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NOSE-POKE RESPONDING AND LOCOMOTOR ACTIVITY IN MICE WITH SEPTAL LESIONS

A Thesis Presented

By

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Submitted to the Graduate School of the
University of Massachusetts in partial fulfillment
of the requirements for the degree of

MASTER OF SCIENCE

August 1978

Psychology Department

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Introduction

Lesions of the septal area result in a generalized hyperreactivity to stimuli, an effect that manifests itself in the septal rage syndrome, and includes an increased responsivity to visual, thermal, auditory, and gustatory stimuli. The septal rage effect, originally described by Brady and Nauta (1953), consists of resistance to handling and aggressive responses toward tactile stimuli. This rage or hyperemotionality in the rat is transient (Brady and Nauta, 1955), and results from damage to areas which connect to the medial forebrain bundle and possibly to areas anterior and ventral to the septum (Albert, 1976); whereas a comparable effect in mice does not dissipate with time and is attributed to the area immediately anterior to the septum (Standish, 1976). Hyperemotionality is not correlated with other behavioral changes produced by septal lesions, such as enhanced response rates on FI schedules of reinforcement (Schwartzbaum and Gay, 1966).

Hyperreactivity to shock produced by septal lesions has been demonstrated by measuring the unconditioned response to shock presentation. Using movement of one inch in any direction as a response, Lubar et al. (1970) demonstrated that septal-lesioned rats respond more frequently to shock between .10 and .14 mA, although magnitude of response of

animals with septal lesions was comparable to that of controls. When uncued escape from 1.0 mA shock delivered through a grid floor requires two-way shuttling to an adjacent compartment, septal-lesioned animals respond with shorter latencies (Brown and Remley, 1971).

Destruction of the septum produces an increased reactivity to mild, novel stimuli such as light, indicated by a shorter latency to escape to an adjacent dark compartment (Donovick, 1968; Green, Beatty, and Schwartzbaum, 1967). A shorter escape latency from thermal and auditory stimuli has also been reported for animals with septal lesions (Brown and Remley, 1971).

Positive and negative taste solutions also elicit enhanced reactivity in septal-lesioned animals. Beatty and Schwartzbaum (1967) reported that when all available fluid was adulterated with quinine, fluid intake of septal-lesioned animals was significantly more depressed than that of controls over a period of days, whereas addition of saccharine differentially enhanced intake of rats with septal lesions. A dysfunction in food regulation cannot account for the enhanced intake of sucrose solution in lesioned animals since differential pre-loading does not abolish or interact with the lesion effect (Beatty and Schwartzbaum, 1968). Donovick et al. (1970) showed that

the quinine effect is the result of lesions of the posterior septum, while the saccharine effect can be produced by lesions of either the anterior or posterior septum.

Septal lesion-induced hyperreactivity to stimuli, particularly gustatory stimuli, suggests that effects on various schedules of reinforcement may be accounted for by an increased responsivity to reinforcement. Septal-lesioned animals consistently exhibit higher response rates on FI schedules of water reinforcement (Ellen and Powell, 1962; Harvey and Hunt, 1965), food reinforcement under deprived conditions (Ellen et al., 1977; Beatty and Schwartzbaum, 1968; Lorens and Kondo, 1969; Pubols, 1966; Schwartzbaum and Gay, 1966), and food reinforcement under nondeprived conditions (Beatty and Schwartzbaum, 1968). When the concentration of sucrose solution used to reinforce FI responding was manipulated, both septal-lesioned and control animals increased response rates at higher concentrations, with septal-lesioned animals exhibiting higher response rates than controls overall. However, lesioned animals did not exhibit a steeper rate-sucrose concentration function, indicating that hyperreactivity to positive gustatory stimuli cannot account for overresponding on FI schedules in septal-lesioned animals (Pubols, 1966).

DRL schedules of reinforcement have been used extensively to examine timing behavior of animals with septal

lesions. Septal-lesioned rats exhibit high rates of responding and a low level of reinforcement on DRL schedules (Ellen et al., 1964), although the deficit can be eliminated by provision of an exteroceptive cue to signal the end of the delay interval (Ellen and Butter, 1969), or by use of a gradual shaping method (Caplan and Stamm, 1967). Consistent with the notion of an increased responsivity to reinforcement, the DRL deficit in septal-lesioned mice is attenuated by cellulose-adulteration of food pellets; lesioned mice responding for cellulose pellets exhibited a decreased response rate and improved efficiency in obtaining reinforcements compared with their performance with standard pellets (Carlson et al., 1976).

DeNoble and Caplan (1977) have demonstrated that septal-lesioned animals are hyperreactive to response-independent food presentation. Responding immediately following the presentation of noncontingent food during a DRL schedule of reinforcement was accelerated in control animals, and this effect was exaggerated in animals with septal lesions. Response-independent food presentation during a conjunctive DRH-FR schedule, a schedule which generates a high rate of responding, caused a localized suppression of responding in control animals; this response suppression was greater in septal-lesioned rats.

The DeNoble and Caplan results suggest that septal

lesion-induced hyperreactivity to food reinforcement is not merely a heightened general activity. However, this experiment examined localized effects of noncontingent reinforcement; high overall response rates of septal-lesioned animals on operant schedules such as FI or DRL may reflect, at least partially, a heightened elicited activity.

General Method

Subjects. Male B6D2F_1/J hybrid mice from the Jackson Laboratory, Bar Harbor, Maine, served as subjects in these experiments. Animals were maintained on ad lib. water and Purina rat chow pellets except as noted. The mice were housed individually in a temperature-controlled room, with a 12:12 light-dark schedule, lights on at 0600 hr. All experimental sessions were conducted in the afternoon of the light period.

Apparatus. Testing took place in four identical operant chambers, each isolated in an insulated chest. The walls of the chambers were constructed of Plexiglas, with a stainless steel grid floor and a Plexiglas lid. Each chamber measured approximately 15 cm x 15 cm in its horizontal cross section, and 24 cm in height. Three round Plexiglas tubes, approximately 2 cm in diameter, protruded from one of the narrower chamber walls 2 cm above the grid

floor. The outer two tubes were plugged with a cylinder of aluminum. A photocell beam passed through the inner tube, such that a nose-poke into the response tube would break the beam. A Plexiglas plug in the outer end of the tube prevented the mice from leaving the box. The photocell lamp provided the sole source of illumination. Food pellets could be delivered directly into the tube via a plastic hose connected to a pellet dispenser. An on-line computer controlled the presentation of stimuli and collection of data.

Surgery. Animals that received lesions were anesthetized with sodium pentobarbital (75 mg/kg body weight) and secured in a Kopf stereotaxic apparatus equipped with a mouse head holder which obviates the use of ear pins (Slotnick, 1972). Flat-skull coordinates for bilateral septal lesions were: anterior, .7 mm; ventral, 1.5 mm; and lateral, ±.4 mm (relative to bregma). Current was passed through a Grass radio-frequency lesion maker insulated with enamel except for .5 to .75 mm at the tip.

For sham operations, holes were drilled in the skull at the same coordinates used for septal lesions, but the electrode was not lowered into position.

Animals were given at least eight days of post-operative recovery time prior to initiation of testing.

Histology. At the conclusion of each experiment, mice with septal lesions were anesthetized with sodium pentobarbital, perfused pericardially with at least 10 ml of .9% saline solution followed by at least 10 ml of 10% formalin in .9% saline. Brains were soaked in formalin/saline for a minimum of three days, and were soaked in 30% sucrose solution overnight before slicing. Frozen sections were taken at 40 μm, and appropriate sections containing the lesions were mounted on microscope slides and stained with cresylecht violet.

Histological examination revealed that extent and location of brain damage did not vary systematically between the individual experiments. Lesions typically destroyed most of the lateral septal nuclei, and most of the medial septal nuclei. The precommissural fornix was generally destroyed, and the columns of the fornix were damaged in approximately 20% of the subjects. The septo-fimbrial nuclei incurred slight damage in approximately 75% of the subjects, and the triangular nuclei were slightly damaged in 35% of the subjects. The vertical limbs of the diagonal band were generally spared, and extra-septal damage was slight. One animal in the lesioned group of Experiment 1 was found to be lacking a lesion; its data were excluded from all figures, graphs, and analyses.

Figure 1 illustrates the largest lesion and smallest

lesion of subjects in the study, at anterior, middle, and posterior levels.

Experiment 1

This study examined the behavior of septal-lesioned mice on an operant schedule in which the reinforced response required a period of relative inactivity, i.e., breaking the photocell beam across the tube for a specified period of time by keeping the head within the tube. Reward value was manipulated by adulteration of pellets with cellulose in order to test the hypothesis that septal-lesioned animals are hyperreactive to food reinforcement.

Method.

Subjects. Sixteen mice werved as subjects. Eight of the mice received septal lesions and four of the mice underwent sham operations.

Apparatus. The mice were trained in the chambers described in the general method section.

