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Age-Dependent Differences in Reorganization of Primary Somatosensory Cortex Following Low Thoracic (T_{12}) Spinal Cord Transection in Cats

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The organization of primary somatosensory cortex was examined in chronic spinal cats that had sustained cord transection at T_{12} at 3 ages: 2 and 6 weeks of age, and as adults. Five months to 1 yr following transection, the deprived cortex was mapped electrophysiologically (multiunit recordings). The topographical organization found at each age was compared to that present in normal adults to study effects of developmental age on the ability of the somatosensory system to adjust to changes in afferent input.

Cortical responses to deprivation of somatosensory input were age dependent. In animals cord transected at 2 weeks of age, the remaining somatic afferent input excited both its normal cortical area and the area normally reserved for the hindlimb. This resulted in 2 somatotopic maps of the rostral trunk and forelimb. In contrast, in cats spinalized at 6 weeks of age, there was only 1 map for the remaining somatosensory input that was distributed across the mediolateral axis of the primary somatosensory cortex. As a result, the remaining somatosensory input was shifted medially from its normal position and was narrower with respect to the rostrocaudal area driven by light tactile input. The amount of cortex that each body region could excite was essentially the same as in normal animals. In adults, a third response was observed; regions normally devoted to forelimb and trunk appeared to be unchanged, and the region previously serving the hindlimb responded only to a limited extent, and only to tactile stimulation of the trunk. In all cases, however, some sites in the cortex could be excited by parts of the body that in normal animals were served by cortical regions from 3 to 10 mm away, a distance much in excess of the maximum extent of reported thalamocortical overlap.

We suggest that the various patterns of cortical organization observed at different ages reflect different developmental processes that are active at the time of transection. Further, we hypothesize that often, in major denervations such as spinal cord transection, a significant component of the reorganization occurs at synaptic levels below the cortex in young animals.

Topographical reorganization of the somatosensory cortex following peripheral denervation or amputation has been reported to occur in a number of mammalian species: raccoon (Rasmusson, 1982; Doetsch and Kelahan, 1983; Kelahan and Doetsch, 1984), monkey (Wall et al., 1982, 1983; Merzenich et al., 1983a, b), rat (Wall and Cusick, 1984), and cat (Kalaska and Pomeranz, 1979; Metzler and Marks, 1979; Franck, 1980; McKinley et al., 1985, 1987). Although most data concern the results of amputation of 1 or 2 digits or partial denervation of a limb segment (see Wall and Kaas, 1985, for review), it has been suggested that cortical capacity to respond to nerve injury may have a distance limit related to the amount of overlap of thalamocortical axon terminal arbors (Merzenich et al., 1983a, b).

Most of the changes reported in the studies cited above have occurred across cortical distances within the reported range of thalamocortical overlap. However, as the amount of thalamocortical overlap in cat has been estimated to be 1–1.5 mm in both the rostrocaudal and mediolateral directions (Landry and Deschenes, 1981; Landry et al., 1986), this mechanism does not offer a satisfactory explanation for cortical reorganization over greater distances such as those reported in young kittens (Kalaska and Pomeranz, 1979; McKinley et al., 1987).

Although there have been numerous reports on the general age dependent effects of lesions within the central nervous system (Finger and Stein, 1982, for review), reports concerning the reorganizing capacity of the cortex are inconsistent with respect to the magnitude of the response. While some reports indicate an increase in reorganizational response in younger animals (Kalaska and Pomeranz, 1979; Waite, 1984; McKinley et al., 1987), others report no difference (Carson et al., 1981; Kelahan et al., 1981), while others find a reduction in response (Wall and Cusick, 1986). These contradictory results may be due to the use of different species that are at various stages of development at birth. For example, if the reorganizational responses can be described as a function of the developmental growth process, then we might expect a variety of responses that are reflective of particular developmental processes active during the period of the injury.

We have chosen to use the cord transected cat (T_{12}) as a model for studying the capacity of the cortex to respond to a large magnitude of deprivation, and we have selected 3 age groups

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(2 week, 6 week, and adult) to distinguish the effect of developmental influences on this response. The 2-week-old spinal kitten was chosen as a representative of the early postnatal developing animal because the somatosensory system is developed, but aspects of it are in various stages of maturation. Electrophysiologically, the somatosensory cortex is approaching maturity, as both response latency (Grossman, 1955; Bruce and Tatton, 1980) and synaptic configuration (Voeller et al., 1963) are reaching the adult state. However, capacity to code and signal information from the peripheral organs is not well developed until 2 months of age (Connor et al., 1984; Ferrington et al., 1984). Likewise, the synaptic effectiveness from primary sensory cortex to the motor cortex remains low until about 8 weeks postnatal (Bruce and Tatton, 1980). In contrast, an animal cordotomized at 6 weeks of age is in a more mature state of development that may more closely reflect the adult situation, and yet when compared to the adult, may still be capable of a more robust response to developmental processes. Our results demonstrate that central responses to spinal cord transection are age dependent and the topographical reorganization at the cortical level may reflect different steps of development at the time of injury. Preliminary reports of some of these findings have been published (McKinley et al., 1985, 1987).

Materials and Methods

Experimental design

Three age groups of laboratory-raised cats were chosen for this study: juveniles of 2 weeks ($n = 6$) and 6 weeks ($n = 6$) of age, and adults ($n = 6$). Control groups of normal adult cats ($n = 4$) and 6-week-old kittens ($n = 4$) were also studied. All experimental cats were allowed to recover from spinal surgery for a period of at least 4 months, thus insuring that the most rapid and largest aspects of reorganization were completed (Merzenich et al., 1983a, b; Kelahan and Doetsch, 1984), and that the cats that had received cord transections as kittens had an adult-size brain. Although the age at which the cord transection had occurred was generally unknown to the primary investigator at the time of the experiment, all researchers in the laboratory were involved in animal care, and the morphological signs of the surgery were self-evident; thus, it was not feasible to do a blind mapping study. To prevent bias during the mapping procedures of the experimental animals, 1 investigator manipulated the electrode while another located and recorded receptive fields in the periphery, and a third recorded the data.

Subject preparation

Surgical procedure and postoperative care. Both the surgical procedure and postoperative care were routine procedures that have been described previously (Smith et al., 1982; Bradley and Smith, 1988; McKinley and Kruger, 1988). All operations were performed under general anesthesia and aseptic conditions using ketamine (25 mg/kg) and Acepromazine (0.5 mg/kg) for 2- and 6-week-old kittens, and nembutal (35 mg/kg IP) for adults. A laminectomy was performed between T_{11} and T_{13}. After topical application of Xylocaine (2%) on the area of the spinal cord to be lesioned, a hook was used to elevate the cord slightly, and it was severed at the segmental level of T_{12}. The completeness of the transection was verified by lifting the hook through the lesioned area and observation of cord retraction. Gelfoam was packed between rostral and caudal segments and the wound was sutured. Figure 1*A* illustrates the somatic region which is spinal cord isolated by the lesion.

For 1 week following surgery, antibiotics were administered prophylactically. Unweaned kittens were placed with the nursing mother immediately after they recovered from the effects of anesthesia. The hindlimbs were massaged daily, cleaned, and the digit, ankle, knee, and hip joints were moved through their range of motion to prevent stiffness. To initiate reflex evacuation of the urinary bladder, light tactile stimulation was applied to the perigenital area twice daily: manual expression of the bladder was used only when tactile stimulation was ineffective.

Once weaned, kittens were housed by litters in spacious cages (3 × 6 × 6 ft) constructed of chain link fence, in which shredded paper covered the floor to prevent decubitus ulcers from forming. Similar housing was provided for adults. This configuration encouraged social interaction, visual and tactile stimulation, and spontaneous play.

Lesion confirmation. At the termination of the mapping experiments, animals were deeply anesthetized and perfused intracardially with 0.9% saline followed by 10% buffered formalin. After perfusion, the spinal cord was removed and processed using a modified Bielschowsky technique counterstained with trichrome to confirm the completeness of the spinal cord transection. The brains were removed, photographed, and placed in 30% sucrose formalin until they sank. Parasagittal sections of 28 μm were cut on the freezing microtome and stained with thionin for histological studies.

Mapping procedure

Animal preparation. The recording procedures were similar to those developed by Merzenich and colleagues (Merzenich et al., 1978, 1983a). Following a preanesthetic injection (s.q.) of atropine sulfate (0.1 mg/kg), ketamine was administered (28 mg/kg i.m.) and maintained at surgical levels throughout both surgical and recording procedures with subsequent 0.1 ml i.m. doses of ketamine. Injections, i.p., of saline (3–5 ml/hr) were given to prevent dehydration. Rectal temperature was monitored and kept at 37°C throughout the experiment by placing the animal on a cushioned heating pad.

The cranium was exposed, and a metal bar was attached to the skull with dental acrylic contralateral to the hemisphere to be mapped and then clamped to a stereotaxic frame so that the animal's head was rigidly stabilized. A craniotomy was performed exposing the entire anterior cortex from a site posterior to the ansate sulcus to a point rostral to the cruciate sulcus. A cotton dam was constructed around the exposed area, saline placed in the well created by the dam and the craniotomy, and the dura was reflected while viewing through a surgical microscope (Zeiss). The saline was then removed, and the exposed cortex was covered with silicone (Accumetrics). A high resolution photograph of the brain surface was taken with high contrast film (Panex), developed and enlarged (25–30 ×). The surface vasculature provided a reference system used to guide electrode penetrations during the experimental recordings. These locations were recorded on the photograph.

