Visuo-motor connections in the anuran mesencephalon

Neil M. Montgomery

University of Massachusetts Amherst

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VISUO-MOTOR CONNECTIONS IN THE ANURAN MESENCEPHALON

A Thesis Presented

By

NEIL M. MONTGOMERY

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

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Psychology Department
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NEIL M. MONTGOMERY

Approved as to style and content by:

Dr. Katherine V. Fite, Chairperson of Committee

Dr. Stephen A. George, Member

Dr. Neil R. Carlson, Member

Dr. Bonnie Strickland, Chairperson
Psychology Department
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ABSTRACT

VISUO-MOTOR CONNECTIONS IN THE ANURAN MESENCEPHALON

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Neil M. Montgomery, B.A., University of Massachusetts
M.S., University of Massachusetts
Directed by: Dr. Katherine V. Fite

The neuroanatomical connections between the visual and motor nuclei of the anuran mesencephalon were investigated using horseradish peroxidase and the Golgi technique. Four distinct cell types were identified within the terminal field of nBOR: stellate neurons, amacrine cells, elongate neurons, and large ganglionic neurons. In addition, cells which lie medial to the terminal field, pyriform and commissural neurons, send dendrites into nBOR. Pyriform neurons project to the nucleus of the medial longitudinal fasciculus (nMLF) and cranial nerve nuclei III and IV, while commissural neurons project to the contralateral nBOR.

Efferent projections from nBOR were observed in the large-celled pretectal nucleus and nucleus lateralis profundus. The large-celled pretectal nucleus was found to project to the tectum, dorsal tegmentum and the brainstem. The motor component of the mesencephalon consists of oculomotor nuclei n.III and n.IV. The n.III and
n.IV receive afferents from pyriform neurons of the peri-nBOR region as well as from the nMLF and MLF. Other afferents originate from a small population of fibers of the tecto-bulbar pathway which were seen leaving the bundle in the peri-nBOR region and descending into n.III. Collaterals of oculomotor axons were found to ramify within the adjacent nMLF.

This study has demonstrated a wider range of connectivity between the retinal terminal fields and motor nuclei within the anuran mesencephalon. Both tectal and accessory optic system neurons project directly to the oculomotor complex in these species.
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CHAPTER I
INTRODUCTION

This thesis will expand our anatomical information on the organization of a number of nuclei within the anuran mesencephalon. In particular, it will trace the fiber connections from the visual nuclei to the motor nuclei.

The analysis of these systems will be accomplished by a combination of old and new neuroanatomical techniques. These include several modifications of the Golgi technique as well as the horseradish peroxidase (HRP) tracer technique. Detailed information on the intrinsic organization and projections of these nuclei will permit the refinement of existing models of the structural-functional relationships within this region.

Man often attempts to draw inference from data obtained from various experimental animals which he may apply to himself. This practice is questionable unless we understand something of the evolutionary history of the species and regions from which the data were obtained. By understanding the degree of phyletic development of a particular neural region we can better evaluate to what extent a given structural-functional relationship represents either an extreme specialization or a more
generalized condition. To facilitate this type of understanding a section has been included which reviews the organization of the mesencephalon in a number of non-mammalian vertebrates.

The anurans have been extensively used as experimental animals in the study of the nervous system since Galvani first demonstrated the electrical properties of neural conduction using the legs of a frog. Recently, the anuran mesencephalon has become the focus of a number of studies central to issues of brain development as well as brain-behavioral relationships. These studies have included those of Sperry (1951) and Gaze and Keating (1969) on the specification of connections between the retina and optic tectum. Other studies by Ingle (1973) and Ewert (1974) have proposed models for the role of the posterior thalamus and tectum in prey catching and avoidance behaviors. Lazar (1973) has shown that some aspects of optokinetic nystagmus may be mediated by the accessory optic and pretectal nuclei. In all of these studies our ability to draw conclusions about functional relationships is limited by a lack of detailed information on the intrinsic organization and connections of these various mesencephalic regions. In particular, the interrelationships between the sensory and motor nuclei within the anuran mesencephalon are almost completely unknown.
General Features of Mesencephalic Organization

The mesencephalon, unlike more rostral neural segments, has retained the classical metameric organization common to the medulla and spinal cord; that is to say, it has retained that primitive organization of linear segments with similar relationships between the alar (sensory) and basilar (motor) plates found in the brainstem and spinal cord. This metameric pattern is the result of the integration of the cell groups related to four cranial nerves within the mesencephalon. Two of these cranial nerves are sensory: the optic n.II, and the trigeminal n.V; and two are motor: the oculomotor n.III, and the trochlear n.IV. At the same time, the mesencephalon shares suprasegmental features found in the diencephalon and telencephalon. While the diencephalon has retained aspects of the metameric pattern in the organization of the dorsal (sensory) and ventral (motor) thalamus this pattern is purely suprasegmental in nature. The telencephalon, on the other hand, is exclusively an alar plate derivative (Senn, 1970) and thus serves as a modulator of motor activity rather than part of the motor system itself. The mesencephalon, then, is a true midbrain in its structure, function, and location.

The primitive features of the organization of the mesencephalon can best be seen by comparing its
organization in cyclostomes with that of the human spinal cord (Figure 1a and 1b). The cyclostomes are one of the most primitive of the extant vertebrates. The primary components of the cyclostome mesencephalon are: the optic tract, the tectum, the motor tegmentum and the IIIrd and IVth cranial nerve nuclei and tracts. Some somatic projections are believed to reach the deep tectum in these animals; however, a true sensory nucleus of n.V is absent. Within the mesencephalon, vision and sensations from the head are integrated with the motor system for the eyes and upper trunk. This is the fundamental design of the mesencephalon that we will see repeated with increasing complexity throughout the vertebrate sequence. The pattern of organization of the cyclostomes mesencephalon can be compared directly to that found in the human spinal cord. The human spinal segment is composed of afferent fibers from the dorsal root ganglions, the neurons of the dorsal horn, the interneurons of the ventral horn and the spinal motor neurons and their fibers. The unique feature of the mesencephalon as compared to spinal segments is that primary afferents are both visual and somatic rather than purely somatic.

Neither the human spinal cord nor the cyclostome's mesencephalon is as simple as described above. In fact, the general trend in vertebrate evolution has been towards
sensory integration by increasing the number of afferents and interneurons in relation to the number of efferent neurons and fibers. This trend towards increasing integration can be exemplified by a comparison of the ratio of dorsal root afferents to ventral root efferents across several vertebrate species (Agduhr, 1934) showing a ratio of 1.4-1 in anurans to 5-1 in man. It is this trend of increasing sensory integration and supersegmental influences that will be charted in the following sections on the organization of the mesencephalon of non-vertebrates.

While we have defined the mesencephalon as that neural segment which has as its intersegmental features optic afferents and ocular motor efferents, the bulk of this thesis will deal with both lower and suprasegmental circuits within this region. Before entering into the comparative organization of the mesencephalon the general subdivisions common to most vertebrates will be reviewed.

The primary component of the alar plate is the tectum. Rostral to the tectum are a number of primary visual fields referred to collectively as the pretectum. The pretectum is one of the most variable yet consistent areas within the mesencephalon. All extant vertebrates have a pretectum but this region may vary from one nucleus in cyclostomes to as many as seven nuclei in mammals. In general, non-mammals have three pretectal nuclei: 1) a
migrated population of neurons or "true" pretectal nucleus, 2) a region of neuropil receiving visual afferents, and 3) a region of the central grey receiving secondary visual input. Caudal and ventral to the tectum is the torus semicircularis which receives primary input from the auditory system as well as some somatic input. The torus is generally considered the homolog of the inferior colliculus found in mammals. In non-mammals, a region of neuropil through which pass auditory fibers projecting to the thalamus is referred to as the nucleus profundus lateralis. The nucleus profundus lateralis has been considered by some as the homolog of the mammalian nucleus of the lateral lemniscus. The caudal component of the alar plate consists of the nucleus isthmi and the secondary visceral nucleus. In most non-mammals the nucleus isthmi represents a tectal relay nucleus. The secondary visceral nucleus receives input from various visceral sensory nuclei of the brainstem and projects to the thalamus. The nucleus isthmi and the secondary visceral nucleus are strictly non-mammalian structures as no mammalian homologs have ever been located.

The basal plate of non-mammals is composed of four main elements: the motor tegmentum, the oculomotor column (nuclei III, IV), the basal optic nucleus, and the interpeduncular nucleus. The motor tegmentum, also referred
to by some as the nucleus reticularis tegmenti, is a
column of central grey sometimes associated with migrated
populations within the neuropil. It is from the motor
tegmentum that the red nucleus of reptiles, birds, and
mammals has evolved. Those regions of the motor tegmentum
closest to the oculomotor column are referred to as the
interstitial nucleus or nucleus of the medial longitudinal
fasciculus in non-mammals. The various accessory nuclei
of the mammalian oculomotor complex have evolved from the
interstitial nucleus. In all vertebrates this region
receives a direct projection from the vestibular nuclei.
The motor tegmentum, as the term implies, projects to the
motor nuclei of the brainstem. The oculomotor complex
consists of the nuclei of the n.III and n.IV. This region
is represented either as a continuous column of cells or
as two distinct nuclei. The basal optic nucleus is a
visual receptive field in the ventral, lateral mesencepha-
lon. In non-mammals, this region may consist of up to
three nuclei as in avians, or may not exist at all, as
appears to be the case in cyclostomes. The interpeduncular
nucleus is a consistent feature of the mesencephalon of all
vertebrates. It consists of a column of cells along the
ventral midline which receives input from the habenular
and projects to the motor tegmentum.

Three commissural bundles join the two sides of the
mesencephalon of most vertebrates. These are the tectal commissure, the posterior commissure and the ventral commissure. The tectal commissure and a large portion of the ventral commissure are composed of tectal efferents while the posterior commissure serves the pretectal grey and motor tegmentum. There is some evidence that the ventral commissure is involved in oculomotor activity. These groups represent the more universal elements of the non-mammalian mesencephalon.

The Comparative Neurology of the Non-Mammalian Mesencephalon

Homology. Brains do not fossilize. However, brains do evolve. These properties make the study of the evolution of the nervous system a difficult, if not impossible, task. With the acceptance of the concept of evolution came the concept of a phylogenetic scale. The notion of a phylogenetic "scale" led to the unfortunate consequence of being translated conceptually into an historical sequence. The frog is seen in this sequence as a primitive form from which reptiles evolved. This fallacious conception is easy to accept but it denies evolution itself and falls back to a belief in the nonmutability of species of the pre-Darwinian period. If we discard cross-species similarities, we end by treating each species as an independent act of creation disassociated from all others.
Given that stem vertebrates did exist, how do we contend with those similarities that result from this common point of origin? To deal with these problems, a number of conceptual models have developed which serve to circumvent them and accent the differences between species which are due to independent evolution. Chief among these concepts are homology and homoplasy.

Homology, in its broadest sense, relates to the degree of resemblances between equivalent parts of different animals. The operational term here is degree. Even equivalent structures will show some differences due to evolutionary modifications such as migration, differentiation and reorganization of primitive structures. Homologies can come in almost as many forms as there are attributes of an organism. Homologies can be either structural or functional. The hairs of different mammalian species can be said to be homologous to one another, or the coils of DNA responsible for pigmentation of those hairs can also be said to be homologous. In the central nervous system, a number of stringent criteria have been generated by different authors to determine a true homology. To qualify as homologous, two structures must have similar developmental histories, topographical position, patterns of connectivity, and function.

