

BEHAVIOR IN ITS RELATION TO THE DEVELOPMENT OF THE BRAIN

PART II. CORRELATION BETWEEN THE DEVELOPMENT OF THE BRAIN AND BEHAVIOR IN THE ALBINO RAT FROM EMBRYONIC STATES TO MATURITY

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That there exists an ontogenetic relationship between the structure of the nervous system and the behavior of an animal scarcely needs further proof, but the specific details of this relationship still require extensive investigation.

Several types of animals have already been studied with this object in view. Stewart Paton's studies were among the pioneer efforts in this field. In 1911 he reported his observations on the reactions of the vertebrate embryo and the associated changes in the nervous system. These investigations were limited to the early embryonic stages of several varieties of fish and amphibia. The most intensive work of this kind has been done upon amblystoma by Coghill who has expressed the opinion that "behavior patterns develop in a regular order of sequence of movements which are consistent with the order of development of the nervous system and its parts." Tracy, working with the toadfish, was led to the conclusion that each characteristic behavior pattern is dependent upon the time when efficient connections between the elements of the nervous system are established. The same general principle appears to hold good for higher vertebrates. Langworthy has shown in the opossum and in the cat that a relation of this kind exists between the development of the nervous system and the capacity of the animal to adjust itself.

¹ I wish to express my deep appreciation to Dr. Orton and Dr. Elsberg for their very valuable assistance and to Dr. Elsberg, through whose efforts funds for publication were obtained.

Similar opinions have been expressed by Angulo concerning the albino rat as well as by Windle, Tilney, and Casamajor with reference to the development of the cat.

Minkowski, as a result of his comprehensive studies of embryonic, fetal, and postnatal stages in man, identified eight stages in the development of reflex activity.

1. The embryonic stage which occurs at about the second intra-uterine month in which the reactions are exclusively idiomuscular (idio-muscular stage).
2. The early fetal stage, occurring at the third or fourth fetal month, in which the spinal cord contributes to the production of responses (spinal stage).
3. The middle fetal stage, about the sixth month, in which the tegmentum of higher centers as well as the spinal cord participates in reactions (tegmento-spinal stage).
4. The late fetal stage during the last months of pregnancy when parts of the corpus striatum (globus pallidus) and the cerebellum come into action (pallido-rubro-cerebello-tegmento-spinal stage).
5. The neonatal phase, in the first weeks after birth which is the initial stage of cortico-subcortical activity (initial cortico-subcortico-spinal phase).
6. The infantile phase during the first two years of life in which cortical activity increases but subcortical control still predominates (infantile cortico-subcortico-spinal phase).
7. The infantile transitional phase at or about the end of the second year when the pyramidal tracts become myelinated and favor the further extension of cortical control (transitional cortico-subcortico-spinal phase).
8. The adult stage, from the third year to adult life which is characterized by the progressive increase in cortical predominance (cortical stage).

With certain modifications determined by the order to which the animal belongs, it is probable that these stages may be observed in the course of all mammalian development. For this reason two important considerations concerning correlations between the structure of the brain and behavior in mammals should be borne in mind. First, that a large integrative element

operates in the neural control of all reactions and that each part of the neuraxis, including spinal cord, hindbrain, midbrain, interbrain, and endbrain, contributes its specific innervation to this control. Second, that the structures of the endbrain assume an increasingly important rôle in the regulation of behavior during the developmental process. In the following study, the brain and behavior of the albino rat have been considered from this standpoint.

The embryonic and fetal material utilized for histological preparations was especially supplied by Professor Donaldson from the experimental colony of the Wistar Institute. Serial sections stained by hematoxylin-orange-G and by toluidin blue, were prepared in eighteen closely placed developmental stages from the 8-mm. embryo to the adult. When applicable in the later stages, the Pal-Weigert myelin stain was also employed. The wax-plate method was utilized to record the progressive changes in the cerebral cortex from stage to stage. This method also proved serviceable in the production of magnified dissections of the corpus striatum, the hippocampal formation and the fiber tracts.

Observations upon the fetal and postnatal behavior of the animals were made, under the supervision of the writer, by Dr. Myrtle McGraw and Miss Minnie Lesnow. In prenatal stages the fetuses were floated out of the uterus into warm saline solution and the reactions studied with the umbilical cord still attached to the placenta in situ. The operative procedures were done under ether anesthesia. The study of behavior was confined exclusively to somatic reactions and no attempts were made to investigate the strictly splanchnic activities at any stage of development. These latter activities constitute a group of reactions which calls for subsequent detailed consideration.

THE NEURAXIS IN EMBRYONIC AND EARLY FETAL STAGES

During the embryonic and early fetal periods, the animals gave little evidence either of spontaneous activities or of response to external stimuli. Yet in these periods structural differentiation has made rapid strides in the formation of organic systems, especially of the nervous system. The 8-mm. rat embryo (13

days, 18 hours) has advanced to the point at which the neural tube is closed and its walls are formed by the massive, deeply staining neural ectoderm. Although little in the way of cellular specialization is yet apparent in the neural walls, the evagination which gives rise to the hemispheres has made its appearance, the eye cup has developed and is connected with the interbrain by a short, thick stalk, the midbrain has assumed its early developmental prominence, the beginnings of the cerebellum are distinguishable from the rest of the hindbrain and the characteristic differences between the afterbrain and the spinal cord are distinct. The relative simplicity of the cellular arrangement in the neural walls is a striking feature at this stage. The cells in the walls of the entire central nervous system constitute a single broad layer surrounding the central canal. Many of the cells in this *germinal* or *ependymal layer* are in various stages of division but in no region of the brain or spinal cord is there evidence of discrete nuclear or cortical specialization.

PHASES OF CORTICAL DIFFERENTIATION

This simple condition of the neural tube thenceforth undergoes a series of significant changes particularly affecting the disposition and arrangement of the nerve cells. These changes have their most striking expression in the cortex of the cerebral hemisphere and make it possible to recognize a succession of three definite phases in the development of this structure, namely,

1. General cortical differentiation
2. Divisional cortical differentiation
3. Local cortical differentiation

As these phases bear a close relation to distinctive periods in the development of reactions, each one of them may be accepted as a structural index of a definite stage in the up-building of behavior.

The first evidence of general cortical differentiation appears in the 10-mm. embryo (15 days). Almost immediately after the endbrain has formed the evaginations from which the hemispheres develop, important alterations take place in the neural ectoderm.

Young cells derived from the germinal layer move outward toward the external surface in such great numbers as to form an easily discernible second layer in the brain wall. This second or *mantle*



FIG. 1. Albino rat embryo, 10-mm. (15 days) showing striatal and suprastriatal portions of the endbrain. Specimen No. 978, slide 4, section 51, magnification $\times 55$.

layer (fig. 1), appears in cross-section, as a broad stratum of cells immediately external to the germinal layer. At this time the wall of the endbrain has the appearance of two concentric bands

surrounding a spacious lateral ventricle. The bands are not separated by any sharp line of demarcation, but are distinguishable by the intense staining reaction of the inner, germinal layer as compared to the relatively lighter staining of the outer, mantle layer. For a long period during development, the germinal layer plays an important rôle both as a prominent part of the brain wall and as a contributing source in the formation of new cells. The mantle layer, however, plays a far more important rôle in both of these respects. Although this layer may not be recognized as such in the fully developed cortex, the marked specialization and local disposition of the cells derived from it ultimately determine the character of all of the highly differentiated parts of the endbrain. This fundamental importance of the mantle layer justifies the closest scrutiny of the progressive changes which take place within it. Shortly after its first appearance, it gives evidence of highly significant specializations in the disposition of its constituent cells. In the first place, the part of this layer which lies immediately beneath the outer surface of the brain wall assumes an appearance less dense than elsewhere and thus gives rise to an outermost zone or *marginal layer*. In consequence, three distinct concentric bands surround the lateral ventricle, the outermost, *marginal layer*, the middle, *mantle layer*, and the innermost, *germinal layer*. The wall of the hemisphere, having successively passed through the one-layer and the two-layer stage, has now reached the three-layer stage of its development. It is not necessary to dwell upon the phylogenetic significance of these early phases further than to note that the development of the hemisphere in some of the lower vertebrates does not pass beyond this three-layer stage.

The activities of the mantle layer in certain localized areas of the brain wall result in changes of even more importance than the formation of the marginal zone. The floor of the lateral ventricle gives evidence of an exuberant production of cells. It becomes thick and massive. Rapid cellular increases both in the mantle and the germinal layers give rise to two longitudinal, parallel ridges which project from the floor into the ventricle. A deep longitudinal furrow separates a lateral from a medial ridge; both

of these ridges participate in the formation of the corpus striatum. The lateral ridge is more distinctly a structure of the endbrain, but both of them are closely connected with the interbrain in the region of the large foramen of Monro. Both ridges extend, to some degree, into the wall of the third ventricle, and their caudal extremities are, therefore, closely associated with the region which subsequently gives rise to the optic thalamus.

In the lateral wall of the hemisphere, above this striatal region, the mantle layer shows much less active expansion. On the other hand, it attains greater proportions in the lateral wall than it does in either pole of the brain or in the roof of the ventricle. Its development is least pronounced in the mesial wall. For this reason and apparently due to localized differences in the rate of cell production, the early changes in the mantle layer make it possible to identify two distinct regions, i.e., the *striatal area* and *suprastriatal area*. The latter ultimately undergoes definite specialization in the lateral and mesial walls as well as in the roof and poles of the hemisphere. These local specializations are general in their nature, inasmuch as they depend upon the massing of mantle cells rather than discrete cellular differentiations. Thus it is that, even before the more decisive processes of cortex-formation have made their appearance, the foundations for the differential changes which are to follow, are laid by the mantle layer. The first of these differential changes occurs in the striatal region of the lateral wall about midway between the occipital and frontal poles of the hemisphere. It is an inconspicuous process in its inception and first appears in the 11-mm. rat embryo.

PRIMARY MIGRATORY LAMINATION

A thin lamina of granule-like cells, with large nuclei and scanty cytoplasm, moves outward from the mantle layer toward the surface of the hemisphere and takes up a position in the marginal zone. In cross-section it has the appearance of a fine dark line, dividing this zone into an inner and outer portion. As a result of the migration of the cells in this lamina, the original marginal zone presents three layers, i.e., an outer layer which becomes the definitive *zonal layer* of the cortex, a middle layer of granule

cells, the *primary granular layer*, and an inner layer, the *intermediate zone*, which assumes great importance in the later stages of development. Since it is the first of a series of similar migra-

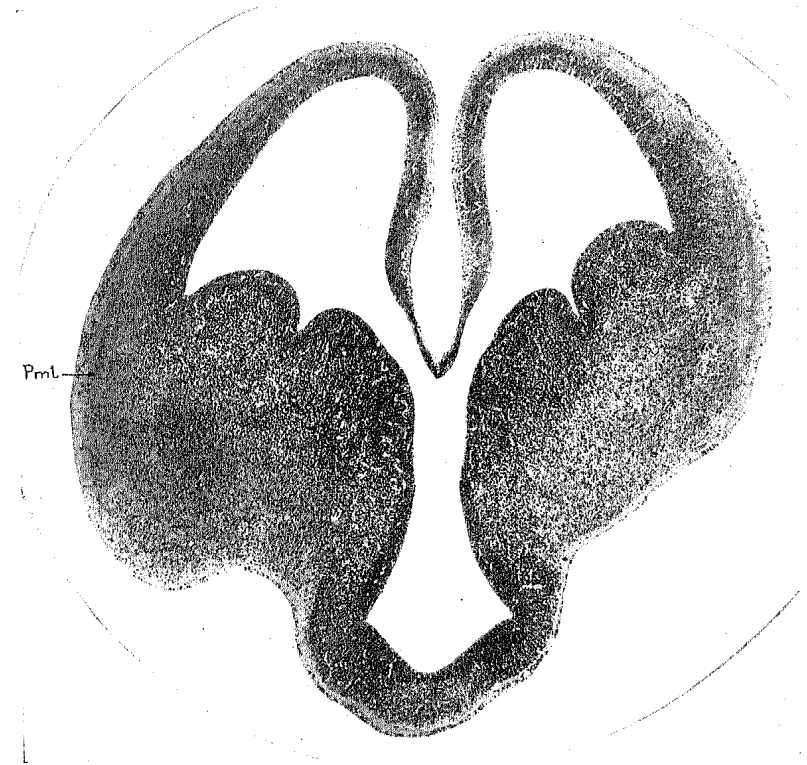


FIG. 2. Albino rat embryo, 11-mm. (16 days) showing primary migratory lamination as it first appears in the striatal and suprastriatal portions of the endbrain. (Pml.) primary migratory lamination. Specimen No. 849, slide 10, section 5, magnification $\times 50$.

tions from the mantle layer, this process may be designated *primary migratory lamination* (fig. 2).

As a process this lamination affects all cortical areas of the hemisphere, with three exceptions to be mentioned later. Its failure to appear in these regions has undoubted significance in

the problem of cortical localization. Moreover, from its beginning, primary migratory lamination draws a line of distinction in the discrete localization of function within the cerebral cortex. Immediately above the striatal area of the lateral wall in which this lamination first appears, a similar migration of granule cells takes place in the supraparietal region. It is then possible to distinguish, even more clearly, the striatal from the supraparietal area. This distinction is not merely a topographical one. The granule cells in the striatal area are relatively large, have lightly staining nuclei and are diffusely arranged in loose cords. The cells in the supraparietal area are smaller, their nuclei stain intensely and they form a compact, continuous strand. The significance of these early histological differences is made clear in the course of later development during which the striatal area takes part in the differentiation of the *paleocortex*, while the supraparietal area participates in the formation of the *neocortex*. These distinctions which occur as early as the 11-mm. stage in the albino rat draw a decisive line between a functional region which is very ancient and one which is relatively new, between the olfactory sphere of the paleocortex and the somatic sphere of the neocortex which subserves the functions of vision and hearing and all qualities of general body sense.

SPREAD OF PRIMARY MIGRATORY LAMINATION

Once it has made its appearance, primary migratory lamination spreads rapidly until it covers all of the supraparietal portion of the lateral wall. It then extends to the roof of the lateral ventricle, to a large part of the mesial surface and finally to the occipital pole. Ultimately it forms a continuous sheet of granule cells throughout all of these regions. The successive stages of its progressive advance may be seen in embryos from the sixteenth day of gestation to the seventeenth day by which time it has reached its ultimate limits (fig. 3).

In the frontal pole the course of events is different. During this embryonic period the frontal region has assumed a tapering form preparatory to the formation of the olfactory bulb. Evidence of primary migratory lamination is lacking in this portion

of the brain wall except at the tip of the pole. The development of a primary granular layer in this apical region marks the area destined to give rise to the olfactory cortex proper. In the

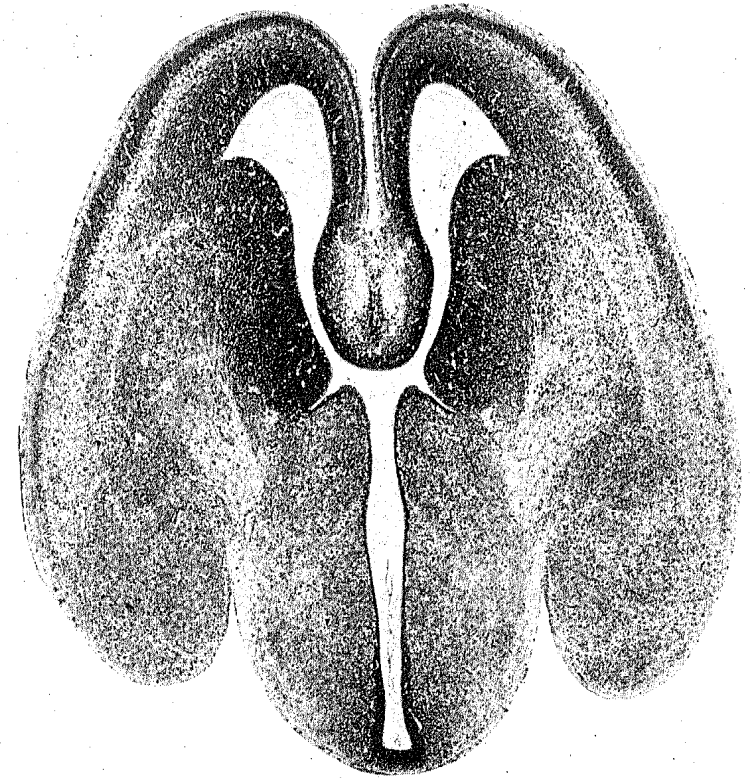


FIG. 3. Albino rat embryo, 16-mm. (17½ days) showing the extensions of primary migratory lamination in the neocortical and paleocortical divisions of the endbrain. Specimen No. 850, slide 15, section 12, magnification $\times 25$.

remainder of the polar region, primary migratory lamination does not occur and, in consequence, the base of the developing olfactory bulb consists of a broad collar of mantle cells entirely

devoid of a granular layer. In this portion of the brain wall cortical differentiation follows a course quite different from that of other areas. It represents one of the three regions already alluded to as exceptional in this respect and ultimately forms the *accessory olfactory cortex* and the *parolfactory area*.

Primary migratory lamination also advances rapidly in the striatal portions of the brain wall. A continuous sheet of granule cells progressively extends downward into the lower portions of the lateral surface and finally makes its appearance in the greater part of the under surface of the hemisphere.

The extensions and growth of the primary granular layer which occur both in the striatal and suprabulbar portions of the brain wall are dependent upon two processes of cellular increment: first, continual additions of new cells from the mantle layer and second, mitotic division of the granule cells in situ. Growth in the granular layer of the suprabulbar region, which gives rise to the neocortex, is much more rapid than in the striatal region from which the paleocortex is derived. The striking contrasts produced by cellular differentiation in these two portions of the hemisphere furnish conclusive histological distinctions between them.

Reference has been made to the fact that primary migratory lamination takes place in the larger part of the mesial wall. In the remainder of this wall such lamination is either totally lacking or occurs as the result of a process not typical of other areas. The region of which this is true constitutes the lower part of the mesial wall and forms an arch over the optic thalamus. In front this arch is in contact with the mantle cells at the base of the olfactory bulb (parolfactory area). It extends upward and backward over the thalamus and has its caudal extremity near the occipital pole in relation with mantle cells which give rise to the amygdalar nucleus. This suprabulbar arch of the mesial wall actually consists of two distinct arches, an outer arch composed exclusively of mantle cells in which no primary migratory lamination has occurred and an inner arch made up exclusively of granule cells.

The granule cells in the inner arch migrate outward to such an

extent that little in the way of marginal zone appears external to them. Collectively these two arches give rise to the several cortical constituents of the *archicortex*. The cornual, subicular and presubicular portions of the hippocampal formation are derived from the outer arch, the fascia dentata, and allied structures from the inner arch.

The mantle layer in a relatively small area of the mesial wall, which is situated immediately in front of the lamina terminalis, exhibits a still different disposition. This region, known as the *septum*, fails to develop any of the embryonic processes essential to cortical formation and remains an uncorticalized portion of the brain wall throughout life.

All of the early changes which occur in the different parts of the hemisphere indicate the decisive rôle of the mantle layer in the phase of general cortical differentiation. They pave the way for the more complicated specializations which finally characterize the divisional regions of the cortex. Special activities of the mantle layer in definite portions of the brain wall are directly accountable for the characteristics of each of the different parts of the endbrain, including the neocortex, the paleocortex, the *archicortex*, the bulbar cortex, the septum, parolfactory area and subcortical nuclei.

SECONDARY MIGRATORY LAMINATION

The importance of activity in the mantle layer is again revealed in neocortical regions during late embryonic stages. In the embryo of 17½ days (16-mm.) the primary granular layer has greatly increased in thickness. Its cells, arranged in dense parallel cords, still retain their earlier characteristics, but the layer as a whole has assumed much more prominence because of its augmented dimensions. A large part of this increment is the result of constant cellular additions from the mantle layer, but multiplication of cells in loco also accounts for a considerable portion of it. During this thickening of the primary granular layer, the intermediate zone has increased in width, preparatory to the next essential step in the differentiation of the neocortex, namely, *secondary migratory lamination* which makes its first

appearance on the nineteenth day (25-mm. fig. 4). This process is determined by the migration of a lamina of granule cells through the intermediate zone to the base of the primary granular layer.

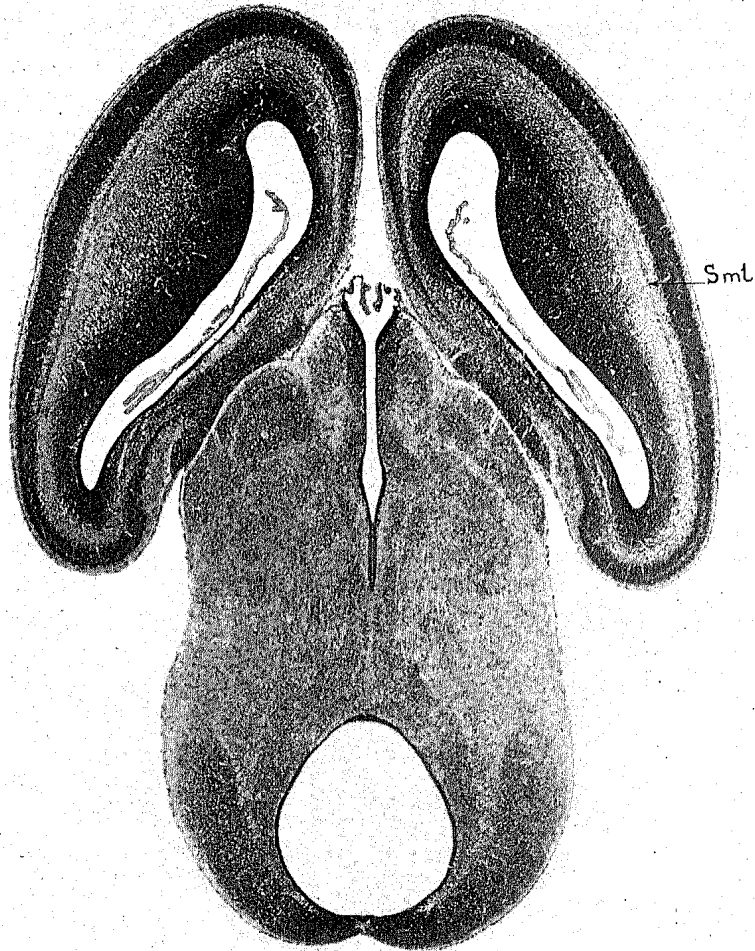


FIG. 4. Albino rat embryo, 25-mm. (19½ days) showing secondary migratory lamination (*Sml.*) in the neocortical division of the endbrain. Specimen No. 1165, slide 11, section 9, magnification $\times 35$.

It has its inception in the same general area in which primary migratory lamination first takes place and gradually spreads until it has involved the suprastratial portion of the lateral wall, the roof, the upper part of the mesial wall, and the occipital pole of the hemisphere. As a process it is limited to the neocortical region of the brain wall. It does not occur in the paleocortical or archicortical regions. This secondary migratory lamination ultimately results in the formation of an internal granular layer.

REACTIONS OF INTRAUTERINE LIFE

In the period during which the early progressive advances of general cortical differentiation are taking place in the hemisphere, the growing embryo is almost entirely devoid of somatic reactions. Occasional isolated twitchings may be elicited by the application of stimuli in this period; but even as late as the seventeenth fetal day these responses are ill defined and inconstant. In the later days of gestation responses to stimulation become sufficiently integrated to indicate that the nervous system has established some of its control. It seems unlikely, however, that the end-brain participates in this control, for despite the fact that the hemisphere has made definite progress in the specialization of its several parts, many stages of development must be traversed before any of its cortical or subcortical constituents acquire the recognizable semblance of mature structures. It is more probable that the structural substratum for the integrative control of embryonic and fetal reactions is located in the segmented portions of the nervous system. This probability is supported by the fact that the spinal cord and brain stem attain most of their definitive specialization long before this is the case in the cerebral hemispheres.

