1971

The Corticomedial Amygdalo-Bulbar Centrifugal Systems in Olfaction in Therat.

Garl Kalman Rieke

Louisiana State University and Agricultural & Mechanical College

Follow this and additional works at: https://digitalcommons.lsu.edu/gradschool_disstheses

Recommended Citation
https://digitalcommons.lsu.edu/gradschool_disstheses/1958

This Dissertation is brought to you for free and open access by the Graduate School at LSU Digital Commons. It has been accepted for inclusion in LSU Historical Dissertations and Theses by an authorized administrator of LSU Digital Commons. For more information, please contact gradetd@lsu.edu.
RIEKE, Carl Kalman, 1942-
The Corticomedial Amygdalo-Bulbar Centrifugal Systems in Olfaction in the Rat.
The Louisiana State University and Agricultural and Mechanical College, Ph.D., 1971
Physiology

University Microfilms, A Xerox Company, Ann Arbor, Michigan

© 1971

CARL KALMAN RIEKE

ALL RIGHTS RESERVED
THE CORTICOMEDIAL AMYGDALO-BULBAR
CENTRIFUGAL SYSTEMS IN OLFACTION
IN THE RAT

A Dissertation

Submitted to the Graduate Faculty of the Medical Center of
Louisiana State University and
Agricultural and Mechanical College
in partial fulfillment of the
requirements for the degree of
Doctor of Philosophy

in

The Department of Anatomy

by

Garl Kalman Rieke
B.S., University of Washington, 1965, 1966
June 1971
ACKNOWLEDGEMENTS

The author would like to express appreciation to Dr. Marvin H. Bennett for his encouragement and assistance throughout the course of this investigation.

He also wishes to thank Miss Mary Lynn Streckfus for her assistance in completion of the critical histology and Mr. Garbis A. Kerimian for his photographic skills. To his wife, Judy, for her support, technical assistance, typing skills, and many dinners cooked in the laboratory, the author is deeply appreciative.
TABLE OF CONTENTS

ACKNOWLEDGEMENTS ......................................................... 1i
LIST OF FIGURES ............................................................... vi
LIST OF GRAPHS ............................................................... viii
LIST OF TABLES ................................................................. ix
ABSTRACT ........................................................................... xii
INTRODUCTION ...................................................................... 1
  Anatomical Background ................................................... 9
  Electrophysiological Background ..................................... 20
METHODS AND MATERIALS .................................................. 33
RESULTS ............................................................................... 43
I. Ipsilateral System ........................................................... 44
  A. Amygdalar Stimulation ............................................... 44
  B. Olfactory Bulb Response to Extraamygdalar Stimulation Sites 48
  C. Forebrain Nuclei Which Respond to Amygdalar Stimulation but not Related to Ipsilateral Centrifugal System .......... 54
  D. Effects of Chronic Lesions ......................................... 58
  E. Summary ................................................................. 62
II. Contralateral System ...................................................... 63
  A. Amygdalar Stimulation ............................................... 63
  B. Extra-amygdalar Stimulation Sites ......................... 68
  C. Effects of Chronic Lesions ....................................... 72
D. Summary ................................................. 74

III. Interaction Studies........................................ 75

A. Ipsilateral Division............................... 76

1) Interactions Between Specific Nuclei.................... 76

2) Effect of Ipsilateral Centrifugal Nuclei on Centripetal Input to Areas Receiving Olfactory Afferents................. 85

B. Contralateral Division............................ 85

1) Contralateral System upon Ipsilateral System............. 85

2) Effects of Contralateral Division upon Antidromically Evoked Olfactory Bulb Response and Orthodromic Bulbar Evoked Responses from Areas of Distribution of the LOT.......... 91

3) Effects of Lesions on the Contralateral System........... 94

C. Summary................................................. 96

IV. Possible Direct Centrifugal Fibers from Periamygdalar Cortex to Ipsilateral Olfactory Bulb................................. 96

DISCUSSION.................................................. 98

I. Interpretation of Evoked Response Studies................ 98

A. Ipsilateral Centrifugal Subdivision................. 98

B. Contralateral Centrifugal Subdivision.............. 105

II. Interpretation of Interaction Studies............. 109

A. Ipsilateral Subdivision......................... 109

B. Contralateral Subdivision...................... 114
1) Inhibitory Influence upon Ipsi lateral System............. 114

2) Facilitatory Influence upon Centripetal Input............... 115

III. Functional Hypothesis............................... 116

IV. General Summary.......................................... 117

BIBLIOGRAPHY.................................................... 120

APPENDIX I......................................................... 130

VITA............................................................. 132
**LIST OF FIGURES**

<table>
<thead>
<tr>
<th>FIGURES</th>
<th>PAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. A: Schematic for generation and delivery of single pulses and for recording evoked responses</td>
<td>38</td>
</tr>
<tr>
<td>B: Schematic for generation and delivery of bursts and single pulses and for recording evoked responses</td>
<td>38</td>
</tr>
<tr>
<td>2. Left half: response from olfactory bulb to stimuli applied to the periamygdalar cortex</td>
<td>45</td>
</tr>
<tr>
<td>Right half: response evoked by stimuli applied to the cortical amygdala, recorded from a) IB, b) AON, c) OTpcl, d) OTpcl, e) BNDB</td>
<td>45</td>
</tr>
<tr>
<td>3. Response evoked in ipsilateral olfactory bulb by stimulation of CAN, BNDB, OT, or AON</td>
<td>49</td>
</tr>
<tr>
<td>4. Change in evoked ipsilateral olfactory bulb response as stimulation electrode was elevated through the periamygdalar cortex into the cortical amygdala and through the amygdala</td>
<td>53</td>
</tr>
<tr>
<td>5. Changes in ipsilateral olfactory bulb response with elevation of the stimulating electrode through the cortical amygdala</td>
<td>55</td>
</tr>
<tr>
<td>6. An example of the inversion of the cortical amygdalar evoked olfactory bulb response as the recording electrode passed through the bulb</td>
<td>56</td>
</tr>
<tr>
<td>7. Effects of chronic lesions in basal forebrain structures upon ipsilateral centrifugal system</td>
<td>59</td>
</tr>
<tr>
<td>8. Cortical amygdalar evoked responses recorded from 1) CB, 2) AON, 3) OT, 4) BNDB, and 5) BNST</td>
<td>64</td>
</tr>
</tbody>
</table>
9. Responses evoked from contralateral forebrain nuclei by stimuli applied to the bed nucleus of stria terminalis (BNST). a) contralateral olfactory bulb (CB), b) contralateral anterior olfactory nucleus (AON), c) contralateral olfactory tubercle (OT), d) contralateral bed nucleus of diagonal band (BNDB).................. 69

10. A: Chronic lesions which abolish responses from the contralateral centrifugal system.................. 73

B: Chronic lesions with no effect upon the contralateral system........... 73

11. A: Inhibition of IB induced centripetal response from the OT by single shocks to the cortical amygdala........ 87

B: Inhibition of IB induced centripetal response from the BNDB by a 20 msec, 200 Hz pulse to the cortical amygdala.................. 87

12. Proposed models for (A) the ipsilateral centrifugal system and (B) the contralateral system........ 119
# LIST OF GRAPHS

<table>
<thead>
<tr>
<th>GRAPH</th>
<th>PAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Following frequencies of cortical amygdalar evoked responses in ipsilateral forebrain nuclei</td>
<td>47</td>
</tr>
<tr>
<td>II. Following frequencies for evoked olfactory bulb responses by stimuli applied to ipsilateral CAN, BNDB, OT, and AON</td>
<td>51</td>
</tr>
<tr>
<td>III. Following frequencies for responses in nuclei of the contralateral system evoked by stimulation of the cortico-medial amygdala</td>
<td>66</td>
</tr>
<tr>
<td>IV. Following frequencies for responses in nuclei of the contralateral system evoked by stimulation of strial bed nucleus</td>
<td>71</td>
</tr>
</tbody>
</table>


## LIST OF TABLES

<table>
<thead>
<tr>
<th>TABLE</th>
<th>PAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Characteristics of the evoked responses recorded from ipsilateral forebrain nuclei and the olfactory bulb</td>
<td>46</td>
</tr>
<tr>
<td>II. Characteristics of evoked responses recorded from the ipsilateral olfactory bulb</td>
<td>50</td>
</tr>
<tr>
<td>III. Characteristics of the corticomedial amygdalar evoked response in the ipsilateral olfactory bulb as the recording electrode passed through the olfactory bulb</td>
<td>57</td>
</tr>
<tr>
<td>IV. Characteristics of responses evoked in nuclei of the contralateral centrifugal subdivision following stimuli applied to the corticomedial amygdala</td>
<td>65</td>
</tr>
<tr>
<td>V. Characteristics of responses evoked in the nuclei of the contralateral centrifugal subdivision following single pulses to the bed nucleus stria terminalis</td>
<td>70</td>
</tr>
<tr>
<td>VI. Comparison of the relative areas of the observed and predicted responses from a single preparation for the test pair CAN—postero-medial OT on IB</td>
<td>78</td>
</tr>
<tr>
<td>VII. Comparison of the relative areas of the observed and predicted responses from a single preparation for the test pair OT—AON on IB</td>
<td>79</td>
</tr>
<tr>
<td>VIII. Comparison of the relative areas of the observed and predicted responses from a single preparation for the test pair CAN—BNDB on IB</td>
<td>81</td>
</tr>
</tbody>
</table>
IX. Comparison of the relative areas of the observed and predicted responses from a single preparation for the test pair CAN--AON on IB................. 82

X. Comparison of the relative areas of the observed and predicted responses from a single preparation for the test pair BNDB--AON on IB............. 83

XI. Comparison of the relative areas of the observed and predicted responses from a single preparation for the test pair BNDB--postero-medial OT on IB................................. 84

XII. Comparison of the relative areas of the observed and predicted responses from a single preparation for the test pair CAN--antero-lateral OT on IB................................. 86

XIII. The suppressive effect of bursts applied to the contralateral corticomedial amygdala on the responses evoked in the ipsilateral olfactory bulb by single pulses applied to ipsilateral forebrain nuclei................. 89

XIV. The suppressive effect of bursts applied to the contralateral striatal bed nucleus on the responses evoked in the ipsilateral olfactory bulb by single pulses to ipsilateral forebrain nuclei.................... 90

XV. The suppressive effect of bursts applied to the contralateral corticomedial amygdala on the responses evoked in the BNDB, OT, and AON by single pulses to the ipsilateral corticomedial amygdala............... 92

XVI. The suppressive effect of bursts applied to the contralateral striatal bed nucleus on the responses evoked in the ipsilateral AON, OT, and olfactory bulb by single pulses to ipsilateral corticomedial amygdala.... 93
XVII. The effect of bursts applied to either the contralateral cortico-medial amygdala or strial bed nucleus on the centripetally or antidromically evoked responses ipsilateral forebrain nuclei.
ABSTRACT

A sensory system in general contains a centripetal and a centrifugal limb. The centripetal limb in olfaction has been well defined. Anatomical and electrophysiological studies have suggested the presence of a centrifugal limb. The present study employed electrophysiological and anatomical methods and defined two, bilateral, symmetrical centrifugal systems in olfaction in Charles River male rats.

The ipsilateral system contained five nuclei: (1) corticomedial amygdala, (2) bed nucleus of the diagonal band, (3) olfactory tubercle, (4) anterior olfactory nucleus, and (5) granule cell core of the olfactory bulb. Centrifugal fibers traversed the basolateral forebrain in association with the allocortex close to the lateral olfactory tract. The contralateral system originated in the corticomedial amygdala and strial bed nucleus. The stria terminalis interconnected these nuclei, and fibers from the strial bed nucleus crossed the midline in the body of the anterior commissure and distributed to the nuclei of the opposite ipsilateral system.

The occlusion observed in olfactory bulb responses during interaction studies between test pairs of
ipsilateral nuclei suggested that the nuclear components of the ipsilateral system shared populations of neurons. Concurrent stimulation of the corticomedial amygdala inhibited the centripetally evoked bulbar responses in the olfactory tubercle or bed nucleus of the diagonal band. Ipsilateral centrifugally evoked olfactory bulb responses were inhibited by concurrent stimulation of nuclei of the opposite contralateral system. Responses evoked in the more caudal nuclei of one ipsilateral system by stimulation of the respective corticomedial amygdala were inhibited by stimulation of the contralateral system. Centripetal responses recorded from areas of distribution of the lateral olfactory tract were facilitated by concurrent stimulation of the contralateral centrifugal system.

It was concluded that the paired centrifugal systems (ipsilateral and opposite contralateral-) were possible antagonists and functioned to regulate the amount of olfactory afferent input which reaches the olfactory cortex and in turn information upon which the brain might act.
INTRODUCTION

A fundamental question associated with a sensory system is the mechanisms of central control or regulation of the quantity and quality of sensory input (Livingston, 1959). This is an encompassing question with many facets. These facets permit multiple disciplinary experimental approaches designed to resolve specific problems fostered by the general question. The present study concerns the definition, interconnections, and functional interactions of those forebrain nuclear centers and related fiber pathways which when electrically stimulated alter the electrical activity of the olfactory bulbs. A centrifugal system is the more centrally situated nuclear groups and the associated fiber paths directed towards the afferent limb of the specific sensory pathway. It has also been referred to as the efferent limb of the sensory loop.

Centrifugal systems have been investigated to variable degrees in most known sensory systems (Hartline, 1954, 1956; Granit, 1955). The centrifugal system of audition has been explored extensively by Rasmussen (1946) and Galambos and associates (1956, 1
1960, 1968). This system has been explored anatomically and electrophysiologically and might serve as a feasible model for a possible multisynaptic centrifugal system in olfaction. Each auditory related nuclear center between the organ of Corti and the auditory cortex is associated with a population of centrifugal neurons. Electrophysiological investigations revealed that direct electrical stimulation of the crossed olivocochlear bundle, defined by Rasmussen (1946), inhibited activity in the cochlea into which the bundle terminated (Fex, 1965; Goldstein, 1968). Electrical stimulation of more centrally situated auditory nuclear centers reduced the tone evoked electrical activity recorded from the cochlear nucleus, but it had no appreciable influence on input from the cochlear division of the eighth cranial nerve (Desmedt, 1960; Mountcastle, 1968). These two observations seem pertinent, because they reveal several general characteristics of a centrifugal system along with inherent problems of the study of a centrifugal system. The afferent ascending centripetal signals can be influenced by the corresponding centrifugal system at several different synaptic levels. The synapse is the site for influence exerted by a centrifugal system through facilitatory or inhibitory mechanisms. The chain of neurons comprising a centrifugal system may present a
high degree of synaptic overlap, in that one nuclear group may synapse with several other centers. Each nuclear group may not necessarily project directly upon the area of the central nervous system receiving primary or first order sensory afferents, and the receptor itself could function independent of centrifugal influences.

These generalities are critical in the selection of the most favorable and informative investigative approaches, in that they reveal inherent technical limitations. The multisynaptic nature of the known centrifugal systems places a severe limitation on direct neuroanatomical degenerative studies. The methods for study of axonal degeneration permit detection of a single fiber system to the point of synapse, and trans-synaptic degeneration is not a common feature of the nervous system. In the case of the corticomedial amygdala, an apparent site of origin for centrifugal elements in olfaction, the extensive and redundant connections of these nuclei with other basal forebrain regions prohibits selection of the specific centrifugal fibers. On the other hand, the combination of selective lesions and electrophysiological techniques provides a more applicable investigative tool. A response from one nucleus evoked by stimuli applied to a distant location
suggests that the two sites are interconnected. The
loss of the evoked response following destruction of
a suspected nuclear group or fiber pathway implies
that the ablated structure was situated in the path-
way between the stimulating and recording sites.

Electrophysiological techniques are not a panacea,
but the limitations are outweighed by the advantages.
The most serious problem is current spread. When an
electrical pulse is applied to a particular region
care must be taken to limit the spread of excitation
to adjacent areas. To partially avert this problem
bipolar stimulating electrodes are employed. The
applied current passes from one lead to the closely
adjacent second lead. Current density is the greatest
on the line between the two leads. Current density is
not a simple relationship. For a specific quantity of
current passed the current density depends upon the
geometry of the electrodes, the exposed area of the
tips of the electrodes, and the characteristics of the
substrate in which the electrodes are placed (Becker
et al., 1961). Extraneous excitations can be further
reduced by delivery of shocks through isolation units
and by setting the shock strength at threshold level or
slightly above threshold. An additional check on the
limitation of current spread is acquired by determina-
tion of the prescribed region where stimuli can evoke
the desired response. If current spread were extensive the boundaries would not be discrete. With these precautions the problem of extraneous current spread can be controlled (Mickle, 1961).

