T140

15 Functional Organization of the Cerebral Isocortex

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Introduction

The great strides that have recently been made in the electrophysiological analysis of brain function has eclipsed the fact that much of our fundamental knowledge about the relationship between brain, behavior, and subjective experience is almost entirely dependent upon clinical and laboratory investigations of brain-lesioned subjects. This eclipse is in part due to the fact that experimental psychosurgical techniques and quantitative neurobehavioral experiments have been performed to a great extent by neuropsychologists who publish in psychological journals (such as the *Journal of Physiological and Comparative Psychology; Psychological Review; Neuropsychologia*) which only occasionally come to the attention of scientists and practitioners with biological and medical training. Further, as with reports made within any well-developed discipline that tackles difficult problems, the experiments and results described are often complex, and an idiosyncratic jargon develops that makes it difficult for those not working in the field to know just what is being reported.

This chapter will be devoted therefore to providing a framework for understanding some of the most significant experimental psychosurgical observations regarding the cerebral cortex that have accumulated in the neuropsychological literature over the past few decades. The overview of the literature will perforce be incomplete but at the same time, hopefully of sufficient scope to stimulate further interest.

The important role of cortical mechanism in mental function has been a focus of scientific interest for the past century and a half. In the early 1800s, arguments raged between physiologists (e. g., Flourens, [34]) and phrenologists, many of whom were good anatomists (e. g., Gall and Spurzheim [37]), as to whether the cerebral mantle functioned as a unit or whether a mosaic of cerebral suborgans determines the complex of psychological experience. During the intervening period, data have been subsumed under one or the other of these two views – almost always with the effect of strengthening one at the expense of the other. In the recent past, the accumulation of data has so markedly accelerated that a reevaluation of the problem promises to prove fruitful. Specifically, the data obtained by the use of electronic amplifying devices to study neural events has raised questions concerning the validity of concepts generated by purely neuroanatomical techniques, and at the same time, the adaptation to subhuman primates of quantitative analysis of problem-solving behavior has stimulated discussion of the validity of concepts derived solely from cliniconeurological material.

Problem of Cortical Organization

First, let us take a look at some neural data and see how they fit current conceptualizations of cerebral organization. Explicitly or implicitly, most of us were trained to think of the cortex as being composed of receiving areas (sensory cortex) that function in some fairly simple fashion to transmit receptor events to adjacent areas of "association" cortex. Here, these neural events are "elaborated" and "associated" with other neural events before being transmitted to the motor areas of the cortex; these motor areas are said to serve as the principal effector mechanism for all cerebral activity. This model was proposed some 75 years ago by Flechsig (33) on the basis of the then available anatomical information. As we shall see, the neural data available today may make it necessary to modify this model considerably.

However, before we can come to grips with a new conception of cortical organization, it is necessary to clarify some definitions. Over the years, many of the terms used in neurology have been imbued with multiple designations. "Neocortex" is such a term. Comparative anatomists use this word to describe the dorsolateral portions of the cerebral mantle since these portions show a *differentially* maximum development in microsmatic mammals (such as primates) as compared with macrosmatic mammals (such as cats). In other branches of the neurological sciences (e. g., see Grossman [40]), the term neocortex has come to cover *all* the cortical formations that reach maximum development in primates. The definition as used in these sciences subsumes portions of the cortex on the medial and basal surface of the cerebral hemisphere, which, though well developed in macrosmatic mammals, do show *some* additional development in primates. Since this mediobasal limbic cortex has been related (74) to behavior of only one part of the neocortex, it seems worthwhile to find an unambiguous term that delimits the dorsolateral cortex. As reviewed in an early publication (99), the cerebral cortex may be classified according to whether or not it passes through a six-layered embryonic stage. The medial and basal limbic structures do not pass through such

a stage and are called "allocortex" and "juxtallocortex"; the dorsolateral portions of the cerebral cortex do pass through such a stage and are called "isocortex".

It has been fashionable to subdivide isocortex according to cytoarchitectonic differences; difficulties in classification have been pointed out (3, 54, 74) that question the immediate usefulness of distinctions based solely on the histological picture of the cortex. We shall, therefore, subdivide isocortex on the basis of thalamocortical relationships since these relationships are determined by several of the most reliable neurohistological techniques available to us: retrograde degeneration of neurons in the thalamus following cortical resection, silver stains, and autoradiography. However, if we are to use this criterion of subdivision of cortex because it is a reliable one, we are forced into looking at the organization of the thalamus as the key to the organization of the cortex. Rose and Woolsey (112) have divided thalamic nuclei into two classes: (1) those receiving large tracts of extrathalamic afferents and (2) those receiving the major portions of their direct afferents from within the thalamus. The former they called extrinsic (primary projection) and the latter, intrinsic (association) nuclei. Thalamocortical connections, demonstrated by retrograde degeneration studies (17, 21, 98, 131), make it possible to differentiate isocortical sectors on the basis of their connections with extrinsic (primary projection) or with intrinsic (association) thalamic nuclei.

It can be seen from Fig. 15–1 that the portions of the cortex labeled as "extrinsic sectors" correspond essentially to those usually referred to as "primary projection areas", while those labeled "intrinsic sectors" correspond essentially to those usually referred to as "association areas". However, the terms "association cortex" and "primary projection areas" have their drawbacks:

1. "Association cortex" implies that in these portions of the cortex convergent tracts bring together excitations from the "receiving areas" of the brain. As we shall see, this implication has been unsupported by fact.
2. Electrophysiological experiments (which will be discussed below) have demonstrated a topographical complexity of organization of the sensory receiving areas, which necessitated labels, such as areas I and II and III. Should the term "primary projection areas" be used to denote the areas I only or should it cover such areas as II and III as well? Additional confusion arises since the intrinsic (association) sectors *do* receive a thalamic projection so that the term "secondary projection areas" has been suggested for these sectors (119). These considerations have led to substituting the currently less loaded terms, "extrinsic" and "intrinsic".

Can the subdivision of cerebral isocortex into extrinsic (primary projection) and intrinsic (association) sectors be validated *when techniques other than histological techniques are used*? Support for the classification comes from electrophysiological data. When receptors are mechanically or electrically stimulated or when peripheral nerves are electrically stimulated, an abrupt change in electrical potential can be recorded from portions of the brain that are connected to these peripheral structures (Figs. 15–2 and 15–3). Under appropriate conditions of deep anesthesia, maps may be constructed on the basis of size of the potential changes evoked and the latency that intervenes between the time of stimulation and the recording of the potential change (Fig. 15–4). As can be seen from the comparison of the maps made by the histological and electrophysiological techniques, there is considerable (though by no means complete) correspondence between various delineations of the extrinsic (primary projection) from the intrinsic (association) sectors of the isocortex.

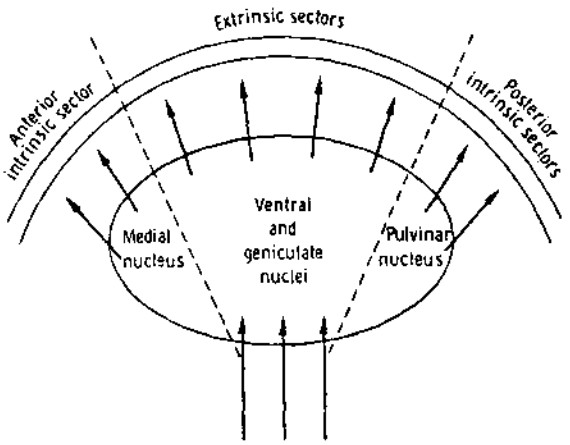


Fig. 15–1 Diagrammatic scheme illustrating the division of isocortex into extrinsic (primary projection) and intrinsic (association) sectors on the basis of thalamic afferent connections. The ventral and geniculate thalamic nuclei that received major direct afferents from extracerebral structures project to the extrinsic sectors; the medial and pulvinar thalamic nuclei do not receive such afferents and project to the intrinsic sectors.

Input-Output Relationships

Note that according to all of the techniques mentioned, input from extracerebral structures reaches the portions of the cortex usually referred to as "motor" as well as those known as "sensory" areas. Electrophysiological experiments demonstrate that somatic afferents are distributed to both sides of the central fissure of primates. Since the *afferents* reaching the precentral motor areas as well as those reaching postcentral sensory areas originate in both skin and muscle nerves (61), the critical differences between the input to the precentral and to the postcentral cortex must yet be determined if the differences in effect of resection of the precentral and postcentral cortex on behavior are to be explained in terms of input. What is important for us here is the

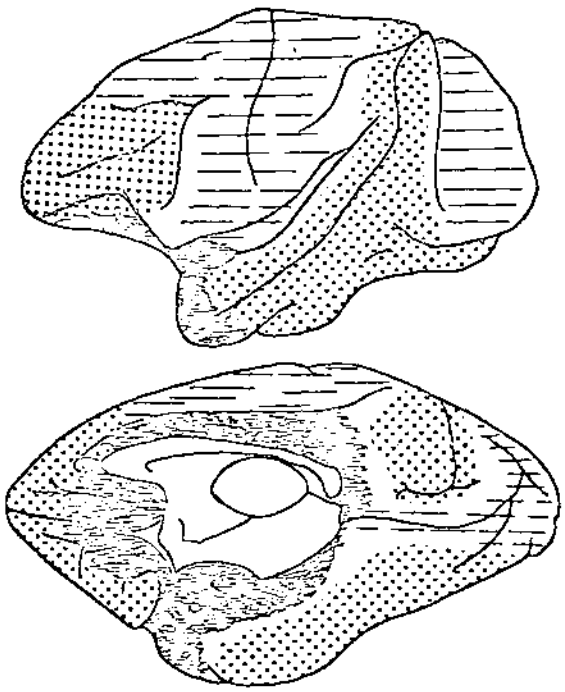


Fig. 15–2 Diagrams of the lateral (above) and mediobasal (below) surfaces of the monkey's cerebral hemisphere showing the divisions discussed in the test. Shading indicates allo-juxtallocortex; hatching indicates extrinsic (primary projection) isocortex; stippling indicates intrinsic (association) isocortex. Boundaries are not sharply delimited; this is, in part, due to minor discrepancies that result when different techniques are used and, in part, to difficulties in classification due to borderline instances and inadequate data (e. g., how should the projections of *n. ventralis anterior* and of *lateralis posterior* be classified?).

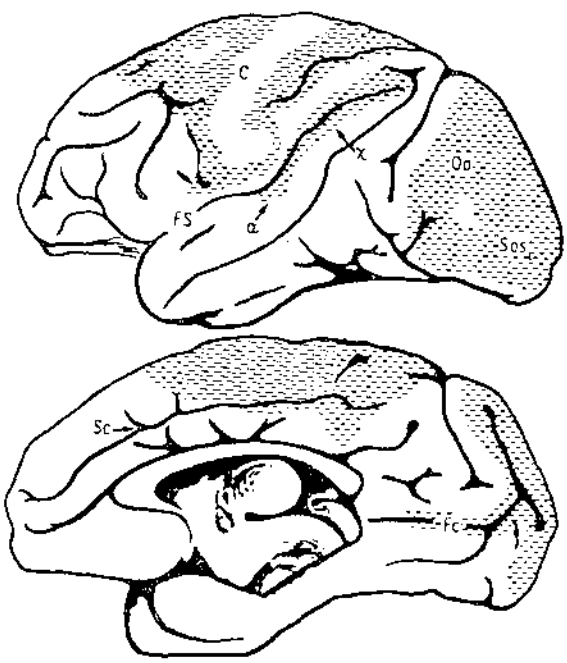


Fig. 15–3 Extrinsic (primary projection) sectors as mapped by staining degenerating axons following thalamic lesions.

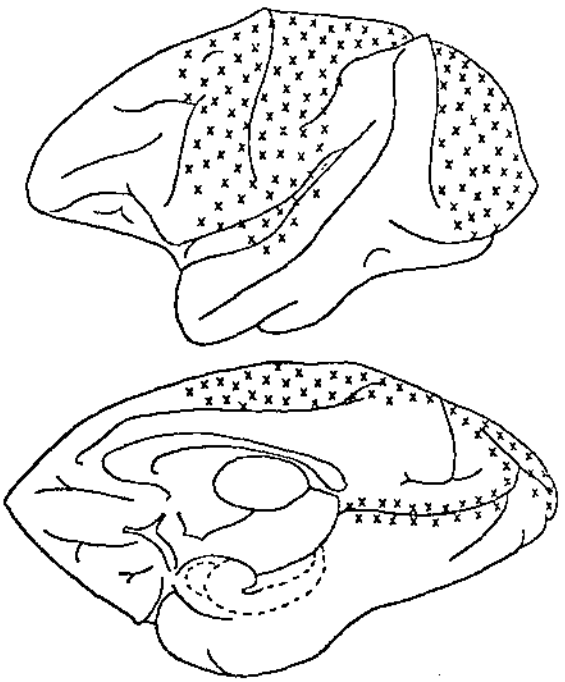


Fig. 15–4 Extrinsic (primary projection) areas as mapped by the abrupt changes in electrical potentials evoked in cortex by peripheral stimulation was compiled from studies using animals sufficiently anesthetized with barbiturates to practically abolish the normally present spontaneous rhythms of potential changes recorded from the brain. Those potential changes were counted that were larger than 50 μV and showed a latency within 3 s of the minimum latency of any abrupt potential change evoked in the particular afferent system investigated. These criteria were chosen as the most likely to indicate major direct afferents from periphery to cortex. The correspondences and minor discrepancies between this figure and Fig. 15–3 indicate the approximate range of such similarities when different techniques and brain diagrams are used.

fact that afferents from the periphery reach motor cortex relatively directly through thalamus, a fact that becomes more meaningful on consideration of the efferents leaving the isocortex.