DEVELOPMENT IN THE SPINAL CORD AND BRAIN STEM IN EMBRYONIC AND FETAL STAGES

Throughout the early embryonic stages, i.e., from the twelfth day (3.5-mm. embryo) to fourteenth day (8-mm. embryo) there is little possibility of control by the nervous system because the spinal cord has not yet established the necessary connections

with receptors and effectors by means of efferent or afferent fibers. This connection is, however, fairly well developed by the fifteenth embryonic day (10-mm. embryo) but it is not until the seventeenth day (16-mm. embryo) that the ventral and dorsal horns of the spinal cord are at all well differentiated (fig. 5). There is still but little distinctive specialization in their nerve

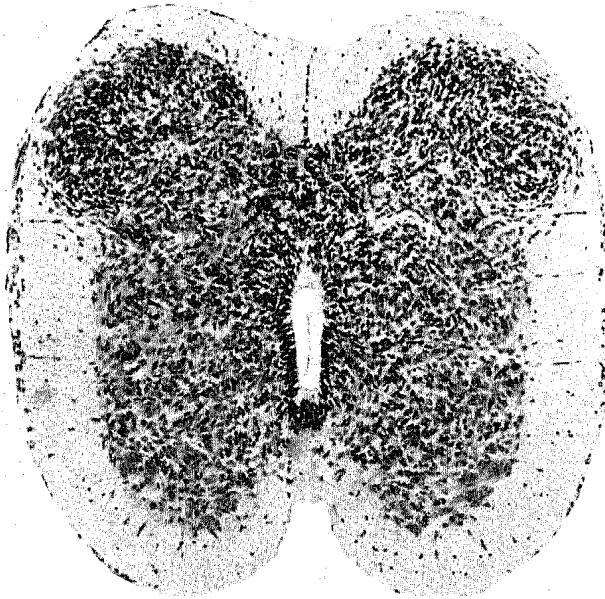


FIG. 5. Cross-section of the spinal cord in an albino rat embryo of 16 mm. showing the degree of differentiation in the ventral and dorsal horns. Specimen No. 855, slide 18, section 25, magnification $\times 90$.

cells. The oblongatal, hindbrain, and midbrain segments are similarly immature. Ventral, dorsal, and lateral tract beds may be traced through the spinal cord into the brain stem. The cerebellar anlage is well developed and presents a thick external granular layer but no lamination or Purkinje cells. Organization in the nervous system up to the eighteenth day thus appears to

be insufficient for the production of spontaneous activities or for constant reflex responses to stimulation.

REACTIONS OF THE EIGHTEENTH AND NINETEENTH FETAL DAYS

The 18-day rat fetus shows little spontaneous activity. Floating in warm saline solution its posture is one of general flexion of the body with the head and limbs closely flexed upon the trunk. When stimulated on the skin by the application of fine bristles or a mild faradic current its reactions are fairly constant and consist of an extension of the head accompanied by opening of the mouth. There is also a slight extension of the trunk. Stimulation usually produces but a single response of this kind. In one litter of 18-day fetuses rhythmical lateral movements of the head from side to side were observed but in general the single response was characteristic of this stage. The reaction pattern was essentially the same without regard to the area of stimulation, although responses obtained from the region of the snout appeared to be more frequent and of greater intensity. Compression of the tail, which was employed as a stimulus in all fetal and postnatal stages, causes reactions similar to those evoked by stimulation of other regions. The results produced by this means of stimulation were considered as especially indicative of the degree of segmental integration in the nervous system. The 19-day fetus shows no increase of spontaneous activity but there is definite evidence of advance in the organization of its reflex capacity. Its posture is characterized by a less extreme degree of flexion of the head, trunk, and limbs. The adduction of the extremities is also less pronounced. When stimulated on the snout the animal rolls from side to side with accompanying lateral flexion of the head and trunk and slight movements in the hind-quarters. A distinct rhythmical alternation of flexion, first to one side and then to the other, is a striking feature of these reactions. A single stimulus usually produces two to three movements of body flexion to either side. In these reactions the extremities are held in an adducted position, although a slight extensor tendency appears in the hindlegs from time to time. Compression of the tail produces a similar series of alternating

rhythmical flexions of head and trunk to right and left. As in the earlier stage, stimulation applied to the snout causes more active responses than could be obtained from any other part of the body. In many respects the alternating lateral flexions of the trunk and head bear a close resemblance to the swimming movements of the rat in early postnatal stages.

STRUCTURAL ADVANCES IN THE NERVOUS SYSTEM OF THE 18- AND 19-DAY RAT FETUS

By their reactions to stimulation, fetuses of the eighteenth and nineteenth days mark the transition from the inactive to the active period of somatic behavior and imply an adequacy in the structural organization of the nervous system not only for segmental reflex response but also for a certain degree of intersegmental integration. The developmental status of the different portions of the nervous system should reveal wherein such adequacy exists.

In the spinal cord of the 18-day fetus (19-mm.) the ventral and dorsal horns may be recognized in general outline but the distinction between them is still somewhat indefinite. Their neurocytes show some tendency to aggregation in groups and those in the ventral horn are conspicuous for their relatively large size. In the neighborhood of the central canal, which is still spacious, the cells are of medium size while those in the dorsal horn are small. The contour of all cells is round or ovoid. The nuclei are large and except for the elements in the ventral horn are surrounded by a small amount of pale, agranular cytoplasm. Prominent tract beds have developed in the ventral, lateral, and dorsal fields and consist of fine protoplasmic strands without apparent fibrils. A similar protoplasmic bed, definitely commissural in nature, connects the two ventral fields.

These conditions in the spinal cord show further advances in the 19-day fetus (25-mm.). The dorsal and ventral horns are more distinct. Several undulations in the outline of the ventral horn indicate the positions of special aggregations of large neurocytes which are now distinctly pyriform in contour. A slight lateral protrusion containing cells of somewhat smaller size indi-

cates the position of the lateral horn, immediately back of which a shallow constriction marks the beginning of the cervix. The dorsal horns have increased considerably in size and are widely separated from each other by the expansion of the dorsal tract beds. The size of the lateral and ventral tract beds has also increased, and the ventral commissure is much more prominent than in the 18-day fetus.

In the oblongatal and pontile portions of the brain stem the connections by nerve roots are well established and the loci of the cranial nuclei (XII, X, VII, and V) are discernible in the general matrix of the gray matter. The reception nuclei of the eighth and fifth cranial nerves are especially well defined and the general outlines of the inferior olive can be recognized. The nerve cells in these nuclear aggregations are all in an early stage of differentiation and the reception nuclei of the dorsal columns are only feebly developed.

Tract beds appear in the dorsal, lateral, and ventral fields although as yet there are no indications of the decussating fibers of the fillet and pyramidal systems.

In the cerebellum, cortical differentiation is characterized by a deep external granular layer, an intermediate molecular layer, and an internal granular layer. No definite Purkinje cells have yet developed. Tract beds forming the cerebellar connections through the inferior, middle, and superior cerebellar peduncles are distinguishable, but the cerebellar and pontile nuclei are still indistinct.

In the midbrain, the tectum is the most prominent feature. It is especially conspicuous because of stratifications which are suggestive of preparatory steps in the formation of a cortex. The several layers are, however, much less definite than those which appear in the endbrain. The mesencephalic tegmentum is particularly diffuse and gives no evidence of special cellular aggregations such, for example, as the nucleus ruber and substantia nigra. Tract beds in the basis indicate the position of the cerebral peduncle and a massive commissural bed represents the posterior commissure.

In the interbrain fairly discrete collections of cells give indica-

tion of the positions of the anterior and lateral groups of thalamic nuclei but none of the ultimate subdivisions of these groups can be distinguished. With the exception of the protuberance which forms the posterior lobe (mammillary body) the cellular constit-

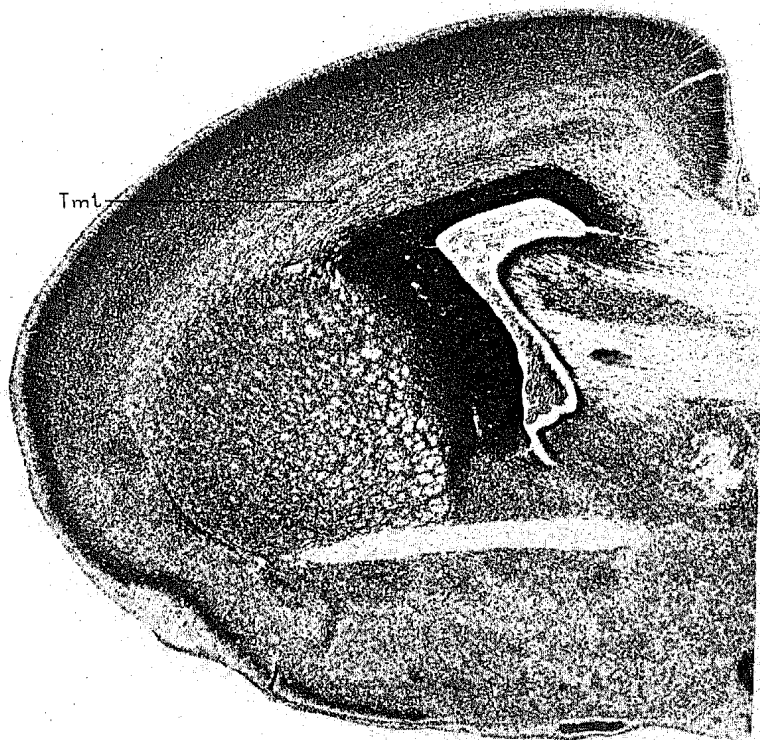


FIG. 6. Twenty-one-day albino rat fetus (35-mm.) showing the beginning of tertiary migratory lamination (*Tml.*) and the six strata forming the neocortex of the endbrain. Specimen No. 1185, slide 19, section 3, magnification $\times 45$.

uents in subthalamic and hypothalamic regions are still too diffuse to permit identification of any of the nuclei of these parts. Immediately subjacent to the epithalamus, a prominent pretectal formation extends forward from the roof of the midbrain. Tract

beds represent the chiasm, optic tract, and the lateral and medial forebrain bundles. The fornix and several mammillo-epithalamic connections are well developed.

In the hemisphere rapid growth in the lateral wall and roof of the endbrain has caused the olfactory bulb to assume a more basal position. The bulb itself is now distinctly delimited from the rest of the brain. It presents two types of cortical differentiation, in its rostral portion, the olfactory cortex proper, in its caudal portion, the accessory olfactory cortex. The rest of the hemisphere, with the exception of the septum, is still in the phase of general cortical differentiation. Almost the entire neocortical region is characterized by the process of secondary migratory lamination and this part of the brain wall now consists of six superimposed strata (1, zonal layer; 2, primary granular layer; 3, intermediate layer; 4, internal granular layer; 5, mantle layer; 6, germinal layer) (fig. 6). The hippocampal portion of the brain wall consists of three layers (1, zonal layer; 2, mantle layer; 3, germinal layer). In the dentatal region, the primary granular and zonal layers alone are present. The subcortical nuclei which may be distinguished are the nucleus accumbens, nucleus caudatus, nucleus lenticularis, nucleus amygdalus, and the claustrum, all in an extremely immature stage of development. Tract beds representing the callosal part of the centrum ovale, the lateral forebrain bundle (internal capsule), the external capsule, the optic chiasm, the lateral olfactory tract, the fimbria, the fornix, and several of the septal fiber systems are well defined. The only interhemispherical connections appear in the tract bed of the anterior commissure. Neither the corpus callosum nor the hippocampal commissure has yet established its connection between the hemispheres.

CORRELATIONS BETWEEN BEHAVIOR AND NEURAL ORGANIZATION IN LATER FETAL STAGES

In interpreting the reactions of the 18- and the 19-day rat fetus, the suprasegmental portions of nervous system may be reasonably excluded on the ground of their extreme immaturity. Differentiation in cortical and subcortical parts of the hemisphere

is in no sense adequate to contribute to the regulation of behavior. The tectum of the midbrain and the cerebellum are likewise but little developed. The mesencephalic tegmentum might conceivably participate in the fetal reactions but the specialization of this region is still too immature to justify such a supposition. On the other hand, the spinal cord and caudal portion of the brain stem are adequately provided with afferent and efferent connections and sufficiently differentiated in their nerve cells to account for the segmental reflexes of the animal at this time. Commissural connections explain the bilaterality of the reactions while spinal and oblongatal tract beds supply the neural substratum for integration of the associated movements in the head, trunk, and limbs. In this light, the early reflex activities of fetal life may be attributed to the spinal cord and brain stem.

BEHAVIOR OF THE TWENTY-FIRST FETAL DAY (35-MM.)

This stage is important because of the approaching transition from intrauterine to postnatal life. The animal is about to give up its total dependency to meet the conditions of a partially independent existence. Its reactions, even in the last two fetal days, are still inadequate for the critical changes in adjustments determined by birth. Spontaneous activity in the twenty-first fetal day has increased but little. If placed upon its back the fetus makes little effort to right itself. It gives no evidence of spontaneity in any of its movements. Responses to stimulation are, however, more vigorous and longer sustained. Body posture is characterized by a greater degree of extension in the trunk. The head is less flexed upon the chest and the limbs are held in partial extension and slightly abducted from the body. When the snout is stimulated, the animal rolls from the lateral into a prone position at the same time flexing the trunk from side to side as in the earlier stages. These flexion movements of the trunk are much more pronounced than those of the 19-day fetus. Not only are they executed with more speed but the increased force in each lateral flexion of the trunk draws the head and hindquarters much closer together. Compression of the tail produces similar reactions, although stimulation of the snout, ear, or any

portion of the face gives rise to responses which are more vigorous and of longer duration. When the manus is stimulated the animal responds by sharp flexion and rotation of the head accompanied by flexion of the trunk. No discretely localized responses could be obtained by stimulation of the individual limbs.

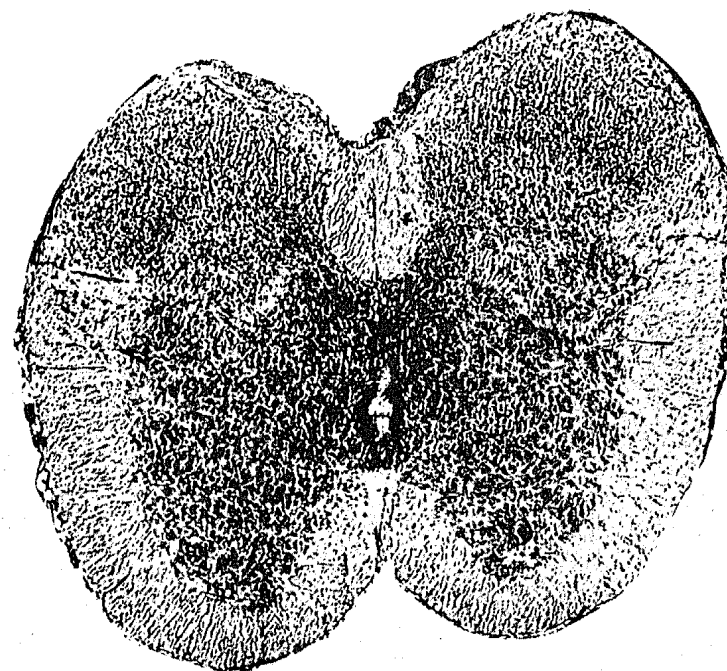


FIG. 7. Cross-section of the spinal cord of a twenty-one-day albino rat fetus (35-mm.). Specimen No. 1180, slide 19, section 3, magnification $\times 35$.

STRUCTURAL ADVANCES IN THE NERVOUS SYSTEM OF THE 21-DAY RAT FETUS (35-MM.)

Progress in neural development is evident in all parts of the nervous system in the twenty-first fetal day but the spinal cord and caudal portions of the brain stem have made the most decisive advance toward conditions of maturity.

In the spinal cord, the dorsal, ventral, and lateral horns as well as the body and cervix of the gray matter are all well defined (fig. 7). The central canal, much reduced in size, has assumed the position and relations characteristic of the adult. Striking cellular differentiation is witnessed both by the definite tendency toward cell-grouping and by the development of specific cellular types. Five distinct types of nerve cells are distinguishable. In the ventral horn the neurocytes are large pyriform elements with extensive agranular cytoplasm and some tapering processes. They are so clustered as to form a ventral, a lateral, and a mesial group. The cells in the body and commissure of the gray matter are of medium size, oval in contour, and diffusely distributed. Cells in the lateral horn have the same general character as those in the ventral horn, although of smaller size. The cervix contains small vesicular cells which stand out in marked contrast to the extremely small neurocytes densely aggregated in the much expanded dorsal horn. All of the tract beds and the ventral commissure have increased in their dimensions. These increments are most pronounced in the lateral field.

In the caudal portions of the brain stem changes similar to those in the spinal cord are apparent. The cranial nerve nuclei have assumed greater definition and their cells have undergone the same progressive alterations seen in spinal segments. There is still little evidence of the decussations of the fillet and pyramidal systems.

In the cerebellum, considerable expansion has taken place and the cerebellar nuclei are discernible, but cortical differentiation has not progressed notably.

In the midbrain, the tectum continues to be the prominent feature. The lamination of its cells covers the large superior colliculus as well as the much smaller inferior colliculus. The outlines of the nucleus ruber, substantia nigra, and nucleus oculomotorius can be distinguished. Cellular differentiation in the mesencephalon is still considerably behind that in the spinal cord and caudal portions of the brain stem.

In the interbrain, the thalamic nuclei have gained in definition. The pretectal region is still prominent. The posterior thalamic

nucleus (pulvinar) and the metathalamic extension which forms the lateral geniculate body have both made their appearance.

In the hemisphere, the progressive changes which have been in process during the embryonic and fetal periods bring the phase of general cortical differentiation to a close. The advances which determine the culmination of this first phase in the formation of the cortex are most decisive in the neocortical regions. They result in a cortical structure of six distinct layers which make their appearance in the following manner after secondary migratory lamination is complete. The first (zonal) layer remains essentially unchanged, but the second (primary granular) layer undergoes marked alterations. This entire layer increases rapidly in thickness, and with the exception of its outermost portion, begins to assume a much looser arrangement of its cells. The reason for this change is probably to be found in the outgrowth of processes from the individual cells, many of which have become pyriform in shape. This feature of development is confined to the deeper portion of the layer, the superficial portion of which still retains its granular appearance. These derivatives of the primary granular layer ultimately form the definitive *external granular layer* and the *external pyramidal layer* of the neocortex.

With the completion of secondary migratory lamination, a second or *internal granular layer* is distinguishable beneath the outer pyramidal stratum.

TERTIARY MIGRATORY LAMINATION

These changes which make their appearance in the 21-day fetus (35-mm.) are followed in the last day of intrauterine life (40-mm.) by a tertiary migratory lamination, in consequence of which many large pyriform and multiform cells migrate outward from the mantle layer. After passing through the intermediate zone they take up positions beneath the internal granular layer to form the internal pyramidal and the multiform layers respectively. The cellular additions resulting from tertiary migratory lamination bring the phase of general cortical differentiation to a conclusion and determine a six-layered neocortex consisting of the following strata (fig. 8).

- | | |
|----------------------------|---|
| 1. Zonal layer | } Derived by primary migratory lamination and subsequent division of primary granular layer |
| 2. External granular layer | |
| 3. External pyriform layer | |
| 4. Internal granular layer | } Derived by secondary migratory lamination |
| 5. Internal pyriform layer | |
| 6. Multiform layer | |

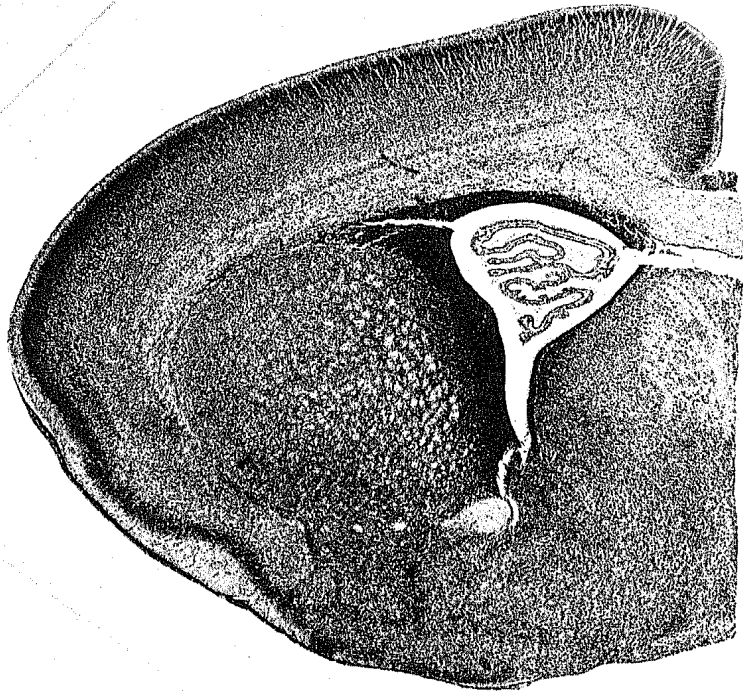


FIG. 8. The six-layered neocortex in the one-day-old albino rat. Specimen No. 1178, slide 7, section 6, magnification $\times 35$.

After these six strata have made their appearance the intermediate zone and mantle layer are no longer distinguishable, and the germinal layer is greatly reduced in thickness to form the ependymal lining of the lateral ventricle.

The process resulting in the formation of six distinct cortical layers is a characteristic of the neocortex exclusively. It does

not affect the bulbar cortex, the paleocortex, or the archicortex. These latter regions in the last days of fetal life have manifested considerable progress in cortical specialization but, like the neocortex, their developmental status falls short of the conditions of maturity.

In this final period of intrauterine life the subcortical nuclei have developed to a point at which it is possible to distinguish the following nuclear structures.

1. Corpus striatum
 - a. Nucleus accumbens
 - b. Nucleus caudatus (poorly developed in the rat)
 - c. Nucleus lenticularis
2. Nucleus amygdalus
3. Claustrum

Cellular differentiation in all of the subcortical nuclei is but little advanced.

The most notable change in the development of the fiber tracts during the last fetal days is the establishment of interhemispherical connections by the callosal and hippocampal commissures. Fibers forming the genu of the corpus callosum have crossed from one hemisphere to the other. These fibers may be traced to the frontal and parietal regions of the brain wall. As they emerge from the mesial surface, the callosal fibers pass beneath the lower margin of the hippocampal formation and carry a portion of the primitive dentatal cortex inward with them so that this cortical area comes to occupy a position on the dorsum of the corpus callosum. Due to this topographical change, the dentate portion of the archicortex in relation with the corpus callosum assumes the characteristic position of the *induseum griseum*. Immediately beneath the corpus callosum, another collection of commissural fibers, the *hippocampal commissure*, has established communication between the hippocampal formation of the right and left hemispheres.

The major functional divisions of the cortex have been foreshadowed in earlier stages of development, but it is not until the last days of fetal life that *divisional cortical differentiation* becomes well defined. This second phase in the formation of the cortex

represents the cumulative effects of progressive structural changes which have long been in process.

Immediately before birth, the olfactory bulb which during a long period of intrauterine life forms an integral part of the cerebral hemisphere, assumes the appearance of a distinct structural division. It still contains a ventricular cavity which communicates with the lateral ventricle and retains its connection with the rest of the hemisphere by means of a massive olfactory stalk.

