Plasticity of Primary Somatosensory Cortex Paralleling Sensorimotor Skill Recovery From Stroke in Adult Monkeys

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Xerrri, Christian, Michael M. Merzenich, Bret E. Peterson, and William Jenkins. Plasticity of primary somatosensory cortex paralleling sensorimotor skill recovery from stroke in adult monkeys. J. Neurophysiol. 79: 2119–2148, 1998. Adult owl and squirrel monkeys were trained to master a small-object retrieval sensorimotor skill. Behavioral observations along with positive changes in the cortical area 3b representations of specific skin surfaces implicated specific glabrous finger inputs as important contributors to skill acquisition. The area 3b zones over which behaviorally important surfaces were represented were destroyed by microlesions, which resulted in a degradation of movements that had been developed in the earlier skill acquisition. Monkeys were then retrained at the same behavioral task. They could initially perform it reasonably well using the stereotyped movements that they had learned in prelesion training, although they acted as if key finger surfaces were insensitive. However, monkeys soon initiated alternative strategies for small object retrieval that resulted in a performance drop. Over several- to many-week-long period, monkeys again used the finger tips to object retrieval that had been used successfully before the lesion, and reacquired the sensorimotor skill. Detailed maps of the representations of the hands in SI somatosensory cortical fields 3b, 3a, and 1 were derived after postlesion functional recovery. Control maps were derived in the same hemispheres before lesions, and in opposite hemispheres. Among other findings, these studies revealed the following: 1) There was a postlesion reemergence of the representation of the fingertips engaged in the behavior in novel locations in area 3b in two of five monkeys and a less substantial change in the representation of the hand in the intact parts of area 3b in three of five monkeys. 2) There was a striking emergence of a new representation of the cutaneous fingertips in area 3a in four of five monkeys, predominantly within zones that had formerly been excited only by propriospinal inputs. This new cutaneous fingertips representation disproportionately represented behaviorally crucial fingertips. 3) There was an approximately two times enlargement of the representation of the fingers recorded in cortical area 1 in postlesion monkeys. The specific finger surfaces employed in small-object retrieval were differentially enlarged in representation. 4) Multiple-digit receptive fields were recorded at a majority of emergent, cutaneous area 3a sites in all monkeys and at a substantial number of area 1 sites in three of five postlesion monkeys. Such fields were uncommon in area 1 in control maps. 5) Single receptive fields and the component fields of mulitiple-digit fields in postlesion representations were within normal receptive field size ranges. 6) No significant changes were recorded in the SI hand representations in the opposite (untrained, intact) control hemisphere. These findings are consistent with “substitution” and “vicariation” (adaptive plasticity) models of recovery from brain damage and stroke.

INTRODUCTION

Since the pioneering work by Flourens (1824) and Munk (1881), functional recovery after brain damage has been studied intensively and is now a rapidly expanding field of research. Evidence of a significant causal link between injury-induced neural network reorganization and functional recovery has been lacking in the great majority of the studies dealing with postlesion functional restoration. At the same time, studies of such reorganization represent an important strategy by which we might gain specific insights into the physiological processes that mediate behavioral recovery. The functional plasticity of the primary somatosensory cortex’s topographic representations has been investigated extensively in adult mammals. A number of studies have addressed the issues of how and to what extent somatosensory maps are reorganized after experimental manipulations (digit amputation, nerve crush or transection, surgical sympathectomy, skin translocation, and dorsal rhizotomy) that induce drastic alterations in the effectiveness of peripheral inputs (for reviews, see Kaas 1991; Merzenich and Jenkins 1993; Merzenich et al. 1988; Snow and Wilson 1991). Cortical map reorganization resulting from deafferentation can be achieved potentially at all levels of the somatosensory system by structures that receive, process, and transfer peripheral information. By contrast, little attention has been paid to the mutability of somatosensory representations after cortical injury and specifically how that cortical plasticity might contribute to functional recovery.

Damage to the somatosensory cortex often results in a reduction or loss of voluntary motor control and of somatic stimulus perception. Behavioral studies conducted in adult macaque monkeys have shown that removal of SI somatosensory cortex distal forelimb representations induces severe functional impairment in hand use and produces deficits in the discrimination of tactile stimuli (Cole and Glees 1954; Lamotte and Mounacaste 1979; Semmes and Meskes 1965; Semmes and Porter 1972). Induction of selective lesions in separate cytoarchitectonic regions (areas 1, 2, and 3b) of the primary SI have resulted in area-specific deficits in the learning of tactile discriminations. Ablation of area 1 affects only texture discrimination, whereas damage to area 2 impaired only size or shape recognition. Lesions of area 3b severely disturbed all types of tactile discrimination capabilities except the gross discrimination of size (Carlson 1981; Randolph and Semmes 1974). These behavioral studies suggest that areas 3b, 1, and 2 are hierarchically ordered networks and that area 3b fulfills a more integrative function than do other SI subdivisions. Complex tactile functions presumably require the concerted activity of specialized somatosensory projection areas in both SI and SII (Glassman 1994; Murray and Mishkin 1984).
Recovery of sensation and of manipulative function develops progressively after restricted SI lesions (Cole and Glees 1954; Glassman 1971). The neurobiological mechanisms underlying functional recovery from cortical lesions still are understood poorly. Two general hypotheses have been proposed to account for this restoration. The first deals with the assumed stability of structure-function relationships in the mammalian brain. On the basis of measurements of somatosensory evoked potentials, Glassman (1971) concluded that ‘‘the tissue immediately surrounding the destroyed region suffered temporary loss of function and regained its original excitability during the course of recovery’’ (p. 25). The author explicitly referred to a theory proposed in 1914 by von Monakow, who stated that a cortical lesion causes temporary suspension (diaschisis) of the normal functioning of healthy cortical structures (or subcortical structures physiologically connected to the damaged region). Accordingly, functional restoration is seen as a result of the alleviation of diaschisis.

A competing hypothesis, in accordance with the vicariance theory first stated by Munk in 1881, postulates that after larger cortical lesions, adaptive reorganization takes place in other regions of the same area or in other cortical areas that may not have been originally involved in the function more directly mediated by the injured zone. In the somatosensory domain, Sasaki and Gamba (1984) reported that the motor function of SI became predominant and compensated for dysfunction of the motor cortex in a monkey after contralateral cerebellar hemispherectomy. In the adult cat, Silakov and Dybowskii (1983) showed that most SI neurons acquired bilateral receptive fields several months after the transection of the opposite hemisphere’s cortical projections.

With somatosensory-evoked potentials, Cole and Glees (1954) invoked mechanisms suggesting that the functional role of the damaged cortical area was maintained by the still intact regions of the postcentral gyrus. More recently, using intracortical microelectrode mapping techniques before and after focal ischemic lesions in area 3b in owl monkeys, Jenkins and Merzenich (1987) demonstrated the emergence of a new representation of the skin surfaces of the hand that formerly had been represented only within the zone of the lesion. This newly emergent representation was evidenced several months after lesion induction apparently within still intact regions of area 3b adjoining the infarct. As the digit map then was represented within a smaller-than-normal cortical sector, its topography was reorganized extensively, and most neurons had exceptionally large receptive fields. Similar results were reported in the raccoon by Doetsch and colleagues (1990).

An extensive series of experiments have shown that cortical fields 3b, 1, and 3a of the SI of normal adult monkeys undergo behaviorally driven remodeling of the hand representation (see Merzenich et al. 1990). These tightly interconnected areas constitute a functional mosaic of interdependent representational zones that plausibly can be subjected to significant reorganization after restricted lesions of area 3b. The corollary assumption is that such representational plasticity within this distributed network potentially can mediate behavioral substitution or restitution after focal cortical lesion.

As a starting point in the investigation of the possible neural substrates of functional recovery after cortical lesions, we designed experiments to search for the possible long-term effects of cortical infarcts restricted to the cutaneous area 3b map of the hand. Injury-induced functional deficits were assessed in owl monkeys and squirrel monkeys previously trained on a digital dexterity task shown to induce specific representational changes within area 3b (C. Xerri, M. M. Merzenich, W. M. Jenkins, and S. Santucci, unpublished results). Cortical infarcts totally destroyed the representations of skin surfaces that were used by the monkeys to guide finger movements in the behavior. Monkeys then were retrained at the same digital dexterity task with functional recovery behaviorally assessed through a postoperative period varying from 2 to 4 mo. Monkeys progressively reacquired high performance abilities with retraining. We then searched for representational changes in SI in the lesioned and opposite intact hemisphere that might account for the recovery of the precise, sensory-guided digital movements recorded in postlesion trained monkeys.

Preliminary findings were earlier reported in abstract form (Xerri et al. 1994a).

METHODS

Behavioral training

Experiments were conducted in three owl monkeys (Aotus nancymai) and in two squirrel monkeys (Saimiri sciureus). All were judged by their histories and their dentition to be young adults. The monkeys were initially trained to retrieve 3.6-mm-diam banana-flavored pellets from a modified Klüver board. This device consisted of a rectangular acrylic plastic (Plexiglas) board containing five food wells of different sizes. It was modified to match the finger dimensions of these small primates. The wells gradually varied in diameter (9, 11, 13, 19, and 25 mm for owl monkeys; 8.5, 9.5, 13, 19, and 25 mm for squirrel monkeys) and depth (6, 7, 9, 15, and 20 mm for owl monkeys; 7, 8, 9, 11, and 13 mm for squirrel monkeys). The Klüver board was attached to the front of the monkey’s home cage. The animal had to reach down through an opening in the front of the cage to recover the pellets. Monkeys were permitted to use either hand to perform this retrieval task.

Each experimental session consisted of 100 trials (20 trials per well in random order) after monkeys were food deprived for 24 h. They were fed ad libitum at the end of each session. The Klüver board was reversed every five or six sessions to assure that the animal’s performance was not dependent on the board orientation. Each trial was recorded on videotape for subsequent analysis. Movement strategies and sequences were reconstructed from frame-by-frame analyses of videotapes recorded throughout all training sessions. For every trial, the number of attempts per successful retrieval, the specific digit surfaces employed by the monkey in retrieval attempts, the failure modes of the monkey, and other specific aspects of the retrieval movement were documented. The training procedure included three sessions per week over a total of 23–42 practice sessions. After practicing for a number of sessions on this limited schedule, as is described in RESULTS, monkeys successfully retrieved food pellets with most attempts from all wells.

At this point in the experiment, detailed maps of the representations of the hand surfaces in cortical areas 3b, 3a, and 1 were derived using sterile surgical procedures in the hemisphere contralateral to the trained hand. After this procedure, a small lesion was induced to selectively and utterly destroy the cortical area 3b representation of hand surfaces that were adjudged to be important for guiding fine movements in the behavior.
Within 3–14 days after lesion induction, monkeys were returned to the training apparatus to assess their small object retrieval capabilities and to reinitiate their retraining at the task. Monkeys again were trained until they could reliably retrieve food pellets with almost all attempts from all wells. That was achieved over a period of ~9–18 wk of postlesion training.

At that point, again, highly detailed terminal electrophysiological response “maps” of somatosensory cortical fields 3b, 3a, and 1 were derived to define possible alternative cortical sources of cutaneous inputs for key hand surfaces in the now-recovered, sensory-guided movement behavior.

**Electrophysiological mapping procedures**

To define the representational status of the somatosensory cortex in trained prelesion and postlesion monkeys, cortical areas 3b, 1, and sometimes 3a were mapped with high sampling densities with methods described in earlier reports. Briefly, monkeys were preanesthetized with 2% halothane in a nitrous oxide:oxygen (75%:25%) mixture and a venous cannulae introduced into the femoral vein. Animals then were weaned from the halothane-nitrous mixture and administered an anesthetic dose of pentobarbital sodium (15–30 mg/kg) to maintain and stabilize a deep, areflexic level of anesthesia. Monkeys were subsequently maintained at an areflexic level by supplemental intravenous administration of dilute pentobarbital. The monkey’s temperature was recorded and maintained at 37.5°C. Heart rate, respiration rate and depth, and skin turgidity were monitored. Lactated Ringer solution was infused continuously at a variable rate (averaging ~6 ml/h) to maintain body hydration.

A wide craniotomy of the anterolateral parietal bone exposed the hand zone of SI cortex. The dura mater was removed by surgical dissection and the cortex bathed in a thin layer of viscous (15 k centistoke) silicon oil. A highly magnified video image of the cortical surface was captured on a Macintosh computer using NIH Image software and a high-resolution Cohn CCD camera. Before surgery was initiated, magnified video images of both surfaces of the hand had been recorded using the same procedure.

With the brain surface vasculature used for locational reference, parallel microelectrode penetrations were introduced into the hand zones of the SI cortical fields on a grid of 30–60 samples/mm². Sampling microelectrode penetration sites were marked with regard to brain surface locations using a data acquisition program designed specifically for conducting these experiments and for managing subsequent data analyses (MAP) (Peterson and Merzenich 1995). Parylene-insulated tungsten microelectrodes (Microprobe) with impedances of 1–1.5 MΩ (1 kHz) were used for unit response recording. All penetrations were parallel to one another. As a rule, multiple unit neuronal response samples in which clearly distinguishable units were evident as a rule were derived 700–800 μm deep to the cortical surface, which in these species corresponds with deep layer 3.

All procedures were conducted under strictly sterile conditions. In the recovery surgery, the dura was closed with 7-O suture, and the skull flap closed using stainless steel sutures. Procedures were limited to an ~14-h-long experimental period. Monkeys recovered from the surgery uneventfully. In the final, terminal procedure, use of sterile procedures ensured cortical integrity throughout the period of a several-day-long mapping procedure. Monkeys were maintained anesthetized at areflexic surgical levels throughout these long procedures.

At the end of each experiment, the monkeys were killed with a lethal dose of pentobarbital sodium and perfused transcardially with 0.9% saline followed by 4% paraformaldehyde in 0.1 M phosphate-buffered saline. The brain then was removed from the skull and placed in 30% sucrose in formalin. The lesioned hemisphere was frozen and cut in 50-μm-thick parasagittal sections. Gelatin-embedded sections were stained for Nissl bodies with cresyl violet.

