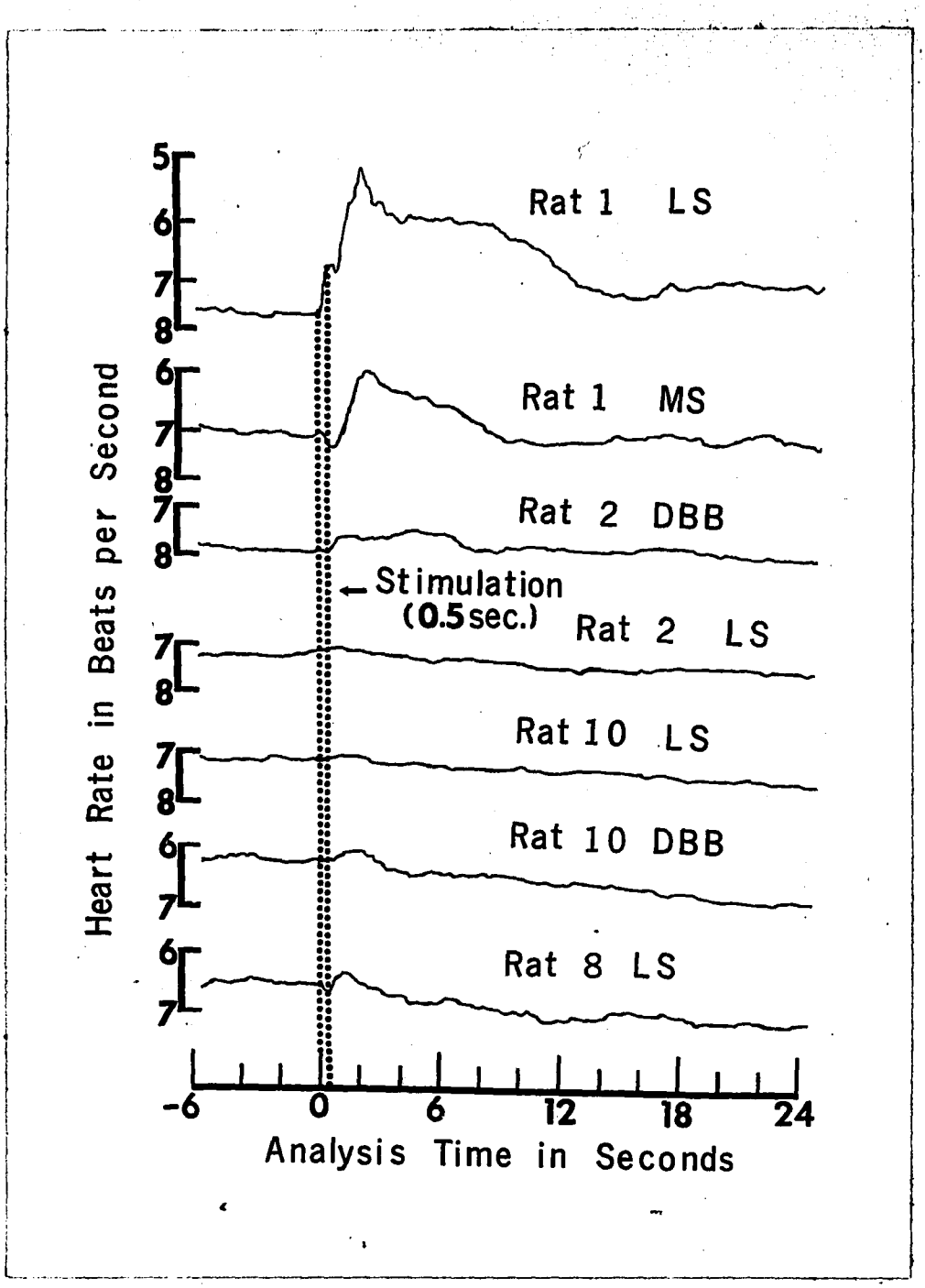

Fig. 2. Averaged heart-rate response to septal brain stimulation. An upward deflection of the tracing represents a deceleration of heart rate.

