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Changes in the Cortical Map of the Hand following Postnatal Median Nerve Injury in Monkeys: Modification of Somatotopic Aggregates

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Median nerves to the hands of 8–15-d-old marmoset monkeys were transected and precluded from regeneration by ligation. Following periods of 0.4–1.5 years, features of organization in the cortical area 3b hand map were assessed neurophysiologically, and compared to features in normally reared monkeys.

Cortical features in monkeys with both histories were *similar* in certain respects. (1) Receptive field organization was similar in terms of tactile thresholds and receptive field size, continuity, and glabrous–hairy specificity. (2) Somatotopic organization was similar in terms of the continuity of the glabrous representation, and progressions of receptive field shifts across some parts of the hand map. (3) Finally, the overall size of the hand map did not change.

In contrast, other cortical features clearly *differed* following these developmental histories. (1) Neurons at virtually all recording sites in normal hand maps responded to light mechanical stimulation, whereas, following injury, neurons at about 8% of the recording sites responded only to high-intensity stimuli. (2) Somatotopic organization differed in terms of the presence or absence of the representation of skin autonomously innervated by the median nerve, the number and continuity of representations of hairy skin, and the spatial interfacing of representations. (3) Finally, there were differences in the areas and widths of representations of parts of the hand. The overall impression is that there is a correspondence between the cortical features that changed most after injury, and the features that varied most in individual normal monkeys: in both circumstances the most variable features involved properties of spatial patterning across large aggregates of neurons as reflected by the size, shape, continuity, and interfacing of representations.

A hypothesis is proposed that suggests that the cortical hand map normally consists of a number of representations that are capable of developing and surviving somewhat autonomously of each other. The features of spatial patterning in the mosaiclike map of these representations are influenced by postnatal availability of inputs from intact hand nerves.

The development of the somatosensory system in human and nonhuman primates begins prenatally and extends into the postnatal period (e.g., Goldman-Rakic and Brown, 1982; Meisami and Timiras, 1982; Rakic et al., 1986; Reisman, 1987; Huntley et al., 1988; Peters and Jones, 1988; Darian-Smith et al., 1990). Peripheral nerve damage in infants and children causes a range of changes in touch perception that may or may not remain apparent in later life (e.g., Weinstein, 1969; Frykman, 1976; Mailander et al., 1989). Given the normal time course of development, it seems likely that this range of perceptual outcomes reflects a corresponding range of brain changes that result from alterations in postnatal development. How is postnatal development altered, and what are these changes?

To address this question, the present experiments assessed how postnatal nerve injury affects processing of touch information in the primate cortex. The specific goal was to determine how features of organization in the primary somatosensory cortical hand map are changed when monkeys were raised under normal conditions, with a usual complement of three nerves from the hand, versus when monkeys underwent postnatal median nerve injury and rearing with two hand nerves. These experiments were pursued in a second study in which organization in these groups was compared to the organization in monkeys that, due to early injury of two hand nerves, were raised with only one hand nerve (see companion article, Wall et al., 1992).

Materials and Methods

Experimental sample. Experiments were conducted on eight marmoset monkeys (*Callithrix jacchus*). Five monkeys developed with normal innervation of the hand. The area 3b hand cortex was sampled completely in three of these monkeys, whereas, in the remaining two animals, mapping was delimited to parts of the hand map. Three monkeys developed with hands innervated by normal ulnar and radial nerves, but with a sectioned and ligated median nerve. The area 3b hand cortex was completely mapped in each of these monkeys.

Nerve transection and ligation. Eight- to fifteen-day-old infant monkeys were anesthetized with halothane and nitrous oxide. Using aseptic procedures, the median nerve was isolated, ligated near the wrist, and transected proximal to the ligature. The epineural sheath of the proximal stump was subsequently slid up the nerve, and the nerve was transected again at this level. The empty sheath was folded and ligated to form a closed ending. Postmortem dissections indicated the transected nerves ended in neuromas. Although it is difficult to rule out fiber regeneration completely, when examined under the dissecting microscope no processes were seen to extend from neuromas or into the wrist.

Neurophysiological mapping. Recordings were made from normal animals that were adolescent or adult in size. For the animals with transected nerves, one monkey was studied at 0.4 years of age, whereas the remaining monkeys ranged from 1.3 to 1.5 years. By size and breed-

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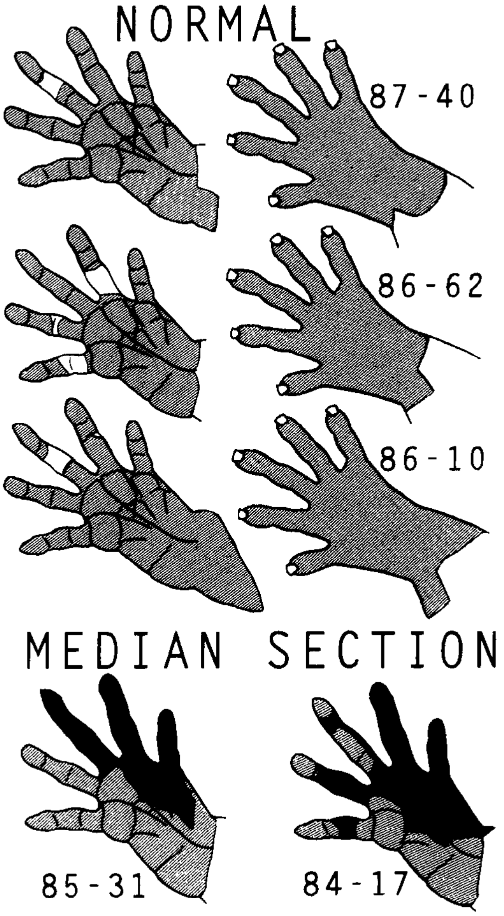

Figure 1. *Shading* indicates the summed receptive field areas of all recording sites in the cortical area 3b hand maps of three normal monkeys (*top*) and two monkeys reared after median nerve section (*bottom*). Except for small, inconsistently located zones (*not shaded*), the complete surface of the hand is represented in the cortical map of each normal monkey. In contrast, following median nerve section, the radial glabrous hand (*black*) was consistently denervated and not represented in the hand map. The denervated zone indicates the autonomous median nerve innervation territory. See Figure 4 for names of hand parts.

ing age for *Callithrix,* the older monkeys were adolescent or young adults.

Recording procedures were similar to those described previously (e.g., Wall et al., 1986). Monkeys were tranquilized and anesthetized (acepromazine, 0.4–0.8 mg/kg, i.m., and ketamine hydrochloride, 25–50 mg/kg, i.m.), and the head was positioned in a stereotaxic frame. Following exposure and photographing of the anterior parietal cortex, an array of penetrations was made across the area 3b hand region and adjacent cortical regions. Penetrations were made with tungsten microelectrodes (1–4 MΩ, measured at 1 kHz) oriented perpendicular to the cortical surface. With some variance due to vasculature, efforts were made to space recording sites about 200 μm apart. At each penetration, attempts were made to define a low-threshold field from multiple-unit discharges. Receptive fields were determined 400–900 μm below the surface, which localized the electrode tip around layer IV; however, similar fields were seen above and below these depths.