Procedure. On the third postoperative day animals were placed on a food deprivation regimen, receiving 2.5 g Purina pigeon chow checkers daily. This regimen was continued during testing, with mice receiving 2.5 g of chow in the home cage after the session. On the eleventh postopera-

tive day testing began in the operant chambers described above. All mice were tested daily for 15 minutes for a total of 24 days. Each animal was tested in the same chamber and at the same time of day throughout the experiment. The operant response consisted of a held nose-poke, and reinforcement (20 mg Noyes pellets, formula A, or diluted pellets consisting of 75% cellulose and 25% formula A) was dropped onto the bottom of the poke tube. On the first day of testing, animals received reinforcement for a held nose-poke of one-second duration; scheduled hold time was increased daily if the animal had received a minimum of 15 reinforcements on the previous day, according to the following schedule: 2, 4, 8, 12, 16, 20 seconds. If an animal had obtained fewer than 15 reinforcements, the previous day's schedule was maintained. Animals that attained the 20-second hold time were maintained on this schedule for the duration of the experiment. The design of the experiment was 2 x 2 factorial, Lesion group (with sham-operates and normals constituting a single control group) x Type of reinforcement.

Results. Since histological analysis revealed that one of the animals in the septal-standard group did not have a lesion, its data were not included in graphs or statistical analyses.

Figure 2 presents the average poke duration data of the four groups as a function of days. It can be seen that on the first day of testing, the average poke durations of lesioned animals were slightly longer than those of control animals. No difference was apparent on the second day, but thereafter all mice increased their mean poke durations, with control mice reaching and maintaining a longer duration than did the lesioned mice. The longest average poke duration, 10.9 seconds, was attained by control animals rewarded with standard (nondiluted) pellets; septal-lesioned animals rewarded with standard pellets attained only a 3.4-second poke duration. Control animals rewarded with standard pellets achieved a longer poke duration than did control animals rewarded with cellulose pellets, but this difference was not statistically significant (see below). Pellet dilution also did not affect the poke durations of animals with septal lesions.

A two-tailed *t*-test compared the average poke duration of sham-operated and unoperated mice, averaging across the last six days of the experiment. Since a significant difference was not found, the two control groups were combined into a single control group for the analysis of variance. Unweighted means analysis of variance was performed on the mean poke duration data, averaging across the last six days of the experiment. The analysis revealed a significant

Lesion effect, $F(1,11)=4.85$, $p<.05$, but no significant Type of reinforcement effect or Lesion x Type of reinforcement interaction.

The criterion poke duration, i.e., the poke duration required for reinforcement, increased across days for all animals. Control mice receiving standard pellets reached the maximum hold time of 20 seconds by the 16th trial, whereas septal-damaged mice receiving standard pellets had attained only an 18.7-second average scheduled hold time by the end of the experiment. Animals receiving cellulose-diluted pellets as reinforcement increased their scheduled hold time more slowly than did their counterparts receiving standard reinforcements.

Since number of pokes made during sessions is contaminated by unequal poke durations, a poke frequency measure was devised as follows: total number of pokes per session/(session length - hold time). Hold time signifies the amount of time during the session that the animal held its head within the poke tube.

Figure 2 presents the poke frequency of the groups throughout the 24 days of the experiment. Poke frequency of control animals was consistently lower than that of the septal-lesioned groups with the exception of the first session, during which all animals emitted approximately the same number of pokes. For mice with septal lesions, poke

frequency per session increased rapidly across the first six experimental sessions and thereafter gradually decreased. Poke frequency of control mice also reached a peak early in the experiment, but their maximum level of poking was much lower than that of the lesioned animals.

A two-tailed *t*-test averaging across the last six days revealed that sham-operated animals and unoperated animals did not differ on poke frequency; the two groups were therefore combined to form a single control group in the analysis of variance. An unweighted means analysis of variance, averaging across the last six experimental trials, was conducted for poke frequency. Lesion produced a significant effect, $F(1,11)=5.47$, $p<.05$, but the factor of Type of reinforcement was not significant and there was no significant interaction of Lesion and Type of reinforcement.

Discussion. Although cellulose-diluted pellets impaired the performance of both septal-lesioned and control mice relative to standard pellets (see Figure 2), this effect was not statistically significant, and there was no significant interaction of Type of reinforcement and Lesion. The theory of an enhanced appetitive value of food reinforcement in animals with septal lesions, therefore, was not assessed by this experiment; the prediction that Type of reinforcement would affect the performance of lesioned mice

more than that of controls was not upheld.

The results of Experiment 1 indicate that septal-lesioned mice are deficient in the acquisition of a task in which the operant response is a held nose-poke. By the third experimental session and for the remainder of the experiment, the average poke duration of lesioned animals was considerably shorter than that of controls. Mice with septal lesions increased their criterion poke duration more slowly than controls; whereas control animals receiving standard pellets as reinforcements attained the 20-second maximum scheduled hold time by the 16^{th} session, lesioned animals had achieved only an 18.7-second scheduled hold time by the end of 24 sessions. With the exception of the first experimental session, mice with septal lesions had a higher poke frequency than control mice throughout the course of the experiment; both groups' levels of nose-poking increased across the first few sessions and declined thereafter.

Interpretation of these findings is included in the discussion section of Experiment 2.

Experiment 2

In order to further evaluate the reliability of the results of Experiment 1, a second experiment was conducted using only standard 20 mg Noyes pellets as reinforcements.

Method.

Subjects. Twelve mice served as subjects; six of the mice received septal lesions and three of the mice underwent sham operations.

Apparatus. The apparatus used was described in the general method section.

Procedure. Procedure was identical to Experiment 1, except that only standard pellets were used as reinforcements.

Results. Two-tailed *t*-tests averaging across the last six days revealed no differences resulting from sham operations for either of the two measures: average poke duration and poke frequency. The two control groups were thus combined to form a single control group for graphs and analyses of data.

The results of Experiment 2 confirm the results of Experiment 1 with regard to the effect of septal lesions on performance of a task requiring a held nose-poke. Figure 3 presents the average poke durations of groups as a function of days. Control animals initially increased their poking durations at a faster rate than did animals with septal lesions, achieving a 10.8-second poking duration by day 17 which declined somewhat thereafter. Septal-lesioned mice

reached only a 4.0-second duration by day 18 which also dropped slightly for the remainder of the experiment.

Control animals reached and maintained the 20-second maximum criterion duration by the 18th day. The longest scheduled duration for septal-lesioned mice was 17.3 seconds which was first achieved on the 19th day.

A two-way (lesion x days) analysis of variance for average poke duration was performed. Both main effects were significant: lesion, $F(1,10)=39.6$, $p < .001$; and sessions, $F(23,230)=20.5$, $p < .001$. The Lesion x Sessions interaction was also significant at the .001 confidence interval, $F(23,230)=4.9$. A two-tailed *t*-test was used to compare mean poke duration of lesioned mice with that of control mice during the final few sessions. A lesion effect was found for this measure, $p < .001$, averaging across the last six days of the experiment.

With respect to poke frequency, lesioned animals displayed a higher frequency than control animals throughout the experiment, as indicated in Figure 3. Highest poke frequencies occurred within several days for both groups, and decreased thereafter, although never reaching original levels (day 1).

A two-way (lesion x sessions) analysis of variance for poke frequency revealed a significant lesion effect, $F(1,10)=8.18$, $p < .025$, a sessions effect which verged on signifi-

cance, $F(23,230)=1.56$, $p < .10$, and no significant interaction of lesion and sessions.

Discussion. In this experiment, as in Experiment 1, septal-lesioned mice displayed a deficit in maintaining a nose-poke for standard reinforcement. The average nose poke duration of septal-lesioned mice was shorter than that of control mice by the end of training, and lesioned mice attained a shorter criterion duration than did control animals. Both groups increased their levels of nose-poking during the early sessions and decreased through the remaining sessions, but septal-lesioned mice exhibited higher levels of nose-poking than controls throughout the 24 sessions.

A response perseveration interpretation of the data from Experiments 1 and 2 is plausible since the scheduled hold time was one second on the first day and was gradually lengthened at a rate which depended on the animal's performance. An increased tendency on the part of septal-lesioned animals to emit a previously reinforced response (i.e., a nose-poke of short duration) could account for their poor performance as training progressed.

It is also possible that a lesion-produced increase in generalized activity may have interfered with lesioned animals' ability to maintain the nose-poke, an interpretation which is suggested by the higher poke frequencies. Animals

with septal lesions may exhibit higher operant levels of nose-poking and/or shorter poke durations, or such effects may have resulted from the food deprivation regimen or non-contingent food presentation.

Experiment 3

In Experiments 1 and 2, lesioned animals exhibited poor performance of a task requiring a held nose-poke. In Experiment 3, animals were tested on a DRO schedule (differential-reinforcement-of-other behaviors) using the nose-poke operant.

