Critical Review

High Precision Systems Require High Precision "Blueprints": A New View Regarding the Formation of Connections in the Mammalian Visual System

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Abstract

■ It is well established that early in development interconnections within the mammalian visual system are often more widespread and less precise than at maturity. The literature dealing with the formation of visual connections has largely ignored differences in developmental specificity among species differing in their phylogenetic status and/or the visual ecological niche that they occupy. Based on a review of the available evidence, we have formulated an hypothesis to account for the varying degrees of developmental specificity that characterize different visual systems. It is suggested that extremely precise systems required for high-acuity binocular vision exhibit fewer presumed developmental errors than do visual systems characterized by poorer acuity and relatively crude depth perception. The developmental implications of the hypothesis are considered, and specific experiments are proposed to further test its validity. ■

INTRODUCTION

One of the "dogmas" of contemporary developmental neurobiology is that the precise patterns of connections in mature mammalian neural systems are achieved through the elimination and pruning of much broader and less precise initial connections. Indeed, a plethora of data dealing with the development of mammalian sensory and motor systems lends strong support for this viewpoint (e.g., Cowan, Fawcett, O'Leary, & Stanfield, 1984; Ebbesson, 1984; Easter, Purves, Rakic, & Spitzer, 1985; Purves & Lichtman, 1985; Finlay, Wikler, & Sengelaub, 1987). Three types of mechanisms have been implicated in the conversion of early widespread projection patterns into the precise and topographically confined connections characterizing mature animals. Broadly defined the mechanisms underlying the sharpening of connectional patterns are (1) selective cell death, (2) retraction of axonal collaterals, and (3) restructuring of terminal fields of neurites (dendritic trees and axonal arbors). In the case of the mammalian visual system all of these phenomena have been documented to a greater or lesser extent at virtually every level of the visual pathway (reviewed by Chalupa & White, 1990). These largely regressive events are thought to be necessary as a mechanism auxiliary to the specification contained in the genome because it is presumed that the complexity of the neuronal system exceeds the genome's information coding capacity (Katz, 1983; Cowan, Fawcett, O'Leary, & Stanfield, 1984; Finlay, Wikler, & Sengelaub, 1987; see also Gierer, 1988). Support for this idea comes from experiments demonstrating that neuronal activity plays a key role in the triggering of at least some remodeling in the developing visual system (e.g., Fawcett & O'Leary, 1985; Fawcett, O'Leary, & Cowan, 1984; O'Leary, Fawcett, & Cowan, 1986; Stryker & Harris, 1986). Thus, the attainment of the mature pattern of connections appears to depend on activity-mediated interactions between subpopulations of cells within a given system.

In recent years, widespread early projections and regressive developmental phenomena "pruning" those projections have been studied, and to a certain extent quantified, in a variety of mammalian species differing in their phylogenetic status and/or the visual ecological

niche that they occupy. By comparing the results of these studies, one can test the relation between the degree of developmental specificity and the complexity and precision of topographic organization in the visual system of a given species. We will argue that the available evidence points to a relation that is largely a reversal of that expected on the basis of the "dogma." In particular, it appears that the precise topographically organized systems required for high-acuity, stereoscopic, focal vision (cf. Trevarthen, 1968; Schneider, 1969; Stone, Dreher, & Leventhal, 1979; Lia, 1989) exhibit fewer presumed developmental errors than do visual systems characterized by poorer visual acuity and relatively crude depth perception. In the present article we will provide a review of the evidence supporting this viewpoint and discuss some implications for our understanding of developmental neurobiological mechanisms.

RETINOFUGAL PROJECTIONS

Four aspects of the development of retinofugal projections are pertinent to our thesis: (1) the transient innervations by retinofugal fibers of "inappropriate" targets, (2) transient intermingling of inputs from the two eyes, (3) the formation of decussation patterns of crossed and uncrossed retinofugal projections, and (4) the establishment of topographically organized projections within retinorecipient nuclei.