The stimuli consisted of hand-delivered contacts and brushes of the skin, hairs, and deep tissues. Cutaneous stimuli were presented so as to monitor the activity of receptors directly beneath the probe, rather than receptors affected by gross stimulus conduction across the skin. The defined receptive fields were judged to reflect the *maximal* field area of the recorded units. For a subsample of recording sites, Semmes–Weinstein filaments were used to estimate pressure thresholds from the centers of glabrous fields. Threshold values are expressed in terms of the markings on the filaments [=log 10(force mg)]. To ensure objectivity in mapping, the investigator defining receptive fields did not know the location of the microelectrode during the experiment.

Upon completion of mapping, microlesions (10 μA, 10 sec) were made at selected recording sites, and the monkeys were overdosed with barbiturate and perfused. The brain was sectioned frozen, and cresyl violet–stained sections were prepared to determine the locations of the microlesions and architectonic borders of area 3b.

Data analysis. Map data were evaluated using previously described procedures (Wall et al., 1986). The rostral and caudal borders of area 3b were determined from cortical cytoarchitecture. The mediolateral extent of the hand map was determined from the borders with the representation of the wrist medially, and the face laterally. The borders and areas of representations of hand parts were delimited and measured with a planimeter using previously described procedures (Wall et al., 1986).

Results

Hand surfaces represented in the cortical map

Hand innervation was evaluated by summing receptive fields in experiments in which the hand cortex was completely mapped. With the exception of small, inconsistent regions on digits, virtually all hand regions were represented in each normal map (e.g., Fig. 1). In contrast, following section of the median nerve there was a consistent loss of glabrous inputs from P2, radial P1-TH, D1–D2, and part of all of D3 (e.g., Fig. 1). These findings indicate that median nerve section resulted in a chronic loss of low-threshold inputs from the pads and digits on the radial glabrous hand.

Cortical activation at single recording sites

Responsiveness

Neurons at virtually all recording sites in normal hand maps were highly responsive to light cutaneous stimulation. Responses from different glabrous subregions had similar pressure thresholds (e.g., Fig. 2). Following section of the median nerve, cortical neurons at most (mean = 92%) recording sites were highly responsive to cutaneous stimulation. Neurons at the remaining 8% of sites responded to harder tap stimuli, but it was unclear whether activation was from high-threshold cutaneous and/or deep inputs. Since inputs were lost from the radial glabrous skin, light pressure thresholds were only measurable from the ulnar glabrous hand (Fig. 2). As in normal monkeys, there were no threshold differences for subdivisions of this skin; moreover, the thresholds for the overall ulnar side of the hand were normal (e.g., Fig. 2).

Receptive field organization

Size. Receptive field sizes in normal monkeys varied within a predictable range. Larger glabrous fields tended to be located proximally, spanning one to three palmar pads, and smaller fields tended to be located distally, on a single digit or digit phalanx (e.g., Fig. 3). Normal hairy fields varied from larger fields extending across much of the proximal hand, to smaller, more distally located fields extending across a single digit or nail bed. Following median nerve section, a normal gradient in relative field size was seen for proximodistal hand locations, and the absolute size of fields on a given hand location was similar to normal (e.g., Fig. 3).

Continuity. In both groups of monkeys, receptive fields typically extended across a continuous skin zone. Exceptions were recording sites with "split" fields on neighboring digits (e.g., Fig. 3). As reflected by similar small percentages of sites with split glabrous digit fields (e.g., normal = 4.7%; median section = 2.2%), rearing with two versus three nerves did not result in major changes in the continuity of receptive fields.

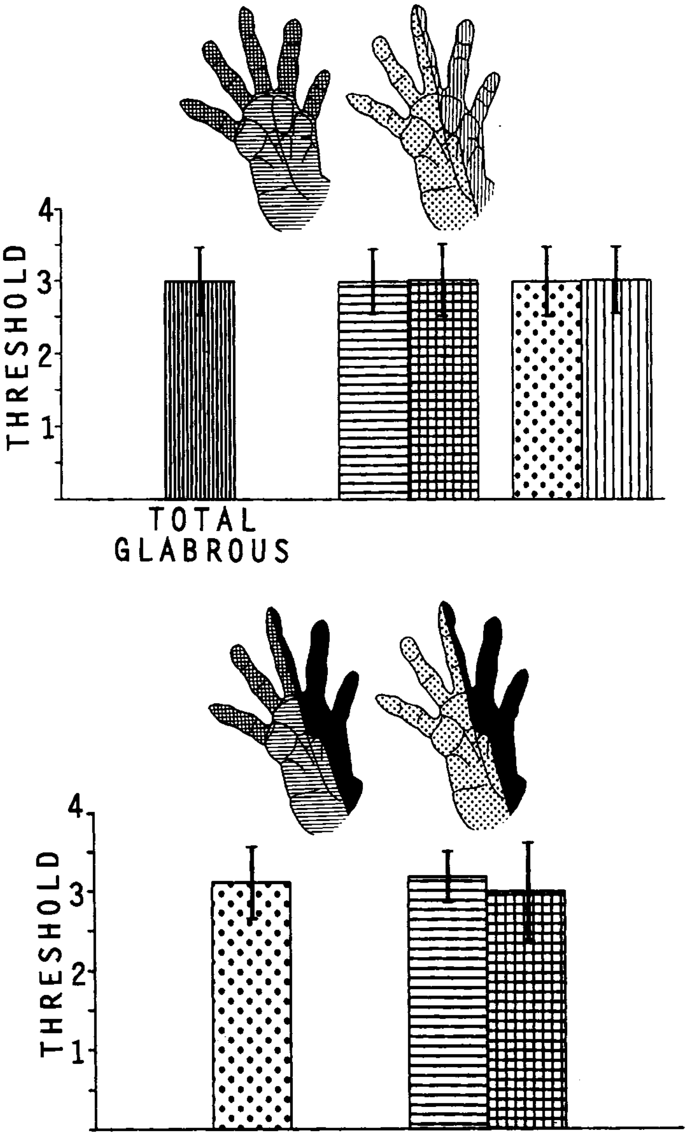

Figure 2. Tactile thresholds of cortical neuron responses to glabrous inputs in normal monkeys (*top*) and monkeys reared after median nerve section (*bottom*). Mean thresholds (±SD) for different subregions of glabrous skin are indicated by the corresponding patterns of *stippling* and *hatching* on the hands and histogram bars. In normal monkeys, there were no differences in thresholds for the indicated radial versus ulnar side of the hand ($t[111] = 0.22$, $p = 0.82$), or palm versus digit skin ($t[111] = 0.25$, $p = 0.80$). In monkeys reared after median nerve section, denervation of the radial glabrous skin (*black*) resulted in no significant differences in thresholds for the indicated palm versus digit skin regions that remained innervated ($t[23] = 1.01$, $p = 0.32$). In addition, thresholds on the innervated ulnar skin of median section monkeys did not differ from the normal thresholds for this skin ($t[91] = 1.10$, $p = 0.27$).

