

Somatosensory Cortical Map Changes Following Digit Amputation in Adult Monkeys

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ABSTRACT

The cortical representations of the hand in area 3b in adult owl monkeys were defined with use of microelectrode mapping techniques 2-8 months after surgical amputation of digit 3, or of both digits 2 and 3. Digital nerves were tied to prevent their regeneration within the amputation stump. Successive maps were derived in several monkeys to determine the nature of changes in map organization in the same individuals over time.

In all monkeys studied, the representations of adjacent digits and palmar surfaces expanded topographically to occupy most or all of the cortical territories formerly representing the amputated digit(s). With the expansion of the representations of these surrounding skin surfaces (1) there were severalfold increases in their magnification and (2) roughly corresponding decreases in receptive field areas. Thus, with increases in magnification, surrounding skin surfaces were represented in correspondingly finer grain, implying that the rule relating receptive field overlap to separation in distance across the cortex (see Sur et al., '80) was dynamically maintained as receptive fields progressively decreased in size.

These studies also revealed that: (1) the discontinuities between the representations of the digits underwent significant translocations (usually by hundreds of microns) after amputation, and sharp new discontinuous boundaries formed where usually separated, expanded digital representations (e.g., of digits 1 and 4) approached each other in the reorganizing map, implying that these map discontinuities are normally dynamically maintained. (2) Changes in receptive field sizes with expansion of representations of surrounding skin surfaces into the deprived cortical zone had a spatial distribution and time course similar to changes in sensory acuity on the stumps of human amputees. This suggests that experience-dependent map changes result in changes in sensory capabilities. (3) The major topographic changes were limited to a cortical zone 500-700 μm on either side of the initial boundaries of the representation of the amputated digits. More distant regions did not appear to reorganize (i.e., were not occupied by inputs from surrounding skin surfaces) even many months after amputation. (4) The representations of some skin surfaces moved in entirety to locations within the former territories of representation of amputated digits in every

Accepted November 15, 1983.

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monkey studied. In man, no mislocation errors or perceptual distortions result from stimulation of surfaces surrounding a digital amputation. This constitutes further evidence that any given skin surface can be represented by many alternative functional maps at different times of life in these cortical fields (Merzenich et al., '83b).

These studies further demonstrate that basic features of somatosensory cortical maps (receptive field sizes, cortical sites of representation of given skin surfaces, representational discontinuities, and probably submodality column boundaries) are dynamically maintained. They suggest that cortical skin surface maps are alterable by experience in adults, and that experience-dependent map changes reflect and possibly account for concomitant changes in tactual abilities. Finally, these results bear implications for mechanisms underlying these cortical map dynamics.

Key words: plasticity, area 3b, somesthesia, cortical magnification, hand

Earlier studies have revealed that somatosensory representations of the skin surface are dynamically maintained in adult monkeys and that cortical map sectors subjected to long-term deprivation effected by cutting the median nerve can reorganize rapidly (Merzenich et al., '83a,b). In that reorganization, representations of skin surfaces in cortical zones bordering a deprived median nerve representation area expanded into it, thereby enlarging the representations of the ulnar insular pad, the third palmar pad, the radial hand dorsum, and the limited skin surfaces on glabrous digit 3 innervated by the ulnar nerve (Merzenich et al., '83a). Such expansion was progressive and it was a number of days after nerve transection before complete territorial reoccupation of the former median nerve zone was observed. Even after complete initial territorial reoccupation, further changes were seen in the cortical topographic map and in receptive field dimensions and overlap (Merzenich et al., '83b).

A quite different sequence was observed in the cortical zone which normally represents the glabrous surfaces of digits 1, 2, and most of 3, also innervated by the median nerve. In that region, there was an immediate "unmasking" of a crude representation of the dorsum of the corresponding sites on the fingers, but on the opposite (dorsal) side of the digits. The "unmasked" representation of the dorsal skin surface was not complete. This crude, incomplete unmasked zone was transformed over time into a large, complete, highly ordered topographic representation of the dorsal surfaces of the digits. In this reorganization, receptive field sizes become progressively smaller, and receptive field overlap as a function of distance across the cortical surfaces changed from a grossly abnormal to the normal condition (Merzenich et al., '83b; Sur et al., '80).

The present experiments examine the effects of a more severe peripheral lesion, the amputation of one or two digits, extending earlier studies of map "plasticity" in several ways.

First, they demonstrate what reorganization occurs after removal of *all* inputs from digits. With digit amputation, the "unmaskable" input from the dorsal digital surfaces is removed along with the normally effective driving input from the glabrous surfaces of the digit(s). What happens, then, when these two inputs are removed together?

Second, they test whether reorganizing inputs can cross the apparent somatotopically discontinuous lines of representation in the cortical map that separate the representations of different digits. Although representations of the

glabrous digits abut each other within the cortex, the glabrous digital skin surfaces are anatomically discontinuous in the skin (except at the extreme base of the digits). The individual cortical representations of the digits are also functionally discrete, in the sense that receptive fields are rarely found to extend over more than one glabrous digit (see Merzenich et al., '78; Nelson et al., '81). (Most recorded exceptions are seen along the 3b-3a border, where occasional receptive fields for neurons extend over more than one fingertip (Merzenich et al., '78). Along the sides of the digits within area 3b proper, such two-digit receptive fields for individual neurons are rare.) Such a lack of overlap in the representations of adjacent glabrous digits might indicate that the representations of adjacent glabrous digital surfaces are anatomically separated throughout the somatosensory projection system. If not, then such representational discontinuities must be *dynamically* established and maintained. Following digital amputation, then, are discontinuous map boundaries crossed? Do they constitute barriers to reorganizational change?

Third, these studies should reveal how the reorganization of the cortical map relates to the neurological changes recorded after amputation. For example, changes in tactile acuity have been recorded on amputation stumps (Katz, '20; Teuber et al., '49; Haber, '55, '58). Are such changes paralleled by changes in the magnification of representation of these skin surfaces, as earlier studies have indicated (Merzenich et al., '83a)?

Finally, these studies should reveal the distance on the cortex over which reorganization can occur. If the deprived zone is large enough, will the surrounding cortical representations expand indefinitely to occupy it? What is the extent of the cortical zone over which territorial occupation can occur? If a single digit is amputated and the cortex reorganizes, what are the dimensions of the surrounding cortical zone that is thereby topographically altered?

The data to be reported here reveal that cortical territories of representation of one or two amputated digits are nearly completely occupied by inputs from the adjacent digits and palm in monkeys studied 2-8 months after digital amputation. The representations of these adjacent surfaces expand into the former territory of the missing digits, while maintaining their overall topographic order and unity. As a result of this expansion and movement of representation, parts of the skin surfaces initially overtly represented in the surrounding cortex come to be represented entirely within the former territory of representations of

the amputated digits. In this process, the former discontinuous borders between digit representations are crossed, although most movement and a disproportionate share of input in the occupied cortical zone is from the digit tips and from the adjacent palm.

These results bear further important implications for the nature of the reorganization process and for the functional meaning of cortical maps and the significance of their internal structure. Some of these implications are discussed. Preliminary reports of these results have appeared earlier (Schoppmann et al., '81; Merzenich and Kaas, '82).

METHODS

Experiments were conducted in eight adult owl monkeys, but most reported data are from six cortical mapping studies in four monkeys. Animals were anesthetized with sodium pentobarbital and maintained at a light level of anesthesia with IV supplementation. In most preparations, maps were derived acutely 62–74 days after amputation of either digit 3 alone, or of digits 2 and 3 together. In one monkey, a detailed map of the hand representation was defined under sterile conditions. After complete recovery from this experimental surgical procedure, digit 3 was amputated. Sixty-two days later, a detailed map of the hand representation was again derived. In another monkey, a detailed map was derived under sterile conditions 64 days after amputation of digits 2 and 3. The hand representation was subsequently remapped acutely 6-1/2 months later.

In all cases, digits were amputated symmetrically on the two hands, to avoid subsequent neglect to an injured side. In every case, care was taken to identify and to tie ligatures around the proximal stumps of all digital nerves in the amputation stump, to prevent their regeneration.

Receptive fields were determined for units or for clusters of units within the middle cortical layers (600–1,100 μm from the cortical surface), in each of 244–342 penetrations within and bordering the area 3b representation of the hand. All penetrations were parallel to each other and were introduced approximately perpendicular to the cortical surface in the flat 3b hand representational zone in the owl monkey. Positions of penetrations were recorded with reference to cortical surface vessels on a 30–40 \times photograph of the brain surface.

All receptive fields illustrated were "minimal receptive fields" (Merzenich et al., '78, '81), defined at the level of just-visual indentation of the skin surface. Receptive fields were determined using manual stimulation with a fine-tipped opaque glass probe. All fields were drawn on scale drawings of an owl monkey hand. Typical fields are illustrated in Figures 7 and 8.

In the studies in which two or more maps were derived in the same monkeys, all but the final maps were conducted under strict sterile procedures, at the end of which the dura was resutured and the bone flap was replaced using stainless steel sutures. As observed in earlier studies (Merzenich et al., '83b), the initial mapping procedure had no apparent effect on the responsiveness of cortical neurons. No surface damage was seen at the time of the second exposure of the hand representation; and neurons were strongly driven by cutaneous stimulation at *all* penetration sites at which they were driven in the first mapping experiment.