Transient Innervation of Inappropriate Targets

Anterograde tracing studies have revealed, in some species, the presence of transient retinal projections to targets that at maturity are not retinorecipient. For example, in the neonatal hamster, Frost (1984) provided clear-cut evidence that retinofugal axons project transiently to several inappropriate targets, including the ventrobasal complex of the dorsal thalamus, a number of nuclei of the hypothalamus, zona incerta, substantia nigra, inferior colliculus (cf. Insausti, Blakemore, & Cowan, 1985), pons, and mesencephalic tegmentum. Transient retinal projections to lateral posterior nucleus (Baisinger, Lund, & Miller, 1977; Perry & Cowey, 1979a,b, 1982) and to the inferior colliculus have also been described in the rat (Yamauchi & Yamadori, 1982; Kato, 1983; Cooper & Cowey 1990a,b); those to the ventrobasal thalamic complex were described in the rabbit (Gayer, Horsburgh, & Dreher, 1989), and to the lateral hypothalamus (Cucchiaro & Guillery, 1980) and the perigeniculate nucleus (Linden, Guillery, & Cucchiaro, 1981; Cucchiaro & Guillery, 1984; Jeffery, 1989) in the ferret. By contrast, in cats retinal terminals throughout development appear to be confined to the regions that in adults constitute retinorecipient nuclei (Williams & Chalupa, 1982; Shatz, 1983; Williams & Chalupa, 1983). The only notable exception appears to be the early retinal innervation of the cat perigeniculate nucleus, in the immediate vicinity of the dorsolateral geniculate nucleus (Sretavan & Shatz, 1987). In fetal macaque monkeys retinal terminals appear to be strictly confined to the regions that in adults constitute the retinorecipient nuclei (Rakic, 1976).

In the cat a more subtle type of misprojection has been detected. Retinal ganglion cells of the β class, which in mature animals do not appear to innervate the superior colliculus (Leventhal, Rodieck, & Dreher, 1985; Leventhal, Schall, Ault, Provis, & Vitek, 1988), have been found during early development to project to the colliculus, including its caudal pole (Ramoa, Campbell, & Shatz, 1989). Whether in other species particular classes of retinal ganglion cells innervate transiently inappropriate retinorecipient nuclei is as yet unknown.

Intermingling of Ocular Domains

More than a decade ago Rakic (1976) in the macaque monkey and Land and Lund (1979) in the laboratory rat provided evidence that retinal projections from the two eyes are more widespread and overlapping within retinorecipient nuclei early in development than at maturity. Indeed, projections from the ipsilateral and contralateral eyes have been reported to occupy, at a certain stage of development, virtually the entire volumes of the principal retinorecipient targets, the dorsolateral geniculate nucleus (LGNd), and/or the superior colliculus (SC) in a variety of mammalian species, including primate (macaque: Rakic, 1976), carnivores (domestic cat: Williams & Chalupa, 1982; Chalupa & Williams, 1984; ferret: Linden et al., 1981; Cucchiaro & Guillery, 1984; Jeffery, 1985, 1989), rodents (laboratory rat: Land & Lund, 1979; Bunt, Lund, & Land, 1983; Laemle & Labriola, 1982; Manford, Campbell, & Lieberman, 1984; hamster: Frost, So, & Schneider, 1979; Insausti, Blakemore, & Cowan, 1985; So, Schneider, & Frost, 1978; So , Woo, & Jen, 1984; Thompson & Holt, 1989; Woo, Jen, & So, 1985), and lagomorphs (rabbit: Crabtree, 1989, 1990).

