UNITED NATIONS EDUCATIONAL, SCIENTIFIC AND CULTURAL ORGANIZATION
INTERNATIONAL CENTRE FOR THEORETICAL PHYSICS
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SMR.853 - 15

ANTONIO BORSELLINO COLLEGE ON NEUROPHYSICS

(15 May - 9 June 1995)

"The Reorganization of Sensory and Motor Maps in Adult Mammals"

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These are preliminary lecture notes, intended only for distribution to participants.

In: The Cognitive Neurosciences. M.S. Gazzaniga, Ed. MIT Press Cambridge, Mass.

4 The Reorganization of Sensory and Motor Maps in Adult Mammals

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ABSTRACT Sensory representations in developing mammals have long been known to be plastic and subject to environmental influences during certain critical periods. There is also a growing awareness that receptive field properties of neurons in cortical maps in adult mammals are dynamically maintained and vary with learning, experience, and conditions of stimulation. In addition, major perturbations in sensory activation, such as those produced by lesions of sensory surfaces, are capable of producing major reorganizations in sensory maps. Such changes have been demonstrated in a range of mammalian species, in auditory, somatosensory, visual, and motor systems, and at both cortical and subcortical levels in these systems. Some of the alterations in maps occur immediately after the sensory manipulation, suggesting the rapid potentiation of previously weak synaptic influences, whereas other modifications develop over days to weeks, time enough for changes in neurotransmitter and neuromodulator expression, synaptic turnover, and neuronal growth. Some types of reorganization clearly suggest the growth of new connections in the central nervous system. Adult plasticity in sensory and motor systems may be responsible for improvements in sensorimotor skills with practice, adjustments to sensory loss and impairments, recovery from central nervous system damage, and misperceptions and mislocalizations after damage to sensory systems.

We are all aware of changes in behavior that must reflect significant, persisting changes in brain microstructure. Most notably, we improve in sensory and motor skills with practice, adjust to visual and auditory impairments, and recover abilities lost immediately after brain damage. It also seems reasonable to suppose that alterations in sensory and motor systems themselves have much to do with these behavioral adjustments. Sensory and motor systems consist largely of interconnected orderly representations of sensory surfaces and body effectors, and such maps occupy most of the cortex in most mammals (Kaas, 1987). Thus, much of the brain of most mammals is directly involved in processing sensory information and in mediating motor performance. If these systems are mutable in adult mammals, much of the brain can be directly involved in behavioral change. However, the widespread belief was that sensory systems are highly plastic only during a short developmental time, the critical period (e.g., Fox, 1992; Hubel and Wiesel, 1970; see also Rauschecker, 1991). Early, innovative efforts to demonstrate plasticity in subcortical somatosensory representations of rats (e.g., Wall and Egger, 1971) and monkeys (Pollin and Albe-Fessard, 1979) were viewed with skepticism, few investigators were drawn into studies of adult plasticity, and a general acceptance of the validity of adult plasticity failed to emerge. This situation changed with investigations of adult plasticity in cortical representations in the early 1980s.

The clear advantage of studying sensory representations in cortex, rather than in subcortical structures, is that cortical maps often are large and easily accessible on the surface of the brain. Thus, it is possible to obtain detailed maps of normal organization using microelectrode mapping techniques (see Welker, 1976), to employ procedures that might alter the internal structure of normal representations, and then to compare detailed maps from experimental and control animals. As in the earlier experiments on reorganization in the spinal cord and brain stem, the initial experiments on plasticity in somatosensory cortex depended on producing major deprivations via nerve cuts or crushes. Such major deprivations, as for eye closures or nerve cuts in studies of developmental plasticity, were believed to be the most likely to produce map changes of magnitudes that could be effectively measured and documented.

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This expectation was realized, and convincing changes in sensory, and now motor, maps have been demonstrated repeatedly in a number of laboratories (for review, see Kaas, 1991).

Although the existence of adult plasticity seems well established, important questions remain. First, what is the functional significance of map plasticity? The plasticity observed in the deprivation and overstimulation experiments appears similar to the more subtle changes in receptive field structure reported after manipulations of sensory stimuli (Pettet and Gilbert, 1992), changes in attention or emotional state (Desimone et al., 1990), and learning (Weinberger, David, and Lepun, 1993). The same neural mechanisms may be mediating map changes and some of these rapidly induced changes in receptive fields. Thus, experiments on the more dramatic forms of adult plasticity may help reveal the neural mechanisms of learning and perceptual modification, and changes in sensory and motor maps after deprivation might be those that mediate sensorimotor adjustments and learning. In addition, changes in maps might mediate recovery after damage to the nervous system. For example, after partial lesions of a cortical representation of the visual field—the middle temporal visual area (MT)—monkeys rapidly recover from a localized deficit in visual tracking (Newsome et al., 1985). Perhaps, as suggested by Yamasaki and Wurtz (1991), remaining parts of MT (or other areas) reorganize to recover and utilize the missing information. Finally, some reorganizations may not mediate recoveries, compensations, or learning, but may produce further malfunction by producing inappropriate responses to sensory stimuli. For example, mislocalization to an amputated arm of sensory tactile stimuli on the face in humans (Ramachandran, Rogers-Ramachandran, and Stewart, 1992) may be a result of the reorganization of somatosensory representations so that cortex normally activated by the arm is activated by receptors in the face, as can occur in monkeys with sensory loss (Pons et al., 1991). Thus, "arm" cortex may not respecify when activated by afferents from the face to help mediate face sensation but may persistently and incorrectly signal inputs from the missing arm. Tragically, similar types of reactivation without respecification could be responsible for the phenomena of phantom and thalamic pain (e.g., Melzack, 1990), where normal tactile stimuli become intensely painful. Because adult plasticity may relate to any or all of these possibilities, experiments on adult plasticity afford opportunities to make significant advances in understanding behavioral phenomena that currently seem mysterious.

Another issue is where does plasticity occur? Historically, there has been some reluctance to believe that primary sensory maps are capable of change in adults because stability in function would seem to depend on stability in representation. Instead, changes reflecting experience were thought to occur in higher-order association cortex. Although it is now clear that plasticity does occur in primary sensory areas, levels of plasticity may vary across levels in a system, and higher areas may be even more plastic. Studies of plasticity in primary sensory areas have not been motivated by the belief that these structures are the most likely place for placticity to occur but by practical concerns. The internal organizations of only primary and a few other sensory representations are known in enough detail, and can be revealed with enough fidelity, that modest changes in organization can be detected. Thus, there has been only limited progress in assessing the relative amounts of plasticity that occur at other levels in sensory systems, and more research is needed. In addition, comparisons across levels can be complicated by differences in the organization of sensory representations at successive levels, so that local changes in the activation pattern at one level may produce widespread effects at subsequent levels. It is important to determine whether changes in map structure observed at one level can be attributed to modifications relayed from another level.

Still another important issue is what mediates adult plasticity? Are the mechanisms similar to or different from those that permit developmental plasticity? Whereas altered growth and the formation of new connections can be important in developmental plasticity, regeneration and growth generally are not considered to be features of adult plasticity. Nevertheless, recent evidence suggests that axonal growth may be important.