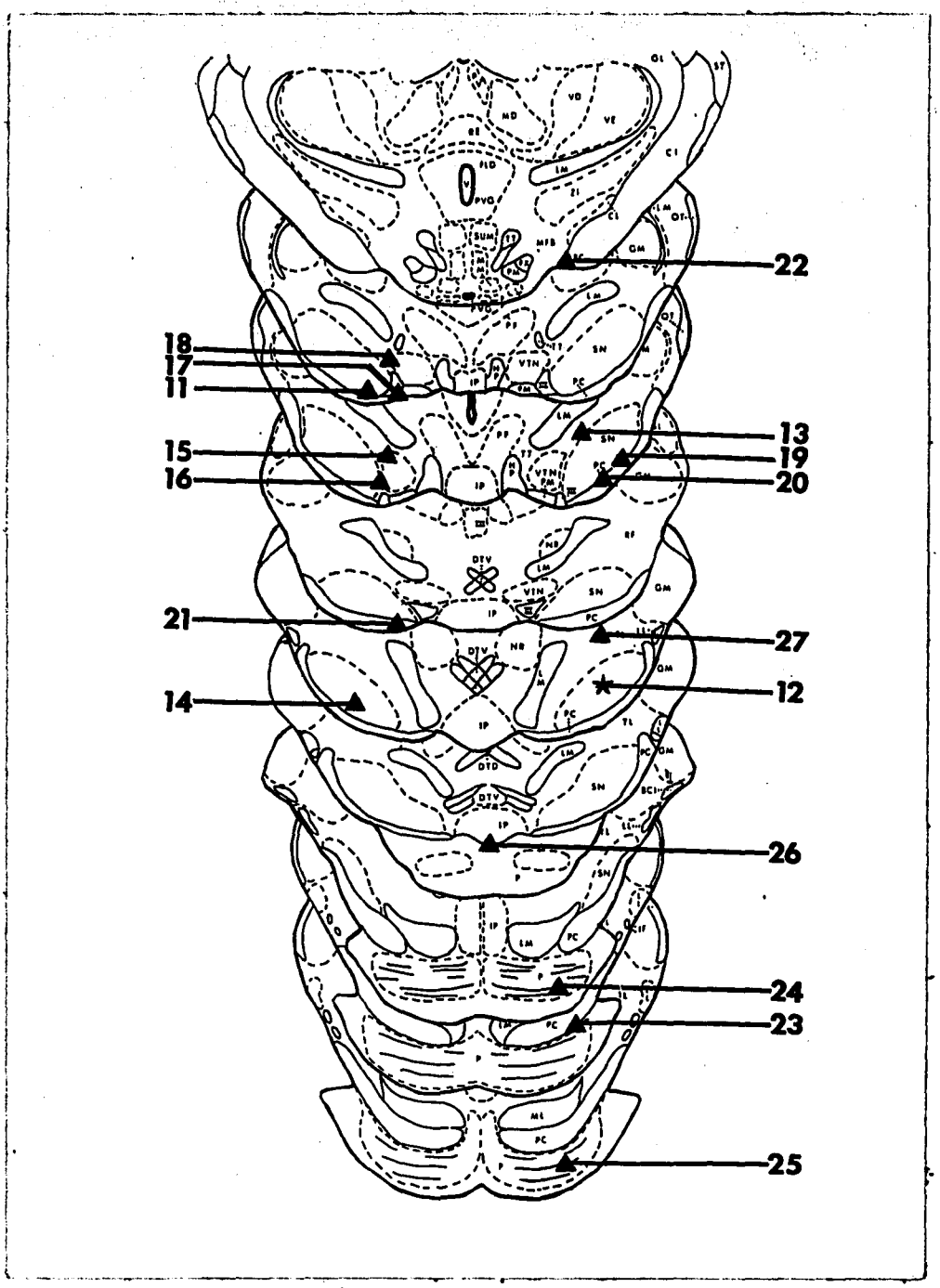

Fig. 3. Histological and self-stimulation findings in the ventral midbrain (Experiment 2). The symbols represent the same response rates as those in Figure 1. Brain section (top to bottom), modified from the Pellegrino and Cushman Atlas (1967) are: 2.0, 3.0, 3.2, 3.6, 3.8, 4.0, 4.8, 5.2, and 5.4 mm. posterior to bregma.