Recording apparatus. Multiunit neuronal activity was recorded with paralene-coated tungsten microelectrodes (Microproduct) having impedances of between 1.5 and 2.0 MΩ (at 1 kHz), attached to a hand-driven triaxial microdrive (Kopf) mounted on the stereotaxic frame. All signals were referenced to a ground attached to the animal, amplified 10,000 × (Dagan), passed through a band-pass filter (100–10 kHz), displayed on a storage oscilloscope (Tektronix), and monitored through an audiomonitor (Grass).

Mapping protocol. During the recording sessions, the microelectrode was lowered to the pial surface and contact with the pial surface was detected using the audiomonitor. Penetrations were made approximately normal to the cortical surface, except in the posterior bank of the coronal sulcus and the anterior wall of the medial and lateral branches of the ansate sulcus, where penetrations were parallel to the cortical surface. A grid-like array of penetrations was spaced at 200–300 μm intervals rostrocaudally and in mediolateral rows spaced 300–700 μm apart across the area of primary sensory cortex that represented the hindlimb, trunk, and proximal forelimb. Mapping in the rostrocaudal direction was terminated when 3 penetrations in a row did not respond to light tactile input. For illustration purposes, only the first nonresponsive penetration is shown at these borders. The cortex normally devoted to forepaw and wrist was not routinely mapped in detail.

At each "in depth" (parallel) penetration near the bank of the sulci, the microelectrode was advanced initially to a depth of 400 μm and then advanced in 200 μm increments to a depth of 1600 μm below the surface. At each recording site, attempts were made to evoke responses to somatic stimuli delivered to the trunk, forelimb, and face, using a handheld probe, brush, or bristle. In areas where there was a response, identification and characterization of receptive fields (RFs) proceeded as described below.

On the crown of the gyrus, the electrode was quickly advanced to a depth of 600–800 μm, where attempts were made to evoke responses to tactile stimuli. If no response was elicited, the electrode was moved up or down 200 μm and the body was stimulated again. When a response was observed, it was recorded and the depth was noted. Electrolytic lesions (10 μA, 10 sec) were occasionally placed at recording sites for verification of penetration depth. Where no evoked responses were observed, efforts were made to stimulate the entire body before the electrode was moved to another site. When no response could be obtained,

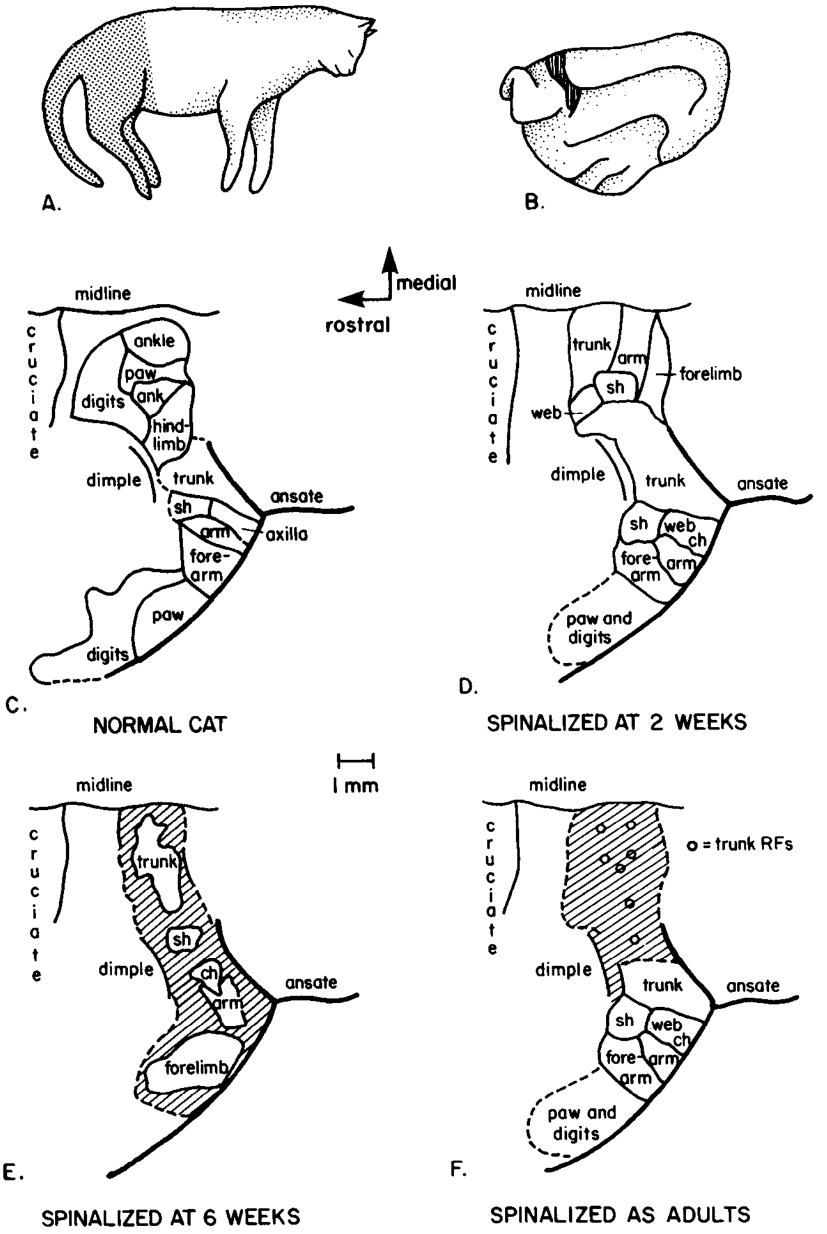

Figure 1. Comparison of reorganization maps in individual cats cord transected at 2 or 6 weeks of age or as adults. *A,* Region of afferent input isolated to the spinal cord after cord transection at T_{12} is shaded. *B,* Region of somatosensory cortex shown in the maps below. *C,* Map of primary somatosensory cortex in normal cat. *D–F,* Cortical maps of individual chronic spinal cats cord transected at different ages: *D,* 2 weeks; *E,* 6 weeks; *F,* adult. *Striped lines* indicate areas of no cutaneous response. *Dashed lines* indicate borders of mapped/unmapped cortex. Abbreviations: *ank,* ankle; *ch,* chest; *sh,* shoulder. *Forelimb* includes forearm, paw, and digits.

the penetration was classified as a nonresponsive cutaneous response (NCR).

Stimulus presentation and classification

Initially, to determine the RF, the researcher lightly touched the hair with the fingers. The entire surface of the animal was stimulated in this manner until a response that was clearly related to the touch was located. Then the researcher used a hand-held nonconductive glass probe and delicately touched the hairs in the area producing responses, until the RF was well delineated. This area was then drawn on a cartoon of the body part and logged in a record book. These neurons were classified as responding to light tactile stimuli. Neurons that responded to more intense stimulation only, such as light scratching, were defined as high-threshold neurons but were still considered to be responsive to cutaneous stimulation. In contrast, if the neurons responded only to tapping or joint movement, they were classified as deep and were not included as part of the population responsive to tactile stimulation.

Preparation of a somatosensory map

After the experiment was finished, an enlargement of the cortical photograph was made by projecting a transparency copy of the photograph against a wall and marking the numbered penetration sites on graph paper. Then, figurines of the cat marked with the appropriate RF location were placed over the corresponding cortical site. From this information a general somatotopic map was drawn with boundary lines placed midway between regions representing separate limb segments or regions of the trunk. Patterns of topographical organization and orientation were also noted, as they could be easily seen with respect to cortical placement on these enlarged maps.

Results

General age-dependent responses

Figure 1 illustrates the major differences in somatotopic maps in chronic cord transected animals of different ages and compares them to that of a normal adult cat. While the maps illustrated in Figure 1, *C–F* are not composites, but taken from individual animals, they are typical of the response of the majority of animals in each age group. Animals cord transected at 2 weeks of age demonstrated the most robust response; the entire expanse of deprived cortex was excited by input arising from