Hand representation maps were drawn by outlining cortical areas over which receptive fields were centered over given skin surfaces (see Merzenich et al., '78). The delimiting lines in these maps were drawn between penetration

sites with receptive fields centered on different labelled skin areas (see, for example, Fig. 1 or 3). Where receptive fields overlapped onto different skin surfaces, the line position was biased to reflect the extent of that overlap. In the illustrated cases, the individual outlined digital representational areas had from 16 to 61 penetrations with receptive fields on the designated digits. (The microelectrode penetration grid is illustrated for a typical case in Fig. 5). At any one point on the margin of the representation with that of adjacent skin surfaces, the possible error in boundary definition was about ± 25 to $150 \mu\text{m}$. However, the boundary was defined at numerous locations on the perimeters of these representational zones, so that overall errors in defined representation areas were small. The consequence of this degree of variability for our experimental measurements of areas illustrated in Figure 5 are as follows: (1) For the digit 4 representation, consisting of 61 sites, the coefficient of variation of the area measurements would be 2.9%, yielding 95% confidence limits that the areas as drawn was correct to within $\pm 5.7\%$. (2) For the digit 1 representation, with 41 sites, the variation would be 3.7%, giving 95% confidence limits of $\pm 12\%$ of the measured area. Therefore, errors in the measurement of representational area associated with the spacing of the microelectrode grid are very small compared to the plasticity observed in this study. Given this high density of penetrations, there was also a highly resolved definition of the detail of internal topography in these maps.

Normal owl monkey area measurements used for comparisons with areas of representation recorded in experimental monkeys were derived from earlier equally detailed complete maps of area 3b from a series of five normal adults (see Merzenich et al., '84). All measurements of area in normal and experimental series were derived with use of a Talos planimeter.

RESULTS

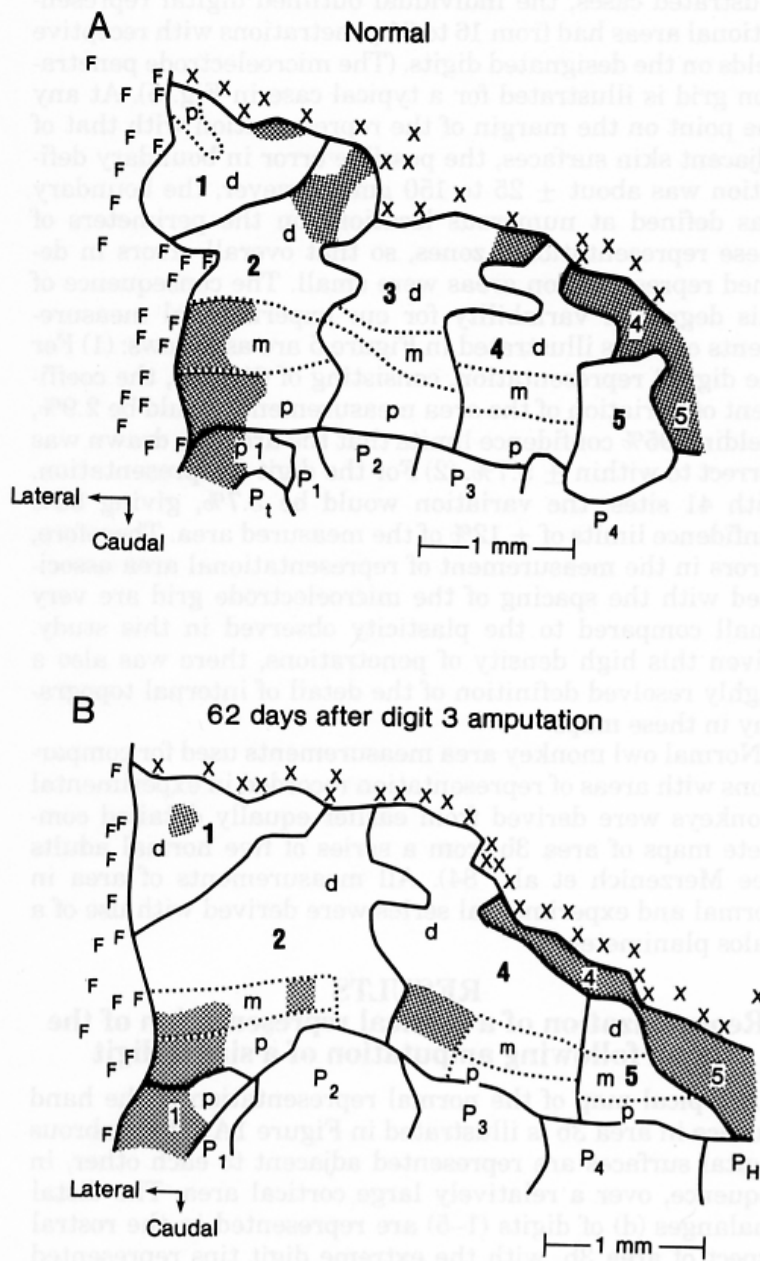
Reorganization of a cortical representation of the hand following amputation of a single digit

A typical map of the normal representation of the hand surface in area 3b is illustrated in Figure 1A. The glabrous digital surfaces are represented adjacent to each other, in sequence, over a relatively large cortical area. The distal phalanges (d) of digits (1–5) are represented in the rostral aspect of area 3b, with the extreme digit tips represented along the area 3b-3a (cutaneous-deep) border. The four palmar pads (P1–P4 in the map; see Fig. 3B) are represented continuously with the bases of the digits and with each other.

In this monkey, digit 3 was amputated 20 days after derivation of this normal map, taking special care to identify, cut, and suture the proximal stumps of the digital nerves in the short amputation stump. Sixty-two days after the amputation of digit 3, a second map of the representation of the hand in area 3b was derived (Fig. 1B).

In every one of 42 penetrations into the former zone of representation of the amputated digit, neurons were driven by cutaneous stimulation of new skin fields. These new "occupying" inputs were from the adjacent digits and the adjacent palmar pads and stump. All but a few receptive fields from the digits were on the facing digit tips. Their locations are illustrated in Figure 2. Most of the new inputs from the palm were from pad 2, normally immediately subjacent to digits 3 and 2. In both the palmar-occupying and digital-occupying zones, receptive fields were in topo-

Owl monkey 80-39



**C REPRESENTATIONAL AREAS
GLABROUS DIGITAL SURFACES**

	D ₁	D ₂	D ₃	D ₄	D ₅
Normal	0.71 mm ²	1.02	1.26	0.99	0.55
After amputation	0.74	1.84	—	1.63	0.46 mm ²
Amputation/ normal	1.04	1.80	—	1.65	0.92

graphic sequence (for an example from another similar case see Fig. 6 and 7), and these sequences were in continuity with the topography of the representation of the remainder of those hand surfaces, in their original representational territories. That is, the representation of digits 2 and 4 and palmar pad 2 expanded in area while maintaining their topography as they occupied this chronically deprived cortical zone.

The locations of the digit 2-digit 1 and the digit 4-digit 5 borders were relatively static. While the representations of digits 4 and 2 both increased greatly in area (by $\times 1.80$ and $\times 1.65$, respectively), the areas of representation of digits 1 and 5 changed little (see Fig. 1C).

A second single-digit amputation case is shown in Figure 3. In this monkey, the apparent occupation of the former digit 3 representation again primarily involved the tips of the adjacent tips, which expanded greatly (Fig. 3C). The expansion of digit 4 was more pronounced than was that of digit 2. The representation of palmar pads 3 and 2 again appeared to invade the normal territory of representation of the digits. Finally, a significant "silent" region was found, within which neurons were not driven by cutaneous stimulation.

Note that around this "silent" zone, there are several intermingled and apparently isolated patches representing distal phalangeal surfaces of digits 2 and 4. One to several such "islands" were found in each reorganization case.

Reorganization of cortical representations of the hand following the amputation of digits 2 and 3

After recording a "silent" zone in two relatively short-survival single-digit amputation cases, two-digit amputations were effected in each of two additional monkeys in an attempt to create a larger chronically deprived zone. When maps were derived in these monkeys 64 and 76 days after amputation, neurons within most of the original territory of overt representation of these digits were driven by inputs from the adjacent digits and palm (Fig. 4, 6). However, a residual region was also seen, within which neurons could not be activated by cutaneous stimulation.

As in single-digit amputation cases, the expansions of the representations of digits adjacent to those amputated were continuous and topographic. Thus, for example, in the case illustrated in Figure 4, digits 1 and 4 were $\times 1.70$ and $\times 1.77$ their normal size; and in the case illustrated in Figure 5, adjacent digits 1 and 4 were $\times 1.48$ and $\times 1.63$ their normal size, respectively. In the monkey mapped 64 days after nerve section (Fig. 6), an extraordinarily large representation of the remaining small digital stump was recorded (see

Fig. 1. A. Representation of the hand surfaces derived in a 244-penetration map within area 3b in a normal adult owl monkey. Xs mark penetration sites at which neurons were driven by deep but not by cutaneous receptor inputs. Fs mark penetrations in which neurons were driven by cutaneous stimulation of the face. Other abbreviations are shown in Figure 3B. The numbers 1-5 are the territories of representation of digits 1 (the thumb) through 5. d, m, and p are the territories of representation of distal, middle, and proximal phalanges, respectively; P1-P4 are the palmar pads at the base of the digits; and PH is the hypothenar eminence. Representational areas of dorsal digital and hand surfaces are shaded. The split representation of digit 1 (the proximal phalanx is represented at the lower left, more than a millimeter from that of the distal phalanx, upper left) is an unusual feature of this normal hand representation map. B. Map derived by defining receptive fields in each of 335 penetrations into and around area 3b, 62 days after amputation of digit 3 and 83 days after derivation of the map shown in A, in the same adult owl monkey. Abbreviations as above (and see Fig. 3B). C. Absolute cortical areas of representation of the glabrous digits derived before and after amputation.