Atnip (1975) investigated the DRO performance of rats after they had been trained to bar-press on a VI 30 schedule. It was found that septal-lesioned rats required a greater number of sessions to suppress responding as well as controls, taking the higher VI rates of septal-lesioned animals into account. However, it is possible that in Atnip's study the initial VI training resulted in response perseveration, so that DRO performance of lesioned animals was impaired more than that of control animals.

In Experiment 3, animals received no pre-training prior to the initiation of the DRO schedule in order to eliminate the confounding factor of response perseveration. This procedure was made possible by a sufficiently high operant level of nose-poking and spatial closeness of the

reinforcement.

Method.

Subjects. Twelve mice served as subjects; three mice underwent sham operations and six mice received septal lesions.

Apparatus. Apparatus was described in the general method section.

Procedure. On the third postoperative day, animals were placed on a 24-hour food deprivation schedule, receiving 2.5 g Purina chow daily. Beginning on the eighth postoperative day, mice were tested for 15 minutes on a DRO 20-second schedule, with standard 20 mg Noyes pellets delivered within the poke-tube. Animals were tested daily at the same time of day for a total of 24 days, and were fed 2.5 g Purina chow after each session. Dependent measures were average waiting time (time elapsed between pokes), number of pokes, and % efficiency (# reinforcements/# responses x 100).

Results. For the three dependent measures--average waiting time, number of pokes, and % efficiency--*t*-tests, averaging across the last six days, revealed no significant differences between sham-operated animals and normal ani-

mals. These two groups were therefore combined to form a single control group for graphs and data analysis.

Figure 4 displays the average waiting time data (time elapsed between pokes) of septal-lesioned mice and control mice as a function of days. An average waiting time of approximately 15 seconds was attained by both groups of animals, although control mice required fewer trials to reach this level. On the first day of testing, control animals exhibited a long average waiting time which dropped rapidly on the second day and rose steadily to asymptote. The average waiting time of septal-lesioned mice was generally much shorter than that of controls; over the course of the experiment, lesioned animals' waiting time also dropped slightly across the first few days and then rose slowly to their peak levels.

An analysis of variance indicated that lesion produced a statistically significant effect, $F(1,10)=10.7$, $p<.01$, performance varied across days, $F(24,240)=27.1$, $p<.001$, and lesion interacted with sessions, $F(24,240)=4.5$, $p<.001$. A *t*-test comparing average waiting time for control mice with that of septal-lesioned mice averaged across the last six days of the experiment revealed no statistically significant difference between the two groups.

With the exception of the last week of the experiment, septal-lesioned animals made more responses (nose-pokes)

than did control animals (see Figure 4). Both groups increased poking during the first few trials and then steadily decreased poking levels, reaching asymptote of approximately 60 pokes per 15-minute session. Control animals reached this low level of poking within 11 days of running, whereas lesioned animals required 19 days to attain this level.

A two-way (lesion x sessions) analysis of variance produced the following significant results: a main effect for lesion, $F(1,10)=15.1$, $p<.005$; a main effect for sessions, $F(24,240)=24.0$, $p<.001$; and a lesion x sessions interaction, $F(24,240)=7.0$, $p<.001$. A *t*-test averaging across the last six days of the experiment revealed that the level of poking of septal-lesioned animals did not differ significantly from that of controls by the end of the experiment.

Percent efficiency (# reinforcements/# responses x 100) of control mice was higher than that of septal-lesioned mice during the first 18 days of the experiment, as revealed by Figure 4. On the first day, control animals exhibited high efficiency which dropped on the second day and then rose steadily, reaching its highest level by about the 17^{th} day. Septal-lesioned animals improved their efficiency more slowly, reaching asymptote by the 19^{th} day.

An analysis of variance was run on the percent effi-

ciency data. The lesion effect approached but did not reach statistical significance ($p < .10$); a main effect was found for sessions, $F(24,240)=25.1$, $p < .001$, and lesion x sessions produced a significant interaction, $F(24,240)=2.7$, $p < .001$. A *t*-test compared percent efficiency across the last six days of the experiment; animals with septal lesions did not differ significantly from controls.

Discussion. Results of this experiment do not confirm the hypothesis of a septal-lesion-induced hyperresponsivity to reinforcement. During the first 18 days of testing on a DRO 20-second schedule, the performance of mice with septal lesions was inferior to that of control mice, with lesioned animals displaying shorter average waiting times, a greater number of pokes, and impaired efficiency (% #reinforcements/# responses). Final performance of lesioned animals did not differ significantly from that of control animals.

The deficient acquisition of septal-lesioned mice cannot be accounted for by response perseveration, since the DRO schedule was instituted at the beginning of the first experimental session to experimentally-naive animals. Another explanation of performance differences--elicitation effects of food presentation--seems plausible. In Experiments 1 and 2, lesioned mice displayed high levels of

poking relative to control mice despite the fact that duration of poking was rewarded rather than number of pokes. In Experiment 3, lesioned animals were unable to refrain from poking even though a period of non-reinforcement followed every poke. These experiments suggest that lesioned animals are predisposed to emit a higher number of nose-pokes, an effect which may or may not require food deprivation and/or food presentation. Elicitation effects on nose-poking behavior of septal-lesioned mice will be examined in Experiment 4.

Experiment 4

Inferior performance of septal-lesioned mice in Experiments 1, 2, and 3 could reflect specific differences in operant level of the nose-poking response or durations of pokes, or a generalized activational effect of the lesion. Such effects could also have been elicited by food deprivation and/or noncontingent food presentation.

Data obtained from a number of experiments indicate that septal lesions produce operant levels of nose-poking that differ from those of control animals. During a single non-reinforced 40-minute session, water-deprived septal-lesioned rats exhibited higher operant levels of nose-poking (Schnelle et al., 1971). Capobianco (1977), using a single 30-minute session of nose-poking as a measure of

exploration, found that septal-lesioned animals did not differ from control animals in terms of number of pokes; however, lesioned animals spent less time poking, indicating that the average nose-poke, when nondeprived and with no reinforcement available, was shorter in lesioned animals than in control animals. Feigley and Hamilton (1971) examined the effects of medial septal lesions on both nose-poking responses and response durations. Under constant conditions, septal-lesioned animals had higher response rates and shorter response durations than control animals. Introduction of a condition in which responding produced light onset at the end of the poke tube increased the response rates of lesioned animals more than that of controls, and whereas the light stimulus increased the poking duration of control animals, poking duration of septal-lesioned animals was not affected.

In addition to operant level of nose-poking, the effects of the food deprivation regimen and noncontingent food presentation on this measure are relevant to the interpretation of Experiments 1, 2, and 3. Such manipulations have not been applied to the nose-poking response of animals with septal damage. With respect to the bar-pressing operant, septal-lesioned animals' rates of responding did not differ from those of control animals when food was delivered noncontingently on a VT 60 schedule (Ellen et al.,

1977). In Experiment 4, the effect of food deprivation and noncontingent food presentation on nose-poke behavior of septal-lesioned animals are investigated, and compared with reinforced nose-poking.

In order to determine whether the proposed elicitation effects are specific to poking behavior, locomotor activity was also measured. Activity of septal-lesioned animals during short daily sessions in a small enclosure has not been investigated. Data from open-field tests suggest that familiarity with the test apparatus is a relevant variable; rats with septal damage show increased open-field activity when their first exposure to the apparatus is postoperative (Donovick and Wakeman, 1969), but are hypoactive if they undergo preoperative testing (Schwartzbaum and Gay, 1966; Corman et al., 1967). Similarly, Douglas and Raphelson (1966) reported that enhanced exploratory activity of septal-lesioned animals occurred only on the first trial. Gotsick (1969) found that lesioned animals showed habituation of exploratory activity both across days and within sessions, whereas control animals' activity remained relatively constant, when tested for one hour daily in 24" cages with activity measured by breaking photocell beams.

The effects of food deprivation and noncontingent food presentation on exploratory activity of septal-lesioned rats

have been investigated. Gotsick (1969) compared the activity of septal-lesioned animals after 48 hours of food deprivation with activity when nondeprived. Septal-lesioned animals displayed greater activity levels during initial nondeprived sessions, but activity dropped well below control levels after several daily sessions. Absolute activity levels of septal-lesioned rats after 48 hours of food deprivation were lower than control levels; however, relative to activity levels when nondeprived, septal-lesioned animals showed a greater increase after food deprivation than did controls.

Anderson (1970) showed that exploratory activity of animals with septal lesions was increased more than controls over the entire session when food was presented noncontingently in various areas of the chamber. When tested under 0-hour deprivation conditions rather than after 22-hour deprivation, no differences in activity were found, suggesting that hunger as well as food presentation is necessary for the enhanced activity of septal-lesioned animals. However, since the food was dropped onto various areas of the photocell cage floor in Anderson's study, it could be argued that increases in activity reflected a search for food. In Experiment 4, food was presented in the same location, so that generalized locomotor activity, independent of searching for food, could be examined.

Experiment 4 also examined the effect of septal lesions on reinforced locomotor behavior.

Method.