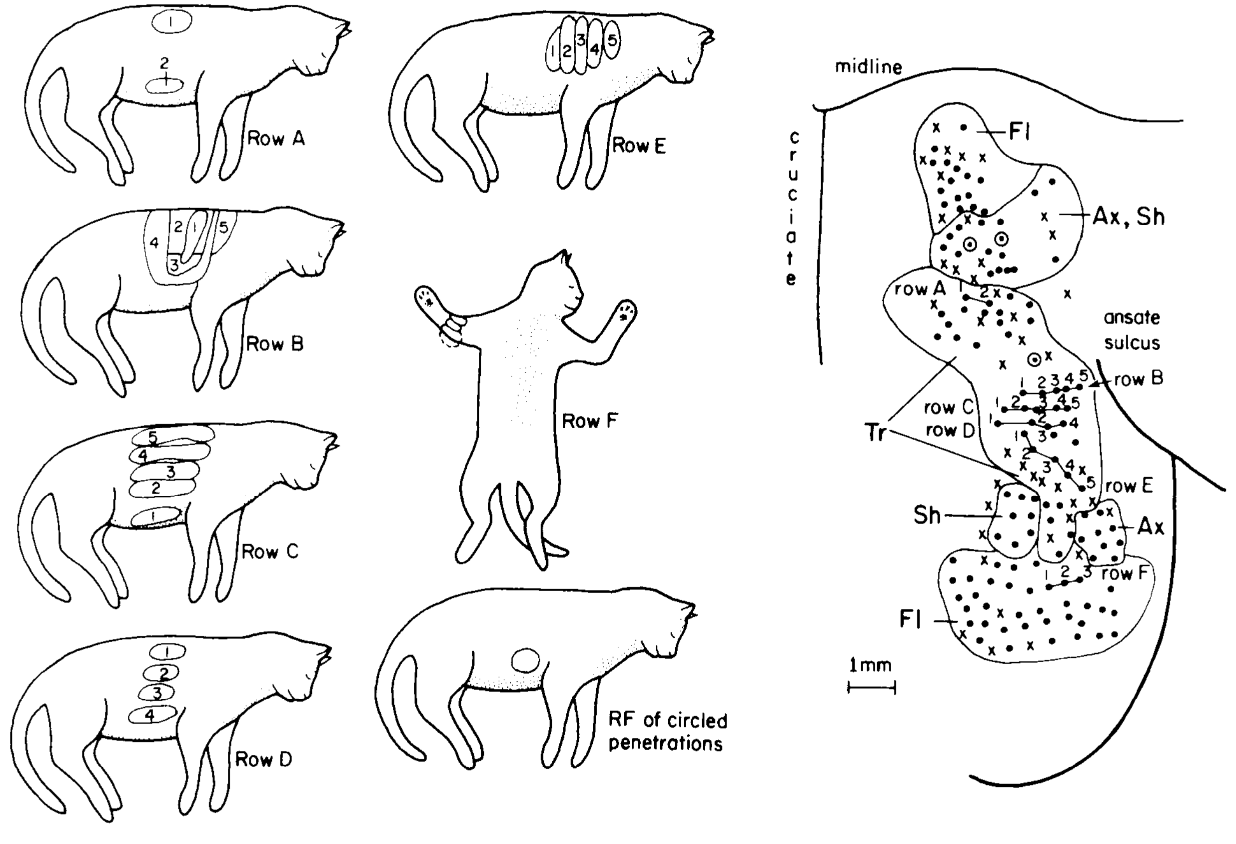

Figure 2. Penetration map of primary sensory cortex in 1 animal cord transected at 2 weeks of age. *Closed circles* represent sites responsive to light tactile stimuli; *X*'s represent sites with NCR. RFs of rows marked *A–F* are illustrated at the *left*. Circled *penetrations* indicate penetrations that could be driven by the same RF. Abbreviations: *Tr*, trunk; *Sh*, shoulder and upper arm; *Ax*, axilla; *Fl*, forelimb.

the trunk, shoulder, axilla, thorax, and forelimb. This resulted in a second, somatotopically organized map of the anterior body (Fig. 1*D*). The cortical neuronal responses of the animals cord transected at 6 weeks and as adults were not as robust as those in animals cord transected at 2 weeks. Only a portion of the deprived cortex was driven by tactile stimulation of the trunk, and none of it was driven by forelimb stimulation. However, the actual placement and organization of RFs within this cortical region were quite different in the 2 groups of older animals. In animals cord transected at 6 weeks of age, trunk RFs were clustered into the middle of the deprived region and extended to the medial boundary, with regions of nonresponsive cortex on the rostral and caudal boundaries of primary somatosensory cortex (Fig. 1*E*). In the adult, the penetrations in the deafferented cortex that could be driven by tactile stimulation of the trunk were sparse and well separated in an expanse of cortex unresponsive to tactile stimulation (Fig. 1*F*).

Description of individual age groups

Animals cord transected at 2 weeks of age

The entire somatosensory cortex devoted to light tactile input was responsive to light tactile stimulation (Fig. 1*D*). While the regions typically designated as forearm, wrist and paws, shoulder, thorax, and upper-arm representations and some of the trunk representation appeared to be organized similarly to normal controls (Fig. 2, rows D–F), the more medially placed trunk and hindlimb regions were reorganized with respect to primary somatosensory cortex in normal animals (Fig. 2, rows A–C).

Trunk organization. The space devoted to the trunk expanded medialward into the region normally occupied by the hindlimb representation (Fig. 1*D*). This resulted in multiple representation of trunk RFs that varied with respect to topographical organization (Fig. 2, rows A–D) in both somatotopically appropriate and inappropriate areas. Normally, the cat primary somatosensory cortex is characterized by topographical arrangement of RFs within the cortex so that adjacent and overlapping RFs are also adjacent and overlapping cortically and maintain an order with respect to somatotopy (Felleman et al., 1983). Examples of this order are illustrated in Figure 2, rows D and E. This order was achieved to an extent in the expanded trunk representation, where often a section of reorganized cortex could be mapped with regular, small, peripherally adjacent overlapping fields, as illustrated in Figure 2, row C. Here, trunk RFs were organized topographically as there was adjacent cortical placement of contiguous trunk RFs. Notice, however, that the most dorsal RF was caudally placed while the most ventral RF was placed more rostrally. This orientation is opposite to that found in normal animals (Felleman et al., 1983) or in the adjacent row of penetrations (Fig. 2, row D). Therefore, while topographical order could be maintained, it was often oriented inappropriately with respect to normal internal cortical topography. This was a common feature of the expanded trunk representation. In addition, the expanded trunk representation was frequently organized in a discontinuous or disrupted manner (Fig. 2, rows A, B). Often, in the deprived hindlimb cortex, a dorsal trunk RF was located adjacent to a ventral trunk RF (Fig.

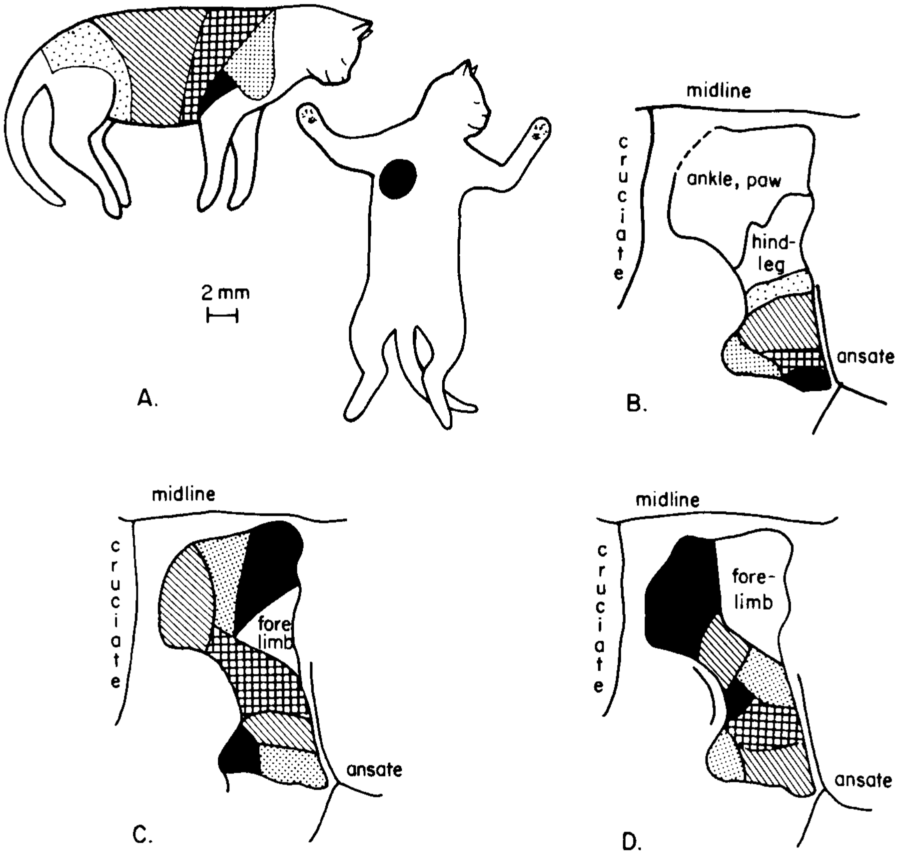

Figure 3. Reorganization of trunk region in cats cord transected at 2 weeks of age. *A*, Cat trunk divided into sectors which were used to generalize trunk location on the cortical maps: *solid*, axilla; *diamonds*, upper shoulder; *grid*, rostral trunk; *diagonal stripes*, midtrunk; *dots*, caudal trunk. *B*, Location of representation of those sectors in the primary somatosensory cortex of normal cat. *C*, *D*, Location of representation of these sites in 2 animals cord transected at 2 weeks of age. Sections devoted to the forelimb include representation of the forearm, wrist, and paw.

2, row A), or a large RF encompassed the entire trunk region which was cortically adjacent to smaller RFs that represented areas within the larger RF (Fig. 2, row B). Additionally, multiple cortical sites could be driven by the same RF (Fig. 2, circled penetrations).

The expanded trunk topography was also idiosyncratic and differed to varying degrees from trunk topography in normal animals. Figure 3 demonstrates schematically how various aspects of the trunk were represented topographically in normal cortex (Fig. 3, *A*, *B*) and compares this topography to the expanded trunk representation in 2 experimental animals (Fig. 3, *C*, *D*). In normal animals, trunk topography is organized such that rostral aspects such as the shoulder and axilla regions are found laterally, while more caudal aspects are found medially. Within a particular trunk division, such as the shoulder/axillary region, dorsal aspects are represented rostrally, and ventral ones caudally on the cortical surface. This organizational principle is illustrated in Figure 3*B*.