It was commonly held during the early part of this century that the pyramidal tract takes origin in the motor cortex, especially that portion close to the central fissure. This view was changed with the publication of a monograph by Lassek (55), which thoroughly documents the evidence for a more extensive origin of the pyramidal tract from the entire extent of the precentral as well as from the postcentral cortex of primates. Another conception held during this earlier period regarding the distinction between pyramidal and extrapyramidal has repeatedly been questioned in the light of these and other data. Woolsey (141) and Woolsey et al (142) have shown that the differences in movement brought about by electrical stimulation of the various parts of the precentral cortex may be ascribed to differences in somatotopic relationships rather than

to differences in the complexity of organization of the movement. Thus, Woolsey found that stimulations in the more forward portions of the precentral region, which had formerly been called premotor, activate the axial musculature, while those close to the central fissure activate appendicular musculature. Since axial muscles are larger, the movements they produce appear grosser than those produced by such discrete appendicular muscular units as those found in the hand – one need not invoke different orders of coordination or complexity to distinguish between the posterior and anterior portions of the motor cortex. Therefore, the distinction between motor and premotor cortex fades and, as a result, makes unnecessary the classical distinction between the locus of origin of the pyramidal and extrapyramidal systems that has already been called into question by anatomical data.

On the other hand, evidence from ablation and stimulation experiments in both man and monkey indicates the continued necessity for differentiating precentral motor from postcentral sensory mechanisms (49). These data called for a thorough reinvestigation of the organization of the input-output relationships of the extrinsic (primary projection) system related to somatic structures. Certainly, the distinction cannot be thought of simply in terms of afferents reaching the postcentral and efferents leaving the precentral cortex.

However the marked overlap of input-output is not limited to the somatic extrinsic (primary projection) system. With respect to vision, eye movements can be elicited from stimulation of practically all the visual extrinsic striate cortex (132); these eye movements can be elicited after ablation of the other cortical areas from which eye movements are obtained. With respect to audition, ear movements have been elicited from the auditory extrinsic system (5). From the portion of the cortex implicated in gustation, tongue and chewing movements can be elicited (2, 125); respiratory effects follow stimulation of the olfactory "receiving" areas (46, 99). Thus, an overlap of afferents and efferents is evident not only in the neural mechanisms related to somatic function but also in those related to the special senses. The overgeneralization to the brain of the law of Bell and Magendie (60), which defines sensory in terms of afferents in the dorsalspinal and motor in terms of efferents in the ventralspinal roots, must, therefore, give way to more precise understanding of the differences in internal organization of the afferent-efferent relationship between periphery and cortex to explain differences such as those between sensory and motor mechanisms. A first step to understanding comes from an examination of the functions of the cortex immediately adjacent to and often overlapping that, which receives a direct input from the sensory systems.

Perifissural Cortex: Perceptual Constancy and Motor Skill

Immediately adjacent to and often overlapping the sensory-receiving cortex, there is a perisensory belt that is complex in organization and function. Some understanding of these complexities must be achieved before a clear view can emerge of the mental functions of the intrinsic cortex. Because research has in some respects proceeded further with respect to visual functions than for those of the other special senses, the focus here will be on the perivisual, i. e., peristriate or circumstriate cortex.

As already noted, this cortex shares with the adjacent sensory-receiving striate cortex the property of electrical excitability, i. e., eye movements can be obtained by electrical stimulation of the peristriate cortex (132). There is therefore good reason to regard the peristriate cortex as a possible visual motor cortex. What then might be the functions of a motor cortex that is anatomically interlinked with afferents from a special sense?

A recently completed experiment by Ungerleider et al (129) provides a key to such analysis. In this experiment, the peristriate cortex was extensively resected in monkeys who were tested for their ability to judge the size of squares placed at different distances. Normal monkeys, in making such judgments, take into consideration both the visual angle subtended by the retinal image produced by the square and the cues that signal distance of that square from the eye. After resection of the peristriate cortex, the distance cues proved no longer effective – judgments were based exclusively on retinal image size. The prestriate resection had interfered with the ability of the monkeys to take into account distance cues either because the mechanism of vergence was interfered with or because retinal disparity between eyes was no longer effective. Mountcastle et al (67) have shown that single cells in the posterior parietal cortex just adjacent to the peristriate cortex specifically respond when a monkey reaches for a piece of food provided that food is within reach and "wanted" by the monkey. Hubel and Wiesel (44) and Zeki (143) also found cells in the peristriate cortex that respond when and only when binocular disparity in the retinal image occurs.

There is, thus, sufficient evidence to indicate that the peristriate cortex is involved in the perception of size constancy. As a guiding hypothesis, one might generalize this evidence to suggest that perceptual constancies of various sorts are derived from the operations of the perisensory belts. What then might these operations be? As is the case in vision, they may be of two sorts – a hierarchical abstraction of features (such as disparity) from those more primary in the sensory projection areas, or they may depend on motor mechanisms, such as vergence. Perhaps both types of mechanisms are involved. The question remains open for future research to explore.

What is clear already, however, is a similarity between the functions of the perisensory cortex of the special sensory systems and the perisensory cortex of the somatosensory system. We ordinarily call the somatoperisensory cortex the precentral motor cortex, but this motor cortex shares with other perisensory systems the task of providing skills in responding to invariant properties in the sensory input. Such invariances – constancies – must be abstracted or apprehended. We know from clinical observation and experiment that somatosensory experience (e. g., Kruger [49]) is predicated on the movement of stimulating event with respect to the sensory surface. When that movement is passively produced, an abstractive process can be inferred to take place. However, in the living sentient organism, the movement is almost invariably the result of an active motor performance that prehends rather than abstracts. (An example of the rare exceptions to such active participation is the experience of being groomed or petted, and such experiences do not ordinarily give rise to the perceptual constancies that we perceive. Rather, such experiences are felt as providing comfort with little reference to what it is that is doing the providing.)

In the clinic, these issues come to a head in the syndrome "apraxia", defined as an inability to execute movements (such as manipulating objects) in the absence of paralysis. There is a long history (reviewed by Hécaen and Albert [41]) of clinical observation of apractic disorders that has posed the following question: are such disorders produced by lesions of the frontal cortex anterior to the precentral motor strip, or by lesions of the parietal cortex, posterior to the postcentral sensory strip, or both? The most recent observations (e. g., Kimura, [48]) suggest that a motor apraxia can be distinguished from a sensory apraxia and that either the frontal or the parietal sites may therefore be involved in the production of apraxia. The question raised by these finding, however, is whether the motor and sensory aspects of the apraxias are intrinsic to the syndrome or whether they are due to involvement of the adjacent primary motor and sensory cortices. This question becomes especially pertinent in view of an anatomical observation (21), which shows that in the monkey the orderly projections of thalamus to precentral and postcentral peri rolandic cortex are the reverse of those to the surrounding frontal and parietal cortex. These histological data and considerations derived from comparative neuroanatomy suggest that the Rolandic central fissure originated on the dorsal margin of the hemisphere, or even on its medial surface, and only recently in phylogenetic histoy, intruded and extended into the lateral surface. The question is raised therefore as to whether the apraxias are due to involvement of elaborations of peri rolandic tissue in man, or of the adjacent intrinsic cortex into which the Rolandic cortex has intruded. This intrinsic cortex was originally a continuous strip (e. g., in the cat, it is the suprasylvian gyrus), which may account for the past difficulty in distinguishing the apraxias originating from lesions of the anterior portions of the strip (frontal in primates) and those originating from lesions of the posterior portions (parietal in primates). When the entire strip is removed in monkeys (Forward, unpublished thesis), a loss of skill results in which a previously learned simple movement of a lever in a T slot becomes disrupted in the absence of any demonstrable muscular weakness or paralysis.

In summary, the neuroanatomical and neuropsychological results reviewed in this section suggest that the perifissural cortex is a sensorimotor cortex, which processes the relationship of the organism to external space. Henry Head gave the name epicritic to such processing because it results in the effective use of local sign (locating and manipulating events and objects in space and time). The perifissural cortex forms a continuous band of tissue that surrounds the three major cerebral fissures: sylvian, Rolandic, and calcarine. The continuity between perirolandic and pericalcarine cortex is established at the apex of the cortical convexity (in the monkey, this is at the confluence of the intraparietal, superior temporal, and lunate sulci). The continuity between perirolandic and perisylvian cortex lies at the foot of the central fissure.

In primates including man, the growth of the cortex surrounding these major fissures has split the remaining cortex into two subdivisions: (1) a posterior focussed on the inferior parietal lobule on the lateral surface and the precuneus on the medial (connected via the medial extension of the confluence between intraparietal and lunate sulci) and (2) the cortex covering the poles of the frontal and temporal lobes (interconnected by the fibers of the uncinate faciculus and adjacent to the orbitofrontal – anterior insular – periamygdaloid cortex, which is a part of the limbic systems). The functional connectione of these divisions and subdivisions of the cortical mantle have been most clearly demonstrated by strychnine neuronography (8, 102) and have been confirmed histologically by the use of silver staining techniques (45, 59).

The behavioral evidence showing that the perifissural cortex processes "external space" while the remaining cortex processes "self" is so extensive that only the highlights are listed here:

1. Beginning with the precentral (prerolandic) cortex, Pribram et al (100) showed that the environmental consequences of movement, not movements or muscle contractions per se, are encoded in this "motor" cortex (see review by Pribram [86]).
2. The postcentral and superior parietal cortex deals with the somatosensory (haptic) discrimination of objects in external space (10, 50, 67, 96).
3. The pericalcarine cortex deals with visual processing (see Weiskrantz [135] for review) and its extension into the inferior temporal gyrus, with making visual discriminations (see Pribram [88], for review).

4. The posterior perisylvian cortex is involved in auditory processing (see Neff [70] for review) and its extension into the superior temporal gyus with auditory discriminations (25, 26, 28).
5. The anterior perisylvian cortex in the depths of the fissure and extending forward to the temporal pole and orbital surface of the frontal lobe processes gustatory information (2, 95) and is also involved in olfactory (12, 13) and temperature discriminations (16).

In short, a useful hypothesis at this state of knowledge, based on the experimental results and observations reviewed thus far, is that the perifissural cortex of primates including man is concerned with the construction and use of a stable relationship between the organism and his external environment. This stable relationship is based on the complementation of organism and environment (35, 86), which rests on the consideration that perceptual constancies are achieved in a manner similar to the achievement of motor skills. Complementation may involve the constitution of a neural representation of the constant relationship or, alternatively, the constitution of an environmental representation as when musical instruments, bicycles, skis and skates, or tools are produced. The perifissural cortex of the primate orients him outward.

This is the first tentative conclusion that can be reached from current experimental results when the ubiquitous occurrence of afferent-efferent overlap in the *extrinsic* (primary projection) systems is taken seriously. A second, which we shall now pursue in detail, is the possibility that the intrinsic (association) systems need not be considered as association centers upon which pathways from the extrinsic sensory sectors converge to bring together neural events anticipatory to spewing them out via the motor pathways. The analysis of the organization of these systems relies largely on psychosurgical experiment. Let us turn, therefore, to such experiments and those that manipulate cerebral isocortex by electrical stimulation and observe the effects of such manipulations on behavior.

Method of Classifying the Functions of the Intrinsic Cortex

As noted earlier, the data that gave rise to the impression that local brain resections do not result in any specifiable deficiency in neural function have been superceded. In my laboratory alone, some 1,500 behaviorally tested rhesus monkeys have been subjected to selective brain operations over the past quarter century. Such studies provide ample evidence that specific impairments in mental functions are produced by local experimental lesions. However, these impairments are deficiencies in *processing* the signals occurring in the extrinsic systems into "information". Information processing critically involves coding that organizes the events occurring in the extrinsic cortex.

The experimental analysis of the problem-solving behavior of primate psychosurgical preparations has, contrary to popular opinion, uncovered a host of very specific behavioral disturbances. The technique by which these brain-behavior relationships were classified is called the method of the "intersect of sums" (74), an extension of what Teuber named the method of "double dissociation" of signs of brain trauma in man. The intersect of sums method is essentially a "multiple dissociation" method that depends on classifying the behavioral deficit produced by cortical ablations into *yes* and *no* instances on the basis of a criterion, then plotting on a brain map the total extent of tissue associated with each of the categories *ablated: deficit* and *ablated: no deficit*, and finally finding the intersect of those two areas (essentially subtracting the noes from the *yeses-plus-noes*). This procedure is repeated for each type of behavior under consideration. The resulting map of localization of disturbances is then validated by making lesions restricted to the site determined by the intersect method and showing that the maximal behavioral deficit is obtained by the restricted lesion (see Table 15–1 and Fig. 15–5).

Once the neurobehavioral correlation has been established by the intersect of sums technique, two additional experimental steps are undertaken. First, holding the lesion constant, a series of variations is made of the task on which performance was found defective. These experimental manipulations determine the limits over which the brain-behavior correlations hold and thus allow reasonable constructions of models of the psychological processes impaired by the various surgical procedures.

Second, neuroanatomical and electrophysiological techniques are engaged to work out the relationships between the brain areas under examination and the rest of the nervous system. These experimental procedures allow the construction of reasonable models of the functions of the areas and of the mechanisms of impairment. Two major divisions of the intrinsic cortex have been delineated by these operations: a posterior and a frontal.

Modal Specificity within the Posterior Intrinsic Systems

Between the sensory projection areas of the primate cerebral mantle lies a vast expanse of parietotemporopreoccipital cortex. Clinical observation has assigned disturbance of many gnostic and language functions to lesions of this expanse. Experimental psychosurgical analysis in nonhuman primates, of course, is limited to nonverbal behavior; within this limitation, however, a set of sensory-specific agnosias (discrimination disabilities and losses in the capacity to identify cues) have been produced. Distinct regions of primate cortex have been shown to be involved in each of the modality-specific mnemonic functions: anterior temporal in gustation

Table 15–1 Simultaneous Visual Choice Reaction[a]

Operates without deficit			Operates with deficit			Nonoperate controls		
	Pre	Post		Pre	Post		Pre	Post
OP 1	200	0	PTO 1	120	272	C 1	790	80
OP 2	220	0	PTO 2	325	F	C 2	230	20
OP 3	380	0	PTO 3	180	F	C 3	750	20
LT 1	390	190	PTO 4	120	450	C 4	440	0
LT 2	300	150	T 1	940	F			
H 1	210	220	T 2	330	F			
HA	350	240	VTH 1	320	F			
FT 1	580	50	VTH 2	370	F			
FT 3	50	0	VTH 3	280	F			
FT 4	205	0	VTH 4	440	F			
FT 5	300	200	VT 1	240	F			
FT 6	250	100	VT 2	200	F			
DL 1	160	140	VT 3	200	890			
DL 2	540	150	VT 4	410	F			
DL 3	300	240	VT 5	210	F			
DL 4	120	100						
MV 1	110	0						
MV 2	150	10						
MV 3	290	130						
MV 4	230	10						
MV 5	280	120						
CIN 1	120	80						
CIN 2	400	60						
CIN 3	115	74						
CIN 4	240	140						

[a] Pre- and postoperative scores on a simultaneous visual choice reaction of the animals whose brains are diagrammed in Fig. 15–5, indicating the number of trials taken to reach a criterion of 90% correct on 100 consecutive trials. Deficit is defined as a larger number of trials taken in the "retention" test than in original learning. (The misplacement of the score H 1 does not change the overall results as given in the text.)

