consistent with the view that the retina and brain had more extensive reciprocal connections earlier in evolution and agrees with the parcellation theory (*17*), according to which neuronal systems evolve by a process that involves the loss of connections rather than the creation of new connections with hitherto unrelated targets.

A second hypothesis must also be considered. In our sample of teleost species, retinopetal systems originating in the tectum and pretectum are best developed in the puffer; they are slightly less obvious in the cichlid and much less striking in the catfish. In the weakly electric fish *Eigenmannia virescens* (*18*) they are even more poorly developed than in the catfish. It may be accidental that the magnitude as well as the frequency of spontaneous eye movements in the species studied follow the same sequence. The puffer has most extraordinary ocular movements and continuously scans its environment, whereas *E. virescens* has almost none of these movements. The catfish and cichlid are somewhere in between, with the cichlid having distinctly more pronounced spontaneous ocular movements than the catfish. Perhaps retinopetal connections are involved in preventing apparent movements of the environment during voluntary eye movements. Of course, further investigations are required to determine whether the correlation between eye movements in a given species and the development of its retinopetal systems is due to our selection of experimental subjects or whether this correlation is generally present.

Note added in proof. The recent finding of two mesencephalic nuclei projecting bilaterally to the eye in a lamprey (*19*) has just come to our attention.

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Regenerating Axons Reclaim Sensory Targets from Collateral Nerve Sprouts

Abstract. *There is a critical period for the sprouting of intact low-threshold mechanosensory cutaneous nerves in rats; functional invasion of adjacent denervated skin does not occur in animals older than about 20 days of age, and it is largely confined to denervated skin within the "domain" of the parent dermatome. These nerves can regenerate readily in the adult, however, and such regenerating nerves do not respect domain borders; moreover, they functionally displace endings of intact nerves that earlier had sprouted into denervated skin.*

One approach to the study of how nerves can establish appropriate connections, and of possible plasticity intrinsic to the connections themselves, is to permit nerves (both intact sprouting and regenerating ones) to compete for targets. In our studies of the reinnervation of denervated cutaneous targets in the rat, we have found that intact low-threshold mechanosensory nerves sprout new functional endings into adjacent denervated skin only during a brief critical period in early life and that these endings are functionally replaced by regenerating nerves that later arrive at the same region of skin.

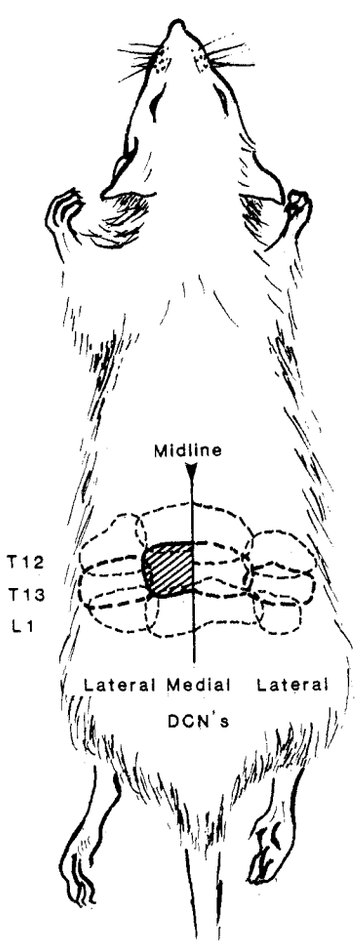

Fig. 1. Typical map of the low-threshold mechanosensory fields of the dorsal cutaneous nerves. The medial and lateral T13 subfields are shown with bold outline; the medial one (mDCN-T13) on the left is hatched.

We electrophysiologically mapped the low-threshold mechanosensory fields (*1*) of the two divisions (medial and lateral) of the segmentally arising dorsal cutaneous nerves (DCN's) (*2*). A hand-held bristle was used to deform skin and to displace hair shafts and so stimulate a variety of low-threshold mechanoreceptors (*3*). Among these were the "touch domes"—epidermal elevations that become visible after depilation. Each dome is supplied by one to three axons that branch to innervate a plate of Merkel cells at its base; displacement of the tylotrich hair associated with the dome or direct mechanical deformation of its surface evokes an irregular, slowly adapting discharge of impulses (*4*). The DCN mechanosensory subfields overlapped only slightly and were similar in size and shape from animal to animal (Fig. 1). In normal animals, the number of touch domes within the field of a given nerve remains stable from at least 15 days of age to maturity (Table 1); as the animal grows and its surface area increases, the domes become farther

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apart. In the rat, the touch domes with their Merkel cells survive denervation (*5*); we have observed denervated domes in the dorsal skin for periods up to 18 months, during which time nerve regeneration was prevented.