The dynamic and changeable quality of sensory representations

Amputation of body parts and section or deactivation of sensory nerves (Metzler and Marks, 1979; Calford and Tweedale, 1988; 1991b; Byrne and Calford, 1991; Nicoletis et al., 1993a), retinal lesions (Chino et al., 1992), and electrical stimulation of cortex (Nudo, Jenkins, and Merzenich, 1990; Recanzone, Merzenich, and Dinse, 1992) all produce immediate changes in

receptive fields of central neurons. These types of rapid changes seem very similar to the alterations produced by other more normal manipulations of neural pathways. For example, receptive field sizes and locations can be rapidly modified by directed attention (e.g., Desimone et al., 1990), associative sensory stimulation and learning (e.g., Delacour, Houcine, and Talbi, 1987; Diamond and Weinberger, 1989; Gonzalez-Lima and Aqudo, 1990; Scheich et al., 1992; Diamond, Armstrong-James, and Ebner, 1993; Weinberger, David, Lepun, 1993), stimuli falling outside the classical receptive field (e.g., Allman, Miezin, and McGuinness, 1985; Fiorani et al., 1992; Gilbert, 1992; Pettet and Gilbert, 1992), and repetitive stimulation (e.g., Bonds, 1991; Lee and Whitsel, 1992). The usual explanation for such rapid changes is the selective potentiation or weakening of various excitatory and inhibitory components of the multitude of synaptic inputs that affect the excitability of any central neuron. The connections within sensory hierarchies are highly divergent and convergent, and the traditional receptive field of a neuron reflects only a portion of its total synaptic input (see Snow et al., 1988; Roberts and Wells, 1990).

Although it is uncertain how the dynamics of synaptic influence shift from moment to moment in the situations just described, a number of possibilities have been discussed in the general context of the unmasking of ineffective synapses (Wall, 1977; Killackey, 1989). More specifically, it has long been obvious that selective denervation could remove feedforward activation of neurons with locally distributed inhibitory connections, thereby reducing the inhibition on neurons to the extent that they express previously subthreshold inputs. Indeed, when local inhibitory mechanisms are chemically suppressed, receptive fields of neurons in the altered cortex immediately enlarge (e.g., Dykes et al., 1984; Alloway, Rosenthal, and Burton, 1989; Jacobs and Donoghue, 1991).

Another possibility is that peripheral amputations and other traumatic manipulations, even in anesthetized animals, briefly activate widespread modulating systems that produce response enhancement. Intense, painful, and otherwise meaningful stimuli could activate the widely distributed noradrenergic and cholinergic brainstem projection systems, both of which have been associated with neuromodulation and potentiation (Armstrong-James and Fox, 1983; Foote and Morrison, 1987). The widespread release of excitatory neurotransmitters could enhance subthreshold activity, thereby enlarging receptive fields. The observation that amputations and denervations produce immediate expansions of receptive fields in both contralateral and ipsilateral somatosensory cortex (Calford and Tweedale 1990, 1991a,b) suggests the involvement of widespread systems. Both noradrenergic and cholinergic systems have been implicated as "permissive" factors in neuronal plasticity induced by learning and experience (Kasamatsu and Pettigrew, 1976; Bear and Singer, 1986; Ebner and Armstrong-James, 1990; however, see Tromblay et al., 1986) and in reorganizations of sensory maps after partial sensory deprivations (Juliano et al., 1990; Kano, Iino, and Kano, 1991; Lee, Weisskopf, and Ebner, 1991; Haniseh et al., 1992). Finally, the rapid strengthening or potentiation of synapses when the presynaptic and postsynaptic neurons are coactive, as suggested by Hebb (1949), is a mechanism of rapid change that may be mediated by *N*-methyl-D-aspartic acid (NMDA) receptors (Brown et al., 1988; Brown, Kairiss, and Keenan, 1990; Bear et al., 1990), perhaps in conjunction with neuromodulating substances.

The ability of all cortical maps to reorganize

In addition to the short-term dynamic changes in sensory representations, there are additional, often more dramatic alterations that take time to be expressed. These slowly developing changes may be dependent on mechanisms that require protein synthesis, structural modifications in neurons, and persisting changes in levels of neuromodulators and transmitters and their receptors.

Many of the early experiments demonstrated slowly developing reorganizations of primary somatosensory (area 3b) cortex of owl and squirrel monkeys. In these monkeys, the central fissure is shallow or absent, and most or all of the hand representation is accessible under visual guidance on the dorsolateral surface of the brain (figure 4.1A) The normal representation of the hand in area 3b is extremely orderly (figure 4.1B, C) in that the glabrous skin of the digits is consistently represented from thumb to little finger (digits 1–5) in a lateromedial cortical sequence, with the tips rostral and the bases caudal, followed by the pads of the palm (Merzenich et al., 1978; Kaas et al., 1979; Sur, Nelson, and Kaas, 1982 . The dorsal skin of the hand activates an extremely small proportion of the hand representation, typically along the margins of the tissue devoted to the glabrous skin. Our original manipulation of the input

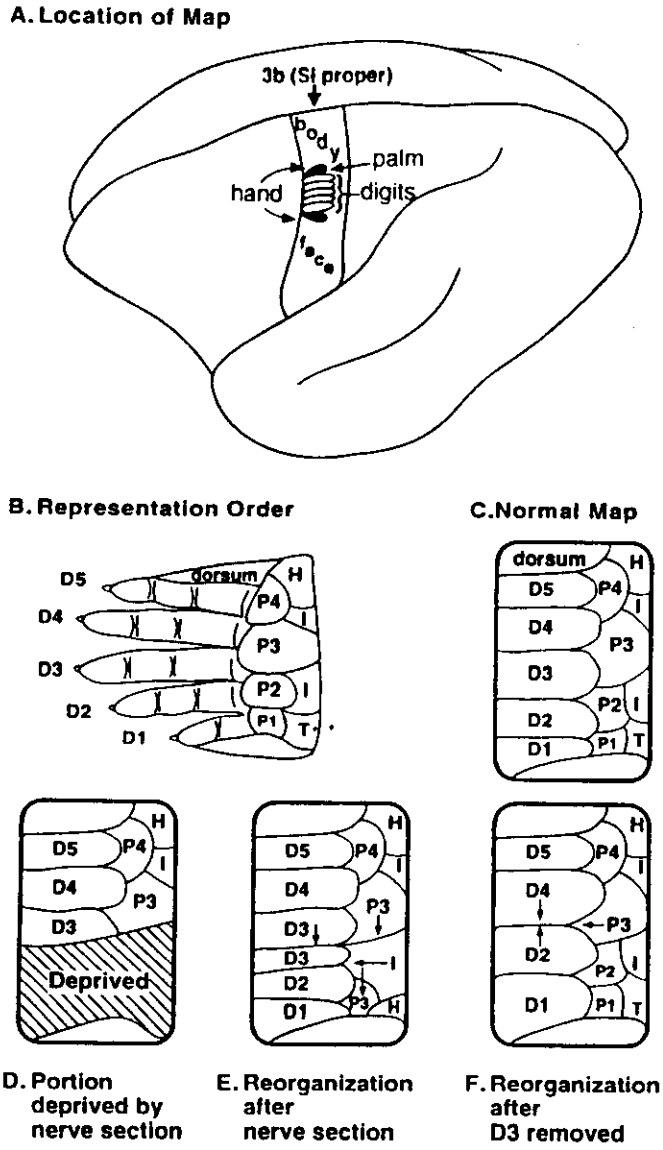

FIGURE 4.1 Reorganization of primary somatosensory cortex (area 3b) in owl monkeys. (A) Dorsolateral view of an owl monkey brain showing the location of the hand representation within area 3b. (B) Ventral surface of the hand split along the palm to reflect the somatotopic pattern of the hand representation. (C) Pattern of the hand representation in area 3b. (D) Portion of the hand representation deprived of normal activation by section of the median nerve. (E) Somatotopic pattern of the reorganized cortex months after median nerve section (based on Merzenich et al., 1983a). Most of the reactivation is from receptors on the dorsum of digits 1–3. (F) Reorganization after D3 removal (based on Merzenich et al., 1984). Digits and pads of the hand are traditionally numbered. Insular (I), hypothenar (H), and thenar (T) pads are indicated.