Less extensive overlap of ipsilateral and contralateral projections has been found by other investigators. For example, Shatz (1983) estimated that during development in the cat the ipsilateral eye innervates at maximum only about 45% of the LGNd, resulting in binocular overlap of retinal terminals of not more than about 30%. In the rat, it has been claimed that at maximum 75% of the LGNd volume is innervated by the ipsilateral eye (Jeffery, 1984). The innervation, during early development by the ipsilateral eye of the LGNd and SC has also been reported to be incomplete in the mouse (Godement, Salaun, & Imbert, 1984), but this has not been quantified. Recently, Crabtree (1990) reported that in pigmented rabbits ipsilateral fibers at a certain stage of development are found within the caudal three-quarters of the LGNd. On the other hand, Gayer, Horsburgh, and Dreher (1989)

estimated that in the pigmented laboratory rabbit the maximal proportion of the LGNd volume occupied by the ipsilateral projection is only about 35%, while the maximal proportion of the collicular volume occupied by the ipsilateral projection is about 45%. Furthermore, in polyprotodont marsupials such as South American opossum (Cavalcante & Rocha-Miranda, 1978; Méndez-Otero, Cavalcante, Rocha-Miranda, Bernardes, & Barradas, 1985), Australian brush-tailed possum (Sanderson, Dixon, & Pearson, 1982), as well as diprotodont marsupials such as tammar wallaby (Wye-Dvorak, 1984) and quokka (Harman & Beazley, 1986), the ipsilateral projection to the LGNd and SC does not appear to innervate the entire volume of those nuclei at any stage of development. To some degree the differences between species, as well as the differences in the data for the same species reported by different laboratories, might be related to methodological factors as well as to dissimilar critieria employed by different investigators for what constitutes label above background levels. Several authors have commented on this point explicitly and excluded lightly labeled regions from their estimates (e.g., Harman & Beazley, 1986; Shatz, 1983).

It is important to note, in this context, that the relative volume of the retinorecipient nuclei occupied by the ipsilateral projection, and the relative magnitude of the population of ganglion cells projecting ipsilaterally, varies markedly among the aforementioned species. In the adult pigmented laboratory rabbit the ipsilateral retinal projection occupies only about 1.5% of the volume of the LGNd (Gayer et al., 1989) and the ipsilateral projecting retinal ganglion cells constitute only about 0.6% of the ganglion cell population (Robinson, Sung, Dreher, & Taylor, 1990). In the LGNd of the adult rat the ipsilateral retinal projection occupies about 14% of the nucleus and ipsilaterally projecting ganglion cells constitute about 1.5–3.0% of the total population of retinal ganglion cells (Dreher, Sefton, Ni, & Nisbett, 1985; Jeffery, 1984). Similarly, the adult population of ipsilaterally projecting cells is very small in the adult hamster (about 1% of all ganglion cells, Hsiao, Sachs, & Schneider, 1984) and mouse (about 3%, Dräger & Olsen, 1980; Godement, Salaun, & Metin, 1987). By contrast, in the adult ferret (Henderson, Findlay, & Wikler, 1988; Morgan, Henderson, & Thompson, 1987), cat (FitzGibbon & Burke, 1989; Illing & Wässle, 1981; Mastronarde, 1984; Stone & Fukuda, 1974; Wässle & Illing, 1980), and macaque (Perry & Cowey, 1984; Perry, Oehler, & Cowey, 1984) ipsilaterally projecting cells constitute, respectively, about 7, 25–30, and 40% of the entire ganglion cell population. In the cat the ipsilateral population occupies about 30% of the volume of the dorsal lateral geniculate (Shatz, 1983). For other species quantitative measurements of the relative geniculate volume occupied by ipsilateral projections are not yet available, but inspection of terminal labeling patterns in the relevant papers indicates that these approximate the proportion of the ganglion cells projecting ipsilaterally (hamster: So et al., 1984; ferret: Cucchiaro & Guillery, 1984; Linden et al., 1981; macaque: Rakic, 1976; R. W. Williams, personal communication).

From our perspective, the key point to be emphasized here is that the relative magnitude of transient retinofugal projections appears to be substantially greater in species with a smaller ipsilateral projection and therefore relatively low degree of binocularity than in animals with a larger ipsilateral projection and more highly evolved binocular vision.