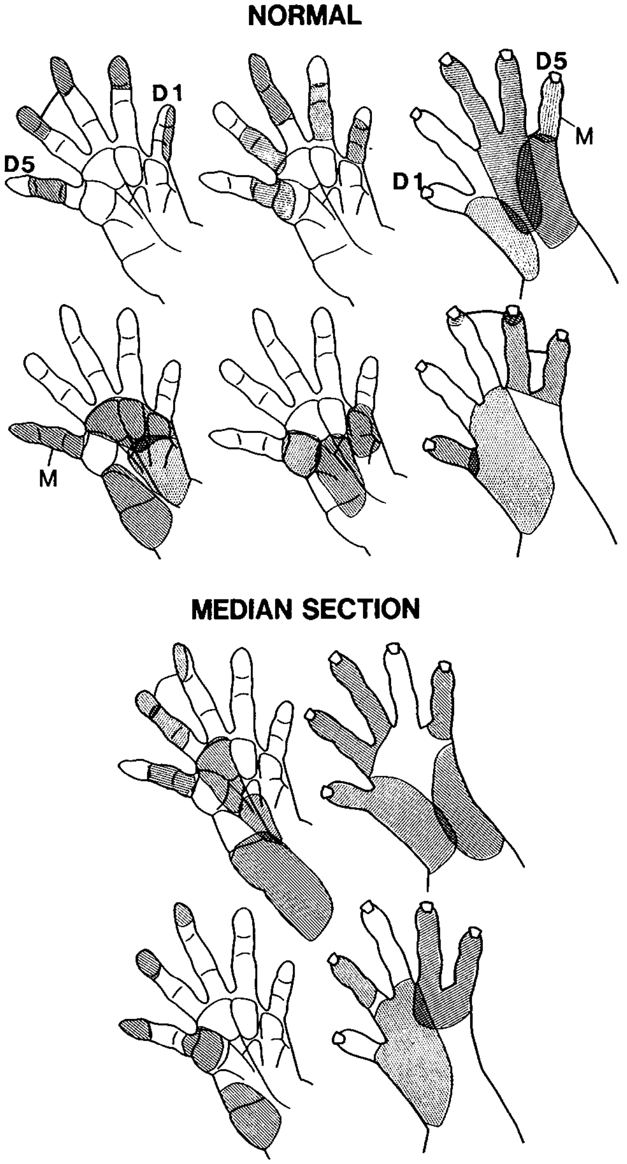

Figure 3. Examples of receptive fields in normal monkeys (*top*) and monkeys reared after median section (*bottom*). Each *hatched* area represents a receptive field defined from a multiple unit response at a single cortical recording site. "Split" fields observed at a single recording site are shown joined by *lines*. A "mixed" glabrous–hairy field is indicated by *M*. There were no major differences in receptive field size, or in the incidence of "split" and "mixed" fields, in normal monkeys and monkeys reared after median section.

Specificity. Receptive fields were normally specific to either glabrous or hairy skin; however, a mean of 2.8% of recording sites in normal monkeys had a "mixed" field involving both types of skin (e.g., Fig. 3). A similar percentage (3.1%) of sites had a mixed field following median section.

Cortical activation across multiple recording sites

Somatotopic organization

The glabrous representation normally occupied a continuous block in the hand map (Fig. 4). Individual palmar pad representations occupied caudal positions, with the representation of P1-TH laterally, PH medially, and P2 and P3-4-I in between (Figs. 4; 5, Row A). Digits D1 through D5 were represented rostrally in a similar lateromedial sequence (Figs. 4; 5, Row B). Caudorostral movements of recording sites generally led to receptive field shifts from proximal palm to more distal digits (Fig. 5, Rows C, D). The hairy representation normally occupied four to six discontinuous cortical regions, consistently located along the medial and lateral edges of the glabrous representation and, to a lesser extent, between the glabrous digit representations (Fig. 4). The medial patch or bandlike region represented the ulnar hairy hand and hairy D5, D4, and, to some degree, D3, whereas the lateral cortical bands or patches represented the radial hairy hand and hairy D1, D2, and, to some degree, D3