Recently, it has been proposed that cell groups must also
have similar axonal terminals and dendritic branching (Winer and Morest, 1979). Few if any structures have undergone this extensive test of homology. If all the criteria were to be met by any two structures, they would be identical rather than similar. Homology in this thesis is used as a phylogenetic hypothesis based mainly on topographical position and connectivity.

To deal with the flaws in considering the phylogenetic scale as a historical sequence, a second concept of homoplasy has been developed. Homoplasy addresses the problem of parallel and convergent evolutionary specializations. Convergent evolution is the process by which species with divergent evolutionary histories arrive by different courses at similar end points. An example of convergent evolution is the development of a structure in the mesencephalon of boney fish and mammals to integrate forebrain and cerebellar activity. Both of these structures are called the "red nucleus;" however, they are not homologous. Our estimations of the state of evolutionary specialization of a given species or class can also be confounded by the process of regressive evolution. Regressive evolution has its greatest effect on species that undergo metamorphosis. Northcutt (1979) believes that some species that appear primordial may in fact be regressive. In particular, the cyclostomes and
urodeles may be the products of regressive evolutionary processes.

Two criteria were used in selecting the species to be examined in the following sections. First, species were chosen which might be expected to display the type of CNS organization which might be similar to that of stem vertebrate at various times in the evolutionary sequence. The second criteria was to choose species whose mesencephalons display a high degree of divergent evolutionary specialization. As a result of this process, species were chosen from the: 1) cyclostomes, 2) elasmobranchs, 3) teleost, 4) dipnoi, 5) urodeles, 6) anurans, 7) reptiles.

**Cyclostomes.** The most primitive known extant vertebrates are the cyclostomes of the class Agatha. While these animals are not part of the line leading to mammals, they are believed to have retained the general features of the early vertebrates. The living representatives of this class are the hagfish (Myxine), the lamprey (Petromyzon), and the slime hag (Bdillatoma). These are soft-bodied, jawless animals unlike many of the early vertebrates which are believed to have been protected by armor. The lamprey are predators which attach themselves to the bodies of bony fish. As an adaptation to this type of predation, it has evolved a single nostril at the top of its head and a
round sucking mouth. The hagfish, on the other hand, are scavengers. The hagfish is a totally marine form while the lamprey, although a marine form as an adult, lays its eggs in fresh water. While the cyclostomes resemble the primitive vertebrates, it must be noted that some of their characteristics are highly specialized, such as the mouth of the lamprey, while others may be degenerate. The lamprey will be the focus of our investigation, as the myxinoids display regressive neuroanatomical relationships due to a reduction in the size of the optic nerve and a lack of eye muscles.

The early neurological studies of the cyclostomes mesencephalon include those of Johnson (1902), Saito (1928, 1930), and Heier (1948). The mesencephalon of these animals displays a very primitive form of organization. Its major components are 1) a neuropil containing various fiber systems, and 2) a periventricular central grey from which neurons send dendrites into the neuropil.

The tectal lamination in these animals is variable with prominent layering in the anterior portions and less in caudal segments (Figure 1). The pretectum is the only true migrated nucleus in the mesencephalon of the cyclostomes. No neurons related to the trigeminal sensory nucleus of V have been located in the deep tectal layers (as is common in other non-mammals). The absence of this
nucleus is believed to be due to the lack of appropriate muscles of the jaw in these vertebrates. Caudal to the tectum is a region of central grey continuous with the periventricular layers of the tectum. This region is considered to represent the torus semicircularis (or mesencephalic auditory area). The secondary visceral nucleus is diffuse and difficult to define. The pretectal grey is a thin plate of neurons.

In the basal plate, the motor tegmentum is a thick plate of cells within which are found three Muller cells. The presence of these Muller cells indicates clearly the motor nature of this segment. The role of the motor tegmentum is more difficult to define in mammals where it is superseded by the pyramidal tract. No nucleus interstitilis or basal optic nucleus have been located in cyclostomes. The oculomotor system is not located in the central grey as in other vertebrates but rather extends ventrolaterally to the superficial margin of the brain. All three oculomotor nuclei are continuous in cyclostomes. The position of the nuclei of III and IV on the superficial margin of the brain and their continuity with the nucleus of VI represent a very primitive or regressive type of organization. With the three cranial nerve nuclei related to eye movement, III, IV, and VI, being nearly continuous with one another and the absence of associated
nuclei of the oculomotor complex such as the basal optic nucleus and interstitilis nucleus, we see an oculomotor system without the complexity found in other non-mammals and mammalian forms.

In general, afferents to the cyclostome mesencephalon are optic input to the tectum and pretectum as well as some somatic input to the deep tectal layers. Vestibular input reaches the nuclei of III and IV. While auditory input reaches the torus, other connections include the habenulo-tectal, thalamo-tectal, and hypothalotectal systems. The efferent systems include descending fibers from the motor tegmentum as well as tectal efferents. In Petromyzon, the commissural systems are clearly defined; however, in Myxinoid (Holmgren, 1919), which have only rudimentary eyes, the posterior commissure and tectal commissure merge. The tectum itself is diffuse in these animals merging with the dorsal thalamus at anterior levels and the torus at posterior levels.

More modern studies of the mesencephalon of cyclostomes have given us some more refined information on the organization of these different systems. These studies include those of Northcutt and Przbylski (1973), and Kennedy and Rubinson (1977) on retinal projections as well as those of Finger and Rovainen (1978) on the oculomotor system. From these studies, it was found that visual
input reaches the contralateral superficial tectum as in other vertebrates; however, an unusual ipsilateral projection reaches the lateral margin of the tectum in the adult but not the larval lamprey. No similar projection has ever been found in any other extant vertebrate. The pretectum also receives an ipsilateral input which was not found in the larval form, nor has it been observed in elasmobranchs or teleosts. Such input is common in amphibians, reptiles and birds. The lamprey is an interesting case in the development of the visual system since this system undergoes drastic changes following metamorphosis from larval to adult. These changes are correlated with a four-fold increase in the size of the eye.

Elasmobranch. The sharks, rays, and skates are generally grouped together under the term elasmobranch which means strap-gilled. This term refers to the fact that these fish have the full complement of 5 gills but lack gill flaps. The sharks are highly specialized animals and represent a somewhat later point of divergence from the stem vertebrates than do the cyclostomes. Within the sharks there are two lines of evolutionary specialization. One line leads to filter-feeders such as the dogfish, while the other leads to carnivorous forms like the great white shark.
The first important neurological study of the shark brain was the Golgi study of Houser (1901) followed by the work of Gerlach (1947). The mesencephalon of sharks displays a higher degree of specialization than does that of the cyclostomes. The tectum is a well-laminated structure and three pretectal regions have been defined (Northcutt, 1979) as superficial, central and periventricular. The two halves of the tectum are joined by the tectal commissure and a trigeminal sensory nucleus of V can be found in the deep tectal layers. The boundary between the mesencephalon and diencephalon is determined by the posterior commissure as in other species. The rostral portion of the torus semicircularis has differentiated into a nucleus rotundus mesencephali. At the caudal portion of the torus, a nucleus isthmi can be defined but it is less-developed than that of amphibians and reptiles. While no secondary visceral nucleus has been located in sharks, it may be represented by a diffuse region caudal to the nucleus isthmi. Within the elasmobranch, the boundary between the alar and the basal plate is easily defined by a prominent suclus limitans. The basal plate of sharks is represented by a diffuse region composed of the central grey and migrated populations of neurons. This pattern differs from that of the cyclostomes where the neuronal populations were restricted to
the central grey. The tectum of elasmobranch differs from that of bony fish in that the main cellular layer is located in the central layer of the tectum rather than in the periventricular region (Figure 2). In conjunction with this type of tectal layering, the optic fibers do not end in the superficial layers of the tectum but enter deep. Within the alar plate a dense nucleus profundus lateralis is found as well as an intercollicular nucleus.

In the anterior regions of the basal plate is the nucleus interstitialis and the nucleus of the IIIrd nerve. The interpeduncular nucleus is particularly dense. Along the lateral margin of the basal plate are a number of forebrain bundles and the basal optic tract. In general, the elasmobranch mesencephalon displays an increase in sub-tectal circuitary related to the migrated pretectal nucleus as well as to the specialized intercollicular nucleus and nucleus profundus lateralis. The large fields of migrate neurons in the dorsal and ventral tegmentum can be expected to have intricate patterns of connectivity which are as yet unknown.

The bony fish. The bony fish or teleost are represented by 16 families, two of which live in shallow water while the rest are deep water forms. According to Romer (1933), at the beginning of the evolution of the bony fish, they diverged into two groups, the Actinpterygii (or rayfinned
fish) and the Sarcoterygii (or fleshy-finned fish). The teleost have developed from the ray-finned fish while the sarcoptergii were ancestral to the land vertebrates. Extant teleost display a wide range of adaptations and associated specializations. Neurologically, the teleost display almost as much divergence from the basic vertebrate pattern as do the advanced mammals. The ganoid and teleost mesencephalon is extremely specialized. Even the application of modern neuroanatomical methods has done little to relieve the confusion. Direct homologs to structures found in mammalian, amphibian, or elasmobranch brains are at best speculative.

Generally, the alar plate is composed of a tectum, pretectal complex, nucleus profundus, nucleus isthmi, torus semicircularis and secondary visceral nucleus. The secondary visceral nucleus is highly developed, as is the trigeminal sensory nucleus of V, in the deep tectum. In addition, there are two nuclei not found in other vertebrates: the nucleus lateralis valvuae related to the valvua cerebellum and the nucleus torus longitudinalis which bridges the tectum and cerebellum.

A number of recent studies of the teleost tectum have made that region better understood than it is in other non-mammals. These studies include the Golgi studies of Vanegas et al. (1974), and Meeks (1978), degeneration
studies of Grover and Sharma (1979), and HRP studies (Sharma, 1980). The teleost tectum sends ascending ipsilaterals to the pretectal region, particularly to the area pretectalis and nucleus pretectalis, as well as to the nucleus rotundus and the nucleus lateral geniculate. Contralateral projections were found to these same nuclei and to the rostral tectum. Descending projections from the tectum were found to reach the dorsal lateral tegmentum and lateral reticular nuclei of the tegmentum, as well as the pons. Contralateral projections also exist to the medial reticular formation of the tegmentum and the pons. Other recent studies of the optic pathways (Campbell and Ebbesson, 1969; Finger and Karten, 1978) indicate that there are a large number of pretectal nuclei which differ in the degree of their differentiation among teleost. Basically, there are two to three migrated nuclei as well as a periventricular group. Detailed studies of the intrinsic organization within the teleost mesencephalon have been restricted to the tectum. The teleost tectum consists of 15 cell types; ten of these have dendrites in the superficial optic layers, while dendrites of the other five types ramify in the deep tectal layers. Data from degeneration studies indicate that two types of neurons give rise to tectal efferents. The use of the HRP technique indicates that a larger
number of tectal efferent cell types exist (Sharma, 1980). The basal plate is composed of the usual complement: the nucleus interstitilis, motor nuclei III and IV, motor tegmentum, and interpeduncular nucleus. Also related to the motor tegmentum is a diffuse region of migrated neurons which receives input from the cerebellum and projects to the brainstem. While this region appears similar to the red nucleus of mammals, it is differentially developed in different species of teleost and is believed to represent an independent development of a rubro-like system in these animals. There is now a dispute as to the nature of the basal optic nucleus in teleost. Ebbesson and Campbell (1969), clearly define a portion of the basal plate as receiving optic input from what they describe as the basal optic root. Finger and Karten (1978) have proposed that this region represents a preoptic area in teleost and that a region ventral to the tectum which projects to the cerebellum should be considered as the accessory optic system. Sharma (1980) believes that a true AOS as found in other vertebrates does not exist in fish but that some species have developed similar connections as an independent evolutionary development.

