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Main Effects of Current and Pimozide on Prepared and Learned Self-Stimulation Behaviors are on Performance not Reward

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MEKARSKI, J. E. *Main effects of current and pimozide on prepared and learned self-stimulation behaviors are on performance not reward.* PHARMACOL BIOCHEM BEHAV 31(4) 845–853, 1988.—This work examined four independent variables which influence behavior of self-stimulating rats: site of electrode placement (cingulate cortex versus lateral hypothalamus), type of operant response (lever press versus nose poke), current intensity (50, 100, 150 μA) and pimozide dosage (0.125, 0.250, 0.500 mg/kg). The dependent measures were: total responding, alternation between two identical manipulanda and mean duration per response. Naive rats made more nose pokes than lever presses, suggesting nose pokes are more "prepared." The cingulate cortex was insensitive to current and pimozide manipulations in contrast with hypothalamic sensitivity, tentatively suggesting a cingulate role in release of prepared behaviors, hypothalamic in plasticity of learned ones. Lever pressing, more prevalent with lateral hypothalamic stimulation, was more affected by current and pimozide manipulations than nose poking. More prepared nose pokes might thus be less susceptible to brain stimulation reward manipulations. Intensifying current produced more but shorter responses, increasing pimozide dosage produced fewer and nonsignificantly longer ones, suggesting a primary effect on motor performance not reward. Decrements in performance over nondrug days were tentatively attributed to long-lasting effects of pimozide.

Current intensity Pimozide Self-stimulation Lateral hypothalamus Cingulate cortex Activation Performance Reward Lever pressing Nose poking Innate Prepared Learned

PHASE 1

Olds and Milner (25) found that rats emit behavior for contingent intracranial stimulation, and brain stimulation reward (BSR) is regarded as a primary reinforcer because it increases antecedent operant behavior (3). According to Valenstein (36), "The behavior produced by brain stimulation reflects innate and perhaps learned prepotent responses which tend to be dominant . . ." (p. 18). No clear attempt, however, has been made prior to experimental manipulations of the reward substrate to distinguish emitted, innate (3) or prepared (29) from elicited, learned, or operant (32) behaviors.

To this end, naive unimplanted rats were first assessed for their nose poking (NP) and lever pressing (LP) proclivity. Kinetic requirements of these responses, which are frequently used in self-stimulation experiments, were expected to differentially affect self-stimulation behavior (11). This is in accord with a statement by Sheer (30), that " . . . reward or punishment is an interactive function of the intensity of excitation and the complex nature of the task animals are called upon to perform." (p. 459). After assessment of the stability of intracranial self-stimulation (ICSS) behavior across days under constant current conditions, the study determined whether varying ICSS current intensity (including a no current condition) differentially affected alternation for LP and NP tasks.

An alternation paradigm was selected in order that the animals traverse the test apparatus to obtain BSR, and thus provide control over possible iterative epileptiform (15) motoric effects of current, or sedative effects of neuroleptic (in Phase 2). Such a paradigm might better clarify whether the major effects of these manipulations are upon performance output or reward duration. Durations per response of ICSS were obtained, because time measures are said to minimize the influence of activity level and performance capacity on the estimate of reinforcement value (37). That duration of ICSS may be used as a quantitative measure of reward is based on the work of Edmonds and Gallistel (8), Faustman and Fowler (12) and Ward (38), and is suggested by the observation that duration decreases as current intensity is increased (16,20).

In view of the statement that "Reward circuits seem to be organized in a hierarchical manner." (p. 125) (27), a diencephalic site, the lateral hypothalamus (LH) and a telencephalic site, the cingulate cortex (CC) were chosen for their contrasting response characteristics (23,24).

The purpose of Phase 1 of the study, therefore, was to conduct an analysis of three factors which influence BSR-

mediated behavior of self-stimulating rats employing a prepared (29), and a learned response. The factors were: self-stimulation task, intracranial site and current intensity of stimulation.

PHASE 2

A substantial body of evidence implicates dopamine (DA) in the control of behavior by reward (11, 14, 26, 39). DA's role in ICSS is however unclear, as the effect of manipulations of DA may be attributed to either changes in performance or reward. Good evidence for DA's role in motor performance comes from Parkinson's disease in which rigidity, lack of voluntary movement, and tremor are associated with DA cell loss from the substantia nigra (18). Furthermore, successful restoraton of movement is achieved by administration of the DA precursor l-dihydroxyphenylalanine (17).

Evidence for DA's role in the control of behavior by reward comes from Poschel and Ninteman (28), who estimated reward value via the proportion of time spent by rats on a platform whereon current was available, versus one on which there was no current. Contrasted with a saline (no drug) condition, the DA agonist methamphetamine increased ICSS time of these rats, whereas the DA antagonist chlorpromazine decreased it.

The purpose of Phase 2 of the study was to examine the effect of DA receptor blockade by pimozide (19) upon activation (activity level), performance and reward aspects of ICSS. This was accomplished by measuring the total number of responses, number of alternations and durations respectively of the two operant responses in the alternating paradigm.