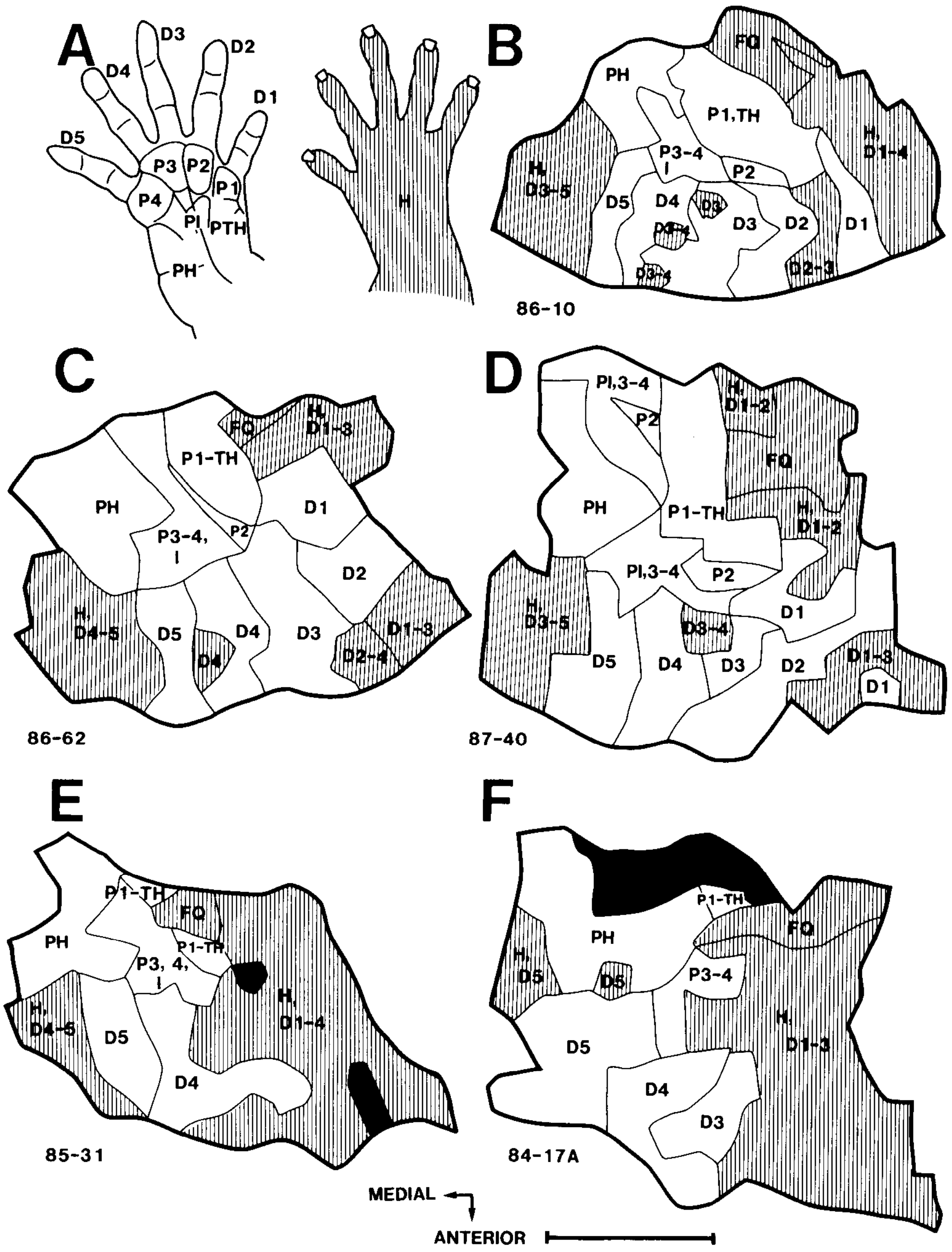

Figure 4. Cortical area 3b maps of the hand indicating the somatotopic organization of the representations of glabrous (*white*) and hairy (*hatched*) surfaces of the hand. *A*, Abbreviations for skin surfaces: *D1–D5*, digits 1–5; *P1–TH*, P1 and thenar palmar pads; *P2–P4*, P2–P4 palmar pads; *PI*, insular palmar pads; *PH*, hypothenar palmar pad; *H*, hairy hand between the wrist and knuckles; *FQ*, forequarter skin on the adjacent forelimb and trunk (not shown). *B–D*, Organization in normal monkeys. Note that there is a high degree of consistency in the arrangement of representations across individual monkeys, while at the same time, there is some variability in terms of the size, shape, continuity, and spatial interfacing of representations. *E* and *F*, Organization in monkeys reared after median nerve injury. Note, first, that there is a high degree of interanimal consistency in the arrangement of representations while at the same time there is some variability in details of organization, and second, that the overall somatotopic pattern seen after median nerve section is clearly outside the range of variability seen in normal monkeys. *Black regions* indicate cortical areas where neurons were only responsive to higher-threshold inputs. The FQ representation was not included in the hand map but is consistently adjacent to the map. Scale bar, 1 mm.

and D4 (Fig. 6). Cortical patches between glabrous digital representations represented hairy D4, D3, and, less consistently, D2.

In monkeys reared with two nerves, the representations of hand parts with intact innervation developed independent of the loss of neighboring representations, but were clearly shaped by the nerve injury. Similar to normal, the representation of the glabrous skin usually occupied a continuous block (Fig. 4). Individual palmar pad representations occupied caudal locations, with the representation of PH medially, and P3-4-I more lateral (Figs. 4; 7, Row, A). Although a small representation of the proximal P1-TH pad was sometimes situated more laterally, there were no representations of radial P1-TH or P2. The representations of the glabrous digits were located rostral to the pad representations with D5 represented most medially and D4 more laterally (Figs. 4; 7, Row B). Although a representation of the ulnar glabrous D3 was sometimes seen, there were no glabrous representations of the radial D3, or D2 and D1. Glabrous digit and palm representations were in register with each other, and as a result, movements of recording sites in the caudorostral dimension led to relatively normal proximodistal shifts (e.g., Fig. 7, Row C). However, since the representation of the radial glabrous hand was absent, this organization only involved ulnar glabrous skin. In further contrast to normal organization, the hairy hand was represented in fewer than normal, that is, two to three discontinuous regions (Fig. 4). There was a high degree of specificity in these hairy representations, with the medial band(s) representing the ulnar hairy hand and hairy D5 and D4, and the lateral band representing the radial hairy hand and hairy D1-4 (Fig. 6). Unlike normal, the lateral band occupied space normally representing the radial glabrous hand, and as a result, the representations of the central parts of the glabrous hand and

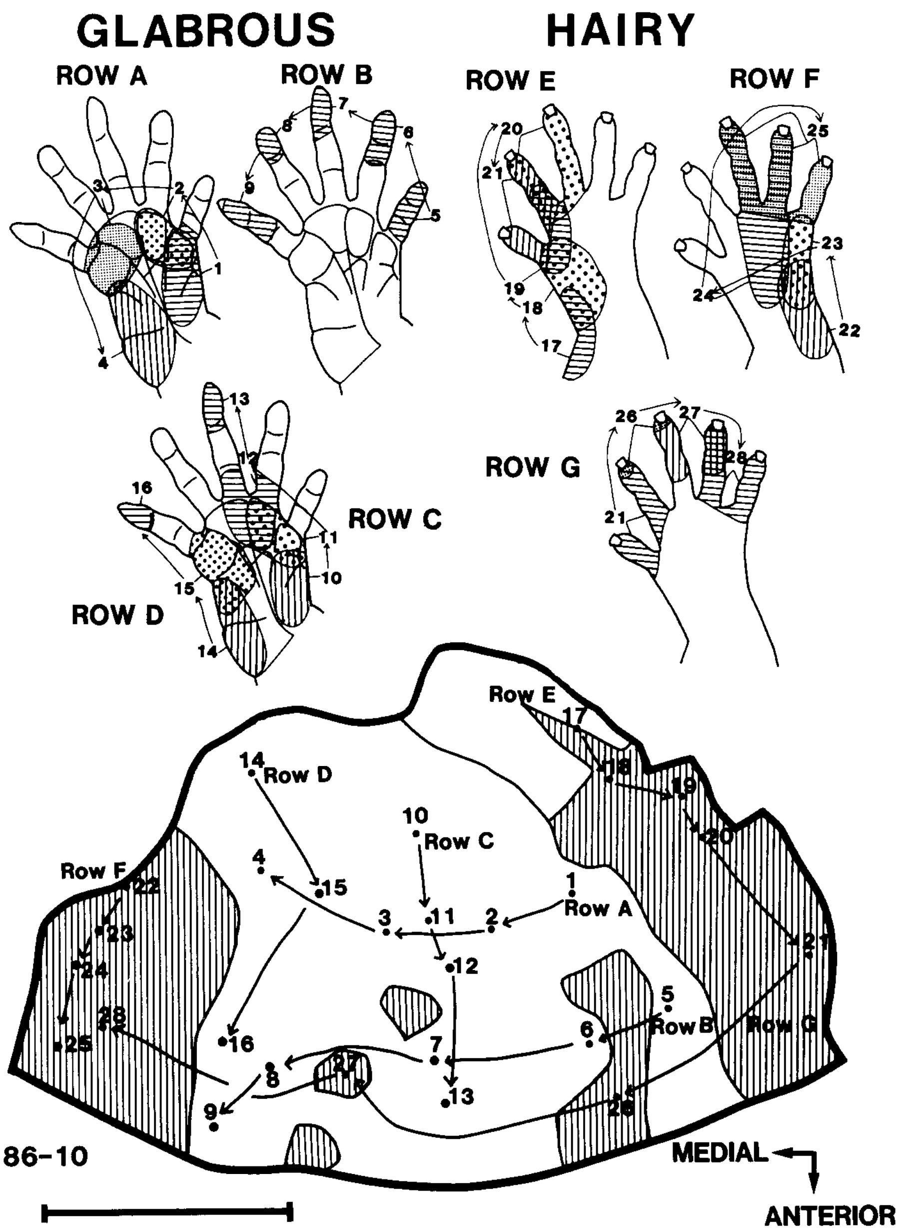

Figure 5. Shifts in receptive field location with lateromedial and caudorostral movements of cortical recording sites in a normally reared monkey. Note that the caudorostral axis of the hand map corresponds to the proximodistal axis of the hand, whereas the lateromedial cortical axis corresponds to the orthogonal axis across the hand. The representations of hairy (*hatched*) and glabrous (*white*) skin are organized in coarse register. Scale bar, 1 mm.

the D1 side of the hairy hand were continuous in lesion monkeys, whereas in normal monkeys the analogous mediolateral continuity was between representations of the central glabrous hand and the D1 side of the glabrous hand (Figs. 4, 5, 7). Thus, median section produced a novel somatotopic interfacing of glabrous and hairy representations.