Electrophysiological techniques provide select advantages. The method of initiating excitation is not physiological, but the events occurring after the initial synchronous depolarization of excitable membranes, the propagation of action potentials, and the processes at synapses between the point of stimulation and recording are biological (Davies, 1968a, 1968b, 1968c). Highly sophisticated methods such as microiontophoresis have been developed to approach biological levels of excitation or inhibition of neurons. Small quantities of suspected transmitter substances have been released in the vicinity of single cells, and the electrical events from the cell have been recorded (Curtis and Eccles, 1958; Curtis et al., 1968; Curtis, 1969). These methods were not utilized since the nature of the synaptic transmitters in the centrifugal system of olfaction are not known. Since a series of biological events are triggered by the artificial stimulus, synapses pose no major obstacle. An intervening synapse can be readily demonstrated by the phenomenon of post-tetanic potentiation (PTP) (Lloyd, 1949; Eccles, 1953; and Hughes, 1958).
J. C. Eccles (1953) attributed the increased response amplitude seen with the cessation of a tetanic stimulus to an increase in the excitable state of presynaptic terminals. Neurons within a synaptic pool are not equally excited by an afferent volley. Excitation is dependent upon the release of sufficient transmitter agent to depolarize the postsynaptic membranes to threshold levels (Mountcastle and Baldessarini, 1968). The mechanisms of transmitter generation and release are properties of the presynaptic elements. The number of excited and subliminal excited neurons in a synaptic pool can be enlarged by increasing the magnitude of the afferent volley (duration, amplitude) or by raising the frequency or duration of the volley. Post-tetanic potentiation apparently involves the latter since a tetanic stimulus is delivered upon the synaptic pool, and a greater number of excitable neurons are recruited. The increase in the post-tetanic response amplitude following cessation of the tetanic stimulus may be due to several factors. The number of excitable neurons and subliminally excited neurons has increased. The mechanism of release of transmitter may have been accelerated. As a result the quantity of synaptic transmitter in the synaptic cleft has been increased. The presence of excess transmitter in the synaptic cleft and the concomitant increase in the
excitatory state of the postsynaptic membrane may, therefore, produce the observed potentiation. The magnitude of the amplitude changes, the shifts in peak latencies, the changes in thresholds, and the frequently occurring post-tetanic depressive phase are related to the frequency and duration of the tetanic volleys (Hughes, 1958). The occurrence of PTP cues the presence of one or more synaptic pools interposed between the stimulation and recording site.

A relative estimate of the number of intervening synapses in a polysynaptic system can be obtained. This is based upon the observation that the frequency of central stimulation which faithfully evokes a response (in a one to one ratio) is inversely related to the number of synapses between the stimulation and recording site. This is referred to as a test of following frequencies. The fewer the number of synapses, the greater the stimulus frequency range over which the response can be evoked. This test allows a distinction to be made as to whether a synaptic system is being driven (orthodromic) or whether processes of neurons (axons) are being excited and the recorded activity is a reflection of non-synaptic activation of the soma (antidromic). An antidromic response can be evoked through high frequencies, because it is not being driven trans-synaptically.
Evaluation of such data gives only a qualitative estimate of the number of synapses.

Responses evoked in the olfactory bulb by stimuli applied to forebrain nuclei denote bulbar connections, but these data reveal nothing in terms of functional relationships. By selecting combinations of stimulation sites, altering the time intervals between stimuli delivered to each group, and employing single shocks or pulses of known duration and frequencies certain conclusions might be drawn with respect to the functional relationships within the centrifugal system.

To facilitate the investigation of a possible centrifugal system in olfaction, keeping in mind as a feasible model the auditory centrifugal system, the areas of distribution of the lateral olfactory tract (LOT) were considered. The lateral olfactory tract is the primary tract over which olfactory input is distributed to widespread areas of the basal forebrain (White, 1965; Heimer, 1968). The LOT is composed of axons of second order neurons (mitral cells) and distributes collaterals and terminals to the anterior olfactory nucleus, the olfactory tubercle, the prepiriform and periamygdalar cortices, and the cortical and medial amygdaloid nuclei. These basal forebrain nuclear centers and their interconnections
are of prime interest to the present study since a current hypothesis considers the cell bodies of centrifugal neurons to be situated within the nuclear areas of distribution of the lateral olfactory tract (Heimer, 1968).

ANATOMICAL BACKGROUND:

The lateral olfactory tract has been shown to contribute collaterals to the anterior olfactory nucleus. The pars externa, pars lateralis, pars dorsalis, and pars rostralis of the anterior olfactory nucleus receive terminal axons and collaterals of mitral cells (Lohman and Lammers, 1967). Cells of the pars externis and pars lateralis receive synaptic terminals from the tufted cells of the ipsilateral olfactory bulb (Valverde, 1964; Lohman and Lammers, 1967), as well as LOT collaterals. Axons from the LOT synapse in the antero-lateral quadrant of the olfactory tubercle (Lohman, 1963; White, 1965) and form axo-dendritic synapses in the superficial plexiform layer of the tri-laminated prepiriform cortex (Valverde, 1965; White, 1965). The periamygdalar cortex receives an LOT input upon the superficial pyramidal cell layer (White, 1965; Heimer, 1968). The cortical and a portion of the medial amygdaloid nuclei are the caudal most projection sites of the lateral olfactory tract (Powell, Cowan, and Raisman,
The areas of distribution of the lateral olfactory tract have been shown to be extensively interconnected (Valverde, 1965). The continuity and interconnections of the basal forebrain areas seem significant in that the potential for functional interactions exists. Through these interconnections the populations of olfactory centrifugal neurons might be regulated by a resultant facilitation or inhibition stemming from the sum of several inputs (Mountcastle and Baldessarini, 1968). Ferrer (1969) reported preterminal and terminal degeneration in the olfactory tubercle (lateral two-thirds), the prepiriform and periamygdalar cortices as well as the corticomedial amygdala following lesions in the anterior olfactory nucleus (pars rostralis). Lesions placed in the medial portion of anterior olfactory nucleus produced degeneration in the basolateral amygdala and the mammillary area. Lesions of the pars rostralis produced, in addition to those sites mentioned, degeneration within the homolateral preoptic region, the lateral hypothalamic area, the lateral habenular nucleus, and the dorsomedial thalamic nucleus (Ferrer, 1969). Ban and Zyo (1962) and Lohman and Lammers (1963) observed similar degeneration within the areas listed above and traced the degeneration through the medial forebrain bundle.
Valverde (1965) has demonstrated neuronal connections between the prepiriform, periamygdalar cortices with one another and with the amygdaloid nuclei. The cortical and medial amygdala are phylogenetically the oldest of the amygdala and were included in the rhinencephalon or smell brain of Papez (Papez, 1937; Crosby, Humphrey, and Lauer, 1962; De Groot, 1966). This major division of the amygdala includes the cortical, the medial and central amygdaloid nuclei and the nucleus of the lateral olfactory tract (De Groot, 1966). The corticomedial group has extensive afferent and efferent relationships and may constitute over several synaptic links a portion of the centrifugal system in olfaction, even though no direct amygdalo-olfactory bulb fibers can be detected (Price and Powell, 1970a). The central amygdala was reported to receive intra-amygdalar inputs and may function in a manner similar to the intralaminar nuclei of the thalamus (Brodal, 1947, 1948; Valverde, 1962). The posterior limb of the anterior commissure interconnects the bilateral amygdaloid complexes and serves as one of the well defined pathways providing input to and output from the amygdala (Ban and Omuki, 1959; Crosby et al., 1962). The stria terminalis and the ventral amygdalofugal system are two additional routes for input to and output from the amygdaloid
complex.

The stria terminalis carries amygdalar efferents to the ipsilateral septal, preoptic, hypothalamic, and epithalamic centers (Fox, 1940, 1943; Valverde, 1963a, 1964, 1965; De Olmos, 1968). Valverde (1964, 1965) employing the Nauta-Gygax (1954, 1957) method and a variant of the Golgi method demonstrated that the stria terminalis arose in part from cells of the central, medial, basal, and lateral amygdaloid nuclei. Both afferent and efferent fibers were demonstrated in the stria terminalis. Fox (1940) gave a detailed description of the distribution of the stria terminalis in the amygdaloid complex which involved the central, medial, cortical, basal nuclei and a component of the posterior surface of the nucleus of the lateral olfactory tract. The stria terminalis in the rat, guinea pig, cat, squirrel monkey, and Rhesus monkey courses from the temporal pole along the inferior concave surface of the fimbria-fornix complex. It then arches around the internal capsule adhering to the infero-medial surface of the tail and body of the caudate nucleus until it reaches the level of its ipsilateral bed nucleus (bed nucleus of the stria terminalis) located superior and caudal to the anterior commissure. At this point the stria divides into five defined components: (1) commissural,
(2) supracommissural, (3) infracommissural, (4) hypothalamic, and (5) stria medullaris or epithalamic division (Gurdjian, 1925; Fox, 1940; Valverde, 1963b; De Olmos, 1968).

The efferent projection field of the stria terminalis represents a complex, highly integrated set of nuclear centers (Gurdjian, 1925; Valverde, 1963b). The bed nucleus of the anterior commissure, the bed nucleus of the stria terminalis, and the bed nucleus of the medial forebrain bundle, bilaterally, form a more or less continuous cellular band along the caudal aspect of the body of the anterior commissure. The bed nucleus of the stria terminalis was considered to be a continuation of the central amygdaloid nucleus (Le Gros Clark and Meyer, 1947). Gurdjian (1925) observed a dorsal continuation of the bed nucleus of the anterior commissure with the ipsilateral septal nucleus. The nucleus medialis septi was shown to possess neurons which synapse in the opposite medial septal nucleus (Fox, 1940; Lohman, 1963). The commissural component of the stria terminalis gives collaterals to the ipsilateral strial bed nucleus and nucleus of the anterior commissure, then enters the anterior commissure and crosses the midline to synapse in the contralateral bed nucleus of the anterior commissure and the strial bed nucleus (Cajal, 1909; Valverde,
1963b). De Olmos (1968) using a silver cupric modification of the Nauta technique reported that the "commissural bundle" or commissural component projects contralaterally to the bed nuclei of the stria terminalis and the anterior commissure, the lateral and medial amygdala, the olfactory tubercle, the prepiriform cortex and the gray matter in the immediate vicinity of the posterior limb of the anterior commissure. The supracommissural component (Fox, 1940), or St₄ component of Valverde (1963b), sends collaterals to the corresponding ipsilateral strial bed nucleus, then passes superiorly to the anterior commissure, turns sharply anteroventrally to project into the septal area and the preoptic region below the anterior commissure. De Olmos (1968) extends the projection field of this component so that it reaches the ipsilateral nucleus accumbens, the laterobasal septum, the olfactory tubercle, and the pars posterior, pars medialis, and pars rostralis of the anterior olfactory nucleus.

A third pathway associated with the amygdala is the ventral amygdalofugal pathway which is a component of the longitudinal association bundle (Johnston, 1923; Valverde, 1963b). This bundle contains both afferent and efferent fibers which project to basal forebrain structures. In rodents the longitudinal association bundle is composed of many neurons with
short axons which interconnect the amygdala with the anterior amygdaloid area and the preoptic region (Valverde, 1965). This bundle also projects over multiple synapses to the prepiriform areas and the nucleus of the diagonal band (Johnston, 1923; Fox, 1940; Valverde, 1962; Valverde, 1963b). The basal forebrain areas served by the longitudinal association bundle are grouped by Valverde (1965) into a collection called the "medial forebrain bundle area". The medial forebrain bundle is closely associated with the basal forebrain in the vicinity of the hypothalamus, the amygdala and the preoptic region. Early investigators did not distinguish between parts of the longitudinal association bundle and the medial forebrain bundle, but in recent studies the distinction is made (Johnston, 1923; Valverde, 1965).

The medial forebrain bundle consists of two principal divisions (Ban and Zyo, 1962; Valverde, 1965). The first system involves long fibers which interconnect basal forebrain, diencephalic, and mesencephalic centers. The second is a system of short neurons connecting the lateral hypothalamus and preoptic area with the mesencephalon (Valverde, 1965). This system relates the hypothalamus and preoptic region, serving as a common effector pathway for (1) axonal processes of the cells of layer IV of the
piriform cortex, (2) axons from the cells of the olfactory tubercle and adjacent cortex, (3) axons of frontal cortex pyramidal cells above the olfactory bulbs and associated with the corpus callosum, (4) the hypothalamic division of the stria terminalis, and (5) axons of cells in the septal nuclei (Valverde, 1965). The basal forebrain regions through which the medial forebrain bundle courses is a complex deep plexus related to the overlying piriform cortex and the lateral hypothalamus, preoptic region, anterior amygdaloid area, the nucleus of the diagonal band, olfactory tubercle, and the anterior olfactory nucleus. The medial forebrain bundle splits into three divisions at the caudal aspect of the bed nucleus: (1) the medial division to the septum, (2) the lateral division along the postero-lateral edge of the nucleus to the amygdala, and (3) the intermediate division, fascicles of which course through the horizontal portion of the bed nucleus of the diagonal band to terminate within the anterior olfactory nucleus. None of the fibers of the medial forebrain bundle terminate within the olfactory bulb (Ban and Zyo, 1962; Lohman and Lammers, 1963; Price and Powell, 1970a).

The complexity of the basal forebrain areas considered above is increased by the fact that each area grades almost imperceptibly with adjacent areas.
Johnston (1923) comparing the basal forebrain areas of various vertebrates demonstrated the phylogenetic progression of complexity, compactness, and the gradations of forebrain nuclear groups. In the turtle the bed nucleus of the diagonal band is composed of a small number of cells and the nucleus is distinct. In the oppossum the nucleus fuses with the amygdala. The bed nucleus in the rabbit is situated on the posterior aspect of the olfactory tubercle, below the preoptic area, lateral to the hypothalamus and optic chiasma. Fascicles of the medial forebrain bundle are interspersed through the bed nucleus, and in the lateral caudal aspect this nucleus fuses with the central and medial amygdala (Johnston, 1923). The bed nucleus of the diagonal band of the rat is described by Price and Powell (1970a) as consisting of two divisions, a vertical limb and a horizontal limb. The large cells of the horizontal limb have branching dendrites which radiate from the cell body in all directions and form a complex, dense plexus. The axons of some of the large multipolar cells of the horizontal limb course laterally towards the posterior aspect of the lateral olfactory tract (Price, 1969; Price and Powell, 1970a). These fibers, upon reaching the LOT, course rostrally deep to the LOT and in the superficial plexiform region of the
overlying cortex. They terminate principally in the granule cell layer and external plexiform layer of the homolateral olfactory bulb (Powell et al., 1965; Price, 1968, 1969; Price and Powell, 1970a, 1970b). These centrifugal fibers have the most caudal origin of the anatomically-defined, rostrally-directed fiber systems terminating in the olfactory bulb. Cragg (1962) reported centrifugal fibers to the olfactory bulb but could not define their precise origin. He suggested that these fibers might arise from the prepiriform cortex. Heimer (1968) reported similar possible origin for the observed centrifugal fibers. Price and Powell (1970a) emphasize that the origin of the centrifugal fibers associated with the deep aspect of the LOT arise in the horizontal portion of the bed nucleus of the diagonal band. They acknowledged that other nuclei may be involved in the centrifugal system, but such fibers were not detected due to the limitations of the Fink-Heimer (1967) method in which trans-synaptic degeneration cannot be observed.