A particular advantage of the present study was that both the effects upon ICSS of varying current intensity and pimozide dosage could be observed in the same animals.

METHOD

Subjects and Surgery

Forty-seven adult Long Evans hooded male rats weighing between 250 and 300 g were housed individually in stainless steel cages and provided free access to food and water. Their environmental conditions were kept nearly constant, with temperature at 21°C, 50% relative humidity, and a reverse 12-hr light 12-hr dark cycle, with darkness commencing at 0800 hr.

Five unoperated rats served as controls to determine baseline response rates. The remaining rats were anesthetized with 60 mg/kg sodium pentobarbitone intraperitoneally (IP), and sterotaxically implanted with twisted bipolar 0.25 mm diameter Plastic Products MS-303/3 electrodes, 22 aimed at the CC and 20 at the LH. The level skull coordinates, with bregma as reference (21), were as follows: CC: 1.8 mm posterior, 0.6 mm left lateral, 2.1 mm ventral to skull surface; LH: 3.1 mm posterior, 1.5 mm left lateral, 8.5 mm ventral to skull surface. Rats were allowed to recover for one week in their home cages before response shaping was begun.

Apparatus

Two Plexiglas alternation boxes (36×32×17 cm) were housed in separate, styrofoam insulated chambers equipped with prompt lights on each side (Fig. 1). Each box was provided at either end with identical, detachable manipulanda for nose poking or lever pressing. Each nose poke manipulandum consisted of a 2.6-cm diameter hole centered 7 cm above the cage floor in a matted Plexiglas panel, and a photocell sensor 1 cm beyond the inner wall of the panel. Each 10-cm wide lever manipulandum was externally positioned below a microswitch, and pivoted 8 cm above the floor in the center of a matted Plexiglas panel. Its internal end was bent downward, and then outward to form a 1.5-cm platform 5 cm above the floor, and extending 5 cm into the alternation box.

Sinusoidal 60 Hz, 100 μA reinforcing current, adjusted by a 10 turn precision potentiometer and monitored on a dual trace oscilloscope, was delivered to the animals through electrical swivels and flexible spring encased leads. Rats were wired in series with a 10,000 Ω resistor to ensure a constant stimulus. Current for prompt lights, as well as signals from either the nose poke photocells, or lever microswitches were routed to standard electromechanical programming equipment housed in an adjoining room.

Procedure

Training. Five unimplanted rats were handled daily for a month. On alternate days, lever press (LP) and nose poke (NP) responses of implanted rats were shaped over seven 30-min sessions. For the next three weeks, their responses were shaped in two daily 30-min sessions, one of LP and one of NP, separated by 30 min in the home cage. Rats had to alternately respond on one side of the box, go to the opposite side, and respond there to obtain ICSS for the duration of the response. Out of sequence responses were not rewarded. The order of manipulanda was randomly determined each day and at the start of each session prompt lights indicated the side of the box from which ICSS was available.

Twelve animals were discarded during training due to nonresponding, lack of electrical contact, loss of electrodes and motoric effects, so that subsequent results are based on 13 LH and 17 CC rats completing the experiment.

Testing, Phase 1. To establish unreinforced fundamental responding proclivity, five unoperated "naive" rats were randomly assigned to an alternation box and tested with NP and LP manipulanda. Total number of responses, number of alternations, and duration of operation of both manipulanda were recorded over two successive 30-min periods on two successive days.

The nature and stability of reinforced responding by self-stimulating rats were assessed on both manipulanda which were presented in random order. Rats were tested for three days under 60 Hz 100 μA constant current conditions. For the next three days, the effects of randomly presented varying current intensities of 50, 100, and 150 μA were assessed. Operant reinforced alternation was taken as an estimate of performance, and mean duration per reinforcement as an estimate of the amount of reward (38). Finally, the effect on behavior of current offset (no current) was assessed.

Testing, Phase 2. Over a 14-day period, five two-day nondrug sessions alternated with four one-day drug sessions. On drug days, pimozide (0, 0.125, 0.250, or 0.500 mg/kg, IP) was injected 4 hr prior to testing. Pimozide was dissolved in boiling tartaric acid and cooled to room temperature prior to injection. All rats received the 0 mg/kg dose (i.e., 1.500 mg/kg of tartaric acid) on the first drug day and the remaining three doses in a randomly determined order for each rat on the next three drug days.

Three measures were obtained during each test: total number of responses, number of operant reinforced alterna-