The paleocortex has likewise established definite boundaries as a division of the brain. The divisional limits of the archicortex and neocortex are also distinct.

All of the specializations which determine the phase of *local cortical differentiation*, take place in these four divisions of the cortex (1, bulbar cortex; 2, paleocortex; 3, archicortex, and 4, neocortex). They begin to make their appearance about the fifth postnatal day.

CORRELATIONS BETWEEN BEHAVIOR AND NEURAL ORGANIZATION IN THE LAST DAYS OF FETAL LIFE

In spite of the fact that the cerebral hemispheres have made such progress in development as is shown by their transition from the phase of general cortical differentiation to that of divisional differentiation, their cellular specialization is still far below the conditions of maturity. It is conceivable, however, that even in this early stage the cells of the hemisphere may, to some extent, contribute to the regulation of behavior. These cells are not only immature but by comparison, are much less advanced than the cells in the spinal cord and brain stem. From this standpoint, it is reasonable to presume that they are still inadequate to exert any pronounced functional influence, certainly much less adequate in this respect than cells in the segmental portions of the neuraxis.

Obviously these estimates of functional adequacy are based on the structural status of cellular organization in the different parts of the nervous system. They may give rise to legitimate doubts as to their validity and require substantiation by other methods

of investigation. As developmental criteria, however, they afford the most reliable index of functional capacity which is at present available. Judged by them, the spinal cord and caudal portions of the brain stem still exercise predominant control over somatic reactions during the last days of fetal life in the rat.

BEHAVIOR IN THE FIRST DAY AFTER BIRTH

Immediately after birth the newborn rat lies on its side and remains in this position for some time after respiration has been established. In most instances the limbs are slightly flexed and abducted, but in others the forelegs are extended. The first somatic activities of the newborn rat consist of a series of spasmodic gasping movements in which the lower jaw is depressed and the mouth widely opened. The muscles of the chest wall and abdomen contract simultaneously. These gasping movements persist for a number of seconds, but the interval between gasps becomes progressively shorter until a regular, respiratory rhythm is established.

Spontaneous activities are at first very limited in extent and variety. Certain "starts" and "twitches" occurring from time to time have the appearance of involuntary movements. They either cause the head to turn, the tail to wag, or else produce convulsive jerkings of the entire body. Under several conditions, spontaneity in action becomes more conspicuous. When placed on its back the newborn rat immediately attempts to turn upon its side and often endeavors to rotate its body into a prone position. All of its movements are slow and feeble. In turning from its back, however, there is a certain degree of order in the sequence of the parts moved. First the forelegs extend and swing in the direction of the ultimate body rotation, then the hindlegs extend and swing in the opposite direction. The head is next extended and turned in the direction taken by the forelegs. During this performance the animal twists and turns its body continuously. As soon as the head and forelegs have been turned in the direction of rotation, the shoulders, then the trunk and finally the pelvic girdle are rotated until the prone position is assumed. In this position the chin, chest, and abdomen rest upon the supporting

surface while the four legs are spreading out sidewise in a sprawling manner. The newborn rat is able to maintain this position for but a short time. Soon the head droops and the animal quickly falls over on its side. In addition to this righting reaction the newborn rat manifests some feeble yet eventually effective locomotor activities. About fifteen minutes after birth and in the momentary periods when it attains the prone position, it begins to move its head from side to side. This movement is accompanied by alternate flexion and extension of the foreleg, first of one side and then of the other. The activities of the limbs provide a locomotor force which propels the animal forward and usually toward the mother. These locomotor efforts, which are extremely slow and complicated by many upsets, serve the purpose of a definite crawling approach reaction and usually result in bringing the young animal to the mother. In the fact that they are largely in the nature of paddling movements which do not lift the body from the supporting surface, they closely resemble the crawling approach reactions observed at birth in certain other mammals such as the cat.

The young rat does not begin to nurse immediately after birth and it is difficult to determine when the sucking reaction first occurs. Milk is not found in the stomach for some hours. The sucking reaction consists of series of integrated muscular activities beginning first with side to side movements of the head which result in securing the nipple. The nose and mouth are thus rubbed against the abdominal surface of the mother. These movements of the head become progressively shorter and finally bring the lips into contact with the nipple. After the nipple has been secured and during the entire suckorial act each foreleg alternates with the other in extending against the mother's breast. Similar alternating movements occur in the hindlegs and are more or less synchronous with those of the forelimbs. All of the movements in the limbs become less active after nursing has continued for a short time.

If placed in water of sufficient depth the newborn rat is able to swim for a number of seconds. The integrated movements of the head, trunk, and limbs in swimming have much in common

with the reflex activities produced by stimulation of the fetus during the last days of gestation. They have sufficient coordination and force to produce locomotor effects, but are inadequate to hold the head above water.

Another spontaneous activity of the newborn rat is the effort made by each animal to gain the closest possible contact with the rest of the litter when the mother is out of the nest or when it is separated by a short distance from its nest-mates. This huddling reaction makes its appearance soon after birth and is constant throughout the nesting period.

The responses to stimulation and especially to compression of the tail immediately after birth present certain features of much significance in their relation to later postnatal stages. If the tail is compressed by forceps the animal emits a sharp squeak and is at once thrown into a convulsive state. This reaction, in many respects, resembles the clonic phase of an epileptic attack. Forceful clonic contractions affect the muscles of the neck, trunk, and limbs. The young rat is turned over and sprawls upon its back, convulsively struggling to right itself. Should it succeed in doing so it makes violent efforts to move forward, only to be immediately overthrown again by the convulsive activity of the muscles. This cycle of spasms continues for several moments and even after the reaction seems to have subsided it recurs at brief intervals until normal equilibrium is at length restored. Three characteristics in the response to this type of stimulation are noteworthy: (1) the apparent participation of the entire somatic musculature; (2) the violent, convulsive nature of the reaction; and (3) the protracted duration of the effects produced by the stimulus.

Stimulation by bristles or by mild faradic currents resulted in consistent withdrawal of the part stimulated.

Since the eyes of the rat are closed at birth no attempt was made to introduce visual stimuli and no responses to auditory stimulation could be elicited at this time. Olfactory stimuli, such as the fumes of dilute ammonia, acetic acid, and volatile aromatics seemed to produce some response in the newborn rat. As a rule the snout is drawn away from the source of stimulation. These

reactions to olfactory stimuli were considered too indefinite to warrant conclusions concerning the availability of the sense of smell in this early postnatal stage.

STRUCTURAL ADVANCES IN THE NERVOUS SYSTEM OF THE
NEWBORN RAT

Evidences of structural differentiation in the first postnatal day are most pronounced in the segmented portions of the neur-

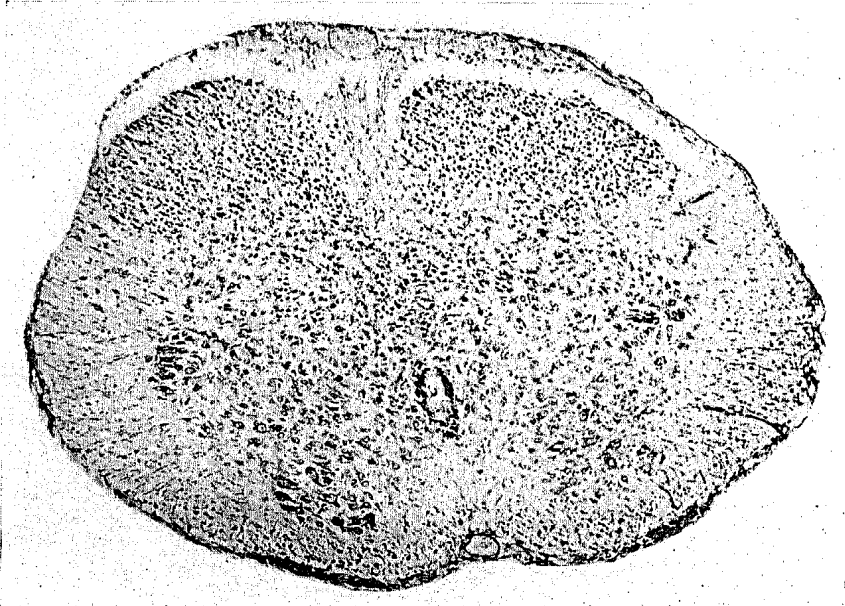


FIG. 9. Cross-section of the spinal cord of the newborn albino rat. Magnification $\times 150$.

axis. This emphasis on segmental development is due to the fact that the structures in the spinal cord and brain stem have made a much closer approach to their ultimate specialization than those in the hemisphere, cerebellum, or tectum. The configuration of the gray matter in the spinal cord has acquired many adult resemblances. A massive ventral horn projects from a short body which is connected with the opposite side by a broad gray

commissure (fig. 9). A short, lateral protrusion from the body forms a well defined lateral horn. The types of cells identified in late fetal stages are still more specifically differentiated and have the same tendencies to grouping observed in the last days of fetal life. The appearance of the large pyriform cells along the margins of the ventral horn is especially striking. These cells are the largest elements in the gray matter and have diameters two or three times greater than those of the cells in immediately adjacent parts. The agranular cytoplasm is relatively extensive, gives off several distinct processes, and contains a large vesicular nucleus. At least three clusters of these large cells may be recognized. Smaller ovoid and pyriform cells are interspersed among them. The cellular details of other groups in the gray matter, while in general similar to those of late fetal life, have acquired better definition.

With the exception of an increase in their dimensions and a greater prominence in the regions of the dorsal and ventral white columns, the tract beds have undergone little change.

In the caudal portions of the brain stem similar advances are apparent. The cellular specializations which distinguish motor and sensory cells are, as in the spinal cord, easily recognized. The motor and sensory nuclei of most of the cranial nerves (XII, X, VIII, VII and V) are sharply defined. Their topography and cellular differentiations indicate the systems to which they belong. The nuclei of the dorsal sensory columns may be identified in outline although their specialization is less advanced than that of other nuclear aggregations. The paleo- and neo-olivary portions of the inferior olive are both distinguishable. The oblongatal and pontile tract beds show some increase in their dimensions but evidence indicating the presence of definite pyramidal decussation was considered somewhat inconclusive. The same reservation applies with reference to the formation of the mesial fillet and the fibers entering into its decussation.

In the cerebellum, cortical formation retains most of its primitive characteristics. A dense external granular layer overlies a narrow molecular zone which covers a deep internal granular layer. Cellular differentiation, in an early stage, indicates the

inception of the Purkinje layer. The cellular collections forming the cerebellar nuclei (dentatus and globosus) are well defined. The external granular layer covering the surface of the cerebellum is thicker in the lateral than in the median regions and the first indications of foliation have made their appearance.

In the midbrain, six indistinct cellular strata may be distinguished in the superior colliculus and five, even less distinct, in the inferior colliculus. The boundaries of the nucleus ruber are clearly outlined and most of the tegmental cells, still in a diffuse reticular formation, show marked advances in their differentiation.

In the interbrain, the thalamic and metathalamic nuclei give evidence of further cellular specialization and the hemisphere is well advanced in its phase of divisional differentiation. These latter advances particularly affect the process of cortical formation in the olfactory bulb, paleocortex, and archicortex. Specialization in the olfactory cortex has been carried to the point at which it is possible to recognize all of its characteristic strata. The paleocortex has likewise attained a large measure of its ultimate differentiation. Advances in the archicortex have resulted in the appearance of the fascia dentata, induseum griseum, intercalary, and preseptal areas together with definite cortical differentiation in the cornual, subicular, and presubicular portions of the hippocampal formation.

CORRELATIONS BETWEEN THE BEHAVIOR AND NEURAL ORGANIZATION OF THE NEWBORN RAT

The exigencies created by birth demand prompt readjustments to the new living conditions of the animal. The newborn rat is abruptly cut off from its source of supplies. It needs oxygen at once, nourishment not too long delayed, and an environment which affords protection and warmth. By what means are these ends attained? To say that such requirements are met by "inherent behavior patterns" or by "instinct" merely begs the question. Any satisfactory explanation must be based primarily on a critical analysis of the organic adequacy of the nervous system. The capacity for adjustment depends, in large measure, upon the degree of efficiency possessed by the brain and spinal cord to

receive afferent impulses, to establish integrative associations and to transmit effector responses. Analysis of the behavior should, therefore, be made in these terms.

The first evidences of somatic independence in the newborn rat are the spasmodic movements of the lower jaw, chest, and abdomen. In a short time, the irregular, initial gasping is replaced by rhythmical breathing. There can be little doubt that the stimulus which excites these respiratory activities is the anoxemia and other chemical changes incident to placental detachment. The oblongatal cells are sufficiently differentiated to respond to this stimulus. Intersegmental connections already existing in the tract beds permit the spinal and oblongatal integrations essential to the coöperations of the respiratory musculature.

The early righting activities and attempts to crawl are open to more question. Whether the spinal cord and lower portions of the brain stem are in themselves adequate to such reactions cannot be decided on the structural evidence alone. It is possible and even probable that higher levels in the tegmentum of the midbrain may be requisite to these important early activities. Any deductions drawn in this connection must, however, be tentative and in expectation of further experimental control.

Several sources of afferent impulses should be considered in relation to the initial attempts of the animal to right itself and to crawl. In the first place, the establishment of respiration introduces an entirely new set of stimuli. The inrush of air into the respiratory passages and lungs provides stimulation for trigeminal and more especially for vagal receptors. The pneumogastric areas of the oblongata must inevitably be influenced by this sensory influx and respond to it throughout the widespread territory of vagal innervation. Evidence of such response is seen in the fact that peristalsis in the stomach and intestines becomes marked after breathing is well established. Contraction in the gastric and intestinal walls is soon pronounced and in this manner may provide the familiar activating impulses of the "empty stomach."

The new contact relations determined by birth offer another possible source of stimulation. Lying upon its side in contact

with a resisting surface to which it is unaccustomed, the newborn animal exposes a large area of its body to sensory stimuli of touch and pressure. Neural mechanisms are adequately developed in the spinal cord and brain stem for response to this situation. Still another possible source of stimulation is the marked drop in temperature surrounding the animal's body after birth. Thermic stimuli may appear to be less pertinent than other stimulation to which the animal is subject at birth, but they introduce factors which cannot be overlooked or minimized. The posture assumed by the animal at birth may likewise be productive of stimuli through still another afferent system, i.e., the semicircular canals and the vestibular division of the eighth nerve. It is probable that such stimuli are essential to the righting activities but it is difficult to conceive in what manner they may serve as incentives to the righting reaction without presuming the existence of an inherent postural pattern in the animal. In estimating the relative values of these several sources of possible stimulation, it seems inadvisable to single out any of them as predominant. It is far more likely that they all contribute stimuli to the reflexes which determine the early righting and crawling activities.

An important question arises as to the portions of the neuraxis which may be operative in these reactions. The spinal cord and caudal part of the brain stem are thought, by some authorities, to be as adequate for all the performances of the newborn rat as they are for those of late fetal stages. Quantitatively, the reactions immediately after birth differ only in their greater degree of force and persistency. Qualitatively, while having the same integrative manifestations, they show a particularly striking difference in that they persist until a definite goal has been attained and cease after its attainment. This quality, which characterizes most of the postnatal reactions, implies a more extensive correlation of impulses than is operative before birth and hence suggests the participation of correlating centers higher than the spinal cord or caudal part of the brain stem. Such a probability is strengthened in view of the ultimate results obtained by the righting and crawling activities. The newborn rat not only reaches the mother but locates a nipple, secures it, and begins

to nurse. In spite of the fact that the righting and crawling efforts are extremely imperfect and often interrupted by complete upsets in posture, they put the animal in a position to meet several of its pressing needs and facilitate the complex activities by which it is enabled to obtain nourishment. If the hemispheres take part in these reactions they must do so in small measure and to a degree far below their ultimate capacity. Neither their cortical or their subcortical structures seem to be adequately differentiated for such participation. Inasmuch as the pathways of vision and hearing are not yet available, the neocortex is incapable of the synthetic associations of visual, auditory, and somesthetic sensibility for which it serves. Its efferent motor organization is still immature, a fact which is further emphasized by the immaturity of the lateral portions of the cerebellum.

By a process of exclusion, the midbrain thus remains as the most likely higher level of the neuraxis to participate in early postnatal activities. The specialization of its subtectal collicular cells and of its tegmental cells is well advanced. Connections with the lower brain stem and spinal cord by means of the dorsal and predorsal ground bundles are already established in the tract beds. From the standpoint of development, the midbrain has made a much closer approach to its final specialization than the hemisphere or interbrain.

In a previous study of behavior in the cat Dr. Casamajor and I were led to the conclusion that the midbrain participates with the caudal portions of the brain stem and spinal cord in early postnatal activities. Our analysis of the "crawling approach reaction," which brings the newborn kitten to the mother, laid special emphasis upon the part played by the midbrain in the performance of this act. We gave particular consideration to the nature of the directing stimuli which guide the kitten to its goal soon after birth. In the absence of evidence indicating the availability of vision, hearing, and probably of smell, we expressed the opinion that the directing influence was thermotropic in nature. In the rat at birth, some facts seem to show that the sense of smell is available. These facts receive considerable support from the advanced state of differentiation in the olfactory

bulb, paleocortex, and archicortex. The development of the three regions just mentioned suggest that these portions of the hemisphere, in their special relations to the sense of smell, may play a part in the reactions of the newborn.

The convulsive responses to compression of the tail seem peculiarly significant as to the neural organization at birth. The avalanche nature of the response as well as its protracted duration indicate the widespread and indiscriminate segmental distribution of the impulse. The reaction is a total and incoördinate one—a confused overflow of motor innervation with scarcely a semblance of objective. It is devoid of selective and inhibitory qualities and utilizes the resources of nervous energy in an extravagant display of ineffectual violence. Its tendency to repeat itself for some time after the application of the stimulus indicates a level of neural organization considerably above that of the immediate, direct reflex response and at the same time much below that of highly integrated reactions. That these convulsive responses in the newborn express the activities of neural segments below the hemispheres becomes progressively clear in their modifications during later development.

Interpretation of the rat's behavior immediately after birth must envisage the greater availability of the segmental portions of neuraxis with the probable participation of the midbrain. It should also include the possibility of activity on the part of those divisions of the hemisphere directly connected with the sense of smell. The rôle of the neocortex in behavior at this time appears to be negligible.

BEHAVIOR IN THE FIVE-DAY-OLD RAT

During the first five days of life, changes in behavior consist largely in the increased vigor of reactions already established. The rat's postural attitude remains essentially unchanged. It lies on its side with legs and body slightly flexed. On the fourth and fifth days the trunk and limbs are continuously held in a greater degree of extension. The body especially is "straightened out."

The postural reaction in this period becomes progressively more

energetic. When placed on its back, during the second day the young rat performs the same wriggling movements observed on the first day. On each succeeding day it is able to lift its head a little more completely and also to use its hindquarters with more vigor in attempting to right itself. On the fourth day there is a discernible improvement in the postural reaction. The performance is quicker and accompanied by less wriggling. This improvement is still more definite on the fifth day when the animal rights itself promptly and with much less struggling. Although the rat now lifts its head more quickly and holds it extended for a longer time, much of the original ataxic oscillation still persists.

Nutritional activities show but slight modification as compared with their initial characteristics. After feeding, the animal lies quietly on its side for several hours. At the expiration of this time the legs, trunk, and head movements preparatory to nursing again reappear, the young rat approaches the mother, secures a nipple, and begins to suck. During this act the fore- and hind-legs are in constant, more or less rhythmical motion. In some instances and as early as the second day, the young continue the sucking movements for a short time after they cease nursing. Some of them protrude the tongue as if licking the lips.

Locomotor activities on the second day continue to show the same degree of inefficiency and lack of coördination as at birth. On the third day these activities are slightly more vigorous and the approach movements to the mother are distinctly stronger. When in the nest alone the young rats crawl over and under one another's bodies quite actively. On the fourth and fifth days they acquire a firmer grasp upon the supporting surface and show some improvement in making headway on a flat surface. Their locomotor efforts are still crawling in nature and drag the body along the supporting surface. The material on the floor of the cage offers them better opportunity to make progress than a smooth table-top. There is so much uncertainty and lack of direction in these locomotor activities that the animal pursues a wandering course with many turnings of the head from side to side. As early as the second day the incipient phases of other definitely purposive reactions make their appearance. The

young rat attempts to scratch behind its ears with its hindpaws. In doing so the animal lifts its hindlegs to its head and makes ineffectual stroking movements in which the paw fails to come into actual contact with the skin. In some instances the forepaw is held against the mouth and licked. That these activities represent the inception of scratching and washing reactions becomes clear on the fourth and fifth days when the hindpaws make actual scratching movements behind the ears, and the forepaws, after being licked by the tongue, are applied in repeated stroking movements to the sides of the face.

Stimulation by compression of the tail produces the same convulsive and protracted reaction until the fifth day when a slight but significant modification appears. Prior to this time, all parts of the body have been about equally affected by the convulsive movements. On the fifth day the head and anterior part of the trunk do not enter into the reaction so vigorously as they did on previous days. The forelegs likewise show less of the convulsive muscular contraction. The pelvic girdle and hindlegs still twitch convulsively and the greatest intensity of the reaction appears in the hindquarters.

The eyelids are still closed and no definite responses to auditory stimulation can be obtained. The animal, as at birth, withdraws its head to one side or the other on the application of olfactory stimuli.

STRUCTURAL ADVANCES IN THE NERVOUS SYSTEM OF THE FIVE-DAY-OLD RAT

In the spinal cord, cellular differentiation has determined many characteristics resembling those of the adult. Some of the large motor elements in the ventral horn contain an occasional tigroid body but these large cells are still densely clustered along the margins of the ventral gray matter. A marked increase in the dimensions of the lateral white matter is especially noteworthy.

In the oblongatal and pontile portions of the brain stem, cellular specialization in all nuclei has resulted in advances similar to those in the spinal cord. The nuclei of the sensory columns of Goll and Burdach have assumed their characteristic outlines and

have increased in size. The increments to the tract beds in the ventral field make it possible to recognize a well-defined pyramid; in the dorsal field the two sensory tracts (Goll and Burdach) are easily distinguishable. Crossing fibers indicate the positions of the pyramidal and fillet decussations. These facts together

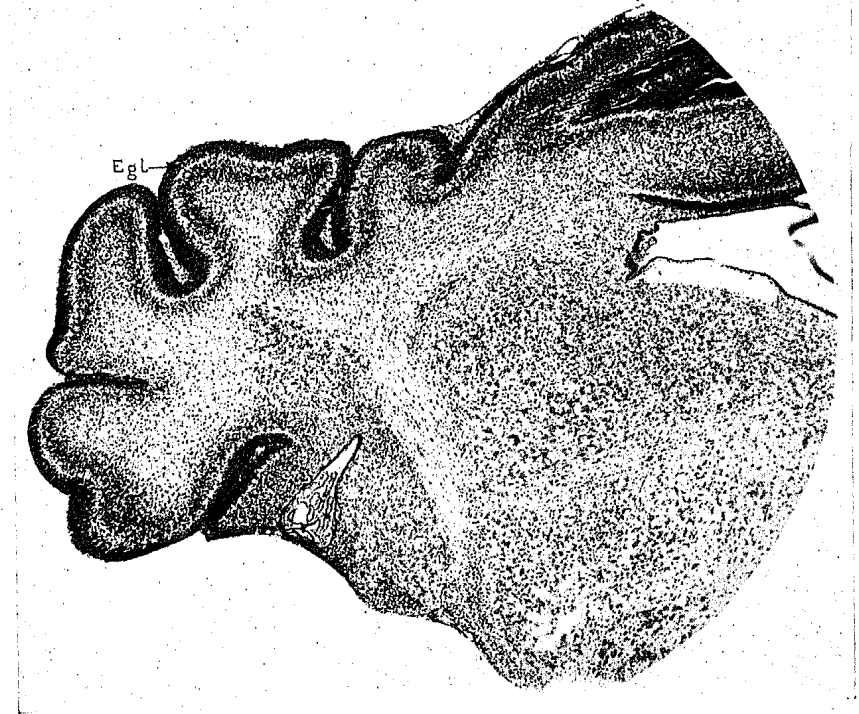


FIG. 10. Section of the cerebellum of a five-day-old albino rat showing the heavy external granular layer (*Egl.*). Specimen No. 1199, magnification $\times 55$.

with the increase of size in the lateral field of white matter in the spinal cord warrant the conclusion that afferent and efferent connections are now established between the neocortex and the axial segments of the neuraxis. Such connections may have existed in even early stages but their presence was considered doubtful on the structural evidence available. In any event the afferent

and efferent pathways of the neocortex are now definite features in the central nervous system.