Four investigators participated in defining cutaneous receptive fields of sampled neurons in the derivation of both prelesion and postlesion; only one of them had knowledge of the monkey’s pellet-retrieval performance history or behavioral progression. Receptive fields were defined by exploring the skin surface of the monkey at each sample site using just-visible skin indentation or hair deflection effected with fine opaque glass probes and thereby determining the skin area over which multiple-unit neuronal clusters recorded in each penetration were reliably excited. These “minimum receptive fields” were drawn using a mouse cursor onto the stored computer images of the hand surfaces that were recorded for each monkey.

Representational maps were elaborated by drawing boundaries enclosing cortical sites at which receptive fields were centered on the same skin region (Canvas software; Deneba). When receptive fields overlapped the boundaries of different skin surfaces, the cortical representational boundary was drawn to reflect the proportional skin surface representations reflected by these boundary fields. Given the sampling densities employed in these experiments, there were usually several to many sampling penetrations introduced into the zones of representations of even small hand surface regions, e.g., representing individual digit phalanges. Thus, for each such area there were usually multiple estimates of the locations of the border positions bounding these representational zones, and estimates of their representational territories are therefore accurate (see Stryker et al. 1987). For example, with the definition of cortical areas from a patch of cortex including 10 samples representing a given skin surface like a fingertips, errors for estimating representational territory would be <10%. No area described in the following text as an emergent or novel representational zone, no matter how small it appears to be in cartoon reconstructions, had fewer than two sampling penetrations within it in which clear and/or strong neuronal responses were recorded. All of the important conclusions of this study were drawn from sampling that provided an appropriate measurement precision for directly compared areal categories that are here determined to be statistically significant.

The significances of differences between experimental and control data were analyzed using analysis of variance (ANOVA) and Fisher PLSD tests. Control groups included data from cortical maps derived before lesion induction, data from cortical maps of the contralateral, untrained hand, and, to a more limited extent, data from maps of corresponding surfaces on the hands of “normal” adult owl monkeys (from Merzenich et al. 1987).

**Induction of cortical microlesions**

The finger surfaces with representations targeted for these lesions initially were defined by videotape analysis of these monkeys’ performances at the trained small-object retrieval task. The territories of the representation of these surfaces were defined in fine grad in the immediately prelesion cortical mapping experiment. Once the representational zone for skin surfaces used to guide movements in the behavior were outlined in area 3b, that zone was destroyed in entirety by the electrocoagulation of surface vessels using bipolar cautery (Cordman) with sharpened microforceps operated under a fine saline drip. Cauterization was applied until visible cortical devascularization (profound blanching) was recorded. Lesions were conservatively induced to extend not more than 200–300 μm across defined representational limits and to extend at least that far across the rostral area 3b border into cortical area 3a. The lesion boundaries were checked at a number of boundary positions and deep within the lesion immediately after induction to confirm that the cortex was profoundly unresponsive across all layers within the lesion and functionally intact within the perileision surround. Cortical infarct boundaries were drawn midway
with the area of unresponsive cortex defined in detail at the time of chronic recording provides a reasonable estimate of the area of the cortical zone that was utterly destroyed or profoundly inactivated chronically by these vascular lesions. For the two owl monkey cases illustrated in detail in this report (OM 2149 and OM 2258), the estimated lesion sizes at the time of induction was 6.4 and 6.9 mm², respectively. The estimation of sizes of the lesion defined chronically were 7.4 and 7.9 mm², respectively. In the illustrated squirrel monkey case (SM 559), the estimated size of the lesion at the time of its induction was 16.8 mm². At the time of cortical mapping, the enduring area of profound damage and loss was estimated to be 11.9 mm². Although this indicates that we significantly overestimated the size of this large lesion at the time of its induction, this discrepancy has no important impacts on the interpretation of results from this case (see further). In the other two cases (not illustrated), there was a reasonably close correspondence between the sizes of the lesions as estimated at the time of their induction and their chronic extents estimated at the time of the chronic recording experiment.

**RESULTS**

**Behavioral study**

**PRELESION.** As described in a previous paper (C. Xerri, M. M. Merzenich, W. M. Jenkins, and S. Santucci, unpublished data), the three owl monkeys and two squirrel monkeys used in the present study exhibited gradual improvement in pellet retrieval during preoperative training. All five monkeys displayed an exclusive hand preference either from the very beginning of training or after a few testing sessions. Retrieval trials were initiated as soon as the experimenter dropped a pellet into one of the five wells. Typically, the monkey would look through the front panel of the Klüver board to locate the well into which the pellet had been deposited. The animal would immediately reach out and insert one or more fingers into the proper well, palpate the pellet, then produce successive flexions and extensions of the digit(s) to grasp it. Once the pellet was captured, the monkey would withdraw the hand and deliver the food to the mouth. It is worth noting that squirrel monkeys generally watched the hand through the grasping phase of retrieval; owl monkeys rarely looked at their hands while attempting to retrieve pellets.

During the early period of preoperative training, all animals exhibited clumsy performance characterized by large and variable numbers of grasps/successful pellet retrieval, heterogeneous combinations of digits used for precision grasping especially in small sized wells, and a significant percentage of pellets ejected from the wells or dropped after retrieval. With practice, all monkeys gradually developed stereotyped and highly successful grasping and retrieval strategies characterized by the ability to place the fingers in a position that matched the size of the wells, and by fine finger coordination (C. Xerri, M. M. Merzenich, W. M. Jenkins, and S. Santucci, unpublished data). For the great majority of grasps performed in the largest wells, the pellet was brought into the palm by the fingers with a smooth grip formation, whereas grasps performed in the small wells consisted of inserting one or two extended fingers into the shallow wells and curling the fingers around the pellet. All monkeys came to reliably engage limited surfaces of the glabrous skin of one, two, or three digits to extract the pellets from
the small wells. Initially, two squirrel monkeys (SM) were more skillful than were seven owl monkeys (OM) at this digital dexterity task (C. Xerri, M. M. Merzenich, W. M. Jenkins, and S. Santucci, unpublished data). Performances by the two species stabilized at similar levels with training. The number of training sessions required to achieve a performance plateau (defined as seven successive days of stable performance with regard to averages and standard deviations of the number of grasps/retrieval, the frequency of finger combinations, and retrieval success on the most difficult wells) ranged from 24 to 42 training sessions for these five monkeys.

### POSTLESION

On the first postlesion day, simple observation did not reveal major functional deficits. Both hands seemed to participate equally in activities such as walking and climbing. Closer inspection indicated, however, that the OM with these microlesions (but not the SMs) did not use the affected hand spontaneously to reach for food. Furthermore, OMs seemed to suffer a loss of successful grasping. For example, a piece of apple or other preferred food item presented to the affected hand resulted in initiation of repeated hand grasps, but the grip could not be sustained without the aid of the other hand. Grasp forces achieved in this gripping appeared to be feeble. This hand weakness did not last more than 2 or 3 days.

Pellet retrieval testing could be resumed 3–8 days after the cortical infarct in four out of five monkeys. Because of its initial reluctance to initiate any retrievals followed by an unavoidable week-long absence of the experimenter that was administering the training, OM 2147 did not begin retraining until the 14th day after surgery (Table 1). On resumption of testing, all five animals in the present study voluntarily used the deprived hand to reach for and retrieve pellets. A sixth owl monkey, not included in the present analysis, was initially ambidextrous. Although it ultimately used one hand exclusively in the pellet retrieval task before lesion induction, only the hand contralateral to the intact hemisphere was used in postoperative training. Because of this enduring shift in hand preference, this case will be reported separately.

Surprisingly, these small area 3b infarcts were found to produce marked deficits in the precision of ballistic movements of the hand as the monkeys reached out for pellets. Indeed, in the early postoperative period, inaccurate hand positioning occurred frequently; fingers often missed their targets as the hand was projected toward the wells. Prehensile movements of the fingers also were affected severely after the area 3b lesion. In particular, the temporal features of the motor sequences of grip formation seemed to be disrupted. For example, in some trials involving a reaching for pellets located in large wells, excessive flexion of the fingers occurred before the fingertips touched the bottom of the wells and contacted the pellet, with a grasp that was too shallow for the fingers to capture the pellets. In this early period of retraining, however, the most obvious prehension abnormality consisted of rough and clumsy finger movements that seemed erratic in nature. The fingers moved in quick alternate sequences of hyperextension and hyperflexion and made only brief contacts with the bottom or the edges of the wells. Furthermore, animals tended to perform grasps at a more rapid rate than before the lesion. In many trials, monkeys failed to dislodge the pellets from wells despite a large number of grasping movements. Videotape recordings showed that close spacing of the fingers was not achieved when the animals grasped for pellets located in the large wells. Moreover, differentiated movements of one or two fingers could not be produced when the monkeys grasped for pellets deposited in the small wells.

Purely sensory deficits were detected in every monkey during the early retesting period. For instance, over a several-to many-day-long epoch, monkeys would frequently supinate the hand after both successful and unsuccessful grasping movements to check visually whether the pellet had been retrieved. In many retrieval trials, animals would continue grasping attempts, even though the pellet had already been retrieved. These two behaviors never were observed before the lesion.

Frame-by-frame video analysis allowed for quantitative measurements of the grasping deficits induced by the area 3b lesion. In all monkeys, the deterioration of manual performance in terms of number of grasps per retrieval (G/R) was proportional to the difficulty of the task, with the strongest deficits observed for the smallest wells (Fig. 2 and 3). The degradation of each animal’s performance was also characterized by a prominent irregularity in performances across retrieval trials, as indicated by the standard deviations in Fig. 3. The effects of the lesion on behavioral performance were found to be more pronounced in OMs than the SMs, particularly for the smallest wells. For the OM and SM case examples illustrated in Figs. 2 and 3, an estimate of control performance was obtained by averaging the mean number of G/Rs and the mean coefficient of variation (CV: mean/SD), calculated over the last three preoperative sessions. To reliably compare the deficits found in these two monkeys at the acute stage of the cortical damage, mean postoperative performance was calculated by averaging over postsurgery days 14, 17, and 20, which corresponded to the first three testing sessions for this OM case. As far as well 4 was concerned, the control performance obtained in this monkey was characterized by a mean number of 1.8 ± 0.2 G/R (SD) and a CV of 40.3 ± 3.3. The postoperative performance of this OM was 5.6 ± 0.7 G/R with a CV of 81.1 ± 12.3, which corresponded to a three- and a twofold increase in the G/R and CV parameters, respectively. A similar degra-

### Table 1. Summary data in three owl monkeys (OM) and two squirrel monkeys

<table>
<thead>
<tr>
<th>Size of Lesion</th>
<th>Time Before Training Resumption, days</th>
<th>No. of Training Sessions</th>
<th>Behavioral Recovery Period, d*</th>
</tr>
</thead>
<tbody>
<tr>
<td>OM 2258</td>
<td>60</td>
<td>8</td>
<td>39</td>
</tr>
<tr>
<td>OM 2147</td>
<td>61</td>
<td>14</td>
<td>46</td>
</tr>
<tr>
<td>OM 2149</td>
<td>62</td>
<td>6</td>
<td>24</td>
</tr>
<tr>
<td>SM 634</td>
<td>76</td>
<td>3</td>
<td>54</td>
</tr>
<tr>
<td>SM 559</td>
<td>100</td>
<td>6</td>
<td>42</td>
</tr>
</tbody>
</table>

* For each monkey case, the table shows the size of the cortical lesion, expressed as a percent of the total digit representational zone in area 3b; the postoperative time before training resumed; total number of postlesion testing sessions; and the time course of behavioral recovery expressed. Values expressed as the number of postlesion calendar days before postlesion performance levels were obtained.
dation in G/R was found in the SM case, which exhibited a control performance of $1.8 \pm 0.1$ G/R and a postlesion performance of $5.1 \pm 0.9$ G/R. It is worth mentioning, however, that retrieval performance consistency was not altered in this monkey, as indicated by the nearly identical CV values obtained before ($60.4 \pm 6.3$) and after the lesion ($62.1 \pm 10.3$). The differences noted between these two representative animals were more pronounced for the grasps performed in the smallest well: comparison of the mean G/R indexes calculated over the pre- and postoperative sessions mentioned above showed a fivefold increase for the OM versus a twofold increase for the SM. The CV parameter increased by a 2.1 factor in the OM, while no change was found in the SM, as indicated by a postlesion/control CV ratio of 1.1.

Close inspection of videotape records revealed that during the very first postoperative sessions, all animals performed the majority of grasps and retrievals with the preoperatively trained digits. These fingers, deprived of area 3b representation, were used either in single-digit manipulations or in combination with other fingers that were either deprived or not deprived after the lesion (Fig. 4). Animals most frequently employed the specific strategy applied stereotypically over the several days preceding the lesion, and the percentage of correct retrievals could be initially sustained surprisingly close to control values (Fig. 5) despite the very obvious degradation in dexterity described above. In the OM case illustrated here, the animal predominantly used digit 3 (well 5) or digits 2 and 3 (well 4; Fig. 4A) in pellet retrieval trials before the lesion. This monkey succeeded in dislodging the food pellets from the smallest wells using digits 2, 3, or 2 and 3 on the earliest postoperative testing sessions, i.e., by the end of the second week after surgery. Some retrievals also were performed using digit 4 (well 4) or digits 3 and 4 (well 5). Similar findings were obtained in SMs (Fig. 4B).

Unexpectedly, performance continued to deteriorate over the following several days in three of the five monkeys (2 OMs and 1 SM) mostly for the smallest wells requiring finer control and coordination of finger movements. The number of grasps per retrieval reached a maximum within the fourth
week postlesion in these three monkeys. The loss of performance homogeneity was attested by a concomitant increase in the standard deviation of the mean performance (Fig. 3A). This late degradation in behavioral performance occurred regardless of the lesion size. Videotape analyses indicated that its occurrence was related to a marked change in retrieval strategy. In all monkeys, the predominant use of previously trained digits in the retrieval task was largely abandoned and followed by the relatively more frequent use of fingers that had not been trained during preoperative testing and had not been deprived of cortical representation (Fig. 4). An exception was SM 559, which had been subjected to a complete area 3b digital representation lesion. In the OMs, the negative consequences of this change for manual performance was also confirmed by the large number of pellets that were flicked away or not retrieved when animals performed on the small wells (Fig. 5A). The inadequacy of using the untrained digits was particularly evident in the illustrated OM 2147, which substantially increased its use of untrained digits 4 (well 4) and/or 5 (well 5) in particular, between the 22nd and 28th postoperative days (Fig. 4A).