(2), superior temporal in audition (28, 136), inferior temporal in vision (7, 65), and occipitoparietal in somesthesis (96, 139). In each instance, the ability to discriminate learning prior to surgical interference, is lost to the subject postoperatively and great difficulty (using a "savings" criterion) in reaquisition is experienced, if task solution is possible at all.

The behavioral analysis of these discrimination deficits is still underway, but the current view of the psychological process involved can be discussed. Perhaps the easiest way to communicate this view is to describe some of the observations, thinking, and experiments that led to the present view.

Information Processing: The Search, Sampling, and Selection of Sensory Invariants

All sorts of differences in the physical dimensions of the stimulus, for example, size (Fig. 15–6), are discriminated less after a bilateral lesion of the cortex of the inferior gyrus of the temporal cortex (64), but this deficit differs from that obtained from resections of the peristriate cortex. The type of dysfunction that occurs is illustrated in the following story.

One day while testing monkeys with such lesions at the Yerkes Laboratories at Orange Park, Florida, I sat down to rest from the chore of carrying a monkey the considerable distance between home cage and laboratory. The monkeys, including this one, were failing miserably at the visual discrimination task being administered. It was a hot, muggy, typical Florida summer afternoon and the air was swarming with gnats. My monkey reached out and cought a gnat. Without thinking, I also reached for a gnat – and missed. The monkey reached out again, caught a gnat, and put it in his mouth. I reached out – missed! Finally, the paradox of the situation forced itself on me. I took the beast back to the testing room. He was as deficient in making visual choices as ever, but when no choice was involved, the monkey's visually guided behavior appeared to be intact. This gave rise to the following experiment (Fig. 15–7), which Ettlinger (31) carried out. On the basis of the informal observation, we made the hypothesis that choice was the crucial variable responsible for the deficient discrimination following inferotemporal lesions. As long as a monkey does not have to make a choice, his visual performance should remain intact. To test this hypothesis, monkeys were trained in a Ganzfeld made of a translucent light fixture large enough so the animal could be physically inserted into it. The animal could press a lever throughout the procedure

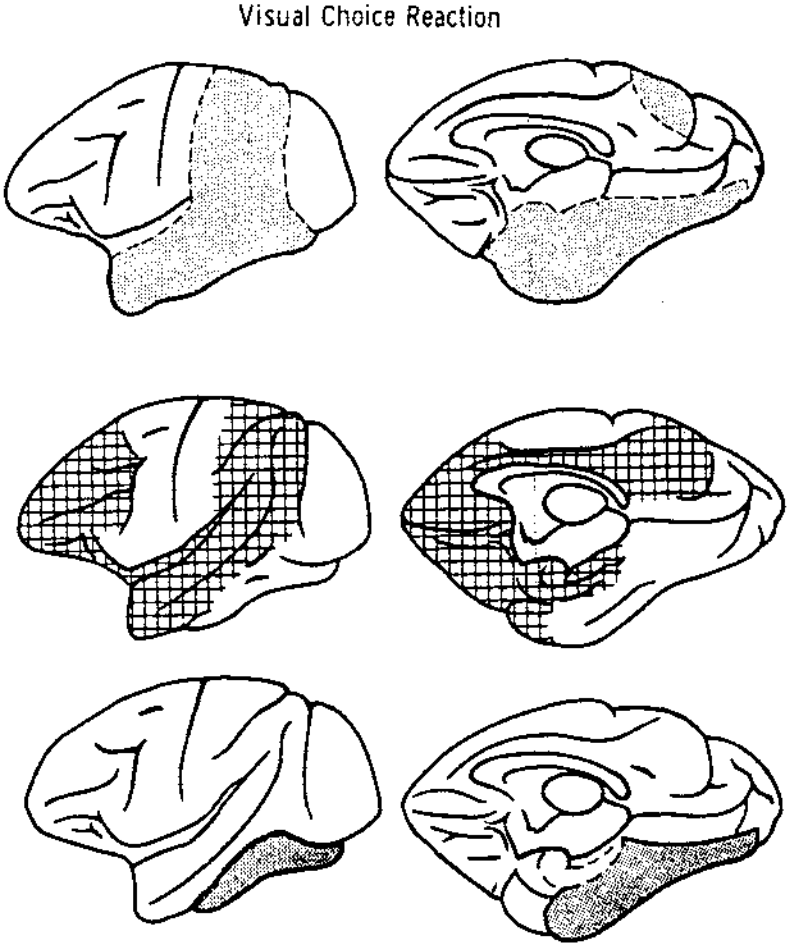


Fig. 15–5 Mapping of intrinsic cortex. The upper diagrams represent the sum of the areas of resection of all of the animals grouped as showing deficit. The middle diagrams represent the sum of the areas of resection of all of the animals grouped as showing no deficit. The lower diagrams represent the intersect of the area shown in black in the upper diagrams and that *not* checkerboarded in the middle diagrams. This intersect represents the area invariably implicated in visual choice behavior in these experiments.

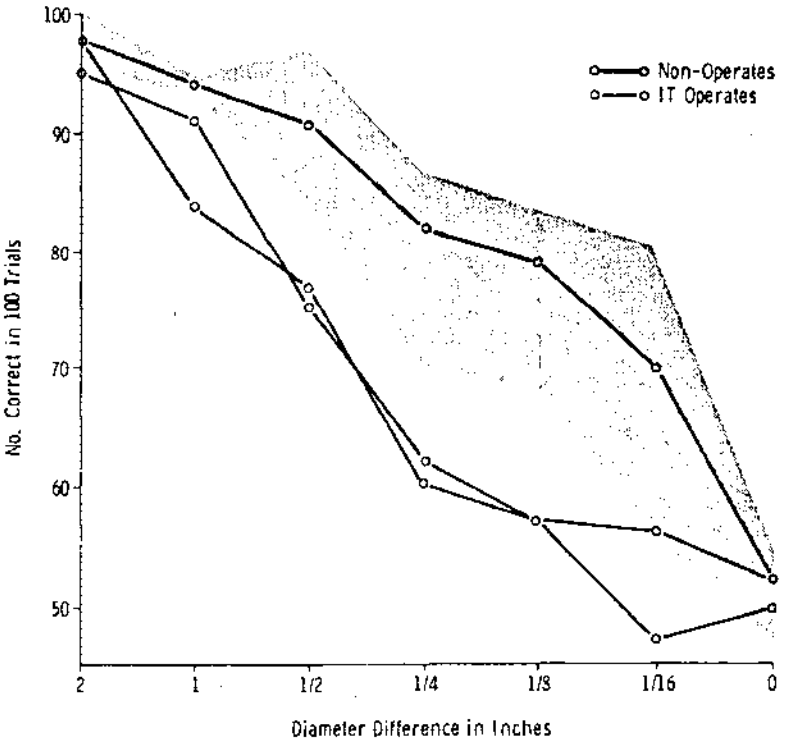
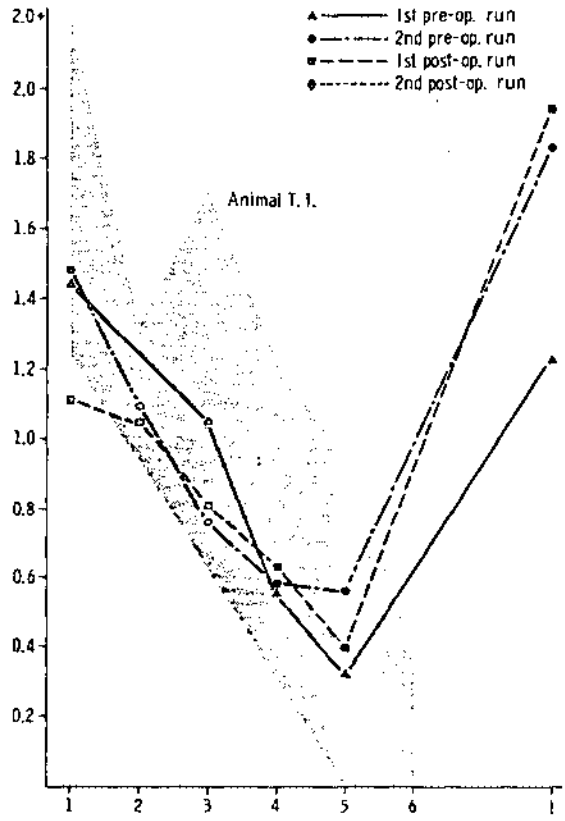


Fig. 15–6 Scores for two operates and four controls on the first run of size discrimination. Shaded area indicates the range of performance of the four nonoperate controls. IT operates-monkeys with resections of inferior temporal cortex.



◀ Fig. 15–7 Single manipulandum performance curves of a single animal in a varying brightness situation. Shaded area indicates variability among groups of four animals.

but was rewarded only during the period when illumination was markedly increased for several seconds at a time. Soon, response frequency became maximal during this "bright" period. Under such conditions, no differences in performance were obtained between inferotemporally lesioned and control animals. The result tended to support the view that if an inferotemporally lesioned monkey did not have to make a choice, he would show no deficit in behavior since in another experiment (65) the monkeys failed to respond differentially to differences in brightness.

In another instance (104), we trained the monkeys on a very simple object discrimination test: an ashtray versus tobacco tin (Fig. 15–8). These animals had been trained for 2 or 3 years before they were operated on and therefore were sophisticated problem-solvers; this, plus ease of task, accounts for the minimal deficit in the simultaneous choice task. (There are two types of successive discrimination: in one, the animal has either to go or not to go, and in the other he has to go left or right.) When given the same cues successively, the monkeys showed a

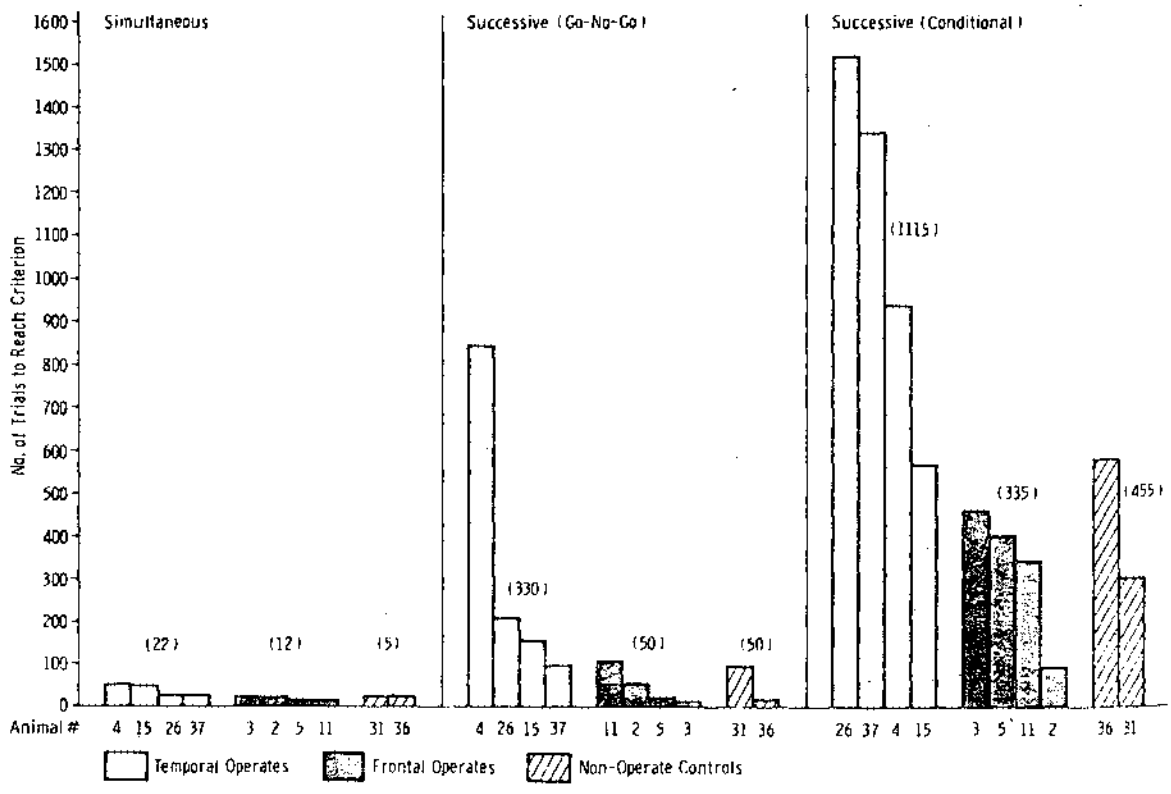


Fig. 15–8 Comparison of learning scores on three types of object discrimination by three groups of monkeys. Note that though the cues remain the same, changing the response that was demanded increased the deficit of the inferotemporal groups.

deficit when compared with their controls, despite this demonstrated ability to differentiate the cues in the simultaneous situation.

This result further supported the idea that the problem for the operated monkeys was not so much in "seeing" but in identifying the *use* of what they saw. Not only the stimulus conditions per se but the whole range of response determinants appear involved in specifying the deficit. To test this idea in a quantitative fashion, we next asked whether the deficit would vary as a function of the *number* of alternative choice possibilities in the situation (76). The hope was that an informational measure of the deficit could be obtained with such a multiple choice problem. Actually, something very different appeared when the number of errors was plotted against the number of alternatives (see Fig. 15–9).

