Neurobiology of Neocortex
eds. P. Rakic and W. Singer, pp. 177–202
John Wiley & Sons Limited

Changing Concepts of Cortical Connectivity: Parallel Distributed Cortical Networks

P.S. Goldman-Rakic

Section of Neuroanatomy, Yale University
New Haven, CT 06510, U.S.A.

Abstract. Recent advances in anatomical techniques have produced new information about thalamocortical, corticocortical, and cortical-subcortical connections. These new facts are changing our views of cortical organization and providing a basis for cortical modeling and physiological investigations.

INTRODUCTION

Development of neurobiological techniques over the past two decades has made possible unprecedented advances in knowledge about the nervous system. Not the least among these advances has been the ability to trace precisely connections in complex structures like the cerebral cortex. It might seem that the technical advances in circuit mapping have meant merely the confirmation or elaboration of knowledge already known from earlier, less definitive, methods. On the contrary, the new methods have provided genuinely new insights into the organization and function of the cortex and its relationship with the rest of the brain. They have allowed examination of the laminar origins and terminal fields of projection neurons, specification of many of the neurotransmitters and neuropeptides in afferent or efferent cell classes, and analysis of the degree of collateralization, reciprocity, convergence, and divergence of neural circuits. With intracellular injection of tracer substances in physiologically identified neurons or injections in physiologically mapped cortical sites, it has become possible to establish relationships between the anatomical location, morphology, connections, and computational properties of specific cells or cell classes. These advances have made possible the understanding of areal and synaptic circuitry at a level of resolution approaching that achieved in simpler structures. In this background paper, I will discuss some general principles that have emerged from the study of three major classes of cortical circuitry: thalamocortical, corticocortical, and cortico-subcortical fiber systems of the association cortices. The subject of local neuronal circuits within cortical areas will be reviewed in the background paper by E.G. Jones (this volume). Since the cerebral cortex does not contain a single molecule or transmitter that cannot be found in other structures of the same brain or in brains of many other mammals and nonmammals, we must look to features of its areal and synaptic organization for answers to the question of what it is that makes the cortex uniquely qualified to regulate the highest functions of language, perception, representational memory, and logic.

ORGANIZATION OF THALAMOCORTICAL CIRCUITRY

Multiple Innervation and Convergence

The application of retrograde axonal transport techniques to the analysis of cortical afferents has brought about some fundamental changes in our way of thinking about thalamocortical organization. Prior to the advent of axonally transported tracers, most studies using retrograde degeneration methods indicated that each cytoarchitectonic area of the cortex received input from one and only one major "specific" thalamic nucleus. Only the intralaminar ("nonspecific") nuclei were thought to provide a diffuse projection to the cortex. However, in a reinvestigation of the thalamic connections of the monkey frontal lobe, Kievet and Kuypers (1977) reported that large injections of HRP into major regions and gyri of the frontal cortex labeled longitudinal bands of cells that extended anteroposteriorly across several thalamic nuclei including the ventral anterior nucleus (VA), the mediodorsal (MD), the medial pulvinar, limitans, and suprageniculate nuclei. The results of more recent studies with smaller injection sites confirm multiple thalamic inputs to the same areas (Baleydier and Mauguiere 1985; Goldman-Rakic and Porrino 1985). For example, we placed HRP injections in seven different, widely separated cytoarchitectonic subdivisions of prefrontal cortex and the anterior cingulate cortex (Goldman-Rakic and Porrino 1985). The results of retrograde tracing showed that for every injection site, large or small, retrogradely labeled cells were present along virtually the entire anterior-posterior extent of the thalamus, e.g., in the anteromedial, ventral anterior, mediodorsal, and medial pulvinar nuclei (Fig. 1). These findings were confirmed by placing anterograde tracers into specific thalamic nuclei. For example, injections of tritiated amino acids or WGA-HRP into the medial pulvinar nucleus anterogradely label axons in prefrontal areas long thought to receive their input exclusively from the mediodorsal nucleus (Baleydier and Mauguiere 1985; Giguere and Goldman-

Rakic 1985). If the medial pulvinar were the only other thalamic nucleus to project to the prefrontal cortex, one might consider whether the boundaries of the mediodorsal nucleus should be extended to include the medial pulvinar. However, the multiple inputs from other nuclei as diverse and distinct as the anteromedial and nucleus limitans argues against redefinition.

The prefrontal association cortex of the frontal lobe is not unique with respect to multiple thalamic innervation and is not a special exception to the classical one-to-one thalamocortical scheme. It is well accepted that area

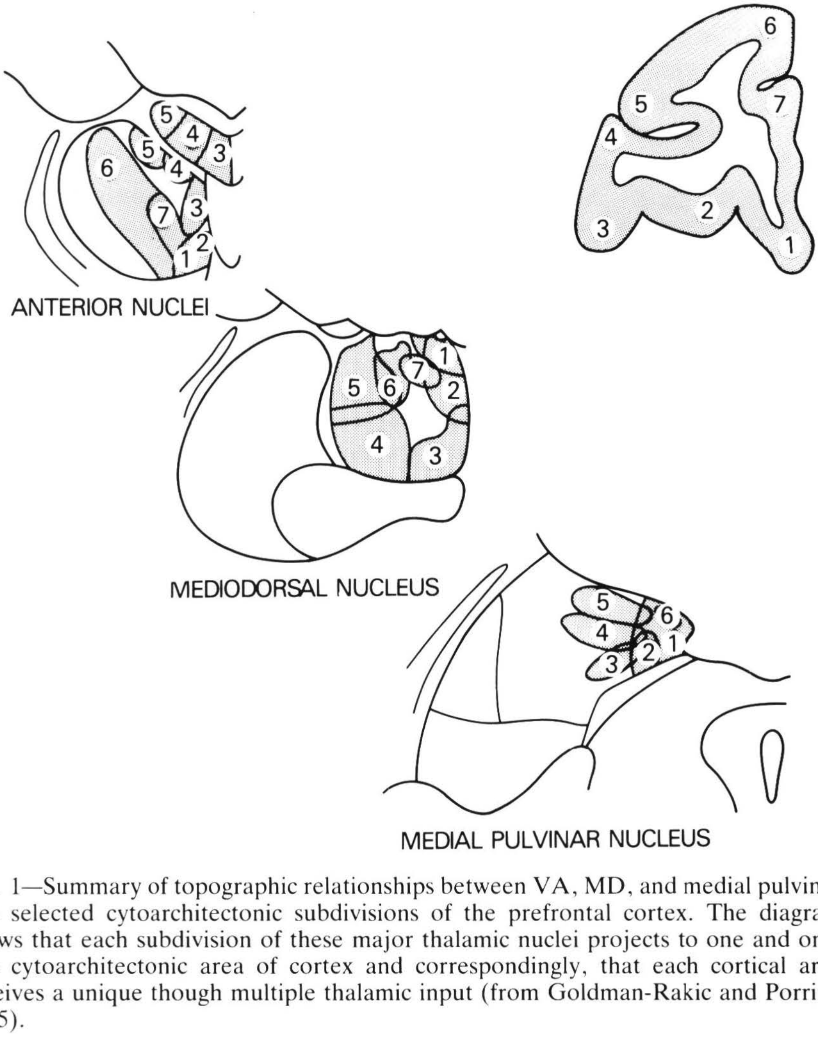

Fig. 1—Summary of topographic relationships between VA, MD, and medial pulvinar and selected cytoarchitectonic subdivisions of the prefrontal cortex. The diagram shows that each subdivision of these major thalamic nuclei projects to one and only one cytoarchitectonic area of cortex and correspondingly, that each cortical area receives a unique though multiple thalamic input (from Goldman-Rakic and Porrino 1985).

17 receives afferents from the pulvinar as well as the lateral geniculate body (e.g., Ogren and Hendrickson 1977; Rezak and Benevento 1979). A recent reexamination of the thalamic relationships of the second somatosensory cortex and neighboring somatosensory fields indicates that each of these areas also receives input from more than one thalamic nucleus (Friedman and Murray 1986). Other cortical regions, such as Brodmann's area 7 of the parietal cortex (Asanuma et al. 1985; Stanton et al. 1977) and also the anterior and posterior cingulate cortex (Baleydier and Mauguiere 1985; Vogt et al. 1979), are all targets of afferents from multiple thalamic nuclei. Convergent thalamic input is not unique to the primate neocortex. Area 17 in cat has long been known to receive a joint innervation from the lateral geniculate and pulvinar complex (Rosenquist 1985).

The nature and degree of the convergence from different thalamic nuclei and even from cells of a given nucleus have not been fully worked out. In area 17 it seems clear that the pulvinar and LGd innervate different layers. For other regions, such as prefrontal cortex, it is not known whether two thalamic nuclei actually innervate the same patch of cortex or different layers within cortical columns, or whether their terminal fields are mutually exclusive or totally overlapping. For example, do the terminals of the medial pulvinar that project to prefrontal cortex converge with the terminations of other thalamic input, e.g., the mediodorsal nucleus, to these same areas? Preliminary findings from double anterograde labeling experiments in my laboratory indicate that they do (Giguere and Goldman-Rakic, in preparation). Given the enlargement and elaboration of the pulvinar complex that has occurred in primate evolution (Harting et al. 1972), large species differences may be expected among the diversity of mammalian species in the number of converging thalamic nuclei and degree of their convergence in specific cortical areas.