During this period, the monkey’s success rate sharply dropped to ~10 and 20% on wells 5 and 4, respectively (Fig. 5A).

During a subsequent period, a substantial improvement in digital dexterity was observed in all monkeys, as shown by a significant decrease in mean G/R over time (Figs. 2 and 3). There was a correlated reduction in performance variability (Fig. 3) and a progressive increase in the correct retrieval rate (Fig. 5). In parallel with the gradual restoration of retrieval performance, animals recovered the ability to reliably fractionate individual finger movements. Furthermore, they appeared to gradually adopt the more exclusive use of the same digits that they had trained during the prelesion training period (Fig. 4).

Ultimately, monkeys’ digital dexterity assessed on the basis of the various performance parameters used in the present study were found to stabilize at an asymptotic level that fell within the preoperative range (Figs. 2–5). To quantitatively assess the recovery of manual dexterity, both the G/R and the CV values obtained for the smallest wells were averaged over the last three preoperative training sessions and compared with the corresponding values averaged over the last three postoperative sessions. Overall, no significant differences were noted between preoperative and postoperative sessions on either G/R \[F(1,8) = 0.09, P = 0.77\] or CV \[F(1,8) = 0.44, P = 0.53\]. However, one monkey (OM 2147) clearly maintained a higher than normal variability in retrieval performance \(t = 10.03; P = 0.001\).
FIG. 4. Postlesion alterations and recovery in digit manipulation. Frequencies of the different finger combinations used for each postoperative session. Twenty pellet retrieval trials from well 4 are plotted for a representative owl monkey (A) and squirrel monkey (B). Finger combinations most frequently engaged in the retrieval task are labeled as “trained digits.”

A qualitatively similar postoperative evolution of manual dexterity was recorded in all monkeys, although interspecies differences were noted. After the maximum deficit period, all OMs displayed continuous improvement, whereas the recovery profiles found in the SMs were subject to significant fluctuations in performance ability (Fig. 3B). Also, the time course of recovery varied among the animals (see Table 1).

Despite the small number of cases used in our study, it was interesting to consider the possible influence of lesion extent, time before resumption of training and amount of prelesion training on the interindividual differences in the
time course of recovery. Because the number of postlesion testing sessions was proportional to the number of calendar days, the relative contribution of the amount of retraining versus spontaneous recovery could not be assessed in our study. Disparities in the time to complete functional recovery did not seem to be accounted for by the size or location of the cortical lesion. In the three OMs, the lesion destroyed ~60% of the digit representation in area 3b and, more specifically, the representation of three digits, two of which were the ones most heavily engaged in the retrieval task. Among these monkeys, the time to recovery occurred toward the end of the second, third, or fourth month postsurgery (see Table 1). Moreover, in SM 559 in which the entire zone of representation of the digits in 3b was damaged, full recovery was achieved within 3.5 mo, i.e., >2 wk earlier than its congener (SM 634), which had been subjected to a smaller cortical infarct (75% of the digit representation).

In OMs, it appeared that the earlier the training was resumed after the lesion, the shorter the time to full recovery (see Table 1). However, this relation was not found in the SMs; in any event, the OM sample is small. As for the influence of the amount of prelesion training on the time to recovery, it is worth mentioning that the shortest period of functional restoration (2 mo) was noted in OM 2149, which was subjected to the largest number of testing sessions (42) before the lesion. This inverse relation between prelesion training and time to recovery did not seem to apply when the remaining two OMs were compared because the animal (OM 2147) that benefited from 31 prelesion training sessions recovered more slowly (4 mo) than the monkey (OM 2258) trained over 25 sessions (3 mo). It remains that SM 559, which had 39 training sessions before the lesion, recovered faster (3.5 mo) than SM 634, which was trained over 30 sessions (4 mo), despite a complete lesion of the hand representation in area 3b.

Cortical lesions

The specific skin surfaces that each individual monkey used to palpate, manipulate and grasp pellets were defined from examination of videotape recordings of the monkey’s final, stereotyped pellet retrieval trials. Our objective in introducing cortical lesions was to completely but selectively destroy the area 3b zones of representation of essential glabrous skin surfaces. To define the lesion perimeter, we mapped the representation of the surfaces of the hand in fine detail (C. Xerri, M. M. Merzenich, W. M. Jenkins, and S. Santucci, unpublished results). A cortical lesion that destroyed all or nearly all of the cortical area 3b representation of the two or three fingers that the monkey predominantly employed to retrieve pellets from the smaller wells in the latter stages of training was then induced. To ensure that all of the cortex representing these behaviorally engaged digits
was destroyed, we extended lesions ~200–300 μm across digit representation borders and across the area 3b border into cortical area 3a. In effect, in three owl monkeys and in one squirrel monkey, this resulted in the removal of the territory occupied by the equivalent of an additional finger (i.e., on average, half of the representation of the two adjacent digits). Destruction of the representations of these two or three digits resulted in the effective ablation of ~60–75% of the digit representational zone in four of the monkeys in this series. In the fifth monkey, the representation of all five digits in area 3b was destroyed completely. Moreover, the lesion also was extended intentionally nearly 2 mm across the entire hand zone into cortical area 3a.

As noted in Methods, chronic measures of the extent of the cortex that was eliminated or destroyed by the lesion were surprisingly close to the extent of the lesion estimated at the time of its induction.

Unit response mapping experiments

Cortical representations of the skin surfaces of the hand were reconstructed from recordings derived in SI cortical areas 3b, 1, and 3a. These somatosensory maps were based on a total of 3,963 electrode penetrations. The cortical sites were recorded before the lesion (1,138 electrode penetrations), in the hemispheres contralateral to the hand trained on the behavioral task, and after the functional recovery had been achieved, in the hemispheres ipsilateral (1,349) and contralateral (1,476) to the lesion.

To assess lesion-induced changes in the SI hand representations, we compared the cortical maps obtained before the lesion in each monkey with the maps reconstructed after monkey retraining in the chronic stage of cortical injury. The major finding of our mapping study was that a subtotal (4 monkey cases) or total (1 monkey case) ischemic lesion in the digit zone of area 3b extending variable distances into cortical area 3a produced substantial long-term reorganization in functionally defined areas 1 and 3a and relatively less prominent remodeling in the lesioned cortical area 3b.

A detailed description of the normal organization of SI hand representations in the OM and SM is not within the scope of the present paper. This organization has been described in several earlier papers (Merzenich et al. 1978, 1987; Sur et al. 1982). However, before describing lesion-induced remodeling in area 3b and area 1, it is important to review some of the general features of topographic maps of the hand surfaces derived from these areas in intact animals.

The hand representation in the primary somatosensory cortex of the OM and the SM share common organizational principles. As already reported in previous studies (Jenkins et al. 1990; Kaas et al. 1984; Merzenich et al. 1978, 1987; C. Xerri, M. M. Merzenich, W. M. Jenkins, and S. Santucci, unpublished results), recordings of the activity of small clusters of middle layer neurons in response to just visible skin indentation have shown that representations of the cutaneous surfaces of the hand in areas 3b and 1 have a somatotopic organization. A basic internal topographic order that reflects neighborhood skin relationships is maintained, despite significant interindividual variability in the details of the somatosensory maps (Merzenich et al. 1987). In recordings in closely spaced rows of parallel electrode penetrations in the lateral-to-medial direction, cutaneous receptive fields progress in orderly shifting overlaps across the digits 1 to 5 glabrous skin surfaces. In rostral-to-caudal penetration sequences in area 3b, the receptive fields (RFs) shift in an orderly way from the distal to the proximal skin surfaces of the hand. The topographic order of the cutaneous RF distribution typically reverses along the caudal and rostral boundaries of 3b, with roughly mirror-image progressions caudally in area 1, and rostrally in area 3a. Thus the fingertips of the hand representation are represented along the caudal boundary of area 1 and the rostral- and caudal-most margins of the cutaneous hand representation of areas 3b and 3a, respectively. As a rule, the boundaries between area 3b and area 3a are defined functionally as the line separating electrode penetrations in which cutaneous RFs are clearly identified in area 3b and nearby penetrations in which neurons are driven by high-threshold deep receptor inputs in area 3a. The caudal borders of the cutaneous representation of the hand in area 1 are also marked in OM and SMs by cutaneous-to-deep receptor transitions.

In accordance with the earlier studies cited above, a single, complete and highly ordered topographic representation of the glabrous hand surface was found in area 3b of all five monkeys used in our study. By contrast, animals exhibited a more fragmented and less complete and much more variable hand representation in area 1 (see Figs. 6–8, top). As a general rule, dorsal skin surfaces were represented in area 3b as small and discontinuous patches inserted in the much larger glabrous skin representation. In the maps derived in our experiments, dorsal skin surface representations were nearly absent from area 1 except in one monkey (OM 2258), the hairy skin representation of which comprised 44% of the total cutaneous prelesion map.

The area 3b cutaneous maps reconstructed in our intact monkeys were not fully representative of the normal maps derived from naive animals to the extent that training on the digital dexterity task was found to selectively produce a significant enlargement of the cortical representation of the glabrous fingertip surfaces that were engaged most heavily in the retrieval task (C. Xerri, M. M. Merzenich, W. M. Jenkins, and S. Santucci, unpublished data). However, all of the measurements based on prelesion maps are valid for comparison with postlesion maps.

Overall, 82 ± 4% of the area 3b, 3a, and 1 SI cortical region of the digit cutaneous representations were devoted to glabrous skin surfaces, whereas dorsal skin surfaces were confined to 18 ± 4% of the total representation. Area 3b accounted for 83 ± 7%, that is, 7.5 ± 0.6 mm² of the SI cutaneous digit representation. Area 1 was found to account for only 17 ± 8% (1.5 ± 1 mm²) of the SI cutaneous digit maps. In area 3b, most of the digit cutaneous map (81 ± 4%) was devoted to the glabrous skin representation. In control prelesion maps, not more than two or three cutaneous response samples were recorded within densely sampling microelectrode penetrations introduced into cortical area 3a, where deep receptor inputs were invariably predominant.

Postlesion alterations of the areal extents of cortical representations

To quantitatively analyze possible long-term changes in cortical territories of digit representation in the 3b regions...
surrounding the zone of cortical damage, we measured the areal extents of the spared representational zones. The spared territory, referred to as the acute ipsilateral postlesion control (ACUTE IPSI POST/C) map, was obtained by subtracting the area of the lesioned sector of the digit representational zone from the area of the overall digit representation derived before the cortical infarct (ipsilateral prelesion control = IPSI PRE/C). For each monkey, this pseudocount map was compared with the map reconstructed on the lesioned side after the behavioral recovery was complete (ipsilateral postlesion experimental = IPSI POST/X). This comparative procedure may have led to an overestimation of the extent of the chronic-map alterations insofar as possible acute changes evidenced by complete remapping over the first few hours or days after the lesion may have reshaped cutaneous representations, particularly within the intact regions bordering on the injury site (see Jenkins et al. 1987). Note that for the two illustrated cases from which most examples cited in this text are drawn (OMS 2149 and 2258: Figs. 6 and 7), the estimated lesion size at the time of the chronic recording experiment was significantly greater than its estimated extent at the time of its induction (see METHODS). Long-term reorganization was documented by comparing the cutaneous representations obtained in areas 3b and 1 to IPSI PRE/C and ACUTE IPSI POST/C maps, as well as to the digital cutaneous SI maps derived contralateral to the chronically lesioned hemisphere (contralateral postlesion control = CONTRA POST/C).

Postlesion reorganizations of cutaneous SI maps were found to be highly variable across monkeys as to the shape and size of hand surface representations. Results are therefore necessarily reported in the present paper from the viewpoint of both statistical significance and idiosyncratic characteristics.

REPRESENTATIONAL CHANGES IN AREA 3B. An ANOVA was performed to evaluate the main effects of animal species, period and side, and skin surfaces (glabrous/hairy). Period and side were not treated separately because no map could be derived from the side contralateral to the lesion either before or just after the cortical lesion was made. This variable therefore had four levels: control, pseudocount, chronic maps ipsilateral to the lesion, and chronic maps contralateral to the lesion. All three variables had a significant main effect: animal species [F(1,3) = 22.04; P ≤ 0.02], period and side [F(3,9) = 20.23; P ≤ 0.0002], and skin surfaces [F(1,3) = 79.62; P ≤ 0.003]. Interaction effects were significant only for the last two variables: [F(3,9) = 23.93; P ≤ 0.0001]. Multicomparison analysis (Fisher PLSD) suggested that the areal extent of the glabrous skin representation of digits derived from 3b on the lesion side were not statistically different in the IPSI POST/X and ACUTE IPSI POST/C maps (P = 0.09). The same conclusion applied to the areal extent of the representation of hairy digit skin (P = 0.18). However, examination of individual cases revealed substantial variability across monkeys. The differences between the ACUTE IPSI POST/C and IPSI POST/X representations were found to be negligible in three monkeys (OM 2147: from 3.09 to 3.27 mm²; OM 2258: from 3.14 to 2.93 mm²; SM 559: from 0 to 0.86 mm²), whereas a substantial increase from ACUTE IPSI POST/C to IPSI POST/X areal extent was observed in two monkeys (OM 2149: from 2.75 to 5.43 mm², 197%; SM 634: from 1.31 to 2.14 mm², 163%). These interindividual differences emerged, regardless of the size of the cortical infarct. The three typical monkey cases shown in Figs. 6—9 illustrate some aspects of these individual differences. Note that in these figures, the lightly shaded and colored areas mark the zones of representation of glabrous digital surfaces. The blue, green, and red zones mark the cortical areas of representation of the glabrous fingertips that the monkey predominantly employed in the recovered small object retrieval behavioral task under the most difficult task conditions (wells 4 and 5) in cortical areas 3b, 1, and 3a, respectively. The darkly shaded zones mark the territories of representation of the dorsal (hairy) hand surfaces.

In OM 2149 (Fig. 6), an increase in the areal extent of the 3b digit map was presumably accounted for by the apparent expansion of glabrous regions of the digit 2 representation into a narrow strip bordering the lateral edge of the lesioned zone: an enlargement of the glabrous and hairy skin zones of the digit 1 representation, which consisted of two discontinuous zones separated by a noncutaneous response area; an increase in the area of the digit 5 representational area spared by the lesion; and a novel representation of digit 4 emerging in a new area 3b location (blue zone, Fig. 6, bottom), i.e., along the most medial flank of area 3b next to the digit 5 representation.