In the experimental animals, there was always representation of the axilla, upper shoulder, thorax, rostral, and midtrunk regions placed within the "normal" confines of trunk designated cortex (between the fork of the ansate sulcus and termination of its medial branch). However, organization within this area was not always similar to that of the normal animals, nor was there any particular consistency to the somatotopic organization. For example, in Figure 3*C*, the most laterally placed trunk RFs were those from the most rostral trunk regions: the axilla and upper shoulder. However, rostrocaudal placement was reversed from that found in normal cats: the ventrally located axillary region was placed rostral to the upper shoulder. Further, the medially adjacent region was not the rostral trunk, as would be expected in the normal animal, but the midtrunk; medially placed to the midtrunk was the rostral trunk. In another animal, as shown in Figure 3*D*, the shoulder placement was correct, in that it was the most rostral and laterally placed region, but the section adjacent to it caudally was not the axilla but the midtrunk. Adjacent medially was the rostral trunk and axilla followed by a repetition of the various trunk regions.

Similarly, in the second representation of the trunk (found within the deprived trunk-hindlimb region), there was no apparent consistency in organization (Fig. 3, *C*, *D*). In the animal represented in Figure 3*C*, the rostral trunk region extended rostromedially in 1 contiguous piece while the rest of the trunk was re-represented medially in adjacent rostro/caudal sections representing midtrunk, upper shoulder, and axilla. In the animal represented in Figure 3*D*, the rostral trunk did not extend into the deprived region rostromedially, although it likewise is represented once. Instead, the shoulder, midtrunk, and axilla are re-represented along a rostromedial axis. On the mediocaudal border, adjacent to rostral trunk representation, the shoulder was re-represented. On the adjacent rostromedial border, the axilla was re-represented, followed rostromedially by regions devoted to the midtrunk, and most medially, a second axilla representation.

Second forelimb representation. Medial to the first cortical region representing the trunk were distinct areas that represented the upper arm, forearm, wrist, and paw. In contrast to the expanded trunk region, the second representation of the forelimb was small in area, but was characterized by well-organized topography and began consistently at the medial termination of

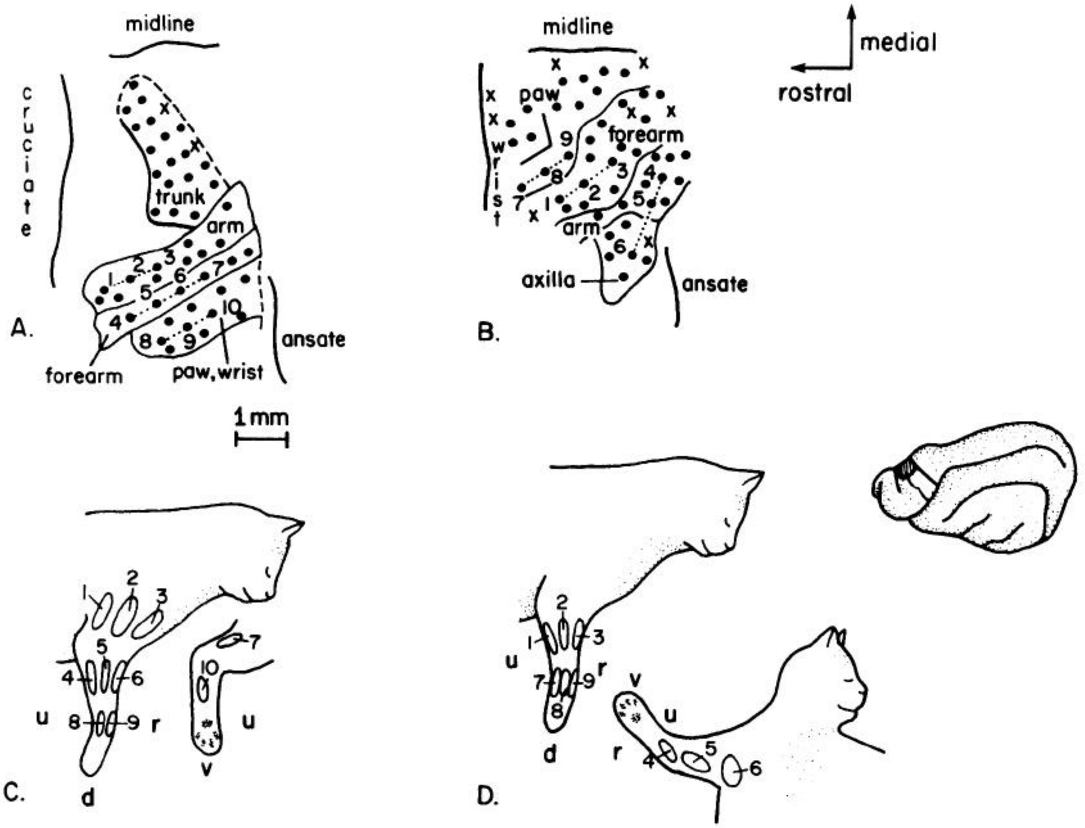

Figure 4. Organization of second forelimb region in cats cord transected at 2 weeks of age. *A, B,* Cortical representation of novel forelimb sites in 2 animals. *C, D,* RF location of corresponding numbers of novel forelimb penetration sites in hindlimb designated cortex. Conventions as in Figure 2.

the ansate sulcus, as can be seen in Figure 3, *C, D.* Each intrasegmental limb topography was organized consistently in separate rostrocaudal strips with sequential dorsal to ventral RFs represented along the rostrocaudal axis (Fig. 4). In contrast, the intersegmental limb organization was idiosyncratic; in some animals, the more proximal segments were represented more medially (Fig. 4, *A, C*), while in others the distal segments were represented in the medial portions of the cortex (Fig. 4, *B, D*).

The RFs were characterized by small size, low threshold, and well defined boundaries. Occasionally, there was considerable overlap between adjacent RFs, but typically, there was little or no overlap of adjacent fields, as illustrated in Figure 4. Rarely was an RF represented more than once, and in no case was more than 1 RF represented at a given penetration site.

Animals cord transected at 6 weeks of age

In general, the reorganizational response in animals cord transected at 6 weeks entailed a restructuring of the entire somatotopic map (Figs. 1*E*, 5). The region responsive to light tactile input was narrowed at the rostral and caudal margins, and there was no second representation of any body segment. Trunk RFs were clustered into the middle of the deafferented region and extended to the medial border, with regions of nonresponsive cortex on the rostral and caudal borders of primary somatosensory cortex. Additionally, there were areas of nonresponsiveness throughout this entire cortical region, including regions representing the forelimb, shoulder, axilla, and thorax. These regions were shifted medialward, and representation in these regions was likewise decreased along the rostral and caudal margins (Figs. 1*E*, 5). Casual inspection of these areas suggested that the axilla and the shoulder regions were more extensively represented in these animals than in normals. However, variable responses of the cord transected animals made it difficult to render a valid judgment with respect to this observation.

Trunk organization. While location of the trunk representation was consistently found along a narrow region in the middle of the deafferented hindlimb cortex, the organization within this region was variable. The trunk representation was not always topographical, and when it was, the topographical order was highly variable with respect to the rostrocaudal or dorsoventral axes. In some cases, as illustrated in Figure 6*A*, dorsal RFs were represented in penetration sites placed laterally and ventral ones in penetration sites placed more medially. In contrast, Figure 6*B* illustrates a reorganized trunk representation where the most laterally placed cortical sites represented RFs located midtrunk, and the more medial penetrations represented RFs both rostral and caudal to these midtrunk RFs. In Figure 6*C*, a third type of organization was demonstrated, as more caudal aspects of the trunk were represented in medially placed penetration sites and more rostral ones in laterally placed sites. As illustrated in all 3 examples of Figure 6, the internal topography was often characterized by adjacent penetrations that shared a common central RF sector, but different peripheral boundaries.

In some animals in this age group, an overall internal topographical organization for the trunk appeared to be absent, although occasional areas of adjacent penetrations within the general trunk region represented contiguous trunk RFs. It was generally easy to define these smaller areas, as they were virtually surrounded by penetrations with no cutaneous response. An example of this is illustrated in Figure 7. Here, in row A, the RF of penetration #1 was large and encompassed the 3 medially placed RFs of the remaining penetration sites. Row B penetration sites represented overlapping RFs from rostral to caudal along the dorsal midline of the trunk, while row C had 3 penetrations representing overlapping RFs that represented lateral to ventral aspects of the anterior trunk. The penetration sites of row D, which were oriented along the rostrocaudal axis of the cortex, represented a series of small RFs that extended along a restricted dorsoventral strip of the trunk that was located behind the shoulder. However, the adjacent penetrations were not always overlapping or contiguous.

Often, responses could only be elicited at very high thresholds, and as illustrated in Figure 7, they sometimes included very large RFs, frequently encompassing the entire trunk (Fig. 7, row A, penetration 1). As in animals cord transected at 2 weeks of age, these large RFs frequently were cortically adjacent to representations of smaller RFs that were within the area encompassed by the large RF.