Subjects. Sixteen mice served as subjects; eight of the mice received septal lesions.

Apparatus. The operant chambers were described in General Method. Locomotor activity was measured via contact-sensitive circuits wired to alternate bars of the chamber's grid floor.

Procedure. Animals were tested for a total of 71 consecutive days divided into six conditions, as described in Table 1.

Table 1

The Six Conditions of Experiment 4

Condition	Description	Number of Sessions
1	nondeprived, no food available during testing	12
2	food-deprived, no food available during testing	13
3	food-deprived, noncontingent food delivered according to a VT 60-second schedule	11
4	food-deprived, VI 60-second nose-poke schedule	13
5	food-deprived, no food available during testing (extinction)	10
6	food-deprived, VI 60-second locomotion schedule	12

Each condition was maintained until individual performance was judged to have stabilized and a minimum of 10 days had elapsed. Testing sessions were 20 minutes in length and were conducted at the same time of day. Food was available ad lib. in the home cages until the first day of the second condition. Condition 1 began on the eighth postoperative day. During condition 1, operant levels of nose-poking, poke durations, and locomotor activity were tested. Throughout condition 2 and for the remainder of the experi-

ment, mice were maintained on a 22-hour food deprivation schedule, receiving 2.5 g Purina pigeon chow checkers after each daily session. During the third condition, mice received 20 mg Noyes pellets, formula A, on a VT 60-second schedule, delivered within the poke tube. The fourth condition consisted of a VI 60-second schedule, with reinforcement contingent on the operant of breaking the photocell beam (a nose-poke). During condition 5, no food was presented (extinction), and during condition 6 food reinforcement was contingent on locomotor behavior on a VI 60-second schedule. Three dependent measures were recorded throughout all 6 conditions: average poke duration per session, number of pokes, and locomotion.

Results. For each of the three dependent measures, three types of analyses were performed. To examine the immediate effects of transition to the next condition, the average of the first three days of a condition were subtracted from the average of the last three days of the preceding condition for each animal, to yield five transitions as the within factor for the analysis. The more lasting effects of each condition were assessed by subtracting the average of the last three days of a condition from the average of the last three days of the preceding condition, again yielding five transitions for the analysis.

In the third analysis of variance, the average of the last three days of each of the six conditions yielded the within factor. Lesion effects within each condition were then assessed with a t-test, using an error term which pools between variance and within variance (Winer, 1971).

Average poke duration. A two-factor mixed design analysis of variance for the immediate effects of transition on average poke duration yielded a significant Lesion effect, $F(1,14)=13.94$, $p < .005$, and a significant Transition effect, $F(4,56)=5.74$, $p < .001$, but no Lesion x Transition interaction. Simple main effects of Lesion were examined within each of the five transitions for immediate effects, using a pooled error term. Only the first transition, i.e., initiation of food deprivation, produced a significant effect of Lesion, $F(1,70)=8.62$, $p < .005$.

Analysis of variance for lasting effects of transition on mean poke duration revealed a significant effect only for the Transition factor, $F(4,56)=6.57$, $p < .001$.

A 2 x 6 analysis of variance with repeated measures for average poke duration revealed a Lesion effect, $F(1,14)=22.4$, $p < .001$, and a Conditions effect, $F(5,70)=12.2$, $p < .001$, but no Lesion x Conditions interaction. Simple main effects of lesion were found with condition 3 (VT 60) and condition 6 (VI 60 locomotion).

Number of pokes. A mixed-design analysis of variance for the immediate effects of transition on number of pokes revealed significant effects for Lesion, $F(1,14)=9.13$, $p < .01$, Transition, $F(4,56)=105.1$, $p < .001$, and Lesion x Transition, $F(4,56)=41.02$, $p < .001$.

Immediate main effects of Lesion on number of pokes were found for transition 2 (food deprivation to VT 60), $F(1,70)=21.23$, $p < .001$, for transition 3 (VT 60 to VI 60 nose-poke), $F(1,70)= 57.64$, $p < .001$, for transition 4 (VI 60 nose-poke to extinction), $F(1,70)=111.05$, $p < .001$, and for transition 5 (extinction to VI 60 locomotion), $F(1,70)= 5.02$, $p < .05$.

Analysis for lasting effects of transition on number of pokes per session revealed a significant Transition effect, $F(4,56)=174.85$, $p < .001$, and a significant Lesion x Transition effect, $F(4,56)=64.69$, $p < .001$, but no significant main effect of Lesion. Analysis of lasting simple main effects of Lesion within Transition for number of pokes yielded significant results for transition 3 (VT 60 to VI 60 nose-poke), $F(1,70)=150.38$, $p < .001$, and for transition 4, (VI 60 nose-poke to extinction), $F(1,70)=167.08$, $p < .001$.

Analysis of variance with repeated measures (2 x 6) for poking revealed significant effects as follows: a Le-

sion effect, $F(1,14)=64.6$, $p < .001$, a Conditions effect, $F(5,70)=148.4$, $p < .001$, and a Lesion x Conditions interaction, $F(5,70)=54.7$, $p < .001$. Examination of lesion effects within conditions revealed significance only for condition 4 (VI 60 nose-poke).

Locomotion. Two-factor analysis for immediate effects of transition on locomotion yielded a significant effect of Transition, $F(4,56)=12.32$, $p < .001$, and a tendency toward significance of Transition x Lesion, $F(4,56)=2.23$, $p < .10$, but no significant effect of Lesion. Analysis of immediate effects of Lesion within each transition yielded significance for only transition 3 (VT 60 to VI 60 nose-poke), $F(1,70)=6.92$, $p < .025$.

Analysis of variance for lasting effects of transition on locomotor behavior yielded a significant effect of Transition, $F(4,56)=17.52$, $p < .001$, and a significant interaction of Transition and Lesion, $F(4,56)=2.91$, $p < .05$, but no significant effect of Lesion. Only transition 3 (VT 60 to VI 60 nose-poke) contained a significant lasting effect of Lesion, $F(1,70)=9.66$, $p < .001$, for locomotion.

Analysis of variance for locomotor behavior with conditions as the within factor yielded significance for Conditions, $F(5,70)=54.7$, $p < .001$, but not for Lesion. A Lesion x Conditions interaction was found, $F(5,70)=4.4$,

$p < .001$, but a t-test revealed no significant effects of lesion within any of the six conditions.

Discussion. Figure 5 presents the average poke duration data of groups as a function of days. In general, septal-lesioned mice exhibited somewhat shorter poke durations than control mice over the six conditions of Experiment 4. The last three days of operant levels of average poke duration did not differ significantly for lesioned and control mice, nor did they differ during food deprivation. However, when food-deprived and presented with food noncontingently, septal-lesioned mice displayed significantly shorter poke durations than control mice. This result is pertinent to the interpretation of Experiments 1 and 2; lesioned mice may have been deficient in maintaining long poke durations for reinforcement because the presentation of food elicited a nose-poke of shorter duration.

At the end of the VI 60 nose-poke condition and the extinction condition, lesioned animals' nose-poke durations did not differ significantly from those of controls. Poke durations of lesioned mice were significantly shorter than those of control mice at the end of the VI 60 locomotion condition.

Differential immediate effects of transition to a new condition on mean poke duration were apparent only when

food deprivation (condition 2) was commenced; whereas control animals increased their poking durations, lesioned animals' durations were essentially unaffected. This lengthened poking duration of control animals was not maintained through the condition.

Number of pokes for the two groups as a function of days is presented in Figure . Although lesioned animals exhibited a higher level of poking throughout the entire course of this experiment, only condition 4 (VI 60 nose-poke) produced a statistically significant Lesion effect. However, lesioned animals seemed to be more sensitive to the conditions of the experiment; differential immediate effects of Transition were found for the implementation of condition 3 (VT 60), condition 4 (VI 60 nose-poke), condition 5 (extinction), and condition 6 (VI 60 locomotion). Lasting effects of Lesion on transition to a new condition were found for condition 4 (VI 60 nose-poke) and condition 5 (extinction).

In general, septal animals' locomotor behavior remained either at or below control levels throughout the experiment (see Figure). Within conditions, none of the comparisons between lesioned animals' activity and activity of control animals yielded significant results. Transitions to new conditions produced few differential effects: only the change from VT 60 to VI 60 nose-poking produced an

effect for Lesion, with septal-damaged animals showing both an immediate and lasting decrease in locomotor activity.

To summarize, Experiment 4 examined the effect of septal lesions on poking behavior and locomotor activity under six consecutive experimental conditions. It is clear that septal lesions in mice result in the emission of pokes of shorter average durations under certain stimulus conditions, i.e., during noncontingent food presentation and when intermittently reinforced for locomotor behavior.

The design of the experiment permitted examination of sensitivity to alteration of experimental conditions. Of the three dependent measures, poking was most differentially susceptible to the changing of conditions, with lesioned animals showing an immediate differential effect for every transition except initiation of food deprivation. Changing of experimental conditions generally produced no differential effect of lesion on poke duration and locomotor activity.