In general, the fish mesencephalon has undergone a number of changes from the basic vertebrate pattern in relation to the development of both the cerebellum and the
forebrain. The development of the telencephalon and cerebellum in mammals greatly altered the configuration of the mesencephalon; however, the development of the cerebellum and forebrain in teleost appears to be an independent evolution of similar systems.

Dipnoi. The earliest studies of the lungfish include those of Holgrem and Van der Horst (1925), and Gerlach (1933). Lungfish are a form of fleshy-finned fish which have lungs rather than gills. As such, they appear to represent a form similar to that from which land vertebrates evolved. With these animals, we return to the basic neurological pattern whose features may be similar to those of vertebrates who first ventured onto the land. The mesencephalon of these animals consists of a central grey and neuropil with no migrated nuclei. The alar plate is composed of an optic tectum which is represented by a thickened central grey plate. A few migrated neurons are associated with the tectum. Northcutt (1979) describes the mesencephalon of these animals as the simplest of the known vertebrates. The pretectum is also a central grey group with optic axons restricted to the neuropil (Figure 4). The only true migrated nucleus is the nucleus isthmi which is represented by a single band of neurons along the superficial margin of the caudal mesencephalon. A torus semicircularis is also located in the caudal
mesencephalon.

The basal plate is composed of a nucleus interstitilis, motor tegmentum, interpeduncular nucleus and the nuclei of III, and IV. A basal optic tract has been recognized. This tract terminates in the neuropil in a cell-free region. Neurons in the nucleus interstitilis send their dendrites into this terminal field.

Amphibia. The amphibians of today are represented by three main lines: the urodeles, anurans, and apoda. Of these three, only the urodeles have maintained the tetrapod body common to the early forms of these vertebrates. The amphibians, in general, have a moist skin which acts as a secondary breathing apparatus. Their skin often contains glands containing toxins to deter predators. Anurans are the largest group and have radiated into a number of habitats: terrestrial, fossorial, arboreal, litteral, and aquatic (Blair, 1976). The primary neurological differences between the urodeles and anurans are in the development of the visual and motor systems. Anurans have a highly developed visual system as well as skeletal alterations in the form of a shortened spinal cord and a saltatorial form of locomotion.

Urodeles. By far the greatest student of the urodele nervous system was C. J. Herrick who in a series of papers
extending over forty years, described in detail the major regions and connections within the central nervous system of the salamander. Herrick was not the only person to study this system. Contributions have been by Kreht (1931, 1933), Rothig (1927), Gruberg (1973) and Northcutt (1979).

The mesencephalon of urodeles displays the generalized pattern which we have seen in the cyclostomes and lungfish rather than the more specialized form found in higher fish and amniotes. The boundary between the mesencephalon and diencephalon is, as in other species, the posterior commissure. At the level of the posterior commissure are located a periventricular pretectal nucleus and a nucleus of the posterior commissure. The optic tract, as it reaches the tectum, divides into dorsal and lateral bundles as well as a diffuse bundle known as the axial optic tract. The tectum is restricted to the central grey with the cells of the trigeminal sensory nucleus of V in its deep layers. These deep tectal layers receive both spinal and bulbar input. The torus semicircularis lies caudal to the tectum as an area of increased cell thickness in the grey. The secondary visceral nucleus is defined as that area of the grey receiving input from the gustatory nuclei of the brainstem. Unlike the lungfish, the nucleus isthmi of urodeles is located in the central
grey and is not a migrated nucleus.

In the basal plate, the most anterior portion is termed the posterior tuberculum. The posterior tuberculum (Figure 5) is a term used by Herrick to refer to the fact that this region of the central grey is shaped like half of a cylinder. The neurons of this region are both large and small and have extensive dendritic spread. The neuropil of the tuberculum is composed of the basal optic tract, efferents from the thalamus and habenula and the median forebrain bundle. Herrick proposed that the tuberculum sends its primary efferents to the hypothalamus. Caudal to the tuberculum is the interstitial nucleus and the nuclei of III and IV. Herrick's drawings show dendrites from this region entering the terminal area of the basal optic tract. From his drawings, the motor tegmentum is composed of two tiers of dendrites, an inner tier of small cells whose dendrites arborize close to the central grey and a second tier of larger neurons whose dendrites extend to the superficial margin of the brain. The interpeduncular nucleus is composed of small cells clustered along the midline. Herrick describes the organization of these cells as a "dendritic glomerulus" referring to the interlocking of the end boutons of the cells within the nucleus with afferent fibers.

Anurans. The anuran mesencephalon has a long history of
investigation dating from the very beginnings of the neuron doctrine. Some of these studies include those of Bellonci (1888), Wlassak (1893), Gaupp (1899), Herrick (1910, 1925), Ariens Kappers and Hammer (1918), Ariens Kappers (1921), Larsell (1924), and Kreht (1930, 1931). These studies used the Golgi and normal cell and fiber stains to outline the major regions, cell types and connections of the anuran mesencephalon. More recently, with the development of modern neuroanatomical techniques such as radioactive tracers, degeneration stains, HRP and electron microscopy, there has been a new burst of interest in the organization of this region. Some of these studies include studies of the terminal fields of the optic projections (Scalia and Fite, 1974; Lazar, 1978; Levine, 1980), studies of the postsynaptic cells of the optic terminal fields (Scalia and Gregory, 1970), the types of optic terminals in the tectum (Scalia, 1976), tectal cell types (Skelezy, 1976; Lazar, 1969), afferents to the tectum (Wilczynski, 1977; Trachtenberg and Ingle, 1974), tectal efferents (Rubinson, 1968; Lazar, 1969), connections of the nucleus isthmi (Grobstein, 1979), the organization of the torus semicircularis (Potter, 1965), projections to the nucleus profundus lateralis (Rubinson and Skiles, 1973). After outlining the general pattern of organization of the anuran mesencephalon some of these more specific studies will be
reviewed in greater detail.

The anuran optic tract, after leaving the chiasm, splits into three components, the marginal, axial and basal tracts. The marginal tract is the largest of these. At mesencephalic levels it splits into lateral and medial components before entering the tectum. There are a number of optic terminal fields in the mesencephalon and along the mesencephalic-diencephalic border. These terminal fields are the posterior thalamic, lateral thalamic, large-celled pretectal, uncinate neuropil and basal optic nucleus (Scalia and Fite, 1974). All of these terminal fields, with the exception of the basal optic, are alar plate components.

The most anterior of these optic nuclei is the lateral terminal field in the central thalamus. This nucleus is represented by a wide band of terminals across the superficial portion of the dorsal and lateral neuropil. Medial to this terminal field are the scattered cells of the posterior lateral cell group, which send dendrites into the terminal field. Around the ventricle is the rounded cell mass of the posterior central thalamus (Figure 6), a region receiving somatic afferents from the obex region and projecting to the striatum (Wilczynski, personal communication). Near the border of the mesencephalon, a rectangular, optic terminal field is
evident. This is the posterior thalamic neuropil. Some of the postsynaptic cells of this terminal field are located in the neuropil while others are found in the central grey. Caudal to the posterior thalamus are the posterior commissure, large-celled pretectal nucleus and the anterior tectum. Behind the posterior commissure is the uncinate terminal field located in a relatively cell-free area above the pretectal central grey. Caudal to this region is the tectal commissure followed by the fusion of the tectal lobes. Ventral to the tectum at this level is the torus semicircularis which has been divided by Potter (1965) into five regions: the subependymal nucleus, the commissural nucleus, the magnocellular nucleus, the principal nucleus and the laminar nucleus. The nucleus profundus lateralis lies superficial to the torus. Caudal to the torus is the nucleus isthmi and the secondary visceral nucleus both of which are highly developed in anurans.

While the alar plate of anurans has been extensively studied, no recent studies of the basal plate exist in the literature. The anterior portion of the basal plate is composed of the posterior tuberculum which resembles that of urodèles both in structure and function. Caudal to the tuberculum is the nucleus interstitilis or the nucleus of the medial longitudinal fasciculus which receives a strong
projection from the MLF. The IIIrd and IVth cranial nerve nuclei form a continuous column in anurans. The central grey dorsal to the nucleus interstitilis is the motor tegmentum. Along the margins of the central grey of the motor tegmentum and in the neuropil are a number of large neurons derived from the motor tegmentum referred to as the nucleus reticularis tegmenti. The nucleus reticularis tegmenti is not equivalent to the red nucleus of mammals; in fact, mammals have both a red nucleus and a nucleus reticularis tegmenti. The nucleus reticularis tegmenti is often considered together with the nucleus lateralis profundus; however, there are clear differences between them. The nucleus profundus is a cell-free area of the alar plate while the nucleus reticularis is a large-celled area of the basal plate. At the level of the third nerve nuclei is the nucleus of the basal optic tract. In anurans, this area is a well-developed cup-like grouping of neurons along the superficial margin of the mesencephalon. The nucleus of the basal optic root, in anurans, is more highly developed than in urodeles where the basal optic tract discharges into a cell-free area.

The anuran tectum is a highly developed structure when compared with that of urodeles. The most current terminology (Szekely and Lazar, 1976) divides the tectum into 9 layers of alternating fibers and cells. The 9th
and most superficial layer is subdivided into seven sub-layers A through G. Layers 2, 4, and 6 are cellular layers with a large but less-concentrated population of neurons in layer 8. Layers 2 and 4 are found in the anterior portion of the tectum. It is within layer 4 that the larger neurons of the mesencephalic nucleus of V are located. The main efferents from the tectum arise from layers 8 and 6 and leave through layer 7. Optic fibers enter in layer 9. These fibers are both myelinated and unmyelinated. Based on myelin stains, layer 9 has been subdivided into a layer A, through which optic fibers enter the tectum, and three terminal layers B, D, and F. Layer F is the thickest of the three and contains the greatest concentration of myelinated fibers. Two cellular lamina are located within the terminal optic layers. These are layers C and E (Figure 7). The most superficial layer of optic fibers is a thin band of densely branching fibers with few terminal arbors. Subgroups of this type may have thorny arbors or no specializations at all. The second major class of optic terminal are bell-shaped (Figures 7, 10).

The cell types of the tectum have been described by Szekely and Lazar (1976). These represent the major types although some variation does exist. Layers 2 and 4 are composed of pear-shaped neurons, 15-20 microns in
diameter. These cells have long apical dendrites extending to the surface of the tectum, often terminating in a number of small branches. Some of the dendrites of these neurons have broom-like endings while others have dendrites which terminate as wide cylinder-like fields with small drum-like terminals. Large pyramidal neurons are found in layers 2, 4, and 6. These neurons have more extensive basilar dendrites and dendritic collaterals with presynaptic specializations. Other large pyramidal cells have short apical dendrites which split into two main branches. These cells have smooth secondary branches from which axons arise and exit the tectum. In the deep layers there are a number of irregular pear-shaped and pyramidal types with differing branching patterns. In layers 6 and 7, large ganglionic neurons make up the second class of efferent in the tectum. Layers 7 and 8 contain bipolar, stellate and amacrine neurons. These small cells located in the optic terminal layers have processes either dendritic or axonal on the efferent cell types of the tectum.