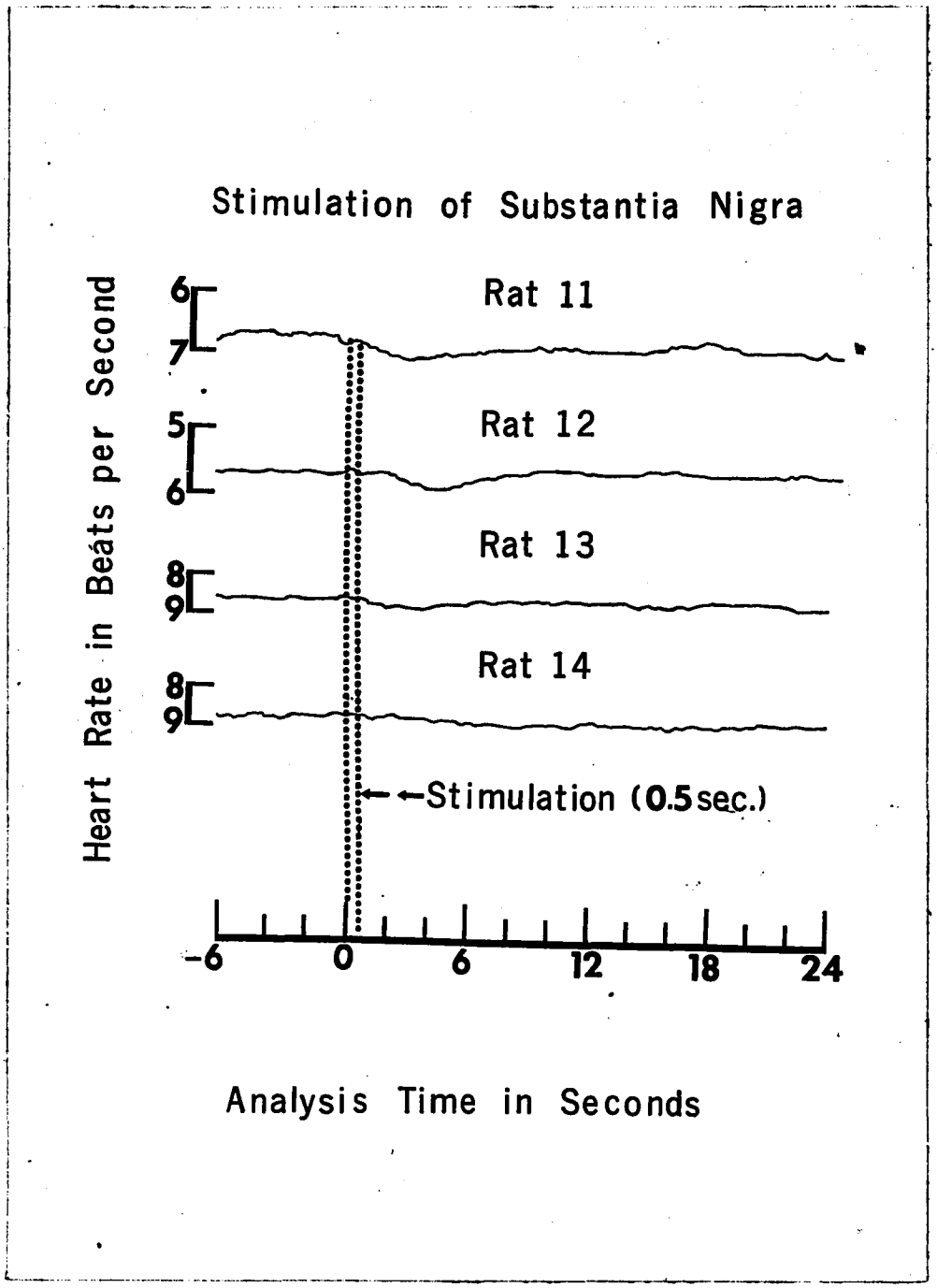

Fig. 4. Averaged heart-rate response to stimulation of the substantia nigra. An upward deflection of the tracing represents a deceleration of heart rate.