General Discussion

In Experiments 1 and 2, mice with septal lesions were deficient in the performance of a task requiring a held nose-poke, displaying shorter average poke durations and a higher level of poking than control animals. Since pellet

dilution in Experiment 1 did not yield a statistically significant effect on performance measures and did not interact with lesion, the hypothesis that septal lesions enhance the reinforcing properties of food could not be assessed.

The literature on nose-poking behavior suggests that septal lesions may produce shorter poke durations (Capobianco, 1977). During testing of operant level in Experiment 4, the lesion effect did not approach statistical significance. A food deprivation regimen produced little difference from operant level of nose-poking behavior, but noncontingent food presentation gave rise to significantly shorter poke durations. It is therefore possible that the deficient performance of septal-lesioned animals in Experiments 1 and 2 may reflect elicitation effects of food reward.

Experiment 3 revealed that septal lesions also produce inferior performance on a DRO 20 schedule, using the nose-poke operant response. During the first 18 days of testing on this schedule, animals with septal lesions received fewer reinforcements than control mice and displayed a higher level of poking and a reduced waiting time. Lesioned animals gradually improved their performance, so that during the final experimental sessions no lesion effects were apparent.

This deficit in acquisition of a DRO 20 schedule by septal-lesioned animals cannot be explained by elicitation effects. In Experiment 4, noncontingent food presentation did not elicit a significantly greater level of poking in lesioned animals, and operant levels under deprived and nondeprived conditions also did not differ from those of controls. These results contradict the findings of previous investigations, in which septal lesions produced higher levels of nose-poking (Feigley and Hamilton, 1971; Schnelle et al., 1971). A response perseveration interpretation of the DRO data can also be ruled out since animals received no pre-training.

Throughout Experiments 1, 2, and 3, control mice obtained a slightly higher number of reinforcements than septal-lesioned mice; it is thus possible that the superior performance of control animals on these schedules may reflect a positive feedback process. At the end of the final session of each experiment, the lesioned group had obtained a total number of reinforcements which control animals had obtained earlier. When performance was compared at these two points, lesion differences remained, suggesting that differences in reinforcement density probably cannot account for the lesion effect. Replication of these experiments with a procedure whereby sessions are terminated when a given number of reinforcements has been obtained would

resolve this issue.

Earlier work has revealed that animals with septal lesions generally exhibit enhanced exploratory behavior upon first exposure to the testing apparatus, but are thereafter hypoactive (Donovick and Wakeman, 1969; Douglas and Raphelson, 1966). In Experiment 4, lesioned animals showed slightly less locomotor activity during all the trials of condition 1. Apparatus differences (e.g., the small size of chamber) and/or procedural differences may account for this result. Whereas Gotsick (1969) found that 48-hour food deprivation increased the activity of lesioned animals more than it increased that of control animals, Experiment 4 found no differential effect of food deprivation. Again, differences in apparatus or the food deprivation regimen may have produced this result. Anderson (1970) reported that exploratory activity of rats with septal lesions was increased more than that of control animals by the presentation of noncontingent food in various areas of the chamber. This effect was not confirmed by Experiment 4; no lasting or immediate effects of transition to the VT condition were found.

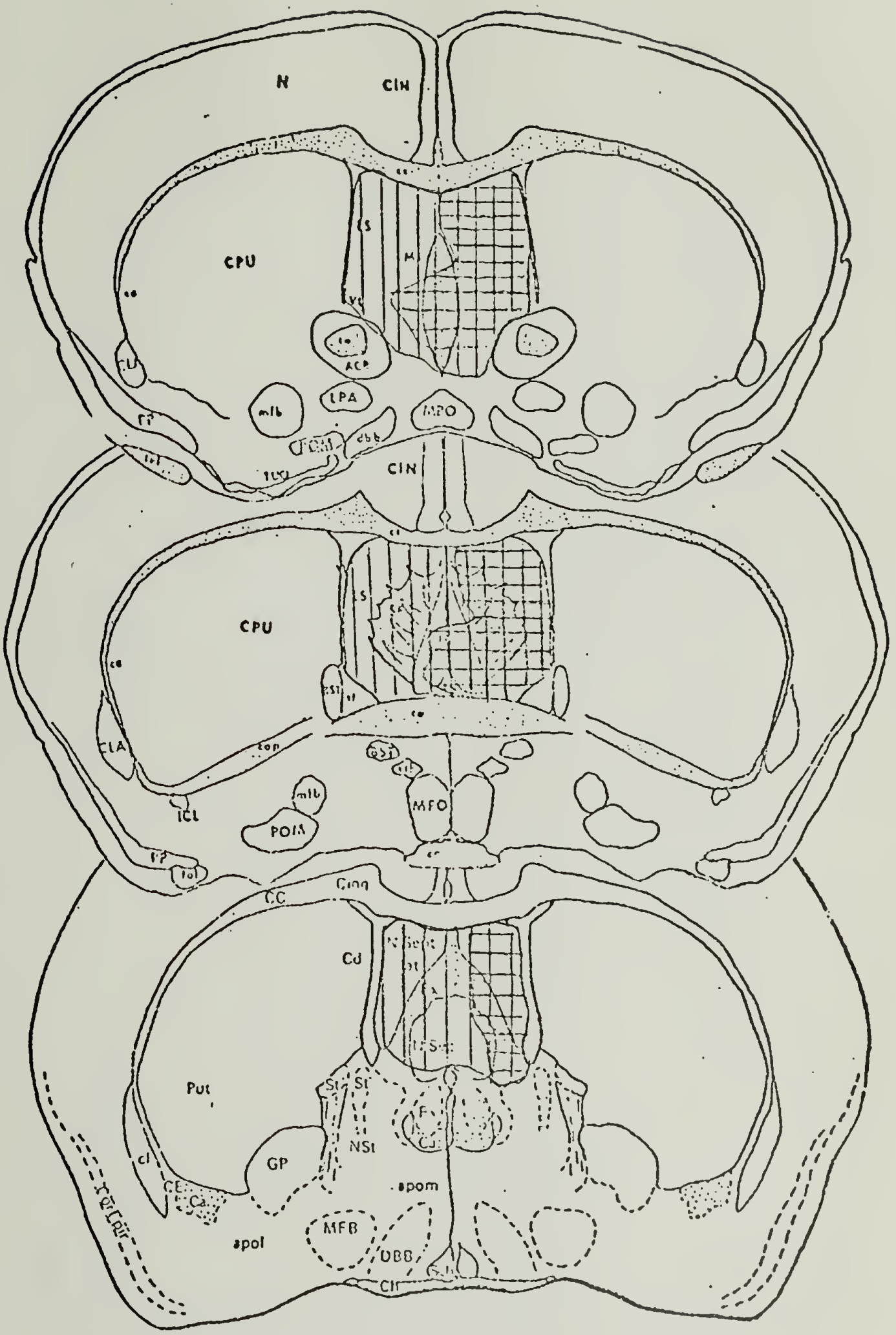


Figure 1. The largest lesion (vertical lines) and smallest lesion (horizontal lines) of subjects in the study at three anterior-posterior levels.