Animals cord transected as adults

The cortical response to deafferentation by cord transection was not robust in this age group, and the pattern of reorganization was different from both the animals cord transected at 2 or 6 weeks of age (Fig. 1*F*). The penetrations in the deprived cortex that could be driven by tactile stimulation of the trunk were usually more sparse and well separated by large areas that were unresponsive to light tactile stimulation. Somatotopic regions typically designated to represent the forelimb, shoulder, axilla, and thorax regions were largely unaffected by the lesions, and representation appeared similar to that in normal animals (Fig. 1*F*). There was also considerable variability in the number of penetration sites that were responsive to tactile input. The map illustrated in Figure 8*A* represents the animal that demonstrated the most vigorous response of the entire group. This animal had the lowest percentage of NCRs in the adult group (44%), which was not significantly different from animals cord transected at 6 weeks (Table 1). However, the pattern of active penetration sites was different from that of the younger animal in that the active sites were interspersed equally throughout the reorganized cortex. This was in contrast to the more highly localized active sites as described for the younger animal. Figure 8*B* illustrates a more typical reorganizational response to cord transection in the adult, with 69% NCRs. There were always areas within the deafferented hindlimb cortex that responded to stimulation, but as the penetration row illustrations reveal, organization varied from "topographical" (Fig. 8*A*, rows A, C; Fig. 8*B*, row B) to nontopographical (Fig. 8*A*, row B; Fig. 8*B*, rows A, C). Most representative, however, were multiple penetrations representing the same RF (Fig. 8*A*, circled penetrations). As found in the other 2 age groups, a large RF shared common boundaries with smaller RFs (Fig. 8*A*, row B).

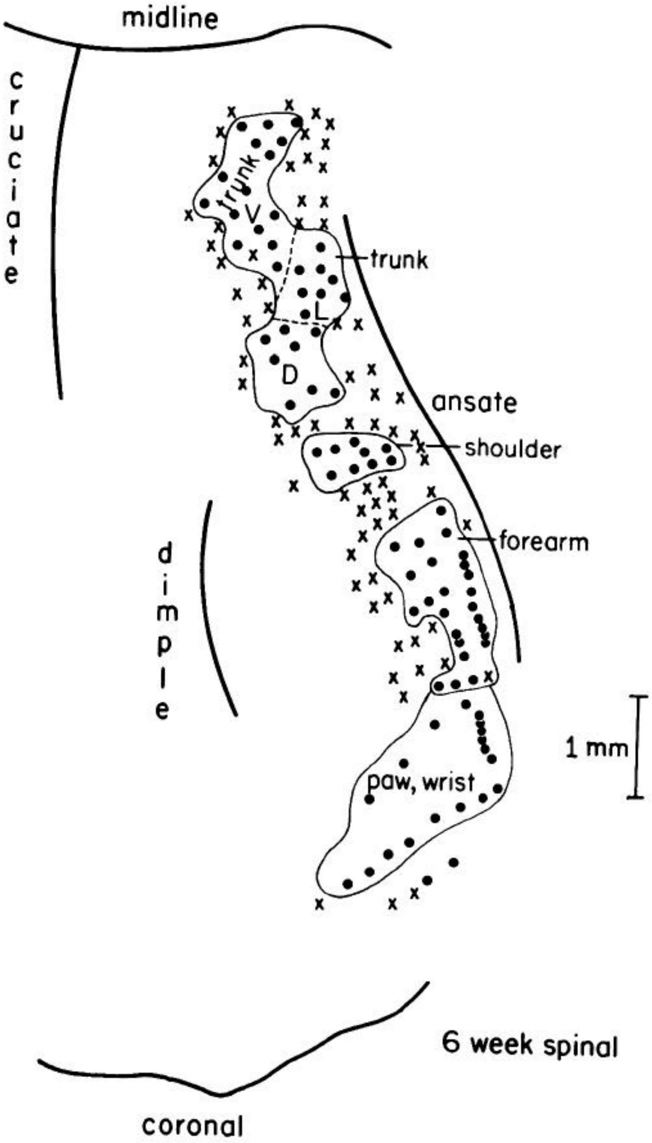

Figure 5. Penetration map of primary sensory cortex in 1 animal cord transected at 6 weeks of age. *X*s represent NCRs; *closed circles*, responsive penetration sites; and symbols represent body parts. *Trunk* includes trunk, axilla, and chest; *shoulder* includes shoulder, upper arm, and dorsal neck.

Definition of deprived-reorganized area

Although it is well documented that the somatosensory cortex is somatotopically organized (cf. Kaas et al., 1983, for review), the organization of each map is individualized, and definitive boundaries using architectural or electrophysiological landmarks are impossible to predetermine before mapping. Therefore, we were concerned about the manner in which the precise boundaries between deprived/nondeprived cortex would be determined. This was made all the more difficult because the RFs eliminated by the lesion were not positioned cortically within a circumscribed area as they are in procedures that partially denervate a limb segment. We initially thought that we could make use of the abnormal RF characteristics described above to determine which part of the cortex had been deprived by the lesion and subsequently "reorganized." In the adult animals it was easier to make this arbitrary decision, as there was often a clear demarcation between organized and disorganized RFs of the trunk. Figure 8*A* illustrates how sharply the cortical responses can change when on the border between "normal" and "reorganized" cortex. In this figure, row A represents contiguous overlapping RFs on the trunk which progress from dorsal to ventral along the rostrocaudal axis. Immediately medial to row

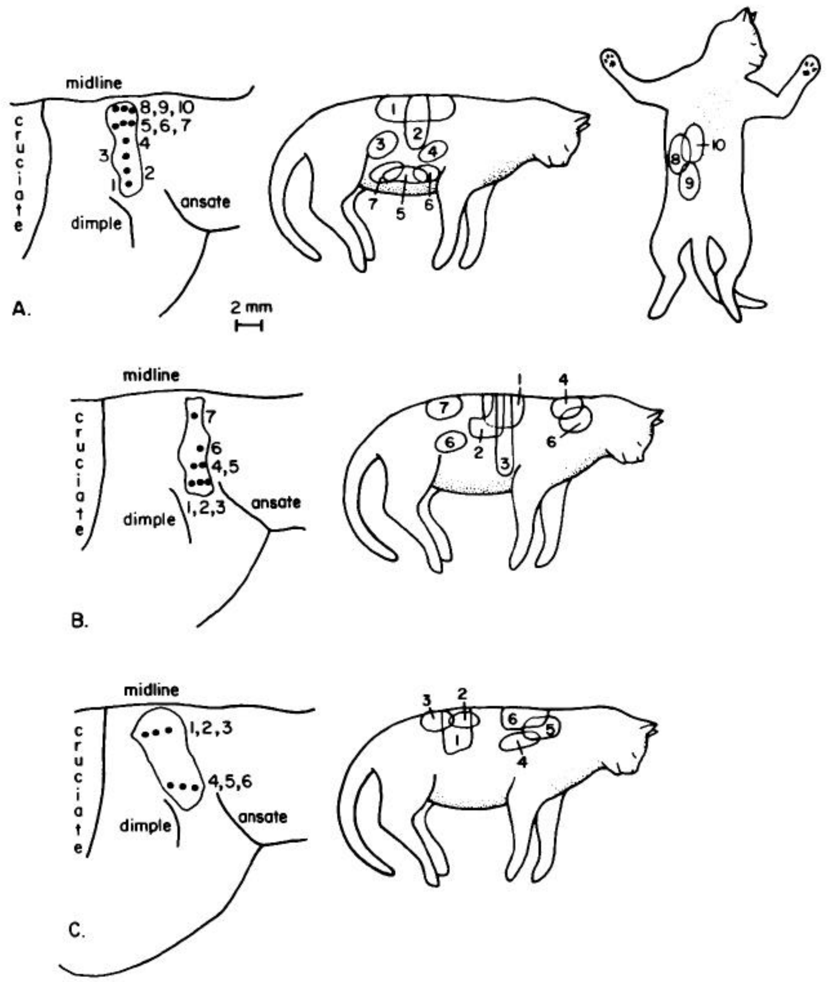

Figure 6. Reorganization of trunk region in cats cord transected at 6 weeks of age. *A–C*, 3 examples of maps of trunk representation in animals cord transected at 6 weeks of age. To the *left* are the cortical maps and selected penetration site locations. To the *right* are corresponding RFs designated by the numbered penetration sites.

A, row B illustrates a rather disrupted organization along the rostral-caudal axis with penetration 1 encompassing a rather large RF on the lateral aspect of the trunk, and penetrations 2 and 3 located inside the RF represented in penetration 1. Penetration 4 was ventrally placed to the other 3 penetrations, but overlapped penetration 1. Additionally, ventral aspects of the trunk were represented more rostrally and dorsal aspects more caudally, an order that is reversed from that of the normal controls. What often made interpretations difficult, however, were sequences such as that illustrated by Figure 8*A*, row C, that demonstrated continuous progression of adjacent RFs around the axilla region of the trunk and thorax. As this row was located in the most medial portion of somatosensory cortex (a region which normally represents the hindpaw or ankle), it was clear that the region was reorganized cortex. However, when more laterally placed deprived cortical regions showed similar topographical organization, it was difficult to decide where boundaries could be drawn between normal and deprived cortex.