A related question is the precision of retinofugal projections in the developing visual system. Conceptually, it is important to separate two types of projection errors, those resulting from chiasmatic factors and those that occur at the target. "Chiasmatic errors" are indicated when ganglion cells from a region of the retina that innervate targets in one hemisphere "misproject" during development to innervate targets in the other hemisphere. For instance, in all mammals projections from the nasal retina to ipsilateral retinorecipient nuclei could be considered chiasmatic errors. In addition, in carnivores projections from the temporal retina to the contralateral thalamic nuclei could constitute a chiasmatic error, while in primates the projection from temporal retina to any contralateral retinorecipient nucleus could be considered such an error. Presumed target errors, on the other hand, are indicated when ganglion cells project to the appropriate hemisphere but innervate either nonretinorecipient nuclei or a topographically inappropriate region of a given retinorecipient nucleus.

The term "error" is used descriptively here to denote connections present during early development that are absent or very rare at maturity. Such transient projections could result from the failure, by a certain contingent of ingrowing axons, to recognize appropriate guidance cues. It is also possible, however, that transient projections are recognizing specific guidance cues, which are expressed only transiently during development. It may even be the case that at early stages of development transient projections play a role in the establishment of later developing appropriate connections. It seems reasonable to assume, however, that the failure to eliminate what we have denoted as targeting or chiasmatic errors would be maladaptive to the functional organization of the mature visual system.

Chiasmatic Errors

Retrograde tracing studies have revealed that in all species a certain proportion of retinal ganglion cells makes apparent chiasmatic errors during development. In terms of *absolute numbers* the magnitude of such errors would appear to be overall not very large and reasonably similar from one species to the next. For instance, in the normally pigmented hooded rat there are about 4800 such

ganglion cells (Jeffery, 1984), in pigmented ferret about 1700 (Morgan & Thompson, 1985), in the cat, about 14,000 (Lia, Kirby, & Chalupa, 1987, and in preparation), and in the rhesus macaque about 6100 (Lia, Snider, & Chalupa, 1988; Chalupa & Lia, 1991). However, when chiasmatic errors are expressed as a proportion of the population of ipsilaterally projecting ganglion cells, substantial variations among species become evident, with a clear trend for the error magnitude to be inversely related to the size of the ipsilateral projection (i.e., the degree of binocularity).

In the newborn hooded rat about 40% of ganglion cells projecting to the ipsilateral hemisphere are located in the "wrong" region of the retina, that is clearly outside the temporal crescent (Jeffery, 1984). By comparison, in the newborn pigmented ferret the proportion of such ectopic neurons is much lower: about 12% of ipsilaterally projecting retinal ganglion cells are located outside the temporal crescent (Morgan & Thompson, 1985). Decussation errors of similar magnitude have been noted in the fetal cat (Lia et al., 1987). Finally, in the fetal rhesus monkey, a species with the most highly developed binocular vision, the relative proportion of such ectopic cells is indeed very small, with less than 0.5% of ipsilaterally projecting neurons located in the inappropriate (i.e., nasal) hemiretina (Lia et al., 1988; Chalupa & Lia, 1991).

It should be noted that the foregoing comparisons refer to the magnitude of errors at virtually equivalent stages in the development of the visual system, from 58 to 65% of caecal period, the time from conception to natural eye opening. Dreher and Robinson (1988) proposed this as the standard temporal unit of mammalian visual system development. In all species the comparisons were made at the beginning of the period of naturally occurring ganglion cell death (for review see Dreher & Robinson, 1988). Thus, when the magnitude of the projection is taken into account, the early ipsilateral retinal projection appears to be characterized by more developmental errors in those species with a relatively smaller uncrossed pathway at maturity.