In SM 634, the gain in cortical territory resulted from an enlargement of the spared representational zones surrounding the lesion. OM 2258 (Fig. 7) also exhibited postlesion area 3b reorganization. The borders separating digit phalanges and adjacent fingers were shifted but with less consequence for the overall measures of digital surface representational territory. Note, however, that a number of penetration sites with multiple receptive fields located on both digits 3 and 4, the representation of which had been destroyed by the lesion, were found within an emergent zone along the rostral margin of the digit 4 representation.

In the squirrel monkey case (SM 559) illustrated in Fig. 8, the cortical lesion destroyed the entire digit representation of 3b, together with a large sector of area 3a situated along the rostral border of area 3b. Postlesion remapping revealed that a large dorsal hairy hand representation had reemerged along the medial edges of area 3b. Novel dorsal digit responses emerged in this medial dorsal hand zone, as well as in a lateral hand representational zone that probably survived the lesion. No glabrous cutaneous digit responses were recorded in area 3b in this recovery case (see Fig. 8, bottom).

To examine the possible occurrence of postlesion representational changes within the intact hemisphere, we compared IPSI PRE/C digital cutaneous maps to the homologous CONTRA POST/C maps. In all five monkeys, hemispheric differences consisted of larger cortical territories of representation in area 3b maps derived for the trained hand (P ≤ 0.005). The differences between IPSI PRE/C and CONTRA POST/C cutaneous maps selectively concerned the cortical zones devoted to the representation of the glabrous fingertip segments predominantly used for pellet retrieval [F(3,41) = 3.06; P ≤ 0.02]. The ‘‘magnification’’ of the representations (cortical area/skin surface area) of those fingertips was larger (0.017 ± 0.008) than the magnification of the repre-
FIG. 6. Postlesion reorganization of the hand representation in owl monkey OM 2149. Topographic maps of representation of different skin surfaces on the hand before (in the right hemisphere) and 63 days after induction of a cortical lesion in the digit representation of area 3b. A contralateral-hemisphere control map for this case is illustrated in Fig. 9. Infarcted zone determined on the basis of electrophysiological recordings during the 1st 2 h after the lesion induction is outlined on the prelesion map. Cortical zones of representation of hand surfaces that were employed most heavily in the final phases of recovered behavior (the tips of digits 3 and 4) are highlighted in these map reconstructions: blue for area 3b representations; green for area 1; red for area 3a. Other glabrous (volar) finger representations are indicated in light gray. Note that the lesion extended into area 3a. Large numbers 1–5 denote the digits (e.g., 1 = thumb); D, M, and P, distal, middle, and proximal phalanges, respectively; multiple digit representations are shown (e.g., 34D indicates cortical zones in which neurons displayed receptive fields located on the tips of digits 3 and 4); P1–P4, palmar pads at the bases of the digits; H, hypothenar eminence; I, insular zone in the center of the palm; T, thenar eminence; W, wrist; F, face; LD, large dorsum surfaces; * zones over which no cutaneous responses could be evoked. Dorsal skin representational zones are indicated in dark gray. --- --- ---, approximate line of reversal in receptive field sequences that functionally defines the area 3b/area 1 border (Merzenich et al. 1978). ---, estimated area 3a-area 3b border. Black infarct area delimits the zone over which neither cortical spontaneous or driven neuronal discharges could be recorded in the postlesion mapping experiment. Constant vascular landmarks are shown in each map in the experimental hemisphere, to facilitate comparisons. Note the emergence of cutaneous representational zones in both area 3a and area 1.

sentations of the same skin surfaces of the opposite untrained hand (0.011 ± 0.003).

REPRESENTATIONAL CHANGES IN AREA 1. As a general rule, the representation of the glabrous surface of digits derived from area 1 before the lesion occupied a much smaller cortical territory than did the corresponding representation obtained in area 3b (1.13 ± 0.97 mm² vs. 5.60 ± 1.0 mm²; P = 0.0005). Moreover, area 1 maps appeared as incomplete usually discontinuous representations characterized by a coarse topography (Figs. 6–8 and 9) (see Merzenich et al. 1987). Layer 3–4 multiple unit samples in this cortical field displayed clear but rarely strong responses to cutaneous stimulation.

Postlesion alterations in the topography of the glabrous skin representation of the digits could be documented in four monkeys in which cutaneous digit maps were obtained both before lesion and after functional recovery. In the remaining monkey (OM 2147), area 1 hand representations could be reconstructed only at the chronic stage of the lesion, in both hemispheres. The ANOVA showed a significant interaction between the period and side and skin surfaces variables [F(2,4) = 16.96; P = 0.05]. On the average, the IPSI PRE/C areal extent of the cortical territories devoted to glabrous skin surfaces of the digits in area 1 was 1.13 ± 0.97 mm², whereas the IPSI POST/X areal extent was 2.16 ± 0.87 mm² (P = 0.0001), which represented an increase of 1.9 times.

Despite individual differences, every monkey exhibited a substantial expansion of the area 1 digit representation. Two monkeys showed a moderate enlargement ranging from 1.18 times (from 2.88 to 3.39 mm²; OM 2258; see Fig. 7, where zones of representation of the most heavily behaviorally engaged area 1 digit tips are highlighted in green) to 1.53 times (from 1.16 to 1.78 mm²; SM 559) as compared with
the other monkeys that displayed a more prominent increase ranging from 2.09 times (from 0.75 to 1.57 mm$^2$; OM 2149; see Fig. 6) to 3.11 times (from 1.0 to 3.11 mm$^2$; SM 634).

In all four monkeys, the cortical territorial gain of the glabrous digital skin surfaces appeared to have resulted largely from shifts in the functionally defined borders separating the cutaneous from the deep receptor input representations within and along the most caudal margins of the cutaneous zone of area 1. From a consideration of the distance of these representational zones from the area 3b-area 1 border (see Merzenich et al. 1987) and because these emergent cutaneous receptive fields were related topographically to those defined more anteriorly, it was concluded that this expansion of representation most likely comes from an enlargement of the digital representational sector of area 1. At the same time, it is difficult to rule out the possibility that a plastic change in the bordering area 2 responses is contributing to some of these recorded changes in the posterior aspect of cortical area 1.

In two monkeys, hand maps derived from area 1 were characterized by the emergence of representational zones with multiple receptive fields, all located on the glabrous surfaces of the fingertips. These representations of discontinuous digital skin territories accounted for most or all of the expansion of area 1 in these cases. In owl monkey case OM 2258 illustrated in Fig. 7, the cortical zone of multiple cutaneous inputs represented 35% (0.72 mm$^2$) of the total map of the digital glabrous skin (2.04 mm$^2$). This multiple digit representation was found to be even larger (70%; 1.05/1.78 mm$^2$) in squirrel monkey case SM 559 (Fig. 8).

The glabrous digit representations that expanded in area 1 seemed to be related consistently to the digit representations directly affected by the area 3b lesion. At the same time, note that the lesions were designed specifically to destroy the representations of skin surfaces that were crucial for the pellet retrieval behavior. For example, in OM 2149 (Fig. 6), the cortical infarct (outlined in dark blue) deprived digits 2–4 and most of the tip of digit 5 of the cutaneous represen-
Postlesion reorganization of the hand representation in squirrel monkey SM 559. Topographic representations of the hand before and 109 days after induction of a cortical lesion damaging the entire digit representation in area 3b and a substantial part of area 3a. Same conventions as for Fig. 6. Representations of most heavily behaviorally engaged digit tips in the recovered behavior are again highlighted in color.

Remodeling was the emergence of a prominent zone of multiple cutaneous receptive fields located on the tips of digits 2–4 (Fig. 7). It is worth mentioning that this reorganization prominently devoted to the glabrous surfaces of digits 3–5. To gain some insight into the possible influence of hand dexterity behavior on the reshaping of area 1, we examined the finger combinations most often involved in the retrieval task during postoperative testing sessions, in particular for the smallest wells that required a larger number of grasps for successful retrieval. Close inspection of the videotapes revealed that OM 2149 consistently used the tip segments of digit 3 or of digits 3 and 4 during most of the later postoperative training sessions. The areas 3b, 1, and 3a, cortical zones representing these digits at prelesion and post-lesion experiment stages are shown in Fig. 6 in blue, green, and red, respectively. Note that digit 2 had been used on a lower schedule earlier in training, during a period when this monkey used broad combinations of fingers (from training resumption to the 36 postlesion day).

In OM 2258, the area 3b lesion (outlined in dark blue in Fig. 7) damaged the cutaneous representation of all of digit 2, most of digit 3, and >50% of the distal phalanx of digit 4. In this monkey, the most remarkable feature of postlesion remodeling was the emergence of a prominent zone of multiple cutaneous receptive fields located on the tips of digits 2–4 (Fig. 7). It is worth mentioning that this reorganization almost exclusively concerned the distal phalanges of fingers the medial and proximal phalanges of which also were deprived of representation in area 3b. At the same time, the representation of digit 1, which was injured to a great extent, did not benefit from a larger representation in area 1 at the chronic stage of the lesion. Examination of the digital skin surfaces most heavily involved in the dexterity task during postlesion recovery showed that OM 2258 favored a retrieval strategy characterized by the use of different combinations of fingers (digits 3 and 2 and 3 and 4) involving mainly the distal phalanges. The area 1 zones of representation of the most heavily behaviorally employed digit tips (2 and 3) are highlighted in green in Fig. 7.

In SM 559, in which the entire cutaneous representation of the digits was destroyed in area 3b, the emergence of multiple receptive fields in area 1 reunified the cutaneous representation, which was fragmented before the lesion (Fig. 8). This multiple digit representation developed at the expense of cortical zones previously devoted to single digit...
FIG. 9. Contralateral hemisphere "control" maps for OM 2149 and OM 2258. Somatosensory cortex (SI) maps from the lesioned hemispheres in the representative cases illustrated in Figs. 6 and 7. Cross-hatched and dotted cortical zones highlight the territories of representation of digit tips in cortical areas 3b and 1, respectively, that correspond to hand surfaces that were employed most predominantly in pellet retrieval in behaviorally recovered monkeys (see Figs. 6 and 7). Lightly shaded zones mark the territories of representation of the rest of the glabrous (volar) finger surfaces. Dorsal (hairy) skin representational zones are darkly shaded. * Zones in which no cutaneous responses were recorded.

In particular, the digit 2 representation that was predominant in the IPSI PRE/C map became confined to a much smaller cortical zone when functional recovery was achieved. Furthermore, digit 1, which occupied a substantial part of the area 1 cutaneous representation before the lesion, was devoid of any representation in the reorganized area. Interestingly, the greater part of the multiple digit representation was devoted to digits 2 and 3 and, to a lesser extent, to digits 4 and 5. Note that a new single digit representation of digit 5 emerged in a topographically correct location, i.e., along the medial border of the digit 4 representation. Analysis of the behavioral data clearly showed that SM 559 predominantly used digits 3, 3 and 4, and 2 and 3 digit combinations over the final sessions of pellet retrieval behavior; digits 4 and 5 were frequently used together on well 4 from the 46th to the 70th day postlesion (see Fig. 4B) and on well 5 from the 52nd to the 70th day postlesion.

In SM 634 (not illustrated here), the area 3b lesion damaged the whole cutaneous representation of digits 1 and 2 and 70% of the tip of digit 3. The IPSI POST/X map derived from area 1 was characterized by a complete and well-differentiated representation of all five fingers in contrast to a
smaller IPSI PRE/C representation that was almost exclusively devoted to the distal phalanges of digits 1–3. The new representational zones emerged in the cortical territory that bordered on the area 1 cutaneous map and had been afferented previously by deep-receptor input. The main feature of the IPSI POST/X map was that it contained a dominant representation for the proximal and distal phalanges of digit 2 and the distal phalange of digit 3 and included a complete representation of all phalanges of digit 4, which was entirely missing in the IPSI PRE/C digital representation. Note that in SM 634, digits 2 and 3 and digits 3 and 4 proved to be the finger combinations most frequently involved in the retrieval task during the postoperative training period.

Postlesion reorganization of area 1 seemed to specifically occur in the infarcted hemisphere, as attested by the fact that the IPSI PRE/C area 1 cutaneous maps obtained in four monkeys did not differ in cortical surface area from the CONTRA POST/C maps recorded on the opposite side ($P = 0.62$). Furthermore, comparisons of the IPSI POST/X and CONTRA POST/C cutaneous maps derived from area 1 revealed interhemispheric differences that corroborated the drastic representational reorganization described above. On the average, the overall area of the representation of the digital glabrous skin surfaces chronically recorded on the lesioned side ($2.16 \pm 0.87 \text{ mm}^2$) in the five monkeys was significantly larger than the corresponding area measured on the intact side ($1.26 \pm 0.76 \text{ mm}^2$; $P = 0.03$) contralateral to the lesion. However, as noted earlier, one monkey case (SM 559) exhibited a larger glabrous digit representation on the contralateral side ($2.26 \text{ mm}^2$) than on the lesioned side ($1.78 \text{ mm}^2$). Interestingly, this monkey displayed a nearly complete CONTRA POST/C map (the middle phalanges of digits 3 and 5 were missing). By contrast, the IPSI POST/X map was characterized by a large multiple-digit representation of distal phalanges along with a smaller single-digit representational zone mostly devoted to the distal phalanges. Novel inputs originating from digit 5 also were observed on the lesioned side. No multiple-digit representations were observed in the CONTRA POST/C maps. As far as dorsal skin surfaces of the digits were concerned, no interhemispheric differences were found in area 1 ($P = 0.87$) in our population of monkeys.

REPRESENTATIONAL CHANGES IN AREA 3A. Striking alterations of the response properties of area 3a neurons were found in the maps derived on the infarcted sides in four monkeys. Area 3a, which is normally devoted primarily to deep-receptor input representation, exhibited emergent cortical regions over which neurons were excited vigorously by light tactile stimulation. The newly expressed cutaneous responses originated almost exclusively from the glabrous surfaces of the fingertips. Most of the recorded cortical sites exhibited RFs on multiple fingers.