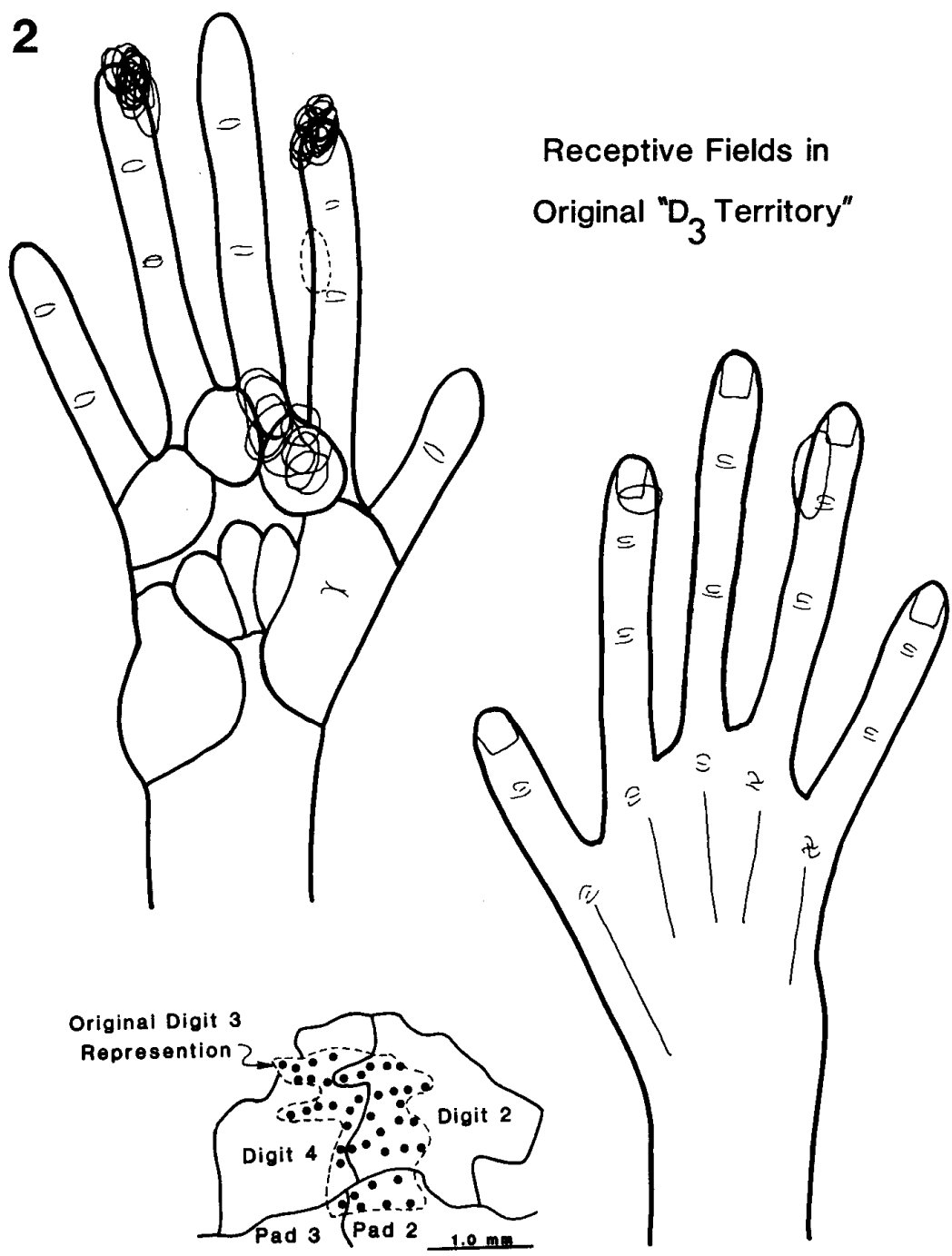


Fig. 2. All receptive fields represented within the original territory of representation of the amputated digit 3, for the case illustrated in Figure 1. The outline of the original digit 3 cortex is shown at the bottom in the inset (outlined by the broken line) in relation to the later-defined outlines of the territories of representation of digits 2 and 4 (solid lines). Dots represent the

42 penetration sites in the second map which fell within the territory of representation of the third digit in the first map. All of the receptive fields derived in those penetrations are shown on the hand drawings. The single field outlined by the broken line was not unequivocally driven by cutaneous inputs.

Fig. 6A), actually about the size of the normal area of representation of an entire glabrous second digit. The representation of the digit 3 stump was expanded from the normal, as were those of digits 2 and 3 (especially the latter) in the other illustrated two-digit amputation study (Fig. 4). In this second case, an especially large representation of palmar pad 2 was recorded, extending far into the presumed former territory of representation of the amputated digits.

The penetration grid for the study illustrated in Figure 4 is shown in Figure 5. When the density of sites (microelectrode penetrations) at which receptive fields have been defined is considered, it is evident that there is little uncertainty inherent in the definition of the basic form of

the map in these reorganized representations (also see Methods). In this typical example, the perimeters of zones representing given skin surfaces were defined at very many sites (more than 25, for either digit 1 or digit 4). While there are small possible errors in boundary definition at any one perimeter site, the overall average error is small, and the locations of borders and especially the measurements of areas of representation must be highly accurate. Thus, evident expansions of territories of representation are, in fact, unequivocally demonstrated by these fine-grained maps.

Similarly, given these fine microelectrode penetration grids, the internal topographies of these reorganized cortical zones are highly resolved. Receptive field sequences are

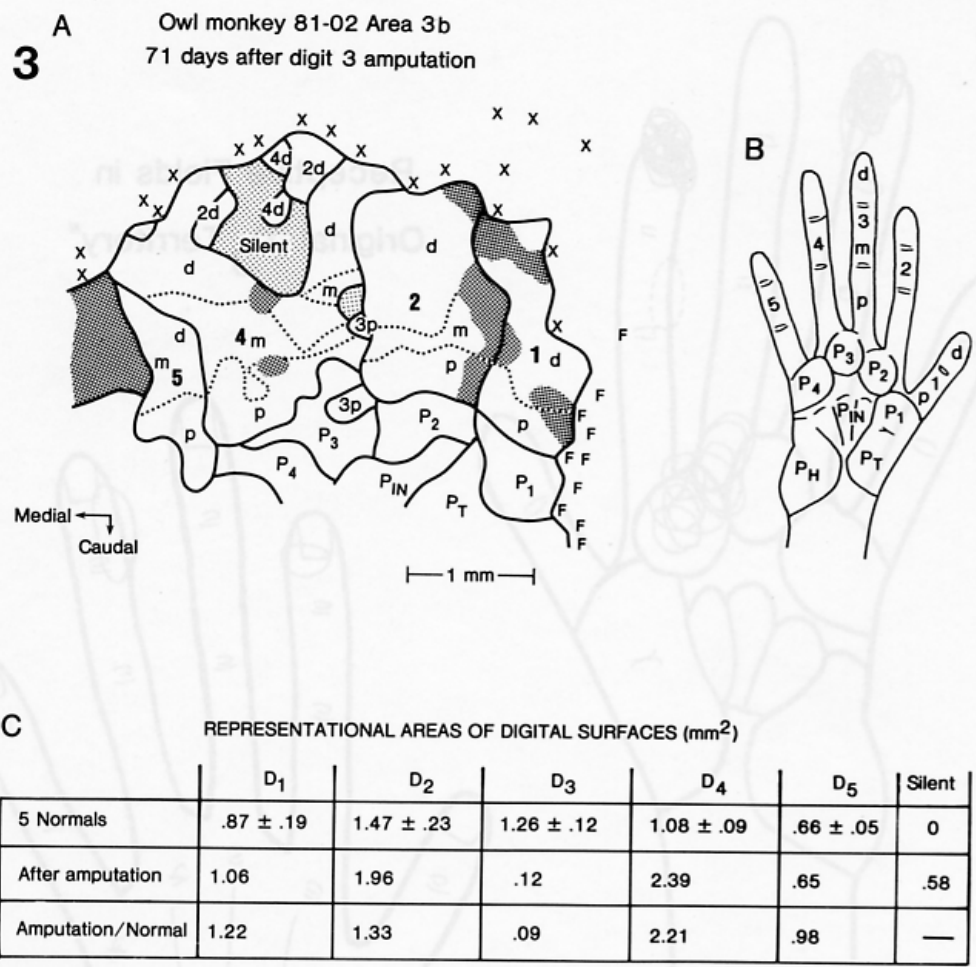


Fig. 3. Topographic representation of the hand surfaces, defined in a 342 penetration map into and across the borders of area 3b, derived 71 days after digit 3 was amputated (A). Abbreviations as in Figure 1, and as in the hand drawing (B). Comparisons of areas of representation of different digital surfaces are contrasted to areas of representation of the same digits in a series of five normal owl monkeys in C.