Rubinson (1968) described the efferent pathways of the tectum using degeneration methods. He found four components to the tectal efferent system. The largest tract descends along the superficial margin of the mesencephalon until it reaches the ventral midline. It crosses
the midline rostral to the interpeduncular nucleus and maintains its midline position until it reaches the brainstem and spinal cord. Rubinson was unable to find any evidence that this tract reaches the cranial nerve nuclei of the brainstem. A second ipsilateral component travels along the lateral edge of the mesencephalon below the lateral marginal tract (Figure 8). This bundle innervates the nucleus isthmi, the superior olivary nucleus, and the nucleus reticularis tegmenti. In the caudal brainstem some of these fibers cross the midline to reach the medial reticular formation. A small ascending bundle of tectal fibers reaches the ipsilateral pretectum and thalamus along a route below the medial marginal optic tract. The largest ascending component travels below the lateral marginal optic tract reaching the lateral thalamic neuropil and corpus geniculatum of both sides and the contralateral central grey and ventral pretectum.

Afferents to the tectum have been studied by Wilczynski and Northcutt (1977). Afferents originate from the ipsilateral nucleus isthmi, large-celled pretectal nucleus, lateral thalamus, posterior thalamus and torus semicircularis. Contralateral projections originate from the tectum and lateral thalamus. In addition, Trachtenberg and Ingle (1974) have reported an ipsilateral
projection from the anterior thalamus to the tectum.

In general, the anuran mesencephalon has developed a large number of specialized nuclei and connections related to the great expansion of the alar plate, in particular, the optic tectum and torus semicircularis.

Reptiles. The reptilian mesencephalon has been the subject of more extensive study than most of the non-mammals. The interest in this region has stemmed from the fact that the mesencephalon of these animals displays several traits pointing towards a mammalian-like organization. Some of the studies of the reptilian mesencephalon have included Delange (1912), Beccari (1923), and Tuge (1932), as well as recent studies by Halpern and Frumin (1973), Northcutt and Butler (1971, 1974), and Reiner and Karten (1978).

Superficially, the reptilian mesencephalon looks much like that of anurans (Figure 9). The similarity, however, is not uniform across reptiles. While the crocodile tectum appears much like that of anurans, the snake tectum is smaller in relation to neighboring structures. In burrowing snakes with reduced optic systems, the torus semicircularis may bulge out behind the tectum thereby creating a formation very much like that of the inferior colliculus in mammals. The inferior colliculus-like formation and the lack of a secondary visceral nucleus (a non-mammalian trait) have been pointed to as
mammalian-like features of the reptilian alar plate.

The basal plate of reptiles shows a true intermediate organization between the anuran and mammalian patterns. Within the motor tegmentum, two nuclei have differentiated into a dorsal and ventral nuclei reticularis tegmenti. Beccari (1943) has described a portion of the basal plate as the forerunner of the substantia nigra. Another mammalian-like feature can be seen in the differentiation of several nuclei around the oculomotor complex including the nucleus interstitilis and a nucleus darkschewitsch.

Summary. The mesencephalon of non-mammals displays a wide range of structural variation. A number of species have retained very primitive forms of organization such as the cyclostomes, dipnoi, and urodeles. Other species have developed extensive systems of first- and second-order visual nuclei related to the tectum such as teleost and anurans. The basal plate of the mesencephalon is relatively consistent showing a series of modifications resulting in the formation of the accessory optic system, red nucleus, and accessory nuclei of the oculomotor system. Reviewing the literature, we find little information on the connections between the optic centers and the motor tegmentum and oculomotor system. It is this question of visuo-motor integration that will be
addressed in the following sections, keeping in mind that some of these connections may not be generalizable to other vertebrates due to the specialization of the anuran alar plate.
CHAPTER II
METHODS

Over 130 *Rana pipiens* brains were examined with the horseradish peroxidase (HRP) method. In *Rana pipiens*, HRP injections were made in a number of regions of the neuroaxis as follows: 12 injections in the cerebellum, 4 injections in the vestibular nuclei, 10 injections in the anterior thalamus, 10 injections in the caudal thalamus, 5 injections in the brainstem, 30 injections in and around the anterior mesencephalon, 12 injections of the pretectal area, 10 injections of the tectum, 1 injection in the torus semicircularis, 1 injection in the endopeduncular nucleus. These brains were processed by the Hanker Yates reaction method, embedded in gelatoni and cut frozen at 40 microns.

Fifteen *Rana pipiens* and 4 *Bufo marinus* were processed with the Sholl (1953) modification of the Golgi-Cox, mercury-impregnation method. Fifteen *Rana pipiens* were also processed according to the Golgi-Kopsch method using the modification described by Hillman (1978) for frog. Brains were dehydrated, embedded in low viscosity nitrocellulose (LVN) and cut at 40 to 80 microns.

In addition, using 4 proline autoradiographic cases
supplied by Dr. Fite, cell counts were made of the neurons within the basal optic nucleus. Cells were classified and counted on the basis of the size and shape of their soma in the central most 190 microns of the terminal field. Cell types counted in ARG-nissl stained sections were correlated as to size and shape with the cells stained by the Golgi technique. In this manner, all the elements within the terminal field could be accounted for. This process was repeated without the cell counts for the large-celled pretectal nucleus.
CHAPTER III

RESULTS

General Features

The mesencephalon of anurans can be seen in normal cell stains to be composed of a central grey and superficial neuropil. Golgi-stained sections indicate that within the neuropil the dendrites of central grey neurons arborize in two tiers (Figure 10). The inner tier is composed of the dendritic arborizations of small neurons of the central grey which ramify in the proximal 90\(\mu\)m of the neuropil. The outer tier is composed of the arborizations of the large neurons of the central grey whose dendrites ramify to the superficial margin of the neuropil. This pattern of dendritic arborization is similar to that found in urodeles (Figure 11). Golgi-stained sections also indicate that stretching across the entire outer tier is a dense population of stellate and amacrine neurons. The stellate-amacrine population extends from the interpeduncular nucleus to the tectum. This morphologically uniform population of stellate and amacrine neurons forms the basic substrate for the organization of all the various nuclei of the outer tier. As we will see, each nucleus within the outer tier has as one of its components elements of this stellate-amacrine population. Along the most medial
margin of the outer tier, medium sized neurons (18-24\(\mu\)m in diameter) can often be found which appear to integrate activity within the outer tier and project to the central grey. Within the outer tier, large reticular neurons have dendrites which arborize across large areas of the neuropil. This type of neuron sometimes aggregates into nuclei such as the large-celled pretectal nucleus or the nucleus reticularis tegmenti.

The anuran mesencephalon can be viewed as a neural segment in which nuclei share many of the same cell types. These nuclei are mainly defined by their location and connectivity. The large-celled pretectal nucleus and the basal optic nucleus are well-known nuclei while the area between these nuclei contain many of the same cell types but are un-named as their connections are as yet unknown.

The Large-Celled Pretectal Nucleus

The large-celled pretectal nucleus (nPT) is an aggregate of second tier neurons defined primarily by its direct optic input. The nucleus is located below the anterior optic tectum and is superficial to the anterior mesencephalic grey. In coronal, plane HRP-soaked optic-nerve tissue (Figure 12), the nucleus appears rectangular in shape with a long dorso-ventral axis. Two general regions of optic terminations can be defined. In the center
of the nucleus there is a dense region of terminations. This area is referred to as the dense core region. Surrounding the dense core is a region of lower density optic terminations. Optic fibers reach the nPT from the lateral division of the marginal optic tract. These fibers are mainly of large diameter and enter the dense core area of the nucleus where each axon branches into smaller finger-like fibers. The branches travel in parallel through the nucleus giving off numerous fine-beaded axonal arborizations which then course tangentially to the primary fiber. This meshwork of fine arborizations forms the diffuse region around the dense core. Along with its primary visual input, nPT also receives secondary input from the nucleus of the basal optic root (nBOR). This projection originates from the ganglionic neurons within nBOR. The axons of the ganglionic neurons travel along the tectobulbar pathway terminating in the dense core of the nPT. These fibers are large-diameter axons with beaded terminals forming a dense meshwork restricted to the dense core region of nPT.

Four types of neurons were found in nPT. Based on the correlation of the size and shape of the somas within the nucleus with HRP and Golgi-stained materials, these types are 1) large neurons, 2) elongate neurons, 3) stellate neurons, and 4) amacrine neurons. The large neurons
(Figure 13), for which the nucleus is named, have elongated soma (18μm in diameter) and a single long dendrite that extends across the dorso-ventral axis of the nucleus for up to 250μm (Figure 13). Some of the large neurons also have short basilar processes. The elongate neurons have 17μm somas from which a primary dendrite emerges as well as a short secondary dendrite. The primary dendrite branches within 25μm of the soma into two processes creating a total dendritic field of 100μm. The stellate neurons have round somas that range from 7-10μm and have spineless dendrites. These dendrites terminate in endbulbs or boutons from which fine processes emerge to terminate on other stellate neurons or upon the larger classes of cells within the nucleus. The smallest neurons in the nPT are termed amacrine since they lack distinct axons. The somas of these cells range from 3-5μm and give rise to several fine processes. The nPT projects to the tectum (Wilczynski and Northcutt, 1977). Both elongate and the large cells contribute to this projection. Two out of five ventral brainstem injections resulted in filled cells within the nPT. Again, this projection originates from both the large cells and the elongate neurons. Due to the size of the injection sites, the exact location of the terminal field of the pretecto-bulbar pathway could not be determined; however, it does appear to reach the caudal portion of the
ventral brainstem.

The Optic Tectum

The optic tectum was not the primary focus of this thesis as its organization has been analyzed previously in great detail by other investigators. In general, the organization of tectal afferents, efferents, and internal structure follows that cited earlier but with a few exceptions. In those tectal injections which entered the deep fiber layers 3, 4, 5 around the trigeminal sensory neurons, a consistent labeling of neurons within the nucleus reticularis tegmenti (nRT) took place. The nRT is located in the caudal mesencephalic neuropil, above the torus semicircularis. The nucleus consists of a diffuse population of reticular neurons within the second tier with a companion population of bipolar and elongate neurons just superficial to the central grey. The large reticular neurons have a 30μm soma and a single 180μm dendrite. Some of the neurons have smaller secondary processes. The smaller neurons situated along the margin of the central grey have a 20μm soma with a 90μm dendritic field. The diffuse nature of nRT made it difficult to determine the relationship of smaller neurons within the field to the larger efferent cell types. The axons of the large reticular and bipolar elongate types project through
the caudal region of the nucleus profundus lateralis and into the deep tectal lamina. Also filled after tectal injections were neurons in the anterior thalamus. These cells were not postsynaptic to the optic terminal fields of Bellonci and geniculatum but were rather neurons deep within the nucleus rotundus along the margins of the ventricle.

The projection of the tecto-bulbar to the anterior mesencephalon described by Lazar (1969) and Rubinson (1968) using degeneration techniques was confirmed with HRP. These fibers were found to be of small caliber and to be restricted to the superficial margin of the grey just ventral to the uncinate field and were not found to enter the nMLF. Collaterals of the tecto-bulbar pathway were also found to emerge just medial to the nucleus of the basal optic root and to terminate in and around the nucleus of the third cranial nerve (n.III).

The Accessory Optic System

Afferents. The course of the basal optic root was revealed in cases where the optic nerve was transected just behind the eye with HRP being transported in anterograde fashion to the retinal terminal fields. Brains were sectioned in either the coronal, sagittal or horizontal plane. The basal optic root (BOR) emerges from the
ventral, posterolateral margin of the optic chiasm and consists of a well-defined tract which courses along the ventrolateral edge of the diencephalon to enter nBOR immediately caudal to the mesodiencephalic junction. The main body of the terminal field of nBOR begins at the caudal edge of the hypothalamus, and extends rostro-caudally to the level of the n.III. The main portion of nBOR has a cup-like configuration, rounded along its medial edge, and is convex along its dorsal and ventral margins. Cells cluster along the inside margins of the terminal field (Figure 14a).

