Behavioral Comparison of Septal Lesioned and Anosmic Rats

Suppes
BEHAVIORAL COMPARISON OF
SEPTAL LESIONED AND ANOSMIC RATS

by
Sharon Kay Suppes

A Thesis
Submitted to the
Faculty of The Graduate College
in partial fulfillment
of the
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Sharon K. Suppes
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Psychology, experimental

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INTRODUCTION

This study is an attempt to compare the similarities of behavioral changes caused by disruptions or irritations in two distinctly different but anatomically connected structures that are components of the limbic system.

Brady and Nauta (1953) presented data that describe the emotional behavior that is characteristic of a rat with lesions in the septal forebrain area. Resistance to capture; resistance to handling; increases in muscle tension, squealing and vocalization, urination and/or defecation; hyperaggressive reactions; and the startle response to aversive stimuli such as a blast of air or loud tone have all been classified as affective changes following septal forebrain lesions in the rat. The specific character of these affective changes and the critical factors limiting their duration was investigated in a follow-up study by Brady and Nauta in 1955. Douglas, Isaacson and Moss (1969) reported that bilateral lesions of the olfactory bulbs resulted in hyperemotionality similar in kind and degree to the rage produced by septal lesions. Brown and Remley (1971) reported that septal rats were reliably hyperreactive to thermal, sound, and shock stimulation, but not to taste or light stimuli
while anosmic rats were hyperreactive to thermal and shock stimulation but not to taste, light, or sound stimulation.

Voluntary types of movement such as rearing, turning, and walking were generally accompanied by the rhythmic theta activity from the dorsal hippocampus, the midbrain reticular formation and the occipital cortex (Iwahara, Oishi, Yamazaki, and Sakai, 1972). Vanderwolf (1971) discussed the association of initiation, performance, and cessation of voluntary behaviors with activation of ascending pathways from the diencephalon to the hippocampus and neocortex. Douglas, et al. (1969) suggest that temporary hyperactivity in both septal and olfactory lesioned animals might be due to changes in amygdaloid activity as a result of either disruption of these pathways or irritation produced by degeneration.

Locomotor activity was studied by Valle (1971) employing the open field apparatus which consisted of a square box with sixteen divisions. The number of squares crossed and the number of times the animal stood up on his hind limbs during a five minute period were used as an effective measure of activity. Klein and Brown (1969) found that bulbectomizing rats and placing them in an open field resulted in increased activity and decreased habituation. Douglas, et al. (1969) measured activity of septal and anosmic subjects using wheel running and cage
exploration as test situations and found that both septal and olfactory bulb lesioned rats were somewhat under-active in the exercise wheel while bulb-lesioned animals were below normal in cage activity compared to the distinctly hyperactive septally lesioned rats. Glickman, Sroges, and Hunt (1964) reported that gross locomotor activity of the rat in a novel situation is primarily under subcortical control and that interruption of the primary sensory pathways can produce hyper-exploratory activity (Glickman, 1958).

Passive and active avoidance situations employing the use of the shuttle box are good testing procedures because the subjects do not need prior training, the procedure is fast and the response measured is an all-or-none task (Theios and Dunaway, 1964). Avoidance training of rats often leads to general response suppression as a result of the occurrence of previous shocks, or the threat of subsequent ones. Response suppression is incompatible with the particular avoidance response being trained (Johnson and Church, 1965). This suppression, caused by increased emotionality or anxiety, is often the subject of drug research (Morrison and Stephenson, 1970; Quinton, 1971; Siegel and Jarvik, 1971; and Penrod and Boice, 1971). The fact that animals with septal lesions appear unable to inhibit activity-contingent shock and also show little activity suppression when placed in the
experimental chamber on subsequent days suggests that the lesions interfere with some central inhibitory mechanism (Slotnick and Jarvik, 1966). Thus the possibility that septal lesions facilitate avoidance learning has been extensively studied (Thomas and Van Atta, 1971; Schwartzbaum, Green, Beatty, and Thompson, 1967; Fox, Kimble, and Lickey, 1964) and two opposing findings have been reported: that septal lesions facilitate avoidance learning; and that septal lesions interfere with the avoidance response. Vanderwolf (1964) offers a suggestion to these contrasted findings; impaired acquisition of a simple avoidance response in animals with lesions in the septal area does not conflict with the findings that septal lesions facilitate active avoidance performance in the shuttle box. In a two-way active avoidance situation the avoidance response is often suppressed in normal animals by the same mechanism that is impaired in septal animals. Freezing behavior is inhibited in subjects with septal lesions and results in an enhanced active avoidance response while this same phenomenon results in a decrement of avoidance responding in a one-trial passive avoidance situation in septal animals.