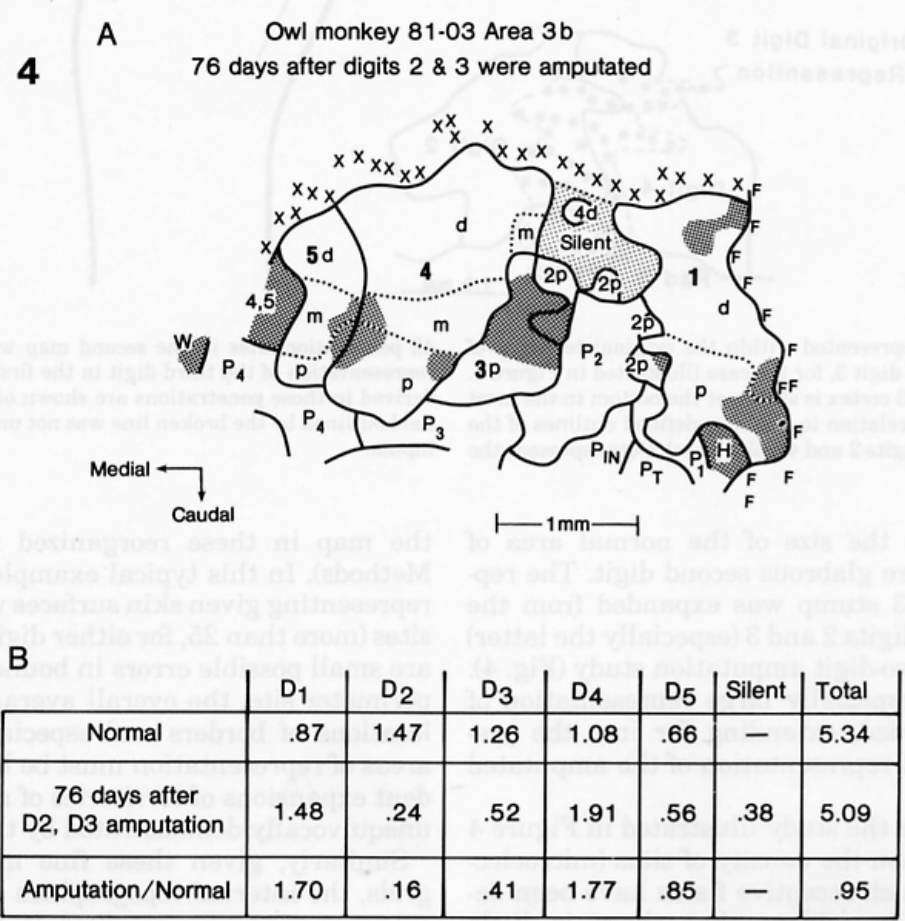


Fig. 4. A. Representation of the hand surfaces defined in a 284-penetration map into and across the borders of area 3b, derived 76 days after digits 2 and 3 were amputated. Abbreviations as in Figures 1 and 3. B. Comparison of the areas of representation of the digits in this monkey with normal areas of representation derived in a series of five adult owl monkeys.

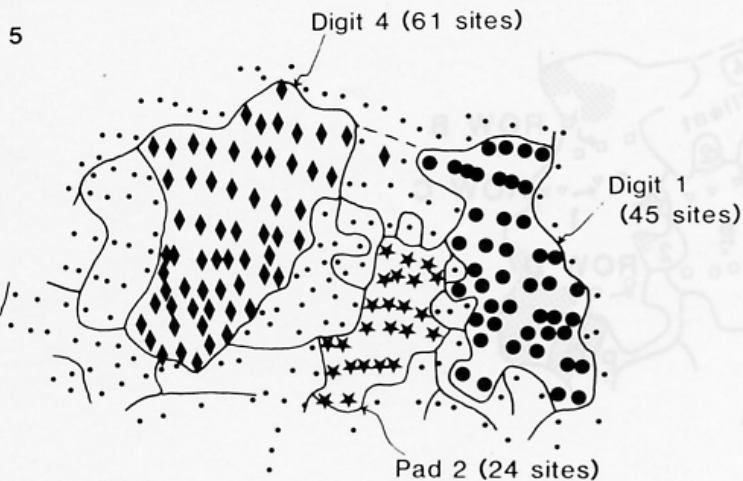
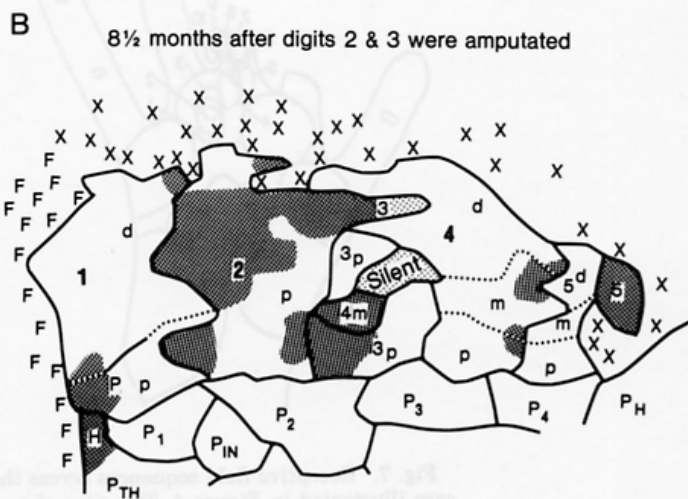
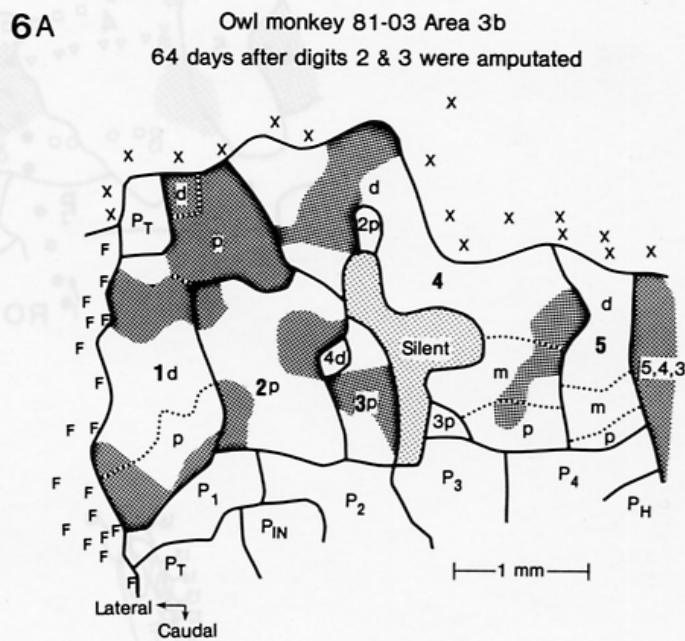


Fig. 5. Penetration grid for the case illustrated in Figure 4. Dots and symbols mark microelectrode penetration sites. Filled diamonds were sites at which neurons had receptive fields centered on digit 4; stars were sites at which the receptive fields of neurons were centered on the second palmar pad; large dots were sites at which the receptive fields of studied neurons were centered on digit 1. Given this grain of definition, the perimeters of these representational zones, their areas, and their internal topographies were highly resolved. Other illustrated maps (that in Fig. 6A is a modest exception) were actually defined with a finer penetration grid than was employed in this representative experiment.

shown for one of these monkeys in Figures 7 and 8. They are representative of the basic internal topography of expanded "occupying" representations recorded in all single and double digit amputation cases. Note that the border of the occupying representations from digits 1 and 4 are biased toward the distal aspect of the digits. At the same time, the representation of the entire radial side of the middle and distal phalanges of digit 4 had almost certainly crossed its original boundary into the former territory of representation of digit 3 (see below). Also note the relatively small sizes of receptive fields in these surrounding zones, especially over the stump, adjacent palm, and digit 4 (Fig. 7B). In general, as territories of representation expanded, magnification of representation increased (Fig. 9A), and receptive field sizes declined roughly inversely (Fig. 9B). That is, as representations expanded, the skin surfaces came to be represented in progressively finer grain.

Finally, note that there was an apparently orderly representation of the expanded stump representation in this case. This was the case in all reported monkeys, although receptive field locations were sometimes more difficult to define on the stump, probably in part because of the abnormal mechanics of its skin. The presence of a topographic order in the stump representation indicates that (1) direct stimulation of stump neuromas with the light tactile stimuli used for mapping was not a factor in the derivation of these maps; and (2) the nerve stump sutures have apparently successfully prevented neural regeneration of new fibers back into the stump skin.

As in single-digit amputation cases, the sizes of the digit 5 representations were little different from those recorded in a normal series of five adult owl monkeys. Comparisons with normal monkeys for one- and two-digit amputation cases are summarized graphically in Figure 10. Over this time course (approximately 2 months postamputation), territorial changes were principally if not entirely within the areas of representation of immediately adjacent digital and palmar surfaces.



C REPRESENTATIONAL AREAS OF DIGITAL SURFACES (mm²)

	D ₁	D ₂	D ₃	D ₄	D ₅	Silent
64 days after amputation	1.73	1.51	0.39	2.06	0.63	0.77
8 1/2 months after amputation	1.48	1.70	0.70	1.63	0.41	0.12
8 1/2 months/64 days	0.86	1.13	1.79	0.79	0.65	0.16

Fig. 6. A. Representation of the hand surfaces defined in a 248-penetration map into and across the borders of areas 3b, derived 64 days after digits 2 and 3 were amputated. B. Map of the representation of the hand surfaces in area 3b, derived in a 303-penetration map obtained 8 1/2 months after digit amputation. C. Absolute areas of representation of digital surfaces and of the "silent" zones defined in these two maps in this adult owl monkey.