Whenever cutaneous responses were found in a cortical zone supposedly included in area 3a and abutted on area 3b, the usual criterion could no longer be used to functionally define the 3b-3a boundary (cutaneous-deep inputs). Reconstruction of this functional boundary was based partially on the assumption that the internal topographic relationship of the representational zones of area 3b spared by the lesion was not disrupted. As illustrated in Fig. 6 for owl monkey case OM 2149, the lateral region of area 3a was defined functionally in the most conservative way by reference to both the ACUTE IPSI POST/C and IPSI POST/X maps reconstructed in area 3b. Although the remaining regions of the IPSI POST/X map of area 3b looked distorted compared with the ACUTE IPSI POST/C map, the topological neighborhood relationships of the representational zones of digits 1 and 2 was maintained to an extent that allowed us to reasonably infer the functional boundaries between area 3b and area 3a. As some recording sites could not be unequivocally assigned to either field 3b or 3a, a possible error in areal extent measurement resulting from this approximation cannot be ruled out. However, most of the emerging multiple-digit cutaneous responses were still found at cortical sites located at least several hundreds of microns away from the 3b-3a boundaries defined functionally before the cortical injury.

The novel, emergent cutaneous regions occupied substantial cortical territories: 0.55 mm$^2$ in SM 634, 1.19 mm$^2$ in OM 2147, 1.60 mm$^2$ in OM 2258, and 3.11 mm$^2$ in OM 2149, which represented 10, 25, 27, and 38%, respectively, of the total surface of the reorganized digital glabrous skin representations in SI (see Figs. 6–8). In Figs. 6 and 7, the area 3a representations of the fingertips that were engaged most heavily in the recovered behavior are highlighted in red. Note that the other digits with emergent area 3a representations also were engaged in recovered pellet retrieval performance (especially digits 2 and 4 in earlier postlesion training periods in OM 2149 and OM 2248, respectively).

As reported above, cortical zones of multiple digit representations were predominant in the cutaneous “maps” of area 3a. They formed 54, 73, 75, and 83% of the overall cutaneous representations in area 3a in OM 2149, OM 2258, SM 634, and OM 2147, respectively. Note that the remaining monkey case (SM 559) did not show any cutaneous inputs in the region of area 3a adjoining area 3b (Fig. 8). This monkey was subjected to an extensive cortical lesion that damaged the entire digit representation within 3b, as already mentioned earlier, but that also damaged a wide hand zone (~8 mm$^2$) of area 3a (see Fig. 8).

The topography of newly expressed cutaneous representations in area 3a varied highly across individuals. For OM 2149 (Fig. 6, bottom; see control hemisphere map in Fig. 9), some representational zones were located along the rostral margin of the hand representation within area 3b, whereas others abutted the rostral borders of the functionally defined infarcted zone or emerged more rostrally within area 3a in the form of discontinuous strips at distances of approximately one millimeter from the edge of the lesion. In this monkey case, a gross topographic organization was observed in the lateral-to-medial (digit 1 to digit 4) direction. The distal phalanges of digits 2–4 and, to a lesser extent, digit 1 were represented in both of the cortical territories where the neurons displayed RFs located at the tip of a single finger or of two, three, or even four fingers. It is interesting to note that these novel cutaneous zones were devoted mostly to the digits deprived of representation in area 3b, i.e., digits 3 and 4. It is also worth recalling that the distal glabrous surfaces of these two fingers, which are specifically what emerged
representationally in area 3a, were the most heavily involved in the digital dexterity task during the later stages of postlesion training.

In owl monkey OM 2258 (Fig. 7), the distal phalanges of digits 3–5 were represented over a large cutaneous sector flanking the rostral edge of the digit 5 representational zone in area 3b, presumably emerging in area 3a. Theoretically, one cannot rule out the possibility that part of this new representation emerged at the extreme margin of area 3b. However, examination of all of the cutaneous maps reconstructed in our monkeys at the chronic stage of cortical lesion suggests that multiple-digit representations were not a feature of area 3b representations. In OM 2258, small cutaneous representations clearly emerged in area 3a along the rostral margin of the infarcted cortical zone. A single-digit representation was devoted to the distal phalange of digit 3, which also was represented in combination with digits 1, 2, and 4 in small patches of the cortex. Surprisingly, the thenar eminence was also represented in area 3a in the form of scattered islands. Nevertheless, the tips of the glabrous surfaces of digits 3 and 4 and, to a lesser extent, digit 2 were represented over the largest cortical territories in area 3a. As already mentioned for OM 2258, these digital surfaces were the most heavily involved in the retrieval task performed during the final weeks of postlesion testing.

In squirrel monkey case SM 634, cortical penetrations with cutaneous RFs located on the distal phalanges of both digits 3 and 4 were found in the regions of area 3a that abutted the representation of digit 4 within area 3b. Two other patches of cutaneous representations identified as being located in area 3a were found at cortical sites situated along the extreme rostral margin of the digit 3 representation in area 3b. In the first region, neurons displayed multiple receptive fields located on the distal phalange of digits 2–4. In the second zone, neurons exhibited single receptive fields located on the tip of digit 4. As in other monkeys, the cutaneous representation emerging in area 3a again favored the glabrous digital surfaces most frequently used in the retrieval task. Interestingly, SM 634, which displayed the smallest emergent cutaneous representation (0.55 mm²) in area 3a, was also the animal that exhibited the largest postlesion increase (about 3-fold) in the cutaneous representation (from 1.0 to 3.11 mm²) derived from area 1.

In OM 2147, digits 2 and 3, half of the tip of digit 4, and most of digit 1 were deprived of a representation within area 3b. In the postlesion map, responses were recorded along the rostral and medial margins of the area 3b representation of digit 5, presumably within area 3a. Indeed, multiple RFs included the glabrous skin surfaces of the distal phalanges of two (digits 2 and 3) or three (digits 2–4 and digits 3–5) different fingers. OM 2147 preferentially used digits 2 and 3 (the tip representations of which are highlighted in color in Fig. 6) on the digital dexterity task, but other digital combinations like digits 3 and 4 were commonly used on well 4 throughout the postoperative period.

In summary the following points are made. 1) Ischemic lesions damaging 60–70% of the cutaneous digital representation in area 3b induced moderate but unequivocal alterations in the shapes and sizes of the remaining cutaneous representation within the region of area 3b surrounding the infarct. Some limited skin surface areas formerly represented only within the lesioned cortical zone could emerge in this region. 2) By contrast, much more extensive map remodeling occurred within the undamaged area 1 ipsilateral to the lesion. Beyond interindividual differences in the extent of the changes, the reorganization of digital representations was characterized by a gain in the cortical territories devoted to the representations of digit skin surfaces. This enlargement in areal extents appeared to occur largely at the expense of formerly deep-receptor input representational zones. The incorporation of these emergent cutaneous responses in the continuous representational topography of the area 1 hand representation, the qualitative area 1-like nature of recorded responses, and the relatively anterior location of these changes with regard to the area 1:area 3b border have led us to conclude that these new input derives from area 1. However, it is possible that the adjacent cortical area 2 is also contributing to these changes. 3) Cortical sectors of cutaneous representation in area 1 were larger for glabrous skin surfaces that were deprived of representation in area 3b and, more specifically, that were more heavily engaged in the digital dexterity task over the postoperative period. 4) In general, reorganized representations appeared to be organized topographically with the important exception that multiple-digit representations of the glabrous skin of the distal phalanges emerged as a major area 1 feature in three of these monkeys. 5) The cortical region of area 3a surrounding the lesion exhibited a remarkable change that consisted of the emergence of cutaneous inputs usually originating from two or three adjacent digits. 6) This novel cutaneous representation was exclusively devoted to the glabrous skin surfaces of the distal phalanges. It favored the fingers that were devoid of an area 3b representation and, more specifically, that were most frequently used during postoperative pellet-retrieval training.

Postlesion changes in receptive-field size

The overall population of digital cutaneous RFs, determined at all cortical recording sites, was classified into two predominant categories: single RFs covering discrete skin surfaces generally restricted to the distal, medial, or proximal phalanges and multiple RFs consisting of separate fields referred to as “subfields,” located on two or more contiguous fingers. Large RFs including several digit phalanges or extending across adjacent digits and/or palmar pad were rare, and were discarded from the analysis.

The substantial interindividual differences encountered in the postlesion remodeling of SI cutaneous representations were accounted for by idiosyncratic changes in RF properties. To characterize these changes properly, the characteristics of the RFs are described here in terms of size, spatial density (relative percentage of RFs over each digit), digital combination (location of subfields from a given recording site), and, whenever data were available, response sensitivity. The sensitivity of the neural response to just-visible indentation was evaluated subjectively on a three-level ordinal scale, and labeled as strong, clear, or weak.

Comparison of the acute ipsi post/C and ipsi post/X maps in area 3b did not show consistent differences in RF size. In only one monkey case (OM 2147) were ipsi post/X RFs
found to be on the average larger than ACUTE IPSI POST/C RFs (Fig. 10); close examination of the data revealed that in OM 2149 only a small number of postlesion recording sites (~12%) exhibited larger RFs after the lesion, whereas no differences in ACUTE IPSI POST/C versus IPSI POST/X RF size were found for the remaining two cases (OM 2258 and SM 634). In all five monkeys, significant differences were observed between IPSI PRE/C and CONTRA POST/C RFs. In accordance with previously reported results (C. Xerri, M. M. Merzenich, W. M. Jenkins, and S. Santucci, unpublished observations), smaller RFs were found in the IPSI PRE/C maps for cortical regions that specifically represented the middle (13.52 ± 4.45 mm² vs. 24.0 ± 7.56 mm²) and distal phalanges (7.24 ± 1.58 mm² vs. 16.18 ± 7.78 mm²) of digits trained on the retrieval task [F(11,48) = 3.61; P < 0.0009].

In monkey case OM 2258, neurons at all cortical sites in the CONTRA POST/C and IPSI PRE/C maps derived from area 1 exhibited single RFs, whereas a relatively smaller percentage of the cortical sites of the IPSI POST/X map displayed single RFs (62% or 33/53). The single RFs recorded in the IPSI POST/X (13.19 ± 7.26 mm²) and CONTRA POST/C hemispheres (14.67 ± 7.56 mm²) were similar; both were smaller, on average [F(2,60) = 3.54; P < 0.03] than were the RFs obtained before the lesion (21.27 ± 15.93 mm²). As shown in Table 2, significant differences in response sensitivity were observed between the IPSI POST/X, IPSI PRE/C, and CONTRA POST/C response samples. No significant difference was observed between the IPSI PRE/C and CONTRA POST/C response categories. In particular, weak responses occurred less frequently (~30% of samples) in IPSI POST/X than in the IPSI PRE/C and CONTRA POST/C maps (~50%), whereas the proportion of clear responses was higher in the former (~60%) than in the latter (~30%) RF populations.

Multiple RFs all located on the fingertips were found at 38% (20/53) of the cortical sites recorded in the IPSI POST/X map derived from area 1 (Fig. 11). On the average, these multiple RFs exhibited 2 ± 0.4 subfields. Subfields were mainly located on digit 3 (42%), whereas relatively smaller proportions of subfields were found on digits 2 (27%) and 4 (27%). Subfields of the cortical sites recorded in area 1 were located either on digits 3 and 4 (40%), digits 2 and 3 (30%), or digits 2–4 (20%), which were the three fingers most heavily engaged in the pellet-retrieval task during postoperative training. Individual subfields covered small skin surfaces (mean size: 9.06 ± 4.04 mm²). Clear (40%) and strong (38%) responses were found to predominate over weak (22%) responses. Strong or clear responses were commonly found for stimulation applied on the tip of digit 3 (53 and 31%, respectively) or digit 2 (42 and 25%), whereas clear responses were most frequently observed for digit 4 (75%). Mixed cutaneous-deep inputs were noted for only 15% of cortical sites. In these mixed fields, rarely recorded in control hemispheres, unequivocal “deep” responses were characterized by very regular discharges that varied in rate

**FIG. 10.** Receptive field (RF) size in area 3b. Frequency distribution and mean values of cutaneous RF size (in mm²) recorded in area 3b before and after the cortical lesion. Data referred to as acute ipsilateral postlesion control (IPSI POST/C) were obtained by subtracting the RFs corresponding to the lesioned zone from the whole population of RFs recorded before the infarct. Data labeled as ipsilateral postlesion experimental (IPSI POST/X) were recorded on the lesioned side after the behavioral recovery was complete. Statistical comparisons between mean RF sizes are shown in the table. An analysis of variance supplemented by a Fisher PLSD posthoc test was used for OM 2147, OM 2258, and SM 634, whereas a Mann-Witney Rank-Sum test was computed for OM 2149 for which the requirement of normally distributed populations was not satisfied.
as a function of the extension or flexion of specific digital joints with sharply mechanically dissociable cutaneous receptive fields.

A particular subfield that was more sensitive to cutaneous stimulation than its associated subfields could be identified for most multiple RFs. Interestingly, the occurrence of the best responses seemed to depend on the topographic locations of cortical sites. For instance, multiple-RF cortical sites adjoining the digit 4 single-RF representation in area 1 tended to display the strongest subfield responses on digit 4.

In this same (OM 2258) case, multiple RFs were also found in a large number of microelectrode penetrations (85%; 22/26) in the region of area 3a bordering the chronic lesion. These multiple RFs displayed a total of 80 subfields with an average of 3.6 ± 1.2 subfields for each RF, which appeared to be larger than the mean number of subfields found in area 1 (2.3 ± 0.4; *t* = 4.92; *P* = 0.0001). The cutaneous subfields were distributed almost evenly across the distal phalanges of digits 3 (26%), 4 (23%), 2 (20%), and 5 (18%), whereas a smaller proportion was observed for digit 1 (13%; Fig. 11). In 55% of the cortical sites exhibiting multiple RFs, subfields were found on digits 2–4. It is worth mentioning that digit 5 was included in 64% of the digital subfield combinations, at all cortical sites adjoining the digit 5 representation in area 3b. On the average, individual subfields recorded in area 3a were larger (11.33 ± 3.76 mm²) than were the subfields found in area 1 (9.06 ± 4.04 mm²; *t* = 3.09; *P* = 0.01). Strong (33%), clear (46%), and weak (21%) responses recorded in area 3a were found for subfields located on all five digits. In most electrode penetrations, a best response could be identified for one of the subfields of each multiple RF. Thirty-six percent of these best responses were observed for subfields located on the tip of digit 5. Note that most cortical sites that exhibited cutaneous responses (16/22; 73%) emerged in the region of area 3a neighboring the representational zone of digit 5 in area 3b.