Size measurements

Total hand map. The mean areas of the hand maps in normal and median-sectioned monkeys were not different (normal = 3.64 mm^2; median section = 3.75 mm^2; $t[4] = 0.17$, $p = 0.87$).

Hairy representations. In normal monkeys, a smaller percentage of the hand map represented the hairy hand (33%) than the glabrous hand (67%) ($t[4] = 6.38$, $p = 0.003$) whereas, following nerve section, the respective representations occupied comparable percentages of 44 and 47% of the map (Fig. 8). Thus, the overall hairy representation increased by about 11% due to median section. Looking at this change more closely, following median section the lateral cortical band representing the radial hairy hand and digits occupied 37% of the map, whereas the more medial band(s) representing the ulnar hand and digits occupied a smaller mean area of 7% (Fig. 8; $t[4] = 5.53$, $p = 0.005$). In contrast, the analogous respective areas of 16% and 17% in normal monkeys were *not different* (Fig. 8). These data reflect two changes. First, the radial hairy representation increased above normal levels (Fig. 8; $t[4] = 3.96$, $p = 0.01$). Consistent with this areal increase, there was an approximate doubling in the mean mediolateral width of this representation (normal = 368 μm; section = 744 μm). Second, following median injury there were decreases in the area and width of bands representing the ulnar hairy skin (Fig. 8; area decrease from 17% to 7%, $t[4] = 2.63$, $p = 0.05$; width decrease from 439 to 303 μm, $t[4] = 2.68$, $p = 0.05$). Thus, a 21% increase in the radial hairy representation and an offsetting 10% decrease in the ulnar hairy representation combined to produce a net increase in the overall hairy representation of 11% above normal. The offsetting

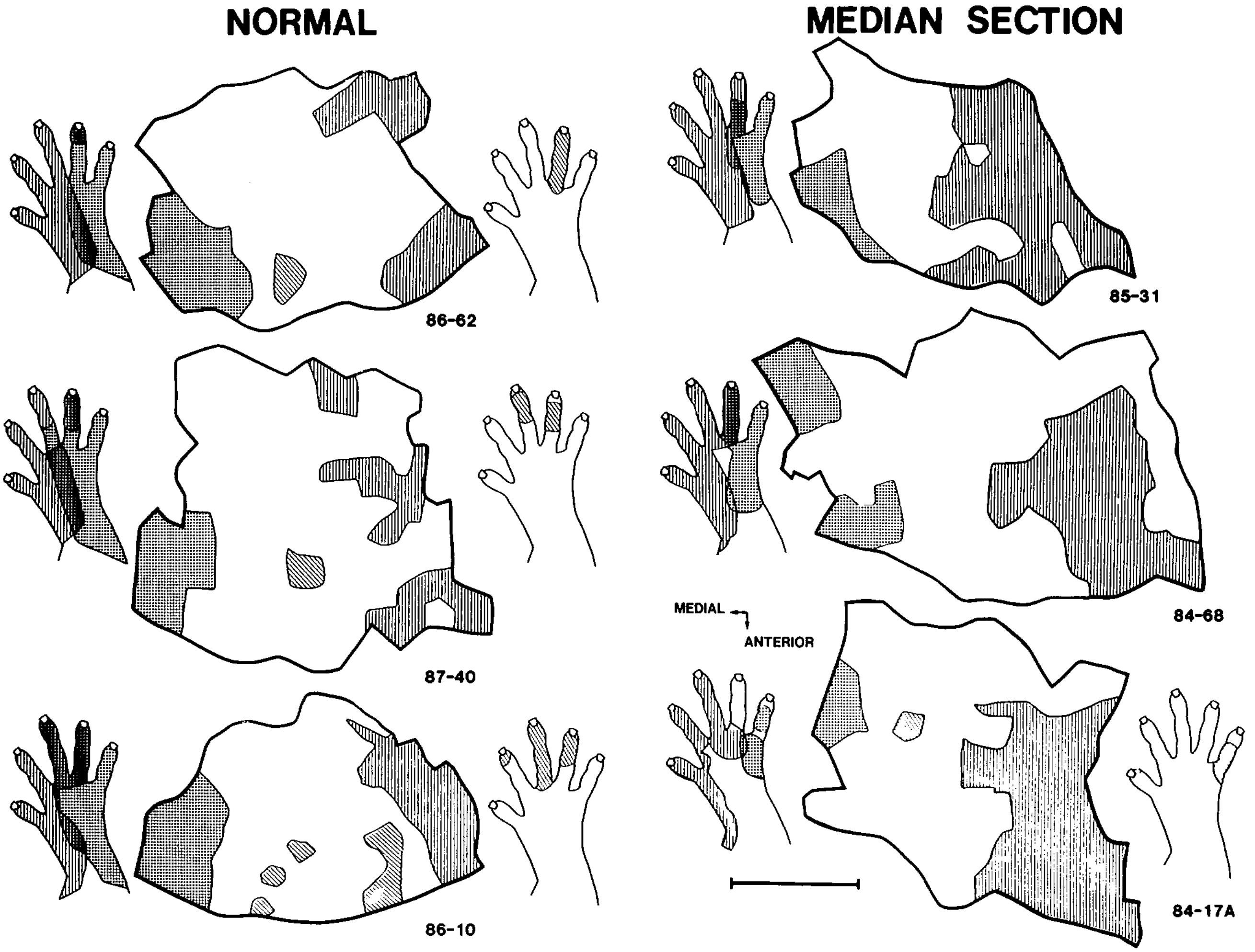

Figure 6. Specificity in the patterns of hairy hand representations in three normal monkeys (*left*) and three monkeys reared after median nerve section (*right*). As indicated by the *stippling* and *hatching* on the hands and maps, in normal monkeys, lateral hairy representations correspond to inputs from the radial hand, medial hairy representations correspond to inputs from the ulnar hand, and intervening patchlike representations correspond to inputs from middle digits. After median nerve section, the hairy hand is represented in fewer patches, the lateral representation of the radial skin increases in area, and the more medial representations of the middle digits and ulnar skin decrease in area. Scale bar, 1 mm.

nature of these changes suggests some interaction in adjustments across the different hairy representations.

Glabrous representations. Insight into the size changes of glabrous representations requires attention to the glabrous innervation of the hand by the median and ulnar nerves. First, the glabrous skin that was not represented in cortex following median section provides an estimate of skin that is autonomously or exclusively innervated by the median nerve (Wall, 1990; J. T. Wall, unpublished observations). By relating the receptive field defined at each cortical recording site to this denervated zone, it was possible to project this skin zone onto the maps of *normal* monkeys to estimate the cortical region that lost median inputs. This region involved a lateral band of cortex occupying a mean area of 30% of the map, with a mean mediolateral width of 499 μm (Fig. 9, right column, hatching). Contrasting with loss of this representation, the sizes of other glabrous representations either increased or remained normal after rearing with two nerves. From previous nerve recording studies (Wall, 1990, unpublished observations), the glabrous skin that retained innervation after median section consists of two proximodistal strips. One strip, which includes the ulnar edge of PH, P4, and the entire glabrous D5, is normally autonomously innervated by the ulnar nerve, whereas the second strip, which includes the central palm and skin on glabrous D3 and D4, normally receives overlapping innervation from both the ulnar and median nerves. Employing the same approach described for defining the autonomous median representation, the autonomous ulnar and overlap strips were projected onto the cortical maps to estimate areas activated by these strips (Fig. 9). The band of cortex representing the autonomous ulnar glabrous skin occupied similar percentages of the maps of normal and median-injured monkeys (Fig. 9; normal = 15%; median section = 16%). Consistent with this areal constancy, the mean widths of this band were similar (i.e., normal = 299 μm; section = 336 μm). In contrast, the representation of the overlap skin occupied 22% of the normal hand map, and a significantly larger 31% of the map after median section (Fig. 9; $t[4] = 3.21$, $p = 0.03$). This areal increase involved a 34% increase in the mean width of this representation. This expanded representation of the middle palmar and glabrous digit skin partially offset the 30% decrease in glabrous representation that would be expected due to median nerve loss.