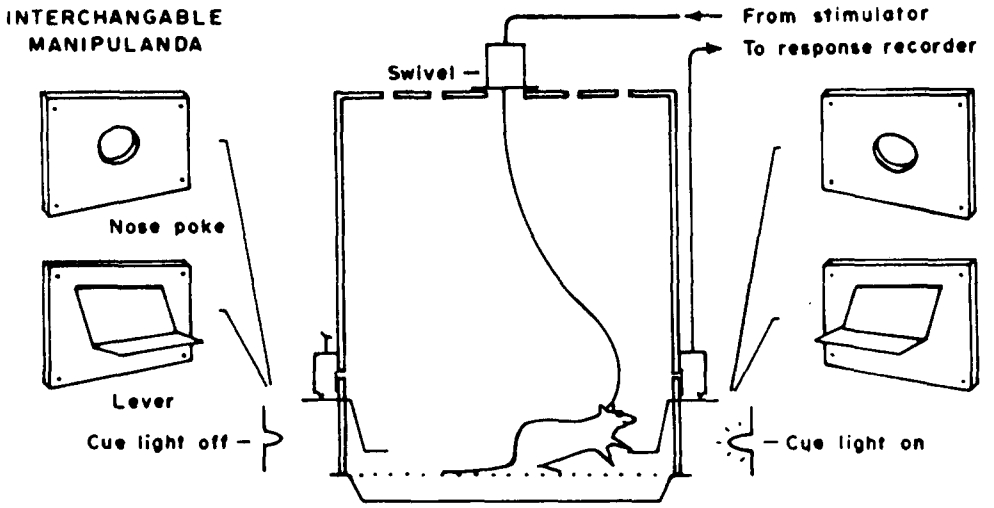

FIG. 1. Intracranial self-stimulation alternation apparatus.

tions, and total duration of operation of manipulanda. Because total duration depends on both the number of alternations and duration of each iteration, the mean duration per reinforced response was calculated.

Histology

At the conclusion of the experiment rats were injected with a lethal dose of sodium pentobarbital, and perfused through the heart with 0.9% saline solution, followed by 10% formalin. Each brain was removed and stored in buffered formalin. Brains were next embedded in paraffin, and sectioned at 7 μm on a rotary microtome. The sections were mounted on slides, stained with hematoxylin, and counterstained with eosin (4). Loci of electrode tips (Fig. 2) were determined by scaling sections to the atlas of König and Klippel (21).

RESULTS

Histology

Histological examination (Figs. 2 and 3) indicated that LH electrode tips clustered in the A 3750 μ plane of the atlas, dorsal and lateral to the medial forebrain bundle. CC tips ranged from A 4890 to A 6790 μ in the antero-posterior direction, from 2.74 to 4.76 mm from the horizontal plane, and from 0.23 to 1.00 mm left lateral to the midsagittal plane.

Phase I

Naive responses (Fig. 4). Standard statistical methods were used for data analyses [Dixon (7)]. Naive unreinforced rats emitted significantly more mean total NPs (133.7) than LPs (21.5), $t(4)=4.97$, $p<0.01$, and they made significantly more mean NP alternations (15.1) than LP alternations (2.7), $t(4)=5.51$, $p<0.01$.

The expectation that LH self-stimulators would emit more NPs than naive rats proved false, $t(16)=-1.49$, n.s., but they did make more LPs, $t(16)=-1.89$, $p<0.05$, than naive rats, as did CC NP self-stimulators, $t(20)=-2.61$, $p<0.01$.

Reinforced alternations, constant BSR intensity (Fig. 4). Among implanted animals, more alternations were made by LH rats in order to LP than to NP, whereas CC rats alternated more frequently to NP than to LP. A distinct site difference was confirmed by analysis of variance (ANOVA), $F(1,28)=14.40$, $p<0.001$, and a task by site interaction was present, $F(1,28)=5.83$, $p<0.05$. Thus, the two tasks differentially reinforced alternation, depending on the site stimulated. Neither the main effect of repeated daily testing, nor any of its interactions were significant, indicating that performance was stable over days during the constant current condition.

Reinforced alternations, varying BSR intensity (Fig. 4). LH rats alternated between manipulanda considerably more often than CC rats, (307.5 to 31.8 respectively), $F(1,28)=20.33$, $p<0.001$. A task by site interaction, $F(1,28)=5.71$, $p<0.05$, showed that LH rats made about 1.4 times as many LPs as NPs, while CC rats made about 1.7 times as many NPs as LPs.

Increasing current intensity increased reinforced alternations, $F(2,56)=10.48$, $p<0.001$. A current by site interaction, $F(2,56)=10.44$, $p<0.001$, confirmed that mean alternations per session of LH rats increased from 198.6 at 50 μA to 389.4 at 150 μA, while those of CC rats remained near 32, unresponsive to current variations.

A task by current interaction, $F(2,56)=7.91$, $p<0.001$, showed that LP alternations increased from an average of 107.9 at 50 μA to 247.1 at 150 μA. Corresponding NPs rose less markedly from 122.2 to 173.8 alternations per session.