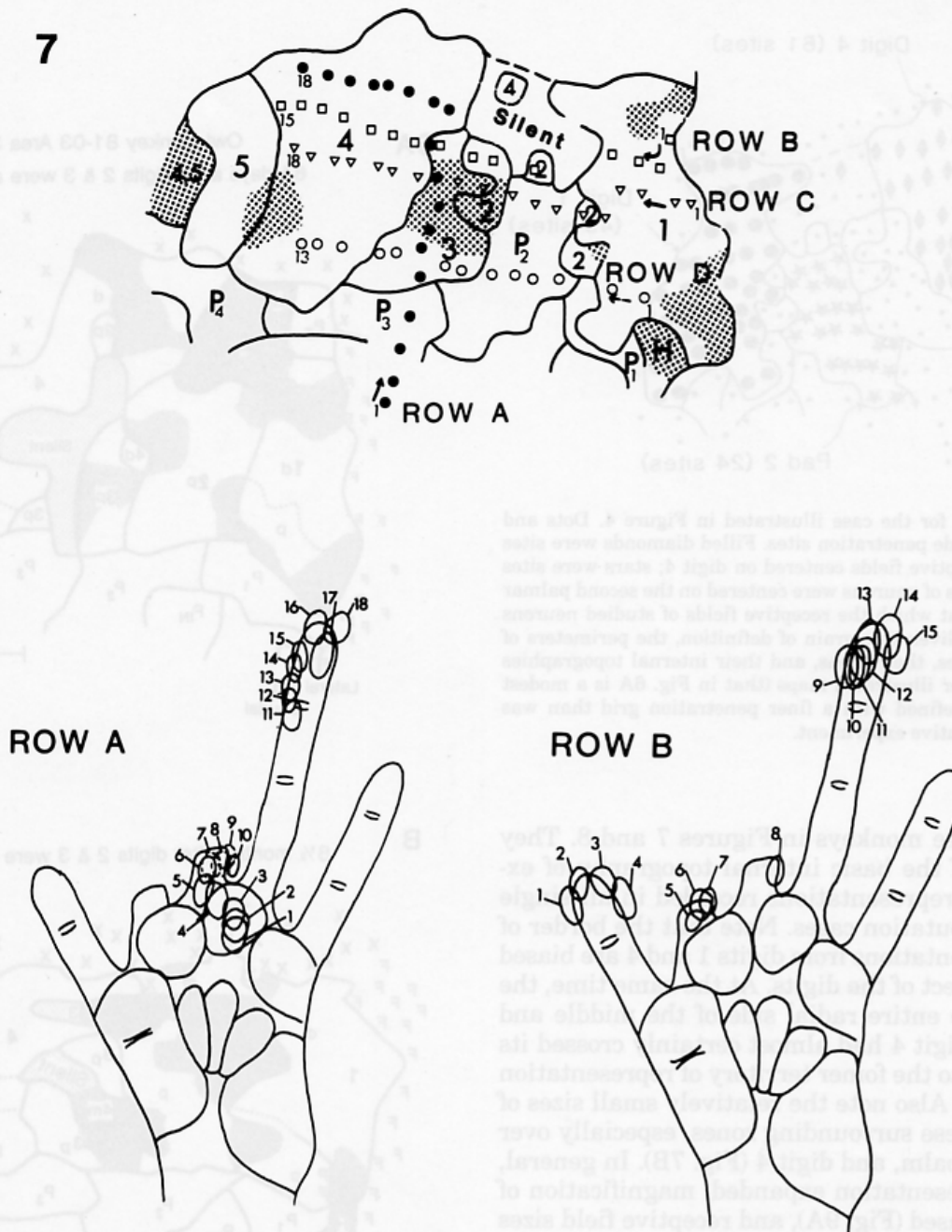


Fig. 7. Receptive field sequences across the reorganized cortical zone for the two-digit amputation case illustrated in Figure 4. The sites of penetrations for which receptive fields are drawn for four rows crossing the reorganized cortical zone are shown in the drawing at the top. Receptive field sequences A and B are shown at the bottom.

Organizational changes recorded in a later remapping of a two-digit amputation case

In a single monkey, a map of the representation of the hand was derived 6-1/2 months after generation of the map illustrated in Figure 6A. The principal objective of this double-mapping experiment was to determine whether or not the "silent" zones recorded in these monkeys would be occupied, over time, by further expansion of surrounding inputs. There were many differences in the internal map structure recorded over this 6-1/2-month period. Note, for example, the unequivocal differences in the representation of dorsal digits 2 and 1, with the stump skin coming to dominate the region of cortex that had earlier represented an expanded digit 1. A number of such differences were recorded over this span of time. Some of these changes are illustrated in Figure 11 by outlining the common areas of

representation of individual digits derived in the two maps, along with areas of digital surface representations gained (black) or lost (crosshatched) from adjacent digital representations over this 6-1/2-month period. Note that substantial changes in the contour and location of the digit 5 representation were recorded in this monkey, as well as in the double-mapping study illustrated in Figure 1—even though its representation changed little if at all in area in any case (Fig. 10). It is important to note that this evident locational dynamism in "normal" representations is real. It shall be the subject of a later, detailed report from this laboratory.

While cortical map changes were substantial, *the silent zone was not eliminated during this 6-1/2-month period* (Fig. 11, lower right). In a small, central core 8-1/2 months after the amputation of digits 2 and 3, neurons within six adjacent penetrations were still not activatable by cutaneous stimulation of any hand surfaces.

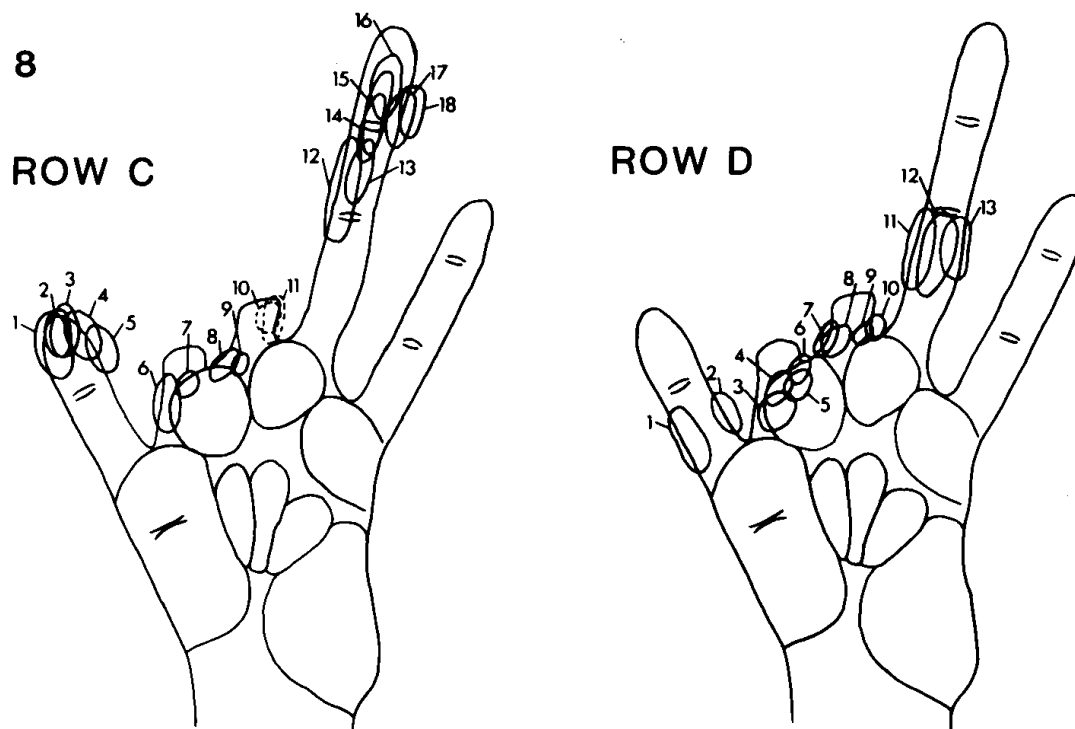


Fig. 8. Receptive field sequences C and D, crossing the reorganized cortical zone, as illustrated at the top of Figure 7.

What skin surfaces lie within and what lie outside the former cortical territories of representation of the amputated digits after reorganization?

Estimations of the expected normal sites of representation of skin surfaces on the hand were derived from normal maps obtained in some monkeys prior to digit amputation and from maps made in a series of normal monkeys. From these data, the locations of representation of different skin surfaces after amputation could be related to their actual or likely sites of representation prior to amputation. In every case, some skin surfaces originally represented outside the deprived zone moved into it, and were ultimately represented *only* in that new cortical sector. Thus, after map reorganization, representations of bordering skin surfaces necessarily involve the deprived cortical zone.

Changes in overt deep-driving inputs within area 3b following digit amputation

In normal maps, inputs from "deep" receptor sources are usually not evident. Of course, one might suppose that deep inputs would to some extent be masked by cutaneous driving. However, inputs from "deep" sources should still be detectable, because unlike cutaneous inputs (1) they usually respond to stimulation of several digits; and (2) they often respond highly characteristically to joint flexion, extension, or rotation. Thus, they should frequently be identifiable even when they are convergent with cutaneous inputs. They are, in fact, only infrequently recorded within area 3b in a normal monkey. On the other hand, they were commonly recorded within the reorganizing cortical zone following digit amputation. As a rule, the farther one proceeded toward the center of the deprived cortex, the more prominent were their contributions, and the weaker the responses to cutaneous stimuli. It should be remembered that all of the maps described herein were drawn from definition of receptive fields with stimulation at levels en-

gaging cutaneous inputs alone; i.e., these deep receptor inputs are not reflected in these maps. They shall be the subject of a later report from this laboratory.