Septal and anosmic rats were compared by Brown, Harrell and Remley (1971) using quinine as the aversive stimulus in a passive avoidance situation. Behavioral similarities produced by septal and olfactory bulb lesions
were found to exist in this study. Thomas (1971) researched the behavioral effects of olfactory bulb removal in several passive and active one-way and two-way avoidance situations. In this study both septally lesioned and bulbectomized subjects were included for the purpose of evaluating the importance of olfactory input for the normal performance of these tasks and to more specifically evaluate the hypothesis that some of the behavioral effects of septal damage are due to changes in the utilization of olfactory input to the limbic system.

The method employing a high frequency alternating current (RF or radio frequency) to destroy brain tissue was used in this study. Kenyon and Kriechhaus (1965) found that acquisition of a shuttle-box avoidance response was pronouncely enhanced to the same degree with small and with unilateral septal lesions as found with large, bilateral lesions of the septal area. Reynolds (1965) placed radio frequency and electrolytic lesions in the septal region of the rat brain and found no postoperative differences between groups as a function of the type of lesion.

Bures, Buresova, and Zahorava (1958) induced spreading depression of cortical electrical activity in rats by applying small filter paper pledgets soaked in 25% solution of KCl. Tapp (1962) demonstrated reversible cortical depression in the rat by implanting chronic
polyethylene cannulae and injecting KCl into the tubes and directly onto the cortex. Mazza (1971) employed a similar technique of applying potassium chloride onto the olfactory bulbs and reported depressed electrical activity of these structures.

Septal lesions and disrupted electrical activity of the olfactory bulb elicited by KCl were investigated and compared in three test situations: a) one-way passive avoidance; b) two-way active avoidance; and c) open field test of activity.
METHOD

Subjects

Forty-five male Sprague Dawley rats from the Upjohn Pharmaceutical Company Colony, Kalamazoo, Michigan were divided into three groups. Group I was implanted with chronic indwelling cannulae placed directly over the olfactory bulbs and cortical recording electrodes positioned anteriorly on the surface of the cortex. Group II received radio frequency lesions in the septal area of the brain. Group III underwent sham operations. The subjects, weighing approximately 350 grams each and approximately 11 weeks old, were housed separately and maintained ad lib. on Purina Rat Chow and water. All of the subjects were naive with respect to experimental procedures prior to this study.

Apparatus

The free field apparatus consisted of a plywood square box measuring 36.0 x 36.0 x 12.0 inches. The floor of the box was marked off into 16 equal squares and delineated with lines drawn and numbered with black ink. There was no lid on the box so that all movement could easily be viewed by the observer. The apparatus
was housed in a sound attenuated, windowless room which was painted flat black. Light was provided by a 100 watt overhead bulb.

A Lehigh Valley\textsuperscript{2} shuttlebox (model no. 146-04) was used for passive and active avoidance procedures. The shuttlebox measured $18.75 \times 8.50 \times 9.25$ inches. The sides and top were constructed of one-fourth inch plexiglas while the floor was constructed of stainless steel rods measuring one-eighth inch in diameter and spaced one-half inch apart. The chamber was housed in another sound attenuated, windowless room. This room was also entirely black. No source of light was supplied other than that which filtered through a 10 inch circular hole in the wall 2 feet above and behind the apparatus. This hole was used as a conduit for the connection of the electromechanical equipment to the shuttlebox. A Grason-Stadler\textsuperscript{3} shock generator was used to deliver shock to the grid floor. A PDP 8 computer by DEC\textsuperscript{4} was interfaced with the electromechanical equipment (Snapper and Walker, 1971) and used to program and record data during the active avoidance procedure.