Several studies have indicated that thalamic terminal fields are disjunctive in association cortex (Giguere and Goldman-Rakic 1985; Jones et al. 1982) as they are in sensory regions (Jones 1985; Jones et al. 1982). Furthermore, Arikuni et al. (1983) have provided some evidence that the reciprocal cortico-thalamic projection neurons in layer VI of prefrontal areas are clustered in .5 mm-wide territories, approximately, alternating with similar size areas that do not contain or contain fewer corticothalamic projection neurons. These findings add to those from the analysis of sensory areas to raise the possibility that the thalamo-cortico-thalamic system is organized in modules such that specific groups of cells in the thalamus project upon and receive input from specific columns of cortical cells. The terminal distribution of thalamocortical fibers does not necessarily reveal the neat geometric pattern of half-millimeter-wide territories interweaving with equally wide unlabeled zones characteristic of corticocortical connections in the same prefrontal territories (Goldman-Rakic and Schwartz 1982). On the contrary, the distribution of thalamocortical terminals appears more coarse and irregular, sometimes spreading in layer 4 over 2–3 mm in the tangential plane. However, it is hard to say whether the spread of thalamic afferents in our tracing studies is due to the precise site or size of thalamic injections that cannot at present be placed, as would be ideal, into one and only one thalamic cell cluster. On the other hand, it is possible that in association regions, thalamic afferents engage a set of side-by-side cortical modules or hypercolumns rather than alternating sets of modules similar to ocular dominance columns (Goldman-Rakic and Schwartz 1982). Although the nature of interaction between converging thalamocortical fiber systems in the primate brain awaits further analysis, it seems clear that a new principle of thalamocortical relations has emerged. This principle emphasizes the convergence of multiple thalamic inputs to a given cytoarchitectonic area and the need to redefine areas by a unique *set* of thalamic inputs rather than by a relationship with a single thalamic nucleus (Goldman-Rakic and Porrino 1985; Kievit and Kuypers 1977). Of course, each thalamic input could be expected to have a distinctive role in cortical function, and multiple thalamic innervation does not rule out the fact that one nucleus could still be the primary nucleus, as LGD is to area 17, for example.

Divergence of Thalamocortical Innervation

Just as a given cortical area may receive afferents from more than one thalamic nucleus, a given thalamic nucleus may project to more than one cortical area. However, these projections are not necessarily divergent in the sense that one or several cells have multiple targets. Indeed, evidence from single and double retrograde labeling studies supports the idea that thalamocortical neurons are organized in cell clusters (Asanuma et al. 1985; Goldman-Rakic and Porrino 1985) or rods (Jones et al. 1979, 1982), and that different groups or types of cells within a given nucleus project to different cortical areas (Asanuma et al. 1985; Goldman-Rakic and Porrino 1985; Ilinsky et al. 1985). The projections of the mediodorsal nucleus to portions of supplementary motor, anterior cingulate, temporal, and parietal cortex appear to originate from distinct clusters of neurons within MD (Giguere and Goldman-Rakic 1985; Goldman-Rakic and Porrino 1985; Ilinsky et al. 1985; Selemon and Goldman-Rakic 1987). Likewise, different clusters of cells in the medial pulvinar appear to project to multiple targets in the parietal, orbital, and dorsolateral prefrontal cortex; superior temporal sulcus (STS); and posterior cingulate, retrospenial, and parahippocampal cortex (Asanuma et al. 1985; Balaydier and Mauguiere 1985; Goldman-Rakic and Porrino 1985; Trojanowski and Jacobson 1974) (see Fig. 4). Yet since these cell clusters are confined within the borders of a defined thalamic nucleus like the MD or pulvinar, a new important principle of thalamocortical organization may be that certain thalamic nuclei, taken as a whole, can activate an entire network of cortical areas that we shall see are linked via corticocortical connections (Fig. 4). Paradoxically, this role was once reserved for the intralaminar nuclei. Recent studies have demonstrated that the projections of these nuclei have topographically organized cortical terminations. Thus rigid distinctions between specific and nonspecific thalamic nuclei may no longer be appropriate (see Macchi and Bentivoglio 1986 for excellent review).

ORGANIZATION OF CORTICOCORTICAL CONNECTIVITY

Heterogeneity of Posterior Association Cortex

A major contribution of pathway tracing has been the parcellation of the large "association" cortical regions into subdivisions according to patterns of connectivity with the remaining cortex. For most of this century, the parietal and frontal (and to a lesser extent the temporal) association areas of the neocortex have often been treated as more or less homogeneous regions. However, closer scrutiny by modern anatomical and physiological techniques has revealed a relatively high degree of compartmentalization in these areas. Further, the most recent data do not fully support the classical concept of association cortical areas as zones of increasing intersensory convergence. In fact, the large association areas, at least in nonhuman primates, can be divided into smaller specialized information centers that retain a large measure of modal specificity, at least as interpreted from anatomical considerations.

A case in point is the posterior parietal cortex (Brodmann's area 7), which has been variously conceived of as a polysensory cortex, a major relay of somatic information to prefrontal cortex, a center for directed attention, and a visuomotor center. Recent analyses of the connections of the separate subdivisions of this area indicate that each subfield is characterized by unique sets of connections with sensory and limbic systems (Cavada and Goldman-Rakic 1986). For example, area 7a, situated caudally and medially on the lateral surface, receives visually related inputs from a recently described visual area (area PO) in the parieto-occipital sulcus (Colby et al. 1988) and from the dorsal bank of the superior temporal sulcus (STS), but few afferents from somatosensory or somatosensory association cortices (Cavada and Goldman-Rakic 1986; Mesulam et al. 1977; Stanton et al. 1977). In contrast, area 7b, the more rostral and lateral part of the posterior parietal cortex, receives a heavy projection from SI but little imput from visual-related cortices (Cavada and Goldman-Rakic 1986; Seltzer and Pandya 1980; Stanton et al. 1977). Parietal cortex in the intraparietal sulcus, variously designated as POa (Seltzer and Pandya 1980), 7ip (Cavada and Goldman-Rakic 1986), and LIP (Asanuma et al. 1985), and cortex on the medial wall of the hemisphere (area 7m in Fig. 2), also receives topographically distinct inputs. For example, 7ip is the target of afferents from the ventral bank of the superior temporal sulcus, including the visuospatial area, MT (Cavada and Goldman-Rakic 1986; Ungerleider and Desimone 1986; Van Essen and Maunsell 1983; Cavada and Goldman-Rakic, in preparation). Based on the anatomical connections with sensory cortices, it would appear that separate subdivisions of posterior parietal cortex, by virtue of their distinctive connections, may be specialized for different, though possibly parallel, information processing functions. This is consistent with available electrophysiological data summarized by Hyvarinen (1982) and Mountcastle et al. (1984). In essence, cellular activity in area 7b may be related more to somatic stimuli while that in area 7a is more related

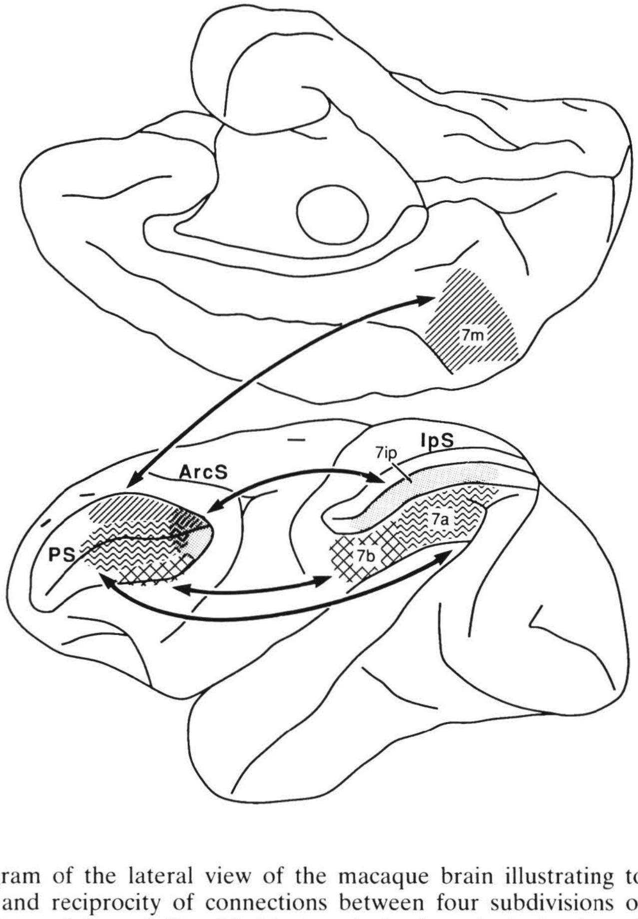

Fig. 2—Diagram of the lateral view of the macaque brain illustrating topography, parallelism, and reciprocity of connections between four subdivisions of posterior parietal cortex and four distinguishable targets in the principal sulcus. Thus areas 7m, 7a, and 7b project to the dorsal rim, lower half of both banks, and ventral rim of the principal sulcus respectively. Area 7ip projects to the caudal end of the sulcus (Goldman-Rakic 1987a).

to visuospatial and visuomotor mechanisms. Within 7b is a weak somatotopy with cells related to mouth located more rostrally than those related to head (Hyvarinen 1982; Robinson and Burton 1980). In addition, the predominant type of neuron so far recorded from 7a and 7ip has been a visually responsive cell, e.g., visual fixation neurons or neurons that fire during reaching movements toward desired visuospatial targets (Mountcastle et al. 1984).