An island of innervated back skin was produced in 10-day-old rat pups by cutting all the branches of the DCN's between thoracic segment 10 (T10) to lumbar segment 3 (L3) on both sides except for the medial branch of DCN-T13 on the left (Fig. 1). The intact fibers of this branch subsequently sprouted to invade adjacent denervated skin; examined at 20 days of age or older, this sprouting was revealed both by an increase in area of the medial DCN subfield, over and above its normal expansion during growth (Fig. 2), and by an increase in the number of touch domes supplied by this medial nerve branch (Table 1). The extra domes were all located in the adjacent skin denervated at the initial operation, and there appeared to be no patches of uninnervated skin or domes in the expanded fields, suggesting that the functional sprouting probably occurred uniformly from the innervated region. We could not obtain any evidence of such sprouting at 15 days of age, however, whether the original denervation was performed at 10 days or even at 5 days of age. It seems then that the earliest age at which functional sprouting occurs is sometime after 15 days; we have not yet excluded the possibility that sprouts are present before 15 days but have not yet acquired mechanosensory function. The extra expansion of the low-threshold field of the medial nerve isolated at 5 to 15 days actually ceased at about 20 days, even though the surrounding skin was still denervated. This apparent cessation of sprouting was indicated by the number of touch domes the nerve supplied, which remained constant after reaching a new level at 20 days (Fig. 2 and Table 1); after this time the expanded field with its increased population of touch domes simply grew *pari passu* with the growth of the animal. Moreover, denervations performed at or after 20 days did not lead to an expansion of a remaining field into adjacent denervated skin (Table 2). We conclude that the functional sprouting of these mechanosensory nerves into denervated skin is limited to a critical period that ends at about 20 days of age and that may well begin at approximately 15 days (*6*).

These results contrast with those reported for high-threshold (nociceptive) nerves in the rabbit (*7*) and the rat (*8*), and with those we have previously obtained from salamanders (*1*) in which the collateral sprouting of intact low-threshold cutaneous nerves can apparently occur at any age. However, the sprouting we found in the rat, as in the salamander (*9*), is essentially confined to the territory of the "parent" dermatome. The enlargement of the receptive field of the (intact) medial branch of DCN-T13 into surrounding denervated skin was found to be almost entirely into the former territory of the lateral branch and only slightly into the adjacent denervated skin of the T12 and L1 dermatomes. That some sort of territorial constraint operates on intact nerves was shown particularly well when the skin of 10-day-old pups was partially denervated so as to leave the entire T13 dermatome normally innervated, with only skin cranial and caudal to it denervated; no invasion of the contiguous denervated skin by the intact T13 axons was subsequently detected. The domain borders (*9*) of these nerves in the rat therefore correspond closely to the dermatomal borders.

In contrast to the sprouting of intact low-threshold axons, the regeneration after a cut or crush of these mechanosensory nerves was not temporally or spatially restricted, and in the adult rat regenerating fibers freely crossed the domain (dermatomal) boundaries into denervated skin. We therefore investigated the consequences of allowing axons to regenerate to skin that earlier (during the critical period) had been reinnervated by collateral sprouts. At various postoperative times, electrophysiological recordings from whole nerves were made to detect low-threshold cutaneous mechanosensory function in regenerated axons or in axons of the intact nerve whose field had been isolated at 10 days of age. In groups mapped at 30 and 40 days of age no functional regeneration of cut nerves was detected, and the enlarged islands of innervated skin (the field of the medial DCN-T13 completely surrounded by denervated skin) contained the appropriately increased number of touch domes that now included those captured by sprouts within the critical period (Table 1); the extra touch domes were almost all formerly supplied by the lateral branch of DCN-T13. Functional regeneration of the originally cut nerves was

Table 1. Domes (mean ± standard deviation) innervated by the medial branch of DCN-T13. In experimental animals, adjacent nerves were cut at 10 days of age to isolate the field of DCN-T13.

Age (days)	Group			
	Control		Experimental	
	N	Domes	*N*	Domes
15	8	18.6 ± 1.5	4	19.0 ± 3.4
20	27	19.0 ± 2.4	8	28.5 ± 2.0
30	18	18.1 ± 1.8	4	28.0 ± 0.8
40	7	18.6 ± 4.7	3	27.7 ± 1.5
60	11	18.8 ± 2.0	11	28.4 ± 3.2
60*			8	19.6 ± 2.2

*Functional regeneration of originally cut nerves was allowed to occur.

Table 2. Mechanosensory field of the medial branch of DCN-T13, isolated at 20 days of age.