Early anatomical investigations revealed centrifugal fibers arising within the ipsilateral basal forebrain. These fibers coursed in the anterior limb of the anterior commissure and terminated within the olfactory bulb (Cajal, 1911; Allison, 1953). Recently Valverde (1965) and Hirata (1965) demonstrated that the
prepirciform cortex contributes fibers to the anterior commissure. The anterior commissure is only one aggregate of centrifugal fibers to the homolateral olfactory bulb. Two other sources of centrifugal fibers are present. In addition to the commissural fibers arising from the contralateral anterior olfactory nucleus reported by Lohman (1963), Valverde (1964c), Powell et al. (1965), and Ferrer (1966, 1967), there are axon collaterals from the LOT (Lohman and Lammers, 1967; Price and Powell, 1970b). The third group are those fibers which course in proximity to the LOT (Cragg, 1962; Powell and Cowan, 1963; Powell et al., 1965; Price, 1969; Price and Powell, 1970a, 1970b). General agreement exists as to the terminal distribution of the centrifugal inputs to the olfactory bulb, in both electron microscopic and light microscopic studies, but the location of cell bodies of neurons constituting the centrifugal system is controversial. The hypothesis of a multinuclear origin for the centrifugal system, involving the corticomedial amygdala, the horizontal portion of the bed nucleus of the diagonal band, the olfactory tubercle, the anterior olfactory nucleus, and periamygdalar and prepirciform cortices, seems most favorable on the basis of the reported anatomical data (Cragg, 1962; Heimer, 1968). Such a hypothesis is further strongly supported by
the accumulated electrophysiological data (Kerr and Hagbarth, 1955; Dennis and Kerr, 1968).

**ELECTROPHYSIOLOGICAL BACKGROUND:**

Early electrophysiological studies involved direct electrical stimulation of the areas of distribution of the lateral olfactory tract, and the effects of such stimuli upon the electrical activity (intrinsic, electrically induced, or odor induced activity) of the olfactory bulbs (Kerr and Hagbarth, 1955). Two general classes of responses were detected: (1) antidromic responses and (2) orthodromic responses. An antidromic response can be recorded from the olfactory bulb by electrical stimulation of the axons of mitral cells which constitute the LOT. The propagation of an action potential proceeds in all directions along the neuron from the point of excitation, but it will stop at synapses where the excited neuron is the postsynaptic component of the synapse. This type of response can be evoked at high stimulus frequencies and has a short onset latency which is directly determined by the conduction velocity of the axon (Gasser and Erlanger, 1927; Davies, 1968). An orthodromic response involves the spread of excitation from dendrite to cell body to axon, and the excitation is propagated along a neuronal chain through synaptic activation. The onset latency of an orthodromic response is dependent upon
the conduction velocity of each neuron and the number of synapses which intervene between the points of stimulation and recording (Davies, 1968; Mountcastle and Baldessarini, 1968). The number of synapses limits the rate at which an orthodromically evoked response can be driven. In the electrophysiological studies both antidromic and orthodromic evoked responses have been utilized in an effort to define and study the mechanism through which the centrifugal system may regulate activity within the olfactory bulb.

Dennis and Kerr (1968) stimulated the prepiriform, periamygdalar, and parahippocampal cortices unilaterally and evoked negative polarity responses in both olfactory bulbs. The pyramidal cell layer of the piriform cortices (prepiriform, periamygdalar, and parahippocampal) demarked two regions, one deep and one superficial to this cell layer, from which evoked responses from both bulbs could be obtained. Stimulation of the lateral aspects of the areas of distribution of the lateral olfactory tract evoked responses in both olfactory bulbs. As the stimulating electrode was moved medially responses could be evoked only in the homolateral olfactory bulb. Stimulation of the anterior amygdaloid area and a portion of the corticomedial amygdala evoked neg-
ative polarity responses in the homolateral olfactory bulb (Dennis and Kerr, 1968).

Kerr and Hagbarth (1955) demonstrated that the intrinsic and odor induced activity of the olfactory bulbs could be altered by electrical stimulation of the areas of distribution of the lateral olfactory tract. The predominant effect was observed upon the activity recorded from the olfactory bulb opposite to the side of central stimulation. These authors reported frequency dependent facilitatory and inhibitory influences upon the intrinsic and odor induced activity, the principal effect being inhibitory. The ipsilateral olfactory bulb activity was only slightly enhanced or was not affected. The reported observations of Kerr and Hagbarth constitute an early attempt to study the centrifugal system of olfaction in light of its function. Fujita et al. (1964) have studied the effects of amygdalar stimulation and stimulation of the anterior limb of the anterior commissure upon the A-wave (electrically induced afferent wave) in the olfactory bulb. Stimulation of the lateral amygdalar area markedly inhibited the A-wave in the ipsilateral olfactory bulb. Stimuli applied to the medial aspect of the amygdala did not inhibit the A-wave. Two types of evoked responses were recorded from the olfactory bulb following
amygdalar stimulation. The $E_1$-wave was a biphasic short latency response obtained following stimulation of the medial aspect of the amygdala. This response was identical to the response evoked by direct stimulation of the lateral olfactory tract. The second response, $E_2$-wave, was monophasic and could be evoked by stimulating the lateral aspect of the amygdala or the plexiform region deep to the lateral olfactory tract (Fujita et al., 1964). Amygdalar stimulation coupled with repetitive stimulation of the mesencephalic reticular formation produced a prolonged inhibition of the electrically evoked A-wave. Stimulation of the anterior limb of the anterior commissure had a reductive effect on A-wave amplitude only while the stimulus was applied. There was no prolonged inhibition of the A-wave after stimulation. This also held for combined mesencephalic and anterior commissure stimulation. Yamamoto (1961) studied the effect of anterior commissure stimulation on the electrically evoked response (electrical stimulation of the olfactory mucosa) in the olfactory bulb. The intrinsic activity of the olfactory bulb and the evoked olfactory bulb response following mucosal stimulation were suppressed during stimulation of the anterior commissure. The evoked response recovered rapidly, and the intrinsic activity showed an enhance-
ment 500 msec after cessation of the anterior commissure stimulus. Yamamoto (1961) concluded that the evoked olfactory bulb response following olfactory mucosal stimulation was of postsynaptic origin. The A-wave of Fujita et al. (1965) and the response designated by Yamamoto (1961) as N_1 and N_2 are the resultant of electrical events involving several cellular elements: (1) mitral cells, (2) tufted cells, and (3) granule cells of the olfactory bulb, since the recording electrodes were deep within the olfactory bulb. The effect of the anterior commissure upon the activity within the olfactory bulb might be attributed to its input upon the granule cells of the olfactory bulb (Baumgarten, Green, and Mancia, 1962; Green, Mancia, and Baumgarten, 1962; Price and Powell, 1970).

The granule cells in the core of the olfactory bulbs were shown by Callens (1965) to be regulated in part by the prepiriform cortex on one side. Stimulation of the prepiriform cortex facilitated, inhibited, or had no effect upon the activity of the granule cells tested. Stimulation of the olfactory bulbs was shown to either augment or depress the excitability of cells in the prepiriform cortex. Clear facilitatory and inhibitory relationships appear to exist between the olfactory bulbs and the
primary olfactory cortices. The functional relationships seem to be mediated through orthodromic activation of the cellular elements of the bulb by the anterior commissure and centrifugal fiber system associated with the areas of distribution of the lateral olfactory tract or by antidromic activation of the lateral olfactory tract (Kerr, 1960; Baumgarten et al., 1962; Fujita et al., 1964; Callens, 1965).

Green et al. (1962) investigated the possibility of regulation (inhibition) of cellular activity in the olfactory bulb through the mechanism of recurrent axon collaterals of mitral cells. They defined inhibition as the reduction of spontaneous firing of the neurons being monitored. Antidromic stimulation of the lateral olfactory tract resulted in: (1) the rapid onset of inhibition (blocks antidromic invasion since onset of inhibition was not much greater than the conduction time of mitral cell axons), (2) inhibition following stimulation at frequencies at which an interneuron could follow but transiently, (3) massive inhibition which involved all cell types, and (4) prolonged inhibition. These observations led to the conclusion that direct inhibition by axon collaterals had occurred and that involvement of interneurons was unlikely. The activity of mitral cells can be inhibited as shown but the mechanism
was disputed. Yamamoto, Yamamoto, and Iwama (1963) recorded from granule cells an excitatory postsynaptic potential (EPSP) of shorter onset latency than the inhibitory postsynaptic potentials (IPSP) recorded from mitral cells following stimulation of the lateral olfactory tract. These authors observed that the granule (deep cell layer) response had features that were common with Renshaw cells. The latency and the configuration of the IPSP (mitral cell) suggested that a rhythmically excited neuron of the deep cell layer (granule cell) makes an inhibitory synapse with the mitral cell. Shepherd (1963) reported that the suppression of mitral cell excitability following direct stimulation of the lateral olfactory tract and the suppression of mitral cell activity following afferent volleys applied to the olfactory nerves are very similar. Antidromic volleys from the lateral olfactory tract also suppressed the spontaneous discharge of the glomerular short-axon cells, and since these cells are inhibited they are not involved in suppressing mitral cell activity. The active elements were tentatively identified as granule cells and tufted cells (Shepherd, 1963; Yamamoto et al., 1963; Rall et al., 1966; Nicoll, 1969).

The granule cells and the pars rostralis of the
anterior olfactory nucleus comprise the massive cellular core of the radially symmetrical, laminated, ellipsoid olfactory bulb. The mitral cell layer (lamina) is separated from the granule cell core by the internal plexiform layer and separated from the glomerular area by the external plexiform layer (Cajal, 1911; Lohman and Lammers, 1967). The external plexiform layer is the location for synapses between ascending processes of granule cells, secondary dendrites of mitral cells and tufted cells (Cajal, 1911). Centrifugal fibers have also been reported to terminate in this area (Price and Powell, 1970b). Much of the electrophysiological data on the electrical activity in the bulbs suggested dendritic interactions (Rall et al., 1966). Theoretical analysis of the generation of potentials within the olfactory bulb also suggested dendro-dendritic synapses between mitral cells and granule cells (Rall, 1964; Rall et al., 1966). Dendro-dendritic synapses and reciprocal synapses have been observed in the olfactory bulb (Rall et al., 1966; Price, 1969; Hinds, 1970; Price and Powell, 1970b, 1970c). The ultrastructure of these synapses revealed paired synapses of opposite polarities on the gemmule or spine (Price and Powell, 1970a, 1970b, 1970c). In other words, the mitral cell dendrite membrane would be presynaptic in one of the paired synapses and
postsynaptic for the other synapse. These synapses are characteristic of synapses of other regions of the nervous system but differ among themselves in terms of their morphology and function (Gray, 1959, 1969; Gray and Guillery, 1966). The mitral to granule synapse has a thickened postsynaptic membrane; while the granule to mitral synapse has no thickened postsynaptic membrane, the synaptic cleft is wider and fewer synaptic vesicles are observed (Rall et al., 1966). Price and Powell (1970b, 1970c) report two additional classes of synapses involving mitral, tufted, and granule cells. Asymmetrical synapses with spheroid synaptic vesicles are situated predominantly upon spines, gemmules, and varicosities of granule cell processes. Symmetrical synapses with flattened vesicles occurred on the shafts of gemmule studded peripheral processes, on deep processes, and on the cell bodies of granule cells. Those fibers of extrinsic origins (centrifugal, fibers from the anterior commissure, and collaterals from the anterior olfactory nucleus) showed only asymmetrical synapses. The centrifugal fibers synapse on spines and gemmules of peripheral processes of the granule cell in the deep aspect of the external plexiform layer. Fibers of the anterior commissure terminated on the deep processes and on some of the granule cells.
The recurrent collaterals from the anterior olfactory nucleus terminated on the most distal parts of the peripheral processes of granule cells. The symmetrical synapses and the reciprocal synapses occurred predominantly between intrinsic elements (mitral, granule, short axon, tufted) of the olfactory bulbs (Price and Powell, 1970c, 1970d, 1970e). Distinct functions have been proposed for the reported types of synapses. The asymmetrical synapses with flattened vesicles are thought to be excitatory, while the symmetrical synapses with spheroidal vesicles are inhibitory (De Iraldi, Duggan, and De Robertis, 1963; Rall et al., 1966; De Robertis, 1967). The asymmetrical terminals upon granule cells may serve to excite this cell which in turn can alter the excitability of those cells in the olfactory bulb which have functional contact with the granule cells. The electrophysiological data and the resultant computations and theoretical reconstructions of electrical events suggest that the granule cell plays a role as an inhibitory interneuron (granule or mitral cell interaction) and that it may serve to integrate several inputs (Rall et al., 1966).

SUMMARY:

The anatomical and electrophysiological data reviewed above gives credence to the existence of a centrifugal system in olfaction. The centrifugal
system in olfaction of the rat has been studied by electrophysiological and neuroanatomical techniques in the present study. The specific problems were: (1) to identify those forebrain nuclear centers and fiber pathways constituting the centrifugal system to both olfactory bulbs, (2) to study the interactions of these centers in reference to their effects upon the electrical activity in both olfactory bulbs, (3) to consider the interactions and effects of these nuclear groups upon their respective electrical activities following electrical stimulation of the olfactory bulb, and (4) to determine if the periamygdalar cortex contributes direct centrifugal fibers to the ipsilateral olfactory bulb. Electrophysiological methods were used to answer the first three problems while a neuroanatomical method, in particular the Fink-Heimer (1967) procedure, was employed in conjunction with electrophysiological techniques to resolve the last problem.

The neuroanatomical and electrophysiological data with regards to the centrifugal system and the conclusions drawn from each discipline are frequently at odds. The anatomical data suggests a restricted origin while the electrophysiological data reveals a more widespread origin of centrifugal fibers from the phylogenetically ancient sensory systems (Heimer,
1968). The technical demands and technique limitations related to the problem of defining and studying the inter-relationships of nuclear groups suspected of contributing neurons to the centrifugal system favored the methods employed in the present study. A carefully designed and thorough exploration of the basal forebrain, with emphasis placed on the areas of distribution of the lateral olfactory tract, might reveal more detailed collections of neuronal centers and related fiber pathways which when stimulated are capable of altering the electrical activity of one or both olfactory bulbs. The electrophysiological definition of nuclear groups can be correlated with the anatomical data, while the observations of altered electrical activity in the olfactory bulb provides evidence in support of a functional hypothesis. A structural basis and a functional basis for a centrifugal system in olfaction is provided by the results of the present study. With this information it is possible to study the effect of the centrifugal system upon odor induced activity in either olfactory bulb. It is then possible with this basic information to do single unit studies where the alterations on specific cells can be observed rather than changes in gross electrical activities. Behavioral studies might be designed on the basis of the centrifugal system in an
effort to determine its role in odor detection or odor discrimination. A firm understanding of the components of the centrifugal system and an insight into the function of such a system is a significant step towards the ultimate resolution of the problem of the mechanisms whereby the central nervous system controls and regulates the degree of sensory input.
METHODS

In the present work 103 Charles River male rats weighing 250-550 g were utilized. The animals were housed two to a cage with food and water available ad libitum. Two general classes of animals were utilized in the electrophysiological portion, normal acutes and chronic lesioned acutes. All acute preparations were anesthetized with sodium pentobarbital (Nembutal) at 35-40 mg/kg, ip with supplementary injections over the course of the experiment (Lumb, 1963; Ben, Dixon, and Anderson, 1969). Atropine sulfate (1/300 g, ip) was administered with the initial anesthetic and periodically throughout the experiment to lessen the development of respiratory problems and the resultant anoxia. If respiratory problems developed the preparation was treated with atropine and artificially respired. If the respiratory problem persisted the experiment was terminated.

The lesions in the chronic preparations were placed in various nuclear centers and fiber tracts. Three methods were employed: surgical transection of the structure, radio-frequency (rf) generated lesions, or direct current (d-c) lesions (Rowland, 1966).
The lesion electrodes were stereotaxically placed using the atlas of Pellegrino and Cushman (1967). The cutting electrode used to make surgical transections or isolation of whole nuclei was constructed from an 18 gauge needle, a piece of hollow stainless steel tubing (Tube Sales, Los Angeles), and a size 1 or 0 insect pin (Clay Adams Co.). The needle served as the mounting strut. The insect pin was bent into the desired configuration and mounted into the hollow tube. This unit was placed into the 18 gauge needle and was free to move 360° on the vertical axis but was held rigidly in all other planes. The entire unit was mounted on a stereotaxic holder and zeroed according to the standard procedures. The unit was stereotaxically placed, the cut made, and the unit withdrawn in the same plane as that of entry.