Heterogeneity of Prefrontal Cortex: Parieto-Prefrontal Projections

The existence of specialized centers within association cortex is further supported by the connections between the posterior parietal and prefrontal areas (Cavada and Goldman-Rakic 1985). Thus, each sector of parietal cortex described above (7a, 7b, 7ip, and 7m) terminates in a different and nonoverlapping part of the principal sulcus (Walker's area 46). For example, area 7m selectively terminates in the dorsal rim and upper half of the dorsal bank of the principal sulcus; area 7a projects to the fundus of this sulcus and area 7b to the rim of the ventral bank (Cavada and Goldman-Rakic 1985) (Fig. 2). Further, these projections terminate in a "feed forward" pattern, i.e., parietal axons terminate in layers I, IV, and VI of prefrontal cortex, whereas prefrontal axons in parietal cortex avoid layer IV but terminate in layers I and VI (Selemon and Goldman-Rakic 1983), i.e., in a "feedback" pattern. On the basis of these studies, we can state that the connections between frontal and parietal association areas are characterized by topographic relationships, reciprocity, and parallelism. Furthermore, the specializations of the posterior parietal subdivisions based on distinctive sensory and limbic input are presumably transposed to the prefrontal areas with which each is selectively connected. Although similarly detailed studies do not yet exist for the superior and inferior posterior temporal gyri, common principles of connectivity and function may apply to these regions as well.

Interconnected Networks: Revelations of a Double Labeling Paradigm

In the study of connections, as in other areas of research, the results and the overview or conception of brain organization that they generate are greatly dependent on the methods and strategies used. Accordingly, for more than a century, our ideas about cortical circuitry have relied on reconstructions of circuits from the study of individual cases with, by current standards, large lesions or large injections of tracers. By necessity, the connections of each area had to be examined in one animal at a time. It is from such analyses that our knowledge of brain circuitry has evolved in terms of source and sink conceptions, i.e., parietoprefrontal, occipitotemporal, prefronto-cingulate, etc. Of course, the limitations of technique have never inhibited the construction of flow diagrams, but these are no substitute for direct determination of how many specific populations of cells are directly linked with one another. This issue can now be addressed more directly with the strategy of double anterograde labeling of two cortical areas that are connected to each other in the same hemisphere (see Fig. 3; Selemon and Goldman-Rakic 1985a, b, 1988). We asked the question of whether two areas that project to each other (e.g., posterior parietal and principal sulcus) also project to other cortical areas in the same hemisphere. If they do, are the connections divergent or convergent? If convergent, do they overlap totally or partially, and what is their relationship to the columnar architecture of the target structures?

The results of our double label study revealed that posterior parietal and dorsolateral prefrontal cortex project in common to virtually the same targets in over a dozen distinct cytoarchitectonic areas: e.g., the supplementary motor area (Brodmann's area 6), the anterior cingulate cortex (Brodmann's area 24), the posterior cingulate cortex (area 23), the presubiculum, the parahippocampal gyrus (area TF), the orbital prefrontal cortex (area 11), the prearcuate area (area 8), the premotor cortex (area 6), the frontoparietal

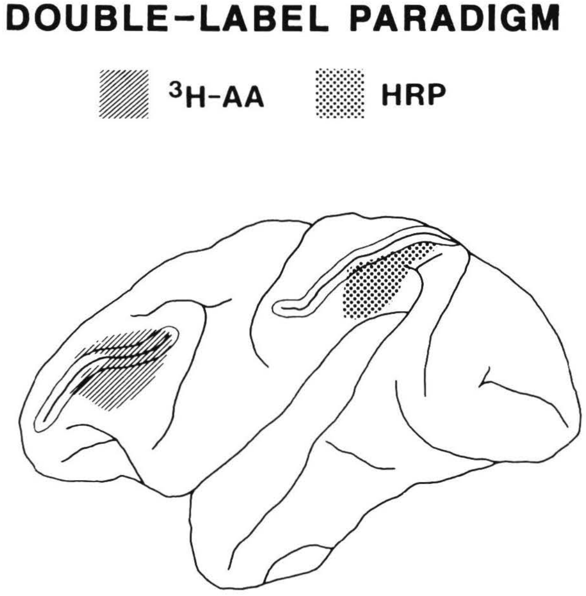

Fig. 3—Double anterograde paradigm for study of cortical networks. One anterograde tracer, tritiated amino acids, is placed in the prefrontal cortex; another, WGA-HRP, is placed in the posterior parietal cortex (and the reverse). Alternate sections are processed for autoradiography and histochemistry. Adjacent sections are charted and superimposed for determination of convergence or lack thereof in potential target areas. In our study, virtually every cortical region innervated by the posterior parietal cortex also received a projection from the posterior prefrontal cortex (Selemon and Goldman-Rakic 1988).

operculum (SI and SII), the superior temporal sulcus (area 20), the medial parietal area (7m), and the medial prestriate cortex (area PO or area 19) (see Fig. 4; Selemon and Goldman-Rakic 1985b, 1987). Moreover, the prefrontal and parietal axons within these "third party" targets terminate in one of two characteristic modes: either as interdigitated, spatially alternating fiber columns or in complementary layers within a single column or set of columns (Fig. 5). In anterior and posterior cingulate cortices, for example, the mode of termination is an interdigitated pattern, i.e., prefrontal and parietal terminals formed adjacent cortical columns, whereas in the parietal operculum and superior temporal sulcus, the pattern was that of complementary laminae (Fig. 5). In the latter case, parietal axons terminate predominantly in layers IV and VI and prefrontal projections are highly concentrated in layer I and much less densely in layers III and V/VI of the same column. The two different patterns of cortical termination suggest that the integration of prefrontal and parietal information differs accordingly. In the cingulate regions, for example, parietal and prefrontal axons probably terminate on different sets of cells whereas in temporal lobe and parietal operculum, it is possible that prefrontal and parietal afferents terminate upon different parts of the dendritic arbor of the very same cells, much as hippocampal inputs are distributed on proximal and distal dendritic segments of pyramidal neurons in Ammon's horn. These anatomical findings open up new issues and possibilities for physiological analysis of cortical networks.

Thus, neurons in a large number of target areas are interconnected with the prefrontal and parietal cortex. These widespread areas are also unified by their thalamic input from the medial pulvinar (e.g., Asanuma et al. 1985; Baleydier and Mauguiere 1980, 1985; Giguere and Goldman-Rakic 1985; Goldman-Rakic and Porrino 1985; Kievit and Kuypers 1977; Selemon and Goldman-Rakic 1987; Trojanowski and Jacobson 1974; Vogt et al. 1979). As mentioned previously, the medial pulvinar projects to the anterior and posterior cingulate and retrosplenial cortices — the paralimbic areas — and also to the superior temporal and frontoparietal operculum as well as to the principal sulcus and parietal area 7a (see Fig. 2). This thalamic nucleus, which is particularly prominent in primates, is thereby in position to recruit an entire neural system defined by corticocortical connectivity and possibly by common dedication to the complex function of being oriented in time and space.

Distributed Parallel Networks versus Hierarchical Models of Cortical Organization

The conclusion traditionally reached in most studies of association cortex connections is that they are organized in a step-wise, hierarchical sequence proceeding from relatively raw sensory input at the primary sensory cortices through "successive stages of intramodality elaboration allowing progressively

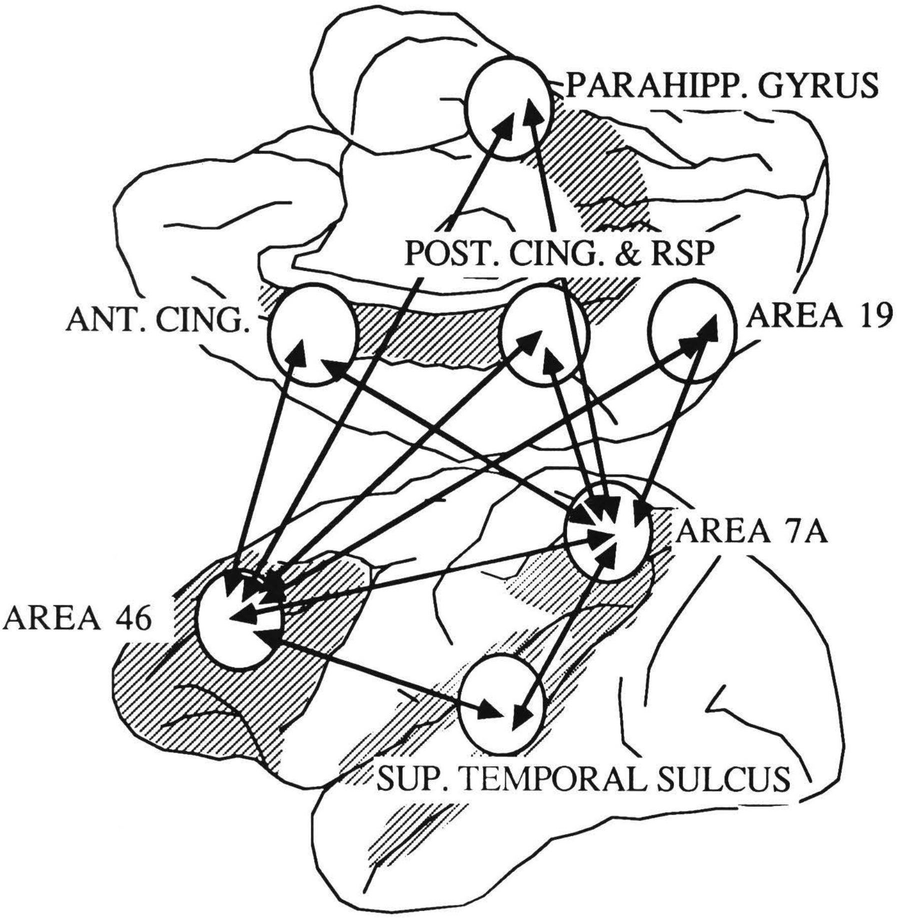

Fig. 4—The results of a double labeling study in which WGA-HRP (or 3-H leucine and proline) was placed in area 7a, and tritiated amino acids (or WGA-HRP) were placed in area 46 in the same hemisphere of the same animal. Alternate sections were processed for HRP histochemistry and autoradiography. Paired sections were superimposed and analyzed. Area 46 and area 7a project over a dozen targets in common (although only five are illustrated). Cross hatched regions represent areas that have been reported to receive afferents from the medial pulvinar. (Baleydier and Mauguiere 1985; Cavada and Goldman-Rakic 1986; Giguere and Goldman-Rakic 1985; Goldman-Rakic and Porrino 1985; Trojanowski and Jacobson 1974).