to this map was to cut and ligate the median nerve to the hand (Merzenich and Kaas, 1982; Kaas, Merzenich, and Killackey, 1983; Merzenich et al., 1983a; 1983b). This nerve subserves the thumb half of the glabrous hand, and cutting it removed all input from cutaneous receptors of the glabrous surfaces of digits 1, 2, and half of 3, and adjoining pads of the palm. The corresponding portion of the map in area 3b was thereby deprived of its normal source of activation (figure 4.1D). Immediately after the deactivation, some of the deprived cortex already could be activated by new inputs, but it took weeks to months before all of the deprived cortex was reactivated, mainly from inputs from the back of the hand (figure 4.1E). Thus, inputs from the back of the hand replaced inputs from the front of the hand, producing a greatly enlarged representation of the hairy surfaces of digits 1–3. In related experiments, Merzenich and colleagues (1984) demonstrated reorganization of the hand map after removing a digit (figure 4.1F). After several months of recovery, the part of area 3b normally devoted to the glabrous surface of the amputated third digit became activated by inputs from the glabrous surfaces of digits 2 and 4 (see Code, Eslin, and Juliano, 1992, for additional results). These experiments established the concept that neurons in the somatosensory cortex of adult mammals can acquire new receptive fields. Subsequently, a number of other manipulations have been shown also to alter map structure in area 3b of these and other monkeys (see Kaas, 1991).

Similar results have been obtained after deprivation from primary somatosensory cortex (S1) of other mammals. After removal of a digit in raccoons, S1 cortex formerly activated by that digit gradually becomes responsive to the adjoining digits (figure 4.2) (Welker and Saidenstein, 1959; Rasmusson, 1982; Kelahan and Doetsch, 1984; Turnbull and Rasmusson, 1991). The reactivation is particularly obvious in raccoons because they have a large hand representation that is exposed primarily on the cortical surface of the brain, and shallow sulci separate the gyral representations of the individual digits. Thus, the location of cortex normally representing any digit is apparent on visual inspection of the cortical surface, and abnormal organization is easily revealed. Reactivations of deprived portions of S1 after removing inputs have also been reported for: (1) rats, in which inputs from the saphenous nerve of the hind paw expanded their cortical territory to occupy partially the sciatic nerve terri-

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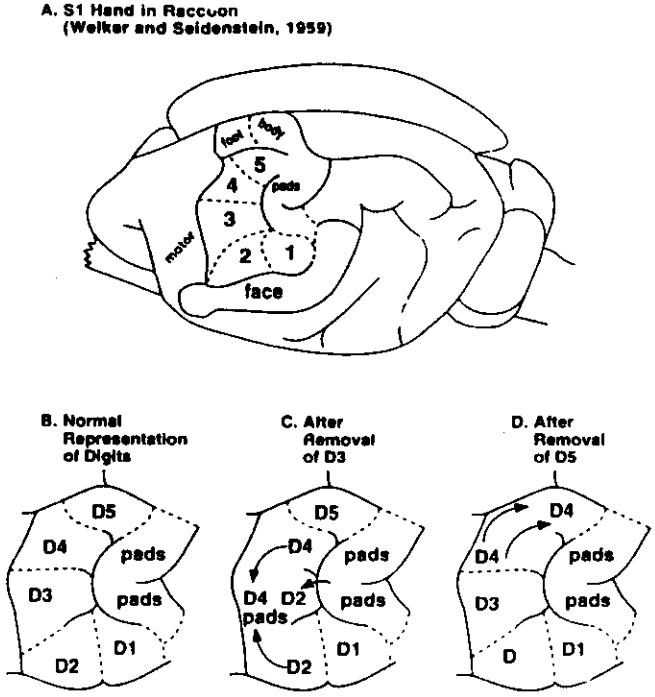

FIGURE 4.2 Reorganization of primary somatosensory cortex (S1) in raccoon after amputation of a digit. (A) Location of S1 on a dorsolateral view of the brain. Digits of the hand are numbered 1–5 from thumb to little finger. (B) Normal representation of the digits in S1. (C) Altered organization of the hand representation after the removal of digit 3. Neurons in the deprived D3 cortex became responsive to stimuli on digits 2 and 4 and the adjoining palmar pad. (D) Activation of the D5 cortex by D4 after removal of digit 5. (Based on Kelahan and Doetsch, 1984; and Rasmusson, 1982.)

tory after sciatic nerve section (Wall and Cusick, 1984; Cusick et al., 1990); and in which the column of cortex activated by a single facial vibrissa enlarged after long-standing lesions of the follicles of other whiskers (Kossut et al., 1988; Levin and Dunn-Meynell, 1991); (2) bats, in which cortex for the climbing digit of the wing became activated by inputs from the adjoining wing after digit amputation (Calford and Tweedale, 1988); and (3) cats, in which some neurons in forepaw cortex acquired receptive fields on the forearm after forepaw denervations (Kalaska and Pomeranz, 1979). Finally, there is recent evidence for the reorganization of primary somatosensory cortex in humans. After the surgical separation of fused fingers, finger representations appeared more distinct when measured with magnetoencephalography (Mogilner et al., 1993). Thus, the somatotopic organization of primary somatosensory cortex is mutable across a range of mammals.

Of course S1 is not the only somatotopic cortical representation. The number of such representations appears to vary across mammalian taxa, and the full number may not have been revealed in any species. In monkeys, seven systematic representations of the body have been identified in cortex, one each in the four architectonic fields of traditional S1 (3a, 3b, 1, and 2) (see Kaas et al., 1979; Kaas, 1983) and additional representations in the second area (S2), the parietal ventral area (PV), and the ventral somatosensory area (VS) (Cusick et al., 1989; Krubitzer and Kaas, 1990). Presumably, all these representations are capable of reorganization, but we presently have direct evidence from only a few. First, in experiments where nerve section in owl and squirrel monkeys produced reorganizations of deprived cortex in area 3b, similar reorganizations occurred in area 1 (Merzenich et al., 1983a,b; see also Garraghty and Kaas, 1991a). Second, although area 3a normally is activated almost exclusively by muscle and other deep receptors, training with tactile stimuli increases the responsiveness of area 3a to tactile stimuli (Jenkins et al., 1990; Recanzone, Merzenich, and Dinse, 1992). Third, the S2 of monkeys normally depends for activation on inputs from anterior parietal cortex (3a, 3b, 1, and 2) (Pons et al., 1987; Garraghty, Pons, and Kaas, 1990). Lesions of the hand representations in anterior parietal cortex partially deprive S2, and the deprived cortex reorganizes to become responsive to the foot and other body parts represented in the intact portions of anterior parietal cortex (figure 4.3) (Pons, Garraghty, and Mishkin, 1988). Thus, areas 3a, 3b, 1, and S2 are all capable of reorganization. However, experiments evaluating the mutability of area 2, PV, and VS have not yet been attempted. Similarly, in other mammals such as cats, where at least five cortical representations of cutaneous receptors exist (Clemo and Stein, 1983; Garraghty et al., 1987), representations outside S1 should be examined for plasticity.