A task by current by site interaction, $F(2,56)=8.67$, $p<0.001$, showed that the task by current interaction was different at the two stimulation sites. For LH rats, as current was

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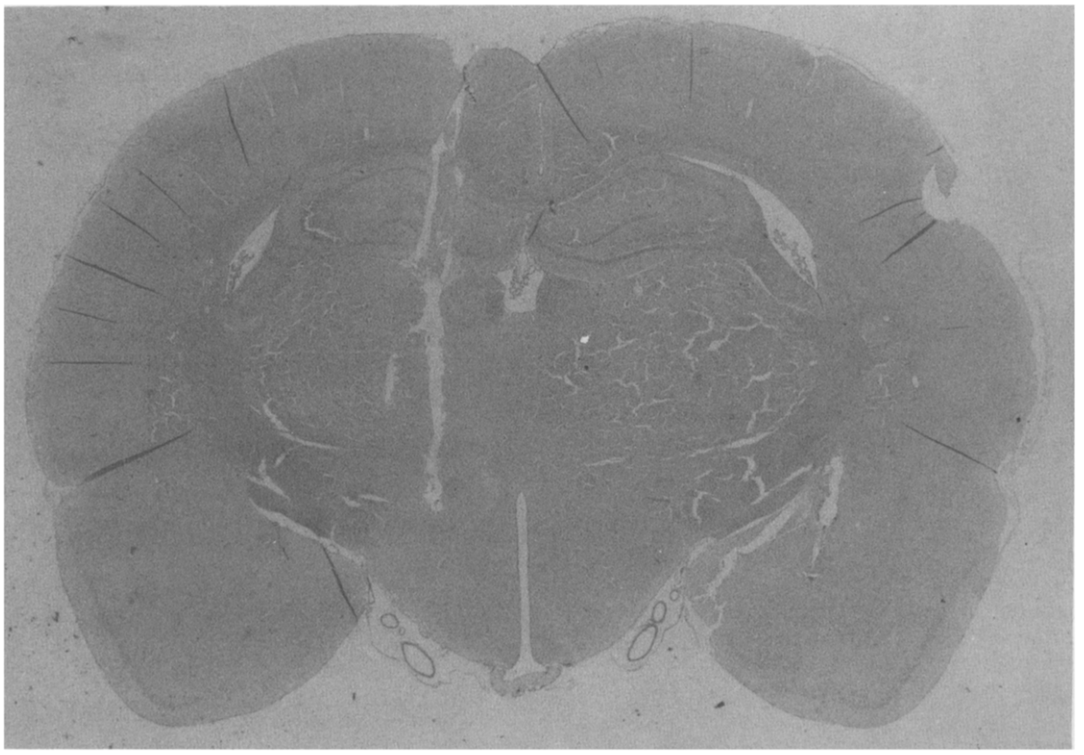
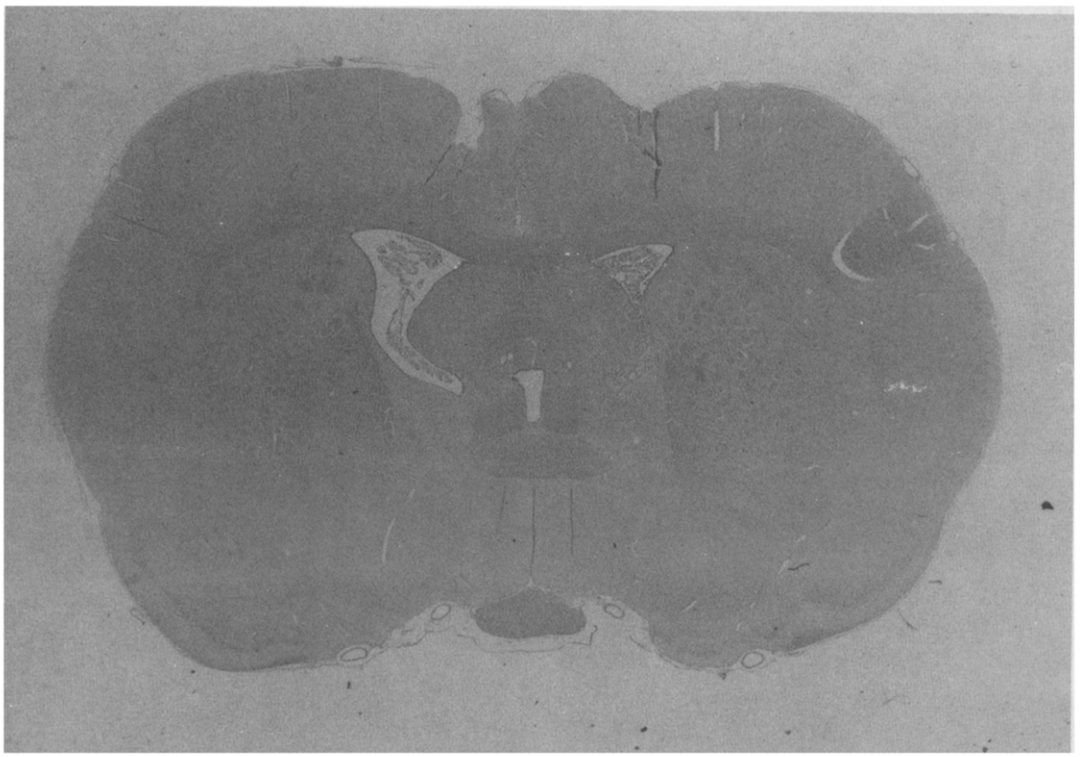
FIG. 2. Representative photomicrographs of hematoxylin/eosin stained coronal sections showing electrode placements: (top) lateral hypothalamus, rat 17; (bottom) cingulate cortex, rat 16.



