same in all solutions. Twenty-five wheat plants were grown in each culture vessel containing 8,600 cc of solution. The solutions were renewed every eight days. Daily records were made of the hydrogen-ion concentrations of the solutions during a culture period of 102 days.

It was found that with low NO_3/NH_4 ratios the pH values of the solution decreased rapidly under the influence of the plants and approached in extreme cases a pH value of 3.0. With high ratios, on the other hand, the pH values increased rapidly, tending to reach a limiting value of 6.5. When a NO_3/NH_4 ratio of suitable value was used, however, a physiologically balanced solution was obtained in which the hydrogen-ion concentration tended to remain approximately constant during the eight-day period between solution renewals. By balancing the partial concentration of NO_3 (the absorption of which removes H-ions from the solution) against that of NH_4 (the absorption of which removes OH-ions from the solution), the various conditions that tend to decrease the acidity may be exactly opposed by conditions that tend to increase the acidity. This method was found to be far more effective than that of attempting to stabilize the solution by greatly increasing the phosphate buffer content.

To maintain a higher pH value, it was necessary to use a higher ratio of NO_3 to NH_4. As the plants grew older, they gradually changed in their ability to alter the reaction of the solution. For the most accurate control of the pH value throughout the life cycle of the plants, it was therefore necessary to employ progressively lower NO_3/NH_4 ratios. Nevertheless, an approximately constant pH value could be maintained throughout the culture period by using a suitably selected intermediate NO_3/NH_4 ratio. Thus a very satisfactory stabilization of the pH value was obtained when NO_3/NH_4 ionic ratios of 50/50, 85/15 and 95/5 were used for maintaining pH 4.3, 5.1 and 6.0, respectively. The average changes in reaction after 8 days of contact with the roots were 0.23 pH, 0.21 pH and 0.08 pH, respectively. The composition of the solution for pH 5.1 is as follows: 0.00670 m KNO_3, 0.00059 m $(NH_4)_2SO_4$, 0.00255 m KH_2PO_4, 0.000079 m K_2HPO_4, 0.00394 m $CaCl_2$, 0.00263 m $MgSO_4$, 0.00005 m $FeSO_4$, 0.00005 m $K_3C_6H_5O_7$. In addition the solution contains 0.11 ppm. Mn, 0.07 ppm. Zn, 0.05 ppm. B, 0.002 ppm. Cu, 0.09 ppm. Al, 0.005 ppm. Li, 0.12 ppm. Na, 0.01 ppm. As, 0.1 ppm. Si, 0.01 ppm. Ni, 0.01 ppm. Co and 0.01 ppm. I.

The results of this study demonstrate clearly that the use of a physiologically balanced culture solution provides an effective and practicable means of stabilizing the hydrogen-ion concentration of the solution, and they indicate that excellent growth of the plants may be secured in a culture solution of this type if due attention is given to the total concentration as well as to the relative proportions of the solution constituents. This method may be recommended for many different kinds of physiological studies in which culture solutions with controlled pH values are required. The general utility and significance of physiological balance as a means of stabilizing the reaction of culture media appear to be worthy of much greater emphasis than they have been given in the literature of physiology, pathology, mycology and bacteriology.

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SPECIAL ARTICLES

THE EVOLUTION OF CEREBRAL LOCALIZATION PATTERNS[1]

THE localization of functions within the brain has been a topic of acute controversy since the beginning of inquiry into the organization of the central nervous system. Without attempting a review of the observations, experiments and speculations in this field, it is evident that the problem has recently entered a new phase with the elaboration of new methods of inquiry and new fundamental conceptions of nervous processes. The divergencies of opinion are to-day more acute and dogmatic than ever before, ranging all the way from a modernized phrenological localization in mosaic patterns of mental faculties of one sort or another to the equally ancient denial of any localization whatever in the cerebrum. On the last point an experimental psychologist has recently written, "Physiology must abandon any theory of cortical activity that rests upon localization of function."

The anatomist, embryologist, physiologist, psychologist and clinician views the problem from his own angle and in the light of his own experience. Too often his general conclusions are derived only from the meager data visible to him within his own contracted horizon. There is truth in each of these partial views, and before a satisfactory solution can be hoped for we must all learn to liberalize our own opinions by looking at the question as judiciously as we can from all points of view. This may justify the presentation of an aspect of the problem which has received scant attention—the phylogenetic approach.