DISCUSSION

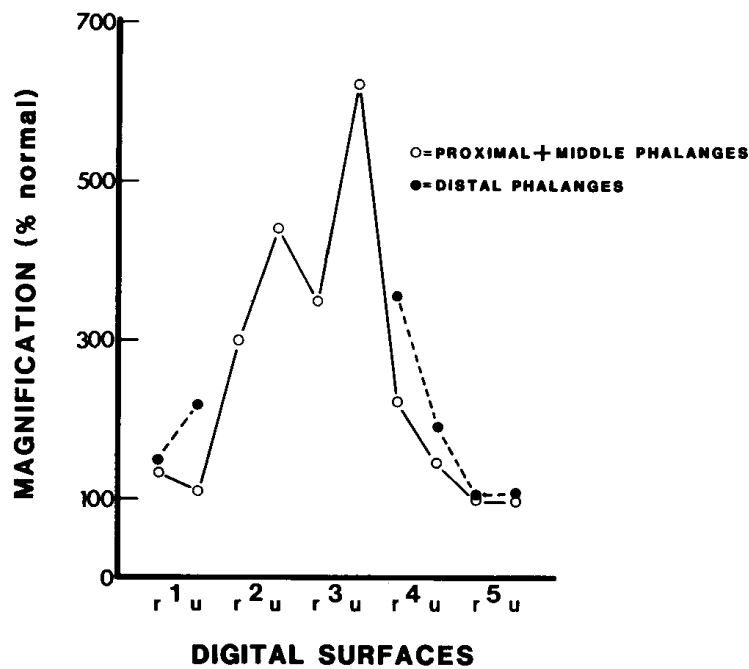
These experiments demonstrate that the somatosensory cortex reoccupies most or all of a small cortical zone deprived of its normal driving inputs by amputation of one or two digits of the hand, within 2 months of digit amputation. Most of the chronically deprived zone in area 3b was occupied by inputs from the adjacent digital and palmar surfaces. The digital input was predominantly (but not exclusively) from the glabrous surfaces of the distal phalanges of neighboring fingers. While the cortical territories of representation of adjacent digits always expanded significantly, those of nonadjacent digits changed little if at all in area.

The occupation of the chronically deprived zone was effected by a *topographic expansion* of the representation of adjacent digits. The enlarged sectors of representation of those digits (and of the "occupying" sectors of palmar pads) were continuous with the representation of the remainder of these surfaces, in always-normal surrounding cortex. Apparent reductions in receptive field sizes were commonly recorded in the reoccupied cortical sector. Such changes were biased toward this zone; i.e., receptive fields on the sides of the digits and palm away from the deprived zone were consistently larger than those in or near it.

In every experiment, one to several small, isolated islands of out-of-place fields were recorded; i.e., there were minor but unequivocal exceptions to the otherwise completely continuous, overlapping representations seen in every experiment.

In reorganization, boundaries of discontinuous representation separating the digits were clearly extended hundreds of microns into the deprived zone, as digital representations expanded.

A. REPRESENTATIONAL MAGNIFICATION



B. RECEPTIVE FIELD AREAS

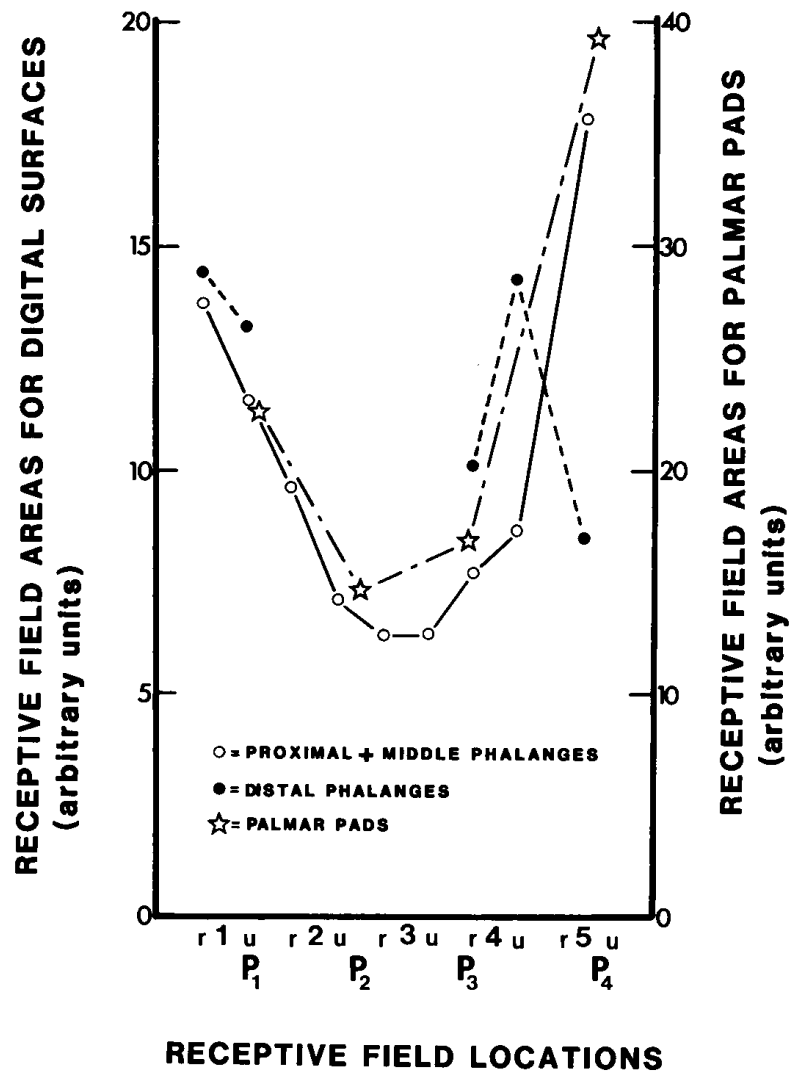


Fig. 9. A. Representational magnification (cortical areas of representation divided by skin surface areas) in area 3b for glabrous skin surfaces of the hand in a monkey mapped 76 days after amputation of digits 2 and 3 (see Fig. 4). Magnification (% normal) was defined for the radial (r) and ulnar (u) halves of the distal phalanges (filled circles) and for the radial and ulnar halves of the proximal and middle phalanges (open circles) of digits 1-5. Normal values were derived from measurements of magnification in a series of nine adult owl monkeys. B. Receptive field areas (arbitrary scale) for neurons in penetrations in which fields were on the glabrous surfaces of the digits (1-5) and the digital palmar pads (P1-4). Receptive field areas were determined for fields centered on the radial (r) and ulnar (u) halves of the distal phalanges (filled circles) and proximal and middle phalanges (open circles) of digits, and for the palmar pads (stars). Charted values are means of 5 to 18 measured fields. Note that the roughly inverse relationship between changes in magnification (A) and in receptive field area (B) indicates a dynamic maintenance of percentage overlap vs. distance as receptive field size is altered (see Merzenich et al., '83b; Sur et al., '80). Note also that the minimum receptive field areas were recorded in the center of the reorganized zone. In this region, mean receptive field areas were roughly one-third to one-sixth their normal size. We have no simple explanation for the unexpectedly small receptive fields on the tip (but not on the rest) of digit 5.

The representation of the skin of the digit stumps commonly expanded significantly (sometimes greatly). In the extreme, it was found to enlarge to approximately the size of representation of the original entire digit. This constitutes a territorial expansion of $\times 10-15$. Some of the observed differences in the expansion of representation of these skin surfaces may reflect differences in the levels at which the digital cutaneous nerves were cut and tied in the stump.

Finally, zones of cutaneously unresponsive cortex were recorded in most amputation cases. In one monkey mapped both 2 and 8-1/2 months after surgical amputation of digits 2 and 3, a small cutaneously nonresponsive zone was recorded in the same region. It was somewhat smaller in the second map than in the first; but a "silent" sector recorded 2 months after amputation was still not eliminated even after a further relatively long (6-1/2-month) survival period.

These results appear to differ from those of recent studies of the consequences of digital amputation in raccoons (see

Rasmusson, '82; Kelahan et al., '82; Carson et al., '82). In the raccoon, the even larger cortical area of representation of an amputated digit was progressively reoccupied by inputs from the adjacent digit(s). However, these "new" representations were described as developing as adjuncts to normal representations of bordering digits. Thus, these "new" representations in the raccoon were described as being nontopographic or only very crudely topographic. These representations were interpreted as duplicating intact, normal representations of occupying digits. In monkeys, by contrast, adjacent digital surfaces expanded topographically *and without duplication*, as they "occupied" amputation-deprived cortical zones. This difference is critical: (1) for consideration of the mechanisms underlying cortical or system reorganization; (2) for consideration of its implications for the establishment and dynamic maintenance of normal map structure; and (3) for its implications for the genesis of perception from topographically organized representational systems.

Reasons underlying these species differences are not completely clear. Maps in these studies in monkeys were derived in much finer grain than in studies in raccoons. However, because the territories of representation of the always-innervated digits in raccoons are very large, it is

3b Representational Areas of Digits (% Change from Normal)

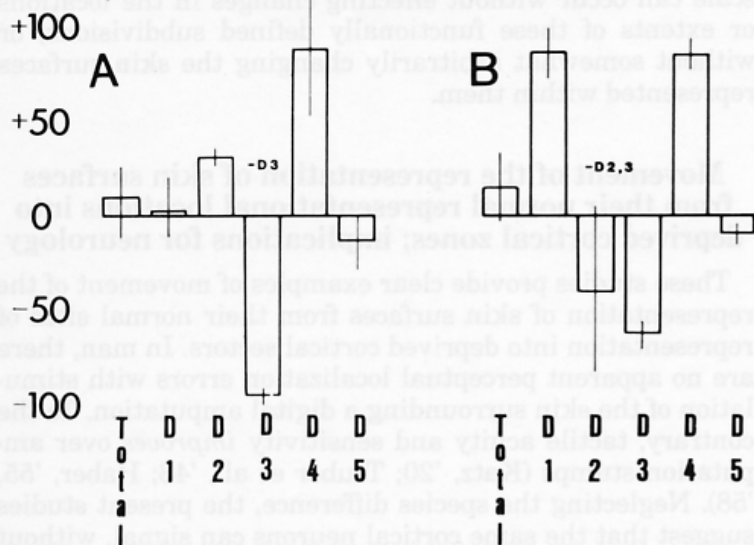


Fig. 10. Graphic illustration of differences in areas of representation of different digits (D1–D5) in these amputation cases as compared with normal adult owl monkeys. These four cases are those illustrated in Figures 1, 3–5. Note that most areal changes over these relatively short postamputation times (2–2 1/2 months) involve adjacent digits. A. Results from amputation of digit 3. B. Results from amputation of both digits 2 and 3.

difficult to see how described reorganizational features in raccoons might be misinterpreted. We have defined receptive fields in this study using stimulation criteria that insures exclusive stimulation of cutaneous afferents. That is not the case in studies in raccoons. Moreover, in contradistinction to raccoon experiments (see Rasmusson, '82), we tied cutaneous proximal nerve stumps to prevent their peripheral regeneration into the amputation stump. Perhaps these methodological differences contribute to some of the apparent differences in described results derived in these two species. It might be noted that there is anatomical evidence in the highly specialized somatosensory system of the raccoon for only relatively limited convergence of lemniscal inputs from different digits in the projections from skin to cortex. Postulated models of the processes underlying map reorganization in monkeys would *require* convergent-divergent projections from lemniscal-source afferents across at least the zones of representation of adjacent digits (see Merzenich et al., '83b). Thus, it is possible that fundamentally different mechanisms underlie the cortical map reorganizations recorded in the hand representations of raccoons and monkeys.