High-threshold representation. The final change involved some switching of cortical neuronal responsiveness from low-threshold to higher-threshold input at penetrations involving areas of about 9% of the hand map.

Cortical variability

There are two main findings regarding cortical variability. First, a few specific features of organization accounted for most individual variability in normal maps. These features involved representation: shapes (Fig. 4; e.g., compare D2), sizes (e.g., coefficient of variation for individual digit and pad representations was about 37%), somatotopic interfacings (e.g., Fig. 4, compare relative adjacency of PH and P1-TH for 86-62 and 86-10), and spatial continuity (e.g., Fig. 4; compare location and number of hairy patches). These features are reflections of spatial patterning across large aggregates of cortical neurons. Second, these features that varied most in normally reared monkeys also changed the most following early nerve injury (see above results). However, it is clear that the cortical changes observed in monkeys reared with two nerves are beyond the range of individual variability seen in normal monkeys (Figs. 4, 6, 9).

Discussion

The present experiments are the first studies of the cortical consequences of neonatal nerve injury in primates. The results indicate how cortical organization is changed after early median nerve injury, and provide insight into somatotopic pattern formation in the hand map. Three main conclusions and a working hypothesis for summarizing the results are discussed.

Conclusion 1. The differences in rearing conditions in the present study resulted in clear changes in spatial patterning, but only modest changes in neuronal response properties

Most response properties surveyed at individual recording sites were similar in both groups of monkeys including, for example, response thresholds to glabrous inputs, receptive field size and continuity, and specificity of receptive fields to glabrous or hairy skin. The one local change detected with the employed methods was that, following injury, neurons at 8% of cortical sites were responsive only to higher-intensity mechanical stimulation. The overall impression from these results is that postnatal development with innervation from two, rather than the normal three, nerves resulted in relatively modest alterations in features of organization reflected at single cortical sites.

In contrast, there were clear differences in the features of spatial patterning reflected in the responses of aggregates of neurons recorded across multiple recording sites. Included in these alterations were (1) increases and decreases in the sizes of glabrous and hairy representations, (2) changes in the spatial continuity and distribution of hairy representations, and (3) changes in the somatotopic interfacing of representations.

The present findings are consistent with reports from nonprimate mammals that demonstrate that cortical neuron response properties can be relatively normal following early peripheral injury (e.g., Kalaska and Pomeranz, 1979; Simons et al., 1984; Wall and Cusick, 1986), but contrast somewhat with other evidence that abnormal response properties can also be developed (e.g., Killackey et al., 1978; Kelahan et al., 1981). At present, the factors that lead to normal versus abnormal response properties remain undefined but probably include the nature of the injury (see Wall et al., 1992). Previous studies in nonprimate mammals have also demonstrated cortical somatotopic reorganization following early peripheral injury (for reviews, see Kaas et al., 1983; Wall, 1988). The novel finding in the present study is that there is a strong correspondence between the features that, on the one hand, vary most in individual normal monkeys, and the features that, on the other hand, change most after median nerve injury. In both circumstances, the most variable features were properties of spatial patterning across somatotopically related aggregates of neurons. This correspondence suggests that the spatial integration features in monkeys reared with two nerves were produced by perturbations of the normal mechanisms for postnatal development and maintenance of these features.

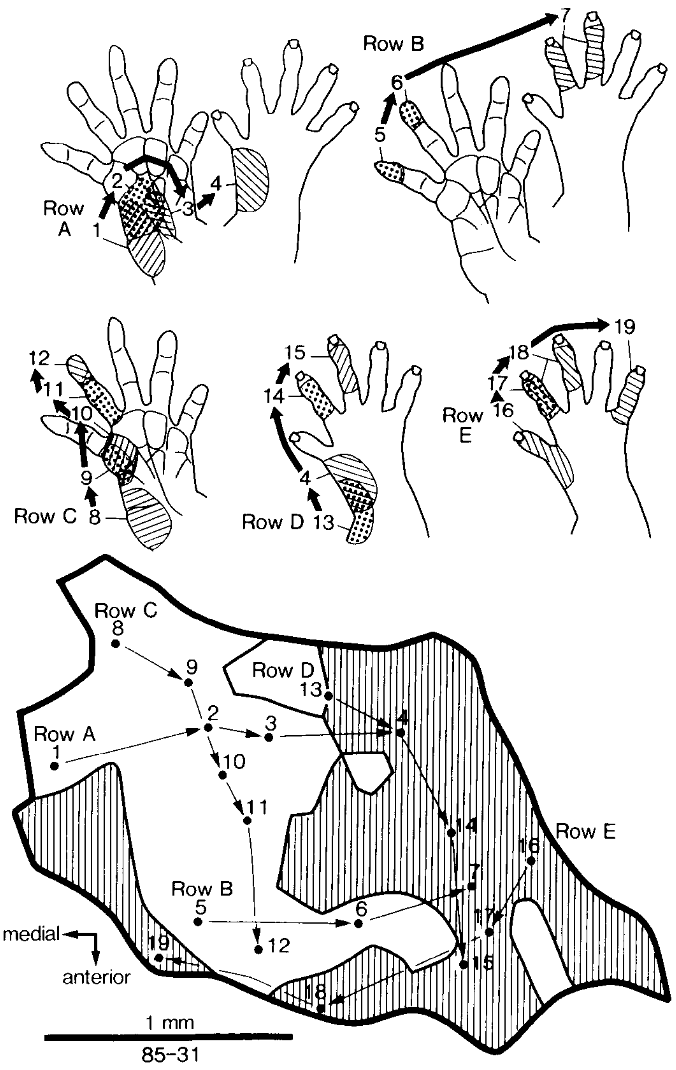

Figure 7. Map of the hand in a monkey reared after median nerve injury showing shifts in receptive fields (*top*) with mediolateral and caudorostral movements of recording sites (*bottom*). As in normal monkeys (e.g., Fig. 5), the caudorostral axis of the map corresponds to the proximodistal axis of the hand, the mediolateral cortical axis corresponds to the orthogonal axis across the hand, and the hairy (*hatched*) and glabrous (*white*) representations are in rough register. In contrast to normal monkeys, loss of the radial glabrous representation results in an abnormal adjacency of radial hairy and midhand glabrous receptive fields. Scale bar, 1 mm.