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One major difficulty in the formulation of any scheme of localization arises from failure to recognize that different types of sensory experience involve very diverse kinds of adjustment to what is going on in the environment, and no single formula can be expected to apply to all of them. Contrast, for instance, the three sensory systems, smell, hearing and vision. Odors have quality and intensity, but no well-defined discrimination in terms of either space or time. The central connections of the olfactory nerve show a minimum of localization, with a diffuse spread, and a maximum of apparatus of summation, intensification and non-specific activation and reinforcement of other sensory-motor systems. Hearing is essentially a time-sense with imperfect localization in space, and the central connections of the auditory nerve are not spread out in space in patterns related with the arrangement of the sensory receptive cells of the cochlea. It is evident that tone analysis is effected by a type of apparatus which does not require that the excitation of specific receptive cells of the organ of Corti be registered centrally in separate places. Vision, on the other hand, is preeminently a space-sense, and here we do find a very precise localization of central tracts and nuclei from the retina to the visual cortex.

The problem of anatomical localization of function within the brain is radically different in these three sensory systems, and it is not to be expected that the pattern of localization which is so clearly shown in the visual system of conductors will be repeated in the auditory and olfactory systems. In primates the various loci of the visual field are accurately projected by the dioptric apparatus upon the retina, the various quadrants of the retina are known to be projected upon precisely bounded parts of the lateral geniculate body, and these in turn are again projected upon definite sectors of the striate area of the cortex. It is probable that the nervous pathway from every point on the retina maintains some measure of individual distinctness up to its discharge into a specific locus of the cortex. This type of localization in space is not required for the sense of hearing, a temporal sense, and in fact the auditory pathway does not show it.

Since the visual pathway is more precisely localized within the brain than that of any of the other senses, it may contribute to our understanding of cerebral localization in general to examine the phylogenetic history of the thalamic visual center—the lateral geniculate body. This survey shows a gradual emergence of this specific and sharply localized center from a non-specific area of central gray and it may illuminate the relation between sharply localized and more dispersed functions in general.

We take our departure from the primitive generalized Amphibia—Necturus and Amblystoma—where the thalamus is very small and undifferentiated. Figs. 1 and 2 give the general orientation and show that the thalamus proper, lying between

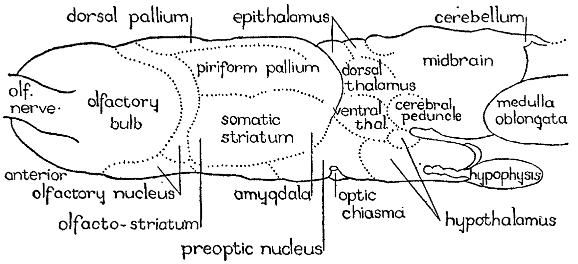

FIG. 1. Lateral aspect of the brain of adult *Necturus maculosus* upon which the boundaries of some of the larger cellular areas are projected in dotted outline. × 6. Figures 1 to 3 are taken from the author's Morphogenesis of the Brain, *J. Morph.*, vol. 54, 1933, pp. 233–258.

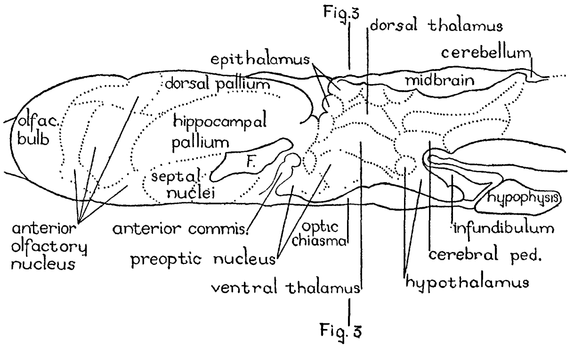

FIG. 2. Median section of the brain of Necturus upon which the outlines of some of the areas of gray substance are similarly indicated. Most of these boundaries are marked by ventricular sulci. In the midbrain and betweenbrain the section is median; in the cerebral hemisphere the plane of section is slightly to one side of the midplane, better to show the relations of the interventricular foramen (*F*) to surrounding gray areas. The approximate plane of figure 3 is indicated.