Electrophysiological recordings of Group I subjects were taken on a Model 7 Grass Polygraph\textsuperscript{5}. Sensitivity settings were placed at 30 mv/cm and filter settings at 1.5 high pass - 15 low pass. The subjects were left in their home cages and placed in a shielded chamber adjoin-
ing the polygraph during recordings.

Surgical Procedure

Surgeries commenced twenty-four hours after the subjects' arrival in the lab. All surgeries were conducted under semi-asceptic conditions. Sodium pentobarbital was used as the anesthetic and 0.1 cc of atropine sulfate was used as a muscarinic blocking agent to reduce respiratory secretions during sedation. Subjects were placed in a Kopf\(^6\) stereotaxic instrument and coordinates for Group II (septal lesions) were consistent with those described in Pelligrino and Cushman (1967). Radio frequency lesions were made through a stainless steel electrode, 0.25 mm in diameter and insulated except for 0.5 mm at the tip, on coordinates 0.5 mm anterior to Bregma, 0.5 mm lateral to the midline, and 5.5 mm in depth from the surface of the dura. Implantation of the chronic cannulae and recording electrodes was accomplished relative to anatomical features. Burr holes were made in the skull according to the location and number necessary. Care was taken during drilling not to disrupt the dura. Two holes for the cannulae were aligned with the anterior portion of the optic globe, and slightly lateral of the midline, approximately 1.0 mm apart. Two silver ball recording electrodes insulated with Formvar\(^7\) except for 0.5 mm at the tip were implanted 1.5 mm posterior to the cannulae.
One anchor screw was placed 3.0 mm posterior to the recording electrodes to give adequate adhesion to the dental cap. The sham subjects received incisions and the drill burr was used to rough up the surface of the skull. All surgeries were done by groups; shams were done first, then the cannulae implants, Group II septal lesions were performed last to control for the time element involving the duration of the septal rage syndrome.

Design

Group I (subjects with chronic indwelling cannulae), II (subjects with septal lesions), and III (sham surgery subjects) were subsequently divided and five subjects from each group were randomly assigned to one of the three behavioral tasks so that each situation would include five sham, five septal, and five olfactory depressed subjects.

Treatment

Electroencephalograph recordings of all subjects in the cannulae implanted group were taken immediately prior to and for 30 minutes subsequent to injections of 12 microliters of 25% solution of KCl. This procedure took place prior to testing of the bulb depressed subjects in each of the three test situations. A non-experimental animal was placed in the shuttlebox and activity chamber.
for five minutes before experimental subjects to control for olfactory cues. Both apparatus were swept of boli and washed with Biosol® after each subject was run.

Each subject involved in the free field test was placed in the apparatus for a period of five minutes. During this time the observer recorded the total number of squares crossed and the total number of rearing movements the subject made. Criteria required that both front feet had to be placed in a new square to be counted as a movement. A return to the same square in which back feet remained was also considered a response. Rearing movements were counted when both front feet were elevated and the subject elongated his body. Grooming responses were carefully excluded. The observer was positioned five feet away from the apparatus and remained stationary during the entire recording session. All subjects were run between the hours of 12:00 P.M. and 3:00 P.M.

The passive avoidance task allowed each subject five minutes of adaptation to the darkened shuttlebox. During this time the total number of crosses made by each subject was recorded. Each time a subject moved across the center of the shuttle cage the toggle floor would tilt in the same direction as the movement. With each tilt the contacts of a microswitch located at the back of the cage would momentarily close and the response was recorded on a counter electromechanically. Immediately following the
five minute adaptation time the subject received 0.8 ma shock upon entering, or if concurrently positioned in, side B of the shuttlebox. A second timer recorded the number of seconds elapsing before the subject returned to side B. The session was terminated if no return response was made within 10 minutes.