In the cerebellum, foliation has made rapid progress, most of the major cerebellar fissures have developed, and the tract connections are all well established. Notwithstanding these advances, the structural details of the cerebellum as a whole offer much evidence of immaturity. The thick, external granular layer, the lack of ultimate definition in the other layers, and the incomplete differentiation of the Purkinje cells reveal how far removed this organ is from its definitive specialization (fig. 10).

In the midbrain, the discrete nuclei and their constituent cells show marked progress. Tegmental cells in the collicular and reticular areas have assumed many of the appearances of their adult state. In the tectum the cellular stratification, which was conspicuous in earlier stages, is now somewhat less distinct.

In the interbrain, the lateral, medial, and mesial groups of thalamic nuclei appear in an advanced stage of differentiation although some details of their final specialization are lacking.

Nuclear aggregations in the epithalamus are well defined. The distinction between the hypothalamus and subthalamus is not clearly established nor are the advances in the posterior thalamic nucleus (pulvinar) and the metathalamus (lateral and medial geniculate bodies) pronounced.

In the hemisphere, a long shallow furrow extends from the base of the olfactory bulb to the occipital pole along the line of junction between the middle and lateral thirds of the lateral wall. This furrow, the rhinal fissure, forms the boundary line between the neocortex which lies above the fissure and the paleocortex which covers the brain wall below it. The neocortex is still characterized by six successive layers of cortical cells. This cellular stratification, typical of the early phases of the neocortex, has undergone some slight regional modifications which are due largely to the varying prominence of the internal granular layer in different areas. In the parietal region the internal granular layer is most prominent. It is also well developed in the frontal and occipital areas, but is less conspicuous in the vertex and mesial surface of the brain. With this exception the cellular stratifica-

tion of the neocortex is similar to that of the late fetal and neonatal stages. The cells constituting each cortical layer still show a relatively low degree of specialization.

Below the rhinal fissure, the characteristic features of the paleocortex may be easily recognized. In this region of the brain wall cortical differentiation lacks many of the stratigraphic details seen in the neocortex. On the other hand, specialization in the paleocortex has entered its final phase of local differentiation and it is possible to distinguish four clearly localized regions as follows:

1. Anterior region (parolfactory area)
2. Intermediate region (tuberular area)
3. Middle region (pyriform area)
4. Posterior region (postpyriform area)

The cortical formation in relation with the rhinal fissure is distinguishable both from the neocortical region above it and the paleocortical area below it. In the upper lip of this fissure the cellular arrangement resembles that of the neocortex, except that the cortical thickness is less and the strata more indistinct. In the lower lip of the rhinal fissure cortical formation is similar to that of the paleocortex, although it is of greater thickness and has more definite cellular stratification.

Like the paleocortex, the archicortex is well advanced in its final stage of local differentiation. The cellular features which characterize the preseptal, induseal, dentatal, subicular, pre-subicular, and cornual areas are approaching their adult appearance. In the portion of archicortical arch having direct relation with the corpus callosum a shallow longitudinal furrow has developed. Topographically it is correctly called the *callosal fissure* but actually it is a fissure in the dentatal portion of the brain wall and may be traced from the splenial end of the corpus callosum into the dentatal fissure of the hippocampal formation. The portion of the archicortical arch caudal to the corpus callosum has undergone considerable invagination into the lateral ventricle within which it forms a much expanded hippocampus major. The dentatal plate participates in this infolding and has assumed its characteristic relations to the tip of the cornu ammonis. Cellular differentiation in all regions of the archicortex is not far

from adult conditions. Cortical formation in the olfactory bulb is in its final stage of local differentiation. Two distinct areas of cortex are distinguishable, the anterior or olfactory cortex proper and the posterior or accessory olfactory cortex. The olfactory cortex consists of its six typically adult layers, i.e., (1) glomerular layer, (2) external granular layer, (3) external gelatinous layer, (4) internal granular layer, (5) internal gelatinous layer, (6) cellular layer. The accessory olfactory cortex is composed of three layers, i.e., (1) zonal layer (very thick) (2) granular layer, (3) gelatinous layer (very thick).

The subcortical nuclei, in some respects poorly defined, show a considerable degree of specialization. The caudate nucleus, which is not well developed in the rat, consists of small and medium-sized cells. The head of this nucleus is fragmented by the passage through it of the many separated fascicles of the thalamo-cortical tract bed as they enter the internal capsule. The slender tail of the nucleus arches with the temporal dip of the lateral ventricle and comes into final relation caudally with the nucleus amygdalus and putamen. The lenticular nucleus is composed of the putamen and the globus pallidus. In the latter structure there are many relatively large and widely scattered pyriform cells. In the putamen the cells are small and but slightly differentiated. The claustrum and amygdalar nucleus are not yet well defined and consist of small and medium-sized cells still lacking in any marked degree of specialization.

One important aspect of the development of the nervous system in the rat is the relatively late appearance of myelin in the fiber tracts. Myelination does not occur, as in some mammals, before birth. There is no evidence of it in the newborn and very little until after the fifth postnatal day. The tract-beds, however, undergo a significant change before myelin makes its appearance. In their earliest development these beds consist almost exclusively of protoplasmic strands interspersed among which are a few scattered cells of small size. In the five-day-old rat there occurs a considerable increase in these cells. The increase affects the optic chiasm and tract, the anterior commissure, corpus callosum, fimbria, hippocampal commissure, and to a lesser degree

the lateral and medial forebrain bundles. In later stages it becomes so intense as to change the staining reaction of the tract-beds from their original glistening white appearance to a dark blue. The cells are small, rod-shaped elements with deeply staining pyknotic nuclei. Their appearance prior to myelination may be significant of an important premyelin stage. But whatever their relations in this respect may be, they increase rapidly in number before myelin is deposited. It is of much interest in this connection to note that these rod-cells are at first more numerous in the spinal cord and oblongatal segments than in the hemispheres. This fact in conjunction with others already cited is evidence of a more advanced stage of specialization in the segmented portions of the neuraxis than in the endbrain.

CORRELATIONS BETWEEN THE BEHAVIOR AND NEURAL ORGANIZATION OF THE FIVE-DAY-OLD RAT

The increased vigor in all somatic activities of the five-day-old rat does not necessarily imply the introduction of neural mechanisms not previously available. The general tendency toward extension of the body and limbs is, however, a fundamental change in relative muscular tone which may not be attributable to increasing strength alone. The early flexion of the fetus is now definitely replaced by a "straightening of the body." Such extension is indispensable to the further development of adjustive activities. It has, as already noted, made its appearance in many of the spontaneous movements at birth, but its increasing prominence in the posture of the animal, quite independent of actual movement, is suggestive of an alteration in the relation between flexors and extensors. To ascribe this alteration in relative tone to adequate specialization in the cerebral cortex does not accord with the developmental advances of this stage. Nor, for that matter, is it well established that this function is ever highly represented in the cortex of the rat since experimental removal of large cortical areas in the adult may not seriously disturb the tonic relation between flexors and extensors. The immature condition of the cerebellum at this time is equally unfavorable to its participation in such tonic activity. On the other hand, advanced spe-

cialization in the midbrain may suffice to explain the new muscular relations in posture, although the claims of the striatum should not be overlooked in this connection. The globus pallidus shows considerable advance in the five-day-old rat. From the lack of distinctly new features in the righting, crawling, nursing, and swimming reactions it may be assumed that the portions of the nervous system originally responsible for these activities are still adequate, nor does the explanation of the early scratching reflex require the introduction of centers other than those in the lower segmental parts of the axis. The conditions involved in the washing reaction are much more complicated. This reaction consists of a correlated sequence of purposive movements the activation of which is open to several questions. The source of stimulation is, as in the scratch reflex, in the region of the head. The structural specialization of the body and the segmental nature of innervation makes the forelimb especially responsive to stimuli from the snout, mouth, and face. The hindlimb is similarly responsive to stimuli from the back of the head and remainder of the body. The selection of the foreleg in the washing reaction thus has its determinants in the structure of the animal. The application of the forepaw to the mouth, the licking movements of the tongue, and even the subsequent stroking of the face by the moistened forepaw do not of themselves imply any higher order of intersegmental organization than that necessary for the simple scratch reflex. But the combination and sequence of these movements in a definite washing reaction seem to require more extensive neural correlations. Correlations of this kind appear to be essential both for the proper assembling of sensory stimuli and for the proper timing of the effector responses. Whether the component elements of this reaction are merely coincidental manifestations of intersegmental reflexes which later acquire higher directive control or whether, from their inception they represent such control, is, of course, a matter open to discussion. When compared with other spontaneous activities the washing reaction has a greater degree of what Coghill calls "individuation." This fact strongly suggests the possibility of correlating levels higher than those necessary to reactions such as crawling and swimming.

If, as seems probable, the pathways of smell and of taste are open, the paleocortex may reasonably be accredited some part in the washing reaction in which case the movements would have the design of removing unfavorable material from the forepaws. All things considered, it is difficult to explain this reaction as a series of intersegmental reflexes. There are likewise objections in attributing it exclusively to axial levels capable of regulating the early postnatal movements of swimming, crawling, and nursing. At this stage the paleocortical division of the hemisphere is sufficiently advanced both in its cellular differentiation and its fiber connections to participate in reactions.

The more obvious contingencies which may influence the afferent influx should not, however, be allowed to overshadow less apparent sensory factors. Cutaneous sensibility is dependent upon many intrinsic as well as extrinsic conditions. Circulatory changes both in the skin and in the conducting fibers are, by experience, known to be sources of stimulation. In pathological conditions the dysesthesia produced by them (tingling, numbness, burning, and pain) give rise to well recognized reactions. During the process of growth many intrinsic factors are operative in the tissues. In the young rat the skin area is rapidly increasing from day to day; cutaneous fat is slowly accumulating, hairs are making their appearance, and the subcutaneous vascular bed is expanding. "In 16-mm. rat fetuses about a dozen anlagen of vibrissae are present in the snout. A reticulum formed by a few nerve fibers at the base of each vibrissa is seen. At birth there are more vibrissae, more fibers to each of them, more tactile fibers to the skin" (Donaldson). Such intrinsic factors are most active in and about the snout, mouth, and face and may be assumed to be constantly augmenting the afferent stream as growth proceeds. That this stream, in early postnatal life, reaches the upper levels of awareness is unlikely but that it has specific sensory registration seems difficult to doubt. Nor is the skin the only source of this increasing volume of afferent impulses. The muscular and articular systems are undergoing simultaneous expansions due both to increments of growth and functional activity. To these impulses must be added the sensory influx from the viscera.

Converging upon the sensory ganglia of the interbrain afferent impulses from these various sources contribute to a constantly changing current of affective influences.

Changes in this sensory current are the result of differences in conduction pressures incident to stimulus variations in the several components of the afferent stream. Nuclear specialization in the thalamic, subthalamic, and hypothalamic portions of the interbrain is, at this stage, well advanced. Connections by means of the medial forebrain bundle and other fiber systems are equally well established. With the exception of its metathalamic structures, this important region of sensory convergence appears to be adequately differentiated for the reception of the afferent impulses which reach it from various parts of the body. To what degree intrinsic sensory factors may influence the activities of the young animal cannot be estimated. On the other hand, they deserve consideration in evaluating the total volume of afferent influx and may play an important rôle in such activities as the washing reaction in which the stimuli and the sources of stimulation are open to so much question.

The response to compression of the tail in the five-day-old rat presents a problem of almost equal difficulty. The fact that the head, neck, forelimbs, and anterior portions of the trunk now show less of the convulsive reaction than the pelvic girdle and hindlegs denotes a selective restriction in the response. The parts of the body in closest proximity to the stimuli still react as vigorously and as incoördinately as on the first day. Yet notwithstanding the availability of the same connections for segmental and intersegmental reflexes throughout the body, the stimulus does not spread to the anterior parts with anything like its previous force. Even at this stage it is perhaps difficult to appreciate what in later periods becomes clearly apparent, namely, that this response is, in essence, an avoiding reaction from its inception. Its original violence and diffusion at first mask its real nature. But its modifications in the five-day-old rat seem to indicate that at least some fraction of the stimulus has gained access to higher correlating centers which eventually impart to the reaction its more coördinate and effectual characteristics.

However uncertain such a conclusion may appear at this period of development, it becomes increasingly convincing in subsequent stages when the direct reflex responses of the reaction are replaced by highly correlated movements. Since the thalamic portion of the interbrain is the ultimate convergence center for all afferent somatic impulses it is reasonable to assume that some part of the stimulus from the tail has reached this level.

In addition to activities of the segmented portions of the neuraxis, the behavior of the five-day-old rat implies the participation of the thalamus and probably of the corpus striatum and the paleocortex.

BEHAVIOR IN THE TEN-DAY-OLD RAT

From the fifth to the tenth postnatal day, the postural attitude and postural reactions of the rat show definite improvements. The animal lies almost continuously in the belly-down position. Its legs are sprawled out on either side of its body and its head is held up with considerable steadiness much of the time. By the seventh day this posture is thoroughly established and, because of its apparent advantages in the initiation of other activities like sitting, standing and walking, it may properly be called the *optimum posture*. The significance of this posture is easily appreciated on the eighth day when the rat makes its first attempts to sit up. It then assumes a partial sitting position by extending the forelegs sufficiently to lift the head and chest clear of the supporting surface. Most of the body weight is borne by the abdomen, rump, and widely abducted hindlegs. On the tenth day this half-sitting posture is more continuously and effectually maintained. It becomes more conspicuous by its association with a reaction which is a prominent feature in the animal's behavior. While sitting half upright, the rat moves its head about in all directions, constantly sniffing as it does so. Since the sniffing reaction of the adult is so obviously exploratory in nature there can be no doubt as to its significance in the ten-day-old rat.

When placed upon its back during the sixth and seventh days the rat rights itself quickly and immediately makes efforts to crawl away. These locomotor attempts have not previously

attended the righting reaction and become more pronounced on the eighth day when the animal turns over from its back almost instantly and begins to move forward. In its efforts to attain the optimum posture, there is still some wriggling of the body but improvement in the righting reaction is shown by greater speed and economy of movement as compared with earlier stages. If placed upon its back on the tenth day the rat, although not entirely free of wriggling movements in the trunk, rights itself without the slightest hesitation.

With the exception of greater strength, spontaneous activities show no additional features up to the eleventh day.

There is little change in the locomotor reactions during the sixth day but on the seventh day the young rat is able to crawl forward five or six inches on a flat surface upon which it appears to have a firmer grasp. Activity in these performances shows a marked increase in vigor. In the nest and cage the animals crawl over and under one another almost continually. Their crawling still retains the characteristic paddling movements of the legs.

The body is not lifted from the supporting surface in locomotion. A notable addition to locomotor activity does, however, appear on the eighth day when side to side movements of the head are accompanied by constant sniffing. On this day also the animal shows its first tendency toward jumping when, for no apparent reason, it suddenly springs clear of the supporting surface. The paddling movements of the legs, on the ninth and tenth days, are longer and more rapid. The animals are constantly moving about and are able to traverse the entire length of the cage to reach the mother.

The scratching and washing reactions acquire greater definition on the seventh and eighth days. Washing appears to be the major occupation on the ninth day. All of the animals are busily engaged in licking their forepaws and applying them to the sides of the face. There is, however, a considerable degree of incoördination in these movements.

The response to compression of the tail shows still further restriction to the rump and hindlegs. The head, trunk, and fore-

limbs now participate but slightly in the reaction. Much of the earlier convulsive character of the movements in the hindquarters is lacking and most of the original violence of the response is limited to forceful wagging of the tail.

By the eighth day convulsive contractions in the forepart of the body are no longer observed in the reaction which now consists of a few wriggling movements of the hindquarters, squeaking, and wagging of the tail. In general this response is less protracted and less diffuse. Its disorganizing effects upon the motor stability of the animal have become much reduced. This change as compared with earlier stages is especially apparent on the tenth day when the rat responds by a short start forward away from the stimulus, a sharp squeak, and pelvic wriggling of brief duration. The residual effects of the reaction are exclusively confined to movements of the tail.

The eyelids are still closed and no positive evidence of response to auditory stimuli could be obtained. The most conspicuous advance, in the sphere of the special senses is the constant sniffing as the animals continually move their heads from side to side.

ADVANCES IN THE NERVOUS SYSTEM OF THE TEN-DAY-OLD RAT

A striking developmental feature in the nervous system of the ten-day-old rat is the appearance of myelin in many of the tract beds. Some indications of myelination are apparent in the spinal cord of the five-day-old rat. Watson (1903) found myelin deposition in the ventral and lateral tract beds of the albino rat as early as two days after birth. This deposition occurs at that time in the cervical segments and was first observed in the thoracic and lumbar segments one day later.²

The extramedullary portion of the ventral roots, according to Watson, are partially myelinated on the second and third days while the extramedullary portions of the dorsal roots begin to acquire their myelin sheaths from the third to the sixth day. The intramedullary portion of both dorsal and ventral roots are par-

² The stages which I have selected for study, unfortunately do not include specimens of the second, third and fourth postnatal days. After careful search in all levels of several one-day-old albino rats, I was unable to find any evidence of myelination.

tially myelinated on the eighth day. In the columns of Goll and Burdach myelin deposition begins on the third to the sixth day. Myelination first occurs in the pyramidal tract in cervical levels on the sixth day, in thoracic levels on the tenth day, and in lumbar levels on the eleventh day.

On the eighth postnatal day myelin is present to some degree as follows:

1. *In the spinal cord.* There is evidence of beginning myelination in the juxtagriseal components of the ventral white column, less marked in the intermediate fasciculi but none in the mesial fiber groups adjacent to the ventral fissure.

In the lateral white column myelin is beginning to appear, to a slight degree, in the circumferential zone and in the juxtagriseal fascicles but is not apparent in the intermediate zone.

In the dorsal white column deposition of myelin has taken place upon the fibers of the circumferential zone, is well marked in the intermediate zone, but lacking in the mesial groups of fascicles.

2. *In the oblongata.* Myelination is marked in the deitersospinal, posterior longitudinal, and predorsal fascicles and in the vestibular division of the eighth nerve, slight in the bundles of Flechsig and Gower, in the descending trigeminal fibers and emergent fibers of the ninth, tenth, and twelfth nerves, and very slight in the dorsal columns of Goll and Burdach, mesial fillet, and internal arcuate fibers, but entirely lacking in the pyramidal tract and pyramidal decussation.

3. *In the pons.* The posterior longitudinal and predorsal bundles are fairly well myelinated and the emergent fibers of the sixth nerve show a slight deposition of myelin.

4. *In the cerebellum.* Myelin is apparent in the inferior cerebellar peduncle and very slightly in the medial folia.

5. *In the midbrain.* With the exception of the posterior longitudinal and predorsal bundles there is little evidence of myelination in any other fascicles.

Although it is unquestionably true that myelin is not essential to impulse conduction through the tract beds, the deposition of this ensheathing substance appears to bear a definite relation to the efficacy of transmission by means of the several conduction

systems of the neuraxis. As a general rule those fibers systems of the greatest phyletic age are first to acquire their myelin sheaths. Whether these sheaths are merely an expression of the growth process in nerve fibers or an index of their capacity for conduction, there can be no dispute that they are a late manifestation in the maturation of those neurones whose axis cylinders become myelinated. Viewed in this light, the myelin sheath affords valuable evidence concerning the degree of neurone

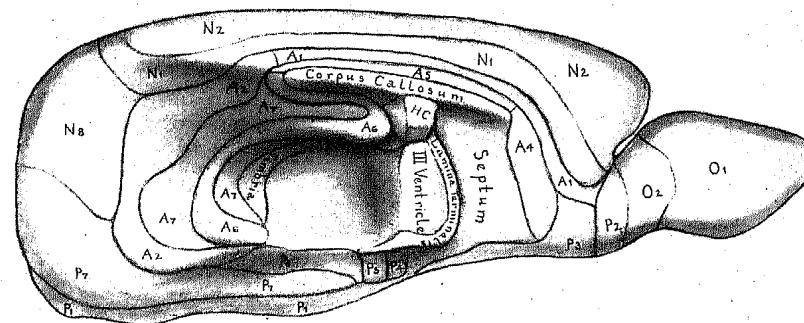


FIG. 11. Mesial surface of a reconstruction of the left cerebral hemisphere of a ten-day-old albino rat. Specimen No. 1194. Neocortical areas: N1, cingular area; N2, marginal area; N8, meso-occipital area. Archicortical areas: A1, intercalary area; A2, presubicular area; A4, preseptal area; A5, induseal area; A6, dentatal area; A7, cornual area. Paleocortical areas: P1, pyriform area; P2, parolfactory area; P3, tubercular area; P4, post-tubercular area; P5, amygdalar area; P6, post-amygdalar area; P7, post-pyriform area. Olfactory areas: O1, olfactory cortex proper; O2, accessory olfactory area; H. C., hippocampal commissure. Histologically different areas and structures in all reconstructions were indicated by using wax plates of different colors.

maturity. The unmyelinated axone, belonging to a system which ultimately becomes myelinated, is a part of a young and immature neurone. The myelinated axone is part of a mature neurone or one approaching maturity.

Developmental advances also appear in other details of the spinal cord (fig. 11). The ventral horn has increased in size and its large motor cells are disposed in five groups which constitute the ventro-lateral, ventro-dorsal, central, ventro-medial, and dorso-medial somatic motor columns. The lateral and dorsal

horns as well as the tract beds have likewise expanded. Changes of a similar character have occurred in the oblongata. In the cerebellum, although the external granular layer is still prominent, the layer of Purkinje cells has become more conspicuous.

Cellular differentiation in the midbrain and in the interbrain shows progressive advances in all of the principal nuclei but it is particularly in the hemisphere that the most decisive progress is apparent. The phase of local cortical differentiation, which is already present in the paleocortex, archicortex, and bulbar cortex of the five-day-old rat, has now extended to the neocortex. Twelve distinct areas may be distinguished in this portion of the brain wall. The distinctions between them depend upon local modifications of the original six-layered neocortex. The internal granular layer is most affected by these modifications. In certain areas this layer assumes marked prominence or is reduplicated; in others it becomes inconspicuous or disappears altogether. It is not, however, these changes in the internal granular layer alone which determine the histological differences in the several localized areas of the neocortex. All of the other layers are subject to considerable variation in passing from one area to another.

Three of these localized neocortical areas appear on the mesial surface of the hemisphere. For purposes of identification they are designated N1, N2, and N8 (fig. 11).

Area N1 (cingular area) extends from the parolfactory region to the occipital pole. It is situated immediately above the outer arch of the archicortex. Its cortical stratification has the following measurements:

	Thickness <i>micra</i>
1. Zonal layer above average thickness.....	200
2. External granular layer well developed.....	200
3. External pyriform layer of moderate thickness.....	120
4. Internal granular layer poorly defined.....	80
5. Internal pyriform layer poorly defined.....	120
6. Multiform layer of considerable depth.....	200

The average total thickness of the cortex in neocortical area N1 is 920 micra.