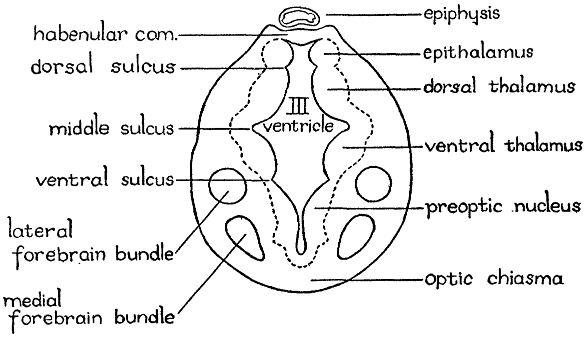

FIG. 3. Transverse section through the diencephalon of Necturus. The outline of the gray substance is indicated by broken lines.

the epithalamus above and the hypothalamus below, is very small. It is divided by a sharp ventricular sulcus into dorsal and ventral parts. The larger ventral part is the precursor of the subthalamus of human anatomy and is a motor adjustor interpolated between the corpus striatum and cerebral peduncle, as in man. The very meagerly developed dorsal thalamus is the precursor of the entire sensory thalamus of mammals. The relations of these parts as seen in cross-section are shown in Fig. 3.

The plan of organization of this primitive sensory thalamus is shown very diagrammatically in Fig. 4.

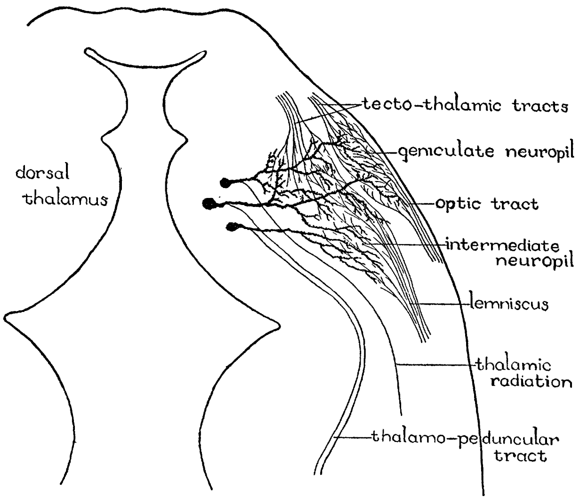

FIG. 4. Diagram of typical connections of neurons of the dorsal, or sensory, thalamus of Necturus, as seen in cross-section. Three neurons of this area are drawn. Their cell bodies lie in a deep periventricular layer of gray. Their dendrites spread widely throughout the white substance, where they are in synaptic connection with terminals or collaterals of various sensory tracts. Their axons may enter the thalamo-peduncular tract (for thalamic reflexes), or they may enter the thalamic radiation which ascends to the cerebral hemisphere. The whole dorsal thalamus is a "nucleus diffusus thalami."

The cell bodies of all neurons are densely crowded in a periventricular gray layer; that is, they retain the embryonic position and no special nuclei are differentiated. Their dendrites and axons pass outward into a superficial white layer, where most of the synaptic junctions are found. These dendrites arborize widely and those of a single cell may spread throughout the entire field of the sensory thalamus. Here they may be activated by terminals of the optic tract, by various lemniscus systems from medulla oblongata and spinal cord, and from the midbrain roof by tecto-thalamic tracts. A thalamic neuron may be activated by any one of these afferent systems or by several of them in various combinations.

The sensory thalamus may be characterized as a nucleus diffusus. Its neurons are not segregated into nuclei each with its own specific connections, as in man. Nevertheless, in the white substance there is an incipient localization, for the incoming fibers tend to end in local fields of neuropil. Thus collaterals from the optic tract arborize in a superficial area of neuropil and they do not pass beyond it. This is clearly the precursor of the lateral geniculate body (Fig. 4, geniculate neuropil). There are few, if any, neurons which are related exclusively with this "geniculate" neuropil; that is, there is no gray nucleus, only a synaptic field. This neuropil, moreover, is not exclusively optic, for it receives terminals of both the optic tract and a strong tecto-thalamic system of fibers from the roof of the midbrain. It is not a geniculate body such as we see in mammals, but it is clearly the precursor of it.

Underlying this "geniculate" neuropil is an intermediate field of neuropil which receives terminals of various lemniscus systems and tecto-thalamic tracts. It is a diffuse synaptic field into which all kinds of exteroceptive sensory impulses may be discharged. In no case do these impulses come directly from the peripheral sense organ, but always by tracts of higher order. Within the gray layer there is a third layer of neuropil (not drawn in the figure) which may be termed the periventricular neuropil. This deep neuropil is a dense entanglement of very slender collaterals and terminals of axons from various sources within which the cell bodies of all thalamic neurons are closely enmeshed.