All of the subjects participating in the active avoidance procedure were presented with 50 trials of tone-shock paradigm comprising one session. The avoidance and escape responses were of identical dimensions and consisted of the subject running to the opposite side of the shuttlebox. A high frequency tone was presented for 10 seconds preceding and during 0.8 ma shock which was delivered if the subject failed to avoid during the tone. A 60 second safety termination was placed on the shock so that if the subject failed to escape, the shock would terminate and the trial would be recorded as "no escape". The total number of crossings by each subject during the inter-trial-interval of 60 seconds was also recorded for each session.
RESULTS

Lesions in the septal forebrain area clearly enhanced active avoidance responses while bilateral spreading depression of the olfactory bulbs did not effect the number of avoidance responses as compared to the sham surgery technique. Unlike the active avoidance results shown in Table 1 on page 14, the passive avoidance results showed a marked similarity between septal and anosmic subjects in that both groups returned to the shock side within closely related time periods while the sham subjects did not return to the shock side within the allowable 600 seconds.

As indicated in Table 2 on page 16, the activity levels of the subjects with septal lesions and the subjects with depressed bulbs were noticeably increased over that of sham surgery subjects. The open field experiment indicated the highest level of activity for the KCl bulb depressed subjects with septal animals less active but clearly superior to the activity level of the sham surgery animals. The active avoidance inter-trial-interval number of crosses again indicated the greatest number of responses for the KCl group as compared to the septal animals whose number of crosses were similar to
### Table 1

#### Active Avoidance

<table>
<thead>
<tr>
<th>Treatment</th>
<th>KCl Group I</th>
<th>Septal Group II</th>
<th>Sham Group III</th>
</tr>
</thead>
<tbody>
<tr>
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<td>26</td>
<td>19</td>
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<tr>
<td>07</td>
<td>36</td>
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</tr>
<tr>
<td>21</td>
<td>29</td>
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<tr>
<td><strong>Total</strong></td>
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<td><strong>159</strong></td>
<td><strong>72</strong></td>
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<tr>
<td><strong>Mean</strong></td>
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<td><strong>31.8</strong></td>
<td><strong>14.4</strong></td>
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#### Passive Avoidance

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<td>600</td>
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<tr>
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<td>06</td>
<td>600</td>
<td></td>
</tr>
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<td>220</td>
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<td><strong>17</strong></td>
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<td><strong>Mean</strong></td>
<td><strong>57.0</strong></td>
<td><strong>4.25</strong></td>
<td><strong>600.0</strong></td>
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those of the sham subjects. While septal lesions enhanced learned avoidance this treatment did not increase the inter-trial-interval number of responses as compared to the number of responses made by the sham treatment group. The passive avoidance pre-trial five minute habituation period revealed further evidence of increased activity responding for KCl and septal subjects over sham number of responses.

The F test one-way analysis of variance (Glass and Stanley, 1970) was utilized in statistical analysis. Tukey's test of comparison of the means was employed when the P values were found to be significant at .05 or less, as shown in Table 3 on page 17. There was a significant difference between the mean of Group I and Group II and between Group II and Group III in the active avoidance (number of avoidance responses) procedure. Analysis of the passive avoidance pre-trial response data showed a significant difference in the means of Group II and III and Groups I and III respectively.

Histological verification of septal lesions showed evidence that all of the subjects in Group II had received bilateral lesions of the lateral septi except one. This information corresponded with the overt behavioral data collected for this subject from the passive avoidance experiment. The score for this subject
Table 2

Open Field
Number of Squares Crossed + Number of Rearing Responses

<table>
<thead>
<tr>
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<th>Sham Group III</th>
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<td></td>
<td>90</td>
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<td></td>
<td>83</td>
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<td>19</td>
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<td></td>
<td>22</td>
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<td>13</td>
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<tr>
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<td>Mean</td>
<td>49.0</td>
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Active Avoidance
Inter-Trial-Interval Responses

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<td>Mean</td>
<td>63.0</td>
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Passive Avoidance
Pre-Trial Responses for 5 Minutes

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<td>Total</td>
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<tr>
<td>Mean</td>
<td>15.0</td>
<td>18.5</td>
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## Table 3

### Analysis of Variance and Comparison of Means

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<tr>
<td>Number of Avoidance Responses</td>
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<td>.008</td>
<td>KCl Group I and Septal Group II</td>
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<td>Septal Group II and Sham Group III</td>
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<td><strong>Passive Avoidance</strong></td>
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<tr>
<td>Seconds to Return</td>
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<tr>
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<td>.151</td>
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<td><strong>Active Avoidance</strong></td>
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<tr>
<td>Inter-Trial-Interval</td>
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<td>.820</td>
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<td>Pre-Trial Responses</td>
<td>6.96</td>
<td>.023</td>
<td>Septal Group II and Sham Group III</td>
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<td>KCl Group I and Sham Group III</td>
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* Not computed because of raw data differences.
was not included in the final results. Investigation of the cannulae implanted subjects also showed reliable indication that all of the cannulae remained open except those of one subject. Data from this subject were also deleted from the results of Group 1 in the passive avoidance task.