In monkey OM 2149, all comparisons of single RF sizes recorded within area 1 in the ipsiPRE/C (21.63 ± 11.59 mm²; *n* = 7), ipsiPOST/X (24.90 ± 27.07 mm²; *n* = 18), and contraPOST/C (29.08 ± 14.13 mm²; *n* = 34) maps showed no statistically significant differences [F(2,57) = 0.56; *P* = 0.55]. Interestingly, comparisons of the three maps in terms of neural response sensitivity revealed that weak, clear, and strong responses were found in equal proportions in area 1 on the IPSI POST/X side, whereas weak responses (71%) predominated over clear (14.5%) and strong (14.5%) responses in the IPSI PRE/C map and clear (53%) or weak (38%) responses were mainly encountered in the CONTRA POST/C hemisphere. As indicated in Table 2, differences between the three populations of RFs were all statistically significant. About 67% of the strong or clear responses were observed for RFs located on either digit 2, 3, or 4 on the IPSI PRE/C side, whereas a smaller proportion (50%) of strong or clear responses was found for RFs located on the homologous digits of the hand representation derived in the CONTRA POST/C hemisphere.

As far as area 3a was concerned, single RFs recorded on the IC side were found for 46% (13/28) of the cortical sites, with a mean RF surface of 10.81 ± 6.37 mm². These RFs were mainly located on the tip of digits 2–4. Clear responses (77%) prevailed over weak ones (23%). Multiple RFs, all located on the fingertips, were observed for 54% (15/28) of electrode penetrations. On the average, these multiple RFs exhibited 2.3 ± 0.6 subfields. Subfields were mainly located on digits 3 (40%) and 4 (37%), and most subfields associated with the same recording site were located either on digits 3 and 4 (59%) or on digits 2–4 (20%), which were the finger segments most frequently stimulated on the pellet-retrieval task during the postoperative period. The subfields generally were restricted to small skin surfaces, as indicated by their mean sizes (11.35 ± 3.41 mm²). Clear responses were most common (45%); strong (26%) and weak (28%) responses were less frequent. As a general rule, responses to cutaneous stimulation were of similar sensitivity for the subfields recorded at a given recording site. In some instances, however, a best response could be defined for a particular subfield. Overall, the occurrence of best responses was similar for subfields on digits 2–4. Mixed cutaneous and high-threshold receptor inputs were encountered at 37% of the recording sites, particularly for about half of the sites with weak responses.

In OM-2147, no recording was done in area 1 before the lesion. Cross-hemispheric comparisons of the RF characteristics in this area were made at the chronic stage of the lesion. The great majority of sampled cortical sites displayed single RFs, both in the IPSI POST/X (20/22; 91%) and CONTRA POST/C hemispheres (16/17; 94%). However, RFs were smaller on the average on the side of the lesion (32.56 ± 20.67 mm² vs. 51.64 ± 33.71 mm²; *t*-test: *P* = 0.04). The majority of the RFs (85%) were located on digits 2 and 3, i.e., on the fingers preferentially used for pellet retrieval. Responses were generally strong (55%) or clear (40%), but all strong responses were found for RFs located on digit 2 (64%) or digit 3 (36%). No data on response sensitivity were available for the intact hemisphere.

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<tr>
<th>TABLE 2. Effects of cortical infarct on the response of area 3b units to hand-delivered cutaneous stimulation</th>
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<tr>
<td><strong>Single RFs in Area 3b</strong></td>
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Cutaneous responses also were found in area 3a in the lesioned hemisphere. The majority of the recorded cortical sites (12/14; 86%) exhibited multiple RFs composed of an average of 2.4 ± 0.51 subfields (total: 29). All of these subfields were located on distal phalanges, predominantly on digits 3 (34.5%) or 4 (34.5%), and to a smaller extent on digits 2 (17%) or 5 (14%). Further analysis indicated that digits 3 and 4 were both included in most combinations of subfields (67%). The mean size of individual subfields was 20.56 ± 21.25 mm². Among the 29 subfields, clear responses were more frequent (59%) than strong (24%) or weak (17%) ones. This held true for all digits except digit 5, the RFs of which more often displayed weak responses (50%).

In SM 559, both single RFs (12/31; 39%) and multiple RFs (19/31; 61%) were encountered in area 1 on the ipsi POST/X side. By contrast, larger proportions of single RFs were found on digits on that side before the lesion (12/13; 92%), and all cortical sites (25) exhibited single RFs in the CONTRA POST/C hemisphere. The size of the single RFs recorded in the IPSI POST/X hemisphere (10.64 ± 3.40 mm²) was comparable with that of the IPSI PRE/C RFs (12.23 ± 5.39 mm²) but was smaller than that of the CONTRA POST/C RFs (23.54 ± 14.07 mm²; F(2,47) = 7.87; P < 0.01). As far as multiple RFs were concerned, they displayed an average of 2.21 ± 0.44 (total = 42) subfields, all of which were located on distal phalanges, generally on digits 3 (38%) or 2 (34%) and less frequently on digit 4 (21%) or 5 (7%). Digits 2–4 were included in 84% of all subfields. Among subfield combinations, digits 2–3 was the predominant combination (53%). Individual subfields were confined to small skin surfaces (7.37 ± 1.40 mm²). No data on response sensitivity were available for the CONTRA POST/C hemisphere.

In SM 634, all IPSI PRE/C cortical sites recorded in area 1 exhibited single RFs. The large majority of the IPSI POST/X cortical sites recorded in the same area still displayed single RFs (43/47; 91%), as was the case for the CONTRA POST/C cortical sites (27/35; 71%). Due to the small size of the sample of area 1 RFs recorded before the lesion (n = 5), our analysis of RF characteristics will be limited to inter-hemispheric comparisons. The RFs recorded on the lesioned side were on the average smaller (21.21 ± 12.45 mm²) than the RFs recorded on the intact side (36.91 ± 18.59 mm²) (t = 3.84; P ≤ 0.0001). IPSI POST/X cortical sites displayed mainly clear responses (58%), with strong (23%) and weak (19%) responses being less frequent. Clear responses were predominant at cortical sites exhibiting RFs on digits 1, 2, and 4, strong responses were mainly observed for RFs located on digit 3 (45%), and weak responses were most common for RFs located on digit 5 (50%).

In area 3a ipsilateral to the lesion, multiple RFs were recorded in 80% (8/10) of the cortical sites exhibiting cutaneous responses (mean number of subfields: 2.3 ± 0.5; total: 18). All subfields were found on distal phalanges, and were
more densely located on digit 3 (44%) or 4 (39%). Cortical sites displayed subfields which were mainly associated with digits 3 and 4 (63%). To a lesser extent, some subfields also combined digits 2 and 3 (12%), or digits 2–4 (25%). Individual subfields were relatively small (9.32 ± 3.0 mm²).

**SUMMARY.**
1) Significant increases or no changes in RF sizes were observed in the still intact territories of area 3b, depending on the monkey case. 2) In all animals, conspicuous positive strength changes in the responses of sampled cortical neurons occurred both in area 3a and in area 1 on the chronic injury side. 3) In area 1, *ipsi post/x* neurons included in the cortical sectors of single-digit cutaneous representations usually displayed RFs that were smaller and responded more vigorously to light cutaneous stimulation than did *ipsi pre/c* neurons recorded before the lesion or than neurons recorded in the *contra post/c* hemisphere. 4) Furthermore, the *ipsi post/x* neurons in area 1 tended to be more responsive to cutaneous stimulation applied on the digits that were engaged in the postlesion behavioral task. 5) Similarly, multiple-RF neurons, exclusively found in the lesioned hemisphere within area 1 or area 3a, exhibited glabrous cutaneous subfields located on digit tips, most densely on the two or three fingers heavily involved in the retrieval task. 6) As a rule, stronger responses to cutaneous stimulation of the trained digits were evoked at multiple-RF cortical sites in both areas 3a and area 1.

**DISCUSSION**

*Functional deficits and the contribution of SI to motor control*

An earlier study conducted in owl and squirrel monkeys revealed that improvements in food-pellet retrieval were paralleled by major representational changes in area 3b mainly consisting of substantial gains in cortical territories with corresponding decreases in RF size in these cortical zones. Changes were related specifically to the digital tip and, to a lesser extent, to middle phalanx skin surfaces that were engaged specifically by the monkey in pellet palpation, ejection, grasping, and retrieval under the most difficult task retrieval conditions (C. Xerri, M. M. Merzenich, W. M. Jenkins, and S. Santucci, unpublished data). Similarly, changes specific to movements in the most difficult task retrieval conditions have been demonstrated to arise in the digit-movement representations in cortical area 4 in squirrel monkeys trained on the same small object retrieval task (Nudo et al. 1996a).

The present study shows that a restricted lesion of area 3b not only impairs tactile sensation but also produces a substantial loss of manual dexterity attested by inadequate grip formation and the inability to execute independent and precisely coordinated finger movements. This result is consistent with the interpretation (C. Xerri, M. M. Merzenich, W. M. Jenkins, and S. Santucci, unpublished data) that area 3b and the cortical areas that it feeds play an important role in fine, tactually guided movement behaviors.

For a several-day-long period after area 3b lesion induction, monkeys behaved as if the digital skin surfaces were insensate; this is consistent with the fact that area 3b neurons are prominently driven by inputs from cutaneous receptors (Hyvärinen and Poranen 1978a; Paul et al. 1972; Powell and Mountcastle 1959; Sur 1980; Tanji and Wise 1981) and corroborates other descriptions of deficits in somesthetic discrimination after area 3b ablation (Pavilides et al. 1993; Randolph and Semmes 1970).

In our experiments, cortical lesions incidentally extended over limited sectors of area 3a. This could theoretically account for some of the observed motor deficits because area 3a neurons predominantly receive afferents from deep mechanoreceptors (Hyvärinen and Poranen 1978a; Iwamuru et al. 1983; Jones and Porter 1980; Powell and Mountcastle 1959) and are activated during hand movement (Fromm and Evarts 1982; Jennings et al. 1983). It seems likely that a partial lesion of the digit representation in area 3b induced a severe degradation of the sensation of fingertip contact because the finger movements brought the food pellet into this cutaneous region of greatest receptor density (Johansson and Vallbo 1979) thereby diminishing the positively reinforcing effects of sensory feedback to the corticospinal system. Indeed, the role of the SI cortex in motor control is still a controversial issue (see Wannier et al. 1991). SI neurons have been shown to discharge before finger movements and electromyographic onset (Favorov et al. 1988; Fromm and Evarts 1982; Soso and Fetz 1980), which suggests that SI contributes to movement initiation. The fact that dorsal rhizotomy can eliminate premovement-related SI activity (Bioulac and Lamarre 1979) provides some support for the view that somatosensory area neurons are driven during movement execution and are involved mainly in the processing of information from peripheral receptors. It is worth mentioning that high-frequency stimulation of the somatosensory cortex was found to induce long-term potentiation at the terminals of its projection fibers to the motor cortex of the cat (Keller et al. 1990; Sakamoto et al. 1987). Our observation that lesions of area 3b induce prominent motor deficits and the fact that SI cooling causes impairment in the motor control of the distal forelimb (Brinkman et al. 1985) are compatible with the hypothesis that SI supplies motor structures with critical feedback during object manipulation and palpation and contributes to the regulation ofprehension strength (Wannier et al. 1991) and precision grasping. This hypothesis also is supported by a recent study showing that anesthesiarestricted to the distal phalanges of the fingers impaired the kinematics of grasp movements. Specifically, the finger-opening phase of grasp movements was lengthened, and the maximal finger aperture increased (Gentilucci et al. 1997).

Area 3b has only sparse direct projections into area 4 in owl and squirrel monkeys. However, it projects topographically to areas 3a, 1, and SII. These cortical areas are interconnected reciprocally, and all of the SI (and SII) fields project in complex combinations to area 4, area 6, to a strip rostral to area 6, and to the supplementary motor cortex areas(s) (Ghosh et al. 1987; Jones et al. 1978; Krubitzer and Kaas 1990; Mountcastle et al. 1992; Stepniewska et al. 1994). All of these fields including area 3b also project to basal ganglia regions implicated in motor learning and movement initiation (Graybiel et al. 1994). This complex network of intimately interconnected cortical areas and subcortical zones, which include feed-forward and feedback loops, forms a physiological substrate that promotes a high degree of integration of somatosensory cues. From its central posi-
tion in this network, lesions of the area 3b digit representation are expected to disrupt this finely tuned organization, and to thereby impair tactually guided motor skills.

**Behavioral strategy in postlesion recovery of digital dexterity**

In macaque monkeys trained on tasks of tactile discrimination and subjected to small lesions of the somatosensory cortex (areas 3, 1, and 2),Cole and Glees (1954) reported that loss of tactile sensation was compensated for by a greater use of visual cues during behavioral testing before functional recovery was achieved. Such a behavioral strategy was not observed in our monkeys. The modified Klüver board used in our experiments was designed to place greater demands on somesthetic cue processing in such a way that the animals visually located the wells in which the pellets were deposited by the experimenter but could not rely on visual cues to compensate for the degradation of cutaneous sensation because pellets were not visible during palpation, ejection, and grasping. Furthermore, the visuomotor loops seems to be too slow to regulate discrete and rapid finger movements (see Jeannerod 1988).

Surprisingly, a cortical lesion that mainly destroyed the representation of the skin surfaces involved in successful pellet retrieval did not result in any immediate change in retrieval strategy, despite the monkey achieving fewer food rewards during testing because of more clumsily produced movements. For several days, the animals continued to use the digital combinations that had come to be highly stereotyped during the final preoperative learning phase. This suggests that despite an apparently high level of motivation in the animals during postlesion retraining, the cortical lesion resulted in the monkey having only a limited awareness of the actual defective finger movements that were produced, hypothetically because the intended action had become automatic. Such a lack of awareness was also reported by Cole and Glees (1954) during the first few days after they introduced small lesions in the hand region of areas 3, 1, and 2. These observations support the idea that a well-learned behavior can be performed with minimal attentiveness and that a robust internal representation of a movement is not “corrected” until the performance becomes poorer or the behavioral context changes.