If one plots repetitive errors made before the subject finds a peanut – i. e., the number of times a monkey searches the same cue – versus the number of alternatives in the situation, one finds there is a hump in the curve, a stage where control subjects make many repetitive errors. The monkeys do learn the appropriate strategy, however, and go on to complete the task with facility. What intrigued me was that during this stage the monkeys with inferotemporal lesions were doing better than the controls! This was paradoxical with respect to all previous data. As the test continued, however, after the controls no longer made so many errors, the lesioned subjects began to

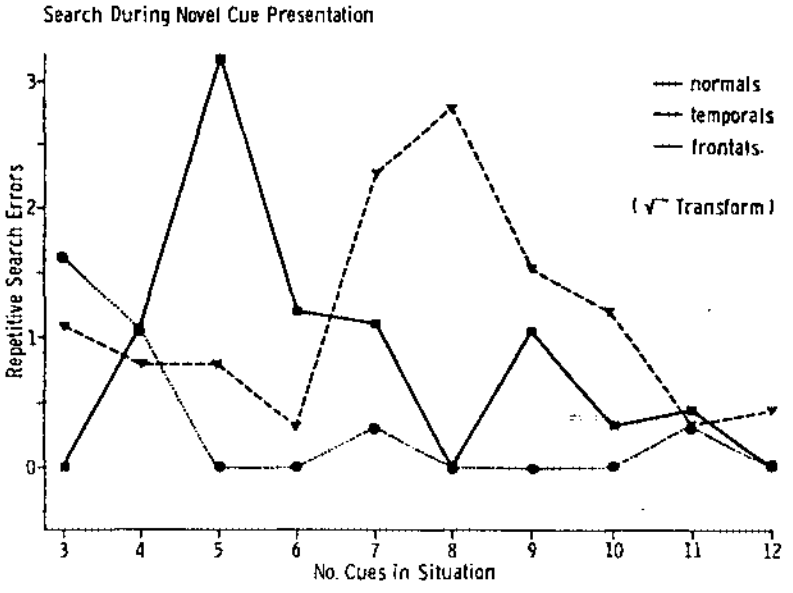


Fig. 15–9 Graph of the average number of repetitive errors made in the multiple object experiment during those search trials in each situation when the additional, i. e., the novel, cue is first added.

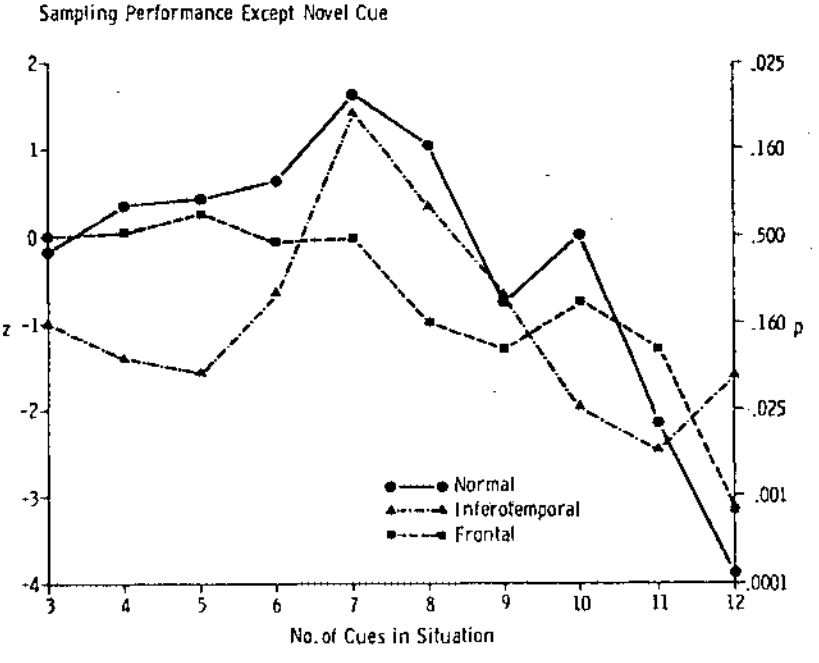


Fig. 15–10 Graph of the average proportion of objects (cues) that are sampled (except novel cue) by each of the groups in each of the situations. To sample, a monkey had to move an object until the content or lack of content of the food well was clearly visible to the experimenter. As was predicted, during the first half of the experiment the curve representing the sampling ratio of the posteriorly lesioned group differs significantly from the others at the 0.024 level (according to the nonparametric Mann-Whitney U test).

accumulate an error "hump" even greater than that shown earlier by the controls.

When a (mathematical) stimulus sampling model was applied to the analysis of the data, a difference in sampling was found to account for these accumulations of errors (Fig. 15–10). The monkeys with inferotemporal lesions showed a lowered sampling ratio; they sampled fewer cues during the first half of the experiment. Their defect can thus be characterized as a restriction in the visual field; however, the limitation is not in the visual-spatial field but in the information-processing field, i. e., in the number of alternatives they can sample or handle at any one time.

In short, the modality-specific defect that results from a posterior intrinsic cortex lesion appears to produce a true agnosia: an information-processing defect best described as a restriction on the number of alternatives (defined as the invariant properties that characterize the problem situation) searched and sampled (86, 88).

Modal Specificity Within the Frontal Intrinsic System

The second major sector of intrinsic cortex is part of an extensive set of neural systems that lie on the medial and basal surface of the brain and extend forward to include the poles of the frontal and temporal lobes (see Pribram [75] and Nauta [69]). This frontolimbic portion of the hemisphere though interrelated phylogenetically and ontogenetically is cytoarchitecturally diverse, and it thus comes somewhat as a surprise that lesions in various locations of the system produce a unitary effect on behavior, which is sharply distinguished from that produced by lesions of the intrinsic cortex of the posterior convexity.

As noted in the previous section, differential discriminations are uniformly impaired by the posterior lesions, but the defects are location specific for sensory mode. In the same manner, lesions of the frontolimbic cortex, irrespective of location (dorsolateral frontal, mediofrontal, cingulate, orbitofrontal temporal polar, and hippocampal) have all been shown to produce disruption of performance of the delayed alternation task (101, 105, 110); though location specificity is shown when variations of the task are used (see below). The alternation task demands that the subject alternate his response between cues (for example, between two places or between two objects) on successive trials separated by a time interval during which the places or objects are hidden from view. On any trial, the correct response is dependent on the outcome of the previous response (whether the monkey had found a peanut in the place or under the object he had chosen).

Variations of the alternation task are numerous and have been especially helpful in distinguishing the functions of different portions of the frontolimbic forebrain. A major variation, called the delayed response task, consists of showing the monkey where the peanut is being hidden from view and randomizing the placement instead of alternating it. Defective performance of the delayed response task is produced *only* by lesions of the dorsolateral frontal cortex (for review, see Pribram [69, 83]).

Another variation of the alternation task is to demand that the subject alternate between going to a single cue and witholding his response, i. e., not going to that cue on the succeeding trial. Defective performance on this "go/no-go" variation of the alternation task is produced by both ventrofrontal and orbitofrontal temporal polar resections (63, 101). However, the effects of these two lesions can be separated by still other variations of the task. In these, cues are presented one at a time, i. e., successively as in the "go/no-go" version, but two different cues are used and the subject's response is made contingent on which cue is presented. Thus, he may be asked to "go" when one cue is presented but withold his response when the other cue is presented. Or he may have to "go" to a box on the *right* to obtain a peanut when faced with one cue and "go" to a box on the *left* when the other cue is tendered. Such successive discrimination problems have distinguished between the ventrofrontal and orbitofrontal temporal polar lesions on the basis of specificity of cues. The effects of orbitofrontal temporal polar resection are nonsensory specific but have been shown to be related to the reinforcing properties of the cues (14, 71, 124). The effects of ventrofrontal lesions, on the other hand, are cue specific to the point that lesions of the lip of the frontal lobe affect successive discriminations cued by kinesthetic stimuli, while those adjacent to the arcuate sulcus involve exteroceptive (visual and auditory) performance.

Taken together, these results indicate that a topographical organization can be distinguished in the functions of the frontal intrinsic cortex. Dorsolaterally placed lesions affect delayed response performance, which has been shown to depend on somatosensory (spatial) cues; ventrally, tasks dependent on kinesthetic (motor) cues are disrupted. In between, around the arcuate sulcus, tasks involving exteroceptive (visual and auditory) stimuli are affected. After orbitally and medially located lesions, the interoceptive limbic connection becomes prepotent.

However, these relationships to modality are very different from those of the intrinsic cortex of the posterior convexity. Note that the relationships are all established by the use of variations of the alternation procedure. Lesions of the posterior intrinsic cortex produce no deficit whatsoever on any alternation task. Thus, the modal specificity of the frontal intrinsic cortex is superimposed on some more basic unitary function shared by and restricted to the frontolimbic forebrain. Let us next examine this function in the following section.

Attaining Assurance: Organizing Responses to Variations in Experiences

The most direct explanation of the basic disturbance produced by lesions of the frontal intrinsic cortex on delayed alternation, delayed response, and a variety of successive discrimination tasks is that short-term memory is disrupted. The term "short-term memory" is ambiguous, however, since it has been used in a variety of ways. For instance, clinical evidence shows that a type of short-term memory usually referred to as iconic, echoic, buffer, or immediate memory is impaired by lesions of the extrinsic and intrinsic systems of the posterior convexity of the brain (133). The deficit produced by lesions of the frontal intrinsic cortex (and related systems) is different and has been labeled a disruption of *"working memory"* (79, 84, 86, 87). The alternation task demands that the subject alternate his reponses between two cues (for example, between two places or between two objects on successive trials). On any trial, the correct response is dependent on keeping in memory the outcome of the previous response. This suggests that the critical variable that characterizes the task is its temporal organization. In turn, this leads to the supposition that the disruption of alternation behavior produced by frontolimbic lesions results from an impairment of the process by which the brain achieves the temporal organization of behavior. This supposition is, as we shall see, in part confirmed by further analysis, but severe restrictions on what is meant by "temporal organization" arise. For instance, skills are not affected by frontolimbic lesions, nor are discriminations of melodies. Retrieval of long-held memories also is little affected. Rather, shorter term mnestic processes are singularly involved. In animal experiments, these are demonstrated especially clearly when tasks demand matching from memory a cue (as in the delayed response variation of the problem) or outcome of the prior trial (as in the classical delayed alternation task) that in the past has shown some complexity in the regularity of its recurrence. Rather than identify an invariant property, the organism must keep track of recurring regularities in the variability of the situation. This is best demonstrated by manipulating the delayed alternation task in a special way. Instead of interposing equal intervals between trials (R-5" – L-5" – R-5" – L-5" – R-5" – L-5" ...) as in the classical task, couplets of RL were formed by extending the intertrial interval to 15" before each R trial (R-5" – L-15" – R-5" – L-15"! – R-5" – L-15" ...). Immediately, the performance of the frontally lesioned monkeys improved and was indistinguishable from that of their controls (106, 109). I interpret this result to mean that for the subject with a bilateral frontal ablation, the alternation task becomes something like what this page would seem were there no spaces between words. The spaces, and the holes in doughnuts, provide some of the structure, the parcellation, parsing of events (doughnuts, alternations, and words) by which they become codable and decipherable (93).

Table 15–2 Percentage of Alternation as a Function of Response and Outcome of Preceding Trial[a]

	Preceding trial[b]			
S	A-R	A-NR	NA-R	NA-NR
Normal				
394	53	56	40	45
396	54	53	36	49
398	49	69	27	48
384	61	83	33	72
Total	55	68	34	52
Frontal				
381	49	51	41	43
437	42	46	27	26
361	49	48	38	35
433	43	39	31	32
Total	46	46	33	33

[a] Comparison of the performance of frontally ablated and normal monkeys on alternations made subsequent to reinforced (R) and nonreinforced (NR) and an alternated (A) and nonalternated (NA) response.
[b] A, alternated; NA, did not alternate; R, was rewarded; and NR, was not rewarded.

More has been learned about the reasons for the deficiency in *working memory* by carefully and extensively analyzing the performance of monkeys with resections of frontal intrinsic cortex in the delayed alternation task.

Thus, Wilson (140) and Pribram et al (106) examined the occasions on which errors were made by the monkeys – did more errors result from a failure in alternation or from an inability to process the outcome of previous behavior, i. e., whether the trial had brought reinforcement or nonreinforcement? In one experiment, both lids over the food well opened simultaneously, but the monkey could obtain the peanut only if he had opened the baited well. Thus, the monkey was given "complete" information on every trial, and the usual correction technique could be circumvented. In the other experiment, an automated computer-controlled apparatus (85) was used. The results were analyzed according to whether the response of the monkey depended on the prior correct or incorrect response or whether the monkey alternated his behavior independently of the location of the peanut. In this manner, the relationship between an error and the trial preceding that error was determined. Notice (Table 15–2) that for the normal monkey the condition of reinforcement and nonreinforcement of the previous trial makes a difference, whereas for the frontally lesioned monkey this is not the case. Both normal and frontal subjects tried to alternate about equally, but frontal subjects are uninfluenced by the rewarding or nonrewarding consequences of their behavior. A similar result was obtained with the multiple choice experiment discussed earlier (76). Here also,

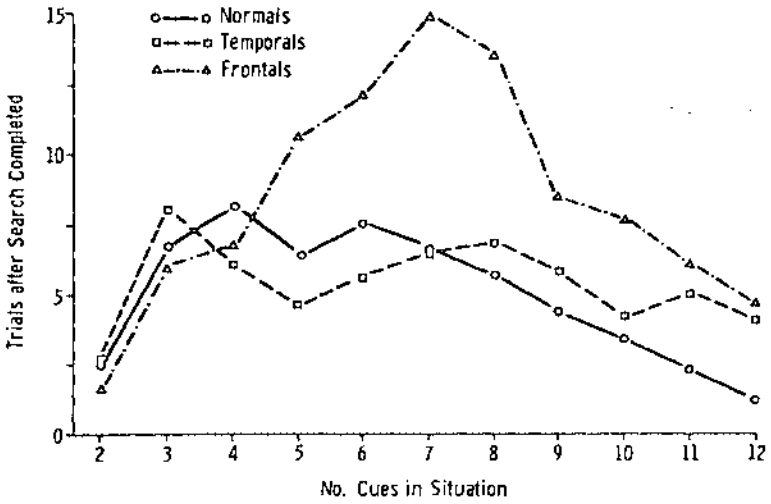


Fig. 15–11 Graph of the average number of trials to criterion taken in the multiple object experiment by each group in each of the situations after search was completed, i. e., after the first correct response. Note the difference between the curves for the controls and for the frontally operated group, a difference that is significant at the 0.05 level by an analysis of variance ($F = S.19$ for 2 and 6 df) according to McNemar's procedure performed on normalized (by square root transformation) raw scores.

this inefficacy of outcomes to influence behavior is demonstrated; it is illustrated (Fig. 15–11) by an increased number of trials to criterion after the monkeys have first found the peanut. The procedure calls for the strategy of return to the same object for five consecutive times, i. e., to criterion. The frontally lesioned animals are markedly deficient in doing this. Again, we see that the conditions of reinforcement are relatively ineffective in shaping behavior once the frontal intrinsic cortex has been removed so that the monkeys' behavior is relatively random when compared to that of normal subjects (94). Behavior of the frontally lesioned monkeys thus appears to be minimally controlled by its (repeatedly experienced and therefore expected) consequences.