The reorganization occurs over a limited distance

Two kinds of evidence strongly indicate that cortical reorganization after peripheral deafferentation reaches a spatial limit. First, changes in magnification and receptive field size were largely if not entirely restricted to the adjacent digits and palmar pads. Thus, for example, with a digit 3 amputation, the sizes of digit 1 and digit 5 representations changed little (there *were* some significant shifts in their defined locations) while the sizes and locations of the adjacent digits 2 and 4 changed dramatically. Moreover, while small receptive fields were found on the expanded facing surfaces of the adjacent digits, receptive fields on the sides of the representations of these digits farthest removed

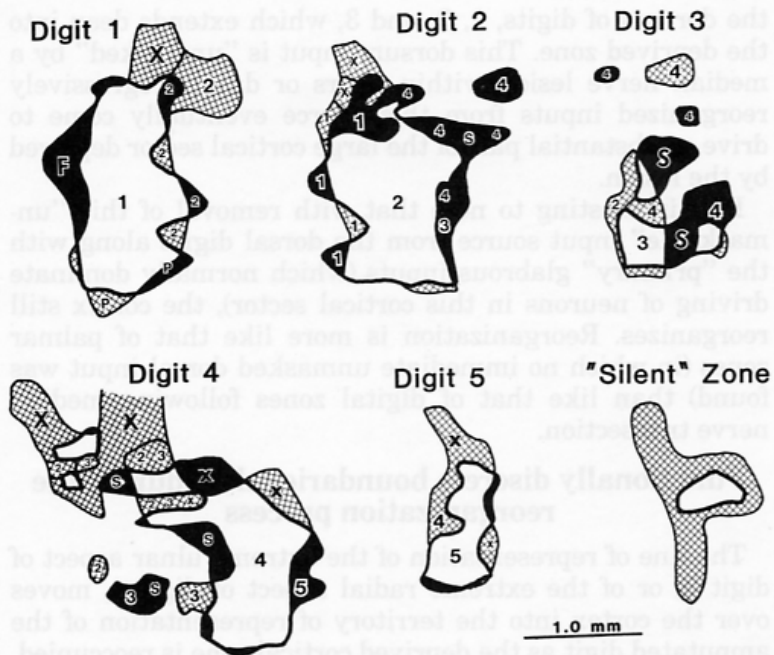


Fig. 11. Differences in the territories of representation of the surfaces of digits 1–5 and the "silent" zone, recorded in a monkey mapped 64 and 255 days after digits 2 and 3 were amputated (see Fig. 6). The two maps were positioned with respect to each other by reference to the cortical surface vessel pattern. The outlined white zones are the common territories of representation of the designated digit, recorded in both maps. Black zones are areas representing that digit in the second map that were driven from different labelled skin surfaces in the first map. Crosshatched zones are areas that were driven from the designated digital surfaces in the first, but not the second map. The skin surfaces from which they were driven in the second map are indicated by the labels in those zones. Abbreviations as in Figure 3.

from the deprived zone were always larger, and on the next removed digit usually approached the normal size. In a single monkey, a two-stage postamputation mapping study revealed that the area of representation of digit 5 was not significantly different at 8-1/2 as compared with 2 months following amputation. These regionally different changes in topographic representation suggest, then, that adjustments in magnification in response to amputation are occurring over a cortical zone with a radius of no more than 500–700 μm .

A spatial limit for reorganization is also indicated by the appearance of a persistent, cutaneously nonresponsive zone within the former territories of representation of the amputated digits. Perhaps more compellingly, the core area of one such zone in a map derived 2 months after digit amputation was still present in a map derived 6-1/2 months later. These studies again suggest that the reoccupation process rapidly approaches a physical limiting distance of some hundreds of microns, beyond which further movement does not occur. It is also possible that deep or other nontactile receptor inputs compete for and then retain a portion of the denervated cortical territory.

It might be noted that the amputation of one or two digits was more severe than the transection of the median nerve. The latter lesion actually deprives a larger cortical territory of representation of its normal effective driving inputs. "Silent" zones were never recorded later than about 4 weeks after median nerve transection (Merzenich et al., '83b). This difference is presumably due to the fact that with a median nerve lesion, large sectors of areas 3b and 1 normally representing the nerve apparently receive a covert input from

the dorsum of digits, 1, 2, and 3, which extends deep into the deprived zone. This dorsum input is "unmasked" by a median nerve lesion within hours or days; progressively reorganized inputs from this source eventually come to drive a substantial part of the large cortical sector deprived by the lesion.

It is interesting to note that with removal of this "unmaskable" input source from the dorsal digits along with the "primary" glabrous inputs (which normally dominate driving of neurons in this cortical sector), the cortex still reorganizes. Reorganization is more like that of palmar zones (in which no immediate unmasked dorsal input was found) than like that of digital zones following median nerve transection.

Functionally discrete boundaries shift during the reorganization process

The line of representation of the extreme ulnar aspect of digit 2, or of the extreme radial aspect of digit 4, moves over the cortex into the territory of representation of the amputated digit as the deprived cortical zone is reoccupied. That is, this functionally distinct representational boundary (a line of representational discontinuity) *moves*. This strongly suggests (as do shifts in dorsal-glabrous boundaries recorded in earlier time-sequence studies conducted in median nerve-section monkeys; see Merzenich et al., '83b) that such representational discontinuities are normally dynamically maintained. They are unlikely to be mere reflections of absolute anatomical discontinuity in the ascending projection system.

In earlier studies, such discontinuities were actually seen to form, as glabrous and hairy representations expanded and moved to occupy the cortical zone "deprived" by chronic median nerve transection (Merzenich et al., '83b). That is, such discontinuities appeared as sharp functional borders within the cortex where representations of the dorsum of the fingers or radial hand approached those of the discontinuously represented expanded glabrous ulnar palm. Neurons across a very sharp line across the cortex responded to stimulation of one or the other but not both of the skin surfaces across these newly created "lines." Similarly, in the present experiments, new discontinuous representational boundaries were established where inputs from non-adjacent digits flanking the amputated digit(s) came into juxtaposition. There, again, newly established borders were sharp, and did not significantly overlap. These observations support the contention (Merzenich et al., '83b) that in zones with competing inputs across lines of map discontinuities, there is a "switching" mechanism by which such cortical map discontinuities are dynamically maintained (Merzenich et al., '83b).

Several investigators, beginning with Mountcastle, have described restricted regions within primary somatosensory cortex within which there are inputs from slowly adapting primary afferents (Mountcastle, '57; Paul et al., '72; Sur, '79; Sur et al., '81; Dykes and Gabor, '81). Mountcastle recognized from the first that dynamic mechanisms are probably involved in sharpening the boundaries of modality or submodality columns recorded in primary somatosensory (SI) cortex (Mountcastle, '57, '79). These current studies indicate that the cortical locations of the boundaries of these columns might also be positionally dynamic. Sur ('79) and Sur and colleagues ('81) have provided carefully derived maps of slowly adapting input zones in area 3b in monkeys. Given the narrow striplike distribution of slowly

adapting input bands in the region of representation of the fingers, it is difficult to see how expansions on the recorded scale can occur without effecting changes in the locations or extents of these functionally defined subdivisions, or without somewhat arbitrarily changing the skin surfaces represented within them.

Movement of the representation of skin surfaces from their normal representational locations into deprived cortical zones; implications for neurology

These studies provide clear examples of movement of the representation of skin surfaces from their normal sites of representation into deprived cortical sectors. In man, there are no apparent perceptual localization errors with stimulation of the skin surrounding a digital amputation. To the contrary, tactile acuity and sensitivity *improves* over amputation stumps (Katz, '20; Teuber et al., '48; Haber, '55, '58). Neglecting the species difference, the present studies suggest that the same cortical neurons can signal, without localization errors, locations of inputs from different skin surfaces at different times. The "cortical map" cannot be regarded, then, as the substrate of a fixed-address "perceptual map" (Merzenich et al., '83a).

Phantoms of amputated digits are sometimes reported in man. What might they correspond to in this reorganizing system? One possibility is that the generation of phantoms does not involve the area 3b representation. To the extent that area 3b is involved in phantoms, they must arise from a largely or completely reoccupied cortical zone. Moreover, that zone formerly representing the now-phantom digit is *required* for the complete representation of newly expanded representations of adjacent hand surfaces. If this cortical zone contributes to the phantom, then, it can do so only if the perception of *both* the phantom and the adjacent expanded digits is generated across the same central somatosensory machinery.