Bipolar side by side electrodes were utilized in the production of the rf or electrolytic (d-c) lesions. These electrodes were constructed from hollow stainless steel tubing and double or triple 0 insect pins (Clay Adams Co.). The end of the tubing was rounded, and the pin and tubing were held together by compressing the pin within the tube. Each single electrode was insulated with Insl-x (Insl-x Inc.), and only the tips of these electrodes were exposed. The single electrodes were approximated, separated by one layer of electri-
cians tape, wrapped several times with the tape, and mounted as a unit on a stereotaxic electrode holder. The tips were less than 1 mm apart. The side by side bipolar electrodes were stereotaxically placed and were used first as stimulating electrodes and then as lesion electrodes in the following procedure. To produce lesions in structures such as the lateral olfactory tract, the anterior commissure, or other neural areas which when stimulated evoke specific and characteristic responses in the homolateral olfactory bulb, the following technique was employed. With a dental burr (#1) a small opening was made over the homolateral olfactory bulb (between the supra-orbital ridges) and a hole was opened at the site for insertion of the stimulating-lesioning electrodes. A micro-electrode was inserted into the bulb with the tip being approximately just under the exposed dura. The structure in which the lesion was to be placed was localized and identified through its characteristic evoked response recorded from the olfactory bulb. The structure was localized by reducing the stimulus strength to the smallest value which produced a consistent response followed by manipulation of the stimulating electrodes to obtain the maximal response. Each electrode in the pair was used as the anode and 250 μamp d-c current was passed for 30 sec. The current delivered was
calculated from the voltage drop across a 10 kilo-
ohm resistor placed in series with the preparation.
Post-operatively the chronic preparations were treated
with oxytetracycline (Terramycin 2 mg/kg im) and
allowed to recover for at least three weeks (Allison,
1953).

In acute preparations the anesthetized animal
was placed in the stereotaxic instrument, and the points
of contact were infused with lidocaine hydrochloride
(Xylocaine, 2% subcutaneously). The dorsum of the
cranium was exposed and the desired areas of bone were
removed with a dental burr and a fine rongeur. The
cranial vault was opened bilaterally and a mid-sagittal
strip of bone was left in place to protect the sagittal
sinus. Both olfactory bulbs were exposed. The dura
was kept moist with physiological saline until it was
opened, and the electrodes had been placed. Mineral
oil was used to prevent dessication after the electrodes
were placed. The dura was not opened above the olfactory
bulbs; instead the fine recording electrode was passed
through the dura. Damage to the olfactory bulbs was
minimized by this method.

The stimuli delivered to the preparation consisted
of either monopolar square wave single shocks or
repetitive pulses of controlled frequency and duration.
The single shock stimuli had a duration of 1 msec and
a repetition rate of 1 Hz. They were uniformly applied at twice the determined threshold voltage. The stimulus voltage range utilized was 2 to 10 volts, and the stimulus was applied through electrodes with resistances in the range of 100-150 kilo-ohms. A tetanic volley was delivered for 15-20 sec during the test for post-tetanic potentiation. The frequency of the tetanic stimulus was 10 Hz; each individual shock had a duration of 1 msec and a magnitude of twice threshold voltage. Repetitive pulse bursts of controlled frequency and duration were employed in the interaction studies. The burst was 20 msec in duration and was delivered once per second. Four to five individual shocks were contained within the burst, and each had a duration of 0.5 msec and a magnitude of twice threshold voltage.

The electronic equipment used for stimulating consisted of a Tektronix 162 wave form generator, a Tektronix 161A pulse generator and a Bioelectric Type ISB 2.5 isolator. The wave form generator was used to trigger the sweep of the Tektronix type 565 oscilloscope and to drive the pulse generator with a sawtooth waveform voltage. The waveform generator controlled the repetition rate at which the scope and pulse generator were driven. The pulse generator provided the means to regulate the duration and
amplitude of the stimulus as well as the delay in delivery of the pulse. The pulse was passed to an isolation unit and then delivered to the preparation (refer to Fig. 1a, Fig. 1b).

Figure 1. A: Schematic for generation and delivery of single pulses and for recording evoked responses.
B: Schematic for generation and delivery of bursts and single pulses and for recording evoked responses.
The evoked responses obtained from the olfactory bulbs and other recording sites were passed to a pre-amplifier (Tektronix 122A) with a band pass of 0.8 Hz to 1 KHz, with a gain of 1000 X. The signal was passed to a Tektronic 3A3 or 3A47 plug-in unit and displayed on a Tektronix type 565 oscilloscope. A model C4N Grass camera was mounted so that 35 mm paper base (Kodak Kind-1732 Paper) records could be taken of the responses displayed. In all records presented an upward deflection represents a response of positive polarity.

At the end of each experiment each stimulating or recording electrode position was marked by passing 100 uamp d-c current for 10-15 sec. The animal was given an overdose of the anesthetic, exsanguinated with a 0.9% saline solution and fixed with 10% neutral buffered formalin delivered through intracardiac perfusion. A 1% solution of potassium ferrocyanide was utilized for the Prussian Blue reaction to the iron deposited at the electrode tip (Green et al., 1962).

Histological confirmation of lesion, stimulation, and recording sites was carried out utilizing several different approaches. The method of Guzman, Alcaraz, and Fernandez (1958) was used for rapid generalized localization of electrode tips. This involved cutting 48 u frozen sections from formalin fixed, 20% alcohol
soaked tissue blocks. The unstained sections were wet-mounted on a glass slide and placed in a photographic enlarger. Positives were printed for the desired lesion containing sections. Detailed studies of brains were carried out on paraffin or parlodion embedded brains. Paraffin serial sections, 10 μ thick were made and the desired sections were mounted and stained with either toluidine blue, hematoxylin and eosin or cresyl violet (Nissl) (Barka and Anderson, 1963; Lillie, 1965). The parlodion blocks were cut at 15 μ on a sliding microtome and stored serially on numbered onion skin paper in 95% ethanol. Each section was stained, cleared in terpinol, and mounted from xylene. Photomicrographs were taken of desired sections. Lesion sites were also plotted to determine their extent.

The anatomical portion of the present study was designed to determine the presence and course of centrifugal fibers directed towards the olfactory bulb. Stimulating electrodes were placed on the cortical aspect of the cortical and medial amygdaloid nuclei of five rats. A recording electrode was placed in the ipsilateral olfactory bulb and a response was evoked following amygdalar stimulation. Once the response was obtained electrolytic lesions were generated by passing 250 μamp d-c current for 30 sec
at five positions on the cortical aspect of the amygdala. The preparations were sacrificed at 2, 4, 6, and 8 days post-lesion respectively. The sham was sacrificed 4 days after the surgical procedures. The animals were perfused with 10% neutral buffered formalin. The brains were left within the cranial vault for several days, then removed and allowed to fix for 2 weeks. The brains were then cut into para-sagittal strips 2 mm thick and placed in a mixture of 10% formalin and 35% sucrose. Each block was cut using the freezing microtome and the 40 µ sections were stored in 2% formalin. Every fifth section was stored in serial order (methods of Dr. J. D. Dunn). The contents of one of the five jars containing the sections were mounted serially on glass slides and were stained with toluidine blue. A second series was stained with hematoxylin and eosin. These staining procedures allowed description to be made as to the location and extent of the lesions. The remaining series were processed by the silver impregnation methods as described by Fink and Heimer (1967). The Fink and Heimer procedure is a modification of the original Nauta method for silver impregnation of degenerating axon cylinders and terminals. The modifications of the Fink-Heimer method were designed to increase the degree of silver impregnation of the degenerating axon cylinders and to suppress impregnation of normal...
fibers. A 0.05% potassium permanganate solution and a 0.5% solution urinyl nitrate sequence were employed to obtain the desired suppression of silver impregnation of normal neurons (Fink and Heimer, 1967).
RESULTS

The data is presented under the general headings (I) the ipsilateral centrifugal system, (II) the contralateral centrifugal system, (III) interactions between defined nuclear groups and interactions between centrifugal systems, and (IV) possible direct centrifugal fibers from periamygdalar cortex to the ipsilateral olfactory bulb.

Two apparent centrifugal systems exist in olfaction in the rat: the ipsilateral and the contralateral. The ipsilateral system includes (1) the cortical and medial amygdaloid nuclei, (2) the horizontal portion of the bed nucleus of the diagonal band, (3) the olfactory tubercle, (4) the pars medialis of the anterior olfactory nucleus, and (5) granule cell core of the corresponding olfactory bulb. These nuclear groups are interconnected as revealed through evoked response studies. Throughout the report the use of the term ipsilateral refers to structures or stimulation sites on the same side from which activity was recorded. The designation contralateral refers to structures or stimulation sites on the side opposite to that from which activity was recorded. A glossary
of abbreviations used can be found in the appendix.

I. IPSILATERAL SYSTEM:

A. Amygdalar Stimulation

A single pulse delivered to the corticomedial amygdaloid nuclei evoked a negative polarity response in the ipsilateral olfactory bulb. The onset latency of this response averaged 24 msec, and it was not evoked beyond the frequency range of 25-31 Hz. Post-tetanic potentiation was demonstrated (Fig. 2a, Table I, Graph I). The response evoked in the anterior olfactory nucleus (particularly pars medialis and to a lesser extent pars dorsalis and pars lateralis) was triphasic. The onset latency averaged 16 msec. The initial negative phase of the response was not evoked beyond the frequency range of 40-50 Hz, while the positive and second negative phases failed to follow amygdalar stimulation beyond 25-31 Hz. Post-tetanic potentiation was observed (Fig. 2b, Table I, Graph I). Two responses related to the centrifugal system were recorded from the olfactory tubercle. One was superior to or upon the pyramidal cell layer of the prepiriform cortex, the other was inferior to this cell layer. The negative polarity response recorded superior to or at the pyramidal cell layer had an average onset latency of 8 msec, could not be evoked beyond 40-50 Hz, and demonstrated post-tetanic potentiation. The second response had an average onset latency
Figure 2. Left half: response from olfactory bulb to stimuli applied to the periamygdalar cortex.

Right half: responses evoked by stimuli applied to the cortical amygdala, recorded from 1) olfactory bulb, 2) anterior olfactory nucleus, 3) olfactory tubercle, 4) horizontal limb bed nucleus of diagonal band.
<table>
<thead>
<tr>
<th>Area Stim.</th>
<th>Area Recd.</th>
<th>Average Onset Latency msec</th>
<th>Following Freq. Hz</th>
<th>% PTP and Dur. sec</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAC</td>
<td>IB</td>
<td>6</td>
<td>76-100</td>
<td>10% 5 sec</td>
</tr>
<tr>
<td>CAN</td>
<td>IB</td>
<td>24</td>
<td>25-31</td>
<td>200 to -52% 36 sec</td>
</tr>
<tr>
<td>CAN</td>
<td>AON</td>
<td>16</td>
<td>1st/2nd pos/neg. 40-50</td>
<td>146 to -242% 29 sec</td>
</tr>
<tr>
<td>CAN</td>
<td>OTpcl</td>
<td>8</td>
<td>40-50</td>
<td>146 to -30% 32 sec</td>
</tr>
<tr>
<td>CAN</td>
<td>OT1pcl</td>
<td>8</td>
<td>40-50</td>
<td>30 to -30% 10 sec</td>
</tr>
<tr>
<td>CAN</td>
<td>BNDB</td>
<td>7</td>
<td>62-76</td>
<td>41 to 3% 26 sec</td>
</tr>
</tbody>
</table>

Table I. Characteristics of the evoked responses recorded from ipsilateral forebrain nuclei and the olfactory bulb.
Graph I. Following frequencies of cortical amygdalar evoked responses in ipsilateral forebrain nuclei.

- CAN on IB
- CAN on AON
- CAN on OT (at pyramidal cell level)
- CAN on OT (inferior to pyramidal cell level)
- CAN on BNDB
of 8 msec and did not faithfully follow beyond 40-50 Hz. Post-tetanic potentiation was observed (Fig. 2c, 2d, Table I, Graph I). The response recorded from the horizontal portion of the bed nucleus of the diagonal band was biphasic with an average onset latency of 7 msec. It was not evoked beyond the frequency range of 62-76 Hz, and short duration post-tetanic potentiation was demonstrated (Fig. 2e, Table I, Graph I).

B. Olfactory Bulb Response to Extra-amygdalar Stimulation Sites

Stimulation of each of the above described nuclear groups produced characteristic responses in the ipsilateral olfactory bulb. The response to corticomedial amygdalar stimulation was previously described (Fig. 2a, 3a, Table II, Graph II). Stimulation of the bed nucleus of the diagonal band resulted in a monophasic negative polarity response in the ipsilateral olfactory bulb. The response had an average onset latency of 14 msec and was not driven beyond the frequency range of 40-45 Hz. Post-tetanic potentiation was demonstrated (Fig. 3b, Table II, Graph II). A monophasic negative polarity olfactory bulb response with an average onset of 10 msec was evoked by stimulation of the olfactory tubercle in the area of the pyramidal cell layer of the prepiriform cortex. The response was not evoked beyond the frequency range of 40-50 Hz, and post-tetanic poten-
Figure 3. Response evoked in ipsilateral olfactory bulb by stimulation of CAN, BNDB, OT, or AON.
<table>
<thead>
<tr>
<th>Area stim.</th>
<th>Area Recd.</th>
<th>Average Onset Latency msec</th>
<th>Following Freq. Hz</th>
<th>% PTP and Dur. sec</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAN</td>
<td>IB</td>
<td>24</td>
<td>25-31</td>
<td>200 to -52%</td>
</tr>
<tr>
<td>BNDB</td>
<td>IB</td>
<td>14</td>
<td>40-45</td>
<td>41 to 3%</td>
</tr>
<tr>
<td>OTpcl</td>
<td>IB</td>
<td>10</td>
<td>40-50</td>
<td>40 to 10%</td>
</tr>
<tr>
<td>AON</td>
<td>IB</td>
<td>4</td>
<td>50-62</td>
<td>246 to 10%</td>
</tr>
</tbody>
</table>

Table II. Characteristics of evoked responses recorded from the ipsilateral olfactory bulb.
Graph II. Following frequencies for evoked olfactory bulb responses by stimuli applied to ipsilateral CAN, BNDB, OT and AON.
tiation was demonstrated (Fig. 3c, Table II, Graph II). A single pulse applied to the pars medialis of the anterior olfactory nucleus evoked a monophasic negative response from the ipsilateral olfactory bulb. This response had an average onset latency of 4 msec and was not evoked beyond the frequency range of 62-76 Hz. Prolonged post-tetanic potentiation was not observed (Fig. 3d, Table II, Graph II). A pulse applied to the periamygdalar cortex superficial to the corticomedial amygdala evoked a large biphasic response in the ipsilateral olfactory bulb. The onset latency averaged 6 msec, and it was evoked through the frequency range of 76-100 Hz. Post-tetanic potentiation was observed but was of short duration (Fig. 2, Table I). Direct stimulation of the lateral olfactory tract evoked a triphasic or biphasic response in the ipsilateral olfactory bulb. The response had an average onset latency of 3 msec and was faithfully driven through 76-100 Hz. The biphasic response obtained following periamygdalar cortex stimulation was evoked over a wide area from anterior 3.3 mm to 5.8 mm and lateral 3.2 mm to 5.2 mm, but was restricted to 300-400 u vertical range. The response recorded from the ipsilateral olfactory bulb changed configuration from a biphasic to a monophasic negative response as the stimulating electrode passed from the cortex to the amygdala (Fig. 4, vertical 32.8
Figure 4. Change in evoked ipsilateral olfactory bulb response as stimulation electrode was elevated through the periamygdalar cortex into the cortical amygdala and through the amygdala.
to vertical 35.5). The monophasic negative response in the ipsilateral olfactory bulb was evoked over a vertical range which corresponded closely to the vertical extent of the cortical amygdaloid nucleus (Fig. 5). The polarity of the olfactory bulb response to corticomedial amygdalar stimulation was reversed as the recording electrode passed through the radially symmetrical bulb. The evoked response had a positive polarity when the tip of the recording electrode was situated at the inferior surface of the olfactory bulb (Fig. 6a, vertical 25.3). As the electrode was elevated through the olfactory bulb the amplitude of the response increased (Fig. 6b-d). At vertical 27.0 (Fig. 6e) the evoked response was biphasic. As the recording electrode was elevated still further the biphasic response assumed a monophasic negative polarity (Fig. 6f-k). The response was lost as the recording electrode reached the dorsal surface of the olfactory bulb (Fig. 6, Table III).