In still other clinical and animal experiments, it was shown that the autonomic components of the orienting reaction are wiped out by lesions of the frontal intrinsic cortex (47, 58). Further, in the absence of such visceroautonomic boosters, the orienting event fails to register and the subject remains reactive to its "novelty" – the origin of the distractibility and hyperreactivity associated with the frontal syndrome.

Finally, a series of computer-controlled experiments (10, 11) has shown that monkeys with resections of frontal cortex are impaired whenever *any* aspect of a task becomes *variable*. In short, the frontal intrinsic cortex is involved in attaining assurance by keeping track of and computing regularities that recur in *variables* whether they be of external or internal (e. g., appetitive) origin. More or less regularly recurring variations in experience are called "episodes," and a great deal of evidence from experiments on human memory has accumulated (90, 114, 115, 127) to show that "episodic" learning and knowing can be clearly separated from the more automatic learning and knowing involved in perceptual and motor skills. Episodic learning demands a visceroautonomic booster or controlled, concentrated effort; the learning of skills demands repetitious persistence and practice to apprehend the invariances that characterize the situation. The psychosurgical and neuropsychological evidence reviewed here has shown that episodic or "working" memory involves the frontal and that the attainment of automatic skills involves the posterior intrinsic systems.

Dimensions of Isocortical Processing

These operations of intrinsic cortex become modulated and differentiated further by corticipetal influences from the brainstem core: mesencephalic reticular, diencephalic (hypothalamic), and forebrain (basal ganglia) in particular. The experiments that demonstrate these influences were inspired by the observation in man that certain lesions of frontal and parietal cortex result in "neglect." Humans and animals who show neglect fail to respond toward contralateral stimuli especially when the stimulation is bilateral (amorphosynthesis). Similarly, neglect can be observed when two stimulations are produced in the contralateral field – only the more rostral of the two elicits a response (extinction). In monkeys, the specific sectors of cortex involved in neglect surround the inferior limb of the arcuate sulcus of the frontal cortex (visual neglect) and the inferior parietal lobule (somatosensory neglect). Recall that in the discussion of apraxia (p 308) it was noted that the Rolandic fissure extends into a region that in nonhuman primates extends continuously from front to back. The cortex that is involved in neglect in primates apparently partakes of this origin and has been split by the intrusion of the central fissure.

In their extensive experimental attack on this problem, Heilman and his associates have demonstrated a relationship between the orienting reaction (an indicator of arousal) and the neglect syndrome obtained from the inferior parietal cortex (reviewed by Heilman and Watson, [43]) and a relationship between intention (as indicated by readiness) and the neglect syndrome obtained from the frontal cortex (42, 134). Heilman's data taken together with those reviewed by Pribram and McGuinness (103) indicate that these frontal and parietal sectors are intimately related to the controls on attention that

originate in the basal ganglia and limbic formations of the forebrain. This relationship has an anatomical substrate as was shown by Pribram and MacLean (102) using strychnine neuronography and more recently with horseradish peroxidase (HRP) by Mesalum et al (62). The relationship is both with subcortical formations that project to the limbic forebrain (such as the mesencephalic reticular formation – locus ceruleus, raphe nuclei, and pretectal region – and intralaminar nuclei of the diencephalic thalamus) and with the limbic cortex per se (cingulate gyrus). Heilman's group has shown neglect to follow lesion of all of these structures.

How are we to conceptualize these data on neglect, which relate limbic cortex and corebrain structures to a select portion of the cortical convexity? One possibility is to distinguish an extrapersonal from intrapersonal dimension. Recall that the perifissural cortex dealt primarily with the organism's construction and use of constancies developed from its interaction with the environment. These constancies are ordinarily projected and attributed to the environment by a process similar to that, which allows the projection of sound to occur forward of and between two speakers in a stereophonic music system (6, 86).

By contrast, the neglect syndrome points to a process by which interactions between organism and environment are referred back to the organism – or at the minimum, that the distinction of an extrapersonal domain is not made. In support of this interpretation are the patients with limbic lesions in the anterior temporal (and inferior frontal?) region who write interminable voluminous descriptions of their subjective experiences – a syndrome that appears to be the opposite of neglect. Tentatively, at least, the delineation of an extrapersonal-intrapersonal (or esthetic-ethical) dimension may provide a suitable heuristic for further study.

The existence of such a dimension has previously been postulated to account for the differences in effects of frontal and parietal lesions (126). A carefully designed experiment (executed by Brody and Pribram [10]) to test this proposal showed, however, that only its extrapersonal-parietal portion could be confirmed. The studies on neglect that were described above suggest that the locus of the intrapersonal portion had been misplaced in the dorsolateral frontal cortex and indicate a more ventral and posterior frontal and inferior parietal locus for the intrapersonal process.

In summary of these data on the localization of functions in the cerebral isocortex, mention must be made of the striking assymmetry of effects of lesions of the two cerebral hemispheres in man. This assymmetry has recently captured the attention of neuroscientists and behavioral scientists to such an extent that evidences of other localizations have been almost totally ignored. Good reviews of the assymmetry literature are available (e.g., Dimond and Blizard [30], Dimond and Beaumont [29]) so here, only a few comments will be tendered.

1. Assymmetry in function between the hemispheres can be shown to be present in the auditory mode even in monkeys when sufficiently complex tasks (auditory delayed matching from sample) are used (25, 26).
2. There is general agreement that in most right-handed persons elaborate speech is primarily a function of the left hemisphere and that visuospatial manipulations are more impaired when lesions occur in the right hemisphere.
3. There is less agreement as to what might be the basis for this assymmetry of function, but in the immediate past those working most intensively in this area of investigation have been concluding that the left hemisphere (in ordinary right-handed persons) is an analytic executive that programs action. It is this executive function that provides seriality to psychological processes since to act it is necessary to perform sequentially.
4. By contrast, visuospatial processing is more parallel in nature. Furthermore, evidence has recently begun to accumulate that affective feeling is assymmetrically involved by lesions restricted to one or the other hemisphere. Lesions of the right hemisphere often lead the patient to become more analytic and therefore dysphoric while lesions of the left hemisphere, though often considerably more debilitating, leave the patient euphoric. Parallel, simultaneous processing, experiencing more holistically, appears to generate positive feelings while analytic processing appears to generate negative feelings.

Once again, to provide a basis for further inquiry, let us encapsulate this huge and varied body of evidence by tentatively suggesting that hemispheric assymmetry in man reflects an effective-affective dimension.

These tentative identifications of "dimensions" allow us to conclude these sections on the localization of functions of the cerebral isocortex. A frontoposterior dimension is reflected in the distinction between the processing of episodically related events to attain assurance on the one hand (frontal), and image and information processing on the other (posterior). This distinction becomes refined in the interaction between frontolimbic and convexal cortex into an intrapersonal-extrapersonal dimension where extrapersonal processes are a function of the intrinsic cortex surrounding the perifissural cortex and intrapersonal processes devolve on the intrinsic cortex more closely related to limbic and corebrain formations. In man, these dimensions become further differentiated by an effective-affective (left-right) dimension involving hemispheric assymmetry. Effective action is perforce serial because of the limited central and motor competency of the organism. Serial ordering is not limited to action on the environment, however. Speech and conceptual action (analysis) also partake of sequentiality. Thus, both extrapersonal and intrapersonal processes are regulated by the effective-affective dimension. The affective aspects enter by virtue of the fact that the more parallel, simultaneous processing performed

by the right hemisphere apparently results in euphoria while analytic processing is apt to result in dysphoria.

So much for localization per se. We need now to examine more closely the mechanisms by which these localizable processes come into being.

An Alternative to the Transcortical Reflex

Models of cerebral organization of the functions of the intrinsic cortex heretofore have been based to a large extent on clinical neurological data and have been formulated with the "reflex" as prototype. Such models state that input is organized in the extrinsic "sensory," elaborated in the intrinsic "associative," and from there relayed to the extrinsic "motor" sectors. According to this view, deficits in function result from disconnections of these sectors from one another. As already pointed out, the afferent-efferent overlap in the extrinsic (primary projection) system makes such notions of cerebral organization suspect. A series of neuropsychological studies by Lashley (53), Sperry (118, 119), Chow (18), Evarts (32), and Wade (130), in which the extrinsic (primary projection) sectors were surgically cross-hatched, circumsected, or isolated by large resections of their surround with little apparent effects on behavior, has cast further doubt on the usefulness of such a "transcortical" model. Additional difficulties are posed by the negative electrophysiological and anatomical findings whenever direct connections are sought between the extrinsic (primary projection) and intrinsic (association) sectors (9, 102). These data focus anew our attention on the problem faced repeatedly by those interested in the relationship between cerebral functions and mental processes. Experimentalists who followed Flourens in dealing with the hierarchical aspects of cerebral organization – e. g., Munk (68) von Monakov (66), Goldstein (39), Loeb (57), and Lashley (51) – have invariably come to emphasize the importance of the *extrinsic* (primary projection) sectors not only in "sensorimotor" behavior but also in the more complex mental processes. Each investigator has had a slightly different approach to the functions of the *intrinsic* (association) sectors, but the viewpoints share the proposition that the intrinsic sectors do not function independently of the extrinsic. The common difficulty has been the conceptualization of this interdependence between intrinsic (association) and extrinsic (primary projection) systems in terms other than the transcortical "reflex" model – a model that became less cogent with each new experiment.

Is there an alternative that meets the objections levied against the transcortical "reflex" yet accounts for currently available data? I believe there is. The hierarchical relationship between intrinsic (association) and extrinsic (primary projection) systems can be attributed to a convergence of the *output* of the two systems at a subcortical locus rather than to a specific input from the extrinsic cortex to the intrinsic. A considerable body of evidence supporting this alternative is already available. Data obtained by Whitlock and Nauta (138) and Reitz and Pribram (111), using silver staining and electrophysiological techniques, show that *both* the intrinsic and extrinsic sectors implicated in vision by neuropsychological experiments are *efferently* connected with the motor structures, such as the basal ganglia and superior colliculus. Lesions of these motor structures have produced effects very similar to those obtained when the comparable intrinsic cortex is resected (113, 123). On the other hand, lesions of their input channels through the intrinsic thalamic nuclei fail to interfere with discriminative behavior (19, 63, 72, 129). Thus, the specific effects on behavior of lesions of the intrinsic (association) systems are replicated when the *output* is to a subcortically located neural mechanism. This output, in turn, affects input to the extrinsic (primary projection) systems either directly or through the efferent control of the receptor (e. g., in vision, Spinelli and Pribram [121], Lassonde et al [56]). According to these new data, the "associative" functions of the central nervous system are to be sought at convergence points throughout the central nervous system, especially in such motor structures as the basal ganglia and not solely in the intrinsic (association) cortex.

The Brain Controls its Input

Much effort has been channeled into an attempt to specify the nature of such efferent control mechanisms. To this end, a series of experiments was undertaken to find out how the intrinsic cortex might affect the processing of visual information. It is appropriate to begin with some facts – or rather lack of facts – about the neuroanatomical relationships of the inferotemporal cortex. There is a dearth of neurological evidence linking this cortex directly to the known visual system, the geniculostriate system. There are no direct pathways to the inferotemporal cortex from the visual cortex or the geniculate nucleus. Connections can be traced via fibers that synapse twice in the preoccipital region, but connections also exist between the visual cortex, and the parietal lobe, the excision of which does not result in visual agnosia (as shown above). In addition, massive circumsection of the striate cortex does not permanently impair visual discrimination (19, 22, 97, 129), although as noted, size constancy becomes disrupted (128). Further evidence that these "corticocortical" connections are not the critical ones can be seen from the following experiment (Table 15–3). A crosshatch of the inferotemporal cortex was performed (much as Sperry [119] had done earlier for the striate cortex), and no deficit was found either in visual learning or in performance. On the other hand, undercutting the inferotemporal cortex

made a vast difference: it precluded both learning and performance in visual tasks. This result indicates that the relationships critical to performance of the visual discriminations are most likely to be corticosubcortical (108, 129). That this is indeed the case has been shown by making lesions (15) within the basal ganglia in the region of the projections from the inferotemporal cortex as determined electrophysiologically (111) and reproducing the visual discrimination deficit ordinarily obtained from resections of the inferotemporal cortex.

Table 15–3 Comparison of the Effects of Undercutting and Crosshatching Infero-Temporal Cortex of Monkeys on Their Performance in Several Discriminations

	Animal	3 vs 8	R vs G	3 vs 8
Crosshatch	158	380	82	0
	159	180	100	0
	161	580	50	0
	166	130	0	0
Undercut	163	[1014]	100	300
	164	[1030]	200	[500]
	167	704	50	0
	168	[1030]	150	[500]
Normal	160	280	100	0
	162	180	100	0
	165	280	100	0
	170	350	100	0

The proposal that the critical relations of the intrinsic cortex are centrifugal, or efferent, has been tested by electrophysiological experiments. Instead of resections, chronic electrical stimulations of intrinsic cortex were performed (121). Records of electrical responses evoked by paired flashes were made from the striate cortex in awake monkeys (Fig. 15–2). The response to 50 such paired flashes were accumulated (averaged) on a computer. The flash-flash interval was varied from 25 to 200 ms. The top traces were recorded prior to the onset of stimulation and the lower ones after electrical stimulation of the frontal or inferotemporal intrinsic cortex had begun. Note that with cortical stimulation the recovery function is depressed by inferotemporal stimulation, i. e., recovery is delayed. During stimulation of frontal intrinsic cortex, the opposite effect is obtained.

Figure 15–13 shows the average of such effects in five subjects. Thus, chronic stimulation of the inferotemporal cortex produces a marked increase, and stimulation of the frontal cortex a decrease in the processing time taken by cells in the visual system.