An inverse relation between the relative magnitude of chiasmatic errors and the relative size of the ipsilateral retinofugal projection is also apparent from comparison of the proportion of ectopically located ipsilaterally projecting retinal ganglion cells in normally pigmented and hypopigmented strains of different mammalian species. The ipsilateral retinofugal projections in hypopigmented strains are substantially smaller than in normally pigmented strains of the same species (Guillery, 1969; Guillery & Kaas, 1971; Lund, 1965, 1975), while the percentage, and to a lesser extent the absolute numbers, of ipsilaterally projecting retinal ganglion cells located in the inappropriate (nasal) part of the retina are significantly greater in hypopigmented than in normally pigmented strains (cf. Siamese cat: Murakami, Sesma, & Rowe, 1982; albino mouse: Dräger & Olson, 1980; albino rat: Lund, Land, & Boles, 1980; Dreher et al., 1985; albino ferret: Morgan et al., 1987; albino rabbit: Robinson et al., 1990).

Topographic Errors

Such errors have also been documented in developing visual systems. In all species the early widespread ipsilateral and contralateral projections to the LGNd and/or the SC are at least crudely retinotopically organized (rat: Martin, Sefton, & Dreher, 1983; O'Leary et al., 1986; hamster: Insausti et al., 1985; ferret: Jeffery, 1985, 1989; cat: Ostrach, Kirby, & Chalupa, 1986; Sretavan & Shatz, 1987). However, with the exception of the work of O'Leary and colleagues (O'Leary et al., 1986; Simon & O'Leary, 1990) and Yhip and Kirby (1990) on the rat, and that of Ostrach et al. (1986) on the cat, little information is available about the extent of topographic targeting errors during development of retinofugal pathways. It should also be taken into account that with current methods it is possible to evaluate only relatively gross topographic errors.

O'Leary and co-workers (1986) reported large topographic errors in the crossed retinocollicular projection of the developing rat. These investigators made small deposits of a retrograde tracer (fast blue) into the caudal aspect of the superior colliculus and subsequently examined the distribution of labeled ganglion cells in the contralateral retina. Topographic errors were defined as those cells projecting to the caudal part of the superior colliculus that were located in the peripheral temporal retina, in the mirror-image region of the nasal peripheral retina in which topographically appropriate ganglion cells were located. At the beginning of the period of naturally occurring ganglion cell death (newborn rat) O'Leary et al. (1986) estimated that for every 100 ganglion cells projecting to the topographically appropriate portion of the contralateral superior colliculus, 14 cells make gross topographic errors. In marked contrast, similar experiments on the contralateral and ipsilateral retinocollicular projection of the fetal cat, conducted at the equivalent stage of visual system development (E39 to 42), revealed a topographic error factor of only about 0.2 per 100 neurons (Ostrach et al., 1986). This suggests that in terms of absolute numbers, at equivalent stages of development, there are about 70 times as many ectopic retinocollicular ganglion cells in the rat as in the cat! Whereas a more recent retrograde labeling study (Yhip & Kirby, 1990) reported a somewhat smaller percentage of ectopic retinal ganglion cell (7–11 per 100 neurons) in the developing rat's crossed retinocollicular projection than indicated by the data of O'Leary et al. (1986), DiI anterograde labeling of terminal arbors revealed that ingrowing retinal axons do mistarget widely within the rat's superior colliculus (Simon & O'Leary, 1990). These

investigators concluded that the crossed retinocollicular projection in the newborn rat is "very diffuse," although "there is some bias for the correct region of the SC."

There is no available information concerning the developing retinofugal pathways in the primate. However, in line with our general theme, the topography of the geniculostriate pathway in the fetal rhesus monkey has been recently shown to be very precise (Lia, Snider, & Chalupa, 1989). In contrast, considerable refinement and elimination of misprojections have been reported in the geniculocortical pathway of the developing golden hamster (Naegele, Jhaveri, & Schneider, 1988).