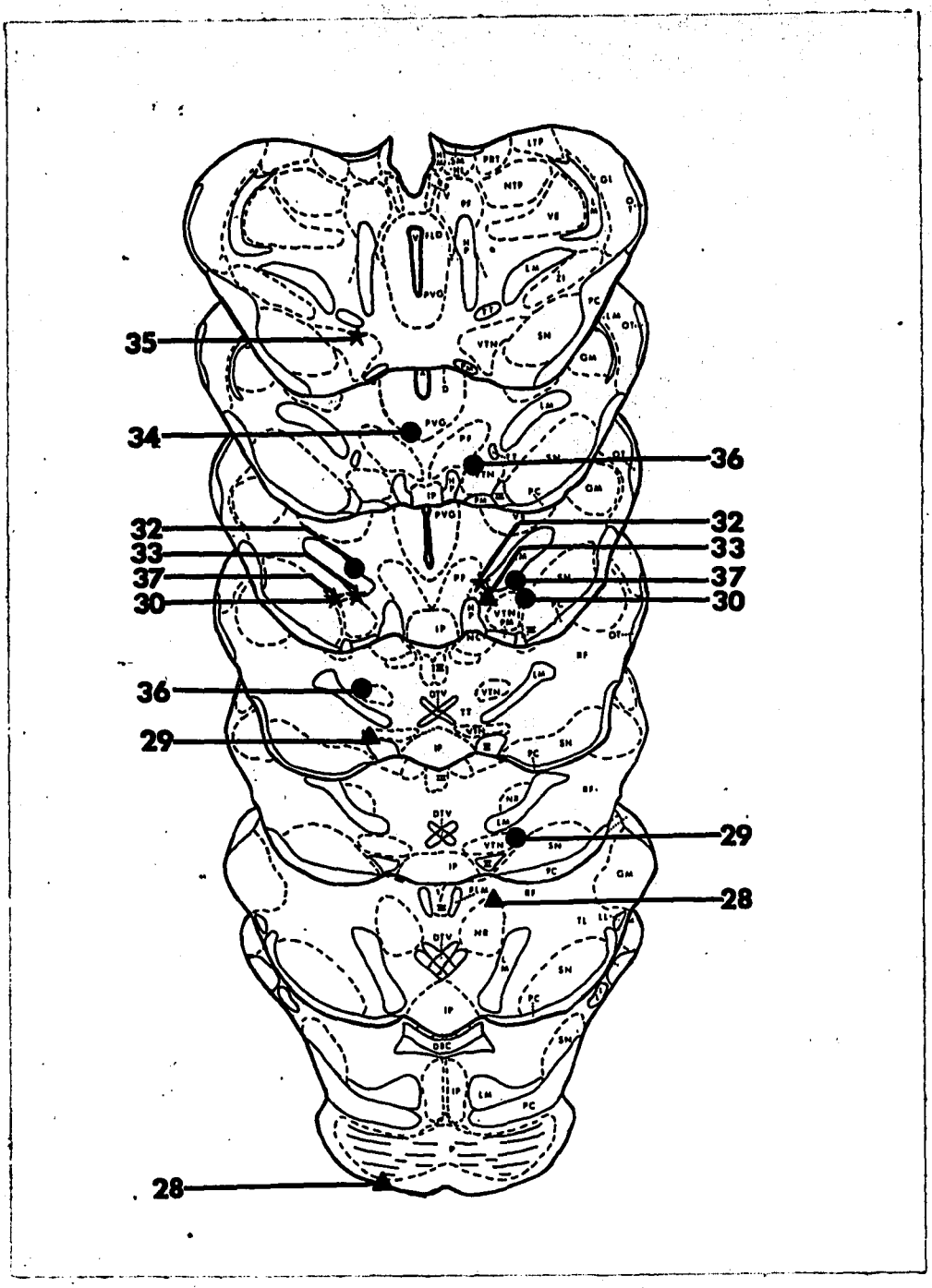

Fig. 5. Histological and self-stimulation findings in the ventral midbrain (Experiment 3). The symbols represent the same response rates as those in Figure 1. Brain sections (top to bottom), modified from the Pellegrino and Cushman Atlas (1967) are: 2.6, 3.0, 3.2, 3.4, 3.6, 3.8, and 4.8 mm. posterior to bregma.