more complex discriminations of the features of a particular stimulus. Then, by a series of further connections, this sensory information, now in a highly complex form, is conveyed to polymodal zones for cross-modal interchange of information, to paralimbic and limbic areas for investment with emotional tone and placement in memory, and to the frontal association areas where

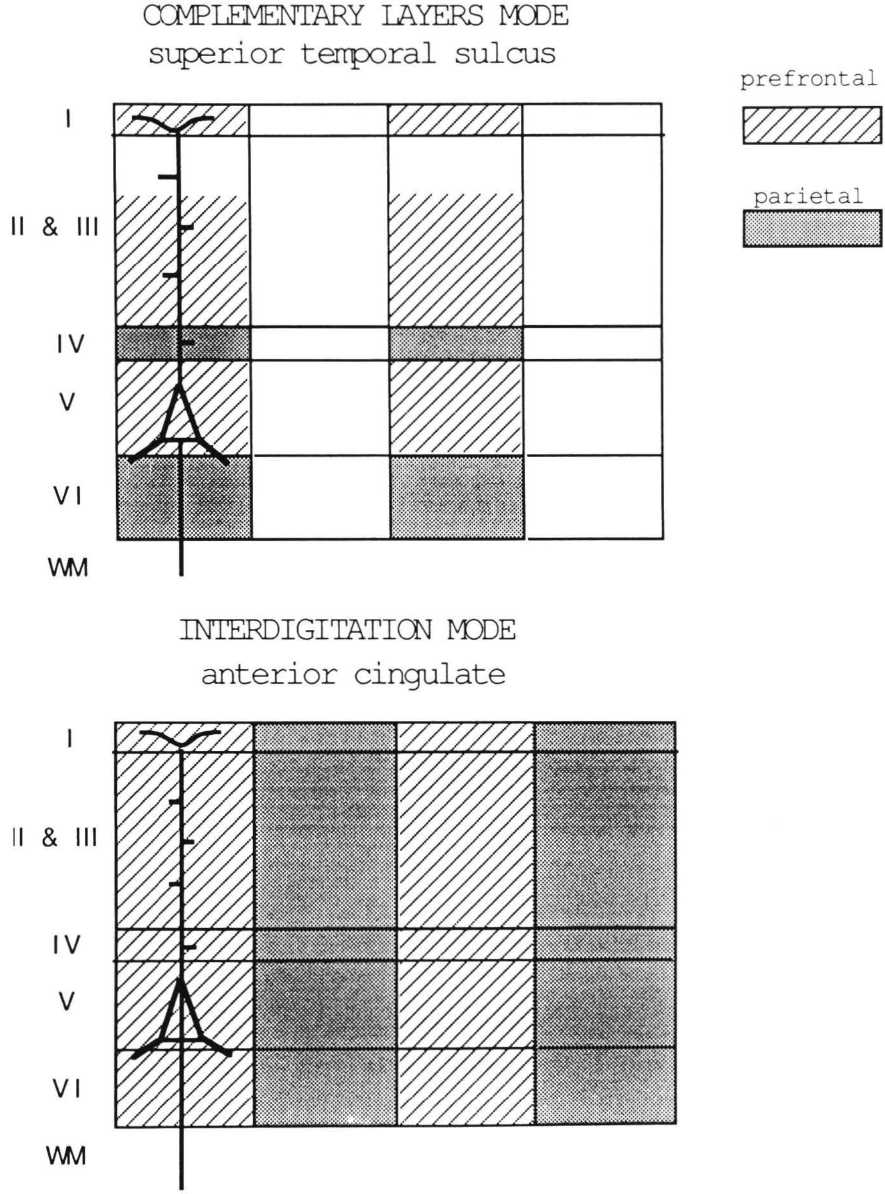

Fig. 5—Modes of distribution of area 7a and area 46 terminals in "third" party targets. In anterior cingulate (and other medially situated) cortex, parietal and prefrontal fibers terminated in the same layers of adjacent columns; in the superior temporal sulcus, and also the frontoparietal operculum, the two areas of cortex project to different layers of the same columns — prefrontal cortex mainly to layer I and less densely to layers III and V.

both sensory and limbic data are integrated in preparation for the organism to respond to sensory stimuli by an appropriate response" (Pandya and Seltzer 1982). According to hierarchical models of cortical function, sensory signals are progressively elaborated in sensory association cortices, and information flow is mainly unidirectional, i.e., from sensory through associational to motor. Further, some sort of convergence occurs and increases at each stage along the hierarchy such that integration of the different sensory inputs takes place in key polymodal areas like the posterior parietal (Mesulam et al. 1977), the superior temporal polysensory area (Bruce et al. 1981) and/or the prefrontal (Bignall and Imbert 1969; Nauta 1971; Pandya and Kuypers 1969) cortex. One has the sense of a pyramidal organization with the areas furthest removed from sensory receptors receiving the most information from convergent sources. However, without denying that some convergence occurs in association cortex, considerations discussed in the present chapter lead toward a different view — one which focuses on the distribution of function in parallel systems with perhaps coequal functions. Some examples of such systems are discussed below.

Parallel Circuits for Guidance of Eye and Hand Movements

As mentioned, the posterior parietal cortex is reciprocally connected with the posterior prefrontal cortex and with at least twelve other cortical areas, as well as with the medial pulvinar of the thalamus. Both prefrontal and posterior parietal areas have been associated with spatial abilities, and physiological studies in these areas suggest possible functional collaborations between them. For example, neurons in the frontal eye field (Walker's area 8a) increase their activity when a monkey withholds eye movements while remembering a target location (Bruce and Goldberg 1985). According to a recent preliminary report of Gnadt et al. (1986) neurons in the lateral bank of the intraparietal sulcus (area 7ip) behave in exactly the same way in delay paradigms. Thus, we may speculate that parietal area 7ip and prefrontal area 8A are part of a common circuit and that both have a role in the guidance of eye movements by visuospatial information. From clinical, neuropsychological, and physiological studies we can surmise that the parietal component may be important for sensorimotor integration and the formation of spatial representations, while the prefrontal component is necessary for the utilization of these representations to generate eye movement commands.

It has occurred to me that the guidance of hand movements by visuospatial representations might similarly be a "distributed" function of a parallel neural circuit — one involving the connections between certain subdivisions of the principal sulcus and posterior parietal subarea 7a (Fig. 3). Neuronal activity recorded from cells in and around the principal sulcus (area 46) has been linked to delayed-response performance primarily in tasks requiring manual responses (cf. Funahashi et al. 1985). Principal sulcus neurons exhibit spatially coded, enhanced firing rates during the delay period of a manual delayed-response trial, i.e., discharging more to a left (or right) visual target when that target is no longer in view (Funahashi et al. 1985; Fuster and Alexander 1971; Kojima and Goldman-Rakic 1982; Kubota and Niki 1971). The discharge pattern of these prefrontal neurons has variously been related to short-term memory (Fuster 1973; Goldman-Rakic 1987a), to intention to move in a particular direction (Niki et al. 1972), or to a sensory representation of visuospatial coordinates (Goldman-Rakic 1987a; Niki and Watanabe 1976).

There is little corresponding information on neuronal activity in area 7a (or any other subdivision) of the posterior parietal cortex on memory tasks, though many neurons in this subarea are strongly related to movement of the hand (Mountcastle et al. 1984). However, in a previous study from this laboratory, we recorded from area 7a in the posterior parietal cortex in one-year-old and adult rhesus monkeys performing the conventional delayed-reponse task and found cells there that discharged during the delay of a delayed-response trial (reported in Rakic and Goldman-Rakic 1982). Although the percentage of delay-related neurons in this region of parietal cortex was lower than in prefrontal cortex and in several other structures, their presence in parietal cortex was at the time surprising. We did not know then what to make of the fact that the activity in parietal neurons resembled that of prefrontal cells. Today, we might conclude that the similar profiles of activation in parietal and prefrontal cortex indicate a commonality of function and shared circuitry. Again, we may speculate that the parietal contribution is presumably to form and maintain the spatial coordinates of an object in space, and the prefrontal contribution is to access and use that knowledge to guide a response, in this case, a hand movement (Goldman-Rakic 1987a). More data would be welcome on the distinctive features of prefrontal and parietal neurons in visuospatial paradigms.