A 3750 μ LH 17



A 5150 μ CC 16

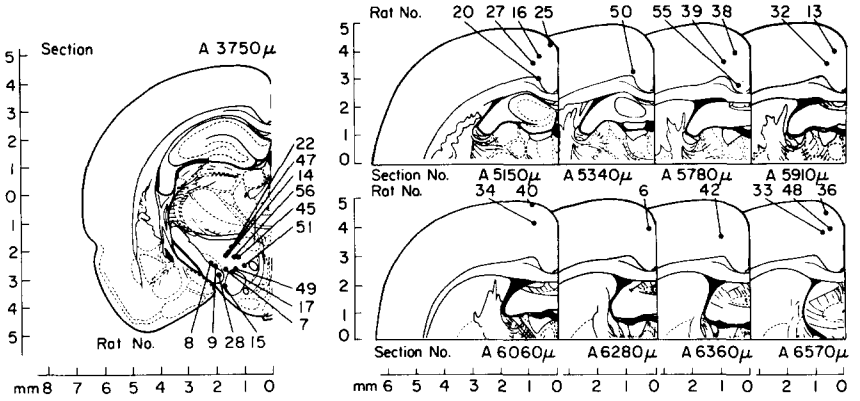


FIG. 3. Location of lateral hypothalamic electrode tips (left) and cingulate cortical electrode tips (right). [Adapted from König and Klippel (21)].

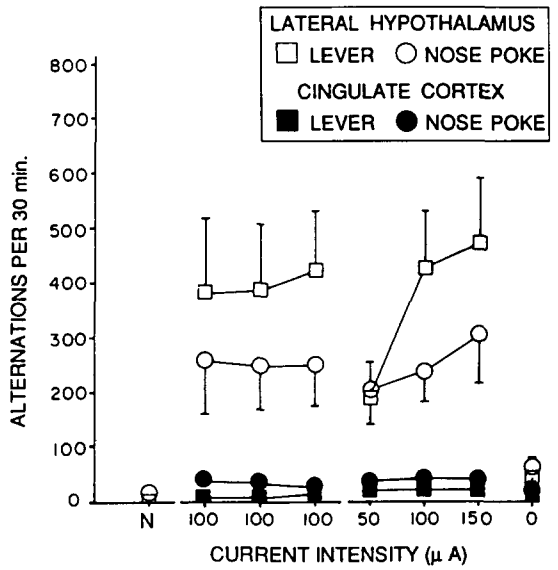


FIG. 4. Number of lever press and nose poke alternations (±sem) in 30 minutes by lateral hypothalamically- (n=13) and cingulate cortically- (n=17) stimulated rats as a function of current intensity. Note that naive (N) and extinction (0) rats were not reinforced.

increased, LPs increased at a greater rate than NPs, while for CC rats both LPs and NPs remained stable.

Alternations, no BSR (Fig. 4). Alternations during extinction were fewer than when 150 μA of intracranial current were available for LH NPs $t(12)=2.82$, $p<0.05$, and LPs, $t(12)=3.81$, $p<0.01$, as well as CC NPs, $t(16)=4.49$, $p<0.001$, and LPs, $t(16)=2.28$, $p<0.05$. During extinction, both LH and CC rats reverted to a low level of performance suggestive of naive rats. LH rats alternated more than CC rats in extinction, $F(1,28)=12.76$, $p<0.01$, with both LH and CC rats making more NPs than LPs, $F(1,28)=9.01$, $p<0.01$.

Naive durations per response (Fig. 5). The mean NP duration per response of naive rats (1.2 sec) was not significantly different from their mean LP duration per response (3.2 sec), $t(4)=-1.79$, n.s.

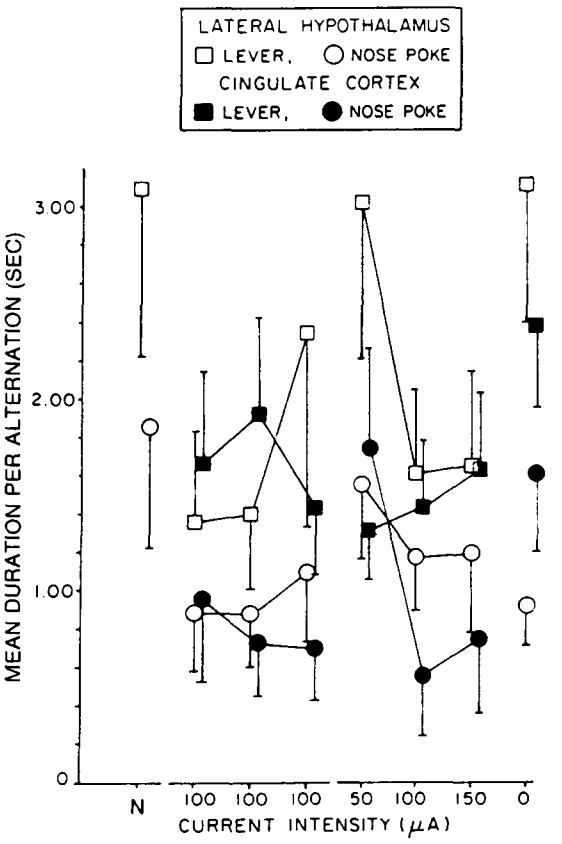


FIG. 5. Mean lever press and nose poke durations per response (±sem) of lateral hypothalamically- (n=13) and cingulate cortically- (n=17) stimulated rats as a function of current intensity. Note that naive (N) and extinction (0) rats were not reinforced.