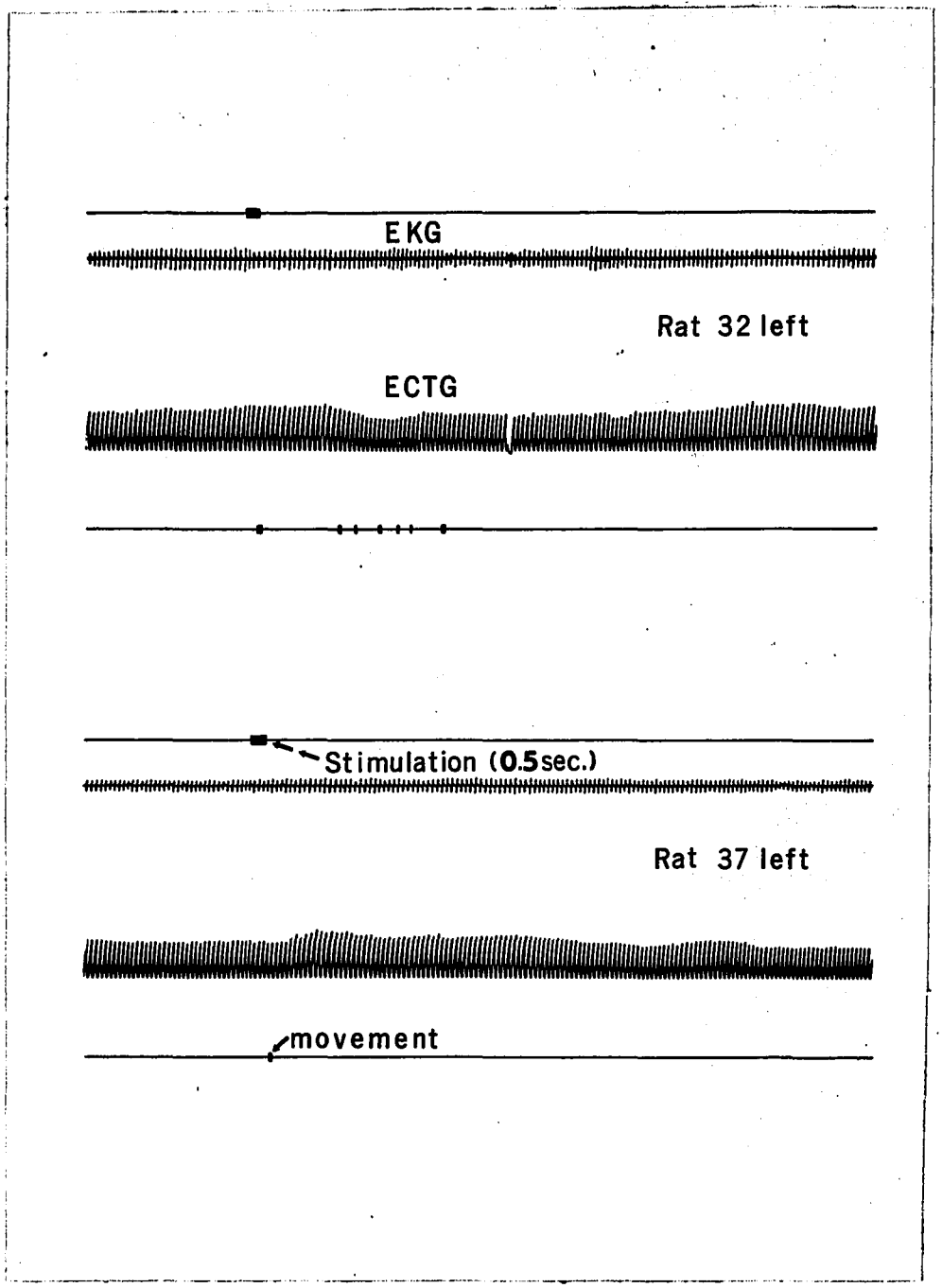

Fig. 6. Representative heart-rate records from Experiment 3. An upward deflection of the ECTG tracing represents heart-rate deceleration.

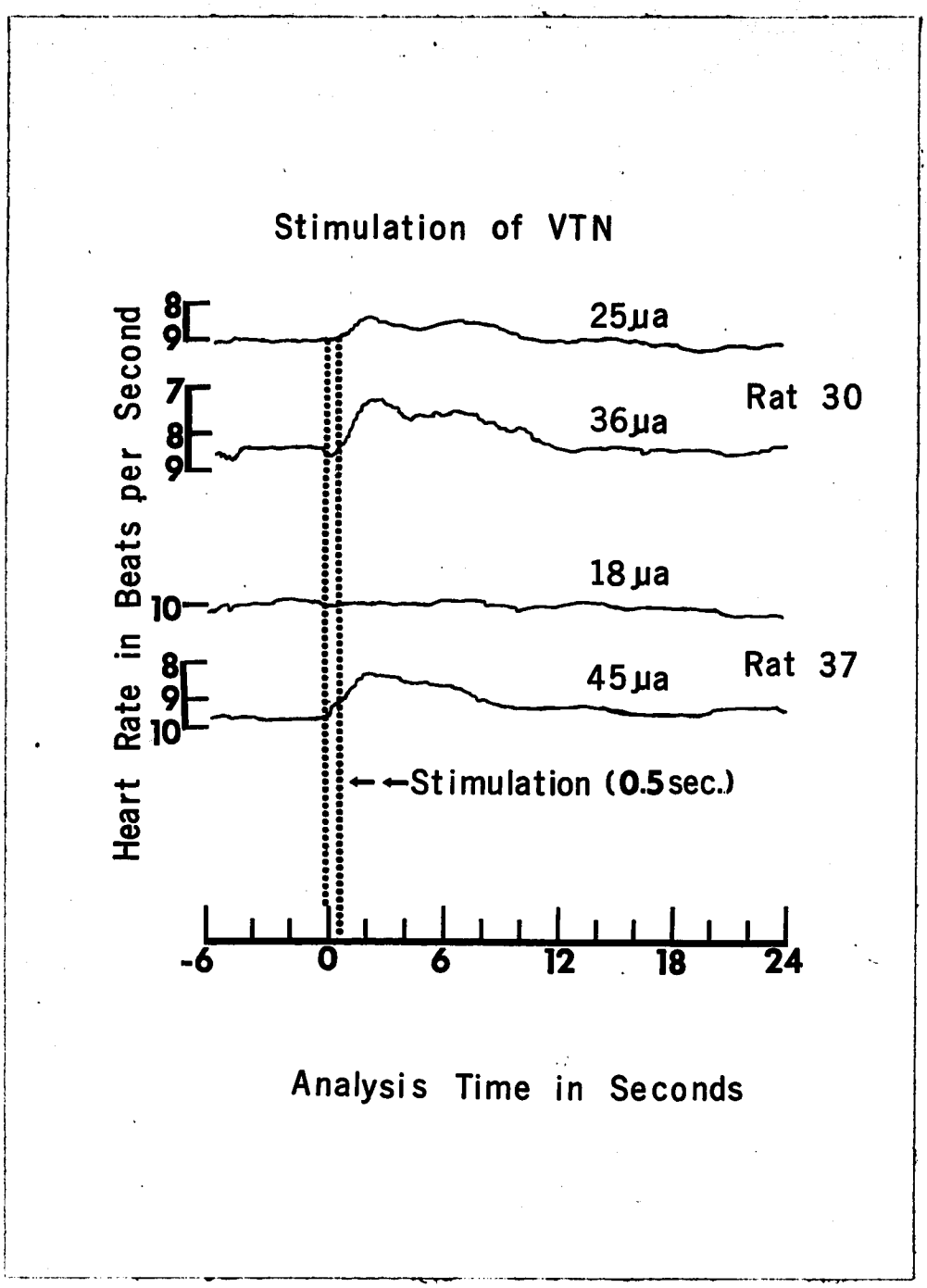

Fig. 7. Averaged heart-rate response to stimulation of the ventral tegmental nucleus. An upward deflection of the tracing represents a deceleration of heart rate.