A second, more diffuse fascicle of optic fibers emerges somewhat more medially from the chiasm and maintains this position as it approaches nBOR and terminates in the medial posterior portion of nBOR (Figure 14b). The large diameter axons often branch along the primary bundle and appear to give off smaller collateral which travel along the main bundle. These large axons enter nBOR along its rostral and superficial margin. Many of the fibers of the diffuse bundle enter nBOR from the surrounding tegmentum. Some of these fibers can be seen turning at right angles before entering the nucleus. Partial transections of the optic nerve and/or BOR have revealed the configuration of axonal terminals within nBOR. Two types of optic afferents were observed: 1) large caliber fibers,
1.5-3μm in diameter, which often form tight spirals before arborizing into smaller branches and give rise to a dense meshwork of terminal arborizations with many boutons; and 2) extremely fine-caliber fibers, 0.5μm or less in diameter, which branch throughout the terminal field with terminal boutons. In horizontal and sagittal sections, a few axons were observed which passed through nBOR and emerged from its caudal margin (see also Steedman et al., 1979). These large-diameter fibers travel along the ventral surface of the mesencephalon and into the brainstem, with occasional terminals occurring along the ventral margin of the caudal mesencephalon and brainstem.

Although the vast majority of BOR axons were contralateral, an ipsilateral component was also observed which appears to travel separately from the main bundle. The ipsilateral nBOR contains a lower density of fibers than does the contralateral but these fibers fill the entire terminal field. The ipsilateral projection is dominated by small caliber fibers, although a few large fibers were also observed.

HRP injections of the anterior thalamus, primarily in the periventricular cell groups referred to as the lateral geniculate nucleus, nucleus rotundus, postero-central and posterolateral nuclei (terminology of Frontera, 1952) produced definitive anterograde labelling of axonal
terminals within nBOR. When HRP injections were made in the ventral mesencephalon including nBOR, retrogradely labelled neurons were seen in the posterocentral cell group and in the nucleus rotundus. These neurons in rotundus had a 13μm soma and a primary dendrite reaching 460μm into both the neuropil of Bellonci and corpus geniculatum (Figure 15). Axons from these cell groups descend around the posterior endopeduncular nucleus and then assume a ventral position as they travel caudally, ultimately entering nBOR from a somewhat more dorsal position than does BOR. This projection consists of fine diameter fibers with larger terminal swellings than BOR axons. Some thalamic axons also project into the ventral tegmentum caudal to nBOR, at least to the level of cranial n.IV.

A group of neurons outside of the terminal field were found to have dendrites extending into nBOR. This region was termed peri-nBOR. Several afferent projections to the peri-nBOR appear to be associated with the AOS in anurans. Axons which originate both from the pretectal grey and also the nucleus of the cerebellum terminate in peri-nBOR. Following HRP injections of the dorsal tegmentum, a fiber pathway was observed from the pretectal grey which enters the posterior commissure and terminates in peri-nBOR, just medial to nBOR. HRP injections restricted
to the nucleus of the cerebellum labelled a fascicle of fibers which could also be traced to the peri-nBOR region. Axonal terminals of these fibers were observed in close proximity to the somas of both pyriform and commissural neurons.

It should be noted that several major fiber systems are located at the boundaries of nBOR; for example, the fasciculus retroflexus courses anterior and ventral to nBOR as it projects to the interpeduncular nucleus, while fibers from the anterior, dorsal and ventral thalamus are located immediately dorsal to nBOR. nBOR is bounded at its caudal extent by fibers from the tectum which cross in the ventral commissure and ascend to the nucleus lateralis profundus dorsalis mesencephali.

**Intrinsic organization.** Neurons occurring within the terminal field of nBOR and in the peri-nBOR region appear to be identical to those found in the superficial layers of the frog optic tectum; therefore, we have adopted the terms amacrine, stellate, ganglionic and pyriform in describing nBOR and peri-nBOR neurons. Within nBOR stellate neurons were the most numerous cell type, comprising 64% of the intrinsic cell population (Figure 16). These neurons were morphologically identical to those described in the LCPTn. The amacrine cell population within nBOR comprises 19% of the intrinsic
neurons. Elongate neurons comprise 14% of the population and have spindle-shaped somas, 7-12μm in diameter. When observed in Golgi material, these neurons could be further subdivided into two distinct morphological types—neurons with a short apical dendrite from which several dendrites emerge, and neurons with a single apical dendrite with spines on both the soma and dendrites. Elongate neurons do not show any consistent orientation; some remain within the terminal field, while others arborize outside of nBOR.

The largest neurons within nBOR are ganglionic neurons with somas 20μm in diameter from which two to three processes emerge in a bipolar configuration. The dendrites of these neurons are 2 microns in diameter and are spineless. These dendrites are long and often reach as far as the nucleus profundus lateralis. These neurons make up only 4% of the population of nBOR.

Neurons in the peri-nBOR region with dendrites which extend into nBOR include: pyriform neurons, commissural neurons which project to the opposite side, and large reticular neurons of the nucleus of the medial longitudinal fasciculus (nMLF) (Figure 16). The largest component of this extrinsic population is that of the pyriform neurons which are located in the peri-nBOR region between nBOR and the central grey. Pyriform neurons have pear-shaped somas, 9μm in diameter, from which a single,
spineless dendrite emerges and enters nBOR. A second, extrinsic neuronal population is composed of commissural neurons located between the central grey and nBOR and lie among the pyriform neurons. These neurons have somas 12\(\mu\)m in diameter from which two dendrites emerge and branch several times before entering nBOR. A third type of extrinsic neuron is located along the lateral margin of the superficial grey, adjacent to the oculomotor complex in the area referred to as the nucleus of the medial longitudinal fasciculus (nMLF). Morphologically, these neurons are part of the nucleus reticularis tegmenti (Kuhlenbeck, 1975), and have large somas, 16\(\mu\)m in diameter. Two large basilar dendrites emerge from the soma and ramify in the central grey. A third, apical dendrite branches several times before entering nBOR.

Within nBOR, the somas of stellate neurons and the dendrites of ganglionic, pyriform, commissural, and large reticular neurons of the nMLF are enmeshed in dense glomerular complexes. The terminal swellings of dendrites of both amacrine and stellate neurons are closely associated with the terminal boutons of afferent axons, thereby creating a glomerular configuration. The somas of stellates, and the dendrites of ganglionic, elongate pyriform, commissural and reticular are associated with glomeruli in nBOR.
Efferents. Two distinct projection systems originate from the AOS in frog. The first arises from the main body of nBOR and projects to the large-celled pretectal nucleus and the nucleus profundus lateralis. A second major projection originates from peri-nBOR and is associated with the oculomotor system and the nMLF. Following HRP injections of the anterior portions the nucleus profundus lateralis and the caudal region of the lateral thalamic neuropil, elongate neurons within nBOR were retrogradely labelled. HRP injections confined to the LCPTn labelled axons and somas of the large ganglionic neurons within nBOR. Elongate and ganglionic neurons comprise the sole efferent neuron population within nBOR.

The projection of neurons lying in peri-nBOR provides the primary route by which information from nBOR reaches the tegmental central grey. Following injections of the nMLF and the nuclei of cranial nerve III and IV, the somas of pyriform neurons located in the peri-nBOR region were retrogradely labelled with HRP. The axons of peri-nBOR pyriform neurons form axonal beads between the neuronal laminae of the nMLF. These axons also bifurcate after entering the nMLF and many of their processes could be traced directly to the proximal dendrites and soma of the motor neurons of cranial n.III. Commissural neurons located among the pyriform neurons were filled with HRP
reaction product after injections of the anterior lateral mesencephalon in and around nBOR on the opposite side. The axons of these neurons enter the posterior commissure, crossing the midline and descending to the opposite tegmental fields. Axon collaterals of these commissural neurons also enter nBOR on the ipsilateral side. The large reticular neurons of the nMLF with dendrites in nBOR were not filled in any of our HRP injections; thus, no axonal connections could be determined in this study. Neurons in nBOR do not appear to project to the cerebellum as they do in a few species, notably avians.

The Central Tegmental and Pretectal Grey

The central grey of the anterior mesencephalon consists of from 4-6 lamina of cell bodies alternating with layers of fibers. At the base of the grey is a thick lamina of fibers representing the peri-ventricular fiber system. This fiber system appears to consist of interconnections between neighbor regions of the grey. The cells of the grey are a mixture of bipolar and spindle-shaped neurons with 6-9\(\mu\)m somas and 90\(\mu\)m dendritic fields. The spindle-shaped neurons have short basilar processes and a primary dendrite that branches twice each time producing two smaller processes. Along the lateral margin of the grey are large reticular neurons that have been described
earlier. Along the dorsal margin of the anterior mesencephalon there is a population of migrated neurons forming 2-3 loose layers above the posterior commissure. These layers represent a configuration similar to that of the denser posterior thalamic group. Above this layer is found the uncinate or hooked field of retinal terminations. This terminal field is 180μm above the margin of the grey and contains both ipsilateral and contralateral fibers which form a dense mesh of fine fibers curving across the medio-dorsal to latero-ventral axis of the grey. At the caudal extent of the uncinate field, fibers from the tectobulbar pathway send fine fibers to the anterior margin of the central grey. These projections coupled with the projection of pyriform neurons of peri-nBOR to the nMLF, indicate that the entire central grey receives either primary or secondary visual input.

Following injections of the dorsal tegmentum (Figure 17), large populations of efferent fibers were found to ascend into the neuropil and form a number of bundles stretching from the dorsal margin of nBOR to the edge of the central grey. These fibers project across the entire ventral brainstem leaving terminals at all levels along its course. Some of the first structures to receive input from these bundles are peri-nBOR and the nMLF. Dendrites from the spindle neurons of the nMLF enter the
more medial bundles of the central tegmental pathway, while
the more lateral bundles reach peri-nBOR (Figure 17).
These fibers course down the brainstem, maintaining a
position between the tecto-spinal and tecto-bulbar path-
ways, terminating in a large number of nuclei including
the nucleus reticularis, the nucleus reticularis isthmi,
the nucleus reticularis superior, the superior olivary
nucleus, the inferior reticularis nucleus, and the nucleus
raphe. Following injections of HRP into the brainstem
this projection was found to originate from both the
small spindle and bipolar neurons within the grey
(Figure 18). Fibers from these cells also cross the mid-
line in the posterior commissure and follow the same route
through the brainstem as the primary bundle. The pro-
jection of these neurons to the optic tectum was also
confirmed.

The Nucleus of the Medial Longitudinal
Fasciculus (nMLF)

The nMLF is only vaguely defined in anurans. Gen-
erally, it is considered to be that section of the central
grey around n.III and n.IV that receives input from the
vestibular complex (MLF). This region lacks the strict
lamination found in the dorsal pretectal grey. While
three cell lamina can be defined at the dorsal margin
of the nMLF, this disappears as one approaches n.III and
n.IV. Along the lateral margin of the nMLF are the large reticular neurons described earlier. The nucleus proper is composed of spindle and bipolar neurons like those found in the dorsal grey. Afferents to the nMLF come from four sources: 1) The largest projection originates in the vestibular nuclei and consists of large fibers that branch to form a dense meshwork of fine-beaded fibers much like those of BOR. 2) A second projection comes from the pyriform neurons of peri-nBOR. These fibers branch thus making contact with the somas of nMLF neurons as well as those of the oculomotor complex. 3) A third projection comes from the dorsal pretectal grey. These fibers project across the posterior portions of the nMLF. 4) The fourth projection originates from the cranial nerve nuclei n.III and n.IV. These oculomotor neurons send collateral fibers into the nMLF.