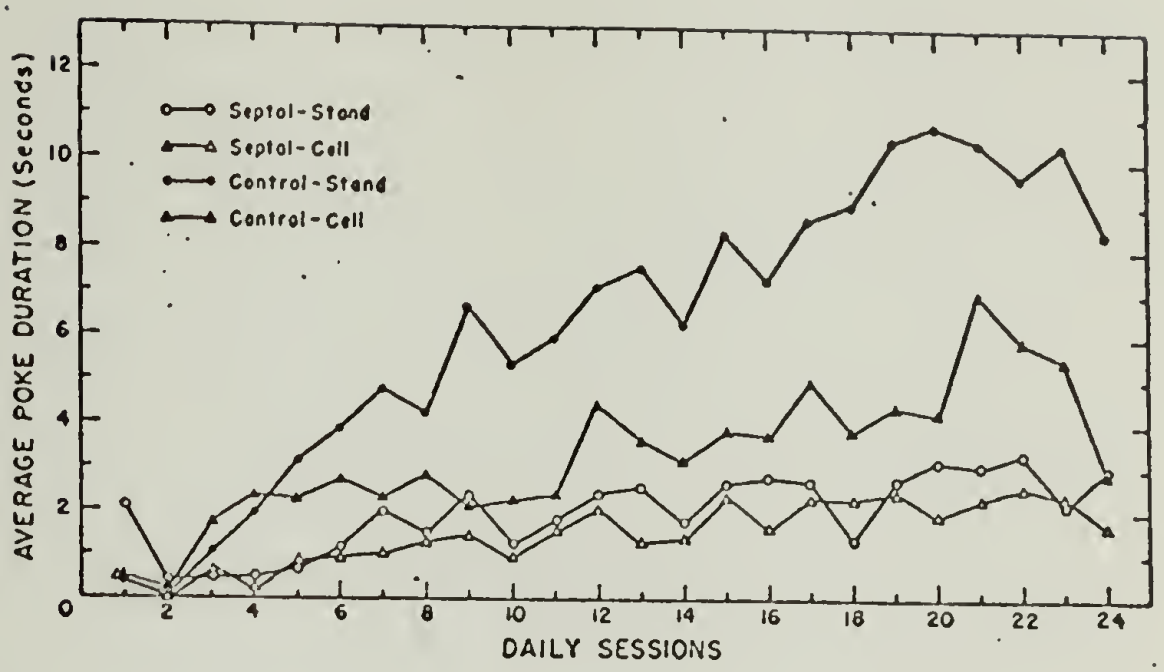
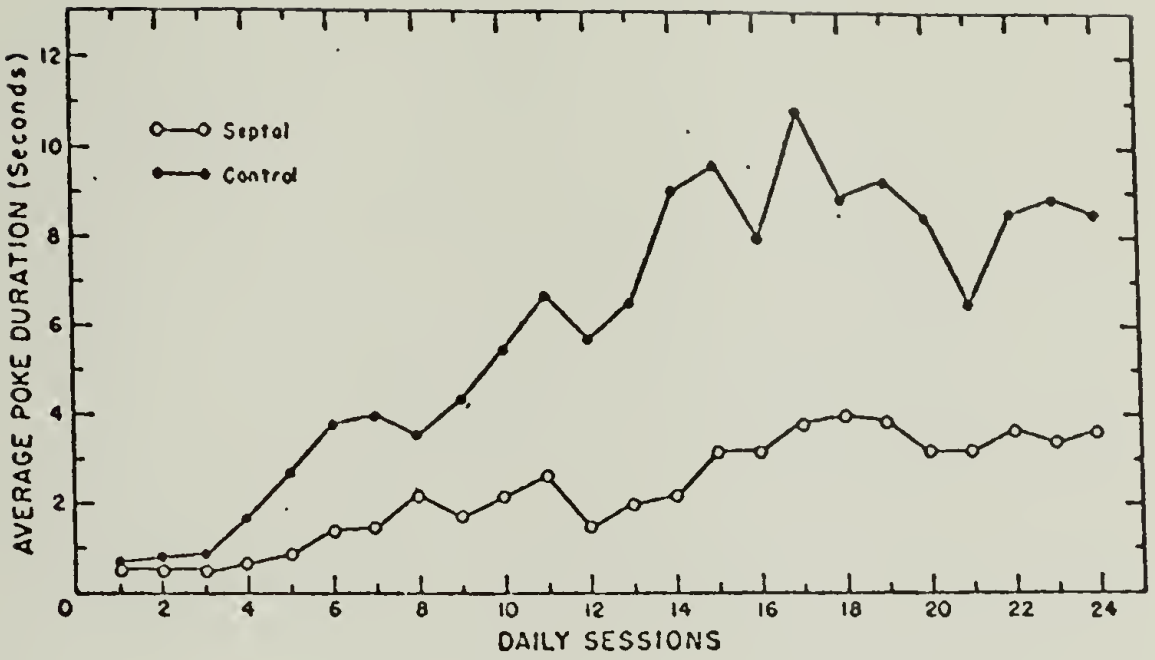


Figure 2. Average poke duration (top) and poke frequency (bottom) as a function of daily sessions for groups in Experiment 1.



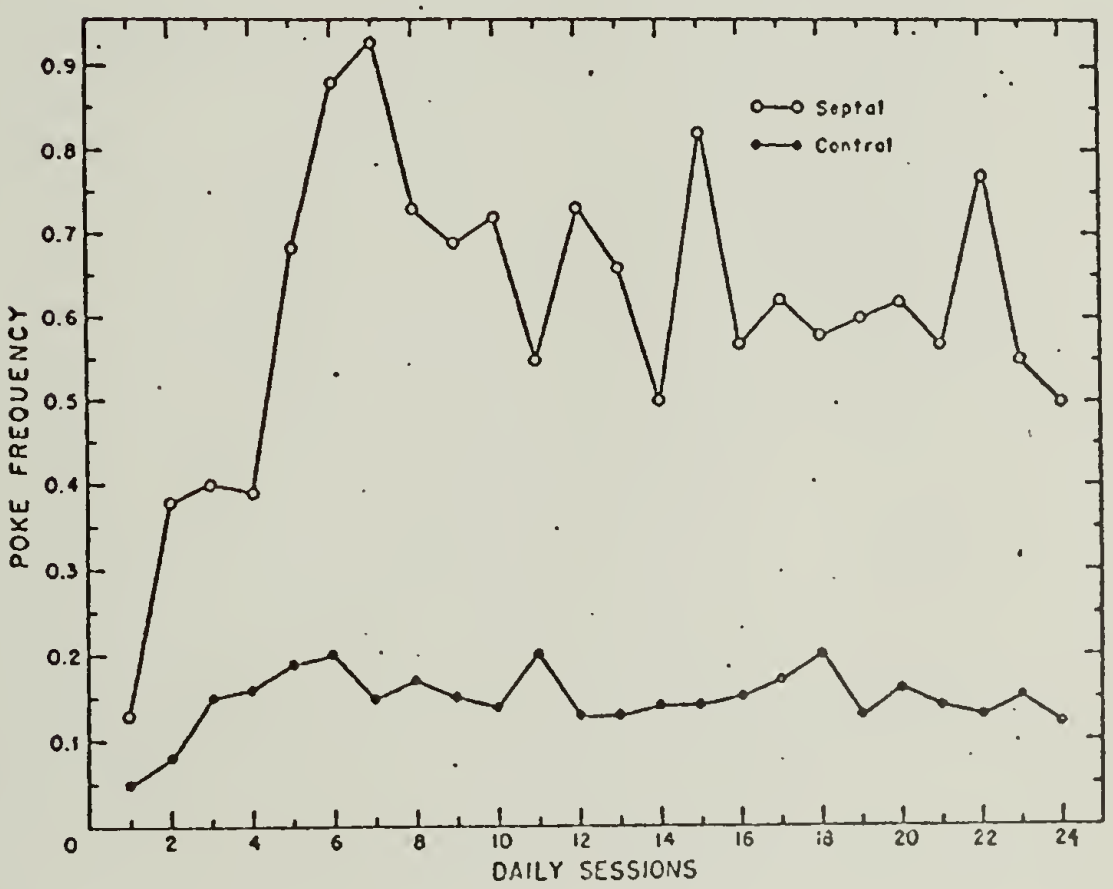


Figure 3. Average poke duration (top) and poke frequency (bottom) as a function of daily sessions for groups in Experiment 2.