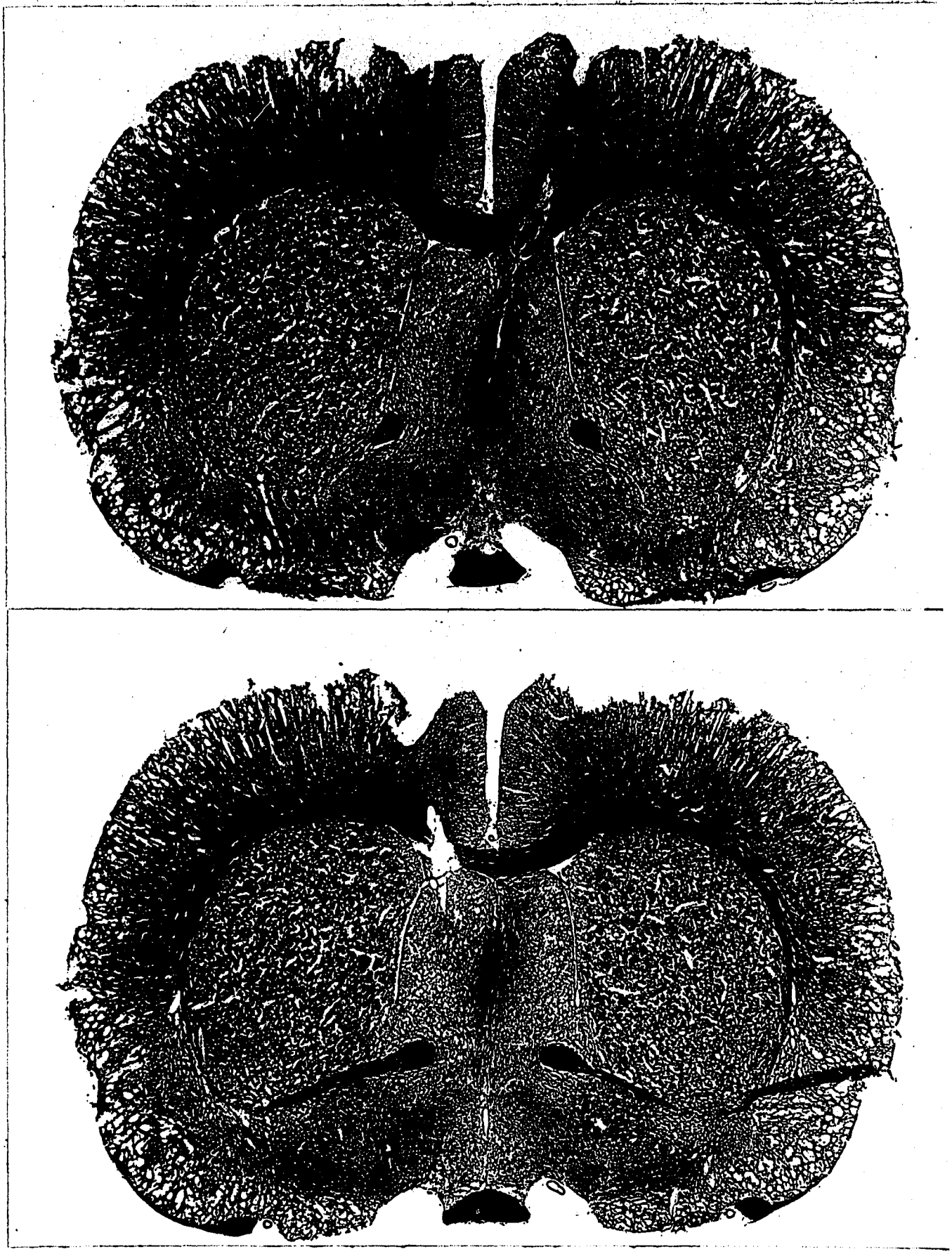

Fig. 8. Electrode placements of Rat 1.