When analyzing maps of animals cord transected at 2 and 6 weeks of age, the task became even more difficult. In animals cord transected at 6 weeks of age, the entire somatotopic map was altered, including regions representing the forelimb, as described above and illustrated in Figure 1*E*. Additionally, while there was organization within the trunk-designated region of the primary somatosensory cortex in this group of animals, orientation of RFs was idiosyncratic and not always well organized topographically, as illustrated in Figure 6. In animals cord transected at 2 weeks of age, there was no obvious change with respect to rostrocaudal boundaries that could be activated, but close inspection of the trunk region indicated that much of the trunk-designated cortex contained areas of cortex that were not topographically organized but contained noncontinuous or disrupted RFs, large RFs, and occasionally, multiple representation of the same RF. A series of sequential rows from medial to lateral (Fig. 2, rows A–D) illustrates this lack of consistent organization throughout trunk-designated cortex of these animals. Therefore, in both groups of animals cord transected as young kittens, it was decided to include the entire trunk region, in

Table 1. Percent somatosensory NCRs

Age group	*n*	Forelimb Range	Forelimb $\bar{X} \pm$ SD	Hindlimb Range	Hindlimb $\bar{X} \pm$ SD
Normals	5	4–10	8.8 ± 3.4	10–14	12.6 ± 1.5
Cord transected					
2 weeks	6	4–14	9.5 ± 3.4	8–23	13.7 ± 5.1
6 weeks	6	20–68	42.4 ± 18.3	40–74	50.0 ± 11.5
Adult	6	3–13	9.1 ± 4.2	44–86	63.3 ± 18.5

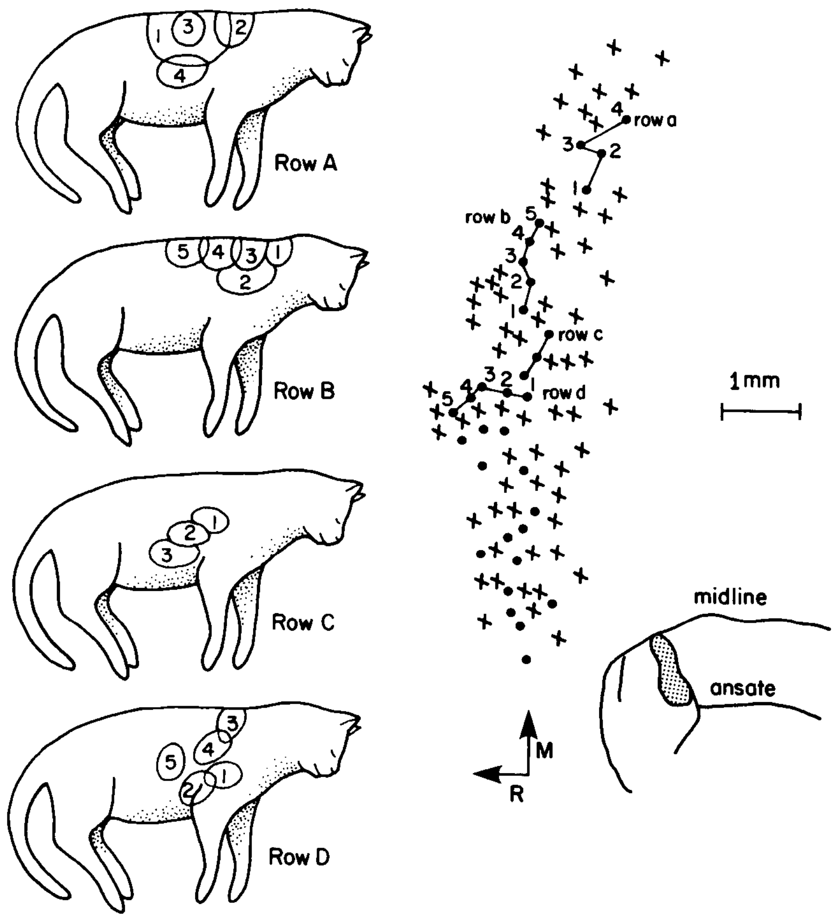

Figure 7. Cortical map of the region activated by trunk RFs in an animal cord transected at 6 weeks of age. Conventions as in Figure 2.

addition to the hindlimb and that portion of the trunk cortex that was physically deprived of its normal peripheral afferent input, in cortex described as "reorganized."

Comparison of active to nonresponsive penetration sites in deafferented cortex

Table 1 lists the percentage of penetrations that did not elicit a response to light tactile stimulation (NCRs) in normal and cord transected animals. Normal animals had a range of 4–10% NCRs in forelimb-designated cortex and 10–14% in hindlimb-designated cortex. A similar but wider range (4–14%) was found for forelimb cortex in the animals cord transected at 2 weeks of age. "Reorganized" (hindlimb and trunk) cortex also had a wider range of 8–23% NCRs. However, this number of active sites was not significantly different from that found in normal animals (Mann-Whitney *U* test; Siegel, 1956). More importantly, however, in the animals cord transected at 2 weeks of age, percent NCRs in forelimb and hindlimb cortex within a given animal was similar for all cases. In one animal, for example, both forelimb and hindlimb had a relatively low percentage of NCRs at 4 and 8%, respectively; another animal demonstrated higher NCRs (14 and 23%) in the fore- and hindlimb cortical regions. Additionally, the animals cord transected at 2 weeks of age had a higher percentage of active penetration sites in the deafferented cortex than did the other 2 groups.

Both the adults and animals cord transected at 6 weeks of age had a larger number of NCRs that were significantly different from those of normals (Mann-Whitney *U* test; Siegel, 1956). As described above, the spatial organization of active penetration sites in these 2 groups differed. This difference was also reflected in a comparison of percentage of NCRs when comparing NCRs in "deprived/reorganized" to those in "normal" cortex. Similar to the animals cord transected at 2 weeks of age, the animals cord transected at 6 weeks showed no significant difference in percentage of NCRs between the 2 regions, averaging about 42 (±18)% in forelimb and 50 (±12)% NCRs in hindlimb cortical regions. However, the adults showed a vast difference between "reorganized" and "normal" cortex in that the number of penetration sites unresponsive in "reorganized" cortex at 44–86% was much larger than those found in the forelimb-designated normal cortex (3–13%). While very large anesthesia-sensitive RFs have been reported to exist in normal adult animals (Rubel, 1971), they are not commonly reported, and we rarely found them in our normal controls. Furthermore, we did not find evidence of multiple cortical sites representing the same peripheral field in the control population.

Cortical responsiveness

In animals cord transected at 6 weeks and as adults, a high number of penetrations were unresponsive to tactile stimulation. It has been suggested that anesthesia state is important for cortical responsiveness to stimulation (Duncan et al., 1982; McKenna et al., 1982). However, recent publications have suggested that this may not be as important as previously suggested, at least in monkey (Stryker et al., 1987) and rat (Chapin and Lin, 1984).

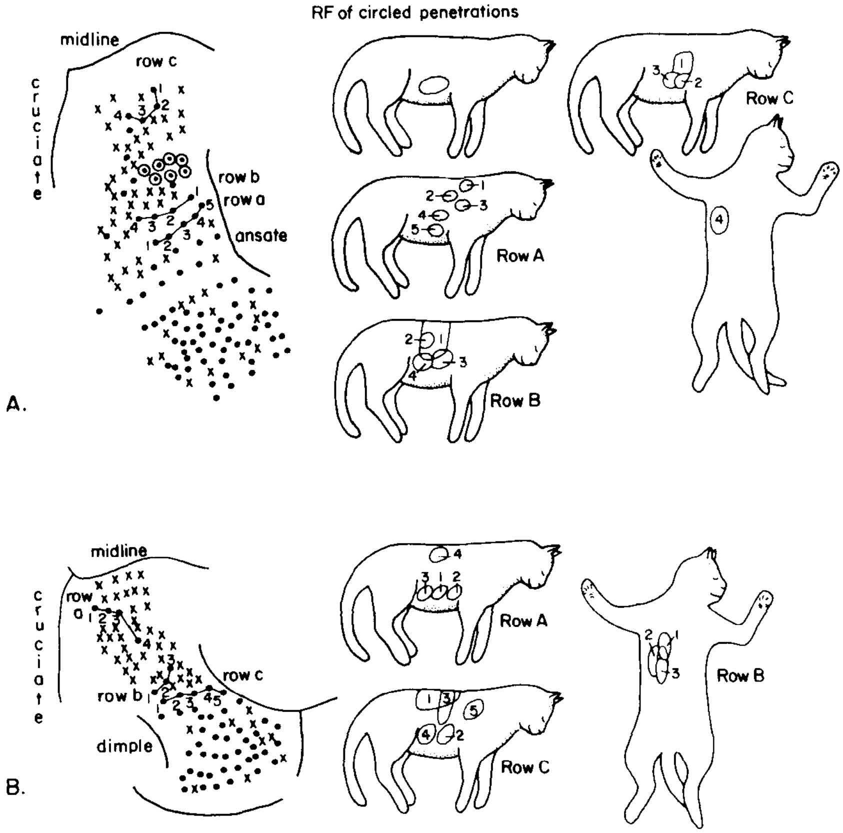

Figure 8. Cortical maps of the deprived regions in primary somatosensory cortex in 2 cats cord transected as adults. Conventions as in Figure 2.

Additionally, our results did not indicate a significant difference in the responses of the animals cord transected at 2 weeks from those of control animals. In the animals cord transected at 6 weeks of age, responses were robust throughout the central portion of the primary somatosensory cortex while diminishing at the rostral and caudal borders. It does not seem likely that only the rostral and caudal borders would be affected by anesthetic and the central portion of primary somatosensory cortex left to respond normally. Likewise in the adults, there was a clear demarcation between normal and deafferented cortex. While the progression of penetration rows sampled was often from medial to lateral in the adult, repeated recording was done in the normal part of the cortex throughout the experiment to insure that the electrode and the preparation were still in good condition.