Among implanted rats, the duration per reinforcement on the first day of self-stimulation was significantly shorter from duration per response of naive rats only for LH LPs, $t(16)=1.86$, $p<0.05$.

Durations per reinforcement, constant BSR intensity (Fig. 5). Analysis of durations per reinforcement confirmed that the only significant effect was that of task, $F(1,28)=12.18$, $p<0.01$, with mean LP duration of about 1.7 sec per reinforcement, and mean NP duration of 0.9 sec per reinforcement. The main effect of stimulation site and its interactions, and the main effect of days and its interactions were not significant, showing that during constant current conditions the durations per reinforcement remained stable.

Durations per reinforcement, varying BSR intensity (Fig. 5). As current increased from 50 to 150 μA, the mean duration per reinforcement decreased from about 1.9 to 1.3 sec. Mean duration per reinforcement did not differ significantly between LH and CC stimulation sites. Stimulation current produced different effects upon the two tasks, $F(1,28)=12.62$, $p<0.01$, with mean LP duration being longer than NP duration. Increasing current intensity resulted in shorter mean durations of stimulation, $F(2,56)=15.58$, $p<0.001$. A significant task by current interaction was found, $F(2,56)=4.89$, $p<0.05$, with the shorter mean NP duration decreasing more precipitously than the corresponding LP duration.

Duration per response, no BSR (Fig. 5). Durations per response during extinction were significantly longer than during self-stimulation with 150 μA of current only for LH LPs, $t(12)=-2.38$, $p<0.05$. With the reward contingency removed, mean duration per response increased to about 2 sec, resembling the performance of naive rats. A significant task effect, $F(1,28)=11.03$, $p<0.01$, showed that in extinction, LPs were of longer duration than NPs, resembling the performance of naive rats.

Phase 2

In ICSS rats, decrements of behavior were revealed by separate ANOVA upon mean measures from nondrug sessions as well as drug sessions from which mean antecedent nondrug or "baseline" responses were subtracted.

Total responses. During nondrug sessions rats stimulated the LH significantly more than the CC, $F(1,28)=22.33$, $p<0.001$. Neither the main effect of task nor of task by site interactions were significant. Daily baseline retesting between drug treatments disclosed a monotonic decrease, $F(4,112)=5.54$, $p<0.001$. A day by site interaction, $F(4,112)=4.81$, $p<0.01$, revealed a performance decrement which could be ascribed to LH but not CC rats. Task did not interact with days, nor was there any task by day by site interaction.

Figure 6 shows drug session deviations from baseline of the total number of reinforced and unreinforced responses as a function of pimozide dosage. The deviation on drug days of LH rats was significantly greater than the deviation of CC rats, $F(1,28)=11.46$, $p<0.005$, however, adjustment of drug responses for corresponding nondrug sessions removed the underlying effect of task. Also, the site by task interaction did not attain significance. Increasing pimozide dosage decreased total responding, $F(3.84)=8.62$, $p<0.001$, and the decrease was more prominent for LH than CC ICSS, $F(3,84)=3.07$, $p<0.05$, Neither task and dose, nor task dose and site interacted significantly.

Reinforced alternations. Analysis of nondrug alternation

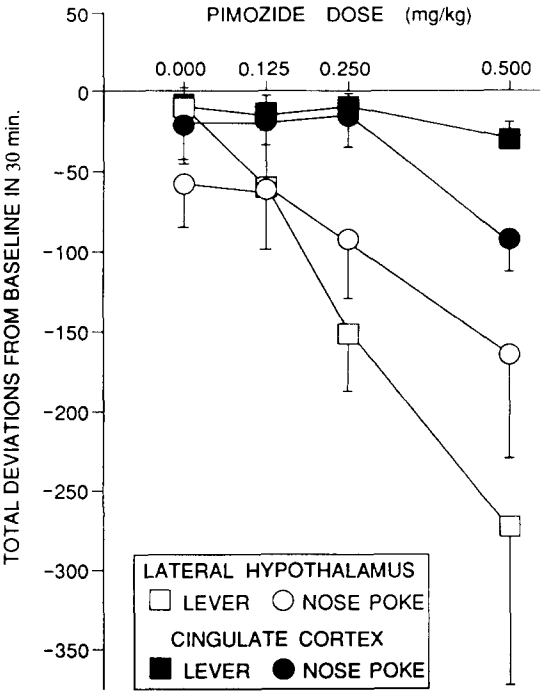


FIG. 6. Deviations from baseline total number of lever press and nose poke responses (±sem) in 30 minutes by lateral hypothalamically- (n=13) and cingulate cortically- (n=17) stimulated rats as a function of pimozide dosage.

responses confirmed that LH rats made significantly more alternations than CC rats, $F(1,28)=23.04$, $p<0.001$. More LPs were made than NPs, $F(1,28)=4.72$, $p<0.05$, and a task by site interaction showed that this difference might largely be attributable to LH rats. CC rats made more NPs than LPs, $F(1,28)=5.53$, $p<0.05$. Daily baseline retesting between drug treatments confirmed a significant decrement in alternations, $F(4,112)=2.51$, $p<0.05$. There were no day by site, task by day, or task by day by site interactions, that is, the task and drug effects were similar across days.