C. Forebrain Nuclei Which Respond to Amygdalar Stimulation but not Related to Ipsilateral Centrifugal System

Stimuli applied to the corticomedial amygdala evoked responses in the lateral hypothalamic area, the lateral parolfactory area, and the caudate nucleus. However, stimuli applied to these nuclear groups did not evoke responses within the ipsilateral olfactory bulb.
Figure 5  Changes in ipsilateral olfactory bulb response with elevation of the stimulating electrode through the cortical amygdala
Figure 6. An example of the inversion of the cortical amygdalar evoked olfactory bulb response as the recording electrode passed through the bulb.
<table>
<thead>
<tr>
<th>Depth in Bulb mm</th>
<th>+Peak Onset Lat. msec</th>
<th>-Peak Onset Lat. msec</th>
<th>+Peak Lat. msec</th>
<th>-Peak Lat. msec</th>
<th>Amplt.</th>
<th>uV</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.8</td>
<td>16</td>
<td>---</td>
<td>30</td>
<td>---</td>
<td></td>
<td>+160</td>
</tr>
<tr>
<td>4.6</td>
<td>14</td>
<td>---</td>
<td>33</td>
<td>---</td>
<td></td>
<td>+360</td>
</tr>
<tr>
<td>4.1</td>
<td>17</td>
<td>---</td>
<td>31</td>
<td>---</td>
<td></td>
<td>+440</td>
</tr>
<tr>
<td>3.6</td>
<td>16</td>
<td>---</td>
<td>30</td>
<td>---</td>
<td></td>
<td>+520</td>
</tr>
<tr>
<td>3.1</td>
<td>16</td>
<td>42</td>
<td>29</td>
<td>52</td>
<td>+230</td>
<td>-180</td>
</tr>
<tr>
<td>2.6</td>
<td>11</td>
<td>32</td>
<td>24</td>
<td>44</td>
<td>+110</td>
<td>-500</td>
</tr>
<tr>
<td>2.1</td>
<td>---</td>
<td>26</td>
<td>---</td>
<td>45</td>
<td>-700</td>
<td></td>
</tr>
<tr>
<td>1.6</td>
<td>---</td>
<td>27</td>
<td>---</td>
<td>41</td>
<td>-800</td>
<td></td>
</tr>
<tr>
<td>1.1</td>
<td>---</td>
<td>27</td>
<td>---</td>
<td>44</td>
<td>-1300</td>
<td></td>
</tr>
<tr>
<td>0.6</td>
<td>---</td>
<td>28</td>
<td>---</td>
<td>43</td>
<td>-1460</td>
<td></td>
</tr>
<tr>
<td>0.1</td>
<td>---</td>
<td>27</td>
<td>---</td>
<td>44</td>
<td>-600</td>
<td></td>
</tr>
<tr>
<td>0.0</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td></td>
</tr>
</tbody>
</table>

Table III. Characteristics of the corticomedial amygdalar evoked response in the ipsilateral olfactory bulb as the recording electrode passed through the olfactory bulb.
D. Effects of Chronic Lesions

An extensive dorsal hemispherical isolation of the amygdaloid complex on one side produced no major change in the corticomedial amygdalar evoked ipsilateral olfactory bulb response. Changes were not observed in the olfactory bulb responses evoked by stimuli applied to centrifugal nuclei rostral to the amygdala in such a preparation (Fig. 7a). Destruction of the ipsilateral stria terminalis and the posterior limb of the anterior commissure had no affect upon the olfactory bulb response, or responses from other ipsilateral forebrain nuclei associated with the centrifugal system (Fig. 7a). Interruption of the lateral olfactory tract and the periamygdalar cortex rostral to the cortico-medial amygdala, at the level of and including the horizontal portion of the bed nucleus of the diagonal band, reduced the number of functional centrifugal fibers such that the olfactory bulb response to amygdalar stimulation appeared only sporadically. The responses evoked in the olfactory tubercle and anterior olfactory nucleus by corticomedial amygdalar stimulation were absent under the previously described conditions (Fig. 7b). Disruption of the lateral olfactory tract with encroachment upon the cortex superior to the tract reduced the amplitude but not the time course of the olfactory bulb response to amygdalar stimulation (Fig. 7c).
Figure 7. Effects of chronic lesions in basal forebrain structures upon ipsilateral centrifugal system (cont. next page)
Lesion destroying the pyramidal cell layer and plexiform layer prepiriform cortex at mid-tubercle level.

Six small lesions in the AON.

Figure 7. Effects of chronic lesions in basal forebrain structures upon ipsilateral centrifugal system.
Disruption of the polymorph, pyramidal cell and plexiform layers of the prepiriform cortex superior to the lateral olfactory tract at mid-olfactory tubercle levels blocked the evoked olfactory bulb response (Fig. 7d). Stimuli applied to structures caudal to the lesions failed to evoke ipsilateral olfactory bulb responses, but the typical responses in the bulb were obtained by stimulating those nuclear groups or parts of nuclear groups anterior to the lesion sites. The biphasic response in the olfactory bulb evoked by periamygdalar cortex stimulation was not observed following disruption of the lateral olfactory tract.

Multiple lesions placed throughout the anterior olfactory nucleus reduced the amplitude of the amygdalar evoked olfactory bulb response, but the time course of the response was not drastically altered (Fig. 7e). Destruction of the anterior limb of the anterior commissure rostral to the olfactory tubercle and within the anterior olfactory nucleus had only a slight reductive affect upon the ipsilateral olfactory bulb response to amygdalar stimulation (Fig. 7a). The olfactory bulb response to olfactory tubercle stimulation was enhanced by destruction of the anterior commissure at the rostral end of the olfactory tubercle. The amygdalar evoked response recorded from the horizontal portion of the bed nucleus of the diagonal band
was present in those preparations with chronic lesions which spared the ventral outflow from the amygdala. The responses evoked in the olfactory tubercle by amygdalar stimulation were altered by disruption of the lateral olfactory tract caudal to the tubercle. The positive phase response recorded from the inferior aspect of the prepiriform cortex was absent. This response was also absent in preparations where the ipsilateral olfactory bulb had been chronically extirpated. Destruction of the lateral olfactory tract had no apparent affect upon the anterior olfactory nucleus response to amygdalar stimulation. Lesions placed in the body of the anterior commissure lateral to the bed nucleus of the stria terminalis, resulted in an increase in the magnitude of the ipsilateral centrifugal response evoked in the olfactory bulb on the side with the lesion. The time course of the evoked responses was not changed but their magnitude increased as compared to the corresponding response evoked by stimuli applied to the same structure on the non-lesioned side.

E. Summary

Stimulation of the corticomedial amygdala produced an evoked response in the horizontal limb of the bed nucleus of the diagonal band, the olfactory tubercle, the anterior olfactory nucleus, and the granule cell core of the ipsilateral olfactory bulb (Fig. 2,
Table I, Graph I). Stimuli applied to each of the above centers evoked monophasic negative polarity responses from the granule cell core of the corresponding olfactory bulb (Fig. 3). The rate at which the response in the olfactory bulb was faithfully driven increased as the site of stimulation was moved to more rostrally situated nuclear groups (Graph I, Graph II). Post-tetanic potentiation was observed for all the reported centrifugal system responses (Table I, Table II). The respective onset latencies of bulbar responses decreased as more rostral nuclear groups were stimulated (Table II).

II. CONTRALATERAL SYSTEM

A. Amygdalar Stimulation

Stimuli applied to the corticomedial amygdala evoked two responses in the opposite olfactory bulb. The first response was monophasic and of positive polarity with an average onset latency of 14 msec. The response was not evoked beyond the frequency range of 31-40 Hz and post-tetanic potentiation of short duration was observed (Fig. 8a, Table IV, Graph III). The second response consisted of an initial positive phase with an average onset of 18 msec and a contiguous large negative phase with an average onset latency of 40 msec. The negative phase was not evoked beyond the frequency range of 20-25 Hz, while the positive
Figure 8. Cortical amygdalar evoked responses recorded from 1) CB, 2) AON, 3) OT, 4) BNDB, and 5) BNST.
<table>
<thead>
<tr>
<th>Recording Site</th>
<th>Average Onset Latency msec</th>
<th>Following Freq. Hz</th>
<th>% PTP and Dur. sec</th>
</tr>
</thead>
<tbody>
<tr>
<td>CB</td>
<td>14</td>
<td>31-40</td>
<td>10% 10 sec</td>
</tr>
<tr>
<td>CB</td>
<td>18</td>
<td>pos. phase 31-40</td>
<td>280 to -50%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>neg. phase 20-25</td>
<td>30 sec</td>
</tr>
<tr>
<td>AON</td>
<td>13</td>
<td>25-31</td>
<td>------</td>
</tr>
<tr>
<td>OTpcl</td>
<td>10</td>
<td>25-31</td>
<td>77 to -8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>35 sec</td>
</tr>
<tr>
<td>BNDB</td>
<td>8</td>
<td>25-31</td>
<td>------</td>
</tr>
<tr>
<td>BNST ips.</td>
<td>6</td>
<td>40-50</td>
<td>260 to 100%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>30 sec</td>
</tr>
</tbody>
</table>

Table IV. Characteristics of responses evoked in nuclei of the contralateral centrifugal subdivision following stimuli applied to the corticomedial amygdala.
Graph III. Following frequencies for responses in nuclei of the contralateral system evoked by stimulation of the corticomedial amygdala.
phase was evoked to 31-40 Hz, and post-tetanic potentiation was observed (Fig. 8a, Table IV, Graph III). The response obtained from the opposite olfactory tubercle on the superior aspect of the prepiriform cortex was biphasic. The onset latency of the response averaged 10 msec, and it was not evoked beyond a frequency range of 25-31 Hz. Post-tetanic potentiation was observed (Fig. 8c, Table IV, Graph III). The response recorded from the ipsilateral bed nucleus of the stria terminalis had an average onset latency of 6 msec and was not evoked beyond the frequency range of 40-50 Hz. Post-tetanic potentiation was observed (Fig. 8e, Table IV, Graph III). Small amplitude, predominantly negative polarity responses were evoked in the contralateral bed nucleus of the diagonal band and the anterior olfactory nucleus. The response evoked in the bed nucleus of the diagonal band had an average onset latency of 8 msec, while the response from the anterior olfactory nucleus had an average onset latency of 13 msec. Neither of these responses were readily evoked by single pulses to the corresponding opposite amygdala, but they were apparent following bursts delivered to the respective corticomedial amygdala (Fig. 8b, Fig. 8d, Table IV). Responses were not detected from nuclear centers other than those reported.
3. Extra-amygdalar Stimulation Sites

A single pulse applied to one bed nucleus of the stria terminalis evoked a monophasic negative polarity response from the contralateral olfactory bulb. The response had an average onset latency of 12 msec and was not evoked beyond the frequency range of 31-40 Hz. Post-tetanic potentiation was observed (Fig. 9a, Table V, Graph IV). A monophasic negative polarity response was recorded from the anterior olfactory nucleus but was more apparent after bursts were applied to the contralateral bed nucleus of the stria terminalis. The onset latency averaged 8 msec, was not evoked beyond the frequency range of 31-40 Hz, and post-tetanic potentiation was observed (Fig. 9b, Table V, Graph IV). Single pulses or bursts applied to one bed nucleus of the stria terminalis evoked a monophasic negative response from the contralateral olfactory tubercle. The average onset latency was 8 msec, and the response was not evoked beyond the frequency range of 31-40 Hz. Post-tetanic potentiation was demonstrated (Fig. 9c, Table V, Graph IV). A monophasic negative polarity response was evoked in the contralateral bed nucleus of the diagonal band following stimulation of the opposite strial bed nucleus (Fig. 9d, Table V, Graph IV). The onset latency was 7 msec, and the response was not evoked beyond 31-40 Hz. Post-tetanic potentiation
Figure 9. Responses evoked from contralateral forebrain nuclei by stimuli applied to the bed nucleus of stria terminalis (BNST). a) contralateral olfactory bulb (CB), b) contralateral anterior olfactory nucleus (AON), c) contralateral olfactory tubercle (OT), d) contralateral bed nucleus of diagonal band (BNDB)
<table>
<thead>
<tr>
<th>Recording Site</th>
<th>Average Onset Latency msec</th>
<th>Following Freq. Hz</th>
<th>% PTP Dur. sec</th>
</tr>
</thead>
<tbody>
<tr>
<td>CB</td>
<td>12</td>
<td>31-40</td>
<td>94 to -3% 16 sec</td>
</tr>
<tr>
<td>AON</td>
<td>8</td>
<td>31-40</td>
<td>107 to 7% 17 sec</td>
</tr>
<tr>
<td>OTpcl</td>
<td>8</td>
<td>31-40</td>
<td>60 to 25% 10 sec</td>
</tr>
<tr>
<td>BNDB</td>
<td>7</td>
<td>31-40</td>
<td>46 to 19% 10 sec</td>
</tr>
</tbody>
</table>

Table V. Characteristics of responses evoked in the nuclei of the contralateral centrifugal subdivision following single pulses to the bed nucleus stria terminalis.
Graph IV. Following frequencies for responses in nuclei of the contralateral system evoked by stimulation of strial bed nucleus.
was observed.

C. Effects of Chronic Lesions

Once the midline was crossed the contralateral centrifugal systems distributed to nuclear groups of the ipsilateral system. The course of the contralateral system was determined by correlation of lesion studies and burst or interaction studies. The body of the anterior commissure was a significant and necessary structure. Destruction of this structure close to the midline, specifically medial to the bed nucleus of the stria terminalis ablated the deep biphasic response recorded from the core of the contralateral olfactory bulb (Fig. 10A). Disruption of the posterior limb of the anterior commissure and stria terminalis on the side of cortical amygdalar stimulation eliminated the biphasic response recorded in the core of the contralateral olfactory bulb. More specific lesions revealed that the stria terminalis had to be disrupted to lose the biphasic response in the contralateral olfactory bulb. Damage to the bed nucleus of the stria terminalis had the same effect as transection of the stria terminalis or disruption of the body of the anterior commissure (Fig. 10A). Destruction of the posterior limb of the anterior commissure and the anterior limb prior to its junction with the body had no affect. Removal of the olfactory bulb on the
Lesions in body of ant., commissure, or bed nuclei stria terminalis, or st: terminalis

Lesions in post. and ant. limbs of ant., commissure, ipsil. bulb removed

Figure 10. A: Chronic lesions which abolish responses from the contralateral centrifugal system
B: Chronic lesions with no effect upon the contralateral system
side of amygdalar stimulation was also without effect (Fig. 10B). Damage to the body of the anterior commissure or the posterior limb of the anterior commissure increased the magnitude of the monophasic positive polarity response evoked in the olfactory bulb on the side opposite the lesion. However the following frequency characteristic of the response and the onset latency remained unchanged. Lesions placed in the anterior olfactory nucleus at three locations did not alter the expression of the contralateral olfactory bulb response to corticomedial amygdalar stimulation.

D. Summary

Stimuli applied to the corticomedial amygdala evoked a response in the homolateral bed nucleus of the stria terminalis, the contralateral horizontal limb of the bed nucleus of the diagonal band, the contralateral olfactory tubercle, the contralateral anterior olfactory nucleus and the granule cell core of the contralateral olfactory bulb (Fig. 8). Stimuli applied to the bed nucleus of the stria terminalis evoked responses in the corresponding contralateral rostral structures as listed above (Fig. 9). Destruction of the stria terminalis, bed nucleus of the stria terminalis, or the body of the anterior commissure eliminated the contralateral evoked responses (Fig. 10A).
Lesions to more rostral structures on the side of corticomedial amygdalar stimulation, including removal of the olfactory bulb, did not alter the evoked response from contralateral nuclei (Fig. 10B). The onset latencies of the amygdalar evoked responses in respective nuclei of the contralateral system increased with the progressively more rostral location of the respective centers. The following frequency range to which the respective amygdalar evoked response recorded from the BNST, BNDB, OT, AON, and olfactory bulb decreased in respect to the more rostral location of these nuclei (Table IV). The onset latencies for strial bed nucleus evoked response recorded from the nuclei of the contralateral system increased with respect to the more rostral location of each nucleus. However, the responses recorded from the BNDB, OT, AON, and olfactory bulb following stimuli applied to the opposite bed nucleus of the stria terminalis (BNST) could be faithfully driven to the same frequency range of 31-40 Hz (Table V).

III. INTERACTION STUDIES:

The interaction studies are presented under two general categories: the ipsilateral and the contralateral. The first major category considers (1) the interactions between specific nuclei of the ipsilateral system as reflected through changes in the centrif-
ugally evoked olfactory bulb responses and (2) the effect of specific ipsilateral centrifugal nuclei upon the electrically induced centripetal input to areas receiving fibers from the olfactory bulb by way of the lateral olfactory tract. The second major category under interaction studies reports (1) the influence of the contralateral system upon the ipsilateral system, (2) the effects of the contralateral system upon the electrically induced centripetal input in the opposite olfactory bulb and the areas which receive input from the olfactory bulb by means of the lateral olfactory tract, and (3) effects of lesions.