Age (days)	Area measurements				Domes in the field			
	Experimental		Control		Experimental		Control	
	N	Area (mm^2)	*N*	Area (mm^2)	*N*	Domes	*N*	Domes
30	6	59 ± 8	31	57 ± 8	6	19.3 ± 2.2	18	18.1 ± 1.8
40	10	105 ± 4	25	112 ± 18	5	19.0 ± 3.0	7	18.6 ± 4.7

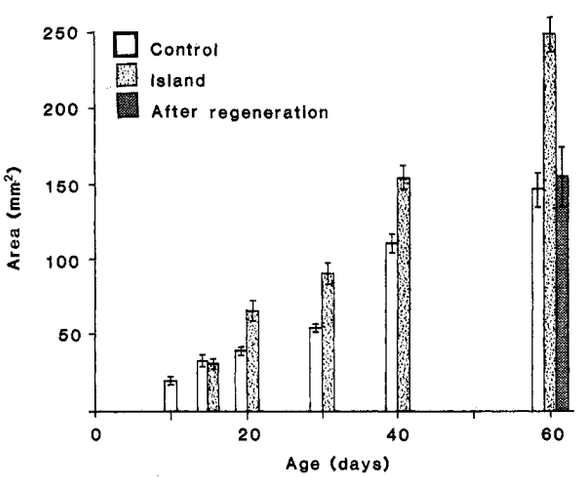

Fig. 2. Area ± standard deviation of the low-threshold mechanosensory field of the medial branch of DCN-T13 (Fig. 1) in control animals and in animals in which the surrounding skin was denervated at 10 days of age. In a third group, shown at 60 days, the originally sectioned adjacent nerves regenerated and successfully reinnervated skin after sprouting of the intact nerve was completed; this reinnervation occurred at about 45 days of age.

first detected in 45-day-old animals, and by 60 days of age the regenerating nerves had well-established mechanosensory fields. In these animals, however, the medial DCN-T13 nerve fields were now no different from those of normal control animals of the same age, and the number of touch domes now supplied by the medial DCN-T13 was normal (Table 1). In 60-day-old animals in which regeneration of the cut nerves was deliberately prevented by ligation of their central stumps, the isolated fields and their population of touch domes remained enlarged (Fig. 2 and Table 1). The regenerating nerves appeared therefore to have replaced the extra population of nerve endings sprouted by intact nerves. In keeping with this result, in the 60-day animals with regeneration of adjacent nerves, the mechanical stimulation of identified domes that had been reinnervated during the critical period by sprouts from intact axons now evoked impulses only in regenerated ones. The recapture of skin and its touch domes by the regenerated nerves occurred sometime between 40 and 60 days of age, commencing about 35 days after the nerves were cut. Interestingly, "foreign" regenerating axons, for example of DCN-T12 or L1, seemed as competent as those of the original nerve (the lateral branch of DCN-T13) in displacing sprouted endings. Regenerating high-threshold nerves have also been shown to recapture skin from sprouted nerves in the rat (*8*).

These results are in marked contrast to findings in the salamander, in which the Merkel cells occur singly, scattered throughout the epidermis (*10*); after their denervation they seem to become permanently captured by the first axon to reach them, whether this is the original axon or a foreign one, and the endings are not thereafter displaced (*11*). In the rat, the target character of the Merkel cell seems to be not totally suppressed upon innervation by sprouted nerves since the cells are apparently still recognized by regenerating axons. Furthermore, only the synapses established by sprouted endings on the Merkel cells in touch domes outside the normal territory of the parent nerve are vulnerable to competition from regenerating nerves; the synapses within the normal field are not. The sizes and maturity of the individual terminal fields of axons, their usage, and the distance between arriving nerve endings, have all been hypothesized to affect the stability of synapses, either during development (*12*), or during the functional replacement by regenerating nerves of other regenerated nerves or of sprouted ones (*8, 13*). In the light of the spatial constraints on collateral sprouting, it is interesting that the seemingly vulnerable endings of low-threshold mechanosensory nerves are those located in the former field of a neighboring nerve, even one within the parent dermatome, suggesting the additional possibility that territorial preference too may be of importance in determining the relative stability of synaptic connections.

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Development of Visual Centers in the Primate Brain Depends on Binocular Competition Before Birth

Abstract. *Removal of one eye before birth permanently changes the cellular organization and synaptic connectivity of visual centers in the primate brain. The most notable alterations are (i) the lateral geniculate nucleus develops only two cellular layers and one interlaminar fiber band instead of the normal six layers and five bands, (ii) aberrant synaptic connections are formed between the intact eye and the geniculate neurons that have lost their normal input, and (iii) ocular dominance columns fail to develop in the visual cortex.*

It has been known for some time that monocular enucleation or sensory deprivation in the neonatal period causes functional and structural alterations in the visual system of mammals (*1*) including primates (*2, 3*). The effect is particularly prominent in the dorsal lateral geniculate nucleus (LGd), which in most Old World primates as well as in humans consists of six horseshoe-shaped cellular layers separated by five fiber-rich interlaminar bands (Fig. 1A). Three of the layers (1, 4, and 6) receive input from the contralateral eye (Fig. 1B) and the remaining three (2, 3, and 5) from the ipsilateral eye (*4*). The LGd neurons subserving each eye project to layer IV of the visual cortex (Fig. 2D) in the form of separate and alternating ocular dominance columns (*5*). The two ventralmost layers of the LGd contain large cells and are termed "magnocellular," while the upper four layers have smaller cells and are called "parvocellular" (Fig. 1A).

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