Discussion

The purpose of these experiments was to examine age-dependent cortical adjustments to spinal cord transection by making RF maps in primary somatosensory cortex from multiunit recordings. The results of these experiments indicate that the age at which the spinal cord is transected in cat had a profound effect on the way the somatosensory map is represented at the cortical level. In cats that had been operated on as kittens at 2 or 6 weeks of age, the lack of afferent input from the caudal trunk and hindlimb influenced the organization of not only the "deprived" cortex, but the "normal" cortex to varying degrees. In the 2-week-old group, it affected primarily the trunk representation immediately adjacent to the deprived region, while in the 6-week-old group, the entire cortical representation was altered. Additionally, in animals cord transected at 2 weeks, the remaining somatic afferent input could drive not only the normal forelimb- and trunk-designated cortex, but the deprived trunk and hindlimb cortex, resulting in two somatotopic maps of the intact input. The animals cord transected at 6 weeks of age demonstrated a different response, redistributing the remaining afferent input across the mediolateral axis of the cortex such that the deprived cortex responded to trunk stimulation, while the regions representing the shoulder, thorax, axilla, and upper arm were shifted medially, and the rostrocaudal borders were narrowed. In the adult, a third response was observed; while regions normally devoted to forelimb and trunk appeared to be unchanged, the deprived hindlimb region responded in a very limited way to trunk tactile stimulation. These results highlight 2 age-dependent variables: the degree of restructuring of the somatotopic map, and the limits on the areal representation at the cortical level of a given somatotopic region.

Restructuring of the cortical map

While reorganization of deprived regions has been described for a number of experimental protocols, concomitant changes in the entire cortex have not been previously documented. Reports of changes in normal cortex topography have been reported, but only when the RF replacements were cortically adjacent. For example, in cat, where the forearm region is separated from the forepaw by the region serving the wrist, Kalaska and Pomeranz (1979) found that when the forelimb nerves were severed above the wrist, forearm RFs could drive the deprived forepaw cortex, but that the normal region representing the forearm was unchanged by the surgical intervention. In contrast, Merzenich and colleagues (1983a, b) reported that after median nerve section in monkeys, the radial and ulnar nerve input (that is both peripherally and cortically adjacent) could drive the deprived cortex previously served by the median nerve. In addition, topographical continuity from the normal into the reorganized region was observed and included reorganization of regions originally served by the ulnar and radial nerves. In the model we used—spinal cord transection—the pattern of restructuring of normal cortex was diverse and age dependent.

Limited responses in adult animals

In adult animals, there was virtually no restructuring of the normal cortex. Indeed, the maps were often characterized by a distinct demarcation between normal trunk penetration sites, which had small RFs, low thresholds, and well organized topography, and the deprived cortex, which had a limited number of penetration sites that could be driven by large amorphous trunk RFs with high thresholds and poor topographic organization. Not only was the degree of response highly variable among animals, it was also characterized by a striking difference between the large percentage of NCRs in the deprived (63.3%) as compared to normal (9.1%) cortex (Table 1). In addition, the active penetration sites were interspersed randomly throughout the reorganized cortex, and were often characterized by multiple representation of the same receptive field. Thus it is possible that the response in the adult may be limited to existing thalamocortical overlap, as the majority of active sites in the deprived cortex were within the range of documented thalamocortical overlap in cat (Landry and Deschenes, 1981; Landry et al., 1986).

A shift in driving force to somatotopically inappropriate input after elimination of somatotopically appropriate input at the thalamocortical interface has previously been proposed as the mechanism by which reorganization occurs in adults with more limited lesions such as peripheral nerve crush or cut or digit amputation (Wall and Kaas, 1985, for review). However, Rasmussen and Nance (1986) have demonstrated thalamocortical overlap is not a factor that affords reorganization in adult raccoon after 5th digit amputation, as thalamocortical connections remained separate, although cortical penetrations in the 5th digit region were driven by stimulation of the 4th digit. Additionally, the recent discovery of the existence of intracortical connections between the glabrous and hairy skin of the digits in raccoons (Doetsch et al., 1988b) suggests that existing intracortical connections could also be the basis for the substitute response seen in our deafferented preparation in the adult age group. Further, both the ability to transmit inappropriate input and the anatomical matrix for this response have been demonstrated at the level of the gracile nucleus in cat (Dostrovsky et al., 1976). These workers showed that in acute preparations under conditions of spinal cooling, units in the gracile nucleus that normally responded to hindpaw stimulation would respond to stimulation on the trunk. Thus, adjustments at levels below the cortex cannot be ruled out.

The variability in response might be simply due to the differences in these connections among animals that are a result of the less than stereotypic manner in which these maps evolve during development. Although it has been recognized for some time that cortical somatotopic maps are a characteristic of mammalian and avian species, each species manifests a map that is unique to that particular species (Kaas et al., 1983). Recently, however, it has been acknowledged that these maps within a given species are highly variable (Wall et al., 1986; Merzenich et al., 1987). The idiosyncratic nature of the maps can be ascribed to variable formation and maintenance of inappropriate connections that are shaped by experience as well as by developmental processes (Spinelli and Jensen, 1979). It is this process that may be manifested in the adult animals.

6-week-old: restructured map

In direct contrast to the adult preparation was the response of the 6-week-old age group. In these animals, the entire map was restructured so that the remaining input from the arm, forearm, paw and wrist, neck, shoulder, and rostral trunk occupied the entire SI mediolateral axis. This redistribution of intact somatosensory imput at the cortical level suggested a gradual shift in representation of receptive fields of intact afferent input. As evidence for sprouting in older kittens is sparse (Beckerman and Kerr, 1976; Kerr, 1975), and the distance over which reorganization took place (3–5 mm) may have been greater than the spread of thalamocortical collaterals, it seems more plausible that "strengthened" synapses of overlapping, existing input at the level of the VB thalamus or the dorsal column nuclei (DCN) may have elicited a gradual reweighting of all existing synapses, effectively shifting the distribution of the trunk, shoulder, axilla, forelimb, wrist, and paw representations medialward. This phenomenon has been demonstrated in the adult cat cortex after dorsal root section (Franck, 1980), and in the rat thalamus after DCN lesions (Ganchrow and Bernstein, 1981) and gracile nucleus after dorsal column lesions (Dostrovsky et al., 1976; Ganchrow et al., 1981; Bernstein and Ganchrow, 1981). Alternatively, there could have been new growth in the DCN or thalamus that was stimulated by the lack of input from below the lesion.

Close inspection of the internal topography of the trunk RFs revealed that often an RF was represented more than once, and while some of the RFs were small, there was often no overlap from cortically adjacent RFs, and frequently RFs were very large, encompassing the entire lateral trunk. In contrast, the forelimb segments as well as the shoulder and axilla showed small overlapping RFs. Thus, while the entire map was restructured, the trunk representation was less well organized when compared to the forelimb, shoulder, and axilla representations. This suggested that while cortical adjustments of the forelimb, axilla, and shoulder representations may have been the result of gradual shifting of emphasis of existing anatomical connections within the nondeprived cortex, the response in the deprived cortex may have included new axonal growth at some point along the neuraxis. While the most parsimonious suggestion is that the alterations are taking place at the first relay (within the gracile nucleus), other possibilities cannot be ruled out, such as ingrowth from other afferent systems such as the spinothalamic tract and the lateral cervical nucleus/posterior nuclei, lateral division (POl) input. These inputs demonstrate characteristics such as increased threshold, and rapidly adapting and less discrete RFs (Methrate et al., 1987) as are reported for the "reorganized" cortex representing the trunk in the 6-week-old animals. These possibilities are currently under investigation in our laboratory.

An additional feature of the restructured map was the large percentage of NCRs found in both the normal (42%) and reorganized (52%) cortex. Typically, the NCRs were located along the rostral and caudal margins and in aggregations between the representations of body parts so that RFs were not overlapping or continuous but demonstrated distinct breaks between lower forelimb and shoulder, and shoulder and axilla, and axilla and trunk. Although these breaks were not electrically silent, they could not be driven by light tactile input, taps, or joint manipulation. This outcome is different from that reported for more restricted lesions in adult monkeys, where amputation of a digit (Merzenich et al., 1984) or a single nerve (Merzenich et al., 1983a, b) resulted in the deafferented region being filled in by substitute input from the adjacent representations, with little or no vacant space between the RFs serving different parts of a limb segment. In contrast, Kalaska and Pomeranz (1979) reported in their studies on reorganization after transection of all nerves serving the forepaw of the cat and kitten, that while the deprived forepaw region was reorganized in varying degrees in both young and adult, there were a large number of NCRs in both age groups. Similar results after partial denervation of the cat forelimb have also been reported by LeClerc et al. (1989), and after sciatic nerve cut in rat by Wall and Cusick (1984). Since the multiple peripheral nerve lesions and spinal cord transections open up a larger territory of deprived cortex than do more circumscribed lesions, it may be that there is a limitation imposed on the amount of cortex that can be controlled by input from a given body part (see below).

2-week-old: partial map restructuring

The response of the 2-week-old animals was also different from the other 2 age groups in that the normal cortex appeared largely unaffected by the lesion, except for the trunk region, which was completely restructured to blend continuously into the deprived but completely reorganized hindlimb cortex. In this case, the representation of the trunk was characterized by continuous adjacent RFs, although the internal topography was not so neatly organized as found in the trunk representation of the normal animal. Often, direction of RF field overlap in a rostrocaudal row of penetration sites would be reversed in the adjacent row, RF boundaries were sometimes amorphous, and a given RF was occasionally represented at more than one penetration site. Typically, the final outcome yielded a map with double representation of the trunk that then extended medialward to include a second representation of the forearm, wrist, and digits. However, the organization of these body parts in the cortical map was idiosyncratic. The origin of this representation can only be conjectured, as our experiments were not designed to investigate this aspect of the response to deafferentation.