The behavioral contribution of other cortical components of the neural networks defined in anatomical studies are much less obvious and more difficult to infer. Neuronal recording in behaving monkeys has not been attempted in many of the cortical areas connected to prefrontal and parietal cortex, e.g., the anterior or posterior cingulate cortex or parahippocampal cortex. Further, in cortical regions like the superior temporal sulcus that have been studied physiologically, delay tasks have not generally been employed (e.g., Bruce et al. 1981). However, it must be noted that delay-enhanced discharge during delayed-response tasks has been reported in several key structures with which posterior parietal areas, the principal sulcus, and frontal eye fields are connected, e.g., the hippocampus (Watanabe and Niki 1985), the head of the caudate nucleus (Niki et al. 1972), and the mediodorsal nucleus of the thalamus (Alexander and Fuster 1973), though not from the cholinergic system of basal forebrain nuclei (Richardson and DeLong 1986). Also, results from ^{14}C-2-deoxyglucose studies of monkeys performing delayed-response tasks show elevated metabolic activity in prefrontal cortex (Bugbee and Goldman-Rakic 1981), in the hippocampus proper (Friedman and Goldman-Rakic 1985), and the mediodorsal nucleus of the thalamus (Friedman et al. 1987) compared with animals performing other types of memory tasks. Thus, while not necessarily revealing the functional specialization of each structure in the network, these physiological and metabolic studies are consistent with the supposition of a distributed, richly interconnected system of neural structures engaged in spatial information processing. In such systems, integrative functions may emerge from the dynamics of the entire network and from its interactions with similarly constructed networks rather than from linear computations performed at each nodal point in the circuit (e.g., Edelman 1979; Goldman-Rakic 1988).

Parallel Circuits for Spatial (Where) and Object (What) Memory

Behavioral and electrophysiological studies support still another division of labor between prefrontal areas. While monkeys with bilateral principal sulcus lesions exhibit profound and selective deficits on spatial delayed-response tasks that require memory for the location of objects in space (e.g., Blum 1952; Butters et al. 1972; Goldman and Rosvold 1970; Goldman et al. 1971; Gross and Weiskrantz 1964; Mishkin 1957), lesions of the orbital prefrontal cortex produce deficits on tasks requiring memory for visual features (e.g., color and shape) of objects and not for their location (Bachevalier and Mishkin 1986; Goldman 1971; Mesulam 1981; Mishkin and Manning 1978; Pandya and Seltzer 1982; Passingham 1972, 1975; Richardson and DeLong 1986; Rosenkilde et al. 1981). Electrophysiological studies support this division of labor in prefrontal areas. For example, neurons expressing delay-activated neuronal activity in spatial delay tasks are found mainly in the area of the principal sulcus, while neurons related to nonspatial memory tasks (e.g., matching-to-sample) are found in the inferior convexity and orbital prefrontal cortex (Rosenkilde et al. 1981). The conclusion drawn from these studies is that the dorsal (principal sulcus, Walker's area 46) and ventral (Walker's areas 11–13) subdivisions of prefrontal cortex may be specialized for working memory of spatial and nonspatial knowledge, respectively, i.e., each area is engaged by different classes of information (Goldman-Rakic 1987a; 1988)). Given that each prefrontal area represents one node in a different distributed circuit, it appears possible that parallel cortical networks subserve spatial and nonspatial mnemonic processing.

Parallel Distributed Functions in Human Cortex

Studies of cerebral blood flow in normal subjects performing pyschological tasks support a parallel distributed processing model of cortical functions

(Roland and Friberg 1985). The act of thinking increases blood flow in multiple cortical fields in homotypical cortical zones outside the immediate sensory association areas, and, predictably, the constellation of cortical areas activated differs with different "types" of thinking or internal operations. Spatial thinking in the form of a mental route-finding task activates the superior occipital, the posterior parietal, and the posterior inferotemporal cortex, as well as several zones within prefrontal cortex; mathematical thinking activates overlapping but some distinctive sets of cortical areas of posterior and anterior association cortex; and linguistic thinking appears to activate still other sets of areas (Roland and Friberg 1985). One cannot escape the conclusion that the constellation of areas activated by spatial thought processes in these studies represents the same type of circuitry that is interconnected by corticocortical and thalamocortical connections described in the nonhuman primate and that mathematical and linguistic thinking engage similarly organized parallel circuits. If this is so, then traditional ideas of hierarchical processing which may apply within some systems is not the dominant or only mode of functional organization of the association cortex. Rather, higher cortical functions seem to be carried out by a finite number of dedicated networks of reciprocally interconnected areas. Further, since we already know that different features of the visual world are processed in parallel in visual cortical areas (e.g., Hubel and Livingstone 1985; Shipp and Zeki 1985), it seems possible that this segregation of input is "respected" and maintained in the association networks. For example, area MT projects mainly to area 7ip while area 7b receives its input primarily from somatosensory association cortex. The opportunity would seem to be at hand for linking the sensory and executive processes of the cerebral cortex.

Integration across Systems

If parallel systems of circuits subserve various distinct information-processing tasks as the foregoing analysis suggests, it is appropriate to raise the issue of integration across cortical networks. The field of cortical systems research will have to address the mechanisms by which knowledge of the color or form of an object is integrated with knowledge of its position in space, as such knowledge would appear to involve crosstalk between two different functional systems. If there is a central executive mechanism in the prefrontal cortex as cognitive studies in humans have suggested (Shallice 1982), then its essence may be elucidated further by taking into account the nature of the interconnections between neural networks. This could take the form of local corticocortical connections between, for example, subdivisions of posterior parietal or prefrontal (Barbas and Mesulam 1981, 1985) cortex (Seltzer and Pandya 1986) or possibly the multiple innervation of all components of a network by a thalamic nucleus. As previously mentioned, the medial pulvinar nucleus projects to the posterior parietal, prefrontal, anterior cingulate, superior temporal sulcus, and other areas of the cortex in primates, i.e., it projects to a system of cortical areas that are interconnected. The question of how the brain organizes its subsystems to produce integrated behavior is perhaps the most challenging one that can be posed. In the last section of this review, we consider this issue again as we take up the motor control and effector mechanism of the cerebral cortex.

ORGANIZATION OF CORTICAL-SUBCORTICAL CIRCUITRY

Motor Control Functions of the Cortex

Are there general principles governing the motor command functions of the cortex? The role of cerebral cortex in motor control is generally considered to involve three major "motor" areas: primary motor cortex (Brodmann's area 4), the premotor cortex (lateral area 6), and the supplementary motor cortex (medial area 6). The functional and anatomical relationships among these areas, as well as between these areas and sensory association cortex, hold one key to understanding the regulation of voluntary motor behavior.

In the study of cortical output, as in the analysis of thalamic innervation, new principles have emerged. An important concept that has evolved in the study of motor control is that the descending corticostriatal pathways are organized in parallel loops rather than as convergent projections (for review see Goldman-Rakic and Selemon 1986; Alexander et al. 1986). Thus, modern anatomical tracing studies affirm that the projections from the dorsolateral prefrontal, orbital prefrontal, frontal eyefields, supplementary motor, and anterior cingulate cortex terminate in topographically segregated areas within the caudate-putamen, and this segregation is presumably maintained in the return pallidal-thalamo-cortical loop to the cortex (Fig. 6). This new knowledge of the organization of the extrapyramidal system raises the question of why these systems should be organized in parallel and whether or where communication takes place among them.

A second new insight into the motor control functions of the cortex comes from analysis of corticocortical connections among the motor centers of the frontal lobe. For example, Muakassa and Strick injected physiologically identified regions of motor cortex with HRP and found that hand, leg, and mouth areas of motor cortex were each connected with four more or less distinct premotor areas. Other studies of premotor cortex indicate that subsets of these premotor centers are interconnected, i.e., the postarcuate mouth area is interconnected with the postarcuate hand area and vice-versa (Matelli et al. 1986). This type of connection may account for the propensity of postarcuate neurons to respond to movement of the hand towards the mouth (Rizzolatti 1983). Thus, within premotor cortex, we can speak of multiple representations of the arm or hand, though little is known as to