A. Ipsilateral Division

1) Interactions Between Specific Nuclei

Several classes of interactive effects were apparent from comparisons of observed changes in the evoked olfactory bulb responses when single pulses were applied in close time proximity to pairs of ipsilateral forebrain nuclear centers. The four observed classes were (1) the influence of CAN and postero-medial OT and postero-medial OT and AON on the ipsilateral olfactory bulb (Tables VI and VII), (2) the influence of CAN and BNDB or CAN and AON upon the ipsilateral olfactory bulb (Tables VIII and IX), (3) the influence of BNDB and OT or BNDB and AON on the ipsilateral olfactory bulb (Tables X and XI).
and (4) the influence of CAN and antero-lateral OT on the ipsilateral olfactory bulb (Table XII). In Table XII the magnitude of the response was reported as the area enclosed between the response curve and baseline. The reported areas for the observed and predicted responses are expressed in relative units. To obtain the area of the predicted response for a particular time period between artifacts of the interacting nuclear test pair, the areas under the bulbar responses evoked by separate stimulation of each member of the test pair were algebraically summed. The artifacts of the separate responses were adjusted to the equivalent period of time between the artifacts of the tested pair.

The areas of the observed responses in the first class (paired CAN and postero-medial OT and postero-medial OT and AON) were 22% to 50% smaller than the predicted areas. The amplitudes of the observed responses were greater than the amplitudes of either individual response of the test pair. The peak latencies of the predicted and observed responses were the same. The inhibitory or occlusive effect was observed over a 0-50 msec range of inter-stimulus interval (Table VI and VII). The second class of interactive effects involved the test pairs CAN and BNDB or CAN and AON. The percent difference in the areas of the observed responses and predicted responses ranged from +17% to
<table>
<thead>
<tr>
<th>Time Between Artifact msec</th>
<th>Area Observed Curve (rel. unit)</th>
<th>Area Predicted Curve (rel. unit)</th>
<th>% Diff.</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>7.52</td>
<td>4.85</td>
<td>-35</td>
</tr>
<tr>
<td>5</td>
<td>8.80</td>
<td>6.87</td>
<td>-22</td>
</tr>
<tr>
<td>10</td>
<td>6.87</td>
<td>3.92</td>
<td>-42</td>
</tr>
<tr>
<td>19</td>
<td>6.94</td>
<td>5.11</td>
<td>-26</td>
</tr>
<tr>
<td>29</td>
<td>6.26</td>
<td>4.84</td>
<td>-29</td>
</tr>
<tr>
<td>40</td>
<td>6.78</td>
<td>4.15</td>
<td>-39</td>
</tr>
</tbody>
</table>

Table VI. Comparison of the relative areas of the observed and predicted responses from a single preparation for the test-pair CA N--postero-medial OT on IB.
<table>
<thead>
<tr>
<th>Time Between Artifacts msec</th>
<th>Area Observed Curve (rel. unit)</th>
<th>Area Predicted Curve (rel. unit)</th>
<th>% Diff.</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.70</td>
<td>1.41</td>
<td>-50</td>
</tr>
<tr>
<td>24</td>
<td>0.88</td>
<td>1.31</td>
<td>-33</td>
</tr>
<tr>
<td>34</td>
<td>0.70</td>
<td>0.99</td>
<td>-29</td>
</tr>
<tr>
<td>-50</td>
<td>0.82</td>
<td>1.09</td>
<td>-25</td>
</tr>
</tbody>
</table>

Table VII. Comparison of the relative areas of the observed and predicted responses from a single preparation for the test-pair OT--AON on IB.
-38% and +6% to -27% (observed vs. predicted). The amplitude of the observed responses was not less than the amplitude of either individual response of the test pair. Whereas the observed responses were consistently less than the predicted in the first class, here, both magnitude and direction of differences changed as inter-stimulus interval was changed. The negative peak latencies of the observed responses were less than the corresponding peak latencies of the predicted response (Table VIII and IX). The third class involved the test pairs BNDB and AON or BNDB and OT. Little or no difference was observed between the area of the observed response and the predicted response. The areas differed by +8% to -8% (BNDB and AON) and +8% to -15% (BNDB and OT). The amplitude of the observed responses was not less than the amplitude of either individual bulbar response from members of the test pair. The negative peak latencies of the predicted and observed responses were identical (Table X and XI). The final class consisted of the test pair CAN and antero-lateral OT. The area of the observed response equaled or exceeded that of the predicted response over the range of 0 to 50%. The maximal effect was observed when the two response artifacts over-lapped. The negative peak latencies of the observed response were 4 msec greater than the predicted, while the duration of the observed
<table>
<thead>
<tr>
<th>Time Between Artifact msec</th>
<th>Area Observed Curve (rel. unit)</th>
<th>Area Predicted Curve (rel. unit)</th>
<th>% Diff.</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.36</td>
<td>1.51</td>
<td>-10</td>
</tr>
<tr>
<td>3</td>
<td>1.81</td>
<td>1.71</td>
<td>+ 6</td>
</tr>
<tr>
<td>10</td>
<td>1.55</td>
<td>1.85</td>
<td>-16</td>
</tr>
<tr>
<td>18</td>
<td>1.60</td>
<td>1.97</td>
<td>-19</td>
</tr>
<tr>
<td>24</td>
<td>1.70</td>
<td>2.11</td>
<td>-19</td>
</tr>
<tr>
<td>30</td>
<td>1.51</td>
<td>2.00</td>
<td>-25</td>
</tr>
<tr>
<td>38</td>
<td>1.20</td>
<td>1.65</td>
<td>-27</td>
</tr>
<tr>
<td>45</td>
<td>1.11</td>
<td>1.44</td>
<td>-23</td>
</tr>
<tr>
<td>50</td>
<td>1.24</td>
<td>1.52</td>
<td>-18</td>
</tr>
<tr>
<td>55</td>
<td>1.30</td>
<td>1.49</td>
<td>-13</td>
</tr>
</tbody>
</table>

Table VIII. Comparison of the relative areas of the observed and predicted responses from a single preparation for the test-pair CAN--BNDB on IB.
<table>
<thead>
<tr>
<th>Time Between Artifact msec</th>
<th>Area Observed Curve (rel. unit)</th>
<th>Area Predicted Curve (rel. unit)</th>
<th>% Diff.</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.88</td>
<td>1.10</td>
<td>-20</td>
</tr>
<tr>
<td>6</td>
<td>1.00</td>
<td>1.19</td>
<td>-16</td>
</tr>
<tr>
<td>12</td>
<td>1.21</td>
<td>1.17</td>
<td>-0.1</td>
</tr>
<tr>
<td>22</td>
<td>1.04</td>
<td>1.68</td>
<td>-38</td>
</tr>
<tr>
<td>26</td>
<td>0.90</td>
<td>1.44</td>
<td>-38</td>
</tr>
<tr>
<td>36</td>
<td>0.94</td>
<td>1.10</td>
<td>-17</td>
</tr>
<tr>
<td>44</td>
<td>1.10</td>
<td>0.93</td>
<td>+17</td>
</tr>
<tr>
<td>56</td>
<td>0.89</td>
<td>1.34</td>
<td>-34</td>
</tr>
</tbody>
</table>

Table IX. Comparison of the relative areas of the observed and predicted responses from a single preparation for the test-pair CAN--AON on IB.
<table>
<thead>
<tr>
<th>Time Between Artifacts msec</th>
<th>Area Observed Curve (rel. unit)</th>
<th>Area Predicted Curve (rel. unit)</th>
<th>% Diff.</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.35</td>
<td>1.28</td>
<td>+5</td>
</tr>
<tr>
<td>12</td>
<td>1.04</td>
<td>1.13</td>
<td>-8</td>
</tr>
<tr>
<td>34</td>
<td>1.18</td>
<td>1.17</td>
<td>+1</td>
</tr>
<tr>
<td>48</td>
<td>1.04</td>
<td>1.01</td>
<td>+3</td>
</tr>
<tr>
<td>70</td>
<td>0.97</td>
<td>0.90</td>
<td>+8</td>
</tr>
</tbody>
</table>

Table X. Comparison of the relative areas of the observed and predicted responses from a single preparation for the test-pair BNDB--AON on IB.
<table>
<thead>
<tr>
<th>Time Between Artifacts msec</th>
<th>Area Observed Curve (rel. unit)</th>
<th>Area Predicted Curve (rel. unit)</th>
<th>% Diff.</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.95</td>
<td>1.08</td>
<td>-12</td>
</tr>
<tr>
<td>14</td>
<td>0.82</td>
<td>0.96</td>
<td>-15</td>
</tr>
<tr>
<td>22</td>
<td>0.81</td>
<td>0.88</td>
<td>-8</td>
</tr>
<tr>
<td>44</td>
<td>0.73</td>
<td>0.82</td>
<td>-11</td>
</tr>
<tr>
<td>56</td>
<td>0.85</td>
<td>0.79</td>
<td>+ 8</td>
</tr>
</tbody>
</table>

Table XI. Comparison of the relative areas of the observed and predicted responses from a single preparation for the test-pair BNDB--postero-medial OT on IB.
response exceeded the predicted by 16 msec (Table XII).

2) Effect of Ipsilateral Centrifugal Nuclei upon Centripetal Input to Areas Receiving Olfactory Afferents

Single pulses applied to the olfactory bulb evoked biphasic responses in those nuclear groups which received input from the lateral olfactory tract. Single pulses applied to the ipsilateral corticomedial amygdala inhibited the biphasic centripetal evoked response recorded from the olfactory tubercle. The inhibition was observed when the centrifugal response preceeded the centripetal response and the interactive period corresponded closely to the duration of the centrifugal response. The centripetal response was completely inhibited when the centrifugal response was initiated 6-8 msec prior to the centripetal response (Fig. 11a). A similar inhibitory effect was observed upon the centripetal response recorded from the horizontal limb of the bed nucleus of the diagonal band, when a pulse (20 msec, 200 Hz, repetition rate of 1/sec) was delivered to the ipsilateral corticomedial amygdala (Fig. 11b).

B. Contralateral Division

1) Contralateral System upon Ipsilateral System

Single pulses applied to the contralateral corticomedial amygdala or bed nucleus of the stria terminalis, when paired in close time proximity with single pulses
<table>
<thead>
<tr>
<th>Time Between Artifacts msec</th>
<th>Area Observed Curve (rel. unit)</th>
<th>Area Predicted Curve (rel. unit)</th>
<th>% Diff.</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>4.52</td>
<td>2.25</td>
<td>+50</td>
</tr>
<tr>
<td>3</td>
<td>4.87</td>
<td>3.88</td>
<td>+23</td>
</tr>
<tr>
<td>12</td>
<td>5.13</td>
<td>4.82</td>
<td>+6</td>
</tr>
<tr>
<td>25</td>
<td>4.19</td>
<td>4.18</td>
<td>0</td>
</tr>
<tr>
<td>30</td>
<td>3.79</td>
<td>3.40</td>
<td>+10</td>
</tr>
<tr>
<td>36</td>
<td>4.32</td>
<td>3.50</td>
<td>+21</td>
</tr>
</tbody>
</table>

Table XII  Comparison of the relative areas of the observed and predicted responses from a single preparation for the test-pair CAN--anterior-lateral OT on IB.
Figure 11.  

A: Inhibition of IB induced centripetal response from the OT by single shocks to the cortical amygdala  

B: Inhibition of IB induced centripetal response from the BNDB by a 20msec, 200Hz pulse to the cortical amygdala
to nuclei of the ipsilateral centrifugal system, demonstrated no repeatable effect. However, application of bursts (20 msec duration, 200 Hz, repetition rate 1/sec) to either the contralateral corticomedial amygdala or striatal bed nucleus paired at variable time intervals with single pulses to any of the four known ipsilateral centrifugal nuclei suppressed the response evoked in the ipsilateral olfactory bulb. A test pair was defined as the nucleus to which a burst was applied and the nucleus to which a single pulse was applied. There were eight test pairs considered. The suppression in general was more pronounced when the burst preceded the single pulse and when the ipsilateral response fell in the duration of the contralateral response. However, the suppression was not restricted to the period of the duration of the contralateral response, and the data presented was the average suppression over the test period of 0-400 msec. The effect of a sequentially applied test pair over an interartifact time delay of 0 to 400 msec (burst preceds single pulse) was to suppress the amplitude of the evoked ipsilateral centrifugal response in the olfactory bulb by 25%-43% or 18%-70% of its pretest amplitude (Tables XIII and XIV respectively). The greatest degree of suppression was manifested by the test pairs (contralateral CAN and ipsilateral OT and contralateral BNST and ipsilateral OT) being 43% and 70% respectively.
<table>
<thead>
<tr>
<th>Burst Site</th>
<th>Single Pulse Site</th>
<th>Recording Site</th>
<th>% Amplitude Change</th>
<th>Duration Post-burst Sup. min</th>
</tr>
</thead>
<tbody>
<tr>
<td>cCAN</td>
<td>ips. CAN</td>
<td>ips.Bulb</td>
<td>35</td>
<td>10</td>
</tr>
<tr>
<td>cCAN</td>
<td>ips. BNDB</td>
<td>ips.Bulb</td>
<td>25</td>
<td>2</td>
</tr>
<tr>
<td>cCAN</td>
<td>ips. OTpcl</td>
<td>ips.Bulb</td>
<td>43</td>
<td>3</td>
</tr>
<tr>
<td>cCAN</td>
<td>ips. AON</td>
<td>ips.Bulb</td>
<td>18</td>
<td>3</td>
</tr>
</tbody>
</table>

Table XIII. The suppressive effect of bursts applied to the contralateral corticomedial amygdala on the responses evoked in the ipsilateral olfactory bulb by single pulses applied to ipsilateral forebrain nuclei.
<table>
<thead>
<tr>
<th>Burst Site</th>
<th>Single Pulse Site</th>
<th>Recording Site</th>
<th>% Amplitude Change</th>
<th>Duration Post-burst Sup. min</th>
</tr>
</thead>
<tbody>
<tr>
<td>cBNST</td>
<td>ips. CAN</td>
<td>ips. Bulb</td>
<td>28</td>
<td>5</td>
</tr>
<tr>
<td>cBNST</td>
<td>ips. BNDB</td>
<td>ips. Bulb</td>
<td>29</td>
<td>3</td>
</tr>
<tr>
<td>cBNST</td>
<td>ips. OTpCl</td>
<td>ips. Bulb</td>
<td>70</td>
<td>5</td>
</tr>
<tr>
<td>cBNST</td>
<td>ips. AON</td>
<td>ips. Bulb</td>
<td>18</td>
<td>2</td>
</tr>
</tbody>
</table>

Table XIV. The suppressive effect of bursts applied to the contralateral striatal bed nucleus on the responses evoked in the ipsilateral olfactory bulb by single pulses to ipsilateral forebrain nuclei.
The amplitude of the respective bulbar response evoked by single pulses to the ipsilateral centrifugal nuclei regained its pretest amplitude slowly; the post-burst suppression ranged from 2 to 10 min. After an interaction test the pretest amplitude of the ipsilaterally evoked olfactory bulb response was readily potentiated following a short (3-5 sec) 10 Hz volley to the respective ipsilateral centrifugal nucleus.

The ipsilateral corticomedial amygdalar evoked centrifugal responses recorded from the anterior olfactory nucleus, olfactory tubercle, and horizontal limb of the bed nucleus of the diagonal band were suppressed by the test pairs contralateral CAN and ipsilateral CAN or contralateral BNST and ipsilateral CAN. The ipsilateral centrifugal responses were suppressed in the range of 34% to 45% less than their respective pretest amplitudes. The post-pulse depression period lasted 1 to 5 min (Table XV and XVI).