The neurons of the sensory thalamus, accordingly, may be activated in any one or all of three ways: (1) By the periventricular neuropil, which effects synaptic junctions directly upon their cell bodies; (2) by the intermediate neuropil or "nucleus diffusus" field; (3) by the superficial or "geniculate" neuropil. Most of the neurons are related with all three of these synaptic fields; all of them are under the influence of the deep periventricular neuropil; and some of the smaller elements may send their dendrites into only one of the layers of neuropil of the white substance, *i.e.,* into the intermediate diffuse neuropil or into the superficial "geniculate" neuropil.

In the most primitive arrangement all neurons spread their dendrites in both the intermediate and the superficial optic or geniculate layers of neuropil. By suppression of one of these dendrites in some cases and the other dendrite in other cases, neurons of physiologically different connections are specialized. But the cell bodies of the two types are mingled; they are not segregated; only the neuropil of the synaptic field is localized. Next the neurons with "geniculate" connections tend to be sorted out from the others. In accordance with Kappers' law of neurobiotaxis, their cell bodies migrate outward from the central gray toward the synaptic field containing the terminals of the optic tract. This migratory movement has begun in the frog and it is consummated in reptiles. There is a true lateral geniculate body in reptiles whose elements are specifically related with the optic and tecto-thalamic tracts and are completely emancipated from connection with the deep periventricular neuropil and the intermediate diffuse neuropil. During this process of segregation of the geniculate body the remaining gray matter of the sensory thalamus is undergoing a similar differentiation and local specialization of other types of nuclei.

In mammals the differentiation and localization of function of the lateral geniculate body has advanced another step. In amphibians and reptiles, as in mammals, the geniculate neuropil receives fibers from the optic tracts and optic tectum, the latter contained in the brachium of the superior colliculus. In these lower vertebrates fibers leave the nucleus diffusus thalami in two directions—downward toward the cerebral peduncle for thalamic reflexes and upward into the cerebral hemisphere as thalamic radiations of the internal capsule system, again as in mammals. But in amphibians and reptiles no specific optic projection tract has been described, passing from the lateral geniculate body into the hemisphere, though Crosby believes that such fibers are probably present in some reptiles. Now in mammals the lateral geniculate body is divided into a dorsal and a ventral part. The ventral part receives optic fibers and the brachium of the superior colliculus and is evidently an apparatus of visual thalamic reflexes. It is strictly comparable with the reptilian geniculate body, for no cortical projection fibers arise from it. The mammalian dorsal nucleus, on the other hand, is a new structure differentiated as the specific nucleus of origin of optic projection fibers terminating in the striate area of the cortex (Brodmann's area 17). It is this dorsal nucleus alone which in primates is greatly enlarged, with neurons arranged in thin convoluted sheets within which both retinal fields and cortical fields are precisely and minutely localized.

This in brief outline is the history of the evolution of the lateral geniculate body, its gradual emergence from a nearly homogeneous and diffuse thalamic gray, with progressive differentiation and segregation in space of neurons and related fiber tracts, until in man every spot on the retina activates a definite spot in the geniculate body, and each of these spots, in turn, registers upon a definite and sharply circumscribed area of the striate cortex, as Dr. Poljak, among others, has so clearly demonstrated.

The evolutionary history of the lateral geniculate body has been selected for description here because it presents in clear and simple outline a sequence of events which is repeated in principle in other parts of the brain. In the corpus striatum and cerebral cortex, for instance, a similar story can be clearly read; but the details are here more complicated and they have been reported elsewhere.[2]

The key to these progressive changes in histological organization is to be sought in the synaptic field, that is, in the neuropil. As in the thalamus, so elsewhere throughout the brain of the generalized Amphibia, this neuropil is arranged in three layers, deep or periventricular, intermediate and superficial.

The periventricular neuropil is spread throughout the gray layer of the entire brain as an entanglement of finest axons within which the cell bodies of all neurons are embedded. Most of these axons are collaterals of long fibers of tracts with well-defined functional specificity, but this neuropil as a whole is of uniform texture, with little evidence of local specialization. It is relatively homogeneous histologically but not physiologically equipotential, for different parts of it are locally activated from different sensory systems—olfactory in front, optic in the diencephalon and mesencephalon, and other senses farther down in the brain stem. This is obviously an integrative apparatus of major importance and probably is concerned chiefly with the most primitive types of mass-action, the regulation of general bodily tone by reinforcement and inhibition, and other generalized functions of the organism as a whole. Here localization of function is at a minimum, though it is not totally absent. This deep neuropil is entirely lacking in the pallial part of the human cerebral hemispheres, but it is more or less well developed throughout the brain stem, being seen in its most characteristic form in the periventricular gray of the thalamus.