In the visual system, retinotopic reorganizations of primary visual cortex (V1), have been demonstrated after lesions of the retina in cats (Kaas et al., 1990; Chino et al., 1992) and monkeys (Gilbert and Wiesel, 1992; Heinen and Skavenski, 1991). As for lesions of the peripheral nerves in the somatosensory system, lesions of the retina do not damage visual cortex directly but only indirectly produce cortical regions of deprivation. However, unlike the somatosensory system, where cutting a single nerve produces a zone of total deprivation, most of the visual cortex is binocularly driven. Thus,

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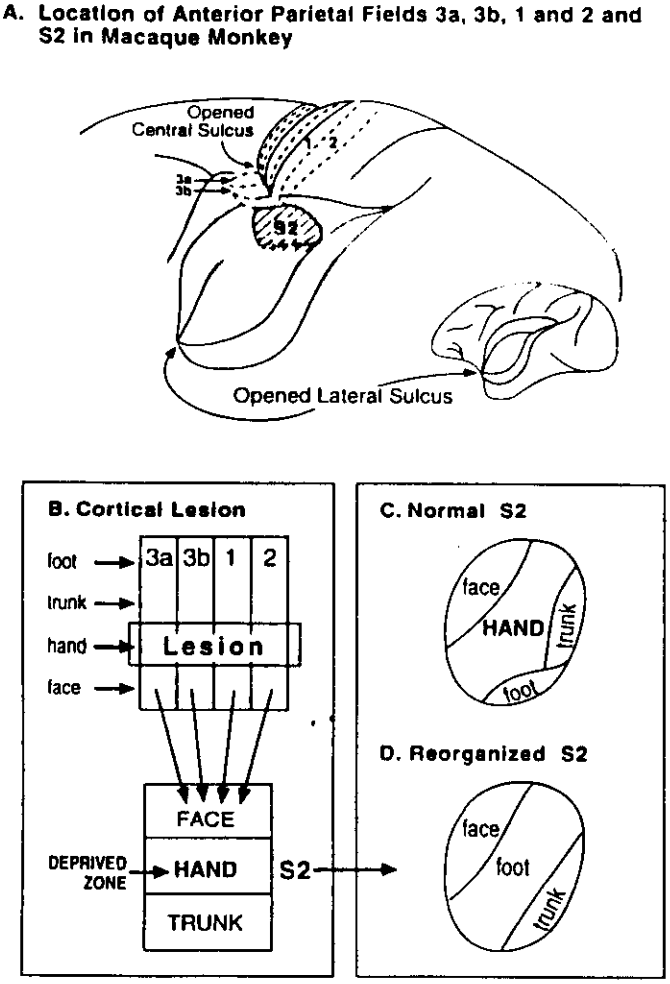

FIGURE 4.3 Reorganization of the second somatosensory area S2 after lesions of the cortex representing the hand in anterior parietal cortex (areas 3a, 3b, 1, and 2). The immediate effect of the lesion is to silence the hand representation in S2. Some weeks later, this cortex becomes responsive to stimuli on the foot. Based on Pons et al., 1988.

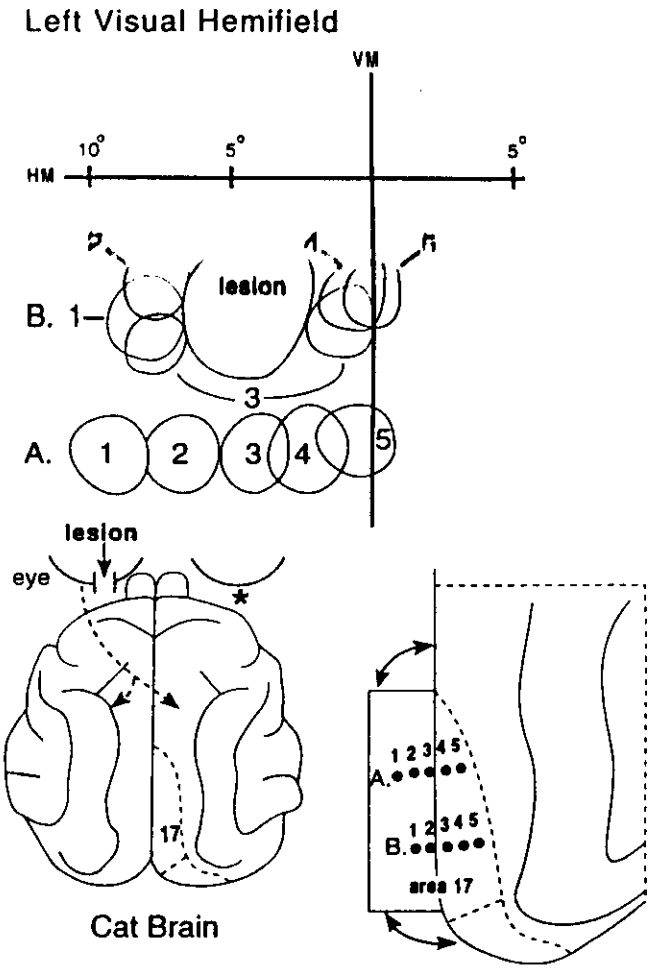

FIGURE 4.4 Reorganization of visual cortex after retinal lesions in cats. A small part of primary visual cortex was deprived of its normal source of activation by totally removing input from the ipsilateral eye and placing a small lesion in the retina of the contralateral eye. Recordings made in rows across area 17 (lower right) normally produce orderly rows of receptive fields in the contralateral visual hemifield (row A, top). In cortex deprived by the lesion, neurons have receptive fields that are displaced from the lesion to parts of the retina surrounding the lesion. Thus, receptive fields are piled up (row B, top), and the representation of the retina surrounding the lesion is expanded. (Based on Kaas et al., 1990.)

total deprivation is produced by placing lesions in matched locations in the two eyes or by removing the complete retina of one eye while placing a restricted lesion in the retina of the other. When retinal lesions are small, on the order of approximately 5° near central vision, a zone of unresponsive cortex is produced in the retinotopic map that becomes reactivated over weeks to months so that neurons acquire new receptive fields involving retinal locations along the margin of the lesion (figure 4.4). Larger lesions may produce a fringe of reorganized cortex around a central core of the cortex that remains unresponsive to visual stimuli.

Recordings in cats with retinal lesions also revealed that area 18 (V2) reorganizes (Kaas et al., 1990). The changes in V2 need not be those simply relayed from V1, as V2 is activated directly via geniculate inputs in cats (see Stone, 1983). The effects of deprivations on the many other visual areas of cats have yet to be determined. Monkeys also have a number of retinotopically organized visual areas (Kaas, 1989), but the potential

for reorganization in adults has not been directly studied in extrastriate fields. However, plasticity has been demonstrated in inferior pulvinar. Bender (1983) found that the immediate effect of area 17 lesions was to abolish visual responsiveness totally in the inferior pulvinar but, after 3 weeks, some 15% of neurons recovered visual responsiveness.

Primary auditory cortex (A1) also reorganizes after partial deprivations. A1 normally represents tones from high to low in a progression across one surface dimension of the field, with lines of isorepresentation of the same frequencies extending across the other surface dimension (see Merzenich and Kaas, 1980). We evaluated the potential for adult plasticity in the auditory cortex of adult macaque monkeys by using ototoxic drugs to create a cochlear hearing loss of high frequencies (Schwaber, Garraghty, and Kaas, 1993). By producing a hearing loss for frequencies above 10 kHz, most of the caudal half of A1 was deprived of its normal source of activation. Two to three months after the hearing loss, recordings in A1 showed that regions formerly responsive to high tones were responsive at normal thresholds to tones of 10 kHz or less (figure 4.5).