Although it is presently difficult to identify specific mechanisms that were perturbed, it is possible to define a range of possibilities. From studies of human and nonhuman primates,

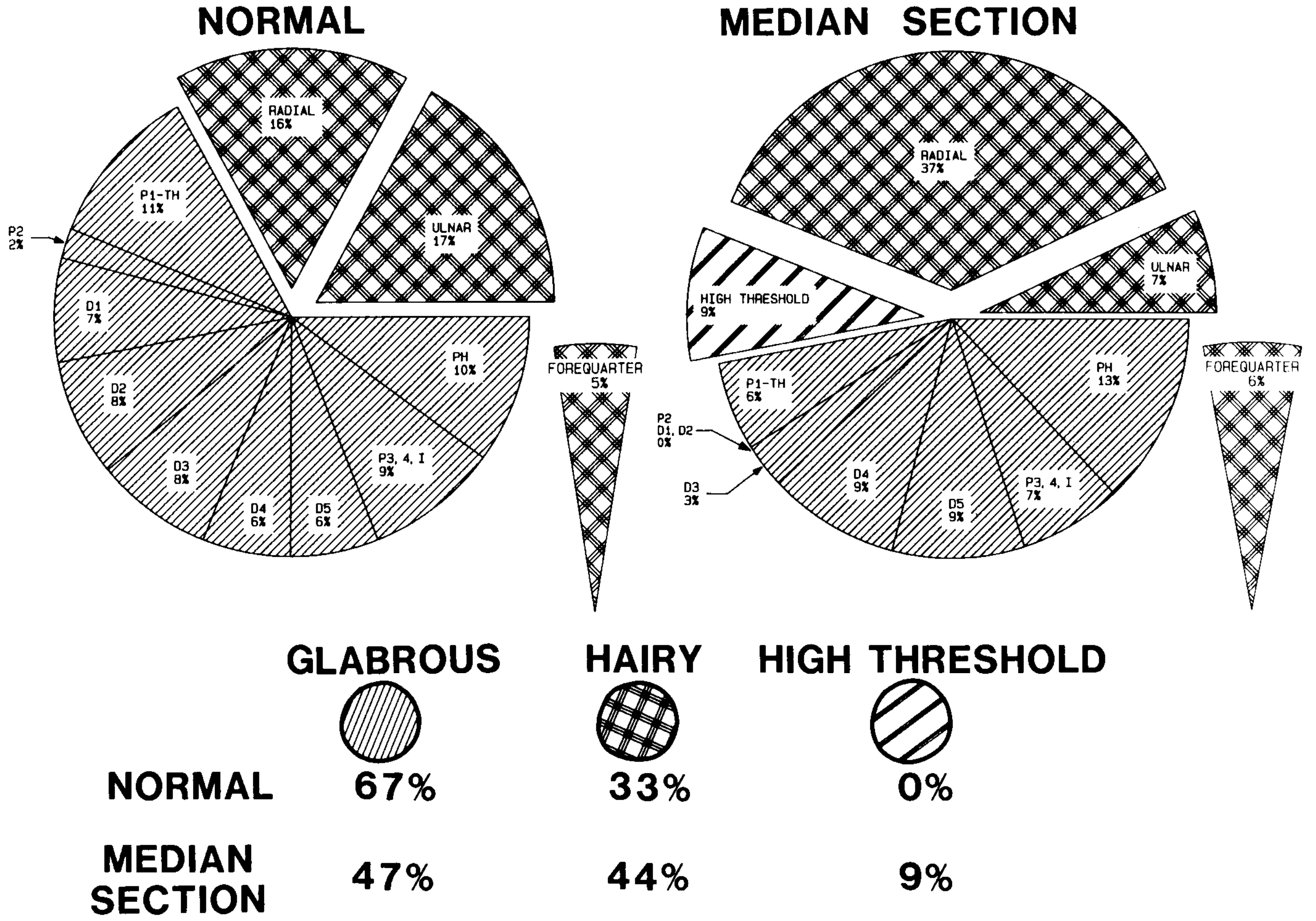

Figure 8. Mean percentage areas of the cortical hand map activated by different parts of the hand in normal monkeys and monkeys reared after median nerve section. The *hatching patterns* identified with glabrous, hairy, and high-threshold inputs (*bottom*) also apply to pie charts. In comparison to normal monkeys, monkeys with sectioned median nerves had (1) a smaller glabrous representation, (2) a larger hairy representation, (3) an area associated with high-threshold inputs, and (4) changes in the areas activated by radial and ulnar hairy inputs.

it is clear that the primate somatosensory system undergoes significant maturation prenatally and that, by birth, the ascending pathways are already formed and functional to some degree (e.g., Rakic, 1985; Rakic et al., 1986; Huntley et al., 1988; Krubitzer and Kaas, 1988; Peters and Jones, 1988; Darian-Smith et al., 1990). It is also clear that a wide range of changes occur postnatally including, for example, changes in functional responsiveness (e.g., Gamstorp and Shelburne, 1965; Sitzoglou and Fotiou, 1985; Thatcher et al., 1987), synaptic density (e.g., Rakic et al., 1986; Johnston, 1988), thalamocortical fiber distribution (e.g., Darian-Smith et al., 1990), and expression of neurotransmitters and neuromodulators putatively related to neurite growth (e.g., Goldman-Rakic and Brown, 1982; Hendry et al., 1987; Huntley et al., 1988). Thus, these or related central mechanisms were potentially influenced by early median nerve injury. Peripheral factors also appear to have contributed to the observed cortical changes. Specifically, the finding that the post-injury features were clearly outside the range of normal variability suggests that central reorganization was guided in specific ways according to the available peripheral inputs. Currently, there is little understanding of how the periphery contributes to development of cortical maps in primates. In adult primates, the sizes of cortical representations are usually presumed to reflect differences in peripheral innervation density (e.g., Mountcastle, 1984). Although the present findings do not refute this view, it is difficult to explain certain changes parsimoniously in terms of innervation density. For example, following median injury the overlap skin representation increased in size despite some loss of innervation. In addition, despite no indications of denervation, the representations of the radial and ulnar hairy skin, respectively increased and decreased in size. Thus, it appears that peripheral factors are pertinent to postnatal cortical development but that innervation density is not the only factor of importance.

Conclusion 2. The representations of parts of the hand can develop and survive somewhat independently of each other

Postnatal section and ligation of the median nerve led to denervation of the radial glabrous hand and loss of the cortical representation of this skin. Despite this loss, highly organized representations were developed for other parts of the hand that remained innervated. These results suggest that the hand map is formed from a collection of representations that are capable of developing postnatally in a parcellated or disjunct fashion somewhat independently of each other.