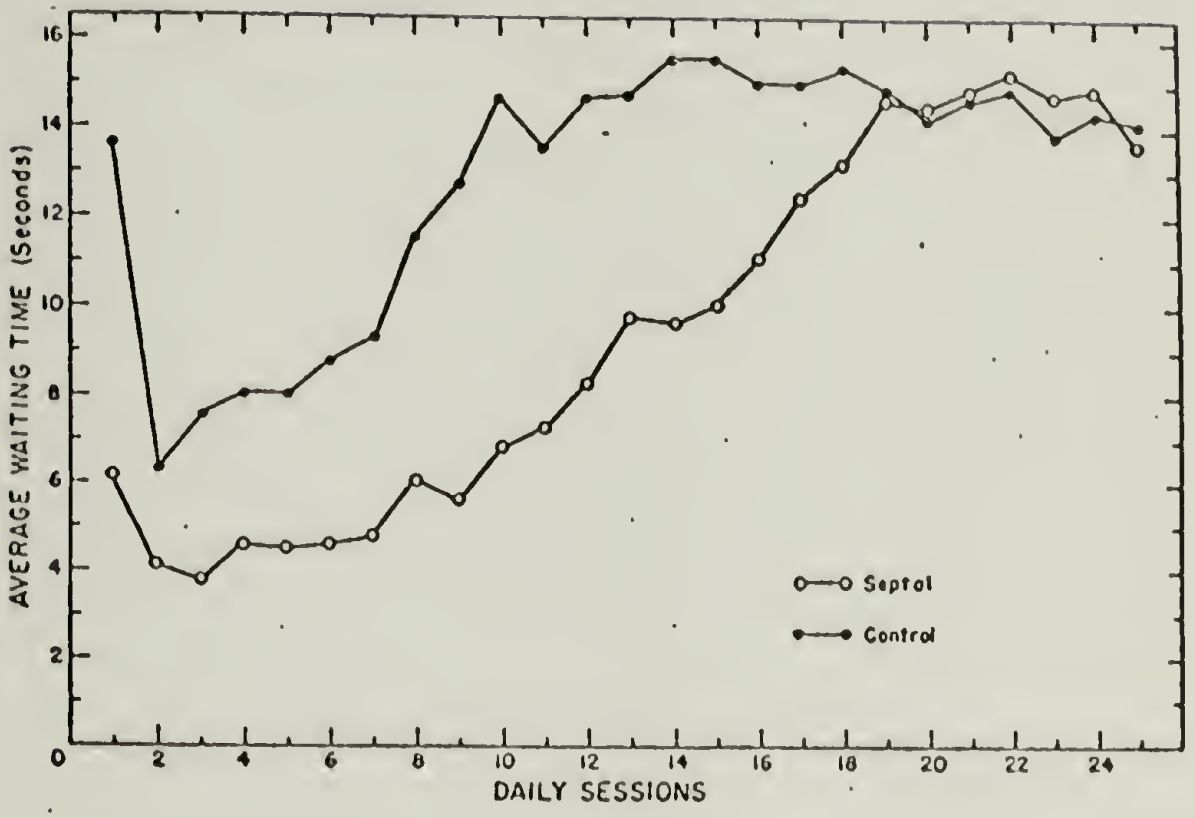
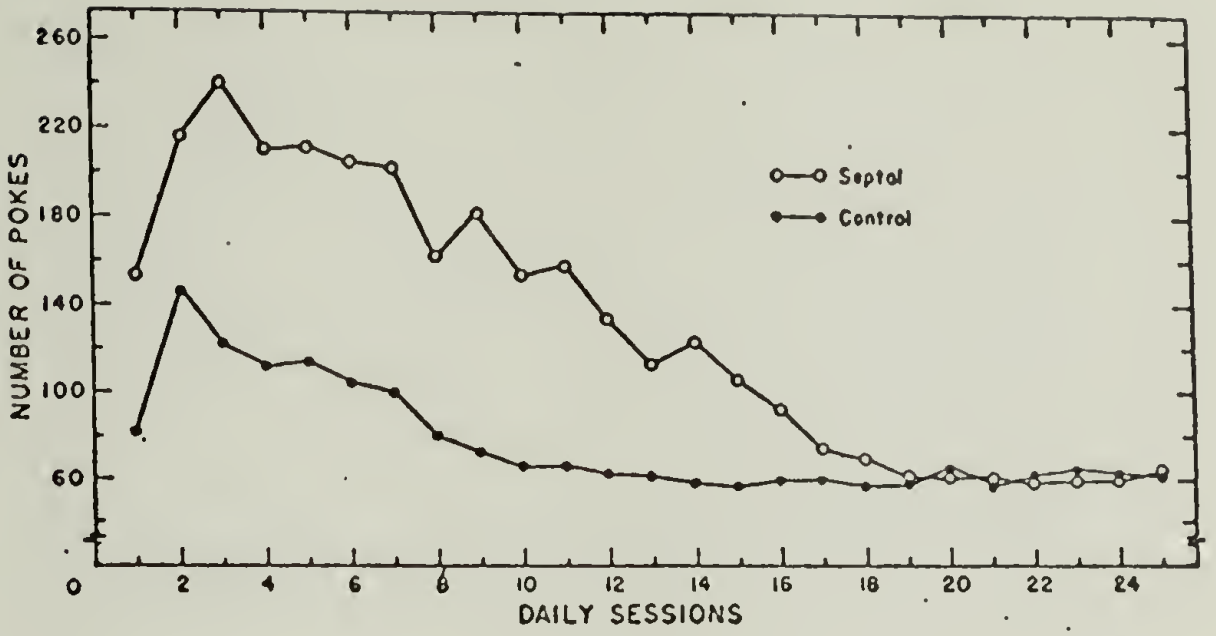


Figure 4. Average waiting time as a function of daily sessions for groups in Experiment 3.



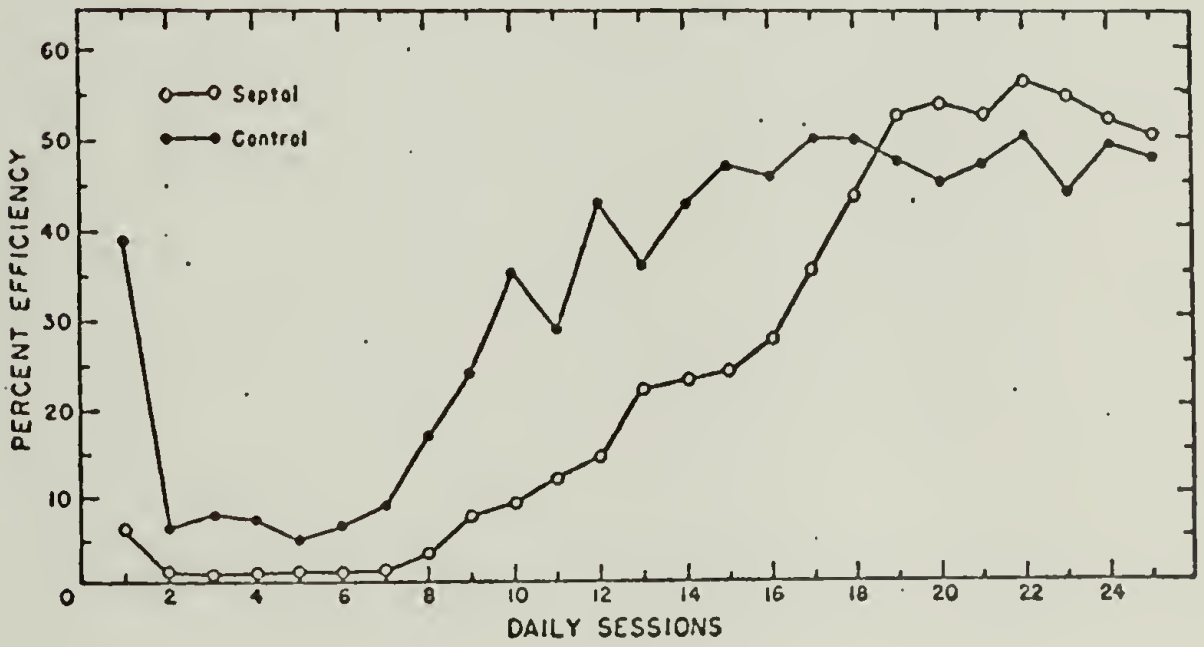
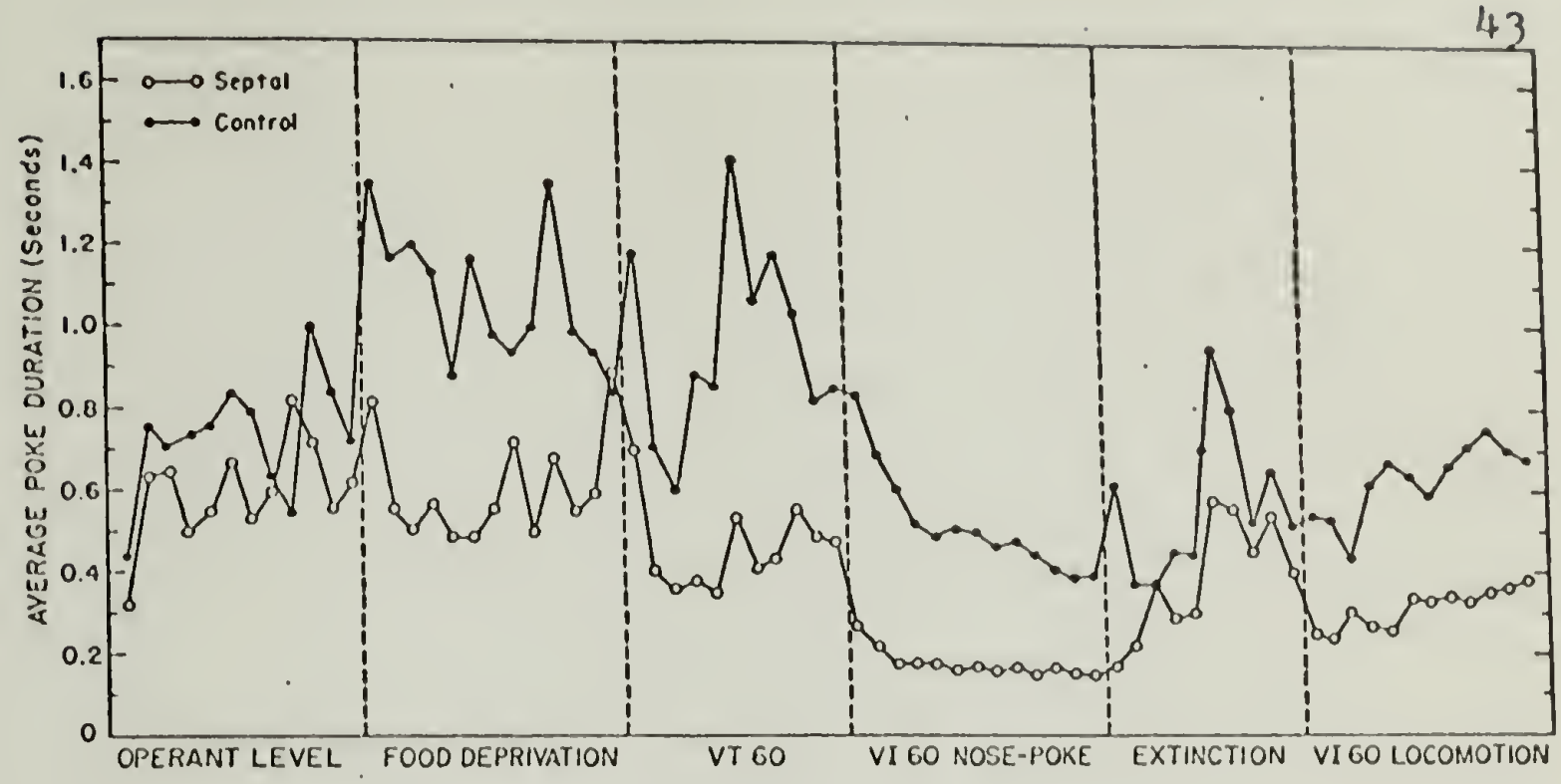


Figure 5. Number of pokes (top) and percent efficiency (bottom) as a function of days for groups in Experiment 3.