CALLOSAL CONNECTIONS

Innocenti and colleagues (1977) discovered that callosal projection neurons have a widespread tangential distribution in areas 17 and 18 of the neonatal cat visual cortex, whereas at maturity such neurons are largely restricted to the representation of the vertical meridian at the border of these two areas. A similar developmental sequence has since been documented in other cortical areas of the cat (somatosensory cortex, Innocenti & Caminiti, 1980; auditory cortex, Feng & Brugge, 1983), as well as in visual and other cortical sensory areas in a number of other species, including two species of rodents (rats: Ivy, Akers, & Killackey, 1979; Ivy & Killackey, 1981; Olavarria & Van Sluyters, 1985; hamster: Rhoades & DellaCroce, 1980), rabbit (Chow, Baumbach, & Lawson, 1981), and macaque (Killackey & Chalupa, 1986). The establishment of mature callosal projections appears to involve the retraction of axonal collaterals rather than cell death (Chalupa & Killackey, 1989; Innocenti, Clark, & Draftsik, 1986; Ivy & Killackey, 1982). Until recently, it was thought that such exuberance characterizes the development of all mammalian interhemispheric connections. However, Dehay, Kennedy, Bullier, and Berland (1988) discovered that area 17 of the rhesus monkey cortex is devoid of callosal projection neurons throughout development. This unexpected finding prompted a reexamination of callosal connections of the striate cortex in the fetal macaque (Chalupa et al., 1989). Although some "ectopic" callosal projection neurons were noted in area 17 of an E119 fetal rhesus monkey, the relative paucity of such cells led to the conclusion that elimination of callosal connections plays only a minor role in the ontogenesis of the striate cortex in this primate (Chalupa et. al., 1989).

Thus, unlike what has been found in developmental studies of other species, in the macaque there appears to be little exuberancy in the establishment of callosal connections of primary visual cortex. It should be stressed that procedures identical to those employed to study the callosal projection neurons of the visual cortex have revealed an exuberant pattern of callosal connections in the postcentral gyrus of the fetal rhesus monkey, including the area considered the primary somatosensory cortex (Killackey & Chalupa, 1986).

DEVELOPMENTAL IMPLICATIONS

The general principle we wish to put forward is that there appears to be a correlation between the degree of precision in a neural system at maturity and the extent of developmental specificity exhibited by that system during development. The correlation is such that the more precise the system at maturity the more specific its developmental "blueprint." This is most clearly evident when comparing the decussation pattern of retinofugal pathways and the callosal connections of the primary visual cortex in the macaque to those of other mammalian species. Support for this viewpoint is also provided by comparing "less visual" and "more visual" mammals in terms of the transient innervation by retinal axons of nonretinorecipient targets as well as their precision in the innervation of retinorecipient nuclei.

The generally accepted explanation of the ubiquity of early widespread projections is that this is the most effective way of forming precise patterns of connections without complete reliance on information encoded in the genome (Easter et al., 1985). A direct implication of this idea is that the more "complex" and topographically precise the system, the greater its reliance on early developmental exuberance and activity-mediated regressive events. Indeed, it has been argued that the development of simpler neural systems, such as those of many invertebrates, is "preordained to a greater degree than neural development in higher animals" (Easter et al., 1985). However, in a mammalian system characterized by extremely precise patterns of connections, such as the parvocellular component of the retinogeniculostriate pathway of the macaque, a high degree of developmental specificity may be essential to ensure the exquisite precision evident at maturity. A developmental strategy characterized by extensive transient connections and subsequent activity-mediated refinements may simply be too risky to achieve such a system. For one thing, such a strategy may leave significant remnants of developmental errors by early ectopic projections. This may account for the appreciable proportion (3.5%) of ipsilaterally projecting ganglion cells being located in the nasal retina of the adult hooded (pigmented) rat (Jeffery, 1984). Such ostensibly ectopic neurons account for a much smaller proportion of ipsilaterally projecting ganglion cells in species with much greater stereoscopic acuity (e.g., adult cat, 0.2%, Jacobs, Perry, & Hawken, 1984; and less than 0.1% in adult macaque, Fukuda, Sawai, Watanabe, Wakakuwa, & Morigiwa, 1989, and Y. Fukuda, personal communication).