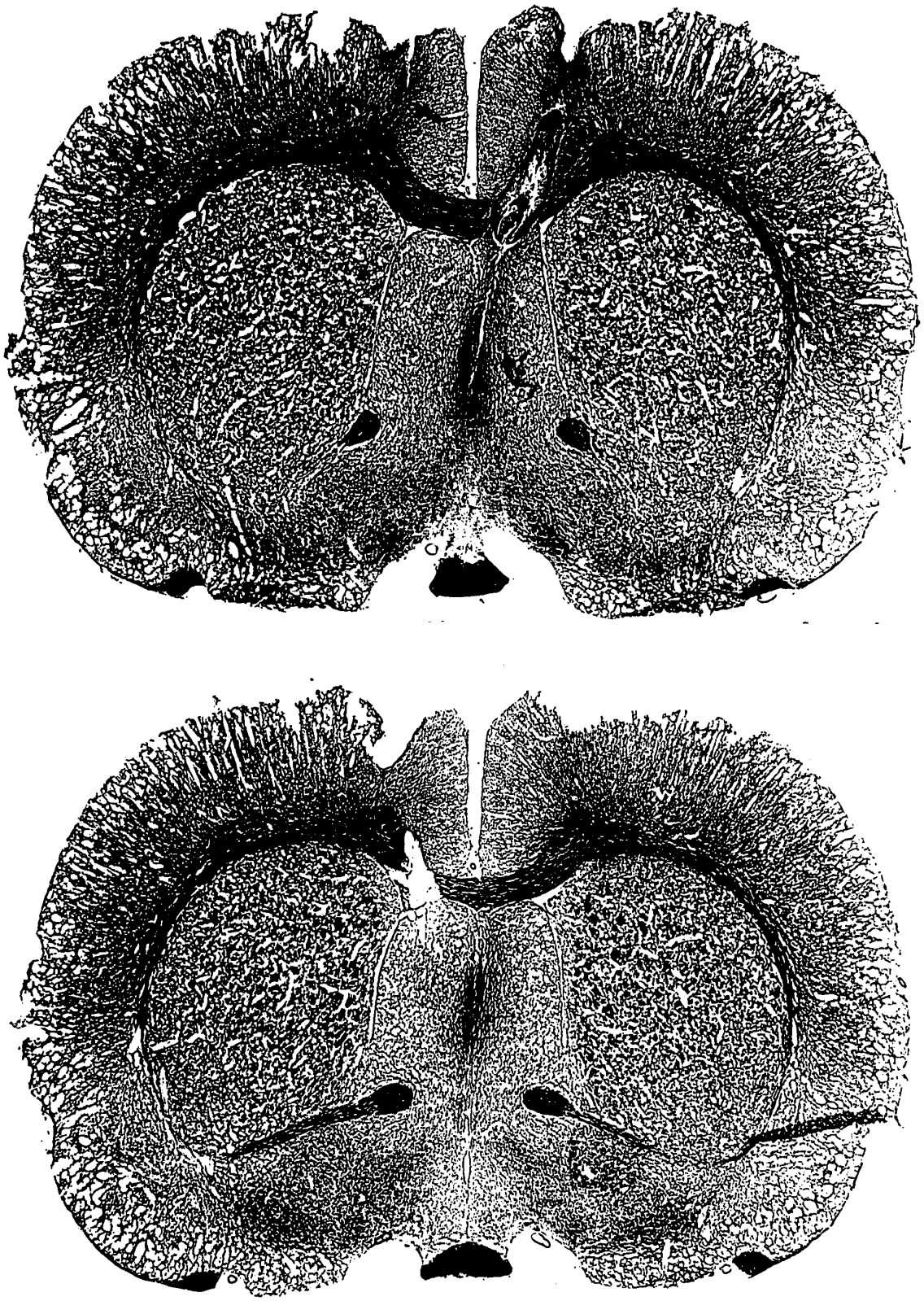

Fig. 8. Electrode placements of Rat 1.

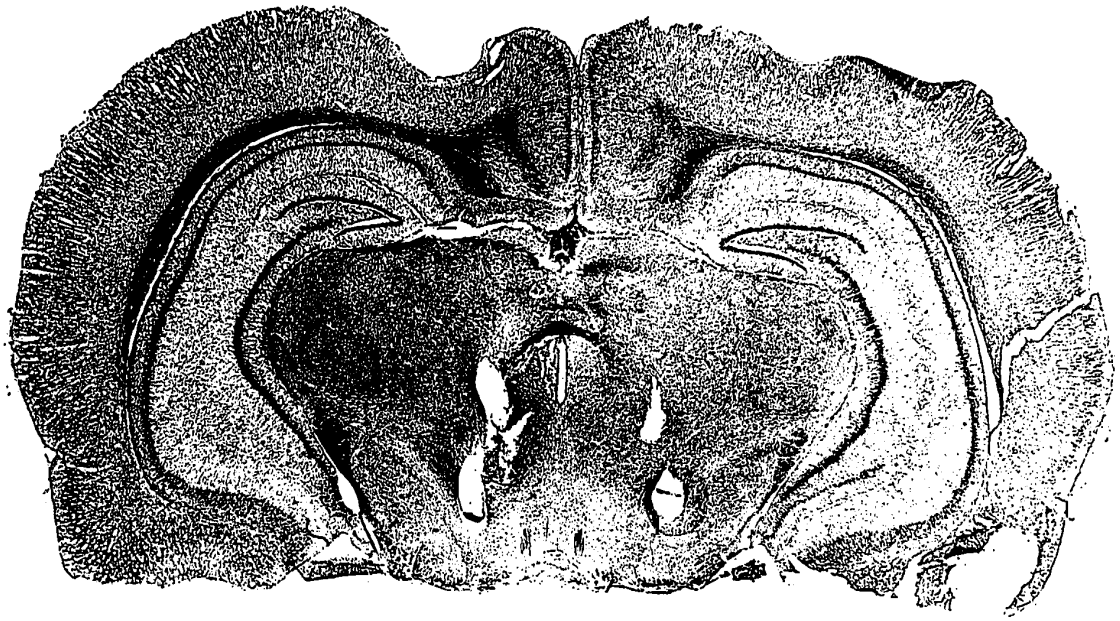

Fig. 9. Electrode placements of Rat 30.