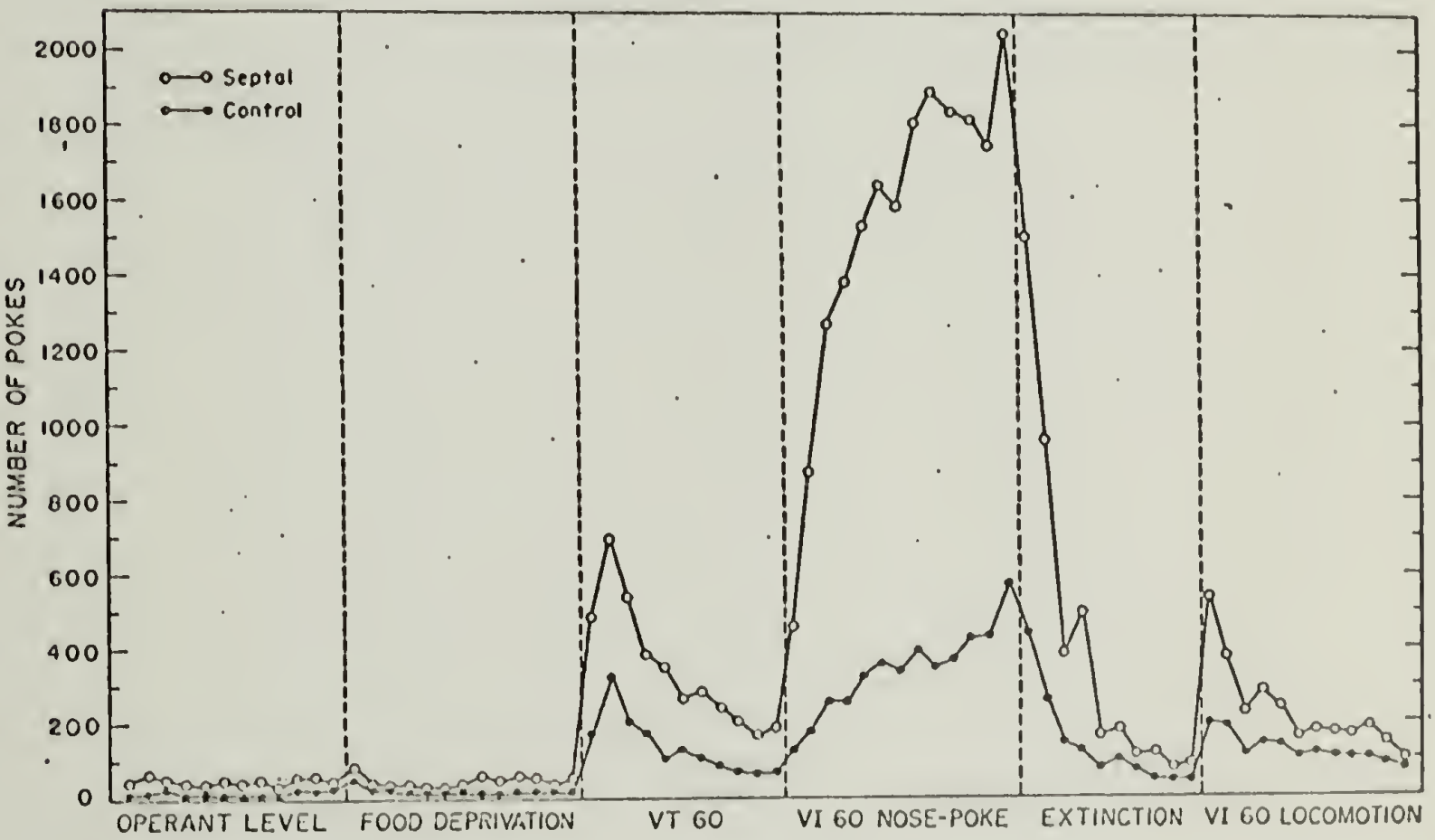


Figure 6. Average poke duration (top) and number of pokes (bottom) as a function of daily sessions for groups in Experiment 4.

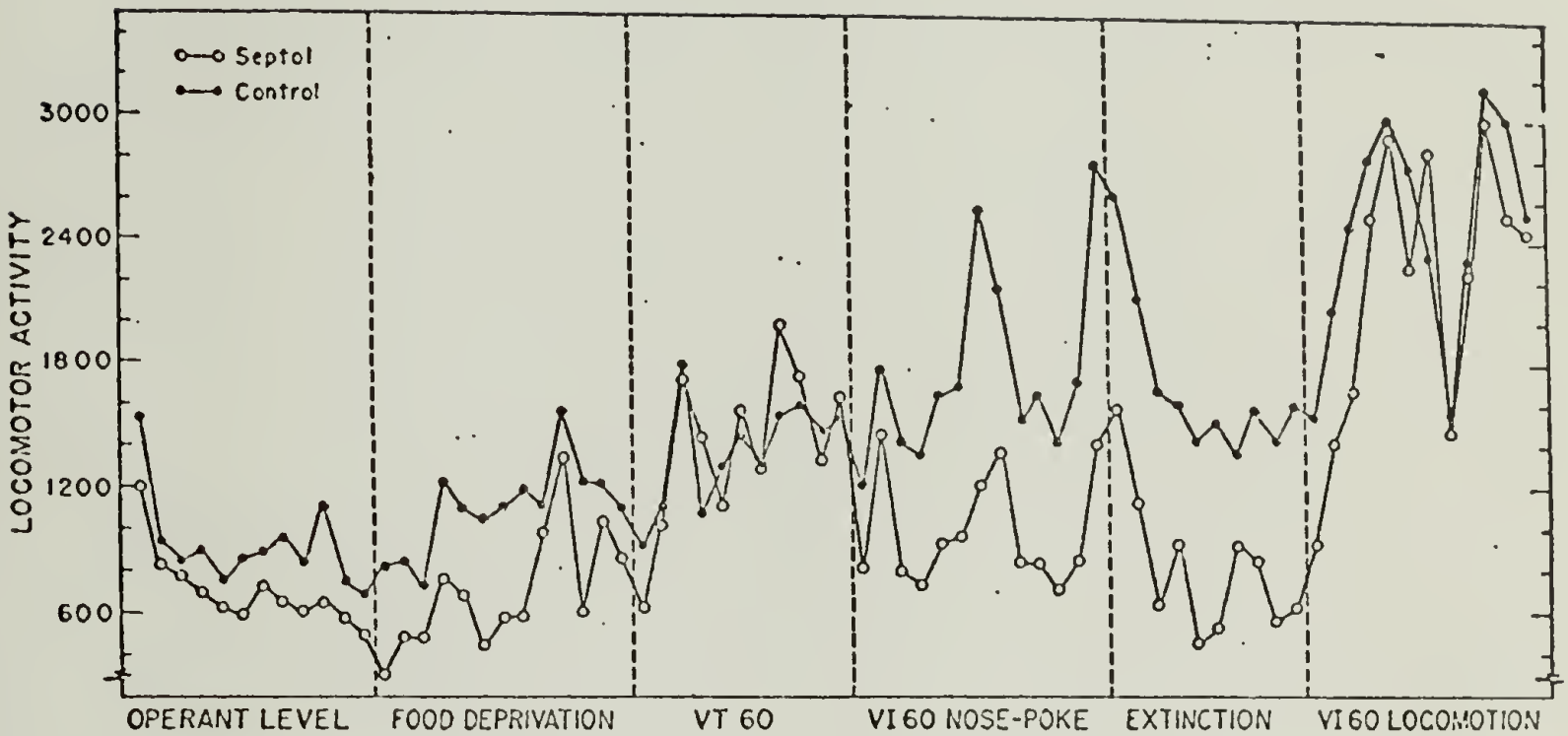


Figure 7. Locomotor activity as a function of daily sessions for groups in Experiment 4.

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