Following HRP injections of the vestibular nuclei, neurons in the nMLF were retrogradely labelled (Figure 19). This projection appears to originate from both the spindle and bipolar neurons within the nucleus and is composed of fine fibers that travel through the MLF to the vestibular nuclei. Injections of the rostral spinal cord also resulted in retrograde labelling of the same spindle and bipolar neurons in the nMLF. A large projection from the nMLF enters n.III and n.IV. This projection forms a
network around the somas of the oculomotor neurons. Finally, HRP injections of the posterior commissure resulted in the labelling of a discrete group of neurons in the caudal nMLF (Figure 20). These cells may represent a commissural population.

The Oculomotor Complex (n.III and n.IV)

The IIIrd and IVth cranial nerve nuclei consist of a continuous column of cells 720µm in rostro-caudal extent. Two distinct types of neurons were found within the column, a large (16-25µm diameter) and a smaller (4-12µm diameter) class. While differences were found between the large cells of n.III and n.IV in the length of their primary dendrites, all cells have the same basic dendritic configuration. Both large and small neurons have a primary dendrite and 1-2 smaller dendrites. The primary dendrite gives rise to 2 second-order and 4 third-order processes. The smaller cells of both nuclei have short (25µm) primary dendrites, while the large cells of n.III have a 60µm-length primary segment and large cells of n.IV have 120µm long primary dendrites.

The n.III and n.IV receive afferents from pyriform neurons of the peri-nBORG region as well as from the nMLF and MLF. Other afferents originate from a small population of fibers from the tecto-bulbar pathway which were seen
leaving the bundle in the peri-nBOR region descending into and around n.III.

Beaded axonal collaterals were observed originating from the smaller dendrites of all neurons within n.III and n.IV. These axons enter the adjacent nMLF. Some collaterals from n.IV enter the periventricular white matter and ascend to the dorsal tegmentum.
CHAPTER IV
DISCUSSION

The Primary Visual Areas

Comparative studies of the vertebrate visual system have demonstrated that the pretectum and accessory optic system are consistent features of both the mammalian and non-mammalian central visual pathways. As we have seen, the relative complexity and degree of differentiation of these nuclei vary across species as does the nomenclature applied to these terminal fields. In anurans, the uncinate, nBOR and LCPTn display a gradient of organization between neuropil and nucleus. Within the uncinate terminal field there are no postsynaptic elements; rather, further processing is carried on by cells outside the terminal field located in the central grey. nBOR has an intermediate type of organization with some postsynaptic elements within the nucleus (ganglionic and elongate types) while other postsynaptic elements (pyriform, commissural and reticular) are positioned outside the region of retinal termination. The large-celled pretectal nucleus is the only "true" nuclear formation of the anterior mesencephalic visual areas. The LCPTn contains all of its postsynaptic elements (large cells, and elongate neurons) within the retinal terminal plexus. This situation
differs greatly from that of the other well-known class of amphibians—the urodeles—where all the visual terminal fields arborize in cell-free areas of the neuropil.

One of the new findings of this study was that the entire superficial margin of the mesencephalon is composed of a morphologically uniform population of stellate and amacrine neurons. The nuclear formations of the second tier appear to be products of this stellate-amacrine population, plus various arrays of medium and large neurons. Since urodeles appear to lack both the stellate-amacrine population as well as their related nuclear formations, a question arises as to the nature of homologies between these groups in the main amphibian lines. A stellate population does exist in the urodele, where Herrick describes a type of "glomerular dendritic" organization. Similar glomerular dendritic formations have been described in the optic tectum of frog by Szekely and Lazar (1976) as well as in the nBOR in this study. In avian species, the superficial layers of the tectum also contain similar stellate populations (personal observation) indicating that the expansion of stellate populations across the lateral margin of the mesencephalon may represent one of the final stages of neural evolution preceding the arrival of amniote types.

While both the LCPTn and nBOR contain stellate and
amacrine populations, the types of retinal axonal arborizations to these nuclei differ greatly. Each large-diameter fiber reaching nBOR creates a dense meshwork of heavily beaded terminals, but this arborization is relatively localized. The large retinal fibers reaching the LCPTn first arborize in the dense core region, but then expand as a series of fine fibers in a radial fashion across a wide area of the nucleus. The uncinate terminal field differs from both of these with fine fibers forming a dense mesh of unbeaded terminals. The functional implications of these differing types of retinal arborizations will have to await the results of electrophysiological recording studies.

In addition to the interneuron types and the classes of retinal arborizations, the efferent cell types within the different optic terminal fields of the mesencephalon were also described. Two features of nBOR's efferent neurons are of interest. First, it appears that each efferent type has a specific target structure such that the ganglionic neurons project to the pretectum while axons of the elongate population reach the lateral thalamic nucleus and the nucleus profundus. Secondly, the efferent neurons of nBOR have dendritic arborizations that extend beyond the terminal field. These cells can be expected to summate not only activity in nBOR, but also that of the
surrounding neuropil. A previously unknown group of neurons related to nBOR were also described as the peri-nBOR region. In the LCPTn a second efferent population was found in the elongate population.

The neurons related to the primary visual fields of the mesencephalon have been shown to have more complex interconnections than had been previously supposed. In particular, connections have been demonstrated between the postsynaptic cell groups of the anterior thalamus (nucleus Bellonci, and corpus geniculatum) and nBOR. Secondly, a projection was found from ganglionic neurons in nBOR to the LCPTn. A variety of other connections between the primary visual nuclei are also known; such as, LCPTn to tectum, reciprocal connections between the tectum and anterior thalamus as well as projections from the posterior thalamic and pretectal grey to the tectum. These connections, taken as a whole, indicate that the anuran visual fields are not discontinuous "islands" but rather these groups are organized in a nearly circular array. Thus, specific visual functions are probably not limited exclusively to particular nuclei; rather, each structure might be expected to add in a qualitative fashion to each behavioral capability. This type of organization-in-series must be an important consideration in any interpretation of electrophysiological recording or lesion-
behavioral studies. These patterns of connectivity are also of interest when we consider that each visual nucleus may receive its input from specific populations of retinal ganglion cells. For example, nBOR receives its input from populations of large ganglion cells which are located in the periphery of the retina as well as from small ganglion cells scattered through the retina (Montgomery, Fite and Bengston, submitted). The dendrites of all of the large ganglion cells arborize in the outer layers of the internal plexiform layer of the retina. As a result of this pattern of arborization, these are one of the first populations of retinal ganglion cells to be activated by impulses reaching the internal plexiform layer. The fibers of these cells form the basal optic root (BOR) which is composed of some of the largest fibers of the optic tract. These large fibers can be expected to be some of the fastest conducting fibers of the optic tract. It may be possible to assume that as an image first crosses the periphery of the retina, nBOR is one of the first structures to be activated. Taking this as a starting point, if we follow the pattern of interconnections, fibers from the neurons of nBOR should reach the LCPTn a little after impulses from the retina to the LCPTn. The projection from nBOR to the LCPTn is to the dense core region of the nucleus which is the first point
of arborization of direct retinal fibers. The projection from nBOR thus seems to be in a position to modulate visual input to the LCPTn. If we follow the circuit, we find the pretectum projecting to the tectum, sequenced perhaps with the arrival of the fine diameter fibers from the retina. The tectum, in turn, projects to the anterior thalamus which then projects back to nBOR, thereby completing the circuit. As we gain more refined information about the types of retinal ganglion cell innervating each nucleus and the pattern of connectivity within and between these groups, we may be able to define the precision timing and interconnections that make up a unified visual field from its individual and diverse components.

Elements of the Somatic and Motor System

In anurans, very few fibers from the spinal cord project beyond the level of the brainstem. This makes the higher-order connections of this system difficult to analyze. Recently, a series of connections have been charted which shed some light on the organization of this system. Projections from the spinal cord are known to reach a region of the brainstem referred to as the obex. Projections have been charted from the obex to the posterior central thalamus (Neary, 1979). The posterior
central thalamus, in turn, projects to a region of the forebrain referred to as the "striatum" (Wilczynski and Northcutt, 1979). The striatum projects to the nucleus reticularis tegmenti. These connections are thought to represent an extrapyramidal system in anurans. In this study, we have shown that the nucleus reticularis tegmenti projects to the deep layers of the optic tectum in the region of the trigeminal sensory nucleus. This connection indicates a link between tecto-trigeminal system and the extrapyramidal system.

The cerebellum, in anurans, is another target of spinal projections. One of the primary targets of the cerebellum is the single nucleus of the cerebellum. In amniotes, one of the targets of the deep nuclei of the cerebellum is the red nucleus. While no red nucleus exists in anurans, an ascending projection was found from the nucleus of the cerebellum. This projection courses just lateral to the MLF as it enters the mesencephalon. Fibers from this tract reach, among other sites, the peri-nBOR region and the posterior central thalamus. The projection of the nucleus of the cerebellum to the deep layers of the posterior central thalamus indicates another interconnection with the system. The projection of the nucleus of the cerebellum to peri-nBOR brings us back to the central issue of this report, the integration of the
Visual and motor system.

**Visuo-Motor Integration**

Neural circuits. First, we have found little evidence for information from the somatic or motor system reaching nBOR, the LCPTn, the uncinate field or the superficial layers of the tectum. This compares favorably with the electrophysiological evidence obtained from these regions where activation is exclusively visual. There is substantial evidence for mixed somatic and visual input to second-order visual cell groups (Fite, 1969). A prime example of this is the projection of the nucleus of the cerebellum to peri-nBOR. The deep layers of the tectum can also be considered a second-order visual area with mixed somatic and visual input. This result again matches the recording data which show mixed somatic and visual responses from regions around the primary terminal fields of the retina in posterior thalamus and anterior mesencephalon (Brown and Marks, 1977). The first step in visuo-motor integration in anurans and perhaps all vertebrates appears to be an interface between the visual and somatic systems.

The next stage appears to take place in the central grey. The anuran central grey is composed of four divisions: 1) a dorsal region with neurons postsynaptic
to the uncinate field, 2) a central region, 3) the nMLF, and 4) the cranial nerve nuclei n.III and n.IV. The entire central grey of the anterior mesencephalon receives either primary or secondary visual input. The dorsal region receives primary visual input from the uncinate. Directly below the uncinate field is the central region of the grey. Lazar (1969) and Rubinson (1968) have reported input to the central region from the tectum. The projection of the tecto-bulbar pathway to this central region was confirmed in this thesis using HRP. This projection consists of small-diameter fibers which are restricted to the superficial margin of the grey. Below this region is the nMLF which receives its visual input from the peri-nBOR region. Finally, the n.III receives input from a small population of fibers also from the tecto-bulbar pathway.