As the number of grasps per retrieval increased over a several day retraining period, the monkeys consistently began to use different finger combinations for pellet retrieval. Behavioral substitution has been reported in other postlesion studies (Goldberger 1988; Xerri and Lacour 1980; Xerri and Zennou 1989). However, this change in behavioral strategy, which also has been observed during early prelesion training sessions, was even less successful for these monkeys. Monkeys ultimately reverted to a predominant use of the deprived digits during the next several postoperative weeks. This resumption of former-strategy use resulted in nearly immediate task performance improvement and, with task-specific practice, in the gradual restoration of preoperative performance levels. Ultimately, progression from a large range of digital combinations to the more consistent use of the same two or three digits trained before these microlesions supports the hypothesis that postlesion restitution of sensory-motor functions depends on a relearning process (see Lacour and Xerri 1981; Schaefer and Meyer 1974; Xerri and Zennou 1989).

The progression of changes in cutaneous cortical representations throughout the early period after these area 3b lesions has not been documented fully. However, given the status of the cortical representations of the hand, it is reasonable to hypothesize that the recovery of high performance levels using the previously learned strategy was due to concurrent changes in SI and other cortical and subcortical representations of the hand.

**Chronic remodeling of hand representations in area 3b**

It has been shown that restricted lesions in the primary somatosensory cortex induce substantial changes in the functional representation of the skin surfaces in the cortical zones surrounding the site of injury several months after lesion induction (Doetsch et al. 1990; Jenkins and Merzenich 1987). Neurons in reorganized cortical sectors developed novel RFs and responded to stimulation of previously ineffective skin surfaces. In the raccoon (Doetsch et al. 1990), the representational zones for digits 2 and 4 were characterized by the occurrence of weaker secondary inputs originating from digit 3, the representation of which was destroyed, but also from other digits. Neurons in reorganized regions displayed larger than normal RFs, with unusual mixtures of responsiveness to glabrous and hairy skin stimulation. These changes degraded the somatotopic precision and response specificity of the SI cortical representation. In the owl monkey (Jenkins and Merzenich 1987), the skin surfaces formerly represented in the lesioned zone gained a new representation as a result of a shift in the RF location of perilesion zone neurons. Cutaneous RFs covered virtually the entire glabrous surfaces previously deprived of representation. Many of these RFs were abnormally large with an irregular topographical order. In the Jenkins and Merzenich study (1987), the postlesion reorganization occurred in area 3b and possibly partly in area 3a; other SI areas were not explored.

In the present experiments, more modest changes were recorded in the cortical zones of area 3b surrounding these lesions. Postlesion changes occurring in area 3b mainly consisted of a limited enlargement of the partially intact representational zones (e.g., OM 2149’s digit 2 representation) and/or an emergence of “new” cutaneous representations of digits formerly represented in the zone of the lesion, now recorded in novel locations, e.g., OM 2149’s digit 4 along the medial border of digit 5. The lesions made in the current experiments were larger and therefore may have limited a wider-scale reorganization of the remaining cortical sectors of area 3b. Indeed, the remodeled cortical representations appeared to be less distorted in our study than in the experiments reported by Jenkins and Merzenich (1987). Moreover, only one monkey case clearly exhibited larger RFs in the remaining digit representation of area 3b. This result is at variance with the studies by Jenkins and Merzenich (1987) and Doetsch et al. (1990) in which postlesion RFs were found to be larger than those recorded before the lesion. In both of these earlier reports, this increase in RF size applied mostly for the emergent novel RFs that again represented the skin surfaces affected by the lesion. Relatively...
few such RFs were recorded in area 3b in these five monkeys. At the same time, the clear emergence of new representations in novel 3b loci confirms its capacity for remodeling intact, perilesion cortex.

It might be noted that the definition of the area 3b-area 3a border on these functional bases is subject to some uncertainty when maps are compared after behavioral training and after these traumatic lesions. We have used the locations of relatively constant vascular features as landmarks (see Figs. 6–8) to facilitate comparisons of border positions and representational zones assigned to area 3b or 3a in prelesion, immediately postlesion and chronically postlesion reconstructions. All of the main conclusions of this report concerning the remodeling of area 3b and area 3a recorded in these trained monkeys after these cortical lesions are based on border locations defined on the basis of these constant vascular landmarks, as well as on the basis of border definitions defined by differences in the functional response properties of recorded neurons.

No reorganization was observed in the homologous area 3b in the opposite control hemisphere. That finding is consistent with the weak interhemispheric connections between homologous SI hand zones recorded in these species (Beck and Kaas 1994; Killackey et al. 1983).

**Chronic remodeling of hand representations in area 1**

Although functionally distinct, areas 3b and 1 share important basic characteristics that may favor a substitution process after injury to one of these areas to the extent that the potential for “interareal substitution” could result in the reinvigoration of similar cutaneous sensory cues. Moreover, because inputs from areas 3b, 1 and 3a are integrated in areas SII and 2, that reinvigoration could result in a restoration of more normal function at a second-stage hierarchical cortical level. Areas 3b and 1 constitute main destinations of thalamic cutaneous input from the dorsal column lemniscal system (Dreyer et al. 1974; Powell and Mountcastle 1959; Tanji and Wise 1981). Most neurons in areas 3b and 1 are phasically or phasic-tonically activated by inputs from low-threshold cutaneous receptors. Neurons in both fields, but to a larger extent neurons in area 1, also receive inputs from high-threshold cutaneous and joint receptors. RFs in area 3b are smaller than in area 1, with the latter being more sensitive to direction and movement (Hyvarinen and Poranen 1978a, b; Sur 1980). Extensive reciprocal connections exist between areas 1 and 3b, particularly between common distal digit regions, and again, these two areas have parallel connections to common somatosensory cortical zones in areas 2, 3a, and in SII (for review see Burton and Fabri 1995).

The digital representational zone of area 1 was remodeled substantially in every monkey in this series in a cortical location that was several millimeters away from the site of injury in the finger zone of area 3b. The territory of the representation of the glabrous surfaces of the digits expanded on the average by nearly two times that recorded in prelesion maps or in opposite hemisphere controls. In three of five monkeys, large zones emerged in which all neurons had cutaneous receptive fields on the tips of more than one digit.

The finding that cutaneous representations in area 1 exhibited a gain in cortical territory after an area 3b hand lesion appears to conflict with the results of a recent acute experiment conducted in the owl monkey and squirrel monkey by Garraghty et al. (1990b). That experiment showed that ablation of areas 3b and 3a eliminated the cutaneous responsiveness of area 1 neurons, suggesting that cutaneous information was sequentially processed across SI areas. Deactivation of the corresponding regions of the hand representation in area 1 was evidenced immediately after area 3b lesions, thus raising the question of the functional role of thalamic projections into area 1 originating in the ventroposterior nucleus. Garraghty et al. (1990b) proposed that these thalamo-cortical inputs may have a modulatory influence, whereas cortico-cortical input from area 3b constitute the main source of activation of area 1 neurons. Similarly, nonactivating, presumably modulatory thalamic input from the ventroposterior inferior nucleus was found in SII (Garraghty et al. 1990a). Our findings demonstrate that discharge patterns of units in area 1 actually become more tightly linked to peripheral input after chronic lesions in area 3b. This finding is consistent with other studies supporting the notion that somatosensory signals are at least partially processed in parallel in areas 1 and 3b (Dykes 1983), e.g., differences in movement-related discharges recorded in these two areas during active texture discrimination are not compatible with sequential transfer and processing of somatosensory information (Chapman and Ageraniti-Bélanger 1991; Nelson et al. 1991b).

Studies on cell and fiber degeneration support the notion that a substantial number of thalamo-cortical axons projecting into area 3b send collaterals to area 1 (Clark et al. 1953; Jones and Powell 1970). One might hypothesize that the degeneration of a subset of target cells within the middle layers of area 3b could result in a strengthening of afferent inputs to target cells in area 1, thereby unmasking formerly ineffective synaptic connections for afferents originating from common skin surfaces. The skin surfaces best represented in the reorganized area 1 did not exactly match those deprived of representation in area 3b but were more specifically related to skin surfaces predominantly engaged in postoperative behavioral training. It therefore seems likely that behaviorally important peripheral stimulation induced the reshaping of thalamo-cortical circuits in a use-dependent fashion, ultimately resulting in the selective expansion of specific cutaneous representations within area 1. This hypothesis theoretically implies that use-driven changes occurring in area 3b in intact animals may be at least partially expressed in area 1. In fact, use-dependent changes in area 3b were not clearly expressed in area 1 in our intact monkeys; this confirms the results of a previous study reporting a lack of significant area 1 changes in cortical sectors representing skin territories selectively engaged in behavioral training in which cutaneous stimuli moved across the skin (Jenkins et al. 1990). These findings seem to be consistent with the observation that area 1 neurons exhibit depressed activity during active manual exploration (Nelson 1987; Nelson and Douglas 1989; Nelson et al. 1991a). Nevertheless, it seems reasonable to assume that after an area 3b lesion, significant alterations in the gating of reafferent input to area 1 during active touching may develop in the long term. It is also conceivable that territorial expansion within area 1 of the representation of the cutaneous regions specifi-
independently stimulated during postoperative training can be accounted for partly by relevant signals provided by the "efference copy" of the motor command potentially originating in area 4. Indeed, in this motor area, which sends projections to area 1 (Ghosh et al. 1987; Jones et al. 1978; Krubitzer and Kaas 1990), the motor representation of distributed finger movements is remodeled substantially in monkeys trained on the digital dexterity task used in the present study (Nudo et al. 1996a).

Ultimately, the existence of postlesion alterations in area 1 cutaneous representations functionally linked to behaviorally trained digits supports the view that this cortical field became increasingly involved in the sensory regulation of tactually guided digital prehension, potentially compensating for the representational deficits induced by the area 3b lesion.

**Emergence of cutaneous representations in area 3a**

In four of our monkeys, cutaneous responses emerged in large, often discontinuous sectors of the hand representation of area 3a. In the remaining monkey, the area 3b lesion expanded over a wide sector of area 3a, probably precluding the emergence of cutaneous input within this cortical field. This finding is consistent with a previous study suggesting the appearance of novel cutaneous representations within area 3a in owl monkeys trained to receive mechanical stimulation moving across the glabrous skin of the fingers (Jenkins et al. 1990). More recently, the emergence of a cutaneous response zone in area 3a was also reported in owl monkeys trained on a frequency discrimination task involving a relatively constant skin locus of a single digit (Recanzone et al. 1992a). In these two studies, cutaneous responses occupied a cortical band neighboring the rostral edge of area 3b. Recanzone et al. (1992a) recorded novel, emergent cutaneous responses in a cortical region extending beyond a narrow (~100–300 μm) cytoarchitectonic transition zone between areas 3b and 3a, in which neurons potentially could respond to either cutaneous or deep-receptor input. However, the authors did not observe cutaneous inputs in territories that were more than ~1 mm rostral to the area 3b-3a border, whereas in our experiments, cutaneous responses were recorded beyond that distance in two monkeys—and thus in a cortical region in which cutaneous inputs have not been demonstrated to emerge in other behavioral training studies conducted in these species. In the current study, animals primarily engaged their fingertips to guide finger movements for small object retrieval. The novel input emerging in area 3a originated exclusively from the tips of the digits in every monkey and primarily from the fingers most frequently engaged in the postoperative behavioral training. By contrast, in the maps reconstructed by Recanzone et al. (1992a) in a behavior that predominantly involved proximal digit segments, the cutaneous representations extended most prominently across proximal digit segments as well as onto large zones all up and down the glabrous surfaces of the directly stimulated and adjacent digits.

Neurons in area 3a are activated predominantly by inputs from receptors that innervate muscles and joints (Costanzo and Gardner 1981; Friedman and Jones 1981; Lucier and Ruegg 1975; Philips et al. 1971). However, cutaneous inputs to area 3a are delivered anatomically from the thalamus (Cusick and Gould 1990; Darian-Smith and Darian-Smith 1993; Lin et al. 1979) and from area 3b (Jones and Powell 1969; Shanks et al. 1985). Area 3a neurons are known to receive subthreshold inputs from cutaneous nerves (Kang et al. 1985; Magillis et al. 1983; Zarzecki and Wiggan 1982).

It has been hypothesized (Jenkins et al. 1990) that the shift in effective input dominance from deep receptor to cutaneous receptor in area 3a reflects an expansion of cutaneous representation in area 3b, presumably through projections of area 3b onto area 3a (Jones and Porter 1980; Jones and Powell 1970; Vogt and Pandya 1977). That could not account for the strongest and most common area 3a responses in the present studies because lesions destroyed a substantial sector of the 3b hand area and the border region of 3a. The emergent representations recorded in these studies therefore cannot be regarded as an expansion of 3b representations. Given the loss of area 3b inputs, they likely result from behaviorally driven strengthening of thalamo-cortical or from other cortico-cortical inputs predominantly from the skin of behaviorally engaged digit tips.

It has been proposed that area 3a exerts a modulating influence during movement; this seems consistent with the observation that this area is linked tightly anatomically to the supplementary motor area and postcentral areas 2 and 5 (Darian-Smith et al. 1993). It is therefore plausible that part of the area 3a reorganization is mediated by changes affecting these cortical fields.

The large-scale emergence of cutaneous representations specifically devoted to restricted skin surfaces stimulated during digital manipulation strongly suggests that the functional contribution of area 3a to this behavioral performance has shifted during the postlesion period by providing new cutaneous sensory feedback formerly arising from area 3b and thus potentially contributing to a representational substitution.

**Neural plasticity mechanisms underlying cortical reorganization**

There are important unresolved questions about the neural plasticity mechanisms that underlie these long-term alterations in cortical maps. Restructuring of neural morphology and changes in the efficacy of synaptic transmission both constitute putative mechanisms that are not mutually exclusive. Theoretically, the expansion of the cortical zones of representation discussed above could be mediated at least partially by morphological change mechanisms such as sprouting of collateral branches of axons, extension of dendritic arbors, and reactive synaptogenesis. Cortical damage in adult rats can lead to an increase in the dendritic arborization of neurons in undamaged regions of the cortex (Colb and Gibb 1991; Colb and Wishaw 1989) assumed to be related to functional recovery (Jones and Schallert 1994). Although sprouting of thalamocortical and/or intracortical fibers over a long distance is very unlikely to occur in the cortex of the adult monkey (for a review, see Snow and Wilson 1991), para-terminal collateral sprouting of intact axons and synaptogenesis as evidenced in many parts of the adult brain almost certainly does occur (see Cotman and Nieto-Sampedro 1982; Cotman et al. 1984). These mechanisms induce changes in local circuits that could contribute...
to restructuring the extrinsic connections to or the intrinsic connections within a local cortical area, thereby mediating representational translocation or expansion.