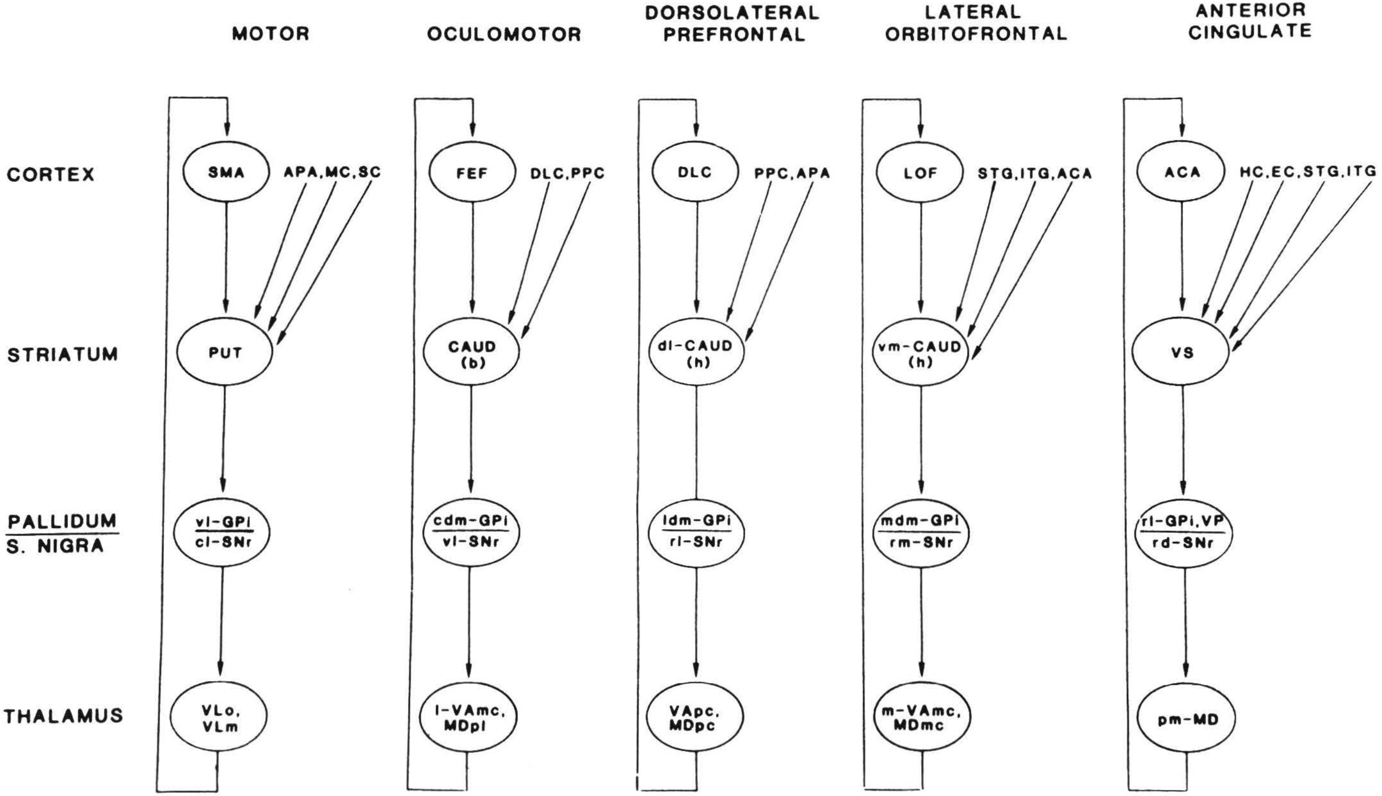

Fig. 6—Example of five parallel systems of connections linking cerebral cortical areas with the basal ganglia-thalamo-cortical pathways (from Alexander et al. 1986).

whether different aspects of movement or intention to move are coded in these separate territories.

A final important step in understanding the motor control functions of the cerebral cortex is the recognition of substantial connections between association areas of the cortex, particularly the prefrontal cortex, and various motor centers. Small injections of WGA-HRP into prefrontal areas 45, 46, or 8a preferentially label several premotor sites including anterior supplementary motor cortex (Jouandet and Goldman-Rakic, unpublished observations) and ventral parts of area 6 (Arikuni et al. 1980; Barbas and Mesulam 1981, 1985; Preuss and Goldman-Rakic 1985),while area 46 is additionally interconnected with SI and SII in the frontoparietal operculum. (Preuss and Goldman-Rakic 1985). Two conclusions can be drawn from these anatomical observations. First, prefrontal sites are but one synapse removed from the primary motor cortex via prefronto-premotor-motor connections. Second, these transcortical connections may supplement, in ways that are not yet understood, the better known projections of prefrontal centers to subcortical "motor" structures via the basal ganglia (Goldman and Nauta 1977; Selemon and Goldman-Rakic 1985a) and deep layers of the superior colliculus (Fries 1984; Goldman and Nauta 1976; Kunzle et al. 1976).

The anatomical and functional evidence supports the thesis that the prefrontal association areas have access to and could direct the output of several motor centers. It is clear, for example, that the anterior arcuate cortex is organized for oculomotor control, and recent behavioral and electrophysiological studies in my laboratory have demonstrated that the caudal principal sulcus can also influence delayed responding in an oculomotor task (Funahashi et al. 1985). However, other regions of the prefrontal cortex may be organized for output of different muscle groups. For example, a projection from the ventral rim of the principal sulcus is specifically related to the hand and mouth representation of SI and SII in the parietal operculum (Preuss and Goldman-Rakic 1985). These findings provide a hint that prefrontal cortex may itself be somatotopically organized and that different subareas are concerned with regulation of behavior expressed through different regions of the body. Without being able to affect directly the performance aspects of a single muscular contraction, prefrontal areas nevertheless may regulate motor output by initiating, facilitating, and canceling commands to structures directly involved in the programming, computational, and performance aspects of specific motor acts.

Somatotopically organized projections to subcortical motor centers also arise from premotor as well as other association cortical areas in the premotor cortex and the parietal and temporal lobes (Lynch et al. 1985; Selemon and Goldman-Rakic 1985a; Yeterian and Van Hoesen 1978). One may wonder whether all of these descending control mechanisms operate in concert and, if not, what rule establishes priority among them. For instance, if all areas that had access to the final common path issued excitatory motor commands simultaneously, the result might be conflict or chaos. The locus of motor control at any given moment is of particular interest in view of the evidence described in the preceding section that many cortical areas with access to subcortical motor centers form an interconnected network. I would like to suggest that the nature of the task to be performed might dictate when and where the final common motor command is issued within our integrated cortical network. For example, if the task at hand involved guidance of a motor act by representational information, instructions, or concepts, e.g., delayed-reponse tasks for monkeys and card sorting for humans, then prefrontal cortical centers might direct the action. If, on the other hand, the task at hand were sensory guided, as in a conditional visual discrimination task (monkeys) or obeying traffic lights (humans), premotor centers might issue the motor command. Finally, if the task was a detection or simple recognition task, the sensory association area most directly involved might control the response without further processing through premotor and/or prefrontal centers.

Neuropsychological investigations in nonhuman primates and in patients with cortical lesions strongly support a dissociation in the neural mechanisms responsible for sensory-guided versus memory-guided regulation of behavior and indicate a prefrontal localization for the latter and premotor involvement in the former (for evidence, see Goldman-Rakic 1987a; Passingham 1984). In addition, reaction time (RT) studies of normal human subjects that show increasing RTs with increasing processing demands would tend to support this view of neural organization and neural cooperativity. The implications of this idea for the operations of cortical networks is that they are functionally labile and can adjust neural activity within their various nodes, depending upon the task at hand. The largely parallel projection systems of the extra pyramidal cortex could then be explained as a mechanism allowing for independent initiation of motor activity by several cortical centers, depending on the level of analysis required by any given task.

CONCLUSION

This chapter has reviewed recent data about the anatomical organization of three major classes of cortical connection: the thalamocortical, corticocortical, and corticostriatal. Studies of each of these systems of connections have led, over the past decade, to remarkable changes in our concepts of the organization of the primate central nervous system. The rigid concept of a one-to-one relationship between a given thalamic nucleus and a given cortical field, which took hold in the 1940's and 1950's, was discussed in light of recent evidence that individual dorsal thalamic nuclei project to widespread cortical areas and that a given cytoarchitectonic region receives afferents from multiple thalamic nuclei. New evidence was also described for parallel networks of intrahemispheric connections that may link numerous separate cortical centers in a single closed circuit. Such circuits may be the basis of parallel distributed functions in the cortex, and their existence should influence our thoughts and experimental approaches to the study of functional localization. Finally, parallel efferent cortical and subcortical projection systems were reviewed from the point of view of the ordering and priority of cortical participation in motor control.

The picture emerging from the new anatomy is that of a highly integrated but distributed cortical machinery whose resources are allocated to several basic parallel functional systems that bridge all major subdivisions of the cerebrum. This view is supported by recent developmental findings that synaptogenesis proceeds at the same rate and reaches peak values at the same age in areas of sensory, motor, limbic, and association cortex, indicating an unexpected degree of integration in maturational sequence (Goldman-Rakic 1987b; Passingham 1975). If subdivisions of limbic, motor, sensory, and associative cortex exist in developmentally linked and functionally unified networks, as the anatomical, physiological, and behavioral evidence reviewed here suggests, it may in the future be more useful to study the cortex in terms of information processing functions and systems rather than traditional but artificially segregated sensory, motor, or limbic components and individual neurons within only one of these components. The new detailed knowledge about specific interconnections at the cortical level can be used to guide physiological analysis of cortical networks. While it is evident that the complexity of the mammalian cortex remains a serious impediment to the study of cortical function, it should be encouraging that major principles of its anatomical and functional architecture have come to light and that the sum of its separate cytoarchitectonic subdivisions can be seen to contribute to the integrated activity of the whole.

REFERENCES

Alexander, G.E.; DeLong, M.R.; and Strick, P.L. 1986. Parallel organization of functionally segregated circuits linking basal ganglia and cortex. *Ann. Rev. Neurosci.* **9:** 357–382.

Alexander, G.E., and Fuster, J.M. 1973. Effects of cooling prefrontal cortex on cell firing in the nucleus medialis dorsalis. *Brain Res.* **61:** 93–105.

Arikuni, T.; Sakai, M.; Hamada, I.; and Kubota, K. 1980. Topographical projections from the prefrontal cortex to the post-arcuate area in the rhesus monkey, studied by retrograde axonal transport of horseradish peroxidase. *Neurosci. Lett.* **19:** 155–160.

Arikuni, T.; Sakai, M.; and Kubota, K. 1983. Columnar organization of prefrontal and anterior cingulate cortical cells projecting to the thalamic MD nucleus in the monkey. *J. Comp. Neurol.* **220:** 116–128.