The dorsal and central regions of the anuran, anterior mesencephalic grey have often been referred to as the motor tegmentum. The term motor tegmentum seems difficult to justify in relation to this region as it does not receive any known somatic or motor projections. The primary rationale for this terminology appears to stem from the projection of these groups to the brainstem. Herrick termed this projection from the grey to the brainstem in urodeles the "central tegmental pathway."
Based on connectivity, the dorsal and central portions of the mesencephalic grey appear to be alar plate structures. The projections of the central tegmental pathways are, in fact, quite similar to that of another alar plate structure, the optic tectum. The course of the central tegmental pathway is between that of the lateral tecto-bulbar and medial tecto-spinal pathways. Neither the tecto-bulbar nor the central tegmental pathways reach the cranial motor neurons of the brainstem; however, both fiber systems innervate a number of reticular nuclei as well as groups in the central grey proximal to the motor nuclei of the brainstem. Both fiber systems leave terminals along their entire course, often entering the same nuclear formations. While the brainstem is one of the least understood regions of the anuran central nervous system, it is clear that some of the reticular nuclei, innervated by both the central tegmental and tecto-bulbar pathways, project to the spinal cord while others act as accessory nuclei of the various cranial nerve nuclei. The central tegmental, tecto-bulbar and tecto-spinal pathways are the dominant descending projections from the mesencephalon. The dual innervation of a number of reticular and central grey groups by these pathways appears to constitute the main substrate of visuo-motor connectivity in the anuran CNS. The large-celled
pretectal nucleus was also found to project to the ventral brainstem. While the exact point of termination of this pathway could not be confirmed, it may be similar to the projection of the pretectum to the inferior olivary nucleus in mammals. A very small population of large axons from the BOR were found to project beyond nBOR. These axons terminate along the ventral margin of the brainstem. As this region of the brainstem contains no known nuclei, the BOR axons are likely to be important in second- or third-order interactions with brainstem nuclei as yet undetermined.

To summarize, influences from the anterior mesencephalon effect motor activity at the levels of the brainstem and spinal cord via five pathways: 1) the tecto-bulbar pathway, 2) the central tegmental pathway, 3) the pretecto-bulbar pathway, 4) the tecto-spinal pathway, and 5) the interstitial-vestibular/interstitial-spinal pathway. Two of these pathways, the tecto-bulbar and central tegmental pathways, project to many of the same brainstem nuclei. These nuclei project to the spinal cord, cerebellum, and brainstem cranial nerve nuclei. The pretecto-bulbar pathway, while its exact point of termination is unknown, may well have similar connections. Finally, the rostral spinal cord receives a direct projection from both the tecto-spinal and
interstitio-spinal pathways. It seems logical to assume that most of the visual activity recorded in the brainstem and rostral spinal cord results from the activity of these pathways.

**Visuo-Motor Integration**

**Functional correlates.** There is ample evidence for visual activity in the frog brainstem and rostral spinal cord. Maeda and co-workers have shown that visual and vestibular inputs are integrated by spinal motor neurons of the neck and forelimbs in frog (Maeda et al., 1977). These spinal units could be found when the tectum was stimulated. However, when the tegmentum was stimulated, postsynaptic potentials of shorter latencies were obtained in spinal motor neurons than were observed following tectal stimulation. Therefore, Maeda et al. suggested that stimulus current may have spread to underlying tegmental structures, and hypothesized the existence of a tecto-tegmental pathway.

This thesis allows an expansion of Maeda's theory to predict that these shorter latencies in spinal motor neuron responses may have resulted from activation of the central tegmental, prepecto-bulbar, or groups of BOR axons.

Visual-vestibular interactions have been described in the vestibular nuclei of toad. Neither the removal of the optic tectum nor removal of the cerebellum abolished
these responses (Chang and Wu, 1959). The most likely source of these responses would seem to be the interstitial-vestibular pathway. Both mossy-fiber and climbing-fiber visual input to the frog cerebellum is well-established electrophysiologically (Chang and Wu, 1959; Dieringer, 1974; Shafa, 1974; Ansorge and Grusser-Cornehls, 1977). Ansorge and Grusser-Cornehls have described two major groups of visually activated neurons—those with receptive field sizes and responses similar to those found in the tectum or thalamus, and those large receptive fields which respond optimally to a moving, patterned surrounding which they believe to be activated via nBOR. Shafa's (1974) studies also provide support for this conclusion. All visually activated units that were tested for visual-vestibular interactions showed stronger responses to combination of visual and vestibular stimulation than to either alone. Although a bisynaptic pathway from the retina to the cerebellum via nBOR has been reported in pigeon (Braith and Karten, 1977), turtle (Reiner and Karten, 1979) and chinchilla (Hendrickson et al., 1978), similar connections do not appear to exist in either rabbit (Simpson, personal communication) or frog (Montgomery et al., 1979). Although the possibility remains that such a pathway has escaped detection with HRP methods, it seems more likely that visual input to
the anuran cerebellum is mediated via the vestibular nuclei and/or the nucleus raphe. This latter structure gives rise to climbing fibers (Larsell, 1967; Cochran and Hackett, 1977), and while anurans do not have a well-defined inferior olive, the nucleus raphe is generally regarded as its primordium (Larsell, 1967). This thesis has shown that neurons of the pretectal and posterior thalamic central grey, which are postsynaptic to two primary retinal terminal fields (uncinate and posterior thalamic) do project in part to the nucleus raphe. The nucleus raphe may also be innervated by the pretecto-bulbar pathway which was first revealed in this thesis following HRP injections in the caudal brainstem at the level of the nucleus raphe. A direct tecto-cerebellar pathway previously reported in anurans (Rothig, 1927) has not been confirmed and several investigators have failed to find evidence of such a pathway using degeneration methods (Lazar, 1969; Rubinson, 1968). The optic tectum may influence visual responsiveness in the cerebellum via the tecto-bulbar pathway. In any event, it seems clear that the anuran cerebellum, which consists of a single, unfolded lobe does not display the richness of connections nor the highly specialized subfields associated with visual, oculomotor and vestibular input which occurs in amniotes.
**Visuo-Ocular Integration**

**Neural circuits.** The connections reviewed so far have related to role of the mesencephalic visual nuclei in the modulation of spinal cord and brainstem activity. By describing the visual input to the oculomotor system, we may gain insights into the way brainstem activity is affected by these same nuclei.

Within the ventral mesencephalon, the n.III and n.IV are surrounded by accessory cell groups referred to as the nMLF. Both the nMLF and the oculomotor column (n.III and n.IV) receive a dense projection from the vestibular nuclei. The nMLF and the oculomotor column have reciprocal interconnections via oculomotor axonal collaterals and the direct projection of the nMLF to the oculomotor neurons. Neurons in the nMLF also project to the vestibular nuclei and spinal cord.

Three types of visual input reach this highly interconnected region of the ventral mesencephalon: 1) The most widely distributed input comes from peri-nBOR. This input reaches both the nMLF and n.III and n.IV. 2) The central tegmental pathway courses over the caudal portion of the nMLF (Figure 19). The dendrites of the neurons in the nMLF enter this bundle. 3) Finally, the tectum sends a small number of fibers in and around n.III. These three precisely organized projections represent a summation of
the activity of all the primary visual fields due to the interconnections of the visual fields themselves. Visually activated eye movements may be effected by any of these three pathways. Each can be expected to have qualitatively different effects on visually guided behaviors. Beyond this, subtle changes in behavior may result from interference with any of the interconnected visual fields.

Functional correlates.

It is obvious that the motor apparatus of the visual organ has to fit the sensory apparatus as the shell does an egg. For, whether one assumes that they were set up according to a wise plan, or that they developed with each other in an inevitable way as the evolutionary series is transversed, in any case, the capabilities of the one have to correspond to the needs of the other (Hering, 1868).

The anuran mesencephalon has been linked to a number of visually guided behaviors. Bilateral lesions of the tectum result in "blindness" towards predators and prey (Ingle, 1973). These animals do show proper orientation to stationary objects. Lesions of the posterior thalamic nucleus and pretectum result in animals which show prey catching behaviors but consistently bump into stationary objects (Ingle, 1976). Lazar (1973) was the first investigator to provide evidence that optokinetic nystagmus (OKN) could be eliminated by lesions of the nucleus of the basal optic root (nBOR) or transection of BOR. In this thesis, a number of neural
circuits have been defined which clear the way for a detailed analysis of these behaviors.

Lazar (1973) made systematic lesions of the anuran visual nuclei. He found that the removal of the entire tectum and large-celled pretectal nucleus could eliminate the OKN response. Lesions of nBOR, however, had the greatest effect on OKN responsiveness. For this reason, Lazar felt that nBOR was the critical element in this behavior. This result has not been obtained in any other species. Complete destruction and deafferentation of nBOR in pigeon and turtle are associated only with a reduction in horizontal OKN response frequencies at the upper range of effective pattern velocities (Fite et al., 1979). Recently, Ingle (1980) has reported the elimination of OKN in frog following knife cuts of the large-celled pretectal nucleus. Evidence has also been obtained in a variety of other species which indicates that the pretectal visual areas may mediate horizontal OKN (Pasik et al., 1969; Collewijn, 1975; Cochran et al., 1980). In an attempt to resolve these conflicting views, a series of twenty-four lesions and knife cuts were made in the accessory optic system and pretectum of anurans (Fite et al., 1980; Fite et al., in preparation). These lesions were evaluated in relation to the neural circuits described in this thesis. Each lesion involved some
combination of three nuclei and three fiber pathways. These nuclei were nBOR, peri-nBOR, or the large-celled pretectal nucleus. The pathways involved in these lesions were BOR, the thalamic afferents to nBOR, and the efferents from nBOR to the pretectum. In addition, three cases also resulted in which the lesions were either rostral or caudal to the accessory optic system. In these control cases no effect on horizontal OKN frequency of saccade versus pattern velocity resulted. In the analysis of these lesions the nuclei and fiber systems were described as intact (+), damaged (-), or destroyed (0). The OKN response was described as normal (no effect), reduced (some decline), no OKN followed by some recovery, and no OKN. Figure 21 shows the results of these experiments. From these lesions, it became clear that damage or destruction of BOR (cases 5-6), the thalamic efferents to nBOR (case 7), nBOR's efferents to the pretectum (case 8) or some combination of these (cases 9-10) results in some decline in the OKN response but does not eliminate it. From these results, it appears that nBOR can be isolated from its known inputs and outputs without the loss of the OKN response. Direct lesion of nBOR can have one of two effects. These lesions can result in a loss of OKN followed by recovery of function after several weeks (cases 15-16) or a loss of OKN for the high range of
effective pattern velocities (cases 11-12-13-14). Lesions in which peri-nBOR was destroyed, consistently resulted in loss of horizontal OKN with no recovery of function observed (cases 17-18-19-20-21-22). Finally, lesions of the large-celled pretectal nucleus and the surrounding region resulted in a great reduction of the OKN response to horizontal stimuli.

How can these data be reconciled with that of Lazar and Ingle? First, reviewing Lazar's published histology, it becomes clear that his lesions were not restricted to nBOR alone but also included the peri-nBOR region. Yet even with this fact, we are still faced with the problem of the dual location in peri-nBOR and the pretectal region for the loss of the OKN response. The pretectal efferents described in this thesis are to the tectum and the ventral brainstem. The tectum gives rise to the tecto-bulbar pathway which passes through peri-nBOR, giving off collaterals which descend in and around the oculomotor neurons of n.III and n.IV. A circuit from the pretectum to the tectum and then to peri-nBOR would seem to fill all the anatomical criteria for our dual points of sensitivity for the loss of the OKN response. There is, however, a major complication. Lesions of the tectum do not abolish the OKN response. The other pretectal projection is to the ventral brainstem. This projection, as stated
earlier, appears to be similar to the projection of the nucleus of the optic tract in rabbit to the inferior olive. The inferior olive in rabbits projects to the cerebellum. In this thesis, the nucleus of the cerebellum has been shown to project to peri-nBOR. Cell groups in the ventral brainstem have also ascended to the nMLF and n.III/n.IV. An outline of this complicated series of circuits can be seen in Figure 22. Briefly: 1) The pretectum projects to the brainstem. Brainstem groups project to the cerebellum and the nMLF and n.III/n.IV. The cerebellum projects to the nucleus of the cerebellum and the nucleus of the cerebellum projects to peri-nBOR. 2) The nBOR projects to the large-celled pretectal nucleus. The pretectum projects to the tectum and the tectum projects to peri-nBOR. 3) The nBOR receives dendrites from peri-nBOR. Pyriform neurons project to the oculomotor complex (n.III/n.IV) and the nMLF. These anatomical relationships may help explain the varied effects of lesion in the anterior mesencephalon on OKN responsiveness. The final common channel for visual input to the oculomotor complex appears to be the peri-nBOR/nMLF region.