2) Effects of Contralateral Division upon Antidromically Evoked Olfactory Bulb Response and Orthodromic Bulbar Evoked Responses from Areas of Distribution of the LOT

Bursts applied to the nuclei of the contralateral system paired with single pulses applied to the lateral olfactory tract or olfactory bulb either increased the magnitude or had no affect upon the magnitude of the
<table>
<thead>
<tr>
<th>Burst Site</th>
<th>Single Pulse Site</th>
<th>Recording Site</th>
<th>% Amplitude Change</th>
<th>Duration Post-burst Sup. min</th>
</tr>
</thead>
<tbody>
<tr>
<td>cCAN</td>
<td>ips. CAN</td>
<td>ips. BNDB</td>
<td>45</td>
<td>2</td>
</tr>
<tr>
<td>cCAN</td>
<td>ips. CAN</td>
<td>ips. OTpol</td>
<td>34</td>
<td>5</td>
</tr>
<tr>
<td>cCAN</td>
<td>ips. CAN</td>
<td>ips. AON</td>
<td>36</td>
<td>1</td>
</tr>
</tbody>
</table>

Table XV. The suppressive effect of bursts applied to the contralateral corticomedial amygdala on the responses evoked in the BNDB, OT, and AON by single pulses to the ipsilateral corticomedial amygdala.
<table>
<thead>
<tr>
<th>Burst Site</th>
<th>Single Pulse Site</th>
<th>Recording Site</th>
<th>% Amplitude Change</th>
<th>Duration Post-burst Sup. min</th>
</tr>
</thead>
<tbody>
<tr>
<td>cBNST</td>
<td>ips. CAN</td>
<td>ips. AON</td>
<td>43</td>
<td>4</td>
</tr>
<tr>
<td>cBNST</td>
<td>ips. CAN</td>
<td>ips. OTpcl</td>
<td>40</td>
<td>3</td>
</tr>
<tr>
<td>cBNST</td>
<td>ips. CAN</td>
<td>ips. Bulb</td>
<td>28</td>
<td>5</td>
</tr>
</tbody>
</table>

Table XVI. The suppressive effect of bursts applied to the contralateral strial bed nucleus on the responses evoked in the ipsilateral AON, OT, and olfactory bulb by single pulses ipsilateral corticomedial amygdala.
responses recorded from the olfactory bulb or those nuclei which received an input from the LOT. The amplitudes of the centripetally related responses (those recorded from areas of distribution of the lateral olfactory tract) increased by 0 to 18%. The antidromically evoked olfactory bulb response increased by 28% as compared to the pretest amplitude. The amplitudes, if increased, remained elevated over a 1 to 3 min post-pulse period (Table XVII).

3) Effects of Lesions on Contralateral System

The general suppressive effect of the contralateral system upon the ipsilateral system was dependent upon an intact stria terminalis and body of the anterior commissure. Transection of these two structures or destruction of the bed nucleus of the stria terminalis abolished the suppressive effect. The inhibitory or suppressive effect was independent of the posterior limb of the anterior commissure and the anterior limb of the anterior commissure anterior to the olfactory tubercle. Disruption of the anterior limb at the junction with the body of the commissure had no apparent affect. Destruction of the lateral olfactory tract or ablation of the olfactory bulb had no influence upon the observed crossed suppression. Disruption of the anterior olfactory nucleus had no apparent affect upon the expression of the crossed inhibition or suppression.
Table XVII. The effect of bursts applied to either the contralateral corticomedial amygdala or strial bed nucleus on the centripetally or antidromically evoked responses ipsilateral forebrain nuclei.

<table>
<thead>
<tr>
<th>Burst Site</th>
<th>Single Pul. Site</th>
<th>Record Site</th>
<th>Preburst Ampl. uV</th>
<th>Max. Ampl. uV</th>
<th>% Diff. Ampl.</th>
</tr>
</thead>
<tbody>
<tr>
<td>right CAN</td>
<td>left Bulb</td>
<td>left OTpcl</td>
<td>1460</td>
<td>1720</td>
<td>+18</td>
</tr>
<tr>
<td>left BNST</td>
<td>right LOT</td>
<td>right Bulb</td>
<td>5150</td>
<td>6600</td>
<td>+28</td>
</tr>
<tr>
<td>left CAN</td>
<td>right Bulb</td>
<td>right CAN</td>
<td>1300</td>
<td>1300</td>
<td>+0</td>
</tr>
<tr>
<td>right CAN</td>
<td>left Bulb</td>
<td>left BNDB</td>
<td>1490</td>
<td>1560</td>
<td>+5</td>
</tr>
</tbody>
</table>
C. Summary

Four classes of interactive effects between pairs of ipsilateral centrifugal nuclei were observed. The response recorded from the areas of distribution of the lateral olfactory tract following single pulses applied to the ipsilateral olfactory bulb was inhibited by single pulses applied to the ipsilateral corticomedial amygdala. Maximum inhibition was observed when the amygdalar stimulus preceded the olfactory bulb stimulus, and the bulbar evoked response fell within the duration of the amygdalar evoked response. The contralateral system had a general suppressive influence upon all levels of the ipsilateral system with maximum effects expressed upon the olfactory tubercle. The contralateral system had no affect or increased the magnitude of the bulbar evoked centripetal response in those nuclei which received input from the lateral olfactory tract, and further increased the magnitude of the antidromic evoked response within the ipsilateral olfactory bulb. The general suppressive influence of the contralateral system was abolished by destruction of the strial terminalis, bed nucleus of the stria terminalis, or the body of the anterior commissure.

IV. POSSIBLE DIRECT CENTRIFUGAL FIBERS FROM PERIAMYGDALAR CORTEX TO IPSILATERAL OLFACTORY BULB

The question arose as to whether the biphasic
response evoked by stimulation of the periamygdalar cortex was orthodromic or antidromic; that is, were there cells in the periamygdalar cortex that sent their axons directly to the olfactory bulb? A short neuroanatomical study designed to answer the above question involved five rats with lesions placed in the periamygdalar cortex at sites where stimulation evoked a biphasic ipsilateral olfactory bulb response. The lesions when examined histologically were larger than expected and had encroached considerably upon the cortical and medial amygdala as well as disrupting a large area of periamygdalar cortex. No definable degeneration arising from outside of the bulb was observed in the ipsilateral olfactory bulbs in the 2 day, 4 day, 6 day, and 8 day preparations. Only limited degeneration attributed to the penetration tract of the recording electrode was observed. The degeneration consisted of a series of large silver droplets which extended diagonally from the dorsal surface of the olfactory bulb to the granule cell core. Some silver deposition was observed around the periphery of the olfactory bulbs, but it was also present in the sham animal.
DISCUSSION

I. INTERPRETATION OF EVOKED RESPONSE STUDIES

Two subdivisions of the amygdalo-bulbar centrifugal system in olfaction were defined. These are referred to as the ipsilateral and contralateral centrifugal subdivisions.

A. Ipsilateral Centrifugal Subdivision

The data in Section I of the results suggested that the ipsilateral subdivision consisted of five nuclear groups. These were (1) corticomedial amygdala, (2) horizontal limb of the bed nucleus of the diagonal band, (3) olfactory tubercle (pyramidal cell layer), (4) anterior olfactory nucleus, and (5) granule cell core of the ipsilateral olfactory bulb. The monophasic negative polarity response recorded from the granule cell core of the olfactory bulb resembled in polarity and recording site the monophasic responses reported by Fujita et al. (1964) and Dennis and Kerr (1968). The onset latencies of the bulbar responses elicited by stimuli applied to progressively more rostral centers shortened, being shortest for stimuli applied to the pars medialis of the AON and greatest for the cortico-medial evoked olfactory bulb response. The long onset
latency of the corticomedial amygdalar evoked olfactory bulb response, the inability of the response to be evoked beyond the frequency range of 25-31 Hz, and the prolonged PTP suggested the presence of at least one synapse between the corticomedial amygdala and the olfactory bulb. The onset latencies, the following frequency levels to which the response could be evoked, and the magnitude and duration of PTP for amygdalar evoked responses recorded in those nuclei previously shown to elicit a monophasic response in the bulb demonstrated a consistent pattern. The difference in onset latencies between the amygdalar evoked responses in the BNDB, OT, and AON might be attributed to the distance between stimulating and recording electrodes and also to the fact that as a fiber diameter decreases the conduction velocity also decreases (Gasser and Erlanger, 1927). These observations suggested that intervening synapses were situated in the BNDB, the OT at the pyramidal cell layer, and the AON. The distinct differences between characteristics of the amygdalar evoked bulbar response and the responses from the BNDB, OT, and AON further suggested that the corticomedial amygdala does not project direct centrifugal fibers to the bulb. Neuroanatomical studies, including those in this study, have consistently reported the absence of direct centrifugal fibers from
the corticomedial amygdala to the ipsilateral olfactory bulb (Price, 1969; Price and Powell, 1970f). Anatomical studies of corticomedial efferents report projections to the bed nucleus of the diagonal band, pyramidal cell layer of the prepiriform cortex and the anterior olfactory nucleus (Cowan et al., 1965; Valverde, 1965; Price, 1969).

The responses evoked in the bulb by stimuli applied to the BNDB, OT, and AON suggested that rostrally directed centrifugal fibers arise from these nuclei and course towards the olfactory bulb. The similarity between the characteristics of the bulbar response evoked by stimuli applied to the BNDB and OT seemed significant (Table II, Section 1, Results). The close similarity in the following frequency characteristics and in the magnitude and duration of the observed PTP suggested that centrifugal fibers from these nuclei either course directly to the bulb or have in their course a common synapse. The anatomical data of Price (1969) and Price and Powell (1970b) demonstrated the presence of centrifugal fibers arising in the horizontal limb of the bed nucleus of the diagonal band which terminated directly within the granule cell core of the olfactory bulb. Heimer (1968) also demonstrated direct tuberculo-bulbar centrifugal fibers which terminated in the granule cell core of the olfactory bulb.
An interpretation of the characteristics of the olfactory bulb response elicited by stimuli applied to the pars medialis of the anterior olfactory nucleus was complicated by the physical location of the structure and the intrinsic organization of this nucleus. The short onset latency was attributed to the close proximity of the AON and olfactory bulb. The change in the slope and the sustained elevation of the curve representing the relationship between the amplitude of the evoked response and the frequency at which the stimuli were applied was attributed to several possible factors (Graph II, Results). This nucleus, particularly the pars medialis, was restricted to the olfactory peduncle, and it was through the peduncle that centrifugal fibers reached the olfactory bulb (Price and Powell, 1970a). Valverde (1964c, 1965) had reported the presence of collaterals from neurons of the pars medialis which were directed into the core of the bulb. One possible interpretation was that the curve was the resultant of activation of both centrifugal fibers and collaterals from the pars medialis. With increased stimulus frequency the number of bulbar directed elements from this elongated nucleus and perhaps centrifugal fibers from the olfactory tubercle or diagonal band were excited. It was also possible that the bulbar input from the anterior olfactory nucleus involved fewer
of the complicated intrinsic synapses in the olfactory bulb itself, which could account for the increased rate at which the response was driven.

The data obtained from chronic lesion preparations suggested that the centrifugal fibers which arose from the nuclei considered, coursed rostrally along the basolateral aspect of the forebrain superficial to the allocortex close to the lateral olfactory tract. The ipsilateral centrifugal neurons in the corticomedial amygdala exit the amygdala through the ventral amygdalofugal system since dorsal hemispherical isolation of the amygdala did not affect the expression of the corticomedial amygdalar evoked responses from the BNDB, OT, AON, or ipsilateral olfactory bulb. The reduction in the amplitude of the amygdalar evoked response in the olfactory bulb following transection of the LOT suggested that a proportion of the centrifugal fibers course close to or in the tract. However, the absence of the bulbar responses following stimuli applied to nuclei caudal to lesions which involved the pyramidal cell layer, the plexiform layer, and the area between the cortex and the LOT suggested that the vast majority of the centrifugal fibers course in this area. It was of interest that stimuli applied to those nuclei rostral to both LOT lesion sites or lesions involving the prepiriform cortex, evoked the
characteristic monophasic negative polarity responses in the olfactory bulb. These observations suggested a widespread origin of centrifugal fibers and supported the hypothesis of Cragg (1962) and Heimer (1968). The present data suggested that the cell bodies of centrifugal neurons, outside of the LOT, were situated in specific nuclei rather than dispersed through the allocortex. This conclusion was based upon the observations that the only response evoked in the ipsilateral olfactory bulb by stimulation of the periamygdalar cortex was a biphasic response. The short 6 msec onset latency, the high stimulation rate at which the response was faithfully evoked (76-100 Hz), the limited degree of PTP, and the absence of the response through chronic transection of the LOT suggested that the response was evoked through antidromic activation of the lateral olfactory tract which terminates in the periamygdalar cortex. That the biphasic response was not orthodromically evoked was further supported by the neuroanatomical investigation (Section IV, Results) in the present study in which no degeneration could be traced from the periamygdalar cortex directly to the olfactory bulb. The suggested multiple nuclear origin of centrifugal fibers proposed in the present study is in contrast to the hypothesis of Price and Powell (1970a). The evoked response studies agreed with Price and
Powell (1970a) that the BNDB does contribute centrifugal fibers to the olfactory bulb, since a monophasic negative-polarity response was evoked in the bulb by stimuli applied to the BNDB. However, centrifugal responses were evoked in the olfactory bulb following stimuli applied to nuclear groups caudal and rostral to the BNDB in normal preparations. Centrifugal responses were also obtained in the bulb by stimuli applied to nuclei rostral to lesions which either destroyed the BNDB or the centrifugal fibers from this nucleus.

In a brief summary, the ipsilateral subdivision of the corticomedial amygdalo-bulbar centrifugal system in olfaction consists of five nuclei: (1) corticomedial amygdala, (2) horizontal limb of the bed nucleus of the diagonal band, (3) olfactory tubercle (pyramidal cell layer), (4) pars medialis anterior olfactory nucleus, and (5) granule cell core of the ipsilateral olfactory bulb. The centrifugal fibers from the amygdala coursed rostrally on the ventrolateral aspect of the allocortex close to the lateral olfactory tract. These fibers synapsed in the BNDB, OT, and AON. Centrifugal fibers from these nuclei proceeded on the basolateral aspect of the forebrain allocortex close to the LOT and terminated within the granule cell core of the ipsilateral olfactory bulb.
B. Contralateral Centrifugal Subdivision

The contralateral subdivision was composed of the corticomedial amygdala and the bed nucleus of the stria terminalis on one side and the nuclei of the opposite ipsilateral subdivision of the corticomedial amygdalo-bulbar centrifugal system. The stria terminalis interconnected the corticomedial amygdala with the ipsilateral strial bed nucleus. Anatomical reports of the origins of the stria terminalis agreed that the amygdala gave origins to components of the stria, but disagreements existed as to the exact nuclei of origin (Gurdjian, 1923; Fox, 1940; Nauta, 1961; Valverde, 1963c; Girgis, 1969; Ishikawa, Kawamura, and Tanaka, 1969). The contralateral response was shown independent of the more rostral nuclei of the ipsilateral system, including the olfactory bulb and the posterior limb and ipsilateral anterior limb of the anterior commissure in that complete disruption of these structures did not abolish the contralateral response. Either destruction of the stria, its bed nucleus, or the body of the anterior commissure abolished the biphasic contralateral olfactory bulb response. Disruption of these structures also eliminated the functional influences of the contralateral system which arose from the side of the brain with the lesion.

The evoked response recorded from the ipsilateral
bed nucleus of the stria terminalis by corticomedial
amygdalar stimulation showed post-tetanic potentiation.
This suggested a possible synapse either intra-amygdalar in nature (Brodal, 1947; Valverde, 1962) or
within the post-commissural gray of which the strial
bed nucleus was a part. The rate of amygdalar stimulation to which the strial bed nucleus faithfully responded
was greater than that for responses from the contra-
lateral olfactory bulb, AON, OT, and BNDB. The onset
latency was also shorter than the contrabulbar, AON, OT,
and BNDB onset latencies. This evidence was sufficient,
but not conclusive, that the strial bed nucleus was
associated with the contralateral system. Stimuli
applied to the strial bed nucleus, however, clearly
demonstrated the involvement of this nucleus. The onset
latencies for the responses evoked in the contralateral
horizontal limb of the bed nucleus of the diagonal
band (7 msec), the olfactory tubercle (8 msec), the
pars medialis of anterior olfactory nucleus (8 msec),
and the granule cell core of the olfactory bulb (12 msec)
suggested a progressively more rostral distribution of
a continuous fiber system with an origin associated
with the strial bed nucleus or post-commissural gray.
The rate of stimulation of the bed nucleus of the stria
terminalis, to which the responses from each contra-
lateral center failed to follow faithfully, was respec-
tively 31-40 Hz. The fibers were dependent upon the body of the commissure using it as a means of access to the contralateral forebrain since destruction of the body eliminated all contralateral responses related to the centrifugal system. The fiber collection appeared to be loosely associated with the anterior limb of the anterior commissure, perhaps coursing in the vicinity, since lesions of the anterior limb where it joined the body, had no affect upon the contralateral system either in terms of the evoked responses or of its functional effects. Since the described lesion had not encroached upon the region of the strial bed nucleus, it was possible that the contralateral centrifugal fibers arising from or passing through the strial bed nucleus entered the anterior limb over a diffuse area. The commissural subdivision of the stria terminalis as reported by De Olmos (1968) crossed the midline in association with the body of the anterior commissure and terminated in the nuclei comprising the commissural gray (bed nucleus anterior commissure, bed nucleus stria terminalis, bed nucleus medial forebrain bundle). Fibers were followed to and terminal degeneration observed in the prepiriform cortex of the olfactory tubercle and the medial and lateral amygdala. This single report was significant in that the lesions were placed in the amygdala (no specifications given), and that
degeneration was found in some of the contralateral nuclei (particularly olfactory tubercle) which, from the present electrophysiological study, appeared intimately associated with the contralateral system.