In the neonate it is possible that thalamocortical projections have a much broader range than in the adult, such that the thalamocortical axons to the forelimb region also project to the hindlimb region and simply do not retract in the cats cord transected at 2 weeks of age. Another possibility is that sprouting of thalamocortical axons occurs from axons projecting from forelimb ventrobasal thalamus to the deprived trunk and hindlimb cortical regions. However, it appears from other experiments in our laboratory that thalamocortical overlap is not the site of this duplicate representation, as separate injections of 2 fluorescent dyes in the 2 cortical forelimb representations did not reveal overlapping thalamocortical projections to these 2 forelimb representations (McKinley and Kruger, 1988). Instead, it appeared that the somatotopic connections of ventral basal nuclei to somatosensory cortex had not been altered due to the lesion. Although use of cortico-cortical polysynaptic pathways cannot be discounted, long-ranging monosynaptic cortico-cortical input could be rejected by these same experiments, as there were no double-labeled cells at the injection sites. Thus developmental processes such as sprouting, or maintenance of exuberant projections, could be rejected with respect to the thalamocortical or monosynaptic cortico-cortical projections.

Since thalamocortical projections were not overlapping in a way to generate such a map, the mechanism that afforded such a response may have enabled the thalamocortical cells that projected to the hindlimb region to receive input from forelimb afferents. This could have taken the form of either increased collateralization of cuneothalamic axons, or of cuneate-bound afferent sprouting into the gracile nucleus. For discussion of these and other possibilities, see McKinley and Kruger (1988).

Areal capacity of the cortex for adaptation

We agree with Wall and Cusick (1986) that whether recovery from lesion is judged as greater or lesser in the neonate as compared to the adult is highly dependent on the state of development of the neonate at the time of the lesion. The response in cats cord transected as kittens of 2 or 6 weeks of age is clearly more robust than that in the adult. Whether the response in cats cord transected at 2 weeks of age is greater or merely different from the response in cats cord transected at 6 weeks of age may be a matter of interpretation. Nonetheless, our results are directly opposite to those reported by Wall and Cusick (1986) in rat after sciatic nerve cut. Their results indicate a real limitation for saphenous replacement of sciatic input in the primary somatosensory cortex that is greater in neonates than in adults. They hypothesize that the areal extent of control is less in neonates because saphenous related thalamocortical projections do not develop as widely during the time that connectivity is being established when sciatic input is missing. It is possible, however, that extended saphenous thalamocortical collaterals never develop in immature rats because at the time of injury, substitute input is equally unavailable to replace appropriate input. Thus, cell regression or death is accelerated in the DCN before any connectivity is established at the first synapse. This would be reflected then at the cortical level, as they have reported. In the adult, it is more probable that established interconnectivity is responsible for the expansion of the cortical region drivable by saphenous nerve input, as the distances reported for reapportionment of afferent input are within the range of thalamocortical collaterals.

However, in contrast to rodents, where cortical response to cutaneous stimulation is not elicited until 6 d postnatal (Armstrong-James, 1975), kitten afferent systems are relatively mature at birth (Skoglund, 1969; Villablanca and Olmstead, 1979). Although the coding of input is not mature, functional connectivity is established (Bruce and Tatton, 1980; Connor et al., 1984; Ferrington et al., 1984) and the somatotopic organization resembles that of the adult in both the cuneate nucleus (Ferrington and Rowe, 1981) and somatosensory cortex (Rubel, 1971). Existence of functional connections (though immature) appears to be important in prevention of cell death, dendrite retraction, or axon retraction when lesions are incurred (Coleman and Buell, 1985). While direct comparisons between species with different developmental time tables for the same lesion are scarce, this phenomenon has been clearly demonstrated for development of the gracile nucleus deprivation of afferent input from hindlimb. In the opossum, where the cuneate-gracile nucleus is not yet formed at birth, hindlimb amputation at birth results in regression of the gracile nucleus (Johnson et al., 1972). In contrast, in cat, where lemniscal neurons and the DCN develop prenatally (Scheibel and Scheibel, 1978), agenesis of the hindlimb late in prenatal development resulted in a gracile nucleus that was relatively normal in size and responded to afferent stimulation in the remaining hindlimb, tail, and trunk regions (Schultz et al., 1981). This might suggest that prelesion connectivity is important in preventing cell death postlesion in immature systems.

While limits on areal control do not seem to be a problem in the animals cord transected as neonates, the pattern of adjustment to spinal cord transection in animals cord transected at 6 weeks of age indicates that there is a limit on the amount of cortex that a given group of afferents can excite, as there does not appear to be expansion of the trunk-represented area, but a shifting of the entire intact afferent input across the mediolateral axis. As the rostrocaudal margins are both narrowed, it would appear that the cortex had rearranged itself to represent remaining input, but had not expanded its influence in somatotopic representation. This suggests that the amount of cortex that each somatotopic representation can drive seems relatively fixed by 6 weeks of age. Although some aspects of the trunk were enhanced slightly in representation (such as the axilla and thorax), and the trunk and forelimb internal topography differed from normal animals, it does not appear that remaining afferent input can increase the amount of cortex it drives to the extent observed in the animals cord transected at 2 weeks of age. This may be due to the maturational state of the nervous system at the time of the lesion and/or the site at which the reorganization process takes place, as reorganization at the first or second relay might afford greater representation of a given body part at the cortical level than reorganization that takes place at the cortex.

In cat, the only previous studies of age-dependent changes after nerve transection have been done on the cat forepaw. While results from these experiments demonstrated a more robust response at both the cuneate nucleus (Kalaska and Pomeranz, 1982) and the somatosensory cortex (Kalaska and Pomeranz, 1979) in animals that had sustained nerve transection as 1.5–3-week-old neonates, reported active penetrations in the deprived region were only 52% of the normal cortical responses (Kalaska and Pomeranz, 1979). Our data demonstrate that only 8–23% of deprived cortex is nonresponsive to cutaneous stimulation in the cord transected neonate. It is curious that such a large deprived region demonstrated a more vigorous capability to be driven by "somatotopic inappropriate" input than the smaller, more circumscribed forelimb region. Since the response after forepaw denervation was limited to drivable units representing the forearm, it is possible that the lesion itself elicited a more circumscribed response than that elicited when input from an entire region of the body was eliminated. Thus, in limited lesions, such as amputation or deafferentation of a limb segment, only local mechanisms such as changes in existing synapses may be employed. In contrast, a massive lesion, such as elimination of afferent input from an entire limb, tail, and caudal trunk, may provoke a more profound change in anatomical connections, at least in the young animal.

Role of the cortex in reorganization

Cortical reorganization is the final outcome of somatosensory system reorganization; that is, it reflects changes that occur at all levels of the projection system and may involve descending as well as ascending projections. Two basic mechanisms have been postulated to explain the dynamic response of the central nervous system to change in somatotopic afferent input: (1) axonal sprouting into areas vacated by deafferentation (Goldberger and Murray, 1985, for review), and (2) unmasking, reweighting, or strengthening of latent existing synapses in the deafferented zones (Changeux and Danchin, 1976). A third mechanism, arrest in developmental processes, such as lack of retraction of exuberant projections, cell specialization, morphological changes, or cell death must also be considered when discussing these events in young animals (Belford and Killackey, 1980; Caminiti and Innocenti, 1981; Innocenti, 1981; Finger and Stein, 1982; O'Leary and Stanfield, 1985, 1986). While our paradigm was not designed to define mechanisms for response, as discussed above, these cortical mapping studies suggest that the mechanisms for response differed with respect to the age at transection.

We agree with Merzenich et al. (1983b) that the anatomic organization of the somatosensory system is consistent with a wide convergence and system filter model, as observed RFs in normal cortex are small when driven by natural stimuli but can be enlarged by various enhancement manipulations, and reorganized cortex RFs undergo a gradual refinement over time (Merzenich et al., 1983b; McKinley and Swyter, 1989). This is consistent with the notion that 1 role of the cortex is to shape and refine RFs and to make minor adjustments that reflect use and small alterations in peripheral input. For example, Dykes and colleagues have demonstrated that the size of a rapidly adapting RF can be enhanced for a brief period of time by iontophoretic application of bicucculine (Dykes et al., 1984) or over a longer period of time by iontophoretic application of ACh coupled with stimulation of an RF (Methrate et al., 1987), or when peripheral field stimulation is paired with stimulation of the basal forebrain (Rasmusson and Dykes, 1988). Other modulatory effects of norepinephrine and acetylcholine have been reported in striate cortical plasticity as well (Bear and Singer, 1985). This may be the mechanism by which the cortex adjusts RF size and degree of magnification to represent use in the periphery.

We must be cautious in our interpretation with respect to the constraints imposed by the methodology in this study, in that data were collected in a nonbehaving, anesthetized animal, using a multiunit recording electrode, and, finally, observations were at least 3 synapses away from the periphery. Thus, changes reported here are with respect to maps generated under these same conditions in normal animals, but do not take into account the effect that descending pathways may have on afferent transmission in the awake, behaving animal. In addition, they reflect the final outcome of changes in synaptic input that could have occurred at any region along the neuroaxis. Nonetheless, we feel that our results demonstrate that neural changes induced by the injury are likely to represent an interactive response of the basic developmental processes active at the time of spinal cord transection. Future investigations as to what extent the processes differ and to what extent they are similar in the 3 age groups may also reveal generalized as well as specific responses to injury.

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