Similarly, Robertson and Irvine (1989) partially deafened guinea pigs by directly lesioning restricted portions of the organ of Corti. After 1 month or longer, the deprived zone of cortex was reactivated by sound frequencies adjacent to the frequency range damaged by the lesions.

Thus, in both monkeys and rodents, the auditory frequency maps reorganized after partial deafness. Comparable results have been obtained also in cats reared after neonatal, bilateral high-frequency loss (Mount et al., 1991), suggesting that reorganizations may occur in adult cats. More recently, Willott et al., (1993) reported that the high-frequency portion of A1 becomes devoted to middle frequencies in a genetic strain of mice that gradually acquires a loss of high-frequency input as a result of progressive sensorineural pathology of the basal region of the cochlea.

Other auditory areas may demonstrate plasticity as well. For example, besides A1, monkeys have rostral (R) and rostrotemporal (RT) fields that are tonotopi-

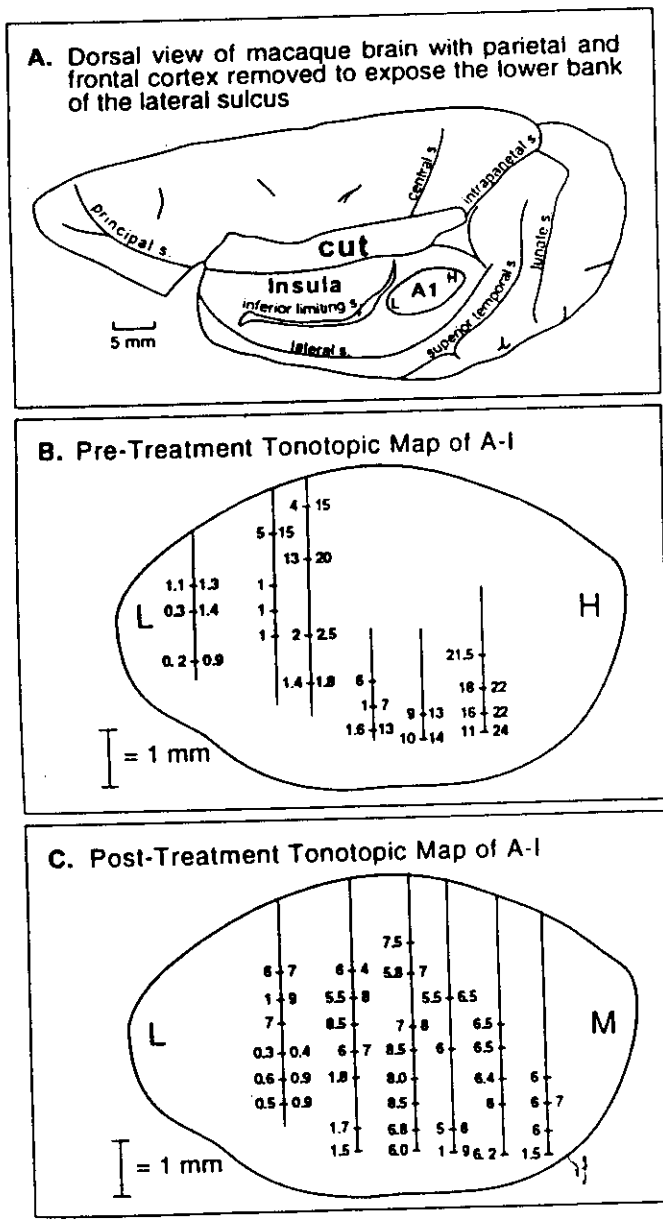

FIGURE 4.5 The reorganization of auditory cortex in macaque monkeys after ototoxic loss of high-frequency hearing. A. Location of primary auditory cortex (A1) on the lower bank of the lateral sulcus. Overlying portions of parietal and frontal cortex have been cut away to reveal the lower bank and insula. A1 represents tone frequencies from low (L) to high (H). Sulci (S) are named as landmarks. (B) Before treatment, a large part of A1 was mapped with microelectrodes that penetrated lateromedially within A1 (lines). Best frequencies for neurons were determined in kilohertz for sites along the penetrations, as indicated. Low tones were represented rostrally and high tones, caudally. (C) Recordings made months after a high-frequency hearing loss (exceeding 10 kHz) revealed a reorganization of A1, with caudal A1 responsive to tones of less than 10 kHz. Thus, the progression across A1 was from low (L) to middle (M) frequencies. (Based on Schwaber, Garraghty, and Kaas, 1993.)

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cally organized (Morel and Kaas, 1992; Morel, Garraghty, and Kaas, 1993). These and other fields need to be examined to determine how they respond to hearing loss.

Recent studies also indicate that motor cortex may reorganize after amputations or section of motor nerves. Several subdivisions of motor cortex exist in monkeys, including primary motor cortex (M1), the supplementary motor area (SMA), and two or more premotor fields (see Stepniewska, Preuss, and Kaas, 1993). At least M1 and probably SMA appear to exist in most other mammals as well (Kaas, 1987). These motor areas contain systematic representations of muscles or movements that can be revealed by electrically stimulating cortex at many sites with microelectrodes. Normal motor maps have somatotopic features that are consistent within a species, and these features appear to be relatively stable over time (Craigs and Rushton, 1976; Donoghue, Suner, and Sanes, 1990). However, removing an effector target by cutting a motor nerve or an amputation changes the motor map in at least M1. This has been shown most clearly in experiments on rats conducted by Sanes, Suner, and Donoghue (1990). Forelimb amputation or facial nerve transection first resulted in a deprived zone in M1, where no movements were evoked by electrical stimulation with microelectrodes. After a recovery period of 1 week or more, representations of other movements expanded in M1 so that stimulation of the deprived cortex evoked movements of intact structures at normal stimulation thresholds (figure 4.6). Similarly, evidence for the reorganization of M1 has been obtained from human patients with long-standing amputations of the arm (Cohen et al., 1991). In these patients, organizations of M1 ipsilateral and contralateral to the amputation were accessed by using local magnetic stimulation through the skull to evoke movements. Muscles of the upper arm in the stump could be activated from a larger area of cortex than could those muscles in the intact arm, suggesting that cortex contralateral to the stump had reorganized to devote more cortex to the remaining muscles.