A parallel experiment in the auditory system was performed. In this study, made with cats, removals of the auditory homolog of the inferotemporal cor-

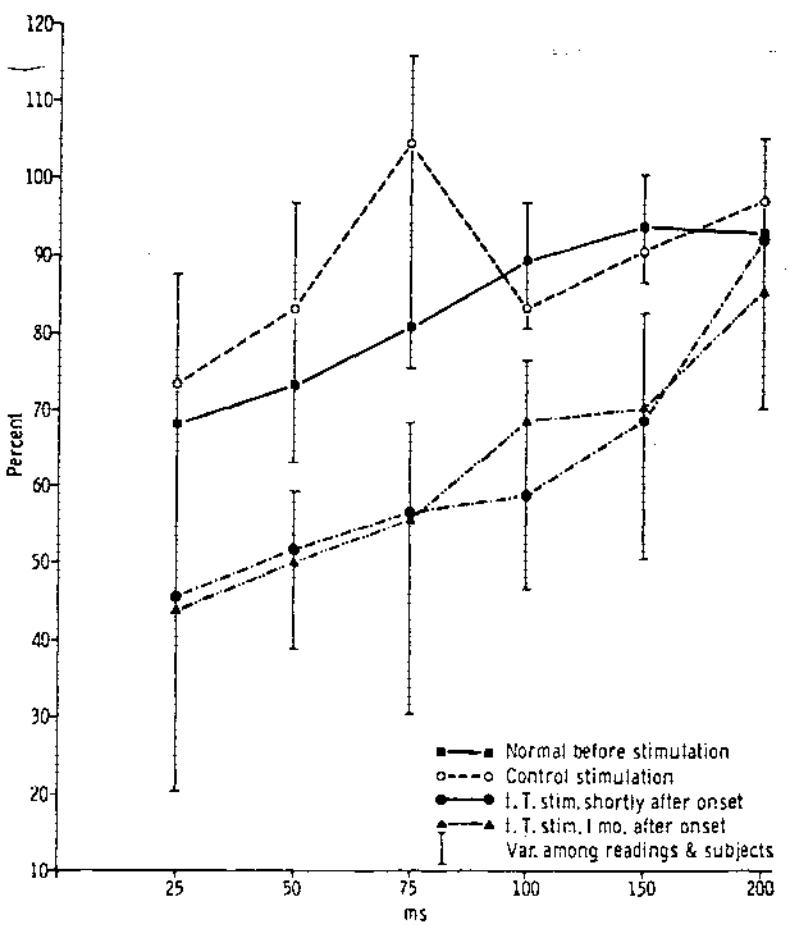


Fig. 15–12 A plot of the recovery functions obtained in five monkeys before and during chronic cortical stimulation: relative amplitude of the second response as a function of interflash interval.

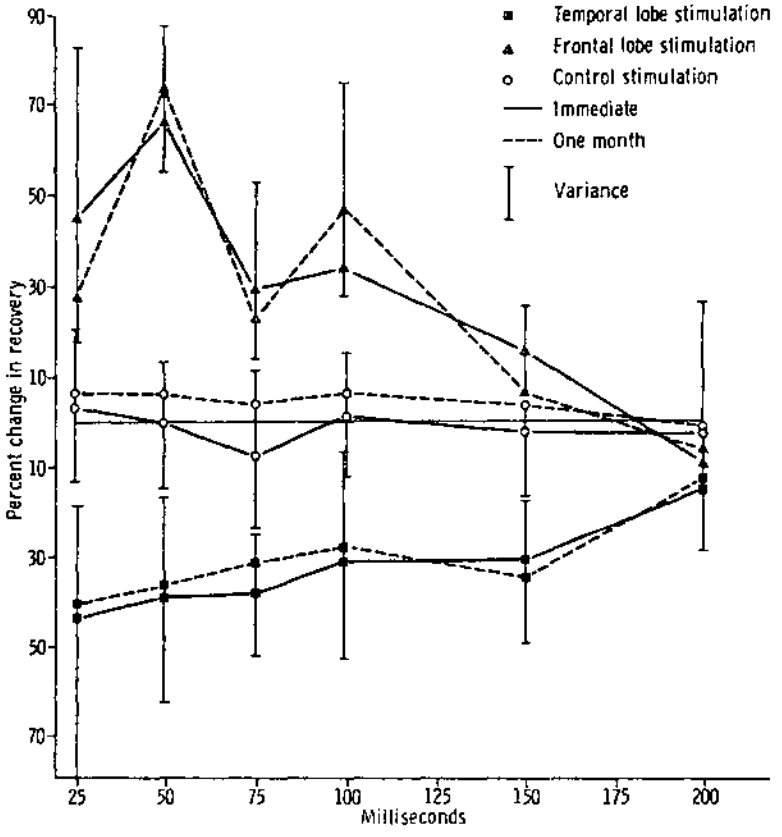


Fig. 15–13 A plot of the percent change in recovery for all subjects in the various experiments. It is thus a summary of the findings.

tex were performed. Dewson (24) has shown that resection of the cortex impairs complex auditory discrimination (speech sounds), leaving simple auditory discriminations (pitch and loudness) intact. In addition, resection shortens paired-click recovery cycles recorded as far peripherally as the cochlear nucleus. Control resections of the primary auditory projection cortex and elsewhere have no such effect. Thus, there is evidence that chronic stimulation of the posterior intrinsic cortex selectively prolongs, while ablation selectively shortens, the recovery time of cells in the related primary sensory projection system.

These results have been extended in both the auditory and visual modes. Microelectrode experiments have shown alterations of visual receptive fields recorded from units at the optic nerve, geniculate, and cortical levels of the visual extrinsic system when the intrinsic cortex is electrically stimulated (56, 122).

The anatomy of the corticofugal pathways from the intrinsic cortex that are responsible for such control over sensory input was also examined. In the auditory system, the fibers lead to the inferior colliculus and from there (in part via the superior olive) to the cochlear nucleus (27). From the inferotemporal cortex, fibers lead to the putamen as already noted, and to the pretectal-collicular region; frontal intrinsic cortex projects to the caudate nucleus. The pathways to the extrinsic sensorimotor systems from the basal ganglia are currently under study with autoradiographic techniques. Preliminary results show that the extrinsic systems are influenced through connections from the globus pallidus (which receives the input from caudate and putamen) to the reticular nucleus of the thalamus, which in turn influences the extrinsic thalamus nuclei (116).

In general terms, the results of these experiments show that the efferents from posterior intrinsic cortex tend to reduce, and those from the frontal intrinsic cortex tend to enhance the number of sensory input channels simultaneously engaged. This is probably accomplished by inhibition and disinhibition of the ongoing interneuronal regulatory processes within the afferent channels (56). When the number of sensory channels simultaneously engaged is few, the channel can be conceived as multiplexed, i.e., each channel can carry different patterns of signals and thus more information can be conveyed at any moment. Thus, the effects of the operations of the intrinsic cortex may be conceptualized as increasing or decreasing the information processing competency of the extrinsic sensorimotor systems (78).

Distribution of Information and the Functions of Extrinsic Systems

This is not the first time in the history of experimental brain research that data have led investigators of mental functions to focus on the primary projection systems. Munk (68), von Monakov (66), and Lash-

ley (52) pursued this course from an early emphasis on the "association" to a later recognition of the importance of the organization of the input systems. Of special interest in this pursuit are the experiments of Lashley that demonstrated that pattern vision remains intact after extensive resection – up to 85% – of the visual extrinsic cortex. Such experiments have been frequently repeated (e. g., Galambos et al [36], Chow [20]). The results make it imperative to infer that input information becomes widely distributed within the visual system. This inference is amply supported by direct evidence that distribution indeed does occur.

For example, in one experiment, monkeys were trained to discriminate between a circle and a set of vertical stripes by pressing the right or left half of a plastic panel upon which the cues were briefly projected (for 0.01 ms). Transient electrical responses were meanwhile recorded from small microelectrodes. Electrical responses were related by computer analysis to the stimulus, response, and reinforcement contingency of the experiment (107). Thus, we could distinguish from the record whether the monkey had looked at a circle or at the stripes, whether he had obtained a reward or made an error, and whether he was about to press the right or the left leaf of the panel. Interestingly enough, not all of these brain patterns were recorded from all of the electrode locations: from some, input-related patterns were obtained best; from others, the reinforcement-related patterns were derived; from still others the patterns were response related. This was despite the fact that all placements were within the extrinsic visual system, which is characterized anatomically by being homotopic with the retina. Therefore, not only are optic events distributed widely over the system but response and reinforcement-related events are reliably encoded in the extrinsic cortex. The mechanism by which such homotopic organization can be utilized to distribute input has been detailed by electrophysiological experiments on single units in the visual and other primary sensory areas and has been extensively reviewed elsewhere (86, 88, 91, 92). Therefore, not only are optic events distributed widely over the system but response and reinforcement-related events are reliably encoded in the extrinsic cortex.

What then is the function of the extrinsic cortex, which has encoded this wealth of experience? Once again, the answer comes from the combined use of psychosurgery and quantitative neuropsychological examination (137). In this instance, a careful resection was performed on a patient to remove a hemangioma, which invaded the cortex. Adjacent cortex appears to have been spared. The result, as expected, was a contralateral homonymous hemianopia. Much to everyones surprise, however, when the patient was tested for possible residual visual function, he performed well above chance in pointing to the location of large objects and even in identifying such coarse grained patterns as large triangles, squares, and circles, the very tasks that are impaired following intrinsic cortex damage. Despite continued excellent performance (to date over a period of several years), the patient insisted that he could not "see" anything, that he was totally blind on the affected side, and that he experienced nothing visual. Several other patients have by now been reported on whom similar observations have been made.

It is clear from these observations that an intact extrinsic cortex is critical to self-awareness, the self-conscious processing of experience. The term a "self-consciousness" or self-reflective consciousness is more appropriate than simply "consciousness" because the latter is ordinarily inferred from the behavior (pointing, identifying) spared in the patients with resections of the visual extrinsic cortex. In animals, self-consciousness is difficult to test (although the ability to recognize oneself in a mirror has been taken as an appropriate indicator – which, by the way, fails with species below the great apes) (see Pribram [89] for review). This may account for the paucity of effects of extrinsic cortex resections when made on nonprimate animals.

Processing Mechanism

Such results surely shake further one's confidence in the ordinary view that input events must be transmitted to the "association" areas for associative learning to be effected. The experimental findings detailed here allow one to specify a possible alternative to account for lesion-produced deficits in mental function. This alternative (78) states that the intrinsic cortex by way of efferent tracts leading to motor structures (such as the basal ganglia) controls and preprocesses the events that occur in the extrinsic systems. Much of this control must, on the basis of the observations on patients described above, be exercised subcortically. In neurophysiological terms (86), when the recovery time of neurons in the sensory projection system is increased by posterior intrinsic cortex stimulation, fewer cells are available at any given moment to receive the concurrent input. Each of a successive series of inputs thus will find a different set of cells in the system available to excitation. There is a good deal of evidence in addition to the ablation experiments noted earlier that there is plenty of reserve capacity – redundancy – so that information transmission is not, under ordinary circumstances, hampered by such "narrowing" of the channel (1). Ordinarily, a particular input excites a great number of fibers in the channel, ensuring replication of transmitted information. Just as lateral inhibition in the retina has the effect of reducing redundancy (4) so the operation of the sensory-specific posterior intrinsic (association) cortex increases the density of information within the input channel.

Conversely, the functions of the frontal intrinsic mechanism enhance redundancy, making more cells available at any given moment to concurrent input.

This diminshes the density of information processed at any moment and enhances temporal resolution.

The model has several important implications. First, the nonrecovered cells, the ones that are still occupied by excitation initiated by prior inputs, will act as a context or short-term memory buffer, against which the current input is matched. A match-mismatch operation of this sort is demanded by models of the process of recognition and selective attention spelled out on other occasions by Craik (23), Sokolov (117), MacKay (59), and Pribram (77, 80, 81, 86, 88). These "occupied" cells thus form the matrix of "uncertainty" that shapes the pattern of potential information, i.e., the "expectancy" that determines the selection of input signals that might or might not occur. The normal functions of the posterior cortex are assumed to increase the complexity of this context, while those of the frontal systems would simplify it and thus allow readier temporal organization and registration.

Second, in a system of fixed size, reduction of redundancy increases the degree of correlation possible with the set of external inputs to the system, while enhancement of redundancy has the opposite effect. The number of alternatives or the complexity of the item to which an organism can attend is thereby controlled (38). This internal alteration in the functional structure of the classic sensory projection system thus allows attention to vary as a function of the spatial and temporal resolution that excitations can achieve, with the result that events of greater or lesser complexity can be attended to. The sharper the spatial resolution, the greater the "uncertainty" and, thus, the more likely that any set of inputs will be sampled for information. Conversely, the greater the temporal resolution, the more likely that attention is focused, and that events become grouped, memorable, and certain. In the extreme, the sharpening of the appetite for information becomes what the clinical neurologist calls stimulus binding. Its opposite is agnosia, the inability to identify events because they fail to fit the oversimplified context of the moment.

Third, this corticofugal model of the functions of the intrinsic (association) systems relieves us of the problem of higher and higher order infinite regress – an association area "homunculus" who synthesizes and abstracts from inputs, only to pass on these abstractions to a still higher "homunculus," perhaps the one who makes decisions, etc. Former ways of looking at the input-output relationships of the brain invariably have come up against this problem (implicit or explicit) of "little men" inside "little men".

According to the model presented here, there is no need for this type of infinite regress. The important functions of perception, decision, etc., are going on within the extrinsic (primary sensory and motor projection) systems. Other brain regions, such as the posterior sensory-specific and the frontal intrinsic systems, exert their effects by altering the functional organization of the extrinsic systems. Thus, these intrinsic systems are not sensory-sensory association systems; they alter the configuration of input-output relationships processed by the sensory-specific projection systems with which they are *associated*. In computer language, the intrinsic systems function by supplying *subroutines* in a hierarchy of programs, subroutines contained within and not superimposed from above on the more fundamental processes. In this fashion, the infinite higher order abstractive regress is avoided. One could argue that in its place a downward regress of subroutines and sub-subroutines is substituted. However, this type of regress, through progessive differentiation, is the more understandable and manipulatable of the two.