Area N2 (marginal area) extends from the olfactory bulb to the occipital region. It is situated between area N1 and the upper

rim of the mesial surface. Its cortical stratification has the following measurements:

	Thickness <i>micra</i>
1. Zonal layer above average thickness.....	160
2. External granular layer poorly developed.....	120
3. External pyriform layer well defined.....	100
4. Internal granular layer very indistinct, in places absent.....	80
5. Internal pyriform layer prominent.....	300
6. Multiform layer of considerable thickness.....	240

The average total thickness of the cortex in neocortical area N2 is 1000 micra.

Area N8 (meso-occipital area) occupies a position in the occipital region of the mesial surface caudal to the descending limb of the archicortex. It differs from other neocortical areas in two important details, i.e., first the richness and reduplication of the internal granular layer; and second, the almost entire lack of pyriform elements. Its cortical stratification has the following measurements:

	Thickness <i>micra</i>
1. Zonal layer of average width.....	110
2. External granular layer prominent.....	120
3. External pyriform layer poorly developed.....	110
4. Internal granular layer (a) broad.....	210
Internal granular layer (b) broad.....	300
6. Internal pyriform layer poorly developed.....	280
6. Multiform layer fairly broad and irregular.....	270

The average total thickness of the cortex in the neocortical area N8 is 1400 micra.

Five of the localized areas of the neocortex appear upon the vertex and lateral surface of the hemisphere. They are designated N3, N4, N5, N6, and N7 (fig. 12).

Area N3 (central area) occupies a narrow strip along the vertex parallel to the mesial rim of the hemisphere. It is immediately contiguous and almost coextensive with area N2. Its cortical stratification has the following measurements:

	Thickness <i>micra</i>
1. Zonal layer of average thickness.....	100
2. External granular layer well defined.....	120
3. External pyriform layer well developed and thick.....	360
4. Internal granular layer indefinite.....	
5. Internal pyriform layer well defined and thick.....	520
6. Multiform layer well developed.....	300

The average total thickness of the cortex in neocortical area N3 is 1400 micra.

Area N4 (frontal area) covers the frontal portion of the lateral surface. It extends obliquely downward and forward from the

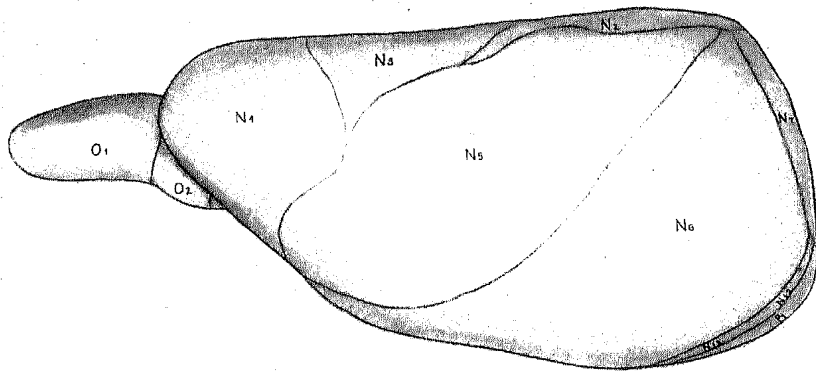


FIG. 12. Lateral surface of a reconstruction of the left hemisphere of a ten-day-old albino rat. Specimen No. 1194. N2, marginal area; N3, central area; N4, frontal area; N5, parietal area; N6, temporal area; N7, latero-occipital area; N12, insular area C; P1, pyriform area; O1, olfactory cortex proper; O2, accessory olfactory cortex.

outer margin of area N3 to the base of the olfactory bulb. Its cortical stratification has the following measurements:

	Thickness <i>micra</i>
1. Zonal layer of average thickness.....	100
2. External granular layer fairly layer well defined.....	110
3. External pyriform layer of moderate thickness.....	110
4. Internal granular layer not well defined.....	70
5. Internal pyriform layer well developed and thick.....	440
6. Multiform layer of average thickness.....	260

The average total thickness of the cortex in neocortical area N4 is 1090 micra.

Area N5 (parietal area) covers the anterior half of the parietal region immediately caudal to area N4. It extends obliquely downward and forward across the lateral surface from the outer margin of area N3 to the upper lip of the anterior portion of the rhinal fissure. Its distinguishing feature is the striking prominence and thickness of the internal granular layer. The stratification of area N5 has the following measurements:

	Thickness <i>micra</i>
1. Zonal layer below average thickness.....	90
2. External granular layer fairly well defined.....	90
3. External pyriform layer above average thickness.....	220
4. Internal granular layer broad and prominent.....	220
5. Internal pyriform layer well developed.....	400
6. Multiform layer of more than average thickness.....	320

The average total thickness of the cortex in neocortical area N5 is 1340 micra.

Area N6 (temporal area) covers the lateral surface caudal to area N5 and forms the temporal region. It extends obliquely downward and forward from the vertex to the rhinal fissure. The transition from area N5 to area N6 is marked by a great reduction in the internal granular layer. The stratification of area N6 has the following measurements:

	Thickness <i>micra</i>
1. Zonal layer of average thickness.....	100
2. External granular layer of less than average thickness.....	95
3. External pyriform layer of moderate thickness.....	130
4. Internal granular layer well developed.....	130
5. Internal pyriform layer of average thickness.....	410
6. Multiform layer of average thickness.....	400

The total average thickness of the neocortex in area N6 is 1265 micra.

Area N7 (latero-occipital area) occupies the occipital region covering the vertex and lateral surface. It is situated immediately caudal to area N6 and extends obliquely downward and forward from the vertex to the upper fold of the posterior por-

tion of the rhinal fissure. The stratification of area N7 has the following measurements:

	Thickness <i>micra</i>
1. Zonal layer below average width.....	75
2. External granular layer prominent.....	110
3. External pyriform layer not well developed.....	100
4. Internal granular layer of average width.....	100
5. Internal pyriform layer fairly well developed.....	350
6. Multiform layer somewhat narrow.....	230

The total average thickness of the cortex in neocortical area N7 is 965 micra.

Area N9 (orbital area) is the only neocortical differentiation on the basal surface of the hemisphere. It occupies a region which extends from the frontal pole to the anterior margin of the parolfactory area. Its stratification has the following measurements:

	Thickness <i>micra</i>
1. Zonal layer broad.....	130
2. External granular layer below average thickness.....	90
3. External pyriform layer, well developed.....	200
4. Internal granular layer narrow and indistinct.....	80
5. Internal pyriform layer narrow.....	190
6. Multiform layer narrow.....	140

The total average thickness of the cortex in neocortical area N9 is 830 micra.

The rhinal fissure in the ten-day-old rat still occupies a position on the lateral surface of the hemisphere. It is not, however, of uniform depth throughout its course. Its anterior portion is the deepest, its middle portion is little more than a shallow groove, while its caudal portion attains considerable depth. In the deeper parts of the fissure the upper fold is formed by neocortex and the lower fold consists of paleocortex. The shallow portion of the rhinal fissure is composed almost exclusively of neocortex, although a small segment of its lower fold contains paleocortex. Neocortical specialization in relation with the entire length of this fissure has distinctive characteristics of its own and forms a narrow strip of cortex situated along the basal margins of areas

N4, N5, N6 and N7. The general appearance of this neocortical strip is fairly uniform from its frontal to its caudal extremity but certain variations affecting the thickness of its several layers establish three distinguishable areas in it. These areas bear definite relations to the three portions of the rhinal fissure (fig. 13).

Area N10 (insular area A) occupies a position in the upper fold of the anterior (deepest) portion of the rhinal fissure. Due to the fissural depth it has but small representation on the surface of

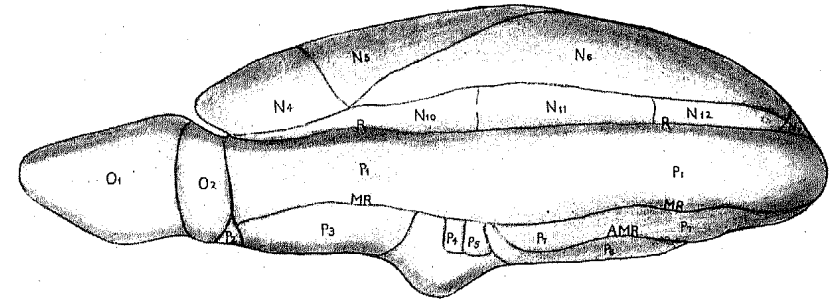


FIG. 13. Basal surface of a reconstruction of the left hemisphere of a ten-day-old albino rat. Specimen No. 1194. N4, frontal area; N5, parietal area; N6, temporal area; N7, latero-occipital area; N10, insular area A; N11, insular area B; N12, insular area C; P1, pyriform area; P2, parolfactory area; P3, tubercular area; P4, post-tubercular area; P5, amygdalar area; P6, post-amygdalar area; P7, post-pyriform area; area O1, olfactory cortex proper; O2, accessory olfactory cortex; R, rhinal fissure; MR, mesorhinal fissure; AMR, accessory mesorhinal fissure.

the lateral wall. Its stratification has the following measurements:

	Thickness <i>micra</i>
1. Zonal layer above average width.....	240
2. External granular layer of average thickness.....	130
3. External pyriform layer well developed.....	280
4. Internal granular layer not distinguishable.....	240
5. Internal pyriform layer fairly well developed.....	240
6. Multiform layer below average thickness.....	220

The total average thickness of the cortex in neocortical area N10 is 1110 micra.

Area N11 (insular area B) covers the greater part of the middle (shallow) portion of the rhinal fissure. Its stratification has the following measurements:

	Thickness <i>micra</i>
1. Zonal layer of average thickness.....	100
2. External granular layer fairly well defined.....	95
3. External pyriform layer well developed.....	110
4. Internal granular layer not distinguishable.....	
5. Internal pyriform layer fairly thick.....	350
6. Multiform layer of average thickness.....	310

The total average thickness of the cortex in neocortical area N11 is 965 micra.

Area N12 occupies the upper fold of the caudal portion of the rhinal fissure. Its stratification has the following measurements:

	Thickness <i>micra</i>
1. Zonal layer above average thickness.....	220
2. External granular layer well defined.....	145
3. External pyriform layer broad.....	320
4. Internal granular layer not distinguishable.....	
5. Internal pyriform layer of moderate thickness.....	236
6. Multiform layer fairly well developed.....	248

The total average thickness of the cortex in neocortical area N12 is 1169 micra.

Arranged in the order of their relative thickness, the several areas of the neocortex have the following measurements in the ten-day-old rat.

	<i>micra</i>
1. Area N3 (central).....	1400
2. Area N8 (meso-occipital).....	1400
3. Area N5 (parietal).....	1340
4. Area N6 (temporal).....	1265
5. Area N4 (frontal).....	1090
6. Area N10 (insular A).....	1110
7. Area N12 (insular C).....	1169
8. Area N2 (marginal).....	1000
9. Area N11 (insular B).....	965
10. Area N7 (latero-occipital).....	965
11. Area N1 (cingular).....	920
12. Area N9 (orbital).....	830

The paleocortex in the ten-day-old rat, like the neocortex, shows an advanced degree of local cortical differentiation. Indications of such differentiation are apparent as early as the late fetal stages. But specialization of cortical regions, in the ten-day-old rat has progressed to such an extent that it is possible to identify nine distinct areas in the paleocortex.

Much confusion exists in the terminology of this part of the hemisphere. Many authorities still prefer to designate it the *pyriform lobe* with certain accessory structures. But Kapper's insistence that this region, by reason of its definite cortical differentiation, should be regarded as a specific part of the cerebral cortex, seems thoroughly justified by the histological conditions of this division of the brain. While the following description of the paleocortex is intended to retain, in so far as possible, the more familiar terms associated with this region, the occurrence of local cortical differentiations has served as the ultimate test for all distinctions.

The paleocortex occupies the lower portion of the lateral wall and the basal surface of the hemisphere. To a small extent it encroaches upon the mesial surface. Its lateral boundary is well defined by the rhinal fissure. Its mesial boundary is much less distinct. Only in places is it indicated by fissural markings such as the anterior endorhinal fissure in the frontal region of the mesial surface and the posterior endorhinal fissure in the occipital region.

The under surface of the paleocortex is subdivided longitudinally by a long shallow groove, the mesorhinal fissure (usually called the endorhinal fissure) which extends from the base of the olfactory bulb to the caudal extremity of the basal surface. The anterior portion of this fissure contains the lateral olfactory tract and several blood vessels. In its posterior portion, the groove, although distinct, is more shallow and contains several large vessels.

Seven areas are distinguishable in the basal surface of the paleocortex. They are here designated areas P1, P2, P3, P4, P5, P6, and P7.

Area P1 occupies a position lateral to the mesorhinal fissure

and extends from the parolfactory area (area P2) to the occipital region. It also covers the lateral surface of the hemisphere up to the rhinal fissure. This area corresponds in general to the pyriform lobe and may be called the *pyriform area*. Its stratification has the following characteristics:

The zonal layer is unusually thick and contains many scattered granule and small pyriform cells. The stratum immediately underlying the zonal layer has the appearance of a dense and prominent external granular layer. Upon analysis it is found to contain but a few scattered granule cells along its outer margin. Most of the cellular elements in this lamina are small and medium-sized pyriform cells closely crowded together and staining deeply in their nuclei and cytoplasm. The external granular layer, consequently, is poorly developed in this region. In many places granule cells are entirely lacking and the pyriform elements are in direct contact with the zonal layer. This partial suppression of the external granular layer and its replacement by a dense external pyriform layer impart a characteristic to area P1 which distinguishes it from adjacent areas.

The internal granular layer is lacking and the internal pyriform layer consists of scattered cells of medium size. There are no large pyriform cells such as those which constitute a striking feature in all regions of the neocortex. The internal pyriform layer as a whole has a loose arrangement which is in contrast to the dense massing of the pyriform cells in neocortical areas.

The multiform layer is relatively narrow and contains scattered cells in a loose arrangement.

Area P2 occupies a small territory adjacent to the base of the olfactory bulb and internal to the anterior portion of the mesorhinal fissure. It also covers a small area of the mesial surface immediately in front of the anterior extremities of the intercalary and preseptal areas. By reason of its relation to the olfactory bulb, it is called the *parolfactory area*. Its stratification has the following characteristics:

The zonal layer is broad, and the external granular layer distinct but poorly developed. The external pyriform layer has considerable depth but is much less prominent than in area P1.

The internal granular layer is lacking. The internal pyriform and multiform layers are both well defined.

Area P3 covers the tuberculum olfactorium. It occupies a position immediately caudal to area P2 and internal to the mesorhinal fissure. A small extension of it appears on the mesial surface below the septum and the preseptal area. It is called the *tubercular area* because of its relation to the tuberculum olfactorium. This area has the most striking histological characteristics of all regions in the paleocortex.

Its zonal layer, although well defined, varies greatly in thickness due to the fact that the external granular layer presents many irregular undulations. The wave-like characteristics of this layer give the area an appearance unlike that of any other part of the entire cerebral cortex. In places the undulations approach so closely to the surface of the brain that the zonal layer is reduced to a mere film. In other places this wavy granular layer recedes far from the surface with the result that the zonal layer becomes a broad lamina. As in the case of area P1 the external granular layer contains many more pyriform than granule cells.

Another peculiarity of area P3 is the dense stratum of small round cells with pyknotic nuclei and scanty cytoplasm which underlies the external granular layer. Its distribution is extremely irregular and undulating. In some cross-sections, clusters of these small cells appear to be detached from the rest of the lamina and form what have been called *islands of Calleja*. Reconstructions, however, show these islands to be irregular protrusions from a continuous lamina. In some instances the protrusions extend deeply into the cerebral tissue and form clusters in the nucleus accumbens. Often they penetrate far into the external granular layer and appear to interrupt its continuity.

The internal pyriform layer is narrow and consists of irregularly scattered pyriform cells of medium size. The multiform layer is difficult to distinguish from the periphery of the nucleus accumbens.

Area P4 is situated immediately caudal to the tuberculum olfactorium and mesial to the mesorhinal fissure. For topographical

reasons it may be called the *post-tubercular area*. It is composed exclusively of a well defined zonal layer and a combined external granular and external pyriform layer. In this combined lamina the granule cells are greatly outnumbered by pyriform elements.

Area P5 occupies a position back of the post-tubercular area and mesial to the mesorhinal fissure. It consists of a broad zonal layer which surrounds the ventral nucleus of the amygdalar complex. Because of its relation to this nucleus it is called the *amygdalar area*. Many nerve fibers from the lateral olfactory tract terminate in this nuclear division of the amygdalar complex.

Area P6, the *post-amygdalar area*, covers the basal surface from the amygdalar area to the occipital region. It also has a slight extension into the mesial surface where it occupies a position below the lower margin of the archicortex. A shallow accessory mesorhinal groove forms its lateral boundary. The stratification of this area consists of a broad zonal layer beneath which is a thick uniform stratum of pyriform cells. The pyriform layer passes over into the caudal nucleus of the amygdalar complex without any sharp line of demarcation.

Area P7 occupies a position between the caudal portion of the mesorhinal and accessory mesorhinal fissures. Because of its relation to area P1 (pyriform area) it is called the *post-pyriform area*. Its stratification resembles that of area P6 from which it is distinguished, however, by the more pronounced development of the external pyriform layer. The two areas seen side by side leave little doubt as to their distinctive histological differences. Both of these areas bear a close relation to the caudal nucleus of amygdalar complex and their topography, at least, warrants the suggestion that together they correspond to the uncus of higher mammals.

Two paleocortical areas appear in the lower fold of the rhinal fissure. They are designated areas P8 and P9.

Area P8 (anterior rhinal area) forms the lower fold of the anterior portion of the rhinal fissure. Its stratification has the following characteristics:

The zonal layer is below average thickness. The next succeeding lamina is a combination of granule cells and small pyriform

elements. As a layer it is relatively narrow and thus in marked contrast to the corresponding stratum in the adjacent area P1 (pyriform area). The transition from the neocortex in the upper fold of the rhinal fissure to this area in the lower fold is signalized by the abrupt termination of the broad external pyriform layer and the massing of pyriform cells in the lamina immediately subjacent to the zonal layer. There is no evidence of an internal granular layer in area P8 and its internal pyriform layer, which is of considerable depth, consists of scattered, medium-sized pyriform cells. The multiform layer is narrow and poorly defined.

Area P9 (posterior rhinal area) forms the lower fold of the posterior portion of the rhinal fissure.

Local cortical differentiation in the ten-day-old rat makes possible the recognition of seven archicortical areas. These areas are designated A1, A2, A3, A4, A5, A6 and A7. They have emerged as specializations from the three original arches of the archicortex which were first identified in the 17-day fetus (25-mm.).

Areas A1, A2, and A3 are derived from the outer or intercalary arch; areas A4, A5, and A6 from the inner or dentatal arch; area A7 from the middle or hippocampal arch.

Area A1 is situated in the frontal region subjacent to the anterior extremity of area N1 and extends backward above the corpus callosum, forming a transition zone between archicortex and neocortex. It is called the *intercalary area*. Area A2 is the somewhat expanded caudal portion of the intercalary area which forms the outer border of the hippocampal formation and is called the *presubicular area*. Area A3 is situated between the presubicular area and the cornu Ammonis. It is called the *subicular area*. The stratification in areas A1, A2, and A3 has the following characteristics:

The zonal layer is relatively thick. It is impossible to identify any definite external granular layer since the stratum underlying the zonal lamina is composed of small and medium-sized pyriform elements. The cells of this external pyriform layer have large vesicular nuclei. They constitute a distinctive feature in the comparatively simple stratification of area A1 which lacks both

internal granular and internal pyriform layers. A thin, diffuse layer of multiform cells is situated beneath the external pyriform layer.

Area A4 is situated immediately behind the anterior extremity of the intercalary area (area A1) and in front of the septum, for which reason it is called the *preseptal area*. Its stratification has the following characteristics:

The zonal layer is narrow and succeeded by a thin but dense layer of small and medium-sized granule cells. The external pyriform layer is poorly defined and relatively narrow. There are no indications of an internal granular or internal pyriform layer. Irregularly scattered cells form a thin multiform layer.

Area A5 rests upon the dorsum of the corpus callosum. It is called the *induseal area* (induseum griseum) and its stratification has the following characteristics:

The zonal layer is much below its average thickness and overlies a stratum of granule cells intermingled with somewhat larger elements, oval in outline and containing large vesicular nuclei.

Area A6 occupies a position below and behind the corpus callosum and also forms the inner rim in the descending limb of the archicortex. This is the *dentatal area* (fascia dentata). Its stratification has the following characteristics:

The zonal layer is narrow and covers a compact, deeply staining lamina of small granule cells intermingled among which are a few small pyriform cells. Subjacent to this dense granular layer is a pale stratum containing widely scattered pyriform cells of fairly large size and a small number of multiform cells.

Area A7 surrounds the dentatal area (A6) in the descending limb of the archicortex. It forms the cornu Ammonis or *cornual area*. Its stratification has the following characteristics:

The zonal layer is thicker than in any other part of the cerebral cortex. It overlies a compact, deeply staining layer of medium-sized pyriform cells. These cells are arranged in cords whose long axes are at right angles to the surface of the area. The stratum, in its entire extent, has about twice the thickness of the corresponding lamina of the dentatal area. It covers a pale, narrow layer which, in addition to numerous multiform cells, contains a number of irregularly scattered large pyriform cells.

At this stage all of the subcortical nuclei are structurally well defined and consist of the corpus striatum, the claustrum, and amygdalar complex. The striate body comprises: (1) the nucleus accumbens which consists of small cells with scanty cytoplasm and large vesicular nuclei; (2) the nucleus caudatus which is also made up of similar small cells; its head is penetrated by many scattered fascicles of the thalamo-cortical radiation; (3) the putamen, which is the most extensive portion of the striatum and is likewise pierced by numerous small fiber bundles; its cells are similar to those of the caudate nucleus; and (4) the globus pallidus which contains many large scattered cells. These cells are oval or pyriform in shape and among them are interspersed numerous smaller granule-like cells.

The claustrum consists of cells somewhat larger and more deeply staining than those in the putamen, in comparison with which it appears to be a more compact and denser structure.

The amygdalar complex comprises six well differentiated nuclei including: (1) the nucleus centralis or princeps; (2) nucleus anterior; (3) nucleus posterior; (4) nucleus ventralis; (5) nucleus ventro-lateralis; and (6) nucleus medialis. These nuclei all contain small oval or round cells. They differ from each other in their cellular dimensions and the degree of compactness in the cellular arrangement. The smallest cells appear in the nucleus medialis, the largest in the nucleus centralis. The cellular arrangement is most compact in the ventral nucleus which receives the majority of the fibers composing the lateral olfactory tract.

CORRELATIONS BETWEEN THE BEHAVIOR AND NEURAL ORGANIZATION OF THE TEN-DAY-OLD RAT

Although the phase of local cortical differentiation is well advanced in all divisions of the hemisphere, the degree to which the neocortex participates in the regulation of behavior at this stage is open to question. Several facts make such participation debatable. The general cellular immaturity in all areas and strata is still pronounced. This immaturity is emphasized by the lack of myelin in any of the afferent or efferent fiber connections. Since the eyelids of the animal are not yet open at this time, it

seems reasonably certain that the visual areas in the cortex are contributing little if any control over somatic activities. In their structural features these visual regions do not appear to be measurably less mature than other neocortical areas. Consequently, when these considerations are taken into account, any marked degree of neocortical influence upon behavior seems dubious.