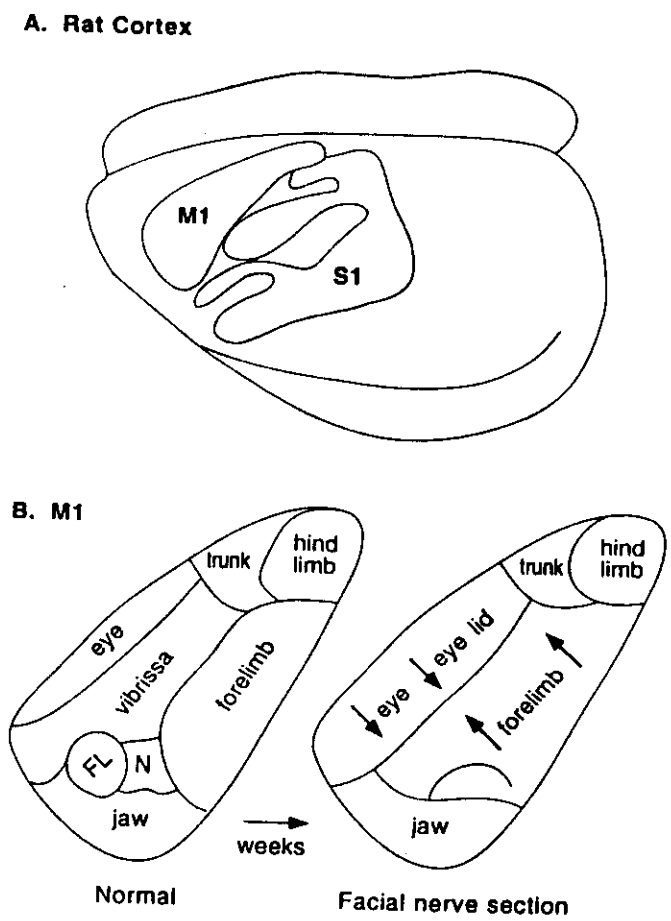

FIGURE 4.6 Reorganization of primary motor cortex of rats after section of the motor nerve to the musculature of the facial vibrissa. (A) Dorsolateral view of a rat brain showing the locations of M1 and primary somatosensory cortex (S1). (B) The somatotopy of M1 (left) becomes transformed (right) by section of the facial nerve. Cortex that formerly evoked vibrissa movements when electrically stimulated evoked eyelid or forelimb movements instead. FL, forelimb; N, neck. (Based on Sanes, Suner, and Donoghue, 1990.)

Where reorganizations occur

Much of the early interest and research on adult plasticity in the somatosensory system stems from the well-known study of Liu and Chambers (1958) purporting to show major axon sprouting of intact peripheral nerve inputs to the dorsal horn of the spinal cortex after synaptic space was made available by selective dorsal root rhizotomies. However, subsequent anatomical studies after such lesions failed to reveal spinal cord sprouting (see Rodin and Kruger, 1984; Rodin, Sampogna, and Kruger, 1983). Likewise, initial electrophysiological studies reported considerable reorganization of the somatotopic map in the spinal cord after such injuries, but later investigations produced more variable results, including no evidence of change (reviewed by Snow and Wilson, 1991). The variable results and lack of agreement about the extent or even existence of somatotopic changes in the spinal cord after injury brought the concept of subcortical plasticity into question. Never-

theless, three general conclusions are supported by the available evidence. First, reorganizations of subcortical structures do occur, and they may occur in all systems and at all subcortical levels. Second, persisting changes in subcortical relay stations of ascending sensory systems are limited in extent; often, they would have little impact on cortical maps. Third, because the anatomical and topographical features of subcortical and cortical maps may differ, there are instances where minor reorganizations at subcortical levels produce major changes in cortical maps.

The dorsal horn of the spinal cord has been rather extensively studied for evidence of plasticity (see Snow and Wilson, 1991, for review). Somatotopic reorganization does appear to occur in the dorsal spinal cord after peripheral nerve or dorsal root injury, but the magnitude of change appears to be close to the level of detectability with microelectrode mapping methods (Wilson and Snow, 1987). Reported changes in somatotopy are spatially limited, and new receptive fields on the skin are very close to original receptive fields. Somatotopic reorganization has also been reported for the dorsal column nuclei after dorsal rhizotomy (Dostrovsky, Millar, and Wall, 1976), but there is no clear evidence of large-scale modifications (see Snow and Wilson, 1991). Furthermore, deactivating parts of the gracile nucleus (McMahan and Wall, 1983) or trigeminal nuclei (Waite, 1984) by nerve section in adult rats produced no clear evidence of plasticity and reactivation. From these studies, it appears that nerve or dorsal root section is followed by no more than limited reactivation of deafferentated portions of the spinal cord and brain stem, yet we have indirect evidence that small changes in the dorsal column nuclei do occur and have large consequences in cortex, as is detailed later.

Reorganization is also expressed at the level of the thalamic relay of somatosensory information, but the evidence is limited. Early evidence that plasticity occurs in the ventroposterior nucleus (VP) of the thalamus comes from a brief report of Wall and Egger (1971). These investigators ablated nucleus gracilis of the medulla in rats, thereby depriving the lateral margin of VP of its normal source of activation from the hind limb. Recordings immediately after the damage revealed no change in somatotopy, but recordings days to weeks later suggested that inputs from the forelimb had expanded their territory to include the deprived hind-limb region of VP. However, the validity of this conclusion has been questioned, in part on the grounds that the magnitude of the reported changes is so small that recordings from distant neurons could explain the apparent expansion (Snow and Wilson, 1991). In another early study, limited recordings from two monkeys 2 weeks after section of fasciculus gracilis suggested an expansion of the forelimb representation into the deactivated hind-limb representation in VP (Pollin and Albe-Fessard, 1979), but the reported results were too sparse to be widely convincing. More recently, Rhoades, Belford, and Killackey (1987) lesioned the principle division of the trigeminal nuclear complex in rats, thereby depriving the face portion of VP (VPM) of its effective source of activation, but leaving the spinal trigeminal inputs intact. Over time, responsiveness to the face returned in VPM, and this return was attributed to the potentiation of the spinal trigeminal input. Finally, there is evidence that major reorganization of the somatotopy in VP occurs after section of the median and ulnar nerves to the glabrous surface of the hand in monkeys (Garraghty and Kaas, 1991b). In monkeys, a large subnucleus devoted to the hand in VP can be distinguished from the rest of the nucleus by partially encapsulating fiber bands. Approximately 90% of this subnucleus is activated by the volar hand (Kaas et al., 1984). After weeks of recovery following nerve section in squirrel monkeys, the complete hand subnucleus was activated by inputs from the dorsal surface of the hand. The reorganization at the level of the thalamus was so extensive that results could not be dismissed as a measurement error. In summary, the experiments of Rhoades, Belford, and Killackey (1987) suggest that alternate inputs can substitute for dominant inputs at the level of the thalamus. The major reorganization demonstrated in the hand subnucleus after peripheral nerve section (Garraghty and Kaas, 1991b) could result from a similar substitution at the thalamic level, but thalamic reorganization in this instance could also reflect changes relayed from the dorsal column nuclei to the thalamus (figure 4.7). Other evidence for reorganization in VP is equivocal.

As for the first relay stations in the somatosensory system, there seems to be only limited reorganization and reactivation in the lateral geniculate nucleus (LGN) of the visual system after retinal lesions (Eysel, Gonzalez-Aquilar, and Mayer, 1981; Eysel, 1982). After photocoagulation of small regions of the retina and weeks of recovery in cats, some neurons of the deprived zone of the LGN recovered responsiveness to visual stimuli directed to regions of the retina just around the

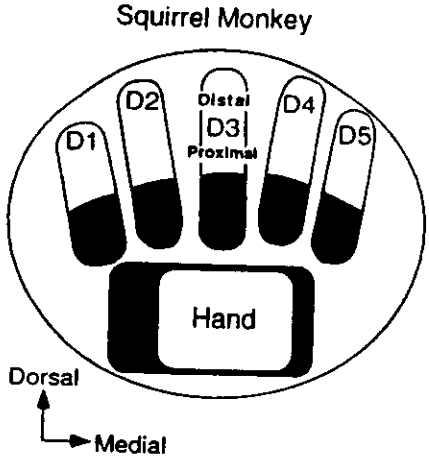

FIGURE 4.7 The somatotopic organization of the cuneate nucleus of the dorsal column–trigeminal complex of the lower brain stem of squirrel monkeys. The glabrous surface of each digit (D1–D5) is represented in a lateromedial sequence just dorsal to the representation of the pads of the palm. Fiber bands separate cell clusters devoted to these body parts. Inputs from the dorsal, hairy skin of each digit and the back of the hand terminate in the same cell clusters as the inputs from the glabrous skin. (Adapted from Florence, Wall, and Kaas, 1991.)

lesion. The results were similar to those obtained from visual cortex (Kaas et al., 1990; Chino et al., 1992), but the magnitude of the filling was much less. Thus, some plasticity does occur at the level of the LGN, but not all the changes observed in cortex are relayed from the thalamus.