A final advantage of the model is that the sensory signal itself is not altered by the associated intrinsic processing mechanism. The invariant properties of a signal are unaffected. It is only the organization of the channel itself – the matrix within which the signal is transmitted – that is altered. Thus, the same signal carries more or less information, depending on the "width" of the channel. The signal carries different *meanings*, depending on the particular structure or organization of the redundancy of the channel.

Concretely, the intrinsic cortex is conceived to preprocess, to program, and to structure an input channel. This is tantamount to saying that the input is being coded by the operation of the intrinsic cortex. In its more fundamental aspects, computer programming is in large part a coding operation. The change from direct machine operation through assembler to one of the more manipulatable computer languages involves a progression from the setting of binary switches to conceptualizing combination of such switch settings in "octal" code and then assembling the numerical octals into alphabetized words and phrases and finally parceling and parsing of phrases into sentences, routines, and subroutines. In essence, these progressive coding operations minimize interference among like events by identifying and registering unique structures among the configurations of occurrence and recurrence of the events.

Thus, the evidence presented here makes it likely that the posterior and frontal intrinsic formations of the forebrain code events occuring within the input systems. The distribution of information (dismembering) within the extrinsic systems implies that the distributed events can become organized and reorganized (re-membered), a process similar to that used by computers when a program organizes events addressed in a random access memory store.

Summary

The advent of electrophysiology has obscured the rich yield of information regarding the cerebral cortex that has been obtained by way of clinical and experimental psychosurgery. Many neurologists and neurosurgeons do not have ready access to the wealth of quantitative neuropsychological data that

has accumulated during the second half of the 20th century, which has often been published in psychological journals. This chapter has attempted to briefly review some highlights of this wealth that bear on the question of cortical function in men.

Isocortex is distinguished from the allocortex and juxtallocortex of the limbic forebrain. Isocortex is then divided according to thalamic input into extrinsic and intrinsic divisions. Extrinsic cortex comprises the classical sensorimotor projection areas. Intrinsic cortex covers the posterior convexity between the projection areas and also the frontal pole.

Evidence is presented that the motor portions of the extrinsic cortex are critical in prehending the constancies, the invariant relationship between organism and environment that characterize not only motor but also perceptual skills. Although the issue is by no means resolved, there are data that suggest that such invariances are indeed prehended by virtue of the actions guided by these motor systems rather than abstracted by some more passive mechanism.

The posterior intrinsic cortex has been shown to consist of sectors, each of which is associated with a specific sensory mode. Paradoxically, however, radically disconnecting the input from the associated sensory mode has surprisingly little effect on the functions ascribed to the intrinsic cortex. By contrast, lesions of structures receiving the output from the intrinsic cortex (such as the basal ganglia) produce effects remarkably similar to those that follow removal of the related cortex. This paradoxical result led to the inference that the intrinsic cortex sends efferents to the input systems, an inference that has been substantiated by a series of electrophysiological experiments.

The functions of the posterior intrinsic systems center on the ability to identify, i. e., choose one invariant organism-environment relationship (i. e., an informative cue) as opposed to another. Evidence was presented that indicates that this function is effected by organizing the neural events taking place in the input systems.

These events reflect not only the input from receptors but also relevant outcomes of actions and properties of the action themselves. The events are encoded in a distributed fashion with no apparent overall organization. Organization is assumed to be achieved by the operation of the efferents from the intrinsic cortex, which emphasize now one constellation of events, now another.

The frontal intrinsic cortex can also be subdivided according to modality. However, the subdivisions are not as clear cut, and some portions (the medial and orbital) are especially closely linked to the limbic forebrain.

The entire frontolimbic sector of the cortex is involved in the processing of recurring regularities in variable relationship between organism and environment, such as eating, drinking, perceiving the appropriate social situations for a particular behavior, and solving problems where external cues present at the time of response are insufficient in themselves to indicate what needs to be done. The mechanism whereby variables are processed appears to be the reciprocal of that by which the processing of invariants is achieved.

Finally, evidence was presented to suggest that the extrinsic cortex is critical to the attainment of self-awareness – self-consciousness. In the same vein, the posterior intrinsic cortex is necessary to cognition – agnosias result when the posterior intrinsic cortex is damaged or resected. As already noted, cognition involves the ability to identify (learn and remember) invariances and to choose among them for a purpose. By contrast, the frontal intrinsic system is critical to the procession of the recurrent regularities of variables that comprises motivated and emotional learning and remembering.

Thus, although psychosurgery yields to electrophysiology when questions of mechanism are asked, more has been learned about brain-behavior relationships from patients and animals with brain lesions that from the application of other disciplines. The opportunities continue to be present especially in the clinic as attested by the recent reports on the role of the visual cortex in consciousness and the vast literature that has accummulated on hemispheric specialization. However, the experimental psychosurgical laboratory also has its contribution to make – take as example the current report that attributes visual constancy to the perivisual cortex. Promise of even greater power is in the offing – the combination of experimental psychosurgery and electrophysiology has as yet not been exploited.

Reference

1. Attneave F: Some informational aspects of visual perception. Psychol Rev 61: 183–193, 1954
2. Bagshaw MH, Pribram KH: Cortical organization in gustation (macaca mulatta). J Neurophysiol 16: 499–508, 1953
3. Bailey P, von Bonin G: The isocortex of man. University Illinois Press, Urbana, Ill 1951
4. Barlow HB: Possible principles underlying the transformations of sensory messages. In: Rosenblith W, (ed): Sensory communication. MIT Press, Cambridge, Mass 1961, 217–234
5. Bechterev von W: Die Funktionen der Nervencentra. Fischer, Berlin 1911, 1859
6. Bekesy G v: Synchronism of neural discharges and their demultiplication in pitch perception on the skin and in hearing. J Acoust Soc Am 31 (3): 338–349, 1959
7. Blum JS, Chow KL, Pribram KH: A behavioral analysis of the organization of the parieto-temporo-occipital cortex. J Comp Neurol 93: 53–100, 1950
8. Bonin G v, Bailey P: The neocortex of macaca mulatta. University Illinois Press, Urbana, Ill 1947
9. Bonin GV, Garol HW, McCullock WS: The functional organization of the occipital lobe. Biol Symp 7: 165–192, 1942
10. Brody BA, Pribram KH: The role of frontal and parietal cortex in cognitive processing: tests of spatial and sequence functions. Brain 101: 607–633, 1978
11. Brody BA, Ungerleider LG, Pribram KH: The effects of instability of the visual display on pattern discrimination learning by monkeys, produced after resections of frontal and inferotemporal cortex. Neuropsychologia 15: 439–448, 1977
12. Brown TS: Olfactory and visual discrimination in the monkey after selective lesions of the temporal lobe. J Comp Physiol Psychol 56: 764–768, 1963
13. Brown TS, Rosvold HE, Mishkin M: Olfactory discrimination after temporal lobe lesions in monkeys. J Comp Physiol Psychol 56: 190–195, 1963

14. Brutkowski S: Prefrontal cortex and drive inhibition. In: Warren JM, Akert K (eds): Frontal granular cortex and behavior. McGraw Hill, New York 1964, 219–241
15. Buerger AA, Gross CG, Rocha-Miranda CE: Effects of ventral putamen lesions on discrimination learning by monkeys. J Comp Physiol Psychol 86 (3): 440–446, 1974
16. Chin JH, Pribram KH, Drake K, Greene LO, Jr: Disruption of temperature discrimination during limbic forebrain stimulation in monkeys. Neuropsychologia, 14: 293–310, 1976
17. Chow KL: A retrograde cell degeneration study of the cortical projection field of the pulvinar in the monkey. J Comp Neurol 93: 313–340, 1950
18. Chow KL: Further studies on selective ablation of associative cortex in relation to visually mediated behavior. J Comp Physiol Psychol 45: 109–118, 1952
19. Chow KL: Lack of behavioral effects following destruction of some thalamic association nuclei in monkey. Arch Neurol Psychiatr 71: 762–771, 1954
20. Chow KL: Integrative functions of the thalamocortical visual system of cat. In: Pribram KH, Broadbent D (eds): Biology of memory. Academic Press, New York 1970, 273–292
21. Chow KL, Pribram KH: Cortical projection of the thalamic ventrolateral nuclear group in monkey. J Comp Neurol 104: 57–75, 1956
22. Christensen CA, Pribram KH: The effect of inferotemporal or foveal prestriate ablation on serial reversal learning in monkeys. Neuropsychologia 17 (1): 1–10, 1979
23. Craik KHW: The nature of explanation. Cambridge University Press, New York 1943
24. Dewson JH, III: Speech sound discrimination by cats. Science 3619: 555–556, 1964
25. Dewson JH III: Preliminary evidence of hemispheric asymmetry of auditory function in monkeys. In: Harnard S, Doty RW, Jaynes J, Goldstein L, Crauthamer G (eds): Lateralization in the nervous system. Academic Press, New York 1977, 63–71.
26. Dewson JH, III, Cowey A: Discrimination of auditory sequences by monkeys. Nature 222: 695–697, 1969
27. Dewson JH III, Noble KW, Pribram KH: Corticofugal influence at cochlear nucleus of the cat: some effects of ablation of insular-temporal cortex. Brain Res. 2: 151–159, 1966
28. Dewson JH III, Pribram KH, Lynch J: Effects of ablations of temporal cortex upon speech sound discrimination in the monkey. Exp Neurol 24: 579–591, 1969
29. Dimond SJ, Beaumont JG (eds): Hemisphere function in the human brain. Wiley, New York 1974
30. Dimond SJ, Blizard DA (eds): Evolution and lateralization of the brain. Ann NY Acad Sci 299: 1977
31. Ettlinger G: Visual discrimination with a single manipulandum following temporal ablations in the monkey. Q J Exp Psychol XI (3): 164–174, 1959
32. Evarts EV: Effect of ablation of prestriate cortex on auditory-visual association in monkey. J Neurophysiol 15: 191–200, 1952
33. Flechsig P: Die Localisation der geistigen Vorgänge insbesondere der Sinnesempfindungen der Menschen. Leipzig 1896
34. Flourens P: Recherches expérimentales sur les propriétés et les fonctions du système nerveux dans les animaux vertèbres. Crevot, Paris 1924, 26–332
35. Fowler CA, Turvey MT: Skill acquisition: an event approach with special reference to searching for the optimum of a function of several variables. Paper presented at CIC Symposium on "Information processing in motor control and learning", Madison, Wisc, April, 1977
36. Galambos R, Norton TT, Frommer CP: Optic tract lesions sparing pattern vision in cats. Exp Neurol 18: 8–25, 1967
37. Gall FJ, Spurzheim G: Research on the nervous system in general and on that of the brain in particular. In: Pribram K. H. (ed): Brain and behavior I. Penguin Books, Middlesex 1969, 20–26
38. Garner WR: Uncertainty and structure as psychological concepts. Wiley, New York, 1962
39. Goldstein K: Die Topik der Großhirnrinde in ihrer klinischen Bedeutung. Disch Z Nervenheilk 77: 7–124, 1923
40. Grossman SP: A textbook of physiological psychology. Wiley, New York, 1967
41. Hécaen H, Albert ML: Human Neuropsychology. Wiley, New York 1978
42. Heilman KM, Valenstein E: Frontal lobe neglect in man. Neurology 22: 660–664, 1972
43. Heilman KM, Watson RT: Mechanisms underlying the unilateral neglect syndrome. In: Weinstein EA, Friedland RP (eds): Advances in neurology, vol 18: Hemi-inattention and hemisphere specialization. Raven Press, New York 1977
44. Hubel DH, Wiesel TN: Receptive fields and functional architecture of monkey striate cortex. J Physiol 195: 215–243, 1968
45. Jones EG: The anatomy of extrageniculostriate visual mechanisms. In: Schmitt FO, Worden FG (eds): The neurosciences third study program. MIT Press, Cambridge, Mass 1973, 215–227
46. Kaada BR, Pribram KH, Epstein JA: Respiratory and vascular responses to monkey from temporal pole, insula, orbital surface and cingulate gyrus: a preliminary report. J Neurophysiol 12: 347–356, 1949
47. Kimble DP, Bagshaw MH, Pribram KH: The GSR of monkeys during orienting and habituation after selective partial ablations of the cingulate and frontal cortex. Neuropsychologia 3: 121–128, 1965
48. Kimura D: Motor control: a multidisciplinary look. Paper presented at 8th annual meeting of the international neuropsychological society, San Francisco, Calif, Feb, 1980
49. Kruger L: Observations on the organization of the sensorimotor cerebral cortex, unpublished Ph. D. dissertation. Yale University School of Medicine, 1954
50. Kruger L, Michel F: A single neuron analysis of buccal cavity representation in the sensory trigeminal complex of the cat. Arch Oral Biol 7: 491–503, 1962
51. Lashley KS: Brain mechanisms and intelligence. University of Chicago Press, Chicago 1929
52. Lashley KS: The problem of cerebral organization in vision. In: Visual mechanisms. Biological symposia. Jacques Cattell Press, Lancaster 1942, vol 7, 301–322
53. Lashley KS: The mechanism of vision. XVIII. Effects of destroying the visual "associative areas" of the monkey. Genet Psychol Monogr 37: 107–166, 1948
54. Lashley KS, Clark G: The cytoarchitecture of the cerebral cortex of Ateles: a critical examination of architectonic studies. J Comp Neurol. 85: 223–305, 1946
55. Lassek AM: The pyramidal tract. Its status in medicine. Charles C, Thomas, Springfield 1954
56. Lassonde M, Prito M, Pribram KH: Intracerebral influences on the microstructure of visual cortex, in preparation
57. Loeb J: Comparative physiology of the brain and comparative psychology. J Murray, London 1901.
58. Luria AR, Pribram KH, Homskaya ED: An experimental analysis of the behavioral disturbance produced by a left frontal arachnoidal endothelioma (meningioma). Neuropsychologia. 2: 257–280, 1964
59. MacKay DM: The epistemological problem for automata. In: Automata Studies. Princeton University Press, Princeton 1956, 235–252
60. Magendie F: Experiences sur les fonctions des racines des nerfs rachidiens. J Physiol Exp 2: 276–279, 1822
61. Malis LI, Pribram KH, Kruger L: Action potentials in "motor" cortex evoked by peripheral nerve stimulation. J Neurophysiol 16: 161–167, 1953
62. Mesalum MM, Van Hoesen G, Pandya DN, Geschwind N: Limbic and sensory connections of the inferior parietal lobule (area PG) in the rhesus monkey: a study with a new method for horseradish peroxidase histochemistry. Brain Res 136: 393–414, 1977
63. Mishkin M: Cortical visual areas and their interaction. In: Karczmar AG, Eccles JC (eds): The brain and human behavior. Springer, Berlin 1972, 187–200
64. Mishkin M, Hall M: Discriminations along a size continuum following ablation of the inferior temporal convexity in monkey. J Comp Physiol Psychol 48: 97–101, 1955
65. Mishkin M, Pribram KH: Visual discrimination performance following partial ablations of the temporal lobe. I. Ventral vs lateral. J Comp Physiol Psychol 47: 14–20, 1954
66. Monakov von C: Die Lokalisation in Großhirn und der Abbau