This apparent trend in the relative magnitude of ectopic retinal projections remaining at maturity is likely to reflect the relative magnitude of more subtle mispro-

jections in the visual pathways of diverse mammalian species. These could include misprojections to the wrong lamina of appropriate target nucleus, innervation of the wrong class of relay cells, as well as small topographic errors beyond the detection of currently available techniques (cf. Dreher & Robinson, 1988; Garraghty, 1985; Hamos, Van Horn, Raczkowski, & Sherman, 1987). In this context, the study by Insausti et al. (1985) dealing with the retinocollicular pathway of the hamster may be of relevance. Using the highly sensitive WGA-HRP anterograde tracing technique these investigators were able to demonstrate a sparse ipsilateral retinal projection in the adult animal that extended to the caudal pole of the superior colliculus. The ipsilateral retinal labeling caudal to the functionally defined binocular segment of the hamster's superior colliculus was interpreted as a remnant of the widespread retinal projection present in the developing animal.

As we have indicated earlier, it could be argued that transient projections should not necessarily be considered as developmental errors. In fact, these might play an important role during development as appears to be the case with thalamic as well as brain stem and basal forebrain projections to the subcortical plate (Marin-Padilla, 1978; Kostovic & Rakic, 1980, 1990; Luskin & Shatz, 1985; Friauf, McConnell, & Shatz, 1990). Similarly, the transient projections of the subcortical plate neurons to the thalamus may prove to be essential for the establishment of the permanent subcortical projections (McConnell, Ghosh, & Shatz, 1989). It might be that all transient projections serve some type of useful developmental purpose. However, transient projections might also carry a price tag in the form of residual errors remaining to maturity. When the demands for precision within a system are very high, the cost–benefit ratio might be such that it is better to forego the benefits stemming from transient projections for the sake of reducing the magnitude of residual error persisting into maturity.

It is unlikely that the differences in developmental specificity exhibited by visual projections among mammalian species are due to differences in the amount of information encoded in their genomes. It also seems unlikely that there are significant qualitative differences among mammalian species in the developmental cues (i.e., molecular markers) responsible for the guidance of ingrowing axons to their appropriate target sites. More likely, the differences in precision we have considered in this review reflect the specialized organization of different systems, including such factors as the tightness of the relationship between birthdays of neurons and their topographic location as well as the degree of morphological (and functional) neuronal heterogeneity within the pathway.

For instance, in terms of the retina and retinofugal projection, in all species there is a spatiotemporal wave of ganglion cell birthdays that begins at or near the area centralis or presumptive fovea and progresses toward the retinal periphery (Kliot & Shatz, 1982; LaVail, Yasumura, & Rakic, 1983; Rapaport, Yasumura, LaVail, & Rakic, 1987; Walsh & Polley, 1985; Walsh, Polley, & Hickey, 1983). In macaque the great majority of ganglion cells born at a given time appear to be located in a well-circumscribed region of the retina (Rapaport et al., 1987). By comparison, the distribution of ganglion cells of a given cohort of cells born at the same time is more widespread in the cat (Kliot & Shatz, 1982; Walsh & Polley, 1985; Walsh et al., 1983), and still more diffuse in the rat (Webster, 1985) or mouse (Dräger, 1985). Since the mammalian retinofugal pathways exhibit a chronotopic organization (Naito, 1986, 1989; Reese & Cowey, 1988; Reese & Guillery, 1987; Torrealba, Guillery, Eysel, Polley, & Mason, 1982; Walsh, 1986; Walsh & Guillery, 1982, 1985), a tight correlation between chronotopy and retinal location allows for the formation of more precise topographic organization within the retinofugal pathway. In turn, more precise topographic organization within the retinofugal pathway may facilitate establishment of more precise topographic maps within the retinorecipient nuclei.

A related factor is that ganglion cells of different classes, located in a given patch of the retina, are born at different times (Walsh & Polley, 1985; Walsh et al., 1983). In the optic tract the fibers of each cell class appear to be largely segregated and organized in at least rough topographic order (Guillery, Polley, & Torrealba, 1982; Reese & Cowey, 1988; Reese & Guillery, 1987; Reese & Ho, 1988; Torrealba et al., 1982). In the macaque, with a retina dominated by a single ganglion cell class, Pβ or B cells (Perry et al., 1984; Leventhal, Rodieck, & Dreher, 1981), there would seem to be less tendency for topographic errors resulting from an intermingling of chronotopic maps of different classes within the fiber groupings of the optic tract. This means that for the overall population of retinal ganglion cells, chronotopy and topographic order are more closely related in the macaque than in a species such as the cat where none of the morphological and functional classes of ganglion cells constitutes a clear majority of the retinal ganglion cells.