In the Amphibia the intermediate level of neuropil is the principal synaptic field. Here the nervous connections are made which serve the standardized mass-movements and local reflexes of locomotion, feeding, etc., and here are the long tracts of fibers which connect the local centers involved. Such incomplete localization of function as these animals exhibit is effected chiefly in this zone of neuropil, and the elaboration of local gray centers or nuclei follows the differentiation of special synaptic areas within this zone.

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[2] C. Judson Herrick, "The Amphibian Forebrain." VI. "Necturus," *Jour. Comp. Neur.*, Vol. 58, No. 1, 1933; VII. "The Architectural Plan of the Brain," *ibid.*, Vol. 58, No. 2, 1933; VIII. "Cerebral Hemispheres and Pallial Primordia," *ibid.*, Vol. 58, No. 3, 1933; IX. "Neuropil and Other Interstitial Nervous Tissue," *ibid.*, Vol. 59, No. 1, 1934; X. "Localized Functions and Integrative Functions," *ibid.*, Vol. 59, No. 2, 1934.

The superficial or marginal zone of neuropil is everywhere present, but in most cases very simply organized. Where it is locally specialized, as in the "geniculate" neuropil, it is composed chiefly of collaterals of long tracts whose fibers make their primary connections elsewhere. In other words, it is subsidiary to the main trunk lines of reflex connection. The deep neuropil is also a subsidiary, or collateral, connection of the long tracts, but without well-defined local areas of specialization. In contrast with this, the specialized superficial areas are more or less definitely localized and each of them receives its own characteristic complex of collateral connections. In brief, the superficial areas of neuropil seem to be well adapted for conditioning of reflexes, and this is probably the rôle which they play.

In the pallial part of the amphibian cerebral hemisphere there is no differentiated cerebral cortex, though primordia of the principal cortical areas can be recognized. In this primordial pallium the three zones of neuropil tend to converge into a single field which pervades the whole thickness of the wall of the hemisphere, and this fusion is more advanced in proportion as the cortical type of organization of the gray substance is approached.

We have here a prodromal stage of cortical differentiation in which all three types of nervous organization which characterize the brain stem are represented—(1) the primitive, relatively non-specific and poorly localized integrative apparatus serving generalized totalizing functions, (2) the apparatus of local reflexes and (3) the mechanisms of conditioning. In further differentiation of the cortex these factors are all preserved, though in anatomical and physiological patterns of organization which are unique and found nowhere else in the nervous system.

In the amphibian pallial primordia there is some localization of function determined by the anatomical arrangement of projection fibers of diverse subpallial connections, but this localization is at a minimum. This pallium obviously acts mainly as a whole to influence nervous activities whose patterns are determined in subpallial territory; that is, its chief functions are the differential inhibition or reinforcement of brain stem activities as going concerns.

With further elaboration of cortical structure in reptiles and mammals and with the segregation in space of specific sensory and motor projection tracts of the internal capsule system, progressively more precise localization of function appears in those cortical fields which are anatomically related with these systems of projection fibers. At the same time the non-specific integrative, activating and associational apparatus increases in still greater amount.

In lower mammals the apparatus of the totalizing functions is mingled with that of the sensory and motor projection systems, and this remains true to a large extent even in man. As we pass from lower to higher primates the apparatus of projection becomes more and more segregated from the far more elaborate apparatus of association, conditioning and rational control, though in the nature of the case this separation is never complete. The so-called associational cortex is differentiated in two directions: (1) There is local differentiation of cell types, lamination patterns and tracts of association fibers which serve stable innate or acquired patterns of behavior or mental processes; this is the permanent organization or architectonic of the hemisphere. (2) There is also a very large amount of unspecialized nervous tissue which infiltrates the permanently organized connections of projection and associational systems and is itself non-specific and labile in structure and function. This non-specific tissue may be very complex structurally, composed in part of small neurons and in part of collateral connections of neurons whose primary connections are those of the stable systems of projection and association tracts. This labile tissue of the second type has no fixed or permanent structurally predetermined reaction patterns of its own; it can be activated only through the nervous elements of the first type; but it pervades the entire cortical organization, and activation of the cortex in any place will affect it more or less extensively. It is a permanent integrator, and it is more than this. Not being a part of the stable architectonic, it possesses a characteristic fluidity. The pattern of its activity at any moment is determined, not by fixed structural connections, but by dynamic factors which are as yet obscure. These transient patterns of activation have no permanent localization.