der Funktion durch korticale Herde. JF Bergmann, Wiesbaden 1914
67. Mountcastle VB, Lynch JC, Georgopoulos A, Sakata H, Acuna C: Posterior parietal association cortex of the monkey: command functions for operations within extrapersonal space. J Neurophysiol 38: 871–908, 1975
68. Munk H: Über die Funktionen der Großhirnrinde: gesammelte Mitteilungen aus den Jahren. Hirschwald, Berlin 1881
69. Nauta WJH: Some efferent connections of the prefrontal cortex in the monkey. In: Warren JM, Akert K (eds): The frontal granular cortex and behavior. McGraw-Hill, New York 1964, 397
70. Neff D: Neural mechanisms of auditory discrimination. In: Rosenblith W. A. (ed): Sensory communication. Wiley, New York 1961, 259–278
71. Oscar-Berman M: The effects of dorsolateral-frontal and ventro-lateral orbitofrontal lesions on spatial discrimination learning and delayed response in two modalities. Neuropsychologia 13 (2): 237–246, 1975
72. Peters RH, Rosvold HE: The effect of thalamic lesions upon spatial delayed alternation performances in the rhesus monkey, unpublished M D thesis. Yale University, 1955
73. Pohl WG: Dissociation of spatial and discrimination deficits following frontal and parietal lesions in monkeys. J Comp Physiol Psychol 82: 227–239, 1973
74. Pribram KH: Toward a science of neuropsychology: (method and data) In: Patton RA (ed): Current trends in psychology and the behavioral sciences. University of Pittsburgh Press, Pittsburgh 1954, 115–142.
75. Pribram KH: Neocortical function in behavior. In: Harlow HF (ed): Neocortical function in behavior. University of Wisconsin Press, Madison 1958, 151–172
76. Pribram KH: On the neurology of thinking. Behav Sci 4: 265–287, 1959
77. Pribram KH: A review of theory in physiological psychology. Ann Rev Psychol: 1–40, 1960
78. Pribram KH: The intrinsic systems of the forebrain. In: Field J, Magoun HW (eds): Handbook of physiology, neurophysiology. American Physiological Society, Washington, DC 1960, vol 2, 1323–1344
79. Pribram KH: A further experimental analysis of the behavioral deficit that follows injury to the primate frontal cortex. Exp Neurol 3: 432–466, 1961
80. Pribram KH: The new neurology: memory, novelty, thought and choice. In: Glaser GH (ed): EEG and behavior. Basic Books, New York 1963, 149–173
81. Pribram KH: Reinforcement revisited: a structural view. In: Jones M (ed): Nebraska symposium on motivation. University of Nebraska Press, Lincoln 1963, 113–159
82. Pribram KH (ed): Brain and behavior II: perception and action. Penguin Ltd, London 1969
83. Pribram KH: Four R's of remembering. In: Pribram K. H (ed): The biology of learning. Harcourt, Brace, and World, New York 1969
84. Pribram KH: Toward a science of neuropsychology: (method and data). In: Patton RA (ed): Current trends in psychology and the behavioral sciences. University of Pittsburgh Press, Pittsburgh, 1954, 115–142. Reprinted in Penguin 1969
85. Pribram KH: DADTA III: an on-line computerized system for the experimental analysis of behavior. Percept Mot Skills 29: 599–608, 1969
86. Pribram KH: Languages of the brain. Prentice-Hall, Englewood Cliffs, NJ 1971
87. Pribram KH: The primate frontal cortex-executive of the brain. In: Luria AR, Pribram KH (eds): Frontal lobes and the regulation of behavior. Academic Press, New York 1973
88. Pribram KH: How is it that sensing so much we can do so little? In: The neurosciences, III. MIT Press, New York 1974, 249–261.
89. Pribram KH: Self-consciousness and intentionality. In: Schwartz GE, Shapiro D (eds): Consciousness and self-regulation: advances in research. Plenum Publishing Corp, New York 1976.
90. Pribram KH: Modes of central processing in human learning and remembering. In: Teyler TJ (ed): Brain and learning. Greylock Press, Stamford Conn 1977
91. Pribram KH: Consciousness and neurophysiology. Fed Proc 37: 2271–2274, 1978
92. Pribram KH: The place of pragmatics in the syntactic and semantic organization of language. In: Temporal variables in speech, studies in honour of Frieda Goldman-Eisler. Janua Linguarum, The Hague, Mouton, Paris 1980.
93. Pribram KH: The role of analogy in transcending limits in the brain sciences. Daedalus, 1980, in press
94. Pribram KH, Ahumada A, Hartog J, Roos L: A progress report on the neurological processes disturbed by frontal lesions in primates. In: Warren JM, Akert K (eds): The frontal granular cortex and behavior. McGraw-Hill, New York 1964
95. Pribram KH, Bagshaw MH: Further analysis of the temporal lobe syndrome utilizing frontotemporal ablations in monkeys. J Comp Neurol 99: 347–375, 1953
96. Pribram H, Barry J: Further behavioral and analysis of the parieto-temporo-preoccipital cortex. J Neurophysiol 19: 99–106, 1956
97. Pribram KH, Blehert S, Spinelli DN: The effects on visual discrimination of crosshatching and undercutting the inferotemporal cortex of monkeys. J Comp Physiol Psychol 62: 358–364, 1966
98. Pribram KH, Chow KL, Semmes J: Limit and organization of the cortical projection from the medial thalamic nucleus in monkey. J Comp Neurol 98: 433–448, 1953
99. Pribram KH, Kruger L: Functions of the "olfactory brain." Ann NY Acad Sci 58: 109–138, 1954
100. Pribram KH, Kruger L, Robinson F, Berman AJ: The effects of precentral lesions on the behavior of monkeys. Yale J Biol Med 28: 428–443, 1956
101. Pribram KH, Lim H, Poppen R, Bagshaw MH: Limbic Lesions and the temporal structure of redundancy. J Comp Physiol Psychol 61: 365–373, 1966
102. Pribram KH, MacLean PD: Neuronographic analysis of medial and basal cerebral cortex. II. Monkey J Neurophysiol 16: 324–340, 1953
103. Pribram KH, McGuinness D: Arousal, activation and effort in the control of attention. Psychol Rev 82 (2): 116–149, 1975
104. Pribram KH, Mishkin M: Simultaneous and successive visual discrimination by monkeys with inferotemporal lesions. J Comp Physiol Psychol 48: 198–202, 1955
105. Pribram KH, Mishkin M, Rosvold HE, Kaplan SJ: Effects on delayed-response performance of lesions of dorsolateral and ventromedial frontal cortex of baboons. J Comp Physiol Psychol 45: 565–575, 1952
106. Pribram KH, Plotkin HC, Anderson RM, Leong D: Information sources in the delayed alternation task for normal and "frontal" monkeys. Neuropsychologia 15: 329–340, 1977
107. Pribram KH, Spinelli DN, Kamback MC: Electrocortical correlates of stimulus response and reinforcement. Science 3784: 94–96, 1967
108. Pribram KH, Spinelli DN, Reitz SL: Effects of radical disconnexion of occipital and temporal cortex on visual behaviour of monkeys. Brain 92: 301–312, 1969
109. Pribram KH, Tubbs WE: Short-term memory, parsing and the primate frontal cortex. Science 156: 1765, 1967
110. Pribram KH, Wilson WA, Connors J: The effects of lesions of the medial forebrain on alternation behavior of rhesus monkeys. Exp Neurol 6: 36–47, 1962
111. Reitz SL, Pribram KH: Some subcortical connections of the inferotemporal gyrus of monkey. Exp Neurol 25: 632–645, 1969
112. Rose JE, Woolsey CN: Organization of the mammalian thalamus and its relationships to the cerebral cortex. Electroencephalogr Clin Neurophysiol 1: 391–404, 1949
113. Rosvold HE, Mishkin M, Szwarcbart MK: Effects of subcortical lesions in monkeys on visual-discrimination and single-alternation performance. J Comp Physiol Psychol 51: 437–444, 1958
114. Schneider W, Shiffrin RM: Controlled and automatic human information processing. I. Detection, search and attention. Psychol Rev 84: 1–66, 1977
115. Shiffrin RM, Schneider W: Controlled and automatic human information processing. II. Perceptual learning, automatic attending, and a general theory. Psychol Rev 84: 127–190, 1977
116. Skinner JE, Yingling CD: Regulation of slow potential shifts in

nucleus reticularis thalami by the mesencephalic reticular formation and the frontal granular cortex. Electroencephalogr Clin Neurophysiol 40: 288–296, 1976
117. Sokolov EN: Neuronal models and the orienting reflex. In: Brazier MAB (ed): The central nervous system and behavior. Josiah Macy, Jr. Foundation, New York 1960, 187–276
118. Sperry RW: Cerebral regulation of motor coordination in monkeys following multiple transection of sensorimotor cortex. J Neurophysiol 10: 275–294, 1947
119. Sperry RW: Preservation of high-order function in isolated somatic cortex in callosum-sectioned cats. J Neurophysiol 22: 78–87, 1959
120. Sperry RW, Miner N, Meyers RE: Visual pattern perception following subpial slicing and tantalum wire implantations in the visual cortex. J Comp Physiol Psychol 48: 50–58, 1955
121. Spinelli DN, Pribram KH: Changes in visual recovery functions produced by temporal lobe stimulation in monkeys. Electroencephalogr Clin Neurophysiol 20: 44–49, 1966
122. Spinelli DN, Pribram KH: Changes in visual recovery function and unit activity produced by frontal and temporal cortex stimulation. Electroencephalogr Clin Neurophysiol 22: 143–149, 1967
123. Sprague JM, Meikle TH, Jr: The role of the superior colliculus in visually guided behavior. Exp Neurol 11: 115–146, 1965
124. Stamm JS: Consequences of prefrontal lesions on locomotor delayed alternation by monkeys. In: Luria AR, Pribram K. H (eds): Frontal lobes and the regulation of behavior. Academic Press, New York 1973
125. Sugar O, Chusid JG, French JD: A second motor cortex in the monkey (Macaca mulatta). J Neuropathol 7: 182–189, 1948
126. Teuber HL: Somatosensory changes after penetrating brain wounds in man. Harvard University Press, Cambridge, Mass 1960
127. Tulving E (ed), Donaldson W: Organization of memory. Academic Press, New York 1972, 423
128. Ungerleider L, Pribram KH: Inferotemporal versus combined pulvinar-prestriate lesions in the rhesus monkey: effects on color, object and pattern discrimination. Neuropsychologia 15: 481–498, 1977
129. Ungerleider L, Ganz L, Pribram KH: Size constancy in Rhesus monkeys: effects of pulvinar, prestriate and inferotemporal lesions. Exp Brain Res 27: 251–269, 1977
130. Wade M: Behavioral effects of prefrontal lobectomy, lobotomy and circumsection in the monkey (Macaca mulatta). J Comp Neurol 96: 179–207, 1952
131. Walker AE: The primate thalamus. University Chicago Press, Chicago 1938
132. Walker AE, Weaver TA, Jr: Ocular movements from the occipital lobe in the monkey. J Neurophysiol 3: 353–357, 1940
133. Warrington EK, Weiskrantz L: An analysis of short-term and long-term memory defects in man. In: Deutsch J. A (ed): The physiological basis of memory. Academic Press, New York, London 1973, 365–395
134. Watson RT, Miller BD, Heilman KM: Nonsensory neglect. Ann Neurol 3: 505–508, 1978
135. Weiskrantz L: Striate and posterior association cortex interactions. In: The neurosciences MIT Press, Cambridge, Mass 1973, vol 3
136. Weiskrantz L, Mishkin M: Effects of temporal and frontal cortical lesions on auditory discrimination in monkeys. Brain 81: 406–414, 1958
137. Weiskrantz L, Warrington EK, Sanders MD, Marshall J: Visual capacity in the hemianopic field following a restricted occipital ablation. Brain 97 (4): 709–728, 1974
138. Whitlock DG, Nauta WJH: Subcortical projections from the temporal neocortex in Macaca Mulatta. J Comp Neurol 106: 185–212, 1956
139. Wilson M: Effects of circumscribed cortical lesions upon somesthetic discrimination in the monkey. J Comp Physiol Psychol 50: 630–635, 1957
140. Wilson WA, Jr: Alternation in normal and frontal monkeys as a function of response and outcome of the previous trial. J Comp Physiol Psychol 55: 701–704, 1962
141. Woolsey CN: Organization of somatic sensory and motor areas of the cerebral cortex. In: Harlow HF, Woolsey CN (eds): Biological and biochemical bases of behavior. University of Wisconsin Press, Madison 1958, 63–81.
142. Woolsey CN, Settlage PH, Meyer DR, Spencer W, Hamuy T, Travis AM: Patterns of localization in precentral and "supplementary" motor areas and their relation to the concept of a premotor area. Res Publ Assoc Res Nerv Ment Dis 30: 238–264, 1952
143. Zeki SM: Representation of central visual fields in prestriate cortex of monkey. Brain Res 14: 271–291, 1969

"Since this manuscript went to press new work from Heilman's group and that of Wright in Australia has shown that in monkeys the neglect syndrome can be reproduced to a large extent by lesions made in the far lateral region of the hypothalamus, lesions which interrupt the nigrostriatal tract. It seems therefore most likely that the neglect syndromes are more closely related to readiness mediated by the basal ganglia system than to arousal which is a function of the amygdala and other anterior limbic structures. The definitions used here are those suggested by Pribram and McGuinness in which arousal is considered to be a phasic response to input while readiness is defined in terms of the tonic behavioral component of the orienting reaction."