The available electrophysiological data, however, did not corroborate the observations of De Olmos (1968). Since the stimulation frequency range to which the contralateral olfactory tubercle response follows faithfully (25-31 Hz) when evoked by corticomedial amygdalar stimulation was less than the range for the tubercle response to BNST stimulation, an intervening synapse was thought to exist, perhaps in the BNST. The uniformity of the frequency range (31-40 Hz) beyond which the strial bed nucleus evoked response from the BNDB, OT, AON, and granule cell core of the olfactory bulb were not elicited suggested that the strial bed nucleus was the source for the contralaterally directed centrifugal fibers.

In a brief summary, the contralateral subdivision consisted of the corticomedial amygdala and the homolateral bed nucleus of the stria terminalis. The stria terminalis carried amygdalar efferents to the strial bed nucleus. A synapse occurred in the strial bed nucleus and the centrifugal fibers from this nucleus crossed to the opposite side of the brain in the body of the anterior commissure. The centrifugal fibers were distributed to the nuclei of the opposite ipsi-
lateral subdivision of the centrifugal system.

II. INTERPRETATION OF INTERACTION STUDIES (Section III, Results):
A. Ipsilateral Subdivision

The results of the interactive tests between pairs of ipsilateral nuclear centers distinguished the olfactory tubercle as an important interactive center. The observed interactive effects either occurred within the tubercle or within the olfactory bulb; however, the distinction could not be made. The posteromedial aspect of the olfactory tubercle appeared to have a different effect as compared to the anterolateral aspect of this structure. The anterolateral OT when paired with the corticomedial amygdala demonstrated an apparent facilitatory influence which may have occurred either in the bulb or at the olfactory tubercle. However, since the anterolateral aspect of the OT was not paired with nuclei other than the corticomedial amygdala, only a limited statement as to the possible interactive influence of this region was made. The consistent interactive influence between the test pair CAN—posteromedial OT or posteromedial OT—AON as expressed by changes in the area of the evoked and predicted response from the olfactory bulb suggested that these nuclei shared common neurons and constituted a distinct subsystem within the ipsilateral centrifugal
system. The proposed pathway involved centrifugal neurons arising in the corticomedial amygdala which synapsed in the olfactory tubercle. The centrifugal fibers from the tubercle projected to the granule cell core of the olfactory bulb and synapsed in addition in the pars medialis of the anterior olfactory nucleus. The anterior olfactory nucleus projected to the olfactory bulb (Fig. 12A, General Summary). The results of the test pairs BNDB--AON or BNDB--posteromedial OT as reflected by the small variation between the areas of the predicted and observed curves suggested a possible independence of the centrifugal input of the BNDB to the olfactory bulb.

A second possible subsystem whose centrifugal neurons arose in the corticomedial amygdala and synapsed in the BNDB which sent neurons directly to the olfactory bulb was proposed. This proposed subsystem was supported by the observation of Price and Powell (1970b) that the centrifugal fibers from the BNDB projected directly to the granule core of the ipsilateral olfactory bulb. The fluctuation between the observed and predicted areas of the bulbar responses evoked by the test pairs CAN--BNDB or CAN--AON could be attributed to an indirect activation of the olfactory tubercle. Single pulses applied to the corticomedial amygdala could directly activate
the OT, while stimuli applied to the BNDB could first excite the corticomedial amygdala which then expressed an influence upon the OT. In the case of the test pair CAN--AON, the OT could also be activated following amygdalar pulses. The observation that the amplitudes of the evoked bulb response obtained in the interactive studies was never less than either response elicited by stimuli to the respective members of the test pair suggested that inhibition had not occurred. Since the observed response was smaller than the predicted response but never less than either response evoked from the respective member of the test pair, it was concluded that occlusion had occurred. The observed occlusion suggested that the tested centrifugal nuclei shared in the rostral course a common population of neurons. One possible site for a population of shared neurons was the granule cell core of the olfactory bulb. All of the reported anatomical studies concluded that centrifugal fibers to the olfactory bulb terminate upon the granule cell core (Cragg, 1962; Heimer, 1968; Price, 1969; Price and Powell, 1970a, 1970b, 1970f). Further, it was clearly demonstrated that centripetal evoked responses recorded from the olfactory tubercle and the horizontal limb of the BNDB could be inhibited by concurrently applied stimuli to the corticomedial amygdala. These data tend to support the conclusion
that the ipsilateral system was involved in the mechanisms of reduction of central transmission of olfactory afferent input.

It has been well established that transection of the anterior limb of the anterior commissure increased the intrinsic activity within the olfactory bulb, and that transection of the olfactory peduncle further increased the intrinsic activity (Orrego, 1962; Callens, 1965; Affani, Morita, and Garcia-Smartino, 1968; Levetreau, MacLeod, and Daval, 1969). These observations suggested that an ongoing regulation of bulbar activity was mediated via the centrifugal input to the olfactory bulb. The anatomical data of Cragg (1962), Heimer (1968), and Price and Powell (1970b, 1970f) revealed that centrifugal inputs to the olfactory bulb were symmetrically distributed and terminated primarily upon the granule cell core. The granule cell population was regarded as the generator for the large extracellular negative polarity responses elicited by stimuli applied to nuclei containing the cell bodies of centrifugal fibers (Dennis and Kerr, 1968). If the granule cell core was the generator or source of the extracellular currents which produced the monophasic response in the bulb, then the change in the polarity of this response as the recording electrode passed through the bulb could be attributed to the change in
the relative position of the tip of the electrode with respect to the generator and the flow of extracellular currents. The granule cells may be activated through a variety of inputs either afferent olfactory inputs or centrifugal inputs. The granule cell has been considered an active element in most theories regarding regulation of mitral cell activity (Shepherd, 1963; Yamamoto et al., 1963; Rall et al., 1966; Nicoll, 1969). Even though the granule cell core of the bulb responds to stimuli applied to each centrifugal nucleus nothing can be concluded as to the exact or specific function of the granule cells affected by the centrifugal input. The interaction data from the present study implies that specific centrifugal inputs, for example that from the BNDB, may influence specific or selective populations of granule cells independently. Callens (1965) demonstrated this possibility by showing that one stimulation site in the pyramidal cell layer of the prepiriform cortex could inhibit a granule cell, facilitate a granule cell, or have no affect upon another cell tested.

In summary the inhibition of evoked centripetal responses by concurrent stimulation of the centrifugal nuclei provides one means whereby the ipsilateral system might regulate transmission of olfactory afferent input outside of the olfactory bulb. The occlusion phenom-
on observed in the interactive studies suggests that activation of a common population of neurons (the granule cells) in the bulb provides through their connections a means whereby the ipsilateral centrifugal system might regulate central transmission of olfactory afferents within the olfactory bulb.

B. Contralateral Subdivision

The interactive effects of the contralateral system are considered under two headings: (1) the inhibitory influence upon the ipsilateral system and (2) the facilitatory influence upon centripetal input.

(1) The suppression of the ipsilateral centrifugally evoked responses at the bulb and in the more caudal nuclei by bursts applied to the corresponding contralateral corticomedial amygdala or bed nucleus of the stria terminalis suggest that the two systems are antagonistic. The ipsilateral centrifugal fibers arising in the corticomedial amygdala excite those centrifugal neurons with which they synapse in more rostral nuclei of the ipsilateral systems. The centrifugal neurons in the BNDB, OT, and AON then influence the next neuron in the rostrally directed chain, which appears to be the granule cells of the ipsilateral olfactory bulb. The contralateral system through the inputs to each of the opposite ipsilateral centrifugal nuclei acts to inhibit the ipsilateral centrifugal
neurons, or the granule cells in the core of the opposite olfactory bulb. All of the ipsilateral centrifugal neurons are not inhibited simultaneously; if simultaneous inhibition were the case no response would be obtained. The suppressive effect of contralateral system upon the ipsilateral system was attributed primarily to inhibition of, rather than fatigue of, ipsilateral centrifugal neurons. If suppression was due to fatigue then the greatest decrease in response amplitude could be expected in the ipsilateral nucleus closest to the point of the applied burst. This was not observed since the suppression was the greatest in the OT and approximately equal in the BNDB, AON, and olfactory bulb. Further if fatigue was the prime cause of the observed suppression, post-tetanic potentiation would not be observed. Post-tetanic potentiation was obtained during the post-burst suppressive phase. A corollary to the suppressive effect of the contralateral system upon the ipsilateral system was the observed increase in the magnitude of the ipsilateral centrifugal evoked responses in preparations where the influence of the corresponding contralateral centrifugal system had been unilaterally removed (lesion in body of AC, lateral to BNST).

(2) The contralateral system appeared to increase the magnitude of the centripetal evoked responses
recorded from nuclei which receive input from the lateral olfactory tract. This was interpreted as the result of the suppressive influence of the contralateral system upon the ipsilateral system. The most pronounced facilitatory effect was observed upon the antidromically evoked response from the contralateral olfactory bulb, which suggested that the contralateral system can directly influence the granule cells involved in the proposed granule-mitral inhibitory loop operating in the opposite bulb.

In summary the contralateral system inhibits the ipsilateral system. As a result of the inhibition of the ipsilateral system there was evidence of an increase in the centrally directed olfactory afferent input.

III. FUNCTIONAL HYPOTHESIS:

It is proposed that one ipsilateral and the opposite contralateral subsystem work in concert, keeping in mind that these are bilateral, symmetrical systems. The contralateral system because of the shorter onset latencies of responses evoked in the opposite bulb as compared to the ipsilateral bulbar response is thought to be prepotent. Both systems are activated by an olfactory cue, the contralateral responds more rapidly and suppresses the tonic-regulatory influence of the ipsilateral subsystem.
This results in an increase in centrally directed olfactory input. The increased afferent drive further excites the ipsilateral centrifugal neurons at the four nuclear groups caudal to the bulb as well as the granule cells of the bulb. This results in the gradual reactivation of the granule-mitral inhibitory loop within the bulb and inhibition of the olfactory afferent input to these nuclei which receive input from the lateral olfactory tract. With the re-establishment of the tonic-regulatory function of the ipsilateral system the olfactory system is "reset" for a new olfactory cue (Cohen, 1964, 1965).

IV. GENERAL SUMMARY:

Two bilateral symmetrical centrifugal subdivisions of the corticomedial amygdalo-bulbar centrifugal system in olfaction have been defined. These are designated as the ipsilateral subdivision and the contralateral subdivision. The ipsilateral system was composed of five nuclei: (1) corticomedial amygdala, (2) horizontal portion of the bed nucleus of the diagonal band, (3) olfactory tubercle (prepiriform cortex at pyramidal cell level), (4) anterior olfactory nucleus (pars medialis), and (5) the granule cell core of the ipsilateral olfactory bulb. The amygdala sent centrifugal fibers along the ventrolateral aspect of the forebrain to the bed nucleus of the diagonal
band, olfactory tubercle and anterior olfactory nucleus. Synapses occurred within these centers and additional centrifugal fibers coursed to and terminated within the granule cell core of the olfactory bulb. Specific interconnections were noted between the bed nucleus of the diagonal band and the anterior olfactory nucleus.

The contralateral system consisted of the cortico-medial amygdala and the homolateral bed nucleus of the stria terminalis. The contralateral nuclei were not distinguishable from those of the ipsilateral system. However, the strial bed nucleus projected to the contralateral horizontal limb of the bed nucleus of the diagonal band, the olfactory tubercle (pyramidal cell layer prepiriform cortex), the anterior olfactory nucleus, and the granule cell core of the olfactory bulb. The stria served to connect the amygdala and homolateral strial bed nucleus. The strial fibers and centrifugal neurons from the homolateral strial bed nucleus crossed the midline via the body of the anterior commissure and cours ed rostrally in loose association with the anterior limb of the anterior commissure. (Fig. 12A,B)

The two centrifugal subsystems had antagonistic influences upon the granule cell core, perhaps activated the granule-mitral cell inhibitory mechanism, and was involved with the ongoing regulation of centrally directed olfactory input. This was
clearly evident by the increase in centrally directed olfactory input when the ipsilateral centrifugal system was inhibited. The contralateral centrifugal system was prepotent with respect to the ipsilateral system. This system served to inhibit or suppress the ipsilateral system at the corresponding olfactory bulb and more caudal nuclear centers receiving ipsilateral centrifugal inputs. As a consequence of the suppression a concomitant increase in centrally directed olfactory input occurred. A hypothesis of a possible interactive mechanism was drawn from the experimental data.

Figure 12. Proposed models for (A) the ipsilateral centrifugal system and (B) the contralateral system.
BIBLIOGRAPHY


Dunn, J. D. 1970. Personal communication.


Gasser, H. S. and J. Erlanger. 1927. The role played by the sizes of the constituent fibers of a nerve trunk in determining the form of its action potential wave. Amer. J. Physiol. 80:522-547.


APPENDIX I

Glossary of Terms and Abbreviations:

1. AC - anterior commissure
2. ALAC - anterior limb of anterior commissure
3. BAC - body of anterior commissure
4. PLAC - posterior limb of anterior commissure
5. CAN - cortical amygdala
6. MAN - medial amygdala
7. IB - ipsilateral olfactory bulb
8. ipsi Bulb - ipsilateral olfactory bulb
9. CB - contralateral olfactory bulb
10. AON - anterior olfactory nucleus
11. OT - olfactory tubercle
12. OTpcl - olfactory tubercle at pyramidal cell layer
13. OTipcl - olfactory tubercle inferior to pyramidal cell layer
14. COTpcl - contralateral olfactory tubercle at pyramidal cell layer
15. BNDB - bed nucleus of the diagonal band (horizontal limb of the bed nucleus of the diagonal band)
16. BNST - bed nucleus of the stria terminalis
17. ST - stria terminalis
18. PAC - periamygdalar cortex
19. LOT - lateral olfactory tract
20. uV - micro-volt
21. msec - millisecond  
22. Hz - frequency unit (cycles/sec)  
23. PTP - post-tetanic potentiation  
24. c - contra or contralateral  
25. rel. unit - relative unit  
26. ipsi - ipsilateral  
27. Pul. - pulse
VITA

Garl Kalman Rieke was born June 30, 1942 in Seattle, Washington. He graduated from high school in 1960 and matriculated at the University of Washington in Seattle in the fall of 1960. He received a Bachelor of Science degree in Zoology in 1965 and a second degree, B.S. in Psychology, in 1966. In the fall of 1966 he was married to Judith Lula Dorman. He registered as a student in the graduate program of the Department of Anatomy at Louisiana State University Medical Center in September 1966. He became a candidate for the Doctor of Philosophy degree in May, 1970 and spent the summer of 1970 as a student at the Marine Biological Laboratory at Woods Hole, Massachusetts. His dissertation was successfully defended on April 26, 1971.
Candidate: Garl Kalman Rieke

Major Field: Anatomy

Title of Thesis: The Corticomedial Amygdalo-Bulbar Centrifugal Systems in Olfaction in the Rat

Approved:

[Signature]
Major Professor and Chairman

[Signature]
Dean of the Graduate School

EXAMINING COMMITTEE:

[Signature]
Melvin Hess

[Signature]
Jack L. Dean

[Signature]
Michael Korser

[Signature]
Glenn B. Qalipos

[Signature]
Herbert L. Lesmann

Date of Examination: April 26, 1971