The sniffing reaction is suggestive of cortical activity in the olfactory portions of the hemisphere inasmuch as the movements of the head which accompany this reaction appear to bear a definite relation to the highly organized exploratory behavior of the animal. Structural immaturity in both the archicortex and paleocortex may, however, be urged as an objection to such an interpretation. The respiratory modifications incident to sniffing do not of themselves imply neural activities more complex than those inherent in the axial portions of the nervous system; but the integration of these modifications with the movements of the head indicate correlations of a higher order.

The springing reactions in this stage of behavior are difficult to explain since the stimuli which excite them are so obscure. In their characteristics, they appear to be related to the locomotor repertory and represent a well integrated performance in which a large part of the somatic musculature acts coördinately. Just as this performance is independent of any discernible stimulus, so at the time of its earliest appearance it is devoid of any recognizable purpose. In this light it may be regarded as comparable to the reflex "starts" and "twitches" of earlier life. But even if accepted as a reflex phenomenon of this nature, the reaction shows such a marked degree of coördinate organization as to suggest the operation of complex correlating centers. In suddenly springing away from its supporting surface, the animal is not thrown out of balance but at once resumes its position without any disturbance of posture. Such a complete act involves kinesiastic and equilibratory components as well as motor factors. It necessitates a definite sequence of innervation in the "take off" in the "posture-maintenance" and in the "alighting." In its execution it gives evidence of complex automatic associations and therefore assumes importance by indicating the probable existence

of centers subserving such correlations. Prevailing current opinion attributes centers of this kind to the striate body and ontogenetic evidence lends some support to this view. On the other hand, more extensive investigation in the experimental and clinico-pathological fields is necessary before the precise relations of the striatum to behavior can be definitely estimated. The relatively advanced state of development in the globus pallidus and putamen of the ten-day-old rat may account for the appearance of the springing reaction and the partial assumption of the sitting posture. It may likewise be the basis for improvements in righting, crawling, and other automatically associated movements of this stage; but the complex interrelations of all the subcortical nuclei and the extensive lateral expansions of the interbrain into the hemisphere call for still more critical analysis, both as to structure and function, than this part of the cerebrum has yet received. It is only with many reservations, therefore, that the more obviously automatic, associated activities of the animal at this or any later period of development are attributed to the corpus striatum, and these reservations, as must be apparent, arise from an unwillingness to accept the functions at present assigned to the striate body as thoroughly established.

The further restriction and modification in the response of the animal to compression of the tail indicate advances in the relations between the receptor and effector mechanisms. The short start forward away from the stimulus and the brief wriggling movements confined to the pelvic region show an increasing degree of individuation in this response. The reaction which was originally characterized by much indiscriminate diffusion is now replaced by one of more effectual concentration. In terms of neural organization this pronounced change signifies a more direct and adequate conduction of impulses to correlating centers with a simultaneous diversion of much of the original segmental overflow. The afferent influx from the point of stimulation apparently reaches the sensory convergence centers of the thalamus and may conceivably attain cortical registration. At this stage the nature of the reaction and the structural status of the cortex make this latter registration appear less probable than in later

periods of development. The effector response should, therefore, be attributed to correlation centers lower than the cortex, either in the striatum or the tegmentum of the midbrain.

In spite of the several debatable points with reference to precise allocation of specific functions, consideration of the ten-day-old rat discloses a distinct tendency on the part of the hemisphere to assume predominance in the regulation of behavior. The segmental portions of the neuraxis, retaining their fundamental responsibilities, have enhanced their integrative capacity by acquiring the additional cooperation of the thalamus, corpus striatum, paleocortex, and possibly to some extent at least, of the neocortex.

BEHAVIOR OF THE FIFTEEN-DAY-OLD RAT

The period between the tenth and sixteenth postnatal days is characterized by several notable features. On the fifteenth day the eyelids usually open. In many instances this reaction does not occur until the eighteenth day. As a rule the complete opening of the eyelids requires about twenty-four hours but as soon as the eyes are completely open the animal is able to follow a moving object by turning its head and eyes. The object must be held within three or four inches of the head. Sight does not, at first, appear to add much to the animal's reactions. In the late previsual period the young rat is capable of many complex motor performances. As early as the fifteenth day it is able to crawl over the top of one cage into another without losing its footing and even before this time, it can make its way directly across the cage to the drinking receptacle. Animals whose eyes opened on the fifteenth day were compared with members of the same litter whose eyes remained closed until the eighteenth day but there were no perceptible differences in behavior. The establishment of sight did not appear to facilitate exploration of the environment nor did it seem to make possible any new adjustments. As an exploratory equipment it was much less utilized than the sense of smell.

The postural reaction, on the eleventh day, is prompt and more complete than on the tenth day. It is devoid of the struggling

and wriggling movements of earlier stages. On the thirteenth day this reaction is thoroughly established. The animal when placed on its back rights itself instantly and starts to crawl away. All of the movements in this performance are well coordinated. The postural attitudes assumed by the eleven-day-old rat are likewise better organized and show an increase in their variety. In the sitting position, the body is held more elevated by the forelegs and the ataxic oscillations have almost entirely disappeared. Standing up is another attitude which makes its appearance at this time. In this act the animals arise on their hindlegs, using their forelegs, which are placed against the wall of the cage, as a means of support. This performance is easily recognized as the incipient phase of an exploratory activity. The adult rat frequently stands up on the hindlegs using the tail for extra support. In this position it moves its head in all directions and sniffs constantly. By the twelfth day many of the animals sit up on their haunches while washing their faces with their forepaws. In this posture they frequently bring the hindpaw to the head in order to scratch behind the ear. Movements in all of these acts are well coordinated and the rat is able to balance itself effectively in either the sitting or standing position.

On the fifteenth day the animals assume a more erect posture in sitting and in this performance the hindlegs are more closely adducted under the body. They stand erect more firmly and for longer periods, although the forelegs are still employed for additional support. Occasionally the attempt is made to stand upright without the assistance of the forelegs, the tail being used for accessory support. This posture is maintained only for a moment or two at a time.

Nutritional activities are still essentially limited to the sucking reaction but on the eleventh day many of the animals protrude their tongues and draw them over the surface of lettuce, excelsior, and other articles in the cage. On the twelfth day they frequently thrust their heads into the meal prepared for the mother and make chewing movements without actually taking the food into their mouths. These licking and chewing reactions become better defined on the thirteenth day. Most of the young rats use

their forepaws to grasp pieces of lettuce or excelsior which they hold up to their mouths and make chewing movements. Neither the lettuce nor excelsior, however, is taken into the mouth. In addition to these licking and chewing reactions the rats begin to nibble with their front teeth on pieces of bread or lettuce on the fourteenth day, although they do not succeed in breaking off pieces by this nibbling.

On the eleventh day most of the animals walk about supporting the weight of the body on all four legs and move their feet so that the advance of the right forepaw is synchronized with that of the left hindpaw and vice versa. Many of them attempt to climb up the walls of the cage, but after ascending three or four inches lose their grasp and fall back. The locomotor activities are quick and vigorous on the twelfth day. Walking is more definitely quadrupedal and shows a complete loss of the paddling movements. The animals can crawl out of the observer's closed hand and push their way through narrow crevices. In some instances they are able to accelerate their locomotion to the extent of running across the cage. By the fifteenth day all locomotor activities are more rapid and the young rats are constantly moving about. They can climb up the wall of one cage into another without losing balance and frequently start forward and run swiftly before they begin to climb.

The scratching and washing reactions also show progressive improvements. On the thirteenth day the animal can scratch all parts of its body with its hind and forepaws. It is also able to wash its hindquarters by lowering its head and licking the caudal portions of the trunk. This act is followed by brushing movements of the hindpaws which are repeated a number of times in succession. The washing reaction is fully established by the fifteenth day when the rat carries on this performance with a certain degree of regular sequence. The forepaw is first held to the mouth and licked; it is then applied to the side of the head and moved in repeated brushing strokes across this area. After many repetitions of these movements the head is lowered, thus enabling the animal to lick its hindquarters which are immediately brushed by the hindpaws. This entire washing process is repeated many times.

The sniffing reaction, on the eleventh day, has acquired all of the characteristics of an exploratory activity. The young rats thrust their noses into corners and crevices and sniff constantly as they move about.

On the fourteenth and fifteenth days gnawing on solid articles becomes a prominent occupation which alternates with such apparently playful activities as pursuing and leaping over one another with a considerable show of animated interest.

In the response to compression of the tail the wriggings and rotations of the pelvis are reduced to a minimum by the eleventh day. The animal now reacts by squeaking, leaping quickly forward, arching its back, and twitching its tail. On the thirteenth day the leap forward is followed by running away for a short distance from the stimulus. By the fifteenth day the response is expressed in a well defined avoidance reaction accompanied by a slight squeak. The animals run away from the stimulus and in some instances, after running forward a short distance, they turn around in such a manner as to face the source of stimulation.

No reactions to sound were observed before the twelfth day but at that time the young rats "start" at any loud noise within or close to the cage. On the fifteenth the animals not only "start" but run away from the source of the sound.

ADVANCES IN THE NERVOUS SYSTEM OF THE FIFTEEN-DAY-OLD RAT

Cellular differentiation in the spinal cord has attained most of its definitive characters. In the cells of the anterior horn of cervical segments, the cytoplasm is extensive, contains distinct tigroid bodies and gives off several long, tapering processes. The nuclei of these cells are large and vesicular. Cellular grouping is particularly well defined in the anterior horn. The largest cells are found in the ventro-lateral group and form a conspicuous cluster in the lateral extremity of the gray matter. An accessory cluster of smaller pyramidal cells occupies a position immediately adjacent to this large group along the ventral margin. The dorso-lateral and dorso-mesial groups are formed by large pyramidal elements whose diameters, however, are somewhat less than those

of the cells in the ventro-lateral cluster. A ventro-mesial and a central group are clearly distinguishable and consist of fairly large-sized cells. The lateral horn is prominent and contains pyramidal cells of small and medium size. A central and a meso-dorsal group form the chief constituents of the body and cervix of the gray matter. The dorsal horn consists of small granule cells with a few very small pyriform elements interspersed among them.

The contrast between the myelination of the eight-day-old rat and that of the sixteen-day-old rat is marked. All of the spinal tracts in the white matter of the latter are myelinated to some degree. The deposition of myelin is heaviest upon the juxtargiseal fibers on the ventral column. In the circumferential zone of the lateral field myelination is also well advanced; it is least pronounced in the intermediate zone of the ventral and lateral fields. Many fibers in the anterior horns are heavily myelinated.

In the oblongata, pons, and midbrain the cells of all the chief nuclei correspond in their development to those of the spinal cord. Most of the large cells contain tigroid bodies. The pontile nuclei, substantia nigra, red nucleus, and oculomotor nucleus are clearly differentiated. Myelination is most pronounced in the deiterso-spinal and the descending trigeminal tracts, in the posterior longitudinal fasciculus and the predorsal bundle. It is less advanced in the tracts of Goll and Burdach, internal arcuate fibers, mesial fillet, cerebellar peduncles, olivo-cerebellar fibers, trapezoid body, lateral fillet, and transverse fibers of the pons. The pyramidal tracts and decussating pyramidal fibers are conspicuous because of their relatively feeble reaction to the myelin stain. Myelination has taken place in the fibers of all the cranial nerves.

In the cerebellum the external granular layer is still present but is much reduced in thickness as compared with earlier stages. The molecular and internal granular (nuclear) layers are broad. On the boundary between them there is an irregular single row of Purkinje cells. The intracerebellar nuclei have attained much of their adult differentiation and the medullary substance of the folia is myelinated.

Most of the twelve areas of the neocortex have increased considerably in thickness, partly because of the expansion of the larger pyriform cells and partly because of a wider separation between the individual cells of this type. The great majority of the pyriform elements retain their original outlines. Many of them stain so deeply throughout their cytoplasm that it is difficult to distinguish histological details. The processes of these cells are poorly developed and appear to be few in number. The greatest increase in cortical thickness occurs in the central (area N3), in the meso-occipital (area N8), the marginal (area N2), the cingular (area N1), and the middle insular (area N12) areas in the order mentioned.

The cells in both granular layers throughout the neocortex contain large vesicular nuclei and their cytoplasm for the most part, stains faintly. In general, the external granular layer is compact and varies in thickness, depending upon the region, from five or six rows of cells to ten or twelve. Its external boundary line is fairly regular except in the central and meso-occipital areas where numerous granule cells appear in the deeper portion of the zonal layer. The internal granular layer is, generally speaking, much less compact and more variable in its thickness.

In only one region do the larger cells of the neocortex present unequivocal pyramidal outlines. For the most part these cells are pyriform and rounded in contour. Most of them stain deeply in their cytoplasm but a considerable number have but a slight affinity for stains. All of the large cellular elements are, however, alike in one particular. They are so oriented that their long axes are at right angles to the cortical surface beneath which they are situated.

The central area is the only region in which some of the larger cells have assumed definitely pyramidal outlines. In scattered patches throughout this area the tendency toward "pyramidization" is pronounced. It appears to be affecting the granular as well as the pyriform layers. The external granular layer consists of granule cells intermingled with small pyramidal cells and forms a stratum eight to ten rows deep. Small and medium-sized pyramids are scattered among pyriform cells in the external pyriform

layer and form a stratum of eight to ten rows. A few granule cells interspersed among large pyriform cells constitute an indefinite internal granular layer while very large pyriform elements with some scattered pyramidal cells of medium size appear in the internal pyriform layer which has a depth of ten to fourteen rows.

In contrast to this central region, the meso-occipital area is characterized by the almost complete absence of pyriform and pyramidal cells. Some of the granule cells, especially at the base of internal granular layer, are exceptionally large and may, for this reason perhaps, be classed as pyriform. On the other hand, their contours are atypical of the pyriform cells as they appear elsewhere in the neocortex. The meso-occipital area is particularly noteworthy because of the marked increase in the thickness and prominence of its granular layers. The external granular layer is exceptionally dense due to the compactness in the massing of its cells which stain deeply. The internal granular layer is conspicuous because of its reduplication. It consists of a broad outer stratum six to eight rows deep separated by a lighter zone from an inner stratum eight to ten rows deep. This preponderance of granule cells gives the area an appearance of intense "granulization."

With the exception of some increase in thickness, the several areas of the paleocortex and archicortex show no advances when compared with these regions of the ten-day-old rat.

Considerable myelinization has taken place in the hemispheres. It is most pronounced in the lateral olfactory tract and well developed in the external and internal capsules, in the centrum ovale, and the anterior commissure. The optic nerve, chiasm, and tract are myelinated to a less degree. Of all the medullary structures which are undergoing myelinization, the deposition of myelin is least well defined in the corpus callosum. A caudal process of medullary substance may be traced from the internal capsule as far back as the meso-occipital area but it appears to be much less intensely myelinated than other fascicles connected with this capsule. Individual rays or fibers from the centrum into the neocortex are difficult to distinguish by means of the myelin stain.

Certain developmental advances are evident in the subcortical nuclei. In the corpus striatum, the nucleus accumbens and caudate nucleus are almost identical in their cellular structure. Both of them consist largely of densely aggregated granule cells with vesicular nuclei and faintly staining cytoplasm. All of these cells are of about the same size and character. The putamen likewise consists of similar densely aggregated granule cells but scattered among them are numerous larger oval cells which stain more deeply. The globus pallidus presents an entirely different cellular constituency. It comprises at least three distinct subdivisions and is in striking contrast to the other portions of the striate body both in the character and arrangement of its cells. The dense cellular aggregation which distinguishes the nucleus accumbens, nucleus caudatus, and putamen is entirely lacking in the globus, the cells of which are irregularly scattered and have wide spaces between them. The most conspicuous cellular elements in this part of the striatum are large and pyriform; loosely interspersed among them are smaller granule cells. The identification of a lateral, a central, and a medial subdivision in the globus is dependent upon the grouping of its pyriform cells according to their size and character. The lateral subdivision consists of large pyriform cells with large vesicular nuclei. In the central subdivision the pyriform cells are very large and somewhat irregular in outline. All of these cells stain faintly. The medial subdivision comprises darkly staining cells whose dimensions are less than those of the pyriform elements in other parts of the globus. The axial orientation of the cells in all three subdivisions is most irregular and the cellular processes are ill-defined.

The claustrum is distinguishable from the putamen by its larger, more densely aggregated, and more deeply staining granule cells.

The amygdalar complex shows little change in advance of the condition in the ten-day-old rat.

CORRELATIONS BETWEEN THE BEHAVIOR AND NEURAL ORGANIZATION OF THE FIFTEEN-DAY-OLD RAT

With the introduction of vision, as evidenced by the opening of the eyelids and the ability to follow moving objects by turning

the head and eyes, there are sufficient reasons to assume that the neocortex is now decisively operative. But even prior to this development and in young rats whose eyelids do not open until the eighteenth day, the animals are capable of many complex performances which imply cortical functions. The manner in which they explore their environment as well as the variety of their apparently playful activities are indicative of more highly organized behavior than can be reasonably ascribed to infracortical levels of neural correlation. The significance of the sense of smell as a directing influence in many of these activities is not difficult to discern. It makes the conclusion that the olfactory portions of the cerebral cortex are now active almost inescapable. Equally, or even more, significant in the animal's somatic behavior are the developments in general body sensibility for without this form of sense, the directing influences of smell, sight, and hearing would prove unavailing. Tactile, pressure, and kinesthetic associations constitute the *sine qua non* upon which discriminations in posture and movement are based. Without adequate representation of the "body image" all of the more highly organized somatic activities are defective. Such complex syntheses in the sphere of general body sense imply the functional participation of the highly differentiated neural mechanisms which the neocortex provides. The structural specializations as well as the fiber connections of the parietal area at this stage are sufficient to indicate that some rôle in the correlations of body sense has been assumed by this region of the neocortex. Likewise the higher degree of discrimination in audition points toward neocortical activities in the realm of hearing. It seems obvious, therefore, that the cerebral cortex which, through earlier stages, has given evidence of a gradual assumption of functional responsibility, now plays a more decisive part in the regulation of behavior. In estimating this steadily increasing importance of the cortex, the progressive advances in the organization of the segmental portions of the neuraxis cannot be overlooked. Unquestionably many of these advances are in the interest of perfecting segmental autonomy, but many of them are determined by the increasing need for intersegmental and especially for supra-

segmental integration. Thus as the cerebral cortex begins to acquire predominance, it does not deprive the lower segments of their individual autonomies but rather augments their functional capacities as operating units in an integrated whole.

In its neural development and behavior, the fifteen-day-old rat gives evidence of this integrative process.

BEHAVIOR IN THE TWENTY-DAY-OLD RAT

By the seventeenth day postural attitudes attain their full development. The animals are able to sit up erectly on their haunches in a manner similar to that of the adult. In this posture they wash and scratch themselves, and with their forepaws hold pieces of lettuce or excelsior up to their mouths. The rats are now able to sit on the rim of the food-cup and maintain their balance perfectly while they carry food to their mouths. Standing erect upon the hindlegs with the extra support of the tail is a posture as easily assumed at eighteen days as it is in the adult.

Lapping water from the drinking cup is an addition to the feeding activities which appears on the sixteenth day but it is not until the eighteenth day that the water or milk lapped up by the tongue is actually swallowed. On the nineteenth day the animals show discrimination in the selection of food. By nibbling they are successful in breaking off pieces of lettuce or bread and using the forepaws to bring these particles to the mouth, they chew and swallow them. The entire process of obtaining food and eating is identical with that of the adult. On the twenty-first day the animals are weaned and thereafter forage for themselves.

Jumping from various heights to the floor of the cage augments the locomotor repertory on the sixteenth day. The animals leap about frequently for no apparent reason. In this act they spring clear of the floor, turning their bodies around sharply and with much agility. Climbing which is the chief activity of the eighteenth day, is so much perfected by the twenty-first day that the animals are able to "walk on the ceiling" by clinging with their claws to the wire netting in the roof of the cage.

In addition to the purposive reactions of scratching and wash-

ing, sniffing and gnawing, the rats manifest a livelier interest in their litter mates. They jump at and pursue one another in an evident spirit of play. By the eighteenth day they frequently engage in what appear to be wrestling bouts. In these performances two of the animals rise on their hindlegs and use the forelegs for grappling. Often they lick each other's bodies and even bite each other. These latter activities are well defined by the twentieth day. Whether they are part of the play behavior or expressions of sexual incipency is difficult to decide. At least some portions of the "play reactions" are obvious in the subsequent development of sexual activity.

The response to compression of the tail is, by the nineteenth day, entirely devoid of its former diffuse wriggings. The animal immediately turns around in such a manner that its head is directed toward the source of the stimulus. It assumes an attitude indicating readiness "to give fight." Even the squeaking, which up to this time has accompanied the response, is now omitted from the reaction.

ADVANCES IN THE NERVOUS SYSTEM OF THE TWENTY-DAY-OLD RAT

The most pronounced change in the spinal cord of the twenty-day-old rat appears in the heavier myelination of the lateral and dorsal white columns. This advance is especially apparent in the intermediate zone of the lateral field and the lateral portion of the dorsal field. In the oblongata deposition of myelin has increased in the pyramidal tracts and in the columns of Goll and Burdach. The transverse fibers of the pons, the pyramidal bundles and cerebral peduncles are also more heavily myelinated.

In the cerebellum, the external granular layer has disappeared and the cortex now consists of its three typical adult strata, *i.e.*, (1) the molecular layer; (2) the Purkinje layer; and (3) the nuclear layer. The Purkinje cells are larger and more prominent than in preceding stages (fig. 14).

In the midbrain, the tectum still retains to some degree the stratifications which are characteristic of this region of earlier periods of development. The cellular laminae are, however, more indistinct. A fairly prominent contingent of myelinated

fibers may be traced from the optic tract to the outer surface of the tectum.

In the hemisphere the only notable change is a general increase in the thickness of the neocortex. Some local advances appear in the central area (area N3) due to extensions in the process of pyramidization as a result of which the number of scattered

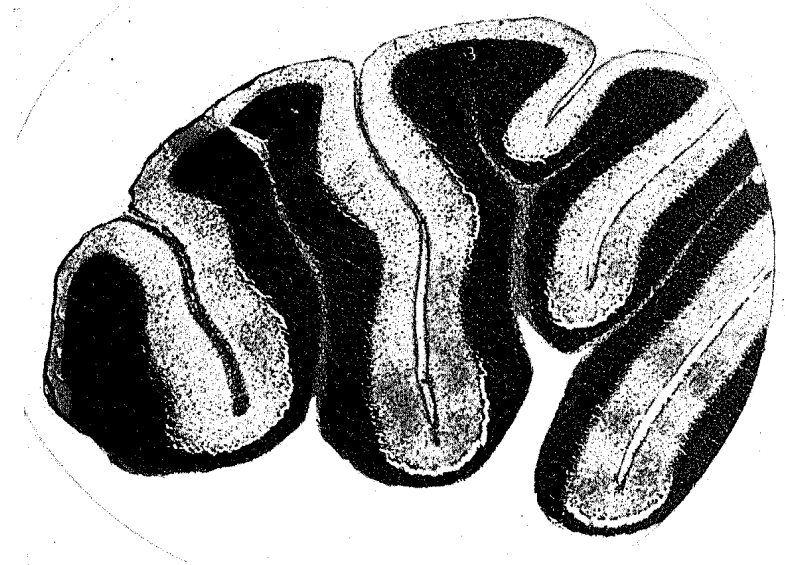


FIG. 14. Section of the cerebellum of a twenty-day-old albino rat showing the three typical adult strata, *i.e.*, 1, the molecular layer; 2, the Purkinje layer; and 3, the nuclear layer. The heavy external granular layer of earlier developmental stages has disappeared from most of the folia. Specimen No. 1182, magnification $\times 60$.

territories containing pyramidal cells has increased. In the meso-occipital area (area N8) the internal pyriform layer is more prominent and contains numerous cells of large size.