Upon completion of this study it was noted that several of the cannulae implanted subjects displayed vicious attacking and biting toward a gloved hand. This behavior was not present prior to or immediately following injections of KCl.
DISCUSSION

The results of this study demonstrate the similarities of affective behavior existing between septal and olfactory bulb disruptions. The superior ability of the subjects with septal lesions to learn active avoidance corresponds to the data reported by Brady, et al. (1953) who found significant increases in both emotional reactivity and startle response magnitude in experimental septals. In addition, the septal group were found to have a reduction in strength of a previously conditioned fear response although such lesions appeared to have no effect upon the acquisition of the conditioned emotional response. Fox, et al. (1964) found that septal lesioned cats showed significantly fewer inhibitions in a passive avoidance task than did the unoperated controls. This same group required substantially fewer trials and learned significantly faster in an active avoidance task than did the normal control animals.

The results of the passive avoidance task in this study agree with the comparison of similar subjects made by Brown, et al. (1971) who investigated passive avoidance in septal and anosmic rats using quinine as the aversive stimulus and found that septal animals had shorter drink latencies than the anosmic animals which
in turn had shorter latencies than did either the sham or normals. The authors felt the results were congruent with the notion that a response inhibition deficit resulted from the experimental manipulations. Slotnick, et al. (1966) felt that freezing was probably the behavioral response underlying activity suppression because of its dominant state in cats, rats, and mice in fear-arousing situations. Interference with this mode of responding was attributed to septal lesions in mice. The data presented in the present study strongly support the response inhibition deficit theory as opposed to the possibility that any deficit in learning occurred as a result of disruptions in the limbic system.

Thomas (1971) evaluated the importance of olfactory input for the normal performance of passive avoidance and active avoidance. His results indicated no significant differences between passive avoidance scores of normal and bulbectomized subjects while the septally lesioned subjects had significantly shorter latencies in returning to the shock source than either of the other two groups. The active avoidance results indicated that all the experimental groups reached criterion of 10 successive avoidance responses significantly more rapidly than the control group with the major difference between the experimental groups and the control group.
being in the number of trials required to make the first avoidance response. The differences in results of the Thomas (1971) study and this study could be due to several factors. The technique of olfactory disruption was dissimilar and the subjects in this study were tested only once, while the results of the active avoidance tasks in the above mentioned study were obtained from subjects that had prior experience in the apparatus. Also, different aspects of the data were used to interpret results.