Consistent with that possibility, stimulation of cut nerves in an amputated limb or manipulation of neuromas of cut nerves results in a perceptual regeneration of the skin field of the nerve (see Cronholm, '51). Following nerve transection, the ultimate cortical target zones of cut cutaneous nerves change little (Merzenich et al., '83a). Thus, the perception of the skin surfaces of the now-amputated digit evoked by stimulation of the proximal nerve stump, like the perception of a phantom (actually probably consequent from spontaneous activity from these cut nerves; see Nystrom and Hagbarth, '81), must involve cortex that is also necessarily involved in the representation of surrounding skin surfaces.

Surprisingly, there have been no evaluations of spatial acuity of skin surfaces around amputated digits, but sensory abilities over amputation stumps of arms and legs have been studied (Katz, '20; Teuber, et al, '48, '49; Haber, '55, '58). There are interesting parallels between the changes in sensation recorded in amputees and the map changes seen in these experimental monkeys. After amputation in man, there is a highly significant increase in tactile spatial acuity on the stump, and significant improvements in acuity extend well away from the end of the stump. However, the zone of increased sensibility has a spatial limit. With an amputation above the elbow, for example, two-point discrimination was found to be normal at the shoulder, but was significantly better than normal over most of the upper arm. Discrimination rapidly im-

proved from the normal, proceeding distalward on the stump (Teuber et al., '49; Haber, '55, '57).

Consider the parallels of these findings with the results of the present experiments. As surrounding skin surfaces expanded to occupy a deprived cortical zone, receptive fields were reduced in size correspondingly, and there was a distance limit for this territorial expansion. We have earlier hypothesized that the finer grain of the representation of surrounding skin surfaces that results from territorial expansion might result in corresponding changes in tactile acuity, and that such territorial and receptive field changes might underly normal use-dependent changes in tactile acuity and skill. These parallel psychophysical and physiological observations in amputees support that hypothesis.

It is interesting to note that the greater the "telescoping" of a phantom limb, the greater the improvements in acuity on the stump (Haber, '58). In "telescoping," the position of the end of the amputee's stump progressively approaches the position of the phantom hand, so that the hand (or foot) is perceived as on a progressively shorter arm (or leg) (Henderson and Smyth, '48). Teuber and colleagues hypothesized that telescoping might be a consequence of expansion of representation of the arm (or leg) stump into territory of representation of the amputated sector of the limb. The farther the expansion progresses in the map the more greatly the stump is enlarged in representation, and hence, the greater the increase in tactile spatial acuity. Another interesting possibility suggested by these parallel observations is the possible relationship of the perceived distances between the stump and the phantom with a cortical map distance (not necessarily in area 3b) separating their representation.

The correspondence between these experimental and clinical observations bears on two deep issues. First, they suggest that tactile spatial acuity may be a product of the "grain" of representation in central projection system maps. Further, they suggest that the grain of representation is altered by relative differences in tactile inputs in adult monkeys and humans. As noted earlier, cutting and tying peripheral cutaneous nerves, as in this amputation model, does not lead to significant loss of connections in the higher levels of this projection system (see Carmel and Stein, '69; Knyihar and Csillik, '76). These amputation studies are believed, then, to constitute a model of severe sensory deprivation, differing only in magnitude from use-dependent alterations occurring in day-to-day life.

The plasticity of somatosensory cortical fields also has implications for the image-generation and recognition functions of cortical representations. The overt-response map may be thought to reflect the consequences of the lifelong operations of this element of an image-recognizing system. Such a machine could be rigidly wired anatomically (studies must be conducted to decide this crucial issue), but in terms of the *details* of the representation of the skin surface, *it could be flexibly, not rigidly, addressed*. In this respect, it especially closely fulfills the requirements of a "group selection" model for recognition processes (see Edelman, '82).

Implications for mechanisms underlying map reorganization

As discussed in earlier reports (Merrill and Wall, '78; Merzenich et al., '83b; also see Wall and Devor, '78) there are two basic classes of mechanisms that might account for observed reorganizational changes following restricted

deafferentations. A normally defined receptive field might arise from a restricted part of a wider convergent projection zone, as a product of a projection system "filter" which has the capacity to shape or select inputs from different locations across this wider input array (i.e., to change receptive field location) and the capacity to alter the dimensions of the effective activation zone (i.e., to change receptive field size). Alternatively, the map at any one time might be directly anatomically determined; in that case, changes in central maps would result from the movement of terminal arbors. In fact, a dominant conclusion of developmental studies is that terminal arbors and the processes of neurons are largely fixed after a critical period of plasticity in early life, and movements of terminals on this distance scale have not been recorded in any sensory system in adults.

For a filter model, the adjustment of system "filters" (or the "selection" of effective driving inputs from a large anatomically delivered repertoire; see Edelman and Finkel, '84) presumably involves alterations in synaptic effectiveness. A driving force (perhaps relative activity) must be present to account for the *movement* of the representation into the deprived zone. The strict maintenance of topographic rules implies the enforcement of a rule restricting active zone overlap during the reorganization process. That is, those selected inputs that drive neurons at any cortical location are maintained in a relatively constant overlapping relationship to neighboring, selected inputs. It has been suggested that simultaneity or sequencing of activity might constitute the force(s) that maintains receptive field overlap relationships and thereby maps continuity through the process of reorganization (Merzenich et al., '83b; also see Hebb, '49; Willshaw and von der Malsburg, '76).

In such a system, reorganization might be expected to reach a limit dictated by the limits of convergence to the cortical sites within the deprived zone. These studies indicate that changes are relatively local, and that a limit in the occupation of deprived zones *is* reached. We interpret them, then, to support a wide-convergence and "receptive field filter" or "input selection" model of system organization (see Merzenich et al., 1983b; Edelman and Finkel, 1984).

This class of model is consistent with anatomical evidence of convergent and divergent projections from level to level in the somatosensory system (Scheibel and Scheibel, '70; Ramón y Cajal, '11). Thus, for example, considering the cortical level alone, terminal arbors in the SI cortex of the owl monkey spread 150–450 μm across the horizontal dimension of area 3b (Pons et al., '81). Imprecision in the correspondences of the peripheral sources of different axons convergent to given cortical sites, and terminal divergence and convergence at the levels of the dorsal column nuclei and ventrobasal thalamus increase the effective cortical convergence, almost certainly to an extent sufficient to account for these recorded movements. This model is also supported by features of topography of the reordered maps seen following median nerve section (see Merzenich et al., '83b).

An alternative hypothesis is that map changes are accounted for by terminal movement (see Merrill and Wall, '78; Merzenich et al., '83a,b). In such models, changes in receptive field structure could be accounted for by dynamic alterations in convergence numbers. So little is known about possible "sprouting" or movement of terminals in the central nervous system (see Cotman et al., '82) that such processes cannot be ruled out as underlying the map

changes found in these experiments. Thus, for example, one might simply postulate that terminal movement also faces a physical limit of direct change, to account for reorganization reaching a distance limit in deprived cortical zones. Interestingly, the recorded reorganization is slow enough so that changes in terminal structure for the required cortical distances over the recorded reorganizational times are reasonable (see Doetsch et al., '82; Merzenich et al., '83b). Of course they cannot account for immediate second-source unmasking phenomena, as others (Wall and Egger, '71; Dostrovsky et al., '76; Millar et al., '76; Metzlar and Marks, '79) have noted.

At what level of the projection system are map changes produced?

Changes in cortical maps reflect changes occurring at all levels within the projection system. Immediately unmasked inputs and subsequent changes have been observed at the level of the dorsal column nuclei following nerve transection in the cat (Dostrovsky et al., '76; Millar et al., '76). The following observations suggest, however, that the changes we have described occur at least to a large extent at the cortical level. (1) Reorganization of area 1 and 3b maps is greatly different following median nerve section, despite the fact that both receive collateral inputs from a common thalamic representation (Clark and Powell, '57; Lin et al., '79). (2) Map reorganization also occurs after *cortical* lesions in area 3b (Jenkins et al., '82). Such reorganization is likely to be effected at the cortical and/or thalamic level. (3) There is a more highly divergent-convergent projection from the thalamus to area 3b than at the level of the dorsal column nuclei or ventrobasal thalamus (Scheibel and Scheibel, '70). For a wide convergence "filter" or "input selection" model to account for these changes and for the maintenance of recorded map detail (continuity, overlap rules, etc.) it is probably *necessary* that reorganization occur to at least a large extent at the cortical level. Further studies of the dorsal column and thalamic representations will ultimately be necessary to determine precisely what they contribute to cortically-recorded map reorganization.

Possible anesthetic effects

In recent studies in unanesthetized and ketamine-anesthetized monkeys, it has been contended that anesthesia can have significant effects on receptive field sizes and even locations (Duncan et al., '82). The present data were generated in lightly sodium pentobarbital-anesthetized monkeys. In our own experience, receptive fields (and map structure) defined under these conditions within the middle cortical layers of area 3b in the owl monkey are similar under light sodium pentobarbital or ketamine anesthesia to those defined *at the same sites* in unanesthetized or nitrous oxide-anesthetized animals. Anesthetic effects may be more profound for neurons in the upper and lower layers, but our experimental strategy specifically excluded derivation of receptive fields from those layers in this study. In any event, the present experiments were conducted under constant conditions of anesthesia for both normal and postamputation cortical maps. This issue is addressed in more detail in another report from our laboratories (Stryker et al., '84).

ACKNOWLEDGMENTS

The authors would like to thank Dr. William Jenkins, Brad Fowler, Kate Sullivan, Annette Lowe, and Joseph

Molinari for technical assistance, and Drs. Gerald Edelman and Gerald Loeb for valuable discussions of some of the implications of these findings. This manuscript was completed during a working visit by Dr. Merzenich to the Neuroscience Institute, New York. Research was supported by NIH grant NS-10414 and the Coleman Fund.

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