We know little yet about the capacity of early stations in the auditory system to reorganize in adult mammals. After hamsters were exposed to tones intense enough to cause stereocilial damage, there was no clear evidence of plastic changes in the tonotopic map in the dorsal cochlear nucleus (Kaltenbach, Gaja, and Kaplan, 1992).

Major reorganizations of cortical sensory maps as a result of minor subcortical reorganizations

Different extents of reorganization imply different mechanisms of change. Small changes could be mediated by the potentiation of ineffective pre-existing connections, whereas major changes would often seem to depend on the growth of new connections. However, maps of the same sensory surface may differ in internal organization from one level to the next, so reorganizations that appear massive at one level may seem less extensive at another level. Topographical differences in maps are most obvious in the somatosensory system. For example, representations of the hand and foot are separated by representations of the limbs and trunk in area 3b of monkeys, whereas they adjoin in S2 (see Krubitzer and Kaas, 1990). These different topographical arrangements may be related to the observations that the foot substitutes for the missing hand input in S2 (Pons, Garraghty, and Mishkin, 1988) but not in area 3b (Florence et al., 1993b). Differences in the somatotopic organizations of maps at different levels may also explain why inputs from the back of the hand so effectively substitute for deactivated inputs from the glabrous hand in area 3b of monkeys (Merzenich et al., 1983a; Garraghty and Kaas, 1991a; Wall, Huerta, and Kaas, 1992). This massive reorganization in cortex largely or completely occurs subcortically, as it is expressed at the level of the VP (Garraghty and Kaas, 1991b). Because the dorsal hand is represented in locations separate from the glabrous hand in VP (Kaas et al., 1984), reorganization at the level of the thalamus would also be extensive. However, the somatotopic arrangement is different at the level of the dorsal column nuclei in the lower brain stem. In the cuneate nucleus of monkeys, the representation of the dorsal hand is distributed in a discontinuous pattern across an array of small clusters of neurons that are isolated from one another by surrounding bands of fibers (see Florence, Wall, and Kaas, 1991). Different cell clusters receive inputs from different digits or pads of the palm, but somewhat segregated parts of the same clusters receive inputs from the volar and hairy surfaces of the same digits (figure 4.8). We hypothesize that the massive substitution of hairy skin inputs for volar skin inputs at thalamic and cortical levels of the somatosensory system of monkeys actually occurs in the cuneate nucleus as a result of short-range substitutions within the cell clusters (see figure 4.8). However, this substitution has not yet been demonstrated in the cuneate nucleus, and a more extensive reorganization at the level of the thalamus remains a viable possibility (figure 4.9) (see Rhoades, Belford, and Killackey, 1987; Garraghty and Kaas, 1991b).

The reversibility of reorganizations

One wonders whether changes in sensory maps produced by partial deprivations or other types of altered sensory activation are reversed if normal patterns of activation return. There is little experimental evidence

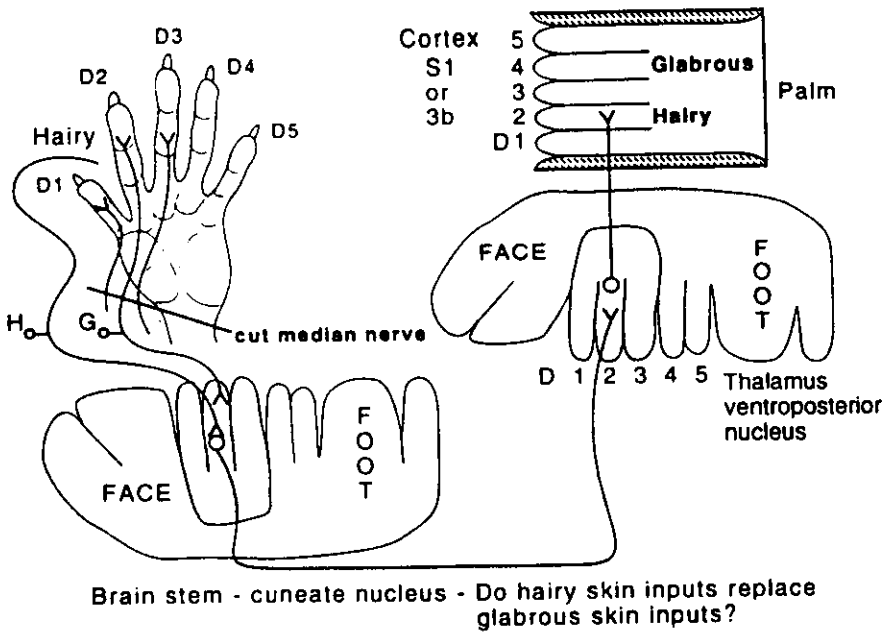

FIGURE 4.8 A substitution of dorsal hairy skin inputs for deactivated glabrous skin inputs in the cuneate nucleus after section of the median nerve may account for the reorganization observed in cortex (Merzenich et al., 1983a) and thalamus (Garraghty and Kaas, 1991b).

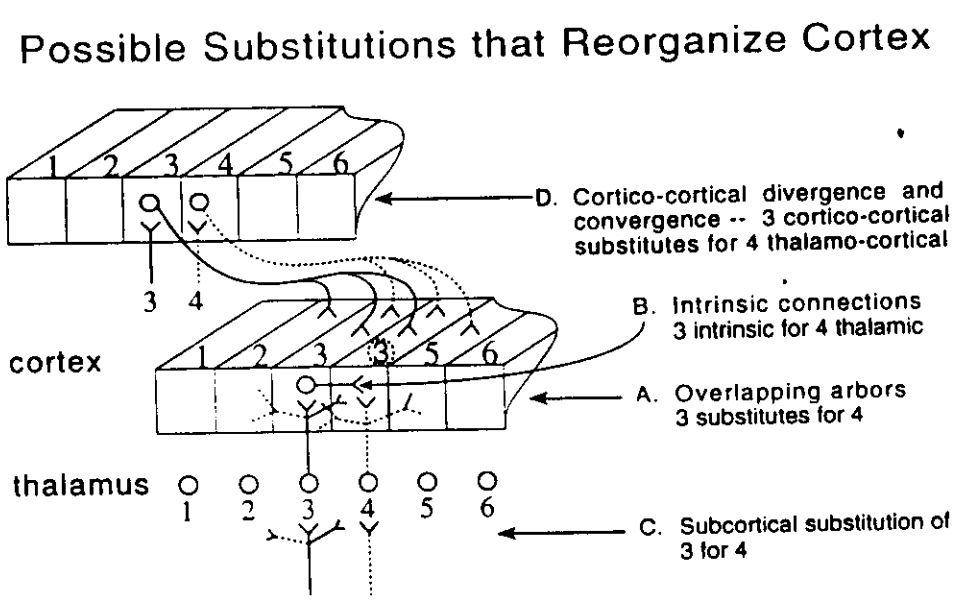

FIGURE 4.9 Most reorganizations probably depend on previously weak inputs substituting for deactivated or less active inputs. Substitutions can take place at all levels of sensory systems.