Previous observations from studies of somatosensory pattern development are consistent with this conclusion. For example, the SI cortex of rodents contains functional representations of

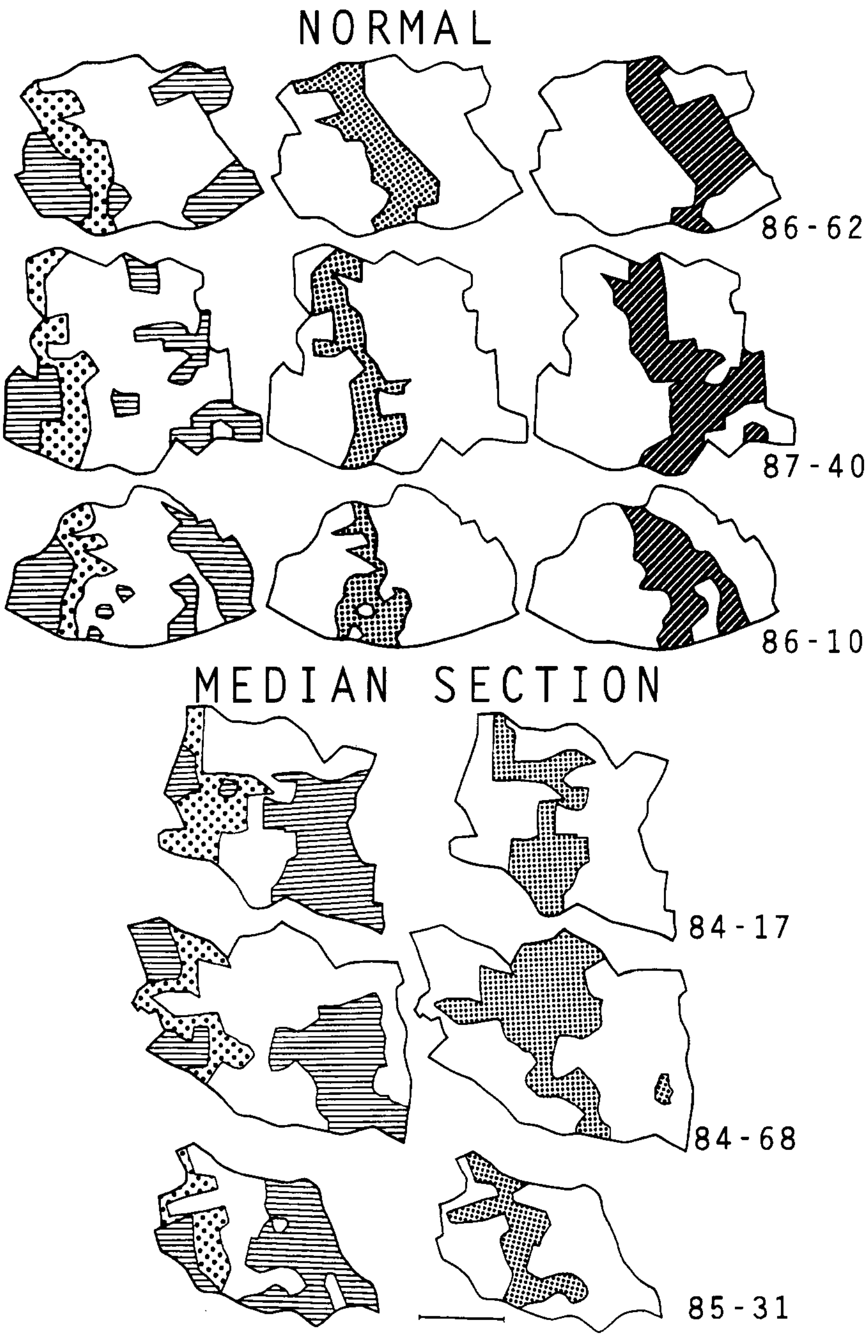

Figure 9. Hand maps showing changes in aggregation patterns of neurons that are activated by low-threshold inputs from skin territories of the hand nerves (and see Wall et al., 1992). Maps from three normal monkeys (i.e., *86-62, 87-40,* and *86-10*) and three monkeys reared after median nerve section (i.e., *84-17, 84-68,* and *85-31*) are indicated. *Hatching in left-column maps* indicates medial and lateral patchlike aggregates associated with hairy skin innervated, respectively, by the ulnar and radial nerves. *Stippling in left-column maps* indicates aggregate for glabrous skin innervated autonomously by the ulnar nerve. *Stippling in middle-column maps* of normal monkeys and *right-column maps* of median section monkeys indicates aggregate for glabrous skin with overlapping innervation from the median and ulnar nerves. *Hatching in right-column maps* of normal monkeys indicates aggregate for glabrous skin innervated autonomously by the median nerve. Following median nerve section, loss of the autonomous median aggregate is correlated with fusion and enlargement of normal radial nerve aggregates in the lateral map and widening of the median and ulnar overlap aggregate in the central map. Medial, left; anterior, down. Scale bar, 1 mm.

vibrissae that are colocalized with organized aggregates of cells and thalamocortical terminations (e.g., Nussbaumer and Van der Loos, 1985; Simons et al., 1989; Killackey et al., 1990; Woolsey, 1990). Each of these aggregates is "place" specialized in that the dominant inputs originate from a "principal" vibrissa (e.g., Chapin, 1986; Armstrong-James and Fox, 1987; Simons et al., 1989). Peripheral injury in neonatal rodents leads to loss of normal functional representations in parts of the map associated with injured vibrissae; however, discrete functional representations still develop for vibrissae with intact innervation (e.g., Jeanmonod et al., 1981; Simons et al., 1984; Killackey et al., 1990; Woolsey, 1990). Thus, findings from both primates and rodents are consistent with the view that there are functional cortical aggregates that are capable of developing and surviving as somewhat independent "units" of a larger map.

If the cortical map of primates is developed in a parcellated fashion, one might expect to see reflections of this organization in the adult brain. Recent findings provide evidence for such adult parcellation. Briefly, rodlike aggregations of afferent terminations relating to a somatotopic part of the hand or face have been described in the spinal cord (Brown et al., 1989; Florence et al., 1989), brainstem (Culberson and Brushart, 1989; Florence et al., 1989; Noriega and Wall, 1991), and ventroposterior nucleus of the thalamus (Jones et al., 1982; Rausell and Jones, 1991) of adult monkeys. The thalamic aggregates, in turn, interface with area 3b cortex via bundles of axons that terminate in patch- or striplike domains (e.g., Jones et al., 1982). These findings suggest that "place" information is processed by parcellated groupings of neuronal elements at different levels of the ascending neuraxis (e.g., see Jones et al., 1982; Wall et al., 1990;

Noriega and Wall, 1991; Goyal et al., 1992). The present findings further suggest that each set of vertically connected aggregates that link a skin zone on the hand to an aggregate of cells in the cortex is capable of developing somewhat independently as a neuraxis "unit."

Conclusion 3. The representations of parts of the hand interact to form maps of larger fractions of the hand surface

Following postnatal section of the median nerve, a bandlike aggregate of cortical neurons in the lateral hand map was deprived of inputs. Inputs from parts of the hand served by intact nerves repartitioned this deprived band with no loss in the overall area of the hand map. These results suggest that inputs from a part of the hand are capable not only of independently establishing a cortical representation, but also of "competing" with inputs from other parts of the hand for a larger cortical space.

"Competition," as suggested by selective enlargement of particular representations, does not, however, appear to be the only possible interaction. For example, following median section the increase in the representation of the radial hairy hand was offset by a decrease in the ulnar hairy representation. These size adjustments were further associated with a decrease in the overall number of patchlike hairy representations. The opposing nature of these size changes, and the coalescence of cortical patches suggest additional interactions also contributed to the changes in hairy representation.

A working hypothesis

The following hypothesis is suggested to summarize the present results. The area 3b hand map normally consists of a collection of representations of all parts of the hand. These representations can develop and subsequently survive somewhat autonomously of each other. Following early median nerve injury, an incomplete map of the hand surface is formed from available ulnar and radial nerve inputs. Under such abnormal conditions, cortical features of spatial patterning change because peripheral factors impact on central mechanisms of somatotopic aggregation when developing parts of the map are interacting in "competitive" or other ways.

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