Difficulty in interpreting spreading depression from the EEG records led to further investigation of this phenomenon through examination of 4 acute preparations. Van Atta (1972) suggested the technique of removing the surface of the skull and recording directly from the olfactory bulbs and anterior cortex. Stimuli applied directly to the surface of the cortex often elicits a depression of local electrical activity which spreads from the point of stimulation and inhibits cortical responses to other stimuli. This phenomenon was labeled spreading depression (Grossman, 1967). Bures, et al. (1958) found that a direct-current shift was involved and that several direct-current shifts could be produced from a single stimulation. Tapp (1962) employed the technique of implanting polyethylene cannulae
over the cortex and applying KCl directly onto the cor-
tex. The results of his experiment showed that the
behavioral deficit was a function of the concentration
of KCl solution, the loss in avoidance behavior was re-
versible, and that loss of the avoidance habit may have
been symptomatic of a general loss in the ability to
perform tasks involving integrated motor behavior.
Electroencephalograph recordings of all subjects in the
cannulae implanted group of this study were taken for
30 minutes subsequent to injections of 12 microliters of
25% solution of KCl. The acute preparations involving
KCl applied directly onto the bulbs showed depressed
electrical activity of the bulb at the point of applica-
tion lasting approximately 90 minutes while the wave of
spreading depression recorded from the cortex existed
only five or six minutes. This would strongly indicate
that in spite of the poor EEG recordings of the electri-
cal activity of the cortex in the chronic implanted
animals, spreading depression did occur at the site of
application and was in effect during behavioral testing.
The amount of time that the wave of depression was
recorded from the bulbs and cortex is consistent with
the findings of Leão (1944) who reported that cortical
SD does not remain confined to the area of application
but spreads over the cortical surface at the rate of
about two to five millimeters per minute and lasts at a
given locus for five to six minutes. EEG recordings of
the acute preparations are shown on pages 25, 27, 29,
and 30. Depression over the cortex could have been un-
impressive in the chronically implanted animals because
of the poor quality of the EEG record caused by inter-
ference from movement of the subjects while recording
took place. The amount of time that spreading depression
was found to exist over the cortex rules out influences
of a decrease in the excitability of motor areas caused
by SD on the cortex as reported by Marshall (1959). A
more reliable method of recording depression of olfactory
electrical activity could be implemented by the use of
stainless steel cannulae which could serve a dual purpose;
for injecting the solution and as a monopolar recording
electrode.

Vanderwolf (1971) has pointed out that septal dam-
age disrupts mechanisms which normally control activity
in a movement trigger system. The septal nuclei form
part of many functional systems, a major role of which is
to inhibit somatomotor activity. A heavy concentration
of points in the septal-preoptic area facilitated move-
ments produced by cortical stimulation while other points
in the same general region had an inhibitory effect. It
has also been shown that stimulation of the septal nuclei
FIGURE 1. Electrophysiological recordings of the electrical activity of the olfactory bulb and the surface of the cortex after application of 12 microliters of KCl to the bulb. Paper speed was set at 15 mm/sec and sensitivity at 30 mv/cm. Acute preparation subject number 1.
Bulb

Cortex

Before Minutes After Injection Recovery

1 sec.

Acute KCl Preparation
FIGURE 2. Electrophysiological recordings of the electrical activity of the olfactory bulb and the surface of the cortex after application of 20 microliters of KCl to the bulb. Paper speed was set at 15 mm/sec and sensitivity at 30 mv/cm. Acute preparation subject number 2.
Acute KCl Preparation
FIGURE 3. Electrophysiological recordings of the electrical activity of the olfactory bulb and the surface of the cortex after application of 12 micro-liters of KCl to the bulb. Paper speed was set at 15 mm/sec and sensitivity at 30 mv/cm. Acute preparation subject number 3.
Acute KCl Preparation

Before | Minutes After Injection | Recovery

Bulb

Cortex

1 sec.
FIGURE 4. Electrophysiological recordings of the electrical activity of the olfactory bulb and the surface of the cortex after application of 12 microliters of KCl to the bulb. Paper speed was set at 15 mm/sec and sensitivity at 30 mv/cm. Acute preparation subject number 4.
results in an increased discharge rate of cells in the centromedian nucleus of the thalamus. Therefore, somatomotor inhibitory as well as facilitatory systems appear to be present in the septal nucleus, and a large lesion could very possibly produce a complex behavioral change. Olfactory bulb fibers project to the olfactory tubercule, the prepyriform cortex, the entorhinal cortex, and probably, the cortico-medial amygdala. Second order connections are with the hypothalamus, septum, hippocampus, and cingulate cortex (Heimer, 1968). This study presents evidence suggesting similar changes in affective behavior of rats as a result of septal lesions and disrupted olfactory input.
FOOTNOTES

1 Ralston Purina Company, St. Louis, Missouri
2 Lehigh Valley Electronics, Fogelsville, Pennsylvania
3 Grason-Stadler, West Concord, Massachusetts
4 Digital Equipment Corporation, Maynard, Massachusetts
5 Grass Instrument Company, Quincy, Massachusetts
6 Kopf Instruments, Tujunga, California
7 General Electric, Bridgeport, Connecticut
BIBLIOGRAPHY


Leão, A. A. P. "Spreading Depression of Activity in the Cerebral Cortex." Journal Neurophysiology, 1944, 7, 359-90.