Asanuma, C.; Andersen, R.A.; and Cowan, W.M. 1985. The thalamic relations of the caudal inferior parietal lobule and the lateral prefrontal cortex in monkeys:

divergent cortical projections from cell clusters in the medial pulvinar nucleus. *J. Comp. Neurol.* **241:** 357–381.

Bachevalier, J., and Mishkin, M. 1986. Visual recognition impairment follows ventromedial but not dorsolateral prefrontal lesions in monkeys. *Behav. Brain Res.* **20:** 249–261.

Baleydier, C., and Mauguiere, F. 1980. The duality of the cingulate gyrus in monkey: neuroanatomical study and functional hypothesis. *Brain* **103:** 525–554.

Baleydier, C., and Mauguiere, F. 1985. Anatomical evidence for medial pulvinar connections with the posterior cingulate cortex, the retrosplenial area, and the posterior parahippocampal gyrus in monkeys. *J. Comp. Neurol.* **232:** 219–228.

Barbas, H., and Mesulam, M.–M. 1981. Organization of afferent input to subdivisions of area 8 in the rhesus monkey. *J. Comp. Neurol.* **200:** 407–431.

Barbas, H., and Mesulam, M.–M. 1985. Cortical afferent input to the principalis region of the rhesus monkey. *Neurosci.* **15:** 619–637.

Bignall, K.E., and Imbert, and Imbert, M. 1969. Polysensory and cortico-cortical projections to frontal lobe of squirrel and rhesus monkey. *Electroenceph. Clin. Neurophysiol.* **26:** 206–215.

Blum. R.A. 1952. Effects of subtotal lesions of frontal granular cortex on delayed reaction in monkeys. *A.M.A. Arch. Neurol. Psychiat.* **67:** 375–386.

Bruce, C.J.; Desimone, R.; and Gross, C.G. 1981. Visual properties of neurons in a polysensory area in superior temporal sulcus of the macaque. *J. Neurophsiol.* **46:** 369–384.

Bruce, C.J., and Goldberg, M.E. 1985. Primate frontal eye fields. I. Single neurons discharging before saccades. *J. Neurophysiol.* **53:** 603–635.

Bugbee, N.M., and Goldman-Rakic, P.S. 1981. Functional 2-deoxyglucose mapping in association cortex: prefrontal activation in monkeys performing a cognitive task. *Soc. Neurosci. Abst.* **7:** 416.

Butters, N.; Pandya, D.; Stein, D.; and Rosen, J. 1972. A search for the spatial engram within the frontal lobes of monkeys. *Acta Neurobiol. Exp.* **32:** 305–329.

Cavada, C., and Goldman-Rakic, P.S. 1985. Parieto-prefrontal connections in the monkey: Topographic distribution within the prefrontal cortex of sectors connected with lateral and medial posterior parietal cortex. *Soc. Neurosci. Abst.* **11:** 323.

Cavada, C., and Goldman-Rakic, P.S. 1986. Subdivisions of area 7 in rhesus monkey exhibit selective patterns of connectivity with limbic, visual and somatosensory cortical areas. *Soc. Neurosci. Abst.* **12:** 262.

Colby, C.L.; Gattass, R.; Olson, C.R.; and Gross, C.G. 1988. Topographic organization of cortical afferents to extrastriate area PO in macaque: a dual tracer study. *J. Comp. Neurol.,* in press.

Edelman, G.M. 1979. Group selection and phasic reentrant signaling: a theory of higher brain functions. In: The Mindful Brain, eds. G.M. Edelman and V.B. Mountcastle, pp. 51–100. Cambridge, MA: MIT Press.

Friedman, D.P., and Murray, E.A. 1986. Thalamic connectivity of the second somatosensory area and neighboring somatosensory fields of the lateral sulcus of the macaque. *J. Comp. Neurol.* **252:** 348–373.

Friedman, H.R., and Goldman-Rakic, P.S. 1985. Enhancement of trisynaptic pathway in the hippocampus during performance of spatial working memory tasks: a 2–DG behavioral study in rhesus monkeys. *Soc. Neurosci. Abst.* **11:** 460.

Friedman, H.; Janis, J.; and Goldman-Rakic, P.S. 1987. Metabolic activity in the thalamus and mamillary bodies of the monkey during spatial memory performance. *Soc. Neurosci. Abst.* **13:** 207.

Fries, W. 1984. Cortical projections to the superior colliculus in the macaque monkey: a retrograde study using horseradish peroxidase. *J. Comp. Neurol.* **230:** 55–76.

Funahashi, S.; Bruce, C.J.; and Goldman-Rakic, P.S. 1985. Visual properties of prefrontal neurones. *Soc. Neurosci. Abst.* **11:** 525.

Fuster, J.M. 1973. Unit activity in prefrontal cortex during delayed-response performance: neuronal correlates of transient memory. *J. Neurophysiol.* **36:** 61–78.

Fuster, J.M., and Alexander, G.E. 1971. Neuron activity related to short-term memory. *Science* **173:** 652–654.

Giguere, M., and Goldman-Rakic, P.S. 1985. Disjunctive distribution of mediodorsal thalamic afferents in the prefrontal cortex of rhesus monkey. *Soc. Neurosci. Abst.* **11:** 677.

Gnadt, J.W.; Andersen, R.A.; and Blatt, G.J. 1986. Spatial memory and motor planning properties of saccade related activity in the lateral intraparietal area of macaque. *Soc. Neurosci. Abst.* **12:** 458.

Goldman, P.S. 1971. Functional development of the prefrontal cortex in early life and the problem of neuronal plasticity. *Exp. Neurol.* **32:** 366–387.

Goldman, P.S., and Nauta, W.J.H. 1976. Autoradiographic demonstration of a projection from prefrontal association cortex to the superior colliculus in the rhesus monkey. *Brain Res.* **116:** 145–149.

Goldman, P.S., and Nauta, W.J.H. 1977. Columnar distribution of cortico-cortical fibers in the frontal association, limbic, and motor cortex of the developing rhesus monkey. *Brain Res.* **122:** 393–413.

Goldman, P.S., and Rosvold, H.E. 1970. Localization of function within the dorso lateral prefrontal cortex of the rhesus monkey. *Exp. Neurol.* **27:** 291–304.

Goldman, P.S.; Rosvold, H.E.; Vest, B.; and Galkin, T.W. 1971. Analysis of the delayed alternation deficit produced by dorsolateral prefrontal lesions in the rhesus monkey. *J. Comp. Physiol. Psychol.* **77:** 212–220.

Goldman-Rakic, P.S. 1987a. Circuitry of the prefrontal cortex and the regulation of behavior by representational memory. In: Handbook of Physiology, The Nervous System V, eds. F. Plum and V. Mountcastle, pp. 373–417. Bethesda, MD: American Physiological Society.

Goldman-Rakic, P.S. 1987b. Development of cortical circuitry and cognitive functions. *Child Dev.* **58:** 642–691.

Goldman-Rakic, P.S. 1988. Topography of cognition: parallel distributed networks in primate association cortex. *Ann. Rev. Neurosci.* **11:** 137–156.

Goldman-Rakic, P.S., and Porrino, L.J. 1985. The primate mediodorsal (MD) nucleus and its projections to the frontal lobe. *J. Comp. Neurol.* **242:** 535–560.

Goldman-Rakic, P.S., and Schwartz, M.W. 1982. Interdigitation of contralateral and ipsilateral columnar projections to frontal association cortex in primates. *Science* **216:** 755–757.

Goldman-Rakic, P.S., and Selemon, L.D. 1986. Topography of corticostriatal projections in nonhuman primates and implications for functional parcellation of the neostriatum. In: Cerebral Cortex, vol. 5, eds. E.G. Jones and A. Peters, pp. 447–466. New York: Plenum.

Gross, C.G., and Weiskrantz, L. 1964. Some changes in behavior produced by lateral frontal lesions in the macaque. In: The Frontal Granular Cortex and Behavior, eds. J.M. Warren and K. Akert, pp. 74–101. New York: McGraw-Hill.

Harting, J.K.; Hall, W.C.; and Diamond, I.T. 1972. Evolution of the pulvinar. *Brain Behav. Evol.* **6:** 424–452.

Hubel, D.H., and Livingstone, M.S. 1985. Complex-unoriented cells in a subregion of primate area 18. *Nature* **315:** 325–327.

Hyvarinen, J. 1982. The Parietal Cortex of Monkey and Man. Berlin, Heidelberg: Springer-Verlag.

Ilinsky, I.A.; Jouandet, M.L.; and Goldman-Rakic, P.S. 1985. Organization of the nigrothalamocortical system in the rhesus monkey. *J. Comp. Neurol.* **236:** 315–330.

Jones, E.G. 1985. The Thalamus. New York: Plenum Press.

Jones, E.G.; Coulter, J.D.; and Wise, S.P. 1979. Commissural columns in the sensory-motor cortex of monkeys. *J. Comp. Neurol.* **188:** 113–136.

Jones, E.G.; Friedman, D.P.; and Hendry, H.C. 1982. Thalamic basis of place- and modality-specific columns in monkey somatosensory cortex: a correlative anatomical and physiological study. *J. Neurophysiol.* **48:** 545–568.

Jones. E.G., and Powell, T.P.S. 1970. An anatomical study of converging sensory pathways within the cerebral cortex of the monkey. *Brain* **93:** 793–820.

Kievit, J., and Kuypers, H.G.J.M. 1977. Organization of the thalamo-cortical connexions to the frontal lobe in the rhesus monkey. *Exp. Brain Res.* **29:** 299–322.