The growth of dendritic arbors and increased synapse numbers have been recorded in numerous environmental enrichment studies targeting the cerebral cortex and have been described to occur within the cerebellar and cerebral cortex of intact animals subjected to extensive learning (e.g., Black et al. 1990; Greenough et al. 1994; Withers and Greenough 1989), whereas simple physical exercise does not result in changes in the numbers of synapses (Black et al. 1990). It is probable that postlesion training induces use-dependent patterns of neural activity that can selectively reshape the neuronal-morphological structure of the undamaged cortical areas of adult animals, thus supporting the representational expansions of behaviorally stimulated skin surfaces.

In our experiments, representational translocations found in area 1 were recorded over cortical distances of <1 mm, i.e., within the estimated anatomic limits of the widespread arborizations of the thalamocortical neurons (Garraghty and Sur 1990; Snow et al. 1988). According to a recent double-labeling study, if the extent of intracortical arborization of single thalamocortical axons is no greater than 600 μm, adjoining cells in the same representational region of the thalamus can project onto cortical targets as distant as 1.5 mm (Rausell and Jones 1995). A limited number of axons give rise to widely distributed connections and display terminal branching scattered over 2 mm (Garraghty and Sur 1990). As shown by Landry et al. (1987), a single thalamocortical axon can form a high concentration of synaptic boutons at the center of its arborization and therefore provide strong input to its main target cells, whereas more peripheral branches provide weaker inputs to more distant cells. It should be noted that most directly driven thalamocortical zone is itself a hypothetical source of effective excitatory inputs via the still more widely dispersed collateral axons of directly engaged neurons. This can create a relatively powerful input source for area 1 or area 3a neurons that are up to ~2 mm distant from the cortical zone that is overtly, directly excited by thalamic inputs.

Unmasking of already existing but formerly ineffective inputs can result from the removal of intracortical inhibition, which is commonly considered to be the main mechanism of cortical map remodeling (Calford and Tweedale 1988; Dykes et al. 1984; Jones 1993). Unmasking of already existing but subthreshold inputs cannot by itself account for the preferential emergence of representational zones of fingertip glabrous surfaces trained on the digital dexterity task. However, it has been shown that relief from inhibitory influences can facilitate the strengthening of synaptic efficacy resulting from tetanic stimulation within the neocortex (Artola and Singer 1987, 1993). This process can facilitate an activity-dependent increase in synaptic plasticity, and thus contribute to the selective reshaping of cortical maps.

Activity-dependent modifications in the synaptic weight via a ‘Hebbian’ mechanism (Edelman and Finkel 1984; Merzenich and Sameshima 1993; Merzenich et al. 1988) can also play a critical role in cortical map remodeling. There is growing evidence that N-methyl-D-aspartate-receptor–based long-term potentiation is, indeed, contributing to progressive changes recorded in cortical plasticity models (Garraghty and Muja 1996). The widespread, divergent, and overlapping arborization of the thalamocortical fibers implies that clusters of thalamic neurons driven by peripheral input from contiguous skin surfaces potentially can gain access to large cortical territories. The long-term emergence of cutaneous input in both areas 1 and 3a is more compatible with behaviorally dependent reweighting of cutaneous inputs than it is with the passive unmasking of already existing input. Selective unmasking of latent connections can mediate the substitution of effective inputs, resulting in the translocation and expansion of representations over formerly noncutaneous cortical sectors for the corresponding regions of the skin.

Cutaneous representations of trained skin surfaces were found to display a topographic expansion within area 1. Such a topographically organized gain in cortical territory also has been found in area 3b in studies in which repetitive stimulation was delivered to specific skin surfaces of the fingers (Jenkins et al. 1990; Recanzone et al. 1992b) and the body ventrum (Xerri et al. 1994b). This phenomenon involves an orderly redistribution of excitatory thalamocortical and intracortical inputs that very likely requires a spatiotemporally structured activation of the relevant cortical circuits through an ongoing, competitive, use-dependent process (Merzenich et al. 1988, 1990; Pearson et al. 1987).

Receptive field plasticity in reorganized cutaneous representations

As a general rule, robust or clear cutaneous responses were found at many cortical sites in sectors formerly devoted to deep-receptor input representation in both areas 1 and 3a of lesioned hemispheres. Neurons with these emergent RFs displayed normal-sized single or multiple cutaneous RFs. Similar results were obtained in area 3a in earlier studies in owl monkeys trained on a frequency discrimination task (Recanzone et al. 1992a). In the present study, the spatial densities of RFs across the behaviorally stimulated fingers were greater than the density of the RFs across the other fingers. Recanzone et al. (1992a) reported that large skin surfaces of the hand were represented in these novel area 3a cutaneous representations despite the restricted skin loci stimulated during the behavioral task. This finding is at variance with our results, in which only directly engaged fingertips—and no other glabrous skin—emerged in representation in area 3a.

The occurrence of multiple RFs in emergent cutaneous representations in the infarcted hemisphere was a conspicuous feature of areas 1 (in 2 monkeys) and area 3a (in 4 monkeys). Furthermore, these multiple RFs were found to exclusively cover the glabrous skin of the distal phalanges, and cutaneous subfields of each RF were more densely located on the two or three fingers most frequently engaged in the postoperative training. Studies on the visual (Ferster and LeVay 1978; Gilbert and Wiesel 1983) and somatosensory cortices (Landry and Deschenes 1983) have reported that many thalamic neurons give rise to terminal arbors bearing dense patches of synaptic boutons separated by zones almost devoid of boutons. These morphological features are likely to favor the occurrence of discontinuous RFs in the somatosensory cortex, especially because noncontiguous
skin surfaces (e.g., several fingertips) are stimulated almost simultaneously during digital exploration and retrieval involving synchronous movements of two or three fingers.

The postlesion representational remodeling influence of use-driven activity was also attested to in our study by a significant decrease in the size of single-digit RFs in cutaneous representational zones of area 1 that were ipsilateral to the cortical infarct. Alteration in RF size is generally assumed to occur via modification of functional inputs rather than through anatomic changes. By that interpretation, a decrease in RF size implies that cortical neurons began responding to a smaller fraction of their anatomicallly delivered inputs, reflecting a dynamic process of segregation of temporally coincident input to cortical cells (Clark et al. 1988; Jenkins et al. 1990; Merzenich et al. 1988, 1990). This mechanism is not limited to the cortex, but can potentially operate at all levels of the somatosensory system. The RF size decrease of the area 1 neurons was correlated with an areal extent increase of the cortical representation of the trained skin surfaces. This finding is consistent with the area 3b results obtained in the same and other animals before the lesion (C. Xerri, M. M. Merzenich, W. M. Jenkins, and S. Santucci, unpublished data) and those obtained in other experiments performed on behaviorally trained owl monkeys (Jenkins et al. 1990) and nursing rats (Xerri et al. 1994b).

The observation that in the lesioned side, area 1 neurons in the representational zones of the trained digits displayed greater sensitivity to cutaneous stimulation than did homologous contralateral untrained digit skin surfaces points out a probable role played by peripheral, temporally coupled inputs in strengthening the effectivenesses and/or increasing the numbers of synaptic connections with cortical cells, and/or of engaged, intrinsically coupled cortical neurons.

Overall, our findings indicate that sensory-motor deficits induced by an area 3b lesion ultimately reflect a severe disruption in complex interareal functional connections and that in the long term, deprivation of a major source of sensory integration resulting from a area 3b lesion can induce a drastic, presumably adaptive reorganization of effective cortico-cortical and thalamo-cortical interactions in the processing of tactile information within areas 1 and 3a. Postlesion changes in the distribution of excitatory and inhibitory input to these areas are assumed to constitute part of the neural substrate of digital dexterity recovery.

Representational remodeling: diaschisis versus vicariation

Von Monakow (1914) originally described diaschisis as a suppression of function in regions adjacent to or remote from, but physiologically connected to, the primary locus of injury. The term diaschisis is used classically for sudden occurrence of symptoms. Von Monakow proposed, however, the possibility of a “slowly creeping diaschisis” (Riese 1984). In the case of focal ischemia, electrophysiologic activity, cerebral blood flow, and metabolism tend to be disrupted within an ischemic penumbral region located beyond the boundaries of the infarct. Indeed, human PET studies of cerebral blood flow and cerebral oxygen metabolic rate have evidenced a “misery perfusion” syndrome in morphologically intact cortical regions in the first 2–4 days after an infarct (Baron 1985). The penumbra is affected by a gradual excitotoxicity process that may lead to neuronal death (Astrup et al. 1981). Recent electrophysiologic mapping of the forepaw representations of SI has confirmed the outward expansion of a focal cortical infarct like those induced in these monkeys during the first 12 h postlesion (Coq and Xerri 1997). Neurological improvement after cortical stroke often has been considered a resumption of function within the cortical area surrounding the lesion affected by a partially reversible diaschisis effect.

Garraghty and colleagues (1990) recently recorded an acute drop in the responsiveness of area 1 neurons after an area 3b lesion. This could represent an acute diaschisis in the von Monakow sense. It is possible that the immediate, dramatic evident skin anesthesia and grasping weakness are related to these hypothetical diaschisis effects in this important second cutaneous SI field and that their recovery after several days is due to a postlesion reactivation of a temporarily inactivated area 1 cortical zone. It is also possible that the loss of movement control over longer postlesion times as assessed by this behavior is also due to such diaschisis effects—and that recovery of excitability in area 1 contributes to progressive behavioral recovery. At the same time, the specificity of plasticity effects recorded in the chronic recovery period for the specific sensory surfaces engaged in the behavior strongly supports the conclusion, especially for the emergence of cutaneous representations over large sectors in area 3a, that strong vicariation effects come into play.

In the present study, alterations in 3b topographical representations within the cortical sectors neighboring the lesion may be overestimated to the extent that some neurons classified as unresponsive at the time of lesion assessment may have been ‘‘silenced’’ by a diaschisis-like effect. This view is, however, not compatible with the clear evidence of a gradual expansion of the dead zone after the induction of this type of lesion (e.g., see Coq and Xerri 1997). Moreover, for all of the cases in which diaschisis could plausibly account for recorded plasticity effects on the margins of lesions induced in this study, the extent of the tissue that was lost or silenced by these lesions appeared to be greater at the time of chronic reconstruction of cortical responses than was the areal estimate of the lesion at the time of its induction. Moreover, emergence of nontopographic representational zones (e.g., digit 4 in OM 2149) in novel locations within 3b that are well removed from their preslesion locations and from lesion boundaries and that fall within zones that were actively driven by other hand inputs immediately after lesion induction cannot be easily reconciled with a simple dissipation of diaschisis.

In other animal studies, investigators have correlated behavioral disabilities (e.g., reaching for food with the appropriate limb) and a depression in sensory evoked potentials recorded in tissue adjacent to small electrolytic lesions induced in the motor cortex. Normalization of the evoked potentials in intact cortex adjacent to the lesions paralleled recovery of behavior (Glassman 1971; Glassman and Malamut 1976). Boyeson et al. (1991) reported that after a cortical laceration or contusion, adjacent cortical regions exhibited a transient elevation of threshold for the evocation of movements. Normal thresholds were again recorded 2 wk after the injury. Although these data support the hypothesis of remote and transient depressive effects of cortical damage,
functional recovery was not attributed to dissipation of a diascisis-like effect but to changes taking place in subcortical structures and in the cerebellum.

Boyeson et al. (1991) also found that after laceration or contusion-induced damage to the hindlimb area of the rat motor cortex, no responses of the affected limb could be evoked from new cortical areas in the injured or the intact hemispheres. The authors concluded that behavioral recovery that occurs after these unilateral cortical lesions (Feeney et al. 1981) is not accounted for by a reorganization of the ability to elicit responses from emergent locations in the motor cortex. This lack of cortical reorganization is at sharp variance with data recorded in another rat model (Castro-Alamancos and Borre 1995) and more pertinently, with data obtained in the monkey, where vicariation in an injured cortical field, area 4, would appear to have been demonstrated. Indeed, Coles and Glees (1954) reported that after undercutting the thumb representation area in motor cortex in thrsus monkeys, the loss of pinch strength recovered within 3 wk. Cortical stimulation in an area 4 zone surrounding the injury, in which no thumb movements could be elicited before the lesion, evoked such movements after the lesion. In contrast, Nudo and Miliken (1996) found that movements formerly evoked from an infarcted zone of hand representations in the primary motor cortex (area 4) in squirrel monkeys did not reappear in the surrounding cortical sector after a focal ischemic infarct. The extent of digit area adjacent to the infarcted zone was even decreased by 40%. However, after rehabilitative training, motor map reorganization marked by evident vicariation was clearly observed. The spared digit and wrist-forearm representations increased by 15 and 58%, respectively. Moreover, new digit motor representations were found in adjacent cortical zones formerly devoted to elbow and shoulder representations (Nudo et al. 1996b). In the present study, we used trained monkeys to assess functional recovery, as did Glees and Cole (1950) and Nudo et al. (1996b). Still, although vicariation is demonstrated to be an unequivocal part of representational remodeling in the current studies, it remains possible that diaschisis is also contributing to some aspects of these behaviorally recorded effects.

At the same time, it is concluded that representational substitution—vicariation—can mediate behavioral restitution after focal cortical stroke. Selective lesions in emergent, reorganized cortical areas aimed at inducing functional compensation could provide decisive support for this conclusion.

Reorganization of SI cutaneous representations does not preclude that postlesion recovery of coordinated finger movements also requires the increased contribution of proprioceptive feedback. Although the basis of the idiosyncratic reorganization of the SI cutaneous fields is still unclear, it very likely relates to individual strategies and sensorimotor experience because the postlesion changes were clearly dependent here on idiosyncratic behavior. More generally, our study supports the view that cortical map plasticity can be very strongly influenced by appropriate rehabilitation programs after brain damage.

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