TABLE 1

Reports of Self-Stimulation

in the Ventral Midbrain

Area or Structure	Investigators
ventral tegmentum	Deutsch, 1964; Deutsch, Adams, & Metzner, 1959; Porter, Conrad, & Brady, 1959; Seward, Uyeda, & Olds, 1959; Spies, 1965; Stein & Ray, 1960.
medial lemniscus	Hawkins & Pliskoff, 1964; Kramis & Routtenberg, 1969; Olds & Olds, 1963; Poschel, 1969; Routtenberg & Malsbury, 1969; Stein, 1962.
red nucleus	Glickman, 1960; O'Donohue & Hagamen, 1967; Routtenberg & Malsbury, 1969; Spies, 1965.
substantia nigra	Kramis & Routtenberg, 1969; O'Donohue & Hagamen, 1967; Poschel, 1969; Routtenberg & Malsbury, 1969; Wurtz, 1965.
ventral tegmental nucleus	Blevings, personal communication; Gallistel, 1966; Hawkins & Pliskoff, 1964; Poschel, 1969; Olds & Olds, 1963.
central gray	Cooper & Taylor, 1967; Glickman, 1960; O'Donohue & Hagamen, 1967; Olds, 1956; Stein, 1962.

TABLE 2

Summary of Self-Stimulation and Phasic HR Changes with Septal Stimulation

Subject	Brain Area	BP/hr	HR Change
1	MS	624	slowing *
	LS	690	slowing
2	DBB	1278	slowing
	LS-CPU	78	speeding
3	DBB	114	none
	LS-CPU	6	slowing *
4	MS	864	slowing *
	LS	408	slowing
5	MS	12	slowing *
	LS-CPU	18	none
6	MPO	690	slowing
	LS	258	slowing
7	DBB	504	slowing
	LS-CPU	18	slowing
8	DBB	678	slowing
	LS	335	slowing
9	MS	816	slowing *
	LS	390	slowing
10	DBB	18	slowing
	LS-CPU	24	slowing (slight)

* denotes initial acceleration following stimulation

Abbreviations: LS, lateral septum; MS, medial septum; DBB, diagonal bands of Broca; CPU, caudate nucleus, putamen; MPO, medial preoptic area

TABLE 3

Summary of Self-Stimulation and Phasic HR Changes with Midbrain Stimulation

Subject	Brain Area	BP/hr	HR Change
11	SN	24	speeding
12	SN	678	speeding *
13	SN	18	none
14	SN	12	none
15	VTA	312	none
16	SN-VTA	0	slowing
17	SN-VTA	24	slowing *
18	SN-VTA	6	slowing *
19	SN-PC	72	none
20	SN-PC	120	none
21	PC	120	slowing *
22	PC	42	none
23	PC	42	speeding
24	P	162	none
25	P	96	speeding (slight)
26	IP	18	speeding
27	TL	18	none

* denotes an initial HR change opposite to the direction noted.

Abbreviations: SN, substantia nigra; VTA, ventral tegmental area; PC, cerebral peduncle; P, pons; IP, interpeduncular nucleus; TL, lateral tegmental nucleus

TABLE 4

Summary of Self-Stimulation and Phasic HR Changes with Midbrain Stimulation

Placement	Brain Area	Current (μa)	BP/hr	HR Change
28 right	at base of brain	25	168	slowing
left	dorsal NR	90	228	slowing
29 right	ventral VTN	50	216	slowing
left	lateral VTN	60	2220	slowing
left	lateral VTN	50	---	none
left	lateral VTN	20	264	---
30 right	ventrolateral VTN	36	378	slowing
right	ventrolateral VTN	25	138	slowing
left	ventrolateral VTN	60	2400	slowing
32 right	medial LM	12	4080	slowing
left	between LM & PF	27	450	speeding
33 right	dorsal VTN	40	456	slowing
right	dorsal VTN	18	96	none
left	dorsomedial VTN	18	96	(none)
34 right	PVG	18	2100	slowing
35 right	VTN	14	582	(speeding)
36 right	lateral VTN	16	2640	slowing
left	dorsal VTN	60	1800	slowing
left	dorsal VTN	20	246	none
37 right	dorsolateral VTN	35	660	slowing
left	dorsal VTN	45	1092	slowing
left	dorsal VTN	18	18	none

( ) denotes visual inspection of HR record due to insufficient data.

Abbreviations: NR, red nucleus; VTN, ventral tegmental nucleus (Tsai); LM, medial lemniscus; PF, parafascicular thalamic nucleus; PVG, periventricular gray