Figure 7 shows drug session deviations from baseline of reinforced alternations as a function of pimozide dosage. On drug days, the deviation of LH rats was more pronounced than that of CC rats, $F(1,28)=17.18$, $p<0.001$. The main effect of task was not significant, but there was a task by site interaction, with LH LPs being more depressed by pimozide than NPs, whereas CC LPs and NPs were affected to about the same degree, $F(1,28)=4.70$, $p<0.05$. Pimozide dose-dependently attenuated alternation responses, $F(3,84)=6.03$, $p<0.001$. A dose by site interaction showed that LH alternations were more attenuated than CC alternations, $F(3,84)=4.57$, $p<0.01$. The task by dose interaction did not attain significance, but there was a three-way task by dose by site interaction, $F(3,84)=3.75$, $p<0.05$, with the task by dose interaction being more pronounced at the LH site, where LPs were progressively more attenuated by increasing pimozide dosage than NPs, whereas at the CC site the differential effect on the two responses was not significant.

Mean durations per reinforcement. Analysis of nondrug mean durations per reinforcement showed a site effect, $F(1,28)=5.95$, $p<0.05$, with more ICSS being obtained via

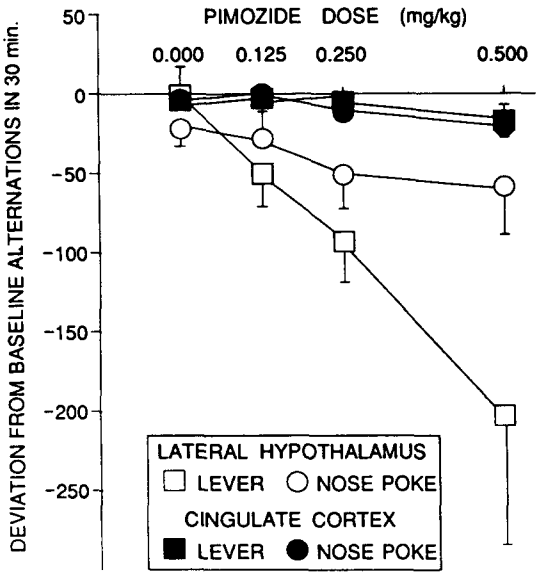


FIG. 7. Deviation from baseline number of lever press and nose poke alternations (±sem) in 30 minutes by lateral hypothalamically- (n=13) and cingulate cortically- (n=17) stimulated rats as a function of pimozide dosage.

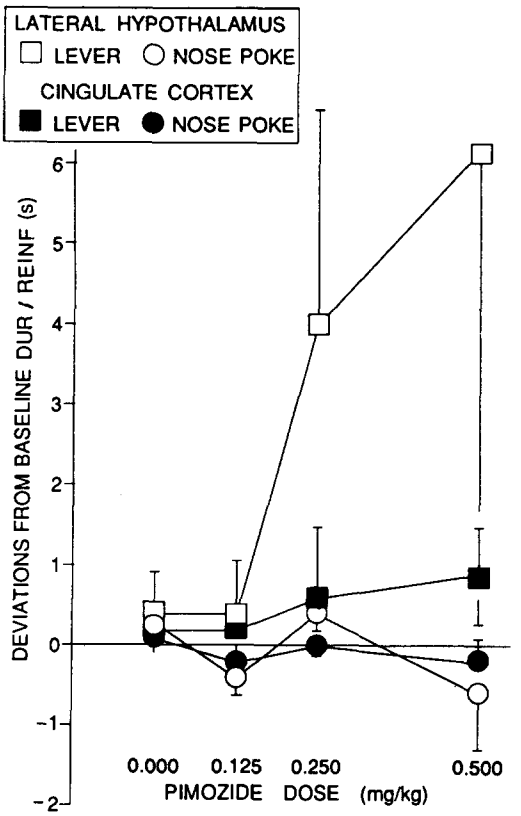


FIG. 8. Deviation from baseline mean lever and nose poke durations per reinforcement (±sem) by lateral hypothalamically- (n=13) and cingulate cortically- (n=17) stimulated rats as a function of pimozide dosage.

the LH than the CC. Nondrug LP durations exceeded NP durations, $F(1,28)=18.41, p<0.001$. The task by site interaction did not attain significance, being similar across the two sites. Mean duration of ICSS increased slightly over the five nondrug sessions, but the effect was not significant. Test days did not interact significantly with site, nor were there any task by day, nor task by day by site interactions. Thus, only site and task were significantly affected during baseline days in that longer ICSS was obtained via the LH, and mean LP durations per reinforcement were longer than corresponding NP durations.