As nBOR does not totally mediate OKN, then what functions are mediated by this nucleus? The prey-catching behavior of animals with nBOR lesions was investigated (Fite et al., 1980). The nBOR is innervated
by retinal ganglion cells located mainly in the periphery of the retina (Montgomery et al., 1979). When frogs with lesions in nBOR were tested for prey-catching latencies, a large increase in latencies was found to stimuli 180° from the center of the visual field. These results may indicate that nBOR deals mainly with peripheral vision; thus, its role in the OKN response.

Anurans and Mammals

The final remaining question is to what extent the connections described in this thesis represent specializations within the anurans or a more generalized condition common to most vertebrates? In particular, do these systems have counterparts in the mammalian central nervous system? To establish whether counterparts exist for these systems, each one was compared with circuits found in the mammalian central nervous system. A complete review of the mammalian central visual and motor pathways is beyond the scope of this thesis. Rather, each specific pathway will be compared with mammalian systems as to similarities in site of origin and their points of termination. This represents a somewhat crude test of homology but it opens the way for future research.

The mammalian structure most like the anuran large-celled pretectal nucleus appears to be the nucleus of the
optic tract (Giolli, 1963). This mammalian pretectal nucleus receives direct optic input as well as a projection from the medial terminal nucleus of the accessory optic complex. Its efferents are to the superior colliculus and the ventral brainstem. These connections parallel exactly those of the large-celled pretectal nucleus in anurans. In general, the projections of the superior colliculus in mammals are similar to those of the anuran optic tectum. The tecto-bulbar and tecto-spinal pathways in mammals seem to mirror those described in anurans. Murray (1978) has described the role of the tecto-bulbar pathway in cat in the control of visually elicited head movements. The descending projections from the anterior mesencephalic central grey to the brainstem found in anurans (this thesis) and salamander (Herrick, 1948) have recently been described in the cat (Rose, 1979). Injections of HRP in the cat, lateral medulla resulted in labelled neurons in the anterior mesencephalic central grey.

The anuran accessory optic system is composed of nBOR and a peri-nBOR region. Similar systems to these appear to exist in mammals in the small-cell, medial terminal nucleus and the large-cell dorsal terminal nucleus. These nuclei appear to have the same location and pattern of connections as does the anuran accessory
optic system. The anuran AOS, however, does not project to the cerebellum as it does in birds and at least one mammal—chinchilla. The development of connections between the AOS and the cerebellum may be thought of as a lemniscal system similar to the evolution of the cortical spinal tract in mammals and may be relatively rare. The anuran nMLF projects to the vestibular nuclei, the rostral spinal cord and cranial nerve nuclei n.III and n.IV. The nucleus interstitilis in cat has a similar pattern of connectivity (Brodal, 1962). Brodal describes both interstitio-vestibular and interstitio-spinal pathways. Visual responses have been reported in the vestibular nuclei and rostral spinal cord of mammals. Visual and vestibular input converge on the vestibular nuclei of the cat (Bauer, 1980). Within the vestibular nuclei, individual neurons respond to visual and vestibular input by a form of linear addition (Robinson, 1977). These visual responses in the vestibular nuclei are not affected by the removal of the cerebellum (Keller, 1978) indicating an independent source for this visual input. Monkeys have been taught to suppress the OKN response by visual fixation (Buettner et al., 1979). This process of suppression of OKN results in changes in the firing rate of vestibular neurons. Visual activity exists in the vestibular nuclei of both anurans and mammals and similar pathways also exist to
deliver this input. Gruberg and Grasse (1980) have recorded visual units along the edge of the anuran nMLF. The projection of the nMLF to the vestibular nuclei would appear to originate from the nMLF in anurans. In anurans, both visual and vestibular inputs were recorded from spinal motor neurons (Maeda et al., 1977). In mammals, the stimulation of the interstitio-spinal tract results in the excitation of neck flexor, spinal motor neurons. The anuran nMLF appears to play an important role in visually guided movements of the head and eyes in both mammals and anurans.

In this thesis, collaterals of oculomotor neurons were described which enter the nMLF. A similar system of oculomotor collaterals exists in the cat (Evinger, 1979). These collaterals may explain the matched firing of the mammalian interstitial nucleus with eye movements. Their presence in anurans suggests similar functional correlates.

In summary, the anterior mesencephalon of anurans is characterized by small, relatively undifferentiated groups of neurons and axonal pathways which undoubtedly subserve a variety of fundamental visuo-motor functions which are mediated by larger and more specific neural populations in mammals. In describing the anterior mesencephalon of urodeles, Herrick (1948) stated:
"This curious tissue is either an undifferentiated primordium of a number of structures which are separately differentiated in more specialized brains, or the retrograde fusion of several structures. The former supposition seems more probable. . . ." Indeed, each of the cell groups and projections seen in the mesencephalon of anurans appear to have counterparts in the mammalian nervous system. A more complete knowledge of the fundamental neural organization of the anuran mesencephalon may thus provide valuable insights into the neural substrates which underlie a variety of visually guided behaviors in all vertebrates.
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>n.III</td>
<td>Oculomotor nucleus</td>
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<tr>
<td>n.IV</td>
<td>Trochlear nucleus</td>
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<td>n.V</td>
<td>Trigeminal nucleus</td>
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<tr>
<td>n.VI</td>
<td>Abducent nucleus</td>
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<tr>
<td>AOS</td>
<td>Accessory optic system</td>
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<tr>
<td>BOR</td>
<td>Basal optic root</td>
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<tr>
<td>CV</td>
<td>Valvula cerebelli</td>
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<tr>
<td>Hy</td>
<td>Hypothalamus</td>
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<tr>
<td>IC</td>
<td>Intercollicular nucleus</td>
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<tr>
<td>L</td>
<td>Lateral thalamic neuropil</td>
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<tr>
<td>MLF</td>
<td>Medial longitudinal fasciculus</td>
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<tr>
<td>Mt</td>
<td>Motor tegmentum</td>
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<tr>
<td>nBOR</td>
<td>Nucleus of the basal optic root</td>
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<tr>
<td>nMLF</td>
<td>Nucleus of the medial longitudinal fasciculus</td>
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<tr>
<td>nPt</td>
<td>Large-celled pretectal nucleus</td>
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<tr>
<td>nRT</td>
<td>Nucleus reticularis tegmenti</td>
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<tr>
<td>OT</td>
<td>Optic tectum</td>
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<td>OKN</td>
<td>Optokinetic nystagmus</td>
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<tr>
<td>P</td>
<td>Posterior thalamic neuropil</td>
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<tr>
<td>Peri-nBOR</td>
<td>Periphery of nBOR</td>
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<td>Ts</td>
<td>Torus semicircularis</td>
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<tr>
<td>U</td>
<td>Uncinate neuropil</td>
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<tr>
<td>VC</td>
<td>Ventral commissure</td>
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Fig. 1a. The cyclostome mesencephalon. (Redrawn from P. Heier, 1948. In The Vertebrate Brain, 1976, Pearson and Pearson.)

Fig. 1b. The human spinal segment.
Fig. 2. The mesencephalon of the spiny dogfish. (Redrawn from G. Northcutt, Retinal pathways in fetal and adult spiny dogfish. Brain Research, 1979, 162, 219-230.)

Fig. 3. The mesencephalon of a teleost. (Redrawn from H. Kuhlenbeck, The Central Nervous System of Vertebrates, Vol. 4, 1975.)
Fig. 4. The mesencephalon of the lungfish. (Redrawn from G. Northcutt, Retinofugal projections in the Lepidosirenid lungfish. Journal of Comparative Neurology, 1979, 174, 553-574.)

Fig. 5. The urodele mesencephalon. (Redrawn from G. Northcutt, Retinofugal projections in the Lepidosirenid lungfish. Journal of Comparative Neurology, 1979, 174, 553-574.)
Fig. 6. Cross section through the anterior mesencephalon of *Rana pipiens*. (Redrawn from F. Scalia, The optic pathways of the frog: nuclear organization and connections. In: *Frog Neurobiology*, R. Llinas and W. Precht (eds.). Berlin: Springer-Verlag, 1976.)
Fig. 7. The organization of the anuran tectum. (From G. Szekely and G. Lazar, Cellular and synaptic architecture of the optic tectum. In: Frog Neurobiology, R.Llinas and W. Precht (eds.). Berlin: Springer-Verlag, 1976.)
Fig. 8. The course of degenerating fibers following lesions of the optic tectum in *Rana pipiens*. (From K. Rubinson, *Projections of the tectum opticum of the frog. Brain Behavior and Evolution, 1968, 1, 529-561.*)
Fig. 9a. The mesencephalon of Lacerta. (Redrawn from H. Kuhlenbeck, *The Central Nervous System of Vertebrates*, Vol. 4, 1975.)

Fig. 9b. The mesencephalon of the Mississippi alligator. (Redrawn from H. Kuhlenbeck, *The Central Nervous System of Vertebrates*, Vol. 4, 1975.)
Fig. 10. The two tier organization of the anuran mesencephalon.
Fig. 11. The two tier organization of the Tigar Salamander mesencephalon. (From The Brain of the Tigar Salamander, 1948, by C. Judson Herrick.)
Fig. 12. Coronal section through the anuran mesencephalon following an optic nerve soak with HRP.
Fig. 13. Coronal section through the large-celled pretectal nucleus following injection of HRP into the optic tectum.
Fig. 14a. Coronal section through the nucleus of the basal optic root following interocular injection of 3H proline.

Fig. 14b. Horizontal section through the nucleus of the basal optic root and optic chiasm following HRP optic nerve soak.
Fig. 15. Coronal section through the anterior thalamus following HRP injection in nBOR and the adjacent tegmentum. Dendrites of these neurons extend into the primary retinal neuropils, n. Bellonci and corpus geniculatum.
Fig. 16. Cell types occurring in each of 3 regions associated with the accessory optic system as determined from Golgi and HRP material (camera lucida drawings). nBOR region: a-ganglionic neuron, b-elongate neuron, c-amacrine cell, d-stellate neuron; peri-nBOR region: e-commissural neuron, f-pyriform neuron; nMLF (nucleus of the medial longitudinal fasciculus): g-reticular neuron.
Fig. 17. Coronal sections through the mesencephalon and brainstem showing the distribution of ipsilateral and contralateral projections to the brainstem from the anterior mesencephalic and posterior thalamic central grey following HRP injections in the grey.
Fig. 18. Drawing of the anterior mesencephalic central grey showing the distribution of HRP filled neurons following injection of the ventral brainstem.
Fig. 19. Drawing of the distribution of HRP filled neurons in the caudal portion of the nMLF following injection of the posterior commissure.
Fig. 20. Coronal section through the nMLF and n.III showing HRP filled neuron and the MLF seen following injection of the vestibular nuclei.
Fig. 21. Analysis of 24 lesions in different mesencephalic targets on optokinetic behavior. (From Fife et al., Visuomotor correlates of the anuran accessory optic system. Neuroscience Abstracts, 1980, 6, 839.)
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Fig. 22. Circuits which may be related to the optokinetic nystagmus response.