CORRELATIONS BETWEEN THE BEHAVIOR AND NEURAL ORGANIZATION OF THE TWENTY-DAY-OLD-RAT

Most of the characteristics of the adult are apparent in the behavior of the twenty-day-old rat. There is, however, a greater

degree of restlessness at this stage than in maturity. The young animals, when not asleep, are constantly in motion and show almost kaleidoscopic variations in their performances. Whether running, jumping, climbing, wrestling, gnawing, nibbling, eating, playing, exploring, biting, scratching, or washing, they pass from one act to another without any purposeful continuity in the sequence of their activities. Such vacillation in objective has its counterpart in the jeunesse of most mammalian species and must, therefore, have profound significance in the development of behavior which now manifests three outstanding characteristics: First, an almost uninterrupted output of energy which finds expression in many somatic performances; second, a high degree of muscular coördination in these reactions; and third, a constantly changing variety of motor patterns.

What is the explanation of the drives which underlie the diffuse and continuous stream of reactions peculiar to the young?

In studying the behavior of the albino rat, Richter has been able to show that the total body activity of the adult animal is definitely periodic and characterized by several distinct rhythms. In one of these rhythms, the rat is active for thirty minutes or more and then becomes inactive again. The alternations of these periods of activity and inactivity are repeated with great regularity and are associated with a rhythm of the stomach. Periodic cycles at much longer intervals have also been demonstrated. Adult female rats show a definite four-day activity rhythm in which they may run as much as ten miles every fourth day and only a fraction of a mile on the three intervening days. This activity rhythm is associated with the cyclical changes of the ovaries. A twenty-two day and a ninety-to-one-hundred-and-twenty-day rhythm have likewise been demonstrated. These longer cycles occur in both sexes. By means of several series of experiments, a close dependence of total activity upon the sex-glands, adrenals, and pituitary has been shown to exist. Contrary to what might be expected, however, the thyroid exerts but little influence upon total activity.

Hunger and thirst are obvious as activating influences in the twenty-day-old rat. The sex drive, however, is less apparent

since the animals are still sexually immature. But the most important difference between the behavior of the adult and that of the twenty-day-old rat is the relative lack of cyclic periodicity in the activity of the young animal. It is difficult, therefore, to attribute the "motor distractability" and constant motion of the twenty-day stage to hormone activation alone. In this connection, the added possibilities for expansion in the sensory influx cannot be overlooked. All parts of the neocortex have, by this time, attained a degree of differentiation sufficient to make them available for the reception of somesthetic, auditory, and visual impulses. The continuous inflow of stimuli from cutaneous and muscular receptors, from the eye, and ear is capable of exciting extensive areas of the cortex. That such cortical excitation has acquired its ultimate elaborations is doubtful because the animal's "flight of activity" manifestly indicates a lack of the selective discrimination and sequential combination which eventually characterize adult behavior. Structurally the hemisphere shows but little development in its intercortical fiber systems until the twenty-fourth day and even then these connections are much less prominent than in the adult. Nor is the portion of the central area (area N3) which ultimately shows the most extensive "pyramidization" completely differentiated, but by the twenty-fourth day this area contains a large number of pyramidal cells and several heavily myelinated bundles connect it with the anterior portion of the internal capsule. As early as the twentieth day many scattered bundles of well myelinated fibers pass through the putamen and caudate nucleus to establish connections with the frontal, parietal, and temporal regions. The significance of these bundles has long been a matter of debate. Many of them unquestionably represent afferent thalamo-cortical connections but the possible existence of efferent, cortico-striate fibers among them cannot be denied. In this light it is not unlikely that the several functional areas of the neocortex may develop efferent connections with the corpus striatum and through this structure with the lower axial segments. Such an interpretation would attribute to the motor area and the great cortico-spinal pathway (pyramidal tract) the regulation of the most highly organized motor activity

which possesses all of the qualities imparted by learning and experience.

The activities of the twenty-day-old rat show little of these qualities as yet and consist largely of random, more or less capricious reactions which in later stages become integrated in the specific sequences of adult behavior.

Afferent impulses of smell and taste add to the activating volume of sensory stimuli at this stage. They also play a highly important rôle in the exploratory drive of the animal; but, like stimuli of vision and hearing, they are chiefly implicated in extra-corporeal orientation. Other drives arising from visceral or endocrine sources may participate in motivation at this time, but the progressively multiplying number of stimuli received by the cortical area of body sense accounts, in some measure at least, for the somatic motor reactions of the young.

The distractibility evident in these reactions is due, in part, to the as yet imperfectly developed selective and discriminative functions of the cortex and, in part, to assertive influences derived from the exploratory drive. The diverting effects of olfactory, visual, and auditory stimuli constantly arising from an environment still incompletely explored and only partially charted in experience can scarcely be questioned.

Two of the three outstanding characteristics of behavior in the stages immediately preceding maturity are thus explained by developments in the cerebral cortex, which, however, has not yet attained its full structural specialization. The third prominent characteristic in the behavior of the twenty-day-old rat, i.e., the high degree of muscular coördination may be attributed to advances in the differentiation of the cerebellum which, at this stage, shows a close approach to maturity as witnessed by the disappearance of the external granular layer, the prominence of the Purkinje cells, and the heavy myelination of the ponto-cerebellar fibers.

Another and less conspicuous feature in the reactions of the animal at this time is evident in the response to compression of the tail. The prompt turning of the body so that the head is directed toward the source of the stimulus brings the olfactory

and visual portions of the exploratory mechanism into effective relation with the new situation which confronts the animal. Similar combinations of several sensory components are evident in many other activities, such as wrestling, jumping, pursuing each other, and scurrying away from sudden noises. The structural substratum of these sensory syntheses depends upon the further development of long association fibers which occupy a position in the outer portion of the centrum ovale and are now fairly well myelinated.

There is strong evidence in the twenty-day-old rat, therefore, that the cerebral cortex has at length assumed an unmistakable predominance in the regulation of behavior.

BEHAVIOR IN THE ADULT RAT

It is difficult to set the exact age of maturity in the albino rat. If the criterion for the beginning of adult life is determined by the establishment of sexual activities in the female, the time of maturity has a wide range of variation. Instances have been reported in which females of especially well fed groups have become pregnant as early as the thirty-third day and have their litters on the fifty-fifth day. According to Long and Evans, the vagina is patent at about the seventy-second day and ovulation begins on or about the seventy-seventh day. Estimated by the structure of the gonads, sexual maturity occurs in both sexes at the age of two months or a little less. In order to cover this range of chronological variation, rats of thirty-five days, forty-five days, and a full grown adult were selected to represent the stage of maturity.

All of the postural reactions as well as the other somatic activities observed in the twenty-day-old rat are seen in the behavior of the adult. Digging makes its first appearance on or about the twenty-fourth day. Nest-making regularly occurs in the pregnant female slightly before term. As the animals grow older they become less playful and their play activities frequently assume more definitely sexual characteristics, such as mounting one another which, still later, eventuates in copulation. The full play repertory is complete about the twenty-fifth day and consists of running, jumping, climbing, wrestling, and sham battles with

pursuits and constant biting of each other's tails. In later stages these playful attacks often result in more vicious encounters. Such conflicts seem to have the effect of cooling the playful ardor. By revealing potent mechanisms for offense and defense, they also appear to engender a new attitude of mutual respect and individual aloofness. When in the cage, but especially when at large, the adult rat spends most of its time exploring. It usually moves forward somewhat deliberately and with many pauses, constantly sniffing as it goes. While thus engaged it stops frequently to wash its snout with its forepaws or to stand erect in order to gain a broader view of its surroundings. It makes cautious explorations, craning its head around corners and over edges. It shows a strong preference to crawl along any ledge and uses its tail as an aid in balancing itself. During these performances, the rat's reaction to any sudden or shrill noise is particularly interesting and appears to consist of two distinct phases. If moving away from the source of the sound, the animal stops abruptly and its body gives a sharp twitch; then it turns its head slowly in the direction of the sound and remains motionless while it sniffs, looks, and listens. After several seconds in this attentive posture it resumes its exploration again. If approaching the source of the sound, the same reaction occurs, although the turning of the head is less pronounced. Periodic activities becomes more conspicuous as the rat grows older. Several of these activity rhythms have already been mentioned (see page 332). Slonaker has observed that the greatest activity in the daily life of the animal takes place between 9 p.m. and 4 a.m. Warden and his co-workers have been able to measure accurately by means of the Columbia Obstruction method the relations, strength, and persistence of several important drives in adult life. They concluded that the normal drives rank as follows in order of their respective strengths: maternal, thirst, hunger, sex, exploratory. This order seems somewhat surprising since several other investigators, using other methods, have rated the maternal tendency rather low. And yet even casual observation, without the aid of control methods, reveals the great potency of the maternal drive in the motivation of adult behavior. Under normal conditions, i.e., in

unsegregated groups, a large part of the female's reactions are represented in maternal activities. The period of gestation is twenty-two days and impregnation is again possible two to three days after the litter is cast. During the breeding period the females ovulate at intervals of five days or less (Long and Evans) but only from April to October do they ovulate fifteen to twenty-four hours after parturition. One litter may thus follow another in such close succession that weaning is scarcely over before the next installment of newborn requires the mother's attention. The average size of the litter varies from six to seven. The largest litter recorded in the Wistar Institute contained eighteen. The large number of the young added to the fact that each of the newborn rats is capable of very limited reactions necessitates a great amount of maternal care. The mother gathers the young into the nest and keeps them in as close contact with her body as possible. During the first few postnatal days, most of her time is spent in brooding the litter and only as the young rats grow older does she leave the nest for any considerable periods of time.

Both sexes make a limited number of sounds. When stroked or taken gently into the hand they click their teeth apparently as a sign of contentment. Certain clucking sounds are made by the mother when in the nest. The short squeaks characteristic of newborn are the most common vocal sounds at all ages. When suffering severe pain or when frightened the adult rat emits a high pitched scream.

A very interesting change occurs in the response of the older adult animals to compression of the tail. This response, which in earlier stages is so diffuse and later manifests such a highly organized behavior pattern, now becomes almost negligible. Unless the tail is compressed with considerable force the full grown rat appears quite indifferent to the stimulus. It continues whatever it may be doing at the time without any change in its reactions. If the pressure is increased, the animal usually withdraws the tail and may turn its head toward the source of the stimulation. This apparent indifference may be reasonably explained by an important structural development of adult life. The tail of the older rat is much tougher than in the young; its

surface is cornified and thus more protected against external stimuli. But, in addition to this cutaneous protection there is the significant fact that biting of the tail is one of the conspicuous features of the play activity. It is of such frequent occurrence that its stimulus value appears gradually to diminish in importance and eventually the stimulation, unless of extreme severity, does not enter into the discriminatory selections which influence behavior. No single reaction observed in the development of the albino rat reveals more graphically the ontogenetic correlations between behavior and the structure of the nervous system than the response to compression of the tail throughout the several stages of growth.

ADVANCES IN THE NERVOUS SYSTEM OF THE ADULT RAT

The principal advances which characterize the adult are found in further specializations of the cells in the cerebral cortex and in the appearance of myelinated intercortical fibers. In the thirty-five-day-old rat, a large portion of the central area (area N3) contains many more pyramidal cells than in the twenty-day stage. It is difficult to distinguish either of the granular layers since most of the cells in the external granular layer now have the form of small pyramids while the granule cells in the internal granular layer have almost entirely disappeared. As a result of these cellular changes, this region consists almost exclusively of pyriform and pyramidal elements of various sizes. The number of definitely pyramidal cells shows a considerable increase as compared with the twenty-day-old rat. In consequence, it is possible to identify in the central area a specialized region which lies immediately in front of the upper anterior margin of the parietal area. The differences in cellular constituency in passing from the parietal to the central area are striking. Not only does the broad internal granular layer of the parietal region disappear abruptly at the boundary line of the two areas but the cells of the central area show the effects of extensive pyramidization. The contrast between these two adjacent regions is even more pronounced in the forty-five day-old rat. These cellular changes, however, do not involve the entire extent of the original central

area (N3). They are limited to the cortical region immediately contiguous to the parietal area but leave a fairly large cortical territory adjacent to the marginal area in which pyramidization is much less pronounced. Consequently two readily distinguishable cortical regions have emerged from the original central area which was first identified in the ten-day-old rat, i.e., a central, highly pyramidized area bordering upon the parietal region and an intermediate central area contiguous to the marginal region (fig. 15).

The cellular differences between the central and intermediate central areas stand out clearly in the full grown adult.

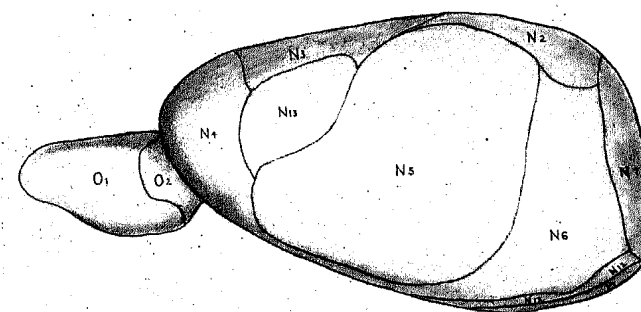


FIG. 15. Lateral surface of a reconstruction of the left hemisphere of an adult albino rat. Specimen No. 1190. N13, central area; N3, intermediate central area; N2, marginal area; N4, frontal area; N5, parietal area; N6, temporal area; N7, latero-occipital area; N12, insular area C; P1, pyriform area; O1, olfactory cortex proper; O2, accessory olfactory cortex.

In the *central area* (now designated area N13 because of the histological characters which distinguish it from the remainder of the original central area (N3)), the zonal layer (I) is relatively narrow and has an average thickness of 100 micra. It contains, near its base, a number of small scattered pyramidal and a few granule cells. The external granular layer (II) is fairly compact and consists of seven to eight rows of small pyramidal and pyriform cells with a few scattered granule cells. Its average thickness is 120 micra. The external pyramidal layer (III) is loose in its cellular arrangement. It is fairly broad and consists of twelve

to fourteen rows of medium and large-sized pyramidal cells with some pyriform elements interspersed among them. It has an average thickness of 360 micra. Most of the larger cells contain tigroid bodies and their axial orientation is perpendicular to the surface of the cortex. The internal granular layer (IV) is lacking although in places several irregular rows of small pyramidal cells appear in the position usually occupied by this stratum. The internal pyramidal layer (V) has a loose arrangement and consists of ten rows of very large pyramidal and pyriform cells, disposed in clusters of four or five. The largest cells contain tigroid bodies, have several long processes and are oriented with their long axes perpendicular to the cortical surface. The average thickness of this area is 560 micra. In no other region of the entire neocortex are the pyramidal cells of all layers in such great preponderance. The multiform layer (VI) is broad and consists of fourteen rows of fusiform oval and small pyramidal cells. Its average thickness is 340 micra. The larger cells are situated at the base of the stratum and their axial orientation is horizontal (fig. 16).

The average total thickness of the central area is 1480 micra.

The *intermediate central area* (area N3) is triangular in outline and bounded by the frontal area anteriorly, the parietal area below and marginal area above. Its zonal layer (I) is relatively narrow and contains some scattered small pyramidal and granule cells near its base. Its average thickness is 100 micra. The external granular layer (II) is fairly compact and consists of six to seven rows of small pyramidal, pyriform and granule cells. Its average thickness is 120 micra. The external pyramidal layer (III) has a loose arrangement and consists of about twelve rows of small, medium- and fairly large-sized pyramidal and pyriform cells, some of the larger of which contain tigroid bodies. The long axes of the cells are perpendicular to the surface. The average thickness of this stratum is 400 micra. The internal granular layer (IV) is somewhat indefinite but may be identified in places as a thin irregular row mostly made up of small pyramidal cells. The internal pyramidal layer (V) has a loose arrangement and consists of ten to twelve rows of fairly large pyramidal and pyriform cells which show no tendency to form clusters.

The axial orientation is perpendicular. The area, unlike area N13, contains no very large cells and its average thickness is 200 micra. The multiform layer (VI) is loose in its arrangement and consists of twelve to fourteen layers of fusiform, small pyramidal, oval, and pyriform cells, the axial orientation of which

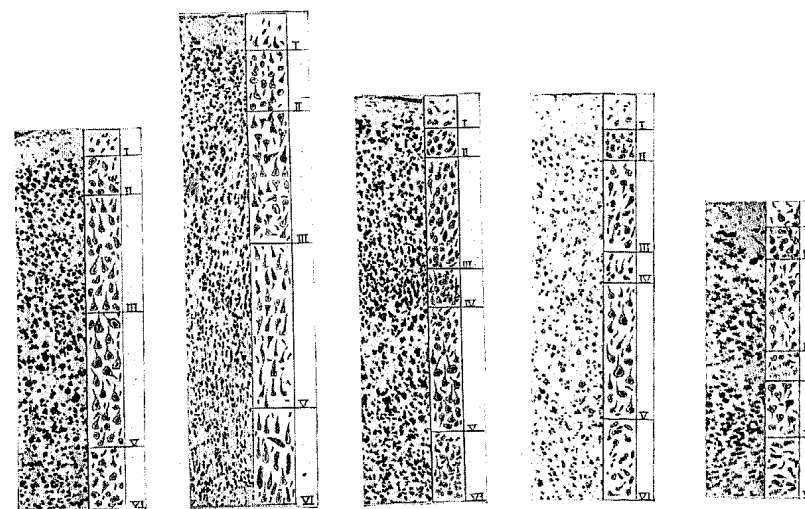


FIG. 16. FIG. 17. FIG. 18. FIG. 19. FIG. 20

FIG. 16. Neocortical area N13 (central area). Adult albino rat. With pen and ink key to strata. Magnification $\times 150$.

FIG. 17. Neocortical area N3 (intermediate central area). Adult albino rat. Magnification $\times 150$.

FIG. 18. Neocortical area N5 (parietal area). Adult albino rat. Magnification $\times 150$.

FIG. 19. Neocortical area N6 (temporal area). Adult albino rat. Magnification $\times 150$.

FIG. 20. Neocortical area N7 (latero-occipital area). Adult albino rat. Magnification $\times 150$.

is somewhat unusual in that it is perpendicular to the surface. Its average thickness is 640 micra.

The average total thickness of the intermediate central area is 1460 micra (fig. 17).

Cytological conditions in the remaining areas of the neocortex merit analysis in that they disclose the ultimate specialization attained by cellular differentiation in the process of development.

In the parietal area (area N5) of the full grown rat, the zonal layer (I) is relatively narrow and contains few cellular extrusions from the subjacent stratum. Its average thickness is 80 micra. The external granular layer (II) is narrow and has a loose arrangement of its cells. It consists of four or five rows of large granule and small pyriform cells, of which the former predominate. Its average thickness is 100 micra. The external pyramidal layer (III) is broad and loosely arranged. It consists of twelve to fourteen rows of small and medium-sized pyriform cells with only an occasional cell of pyramidal form. The smaller elements occupy the more superficial rows. The long axes of the cells are perpendicular to the surface and the average thickness of the layer is 300 micra. The internal granular layer (IV) is well defined and gives a distinguishing feature to the parietal area. It is broad, fairly compact, and consists of about ten rows of small granule and small pyriform cells. Its average thickness is 140 micra. The internal pyramidal layer (V) is broad, loosely arranged, and consists of ten to twelve rows of large and medium-sized pyriform cells which contain tigroid bodies. There are very few pyramidal cells in this layer and no tendency toward the clustering seen in the central area. The larger cells are situated near the base of the stratum and their long axes are perpendicular to the surface. The average thickness of the layer is 460 micra. The multiform layer (VI) is broad and loosely arranged. It consists of fusiform, oval, and small pyriform cells whose axial orientation is generally horizontal. Its average thickness is 400 micra.

The average total thickness of this area is 1480 micra (fig. 18).

In the temporal area (area N6) the zonal layer (I) is narrow, having an average thickness of 100 micra. The external granular layer (II) is broad, fairly loose, and consists of eight or ten rows of granule and small pyriform cells. Its average thickness is 130 micra. The external pyramidal layer (III) is relatively narrow and poorly developed. It consists of eight to ten rows of small and medium-sized pyriform cells with only a few cells of distinctly pyramidal outline. Its average thickness is 220 micra. The internal granular layer (IV) is narrow and loosely arranged.

It is much less prominent than in the adjacent parietal area. It consists of six to eight rows of granule and small pyriform cells. Its average thickness is 100 micra. The internal pyramidal layer (V) has an unusual feature in that it contains alternating areas composed of two distinctly different types of cells. These areas stand out in marked contrast to each other and are not distinguishable in any of the earlier stages. The first type of cells has a loose arrangement and consists of eight or ten rows of long, slender pyramidal elements with well defined tigroid bodies and long apical processes. These cells show no tendency to clustering. The second type forms a more compact stratum of eight to ten cells of large broad pyriform elements many of which have tigroid bodies. The cells are arranged in clusters of two or three. The average thickness of the internal pyramidal layer is 510 micra. The multiform layer (VI) has a loose arrangement and consists of twelve to fourteen rows of fusiform, oval, and small pyriform cells whose long axes are generally oblique to the surface of the cortex. Its average thickness is 230 micra.

The total average thickness of this area is 1290 micra (fig. 19).

In the latero-occipital area (area N7) the zonal layer (I) is narrow and has an average thickness of 75 micra. The external granular layer (II) is narrow and loosely arranged. It consists of six to eight rows of unusually large granule cells and a few small pyriform cells. The average thickness is 90 micra. The external pyramidal layer (III) is relatively narrow, inconspicuous and loose in its cellular arrangement. It consists of eight to ten rows of small pyriform and oval cells whose longitudinal axes are perpendicular to the surface. Its average thickness is 260 micra. The internal granular layer (IV) is somewhat narrow and consists of five to six rows of relatively small granule cells. Its average thickness is 110 micra. The internal pyramidal layer (V) is broad and loosely arranged. It consists of ten to twelve rows of medium cells near its base. There is some clustering of the pyriform cells but the pyramidal cells are scattered and isolated. The axial orientation of these cells is perpendicular to the surface. The average thickness of this layer is 200 micra. The multiform layer (VI) is narrow and somewhat compact. It consists of six

to eight rows of fusiform, oval and small pyramidal cells whose axial orientation is horizontal. Its average thickness is 230 micra (figs. 20 and 21).

The total average thickness of this area is 965 micra.

The three insular areas in the upper fold of the rhinal fissure (areas N10, N11, and N12) have distinctive histological features. Insular area A (area N10) is in relation with the anterior and deepest portion of the rhinal fissure. Its zonal layer (I) is relatively broad and has an average thickness of 200 micra. The external granular layer (II) is broad, fairly compact and consists of ten to twelve rows of granule and small pyriform cells. Its

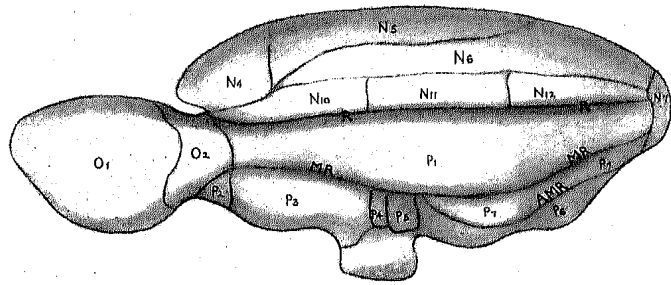


FIG. 21. Basal surface of a reconstruction of the left hemisphere of an adult albino rat. Specimen No. 1190. N10, insular area A; N11, insular area B; N12, insular area C; N4, frontal area; N5, parietal area; N6, temporal area; N7, latero-occipital area; P1, pyriform area; P2, parolfactory area; P3, tubercular area; P4, post-tubercular area; P5, amygdalar area; P6, post-amygdalar area; P7, post-pyriform area; O1, olfactory cortex proper; O2, accessory olfactory cortex; R, rhinal fissure; MR, mesorhinal fissure; AMR, accessory mesorhinal fissure.

average thickness is 200 micra. The external pyramidal layer (III) is narrow and consists of eight or ten loosely arranged rows of small and medium-sized pyriform cells. It contains but a few pyramidal cells. The axial orientation is perpendicular. Its average thickness is 210 micra. The internal granular layer (IV) is poorly developed and consists of three to four loosely arranged rows of granule cells. Its average thickness is 100 micra. The internal pyramidal layer (V) is also poorly developed and narrow. It consists of five to six loosely arranged rows of small and medium-sized pyriform cells with only a few pyramidal cells.