The human cerebral cortex, then, exhibits three types of localization of function. The first is in the projection areas, which can be mapped in mosaic patterns on the surface. These are determined primarily by their respective subcortical connections. Probably all parts of the cortex have some subcortical connections, but the principal systems of projection fibers are related with specific and clearly defined cortical areas. The second type is an expression of the architecture of the intracortical association systems. These stable arrangements of cell bodies and related association fibers constitute the apparatus of our standardized patterns of behavior and mental activity. This apparatus is present throughout the cortex. The functions performed by it are more or less permanently localized, but the pattern of this localization is very intricate and it can not be projected upon the surface of the brain in mosaic designs like those of the projection centers. Third, in addition to the localized systems of projection and associational neurons, there is in the cortex an enormous mass of non-specific tissue. This is everywhere abundant; it varies in structure from place to place and in function from moment to moment. It integrates all cortical activities, synthesizes experience and provides the plasticity of structure requisite for learning and higher mental processes in general.

Reviewing what is known of the phylogeny of the cerebral cortex, it appears that the integrative, associational and synthetic functions have predominated from its inception. Some measure of localization is always present. Only the analytic functions of the projection systems can be charted in mosaic patterns. The segregation and separation in space of the data derived from diverse sensory experiences seems to be an essential prerequisite for the association and synthesis of these experiences and their conversion into appropriate patterns of response. In lower mammals the localization of systems of projection and stable patterns of association is far less refined than in man and the mass-action of the cortex bulks larger. The more refined localization of these two types in the human brain is of great significance in clinical neurology and especially in surgery. The elaboration of these localization patterns goes hand in hand with a still greater increment in the poorly localized synthetic and integrative functions. It is these latter which have most significance for psychology and psychiatry.

The evolutionary history of the lateral geniculate body shows how a highly specific pattern of localization has gradually emerged from a diffuse and non-specific arrangement. The totalizing functions of correlation and integration have not been impaired by this process of local differentiation; on the other hand, they have been amplified and special apparatus has been elaborated (chiefly in the cerebral cortex) to ensure their progressive enhancement and to maintain their dominance over all other components of the behavior pattern.

The evolutionary history of those sensory-motor systems, like the olfactory and auditory, where precise localization in space is not an important factor, presents a radically different morphological picture, the details of which can not here be entered into.

Some cerebral functions are very precisely localized, as every clinical neurologist knows. Having determined the exact pattern of this localization for some one sensory-motor system, the clinician or the experimentalist is inclined to generalize and try to fit all his experience into this pattern. But a point is soon reached where this attempt breaks down. The observed facts do not fit the pattern. The functions performed are extremely diverse. Some of these functions are performed by local areas of gray that can be charted on the surface in mosaic patterns, like the projection fields of the cortex. These fields are interconnected by a complex web of fiber tracts which are stable structural features; these also are localized in space, though in patterns which can not be charted on the surface in mosaic designs. And permeating all this stable architectural fabric there is an enormous mass of neuropil and other less specific tissue whose structure is generalized and whose functions are more labile and modifiable.

This interstitial nervous tissue serves the primitive integrative or totalizing functions and also correlation and conditioning of reflexes and all higher mental processes, including the semantic or symbolic activities. This type of tissue is highly elaborated in the cerebral cortex. It is not structurally homogeneous or physiologically equipotential, yet it has no stable patterns of anatomical localization comparable with those of reflex arcs or cortical projection centers. The pattern of performance varies from place to place and from time to time. But this pattern is not self-determined; for its action at any moment depends on the structural organization and physiological activation of the more stable tissues with which it is organically related.

It is evident, accordingly, that no single formula of cerebral localization of function can be written. Each type of performance has its own anatomical pattern which must be discovered by patient research. For some types of function there are no local organs with stable or rigid arrangements of neurons, for these organismic or totalizing activities are general in their reach and fluid in character. Yet the tissues which perform them are not structurally homogeneous or physiologically equipotential. In these integrating functions the amount of tissue activated is a factor in the situation, as Lashley has shown, but diversification of structure and of pattern of activation is essential, for this is the apparatus of our mental life in both its analytic (sensory) and its synthetic (rational) aspects.

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Ditmars, Raymond L. *Reptiles of the World.* Revised edition. Pp. xx + 321. 89 plates. Macmillan. $5.00

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