Kojima, S., and Goldman-Rakic, P.S. 1982. Delay-related activity of prefrontal cortical neurons in rhesus monkeys performing delayed response. *Brain Res.* **248:** 43–49.

Kubota, K., and Niki, H. 1971. Prefrontal cortical unit activity and delayed cortical unit activity and delayed alternation performance in monkeys. *J. Neurophysiol.* **34:** 337–347.

Kunzle, H.; Akert, K.; and Wurtz, R.H. 1976. Projection of area 8 (frontal eyes field) to superior colliculus in the monkey. An autoradiographic study. *Brain Res.* **117:** 487–492.

Lynch, J.C.; Graybiel, A.M.; and Lobeck, L.J. 1985. The differential projection of two cytoarchitectonic subregions of the inferior parietal lobule in macaque upon the deep layers of the superior colliculus. *J. Comp. Neurol.* **235:** 241–254.

Lynch, J.C.; Mountcastle, V.B.; Talbot, W.H.; and Yin, T.C.T. 1977. Parietal lobe mechanisms of directed visual attention. *J. Neurophysiol.* **40:** 362–389.

Macchi, G., and Bentivoglio, M. 1986. The thalamic intralaminar nuclei and the cerebral cortex. In: Cerebral Cortex, vol. 5, eds, E.G. Jones and A. Peters, pp. 355–402. New York: Plenum Press.

Malmo, R.B. 1942. Interference factors on delayed response in monkeys after removal of frontal lobes. *J. Neurophysiol.* **5:** 295–308.

Matelli, M.; Camarda, R.; Glickstein, M.; and Rizzolatti, G. 1986. Afferent and efferent projections of the inferior area 6 in the macaque monkey. *J. Comp. Neurol.* **251:** 281–298.

Mesulam, M.-M.; Van Hoesen, G.W.; Pandya, D.N.; and Geschwind, N.. 1977. 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.

Mishkin, M. 1957. Effects of small frontal lesions on delayed-alternation in monkeys. *J. Neurophysiol.* **20:** 615–622.

Mishkin, M., and Manning, F.J. 1978. Non-spatial memory after selective prefrontal lesions in monkeys. *Brain Res.* **143:** 313–323.

Mountcastle, V.B.; Motter, B.C.; Steinmetz, M.A.; and Duffy, C.J. 1984. Looking and seeing: the visual functions on the parietal lobe. In: Dynamic Aspects of Neocortical Function, eds. G.M. Edelman, W.E. Gall, and W.M. Cowan, pp. 159–193. New York: John Wiley & Sons.

Nauta, W.J.H. 1971. The problem of the frontal lobe: a reinterpretation. *J. Psychiat. Res.* **8:** 167–187.

Niki, H.; Sakai, M.; and Kubota, K. 1972. Delayed alternation performance and unit activity of the caudate head and medial orbito-frontal gyrus in the monkey. *Brain Res.* **38:** 343–353.

Niki, H., and Watanabe, M. 1976. Prefrontal unit activity and delayed response: relation to cue location versus direction of response. *Brain Res.* **105:** 78–88.

Ogren, M.P., and Hendrickson, A.E. 1977. The distribution of pulvinar terminals in visual areas 17 and 18 of the monkey. *Brain Res.* **137:** 343–350.

Pandya, D.N., and Kuypers, H.G.J.M. 1969. Cortico-cortical connections in the rhesus monkey. *Brain Res.* **13:** 13–36.

Pandya, D.N., and Seltzer, B. 1982. Intrinsic connections and architectonics of posterior parietal cortex in the rhesus monkey. *J. Comp. Neurol.* **204:** 196–210.

Pandya, D.N., and Yeterian, E.H. 1984. Proposed neural circuitry for spatial memory in the primate brain. *Neuropyscho.* **22:** 109–122.

Passingham, R. 1975. Delayed matching after selective prefrontal lesions in monkeys (Macaca mulatta). *Brain Res.* **92:** 89–102.

Passingham, R.E. 1972. Visual discrimination learning after selective prefrontal ablations in monkeys (Macaca mulatta). *Neuropsycho.* **10:** 27–39.

Passingham, R.E. 1984. Cortical mechanisms and cues for action. *Phil. Trans. R. Soc. Lond. B.* **299:** 101–111.

Preuss, T.M., and Goldman-Rakic, P.S. 1985. Somatosensory representation in primate prefrontal cortex: connections of the principal sulcus with S-I, S-II, and adjacent areas of the frontoparietal operculum. *Soc. Neurosci. Abst.* **11:** 677.

Rakic, P.; Bourgeois, J.-P.; Zecevic, N.; Eckenhoff, M.F.; and Goldman-Rakic, P.S. 1986. Isochronic overproduction of synapses in diverse regions of the primate cerebral cortex. *Science* **232:** 232–235.

Rakic, P., and Goldman-Rakic, P.S. 1982. Development and modifiability of the cerebral cortex. *Neurosci. Res. Prog. Bull.* **20:** 429–611.

Rezak, M., and Benevento, L.A. 1979. A comparison of the organization of the projections of the dorsal lateral geniculate nucleus, the inferior pulvinar and adjacent lateral pulvinar to the primary visual cortex (area 17) in the macaque monkey. *Brain Res.* **167:** 19–40.

Richardson, R.T., and DeLong, M.R. 1986. Nucleus basalis of Meynert neuronal activity during a delayed response task in monkey. *Brain Res.* **399:** 364–368.

Rizzolatti, G. 1983. Mechanisms of selective attention in mammals. In: Advances in Vertebrate Neuroethology, eds. J.-P. Evert, R.R. Capranica and D.J. Dugle, pp. 261–297. London: Plenum Press.

Robinson, C.J., and Burton, H. 1980. The organization of somatosensory receptive fields in cortical areas 7b, retroinsular, postauditory and granular insula of M. fascicularis. *J. Comp. Neurol.* **192:** 69–92.

Robinson, D.L.; Goldberg, M.E.; and Stanton, G.B. 1978. Parietal association cortex in the primate: sensory mechanisms and behavioral modulations. J. Neurophysiol. **41:** 910–932.

Roland, P.E., and Friberg, L. 1985. Localization of cortical areas activated by thinking. *J. Neurophysiol.* **53:** 1219–1243.

Rosenkilde, C.E.; Bauer, R.H.; and Fuster, J.M. 1981. Single cell activity in ventral prefrontal cortex of behaving monkeys. *Brain Res.* **209:** 275–294.

Rosenquist, A.C. 1985. Connections of visual cortical areas in the cat. In: Cerebral Cortex, vol 3, eds. A. Peters and E.G. Jones, pp. 81–118. New York: Plenum Press.

Selemon, L.D., and Goldman-Rakic, P.S. 1983. Organization of prefrontal and parietal terminal fields in the caudate nucleus of the rhesus monkey. *Anat. Rec.* **205:** 108A.

Selemon, L.D., and Goldman-Rakic, P.S. 1985a. Common cortical and subcortical target areas of the dorsolateral prefrontal and posterior parietal cortices in the rhesus monkey. *Soc. Neurosci. Abst.* **11:** 323.

Selemon, L.D., and Goldman-Rakic, P.S. 1985b. Longitudinal topography and interdigitation of corticostriatal projections in the rhesus monkey. *J. Neurosci.* **5:** 776–794.

Selemon, L.D., and Goldman-Rakic, P.S. 1988. Common cortical and subcortical target areas of the dorsolateral prefrontal and posterior partietal cortices in the rhesus monkey: a double label study of distributed neural networks. *J. Neurosci.*, in press.

Seltzer, B., and Pandya, D.N. 1980. Converging visual and somatic sensory cortical input to the intraparietal sulcus of the rhesus monkey *Brain Res.* **192:** 339–351.

Seltzer, B., and Pandya, D.N. 1986. Posterior parietal projections to the intraparietal sulcus of the rhesus monkey. *Exp. Brain Res.* **62:** 459–469.

Shallice, D. 1982. Specific impairments in planning. *Phil. Trans. R. Soc. Lond. B.* **298:** 199–209.

Shipp, S., and Zeki, S. 1985. Segregation of pathways leading from area V2 to areas V4 and V5 of macaque monkey visual cortex. *Nature* **315:** 322–325.

Stanton, G.B.; Cruce, W.L.R.; Goldberg, M.E.; and Robinson, D.L. 1977. Some ipsilateral projections to area PF and PG of the inferior parietal lobule in monkeys. *Neurosci. Lett.* **6:** 243–250.

Trojanowski, J.Q., and Jacobson, S. 1974. Medial pulvinar afferents to frontal eye fields in rhesus monkey demonstrated by horseradish peroxidase. *Brain Res.* **80:** 395–411.

Ungerleider, L., and Desimone, R. 1986. Cortical connections of visual area MT in the macaque. *J. Comp. Neurol.* **248:** 190–222.

Van Essen, D.C., and Maunsell, J.H.R. 1983. Hierarchical organization and functional streams in the visual cortex. *Trends Neurosci.* **6:** 370–375.

Vogt, B.A.; Rosene, D.L.; and Pandya, D.N. 1979. Thalamic and cortical afferents differentiate anterior from posterior cingulate cortex in the monkey. *Science* **204:** 205–207.

Watanabe, T., and Niki, H. 1985. Hippocampal unit activity and delayed response in the monkey. *Brain Res* **325:** 241–254.

Yeterian, E.H., and Van Hoesen, G.W. 1978. Cortico-striate projections in the rhesus monkey: the organization of certain cortico-caudate connections. *Brain Res.* **139:** 43–63.