The axial orientation is perpendicular and the average thickness of the layer is 280 micra. The multiform layer (VI) is fairly broad and consists of eight to ten rows of fusiform, pyriform and oval cells whose axial orientation is generally oblique. Its average thickness is 240 micra (fig. 22).

The total average thickness of this area is 1230 micra.

Insular area B (area N11) is in relation with the middle, shallowest portion of the rhinal fissure. Its zonal layer (I) is rela-

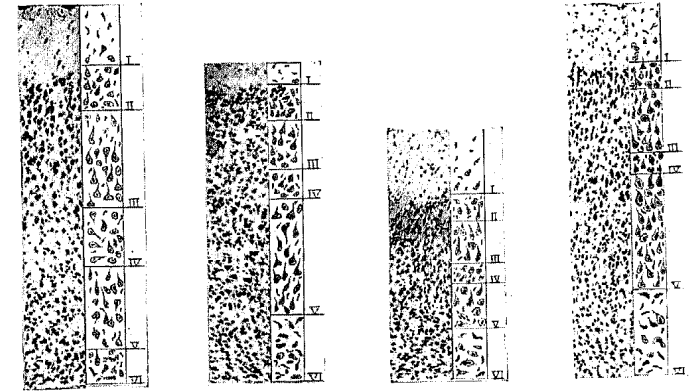


FIG. 22

FIG. 23

FIG. 24

FIG. 25

FIG. 22. Neocortical area N10 (insular area A). Adult albino rat. Magnification $\times 150$.

FIG. 23. Neocortical area N11 (insular area B). Adult albino rat. Magnification $\times 150$.

FIG. 24. Neocortical area N12 (insular area C). Adult albino rat. Magnification $\times 150$.

FIG. 25. Neocortical area N1 (cingular area). Adult albino rat. Magnification $\times 150$.

tively narrow and has an average thickness of 100 micra. The external granular layer (II) is narrow and fairly compact. It consists of four to five rows of granule cells. Its average thickness is 120 micra. The external pyramidal layer (III) is narrow and consists of three to four rows of loosely arranged small and medium sized pyriform cells. Its average thickness is 170 micra. The internal granular layer (IV) is narrow and consists of four to five loosely arranged rows of granule and small pyriform cells.

Its average thickness is 90 micra. The internal pyramidal layer (V) is broad and consists of ten to twelve loosely arranged rows of medium-sized and large pyriform cells. It contains but a few fairly large pyramidal cells. Its average thickness is 380 micra. The multiform layer (VI) consists of eight to ten rows of fusiform, oval and small pyriform cells whose axial orientation is oblique. Its average thickness is 260 micra.

The total thickness of this area is 1020 micra (fig. 23).

Insular area C (area N12) is in relation with the posterior portion of the rhinal fissure. Its zonal layer (I) is relatively broad and has an average thickness of 190 micra. The external granular layer (II) is narrow and consists of four to five loosely arranged rows of granule and small pyriform cells. Its average thickness is 100 micra. The external pyramidal layer (III) is narrow and consists of five to six loosely arranged rows of small pyriform cells. Its average thickness is 160 micra. The internal granular layer (IV) is narrow, poorly developed and interrupted. It consists of three to four loosely arranged rows of granule cells with an occasional small pyriform cell. Its average thickness is 80 micra. The internal pyramidal layer (V) is fairly narrow and consists of eight to ten rows of loosely arranged medium-sized pyriform cells with some clustering. It contains only a few pyramidal cells and no large pyriform cells. Its average thickness is 160 micra. The multiform layer (VI) is fairly broad and compact. It consists of eight to ten rows of fusiform, oval, and small pyriform cells whose axial orientation is generally horizontal. Its average thickness is 140 micra (fig. 24).

The total average thickness of this area is 830 micra.

The three neocortical areas of the mesial surface of the hemisphere (areas N1, N2, and N8) show some advances in the cellular differentiation of the adult when compared with the twenty-day-old rat. In the cingular area (area N1), the zonal layer (I) is relatively broad and has an average thickness of 200 micra. The external granular layer (II) is compact. It consists of five to six rows of granule cells for the most part arranged as cords or chains. Its average thickness is 120 micra. The external pyramidal layer (III) consists of eight or ten rows of loosely arranged small and

medium-sized pyriform cells with very few pyramidal cells. Its average thickness is 180 micra. The internal granular layer (IV) is narrow and consists of four to five loosely arranged rows of granule and small pyriform cells. The average thickness is 110 micra. The internal pyramidal layer (V) consists of twelve to fifteen rows of loosely arranged small and medium-sized pyriform cells with a very few pyramidal cells. Its average thickness is 360 micra. The multiform layer (VI) is relatively broad and consists of six to eight rows of fusiform, oval, and small pyriform cells. Its average thickness is 200 micra (fig. 25).

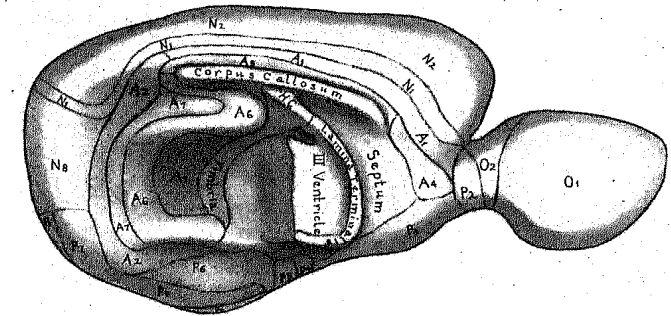


FIG. 26. Mesial surface of a reconstruction of the left hemisphere of an adult albino rat. Specimen 1190. N1, cingular area; N2, marginal area; N8, meso-occipital area; A1, intercalary area; A2, presubicular area, A4, preseptal area; A5, induseal area; A6, dentatal area; A7, cornual area; P1, pyriform area; P2, parolfactory area; P3, tubercular area; P4, post-tubercular area; P5, amygdalar area; P6, post-amygdalar area; P7, post-pyriform area; O1, olfactory cortex proper; O2, accessory olfactory cortex; HC, hippocampal commissure.

The total average thickness of this area is 1170 micra.

In the marginal area (area N2), the zonal layer (I) is relatively broad and has an average thickness of 160 micra. The external granular layer (II) is compact. It consists of eight to ten rows of small pyramidal, granule, and small pyriform cells arranged, in places, as cell cords or chains. Most of the cells are pyriform. Its average thickness is 110 micra. The external pyramidal layer (III) is fairly broad and consists of ten to twelve rows of small and medium-sized pyriform cells with only an occasional pyramidal cell of medium size. Its average thickness is 250

micra. The internal granular layer (IV) is narrow and irregular. Its average thickness is 100 micra. The internal pyramidal layer (V) is broad and consists of ten to twelve rows of loosely arranged pyriform cells of medium size and only a few pyramidal cells. There is no clustering of cells in this layer whose average thickness is 300 micra. The multiform layer (VI) is narrow and

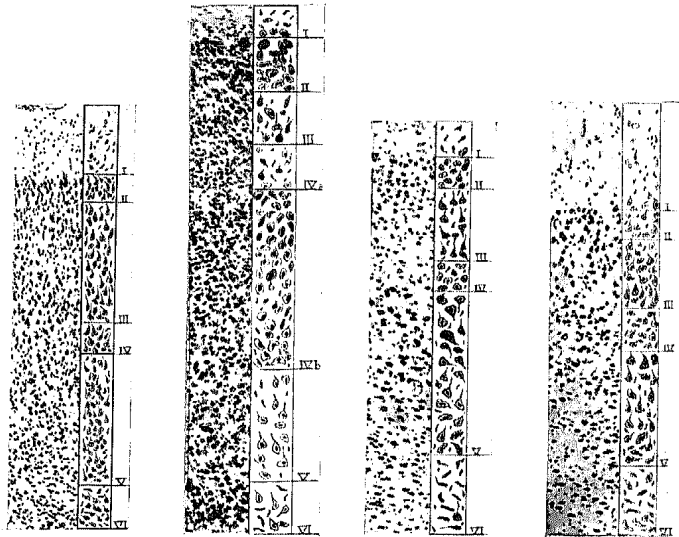


FIG. 27

FIG. 28

FIG. 29

FIG. 30

FIG. 27. Neocortical area N2 (marginal area). Adult albino rat. Magnification $\times 150$.

FIG. 28. Neocortical area N8 (meso-occipital area). Adult albino rat. Magnification $\times 150$.

FIG. 29. Neocortical area N4 (frontal area). Adult albino rat. Magnification $\times 150$.

FIG. 30. Neocortical area N9 (orbital area). Adult albino rat. Magnification $\times 150$.

consists of twelve to fourteen irregular rows of fusiform, oval and small pyriform cells. Its average thickness is 120 micra.

The total average thickness of this area is 1240 micra (fig. 27).

The meso-occipital area (area N8) occupies the caudalmost region of the mesial surface and is situated immediately behind the descending limb of the hippocampal formation. Its zonal

layer (I) is relatively narrow and contains a few granule cells near its base. Its average thickness is 110 micra. The external granular layer (II) is very broad and compact. It consists of eight to ten rows of closely crowded small and large granule cells and has an average thickness of 190 micra. The external pyramidal layer (III) is narrow and appears in cross section as a light longitudinal zone containing four to five very loosely arranged rows of faintly staining medium-sized pyriform cells. Its average thickness is 140 micra. The internal granular layer (IV) is very broad and compact. In certain regions it is reduplicated and consists of about eighteen rows of small and large granule cells with a few small pyriform cells. Its average thickness is 370 micra. The internal pyramidal layer (V) is fairly broad and compact. It consists of eight to ten rows of medium-sized pyriform cells with an occasional large pyriform and large pyramidal cell. The axial orientation of these cells is perpendicular. Its average thickness is 240 micra. The multiform layer is narrow and consists of five to six layers of oval and fusiform cells. Its average thickness is 150 micra (fig. 28).

The average total thickness of this area is 1200 micra.

The neocortex covering the frontal extremity of the hemisphere is the least differentiated of all neocortical regions. Its cells retain many features characteristic of early postnatal stages. The frontal area (area N4) occupies a position on the lateral surface of the hemisphere. Its zonal layer (I) is fairly broad and has an average thickness of 120 micra. The external granular layer (II) is narrow and consists of five to six rows of loosely arranged granule and small pyriform cells, in addition to a smaller number of small pyramidal cells. Its average thickness is 110 micra. The external pyramidal layer (III) is relatively narrow and consists of six to eight rows of very loosely arranged medium-sized pyriform cells whose axial orientation is most irregular. A few medium-sized pyramidal cells also appear in this stratum whose average thickness is 180 micra. The internal granular layer (IV) is poorly defined and irregularly interrupted. It consists of three to four rows of large granule cells and its average thickness is 100 micra. The internal pyramidal layer (V) is relatively broad and

consists of twelve to fourteen rows of medium-sized pyriform cells with some tendency to clustering but irregular axial orientation. Its average thickness is 390 micra. The multiform layer (VI) is fairly broad and consists of six to eight rows of fusiform and oval cells. Its average thickness is 210 micra (fig. 29).

The average total thickness of this area is 1110 micra.

The orbital area (area N9) occupies the basal surface of the frontal region. Its zonal layer (I) is very broad and has an average thickness of 260 micra. The external granular layer (II) is narrow and consists of three to four rows of granule and small pyriform cells. Its average thickness is 100 micra. The external pyramidal layer (III) is narrow and consists of five or six rows of very loosely arranged medium-sized pyriform cells. Its average thickness is 230 micra. The internal granular layer (IV) is indefinite and irregular. It consists of three to four rows of granule cells and its average thickness is 160 micra. The internal pyramidal layer (V) is narrow and consists of six or eight rows of loosely arranged medium-sized pyriform cells the axial orientation of which is irregular. Its average thickness is 230 micra. The multiform layer (VI) is narrow and consists of two to three rows of oval and a few fusiform cells. Its average thickness is 130 micra.

The average total thickness of this area is 1110 micra (fig. 30).

In the twenty-four-day-old rat numerous myelinated fibers may be traced from the centrum ovale to the superficial layers of the neocortex. Many of them enter the external granular layer. At this time, there is no evidence of myelination in the intercortical fiber systems. As early as the thirtieth day, however, two distinct strata of myelinated fibers make their appearance within the cortex, one of them in relation with the superficial portion of the external pyramidal layer, the other in the internal pyramidal layer. In their general direction, these fibers follow the coronal plane but on closer examination each stratum is seen to have a highly plexiform organization and thus makes provision for extensive intercellular connections. It has previously been noted, in discussing the significance of myelination (page 306), that neither the deposition of myelin nor the degree of develop-

ment in the medullary sheath is necessarily an index of the availability of the nerve-fibers for conduction. The transmission of impulses may occur through axones which fail to develop myelin sheaths as well as through axones before they have ultimately acquired such sheaths. The appearance of myelin in the intercortical fiber systems, therefore, does not imply that the conduction of impulses between the cells of the cortex is primarily dependent upon myelination. It does, however, indicate that the neurones of which such myelinated fibers are parts, have attained an advanced degree of differentiation and for this reason have increased their functional capacity. Consequently the appearance of myelinated intercortical fibers has critical significance as a gauge of cortical maturity.

CORRELATIONS BETWEEN THE BEHAVIOR AND THE NEURAL ORGANIZATION OF THE ADULT RAT

The behavior of the adult albino rat is much less complex than that of many of the higher mammals. Indeed, it is difficult to discern wherein the major drives which motivate reactions in the rat, are more effective than those of most inframammalian vertebrates. The activating effects of hunger and thirst, of sexual urge, reproduction and parental care, of exploration, gregariousness, and self-protection are no more successfully expressed in the rat than in many fish, reptiles, and birds; some capacity to learn and to form habits is common to all vertebrates regardless of the degree of development in the nervous system. Such differences in behavior as do exist are often subtle and extremely difficult to analyze. They depend in no small measure upon the ecological factors which condition the animal.

If it is obvious that a simple program of living requires a controlling mechanism commensurately simple and that more complicated adaptations call for a complex neural control, it seems equally clear that the cerebral cortex, especially the neocortex, provides the means for the highest adaptive elaborations. But the functional capacity of the neocortex varies extensively in different species of mammals. It also varies in its structural specialization. In such mammals as the opossums, the skeletal

structure of which has remained almost entirely unaltered since the Cretaceous stage, the neocortex gives evidence of extreme primitiveness.

Neocortical differentiation in the carnivores, on the other hand, shows many structural advances which become progressively more pronounced in the primates.

The primitive cortical structure of lower mammals has numerous features which warrant the term "dawn cortex" and in many respects the neocortical specialization of the rat belongs to this category. The smooth, unconvoluted hemisphere denotes primitiveness. The simplicity of the localized areas and the relatively low degree of development in intercortical fibers have a similar significance. A prominent feature of the adult rat's neocortex is the preponderance of pyriform cells as compared with pyramidal elements. In this respect the rat's cortical specialization aligns itself much more closely with the "dawn cortex" of the opossum than with that of higher mammals. Many of its adult reactions are dependent upon infracortical parts of the nervous system. Its entire somatic behavior is the result of an integrative process to which all divisions of the neuraxis contribute and over which the cerebral cortex exercises a discriminating regulation. In contrast to more highly developed mammals, the capacities of the rat for this type of regulation are relatively limited. Discriminating selection, such as the choice of suitable foods and fluids, is apparent, however, in the reactions of the full-grown animal. A more reserved behavior and individual aloofness gradually emerge as the animal detaches itself from the active huddling of its litter stage. In its cautious exploration, and in its reactions to sharp sounds, the reactions of the adult manifest well defined discriminations which likewise appear in its sexual and maternal activities. When cornered or attacked the adult rat usually shows fight and either brings all of its defensive equipment into action or makes vigorous efforts to escape. The indifference with which the full-grown animal tolerates compression of the tail has already been mentioned. A tougher tail may account for this apparent complacency but the discriminative allowances of an animal accustomed to repeated, playful assaults upon its caudal member should not be lost sight of in the explanation.

In direct proportion to the degree in which the syntheses of general body sense, sight, hearing, smell, and taste enter into discriminating behavior, the combinations and sequences of sensory impressions require a cortical structure for their proper utilization. The cortical structure of the adult albino rat does not attain a high degree of specialization as compared with many other mammals but it plays a dominant rôle in the adult reactions of the animal.

SUMMARY

Based on the general principle that there is an ontogenetic relationship between the structure of the nervous system and behavior, the specific details of this relationship were studied in the albino rat from embryonic stages to maturity.

Observations of behavior were confined to the somatic reactions of the animals, largely because splanchnic activities require separate and extensive investigations of their own. The chief purpose of the study was to follow the natural process of development as objectively as possible and without the introduction of experimental conditions. In all of the interpretations, an effort was made to avoid the implications of "instinct" and "inherent behavior patterns" on the ground that such implications merely beg the question involved in the major problems of the investigation. The analysis of reactions proceeded upon the assumption that a structural adequacy in the nervous system is essential to the several activities which make their appearance in the different periods of development and that such adequacy is founded upon the neural capacity for afferent conduction, neuraxial integration, and efferent transmission. In pursuing this proposal the developmental processes in the spinal cord, oblongata, pons, midbrain, cerebellum, and forebrain were followed through a series of stages from embryonic to adult life. Although it is recognized that the correlations which are here discussed have been made solely on the coincident status of structure and behavior during development, it is nevertheless felt that they offer as satisfactory deductions as are, at present, possible. During the development of the cerebral cortex, three significant phases were distinguished. Each of these phases represents a distinct period in the upbuilding

of behavior, and serves as a convenient index of the relative degree of specialization in the entire nervous system.

1. The first phase (general cortical differentiation) covers the embryonic and fetal periods during which the animal's reactions are at first limited to circumscribed muscular twitchings, then manifest more definitely reflex qualities, and finally are characterized by simple but distinctly integrated responses to stimulation.

In this period, the foundations for all of the progressive changes which determine the specialized structures of the end-brain are laid in the mantle layer. By a series of migratory laminations from this layer and by cellular differentiation in the strata derived from it, a six-layered neocortex makes its appearance at about the time of birth. Cortical differentiation also occurs in the olfactory bulb and in the paleocortical and archicortical portions of the end-brain. Cellular specialization, however, advances much more rapidly in the spinal cord and caudal portion of the brain-stem than elsewhere in the nervous system. In this prenatal period, structural immaturity in the hemisphere, interbrain, midbrain, and cerebellum is sufficient to warrant the exclusion of these structures as participants in the control of behavior. Such influence as the nervous system exercises over the reactions of the animal must, therefore, be attributed to the more advanced conditions of development in the segments of the spinal cord and caudal portion of the brain-stem.

2. The second phase (divisional cortical differentiation) begins at birth and continues into the fifth or sixth postnatal day. During this time the animal develops activities sufficient for the immediate adjustments to extrauterine life, such as breathing, crawling, righting, and sucking. In spite of the fact that the four major divisions of cerebral cortex [(1) bulbar cortex, (2) paleocortex, (3) archicortex, and (4) neocortex] are now well defined, their structure is still too immature to permit of decisive activity in the regulation of behavior.

The reactions immediately after birth are attributed to the spinal cord, the caudal portion of the brain-stem, and the tegmentum of the midbrain. Late in this phase the young rat

develops greater vigor in its postural and nutritional activities. Its locomotion is somewhat more effective, although all movements of this kind still retain their original, neonatal characteristic of paddling. Ineffectual attempts at scratching also make their appearance at this time.

The reasons for associating these later reactions with developments in interbrain, corpus striatum, and probably in the olfactory portions of the cerebral cortex are discussed.

3. The third phase (local cortical differentiation) begins on or about the fifth postnatal day and is well advanced by the tenth day. It results in the ultimate differentiation of thirty-one distinct cortical areas as follows:

In the bulbar cortex:

1. The olfactory cortex proper (area O1)
2. The accessory olfactory cortex (area O2)

In the paleocortex:

1. The pyriform area (area P1)
2. The parolfactory area (area P2)
3. The tubercular area (area P3)
4. The post-tubercular area (area P4)
5. The amygdalar area (area P5)
6. The post-amygdalar area (area P6)
7. The post-pyriform area (area P7)
8. The anterior rhinal area (area P8)
9. The posterior rhinal area (area P9)

In the archicortex:

1. The intercalary area (area A1)
2. The presubicular area (area A12)
3. The subicular area (area A3)
4. The preseptal area (area A4)
5. The induseal area (area A5)
6. The dentatal area (area A6)
7. The cornual area (area A7)

In the neocortex:

1. The marginal area (area N1)
2. The supramarginal area (area N2)
3. The intermediate central area (area N3)
4. The frontal area (area N4)

5. The parietal area (area N5)
6. The temporal area (area N6)
7. The latero-occipital area (area N7)
8. The meso-occipital area (area N8)
9. The orbital area (area N9)
10. The insular area A (area N10)
11. The insular area B (area N11)
12. The insular area C (area N12)
13. The central area (area N13)

During this phase the subcortical nuclei, the interbrain, and the cerebellum attain their full development much earlier than the neocortex. Complete local differentiation occurs in the paleocortex and archicortex considerably before the final specializations have taken place in the neocortical division of the hemisphere.

In this phase myelination slowly advances in the nerve roots, spinal cord, caudal portions of the brain-stem and cerebellum. Subsequently it affects the midbrain and still later the cerebral hemisphere. The first fiber systems to become myelinated in the endbrain are the lateral olfactory tract, the septal fasciculi, the anterior commissure, the medial forebrain bundle, and the mesial portion of the centrum ovale. Deposition of myelin occurs later in the optic fibers, the lateral forebrain bundle, corpus callosum, and intracortical radiations. The lateral portion of the centrum ovale and the intercortical fibers are last to be myelinated.

While local cortical differentiation is in process the animal gradually increases the number and effectiveness of its reactions until it has acquired the full repertory of its postural, nutritional, locomotor, exploratory, play, sexual, parental, and protective activities. As it slowly emerges from its litter-stage, it manifests an increasing number of adaptations in which discrimination is progressively more evident. These later developments in the behavior of the adult rat are attributed to the cerebral cortex and particularly to the neocortex.

The early maturing of the segmental portions of the nervous system and the relatively late specialization in suprasegmental structures are clearly demonstrated in the course of the three

phases of cortical differentiation. The more rapid advances toward maturity seen in the neuraxial segments indicate the importance of the spinal cord and brain-stem in fetal and early postnatal activities. Ultimate specializations in the hemisphere, serve to expand and amplify these activities. In many respects the cortical differentiation in the adult is extremely primitive. This fact, no doubt, accounts for the comparatively limited rôle of the cortex in the neural integrations which control the somatic behavior of the albino rat.

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