Figure 8 shows drug session deviations from baseline of mean durations per reinforcement as a function of pimozide dosage. Stimulation of the LH and CC produced similar mean durations. In spite of the fact that LH LPs slowed down from about 0.4 sec to about 6.2 sec, and CC LPs slowed down from about 0.2 sec to about 0.9 sec, the effect of task was not statistically significant, and task did not interact with site. While mean durations per reinforcement became longer with increasing pimozide dosage, the effect did not attain statistical significance. There were no dose by site, task by dose, or task by dose by site interactions.

In sum, the effects of increasing pimozide dosage were opposite to those of intensifying current. They were mediated mainly by the LH rather than the CC site, and significantly affected alternation performance rather then reward duration. The major impact of these manipulations was on lever pressing rather than on nose poking.

DISCUSSION

Phase 1

Naive unreinforced rats emitted a greater number of NPs than LPs, although their durations per response were not significantly different. This intrinsic preference for more NP alternations suggests that nose poking might be innate (22, 35, 36), i.e., genetically or maturationally organized to occur more frequently than learned lever pressing.

Behavioral ouput of LH self-stimulators was greater than that of naive animals, confirming that the LH site subserves BSR, while CC NPs were significantly greater than their naive counterparts, which might be taken as evidence that the CC subserves reward.

Subsequent to the fundamental task difference, self-stimulation produced a main effect of task or a task by site interaction in alternation performance. In both the constant and varying current conditions, LPs were more frequent than NPs. It is possible NP may be an activity normally having an exploratory function. If so, it should occur de novo with higher frequency than LP, and be more resistant to modification by manipulation of the ICSS substrate, as in the present case.

Duration per reinforcement in the constant current condition showed that mean LP was almost twice as long as NP when averaged for both stimulation sites (1.7 sec and 0.9 sec respectively). It may be that the two tasks required different amounts of reward for a given intensity of stimulation, or that task kinetics differed. A task by site interaction suggests that LH stimulation activated LPs to a greater extent than NPs, while the reverse may be seen for CC stimulation (Fig. 5).

A greater effect of intensifying current upon LPs than NPs may indicate that BSR seems to be modulated by the

nature of the self-stimulation task. Further, the task effect appears to be primarily motoric, i.e., on alternation performance output rather than on reward duration. One way to explain the task differences is to take an ethological approach (2, 22, 35). Unlike topographically novel responses such as LP, those which are prepared (29), or have a role in the animal's preexperimental life, have limits to which they can be altered "by consequences that may have little relationship to their normal function or causation" (p. 244) (31). In accord with this, NPs (which occurred more frequently in unimplanted rats) seemed to be less modifiable by current variations.

Stimulation of the LH resulted in more alternation performance, and accumuated longer durations of stimulation (reward) over test sessions than the CC. The stimulation site difference was therefore robust, and in substantial agreement with existing literature (9, 13, 38). This shows the sensitivity of the LH in contrast with the CC when challenged by changes in stimulus conditions. The result resembles the effects reported for the habenula (33), hippocampus (23), and septum (24), in contrast with sensitivity reported for the hypothalamus (23,24). One may infer, therefore, that increasing hypothalamic current was of increasing motivational, or hedonic value to the animal. These divergent response characteristics suggest that the two sites may have different functional roles. Conceivably, the LH is more active in attaching hedonic valence or biological significance to learned responses or homeostatic states, whereas the CC might be more concerned with stimuli, and the release of prepared responses.

Phase 2

The presumably more prepared (31) or innate (35) NP response which occurred more frequently in unimplanted rats, and was more resistant to current intensity manipulations of the ICSS substrate, was also less depressed by pimozide than the learned LP response. Only total responding (activation) and alternation performance measures were significantly affected by pimozide manipulations, which does not support the hypothesis (39) that neuroleptics blunt the hedonic impact of reward before impairing performance capacity. It is in accord with the suggestion (10) that neuroleptics have a direct motor debilitating role.

It is conceivable that pimozide's effects on performance might be mediated via impairment of immediate memory (1) or via impairment of recognition and recall of behavioral subroutines (34). In addition, pimozide might also affect incoming sensory channels (5,6).

Results of the present experiment showed decrements of total responding and alternation measures not only on drug days, but during intervening nondrug days. One possibility is that this decrement occurred because the relatively high ICSS current used might have produced neuronal damage around the electrode tips, but this was not evident on histological sections (Fig. 2). Furthermore, the rats were tested without drugs during Phase 1, prior to drug trials, and response rates were seen to be stable. Therefore, the observed response decrements probably resulted from repeated pimozide administration on drug days. Such baseline decrements might additionally entail a conditioned drug effect, but further experiments are needed to understand this.

Analysis of data from drug days showed a pronounced stimulation site difference in that LH rats emitted more and longer responses than CC rats. This points to different functional aspects of the two sites, and might argue against a uniform reward system. However, it must be noted that the small CC response decline may be partly attributed to a floor effect caused by initially low response rates. Future studies in which rates at different sites are equated by adjusting current may allow a resolution of this question.

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