The hypothesis we have put forward in this article is testable in a number of respects. One possibility is that the differences in developmental specificity we have discussed are not necessarily related to the phylogenetic status of a given species. Rather, these could be related to the high degree of precision required in high acuity focal vision and stereopsis. If so, one would predict that New World monkeys with high acuity stereoscopic vision, such as the squirrel monkey (cf. Merigan, 1976), would have a similar degree of developmental specificity in forming their visual pathway as the macaque, an Old World monkey with high acuity stereoscopic vision (DeValois, Morgan, & Snodderly, 1974). By contrast, another New World monkey, the owl monkey, a nocturnal primate with relatively poor visual acuity (Jacobs, 1977),

would be expected to have a higher magnitude of ectopic neurons and exuberant connections in the development of its visual pathways, particularly in terms of the retinal decussation pattern and callosal connections of the primary visual cortex.

Another implication of our hypothesis is that in a given species those components of the visual pathway that are specialized for high acuity, spatial and stereoscopic vision would exhibit a high degree of developmental precision. Thus, in the primate we would expect the retinoparvocellular–LGNd–striate pathway to be more highly specified than the magnocellular–LGNd–striate pathway. Such differences might also characterize the visual pathway of other species. For example, one would expect that in the cat, the β class of retinal ganglion cells would exhibit more precision in forming connections than the other two main classes of ganglion cells. With current methods, distinguishing different ganglion cell classes is problematic until quite late in development. However, support for this idea is provided by studies dealing with retinal decussation patterns in the postnatal cat. The chiasmatic errors that have been noted in the nasal retina of the newborn kitten appear to be comprised mainly of γ cells (Jacobs et al., 1984). Furthermore, while some β cells in the temporal retina have been found to misproject to the thalamus of the inappropriate hemisphere, the magnitude and extent of such chiasmatic error appear greater for α and γ neurons (Leventhal et al., 1988).

Highly precise interhemispheric connections in the primate are presumed to be of vital importance for high acuity stereoscopic vision, and in our view this accounts for the relative paucity of exuberant projections in this system. We would expect that the difference in developmental exuberancy that has been found in the callosal connections of the macaque cortex, with the striate cortex being highly specified (Killackey & Chalupa, 1986; Dehay et al., 1988; Chalupa et al., 1989), to be present in comparisons of sensory systems of other species. This might be the case whenever there is a marked disparity in the degree of topographic precision that is exhibited by different modalities in a given species. One might expect, for instance, connections of the barrel-fields of the rodent somatosensory cortex to be more highly specified developmentally than the connections of the rodent visual cortex. Such cross-modality differences may even be evident at subcortical levels of certain sensory pathways.

CONCLUDING REMARKS

Most probably, some refinement occurs in the formation of all neural connections in the mammalian brain. Nevertheless, there is reason to believe that in recent years we have been somewhat overexuberant about developmental exuberance. In particular, relatively little attention has been paid to the possibility that different strategies might be employed during the development of different components of the mammalian visual pathways to form unique patterns of connections. The diversity in the functional capabilities of the visual system among mammalian species (cf. Pettigrew, Dreher, Hopkins, McCall, & Brown, 1988) would make it surprising if the laboratory rat, with a visual system capable of resolving no more than 1.2 cycles/degree, followed the same strategy in forming connections as the visual system of the human, with a resolution capability of over 60 cycles/degree. We believe that a closer consideration of developmental differences—both among species and among different components of the visual system in a given species—will prove to be important in furthering our understanding of how connections are formed in the mammalian visual system.

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