on the reversibility of the effects of partial deprivation on cortical maps, largely because the methods of producing deprivation are either short-term, such as in anesthetizing a sensory nerve, or irreversible because of damage, such as in an amputation. Even allowing a cut nerve to regenerate does not fully restore a previous pattern of activation of central maps, because the regeneration of cut nerves is generally very disorderly (Wall

et al., 1986). Changes in cortical maps produced by anesthetizing a peripheral nerve (e.g., Metzler and Marks, 1979) are reversible after the anesthesia wears off but, of course, this is expected as the period of deprivation seems too limited to produce structural and, hence, persistent changes in the sensory network. In contrast, nerve crush can produce a long period of deprivation. For example, regeneration of the median nerve to the hand crushed at the level of the forearm takes more than 1 month (see Wall, Felleman, and Kaas, 1983). During the course of denervation produced by median nerve crush in monkeys, deprived parts of areas 3b and 1 of somatosensory cortex gradually reorganize, largely over the first 3 weeks, to become fully responsive to new inputs (Merzenich et al., 1983b). If these slowly developing activation patterns were based on major structural changes in the central nervous system, the altered cortical maps could persist after nerve regeneration. However, maps of area 3b and 1 made in individual monkeys before median nerve crush and after regeneration revealed that the normal maps returned completely (Wall, Felleman, and Kaas, 1983). Furthermore, the recovered organizations appeared to match closely the original maps in specific individuals. Thus, the original structural framework must have been maintained during deprivation, and the changes in activity patterns were completely reversible. This reversibility is consistent with the considerable behavioral evidence that normal tactile abilities return after regeneration of crushed nerves in humans (see Wall and Kaas, 1985).

The extent of reorganizations of primary somatosensory areas

The proportion and absolute amount of S1 (3b) that can be reactivated after deprivation varies considerably. At one end of the reorganization spectrum, only approximately 0.3 mm^2 of hind-paw cortex is reactivated by saphenous nerve inputs after sciatic nerve section in rats, and most of the deprived cortex persistently remains unresponsive to tactile stimuli (Wall and Cusick, 1984; Cusick et al., 1990). Similarly, after removal of a single digit, the deprived cortex is reactivated by inputs from adjoining digits in area 3b of monkeys, but digit cortex is not fully reactivated if two or more digits have been lost (Merzenich et al., 1984). In contrast, half to most of hand cortex in area 3b is deprived and then becomes responsive to inputs from the back of the hand after median or median–plus–ulnar nerve section in owl and squirrel monkeys (Merzenich et al., 1983a; Garraghty and Kaas, 1991a; Wall, Huerta, and Kaas, 1992). However, most or all of this reorganization occurs subcortically (Garraghty and Kaas, 1991b), perhaps at the level of the cuneate nucleus, where local modifications in connections could mediate the changes. When the radial nerve to the back of the hand is sectioned in combination with one of the two nerves to the glabrous hand—the median and ulnar nerves—most of the deprived cortex remains unresponsive to cutaneous stimulation (Garraghty et al., 1992). Furthermore, in macaque monkeys, where the median nerve may innervate part of the dorsal, hairy hand in addition to part of the glabrous hand, and the innervation pattern of the cuneate nucleus may differ from that in New World monkeys (see Florence, Wall, and Kaas, 1989), section of the median nerve produces a zone of deprived cortex in area 3b that does not completely recover responsiveness to cutaneous stimuli (unpublished studies). Thus, it appears that S1 or area 3b usually has only a limited capacity for reorganization after partial deprivations. However, there are situations where major changes have been demonstrated.

The most dramatic demonstration of major reorganization in cortex as a result of deprivation comes from the experiments of Pons and colleagues (1991) on monkeys in which all the sensory inputs from the forelimb had been removed by sectioning the dorsal roots of peripheral nerves as they enter the spinal cord. As part of an unrelated study, these monkeys had been deprived of sensory information from the hand, forearm, and upper arm, but not motor outflow, and had received training to use the deafferented limb. Twelve or more years after deafferentation, recordings in these monkeys showed that the complete hand, wrist, forearm, and upper arm regions of areas 3b and 1 were responsive to tactile stimuli on the face. In related experiments, we have studied cortex in monkeys that have had digit or hand amputations as a result of accidental injuries. In one macaque monkey studied 8 years after amputation of an injured hand, much of the deprived cortex in area 3b was responsive to remaining inputs on the wrist, although some of the cortex was unresponsive (Florence et al., 1993b). We do not yet understand how these massive reorganizations occur, but such results imply the growth of new connections (figure 4.10).

It remains uncertain whether primary auditory and visual areas of cortex also differ in the extent of reorgani-

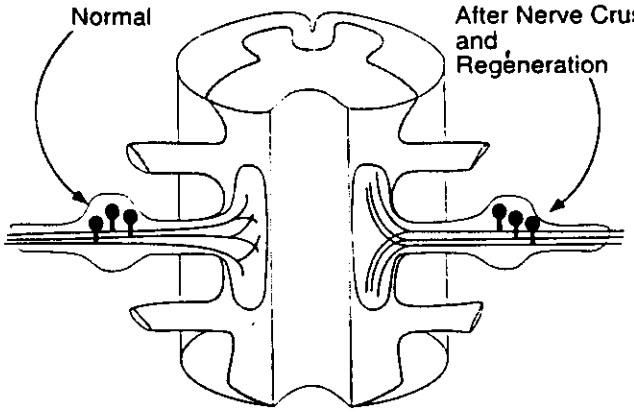

FIGURE 4.10 Some reorganizations may be the result of the growth and formation of new connections. Crushing the median nerve in adult monkeys induces growth in the central arbors of the regenerating afferents so that they overlap more extensively in the dorsal horn of the spinal cord. (Based on Florence et al., 1993.)

zation with variables such as the type or length of deprivation. After larger lesions of the retina in cats, deprived portions of areas 17 and 18 are not completely reactivated, at least within a period of months (Kaas et al., 1990), but longer recovery periods have not been tested. Also, after partial damage to the cochlea, reactivations of auditory cortex have been complete (Robertson and Irvine, 1989; Schwaber, Garraghty, and Kaas, 1993; Willott, Aitkin, and McFadden, 1993). Clearly, the limits of reorganization have not yet been determined.

How reorganizations are mediated

Rapid changes in sensory representations probably are mediated largely by three mechanisms: (1) immediate adjustments in the dynamics of the sensory network by changes in afferent drive (see Nicoletis et al., 1993a,b); 2) the release of neuromodulators that alter the effectiveness of pre-existing synapses (see Dykes, 1990; Juliano et al., 1990; Grasse, Douglas, and Mendelson, 1993); and (3) the potentiation of pre-existing synapses via the NMDA class of glutamate receptors and Hebbian rules (see Bear, Cooper, and Ebner, 1987; Brown, Kairiss, and Keenan, 1990; Diamond, Armstrong-James, and Ebner, 1993). Persisting changes in map structure can result from mechanisms that maintain the rapid alterations and from slowly developing, self-regulatory modifications in neuron structure and function.

Many of the rapidly induced changes in sensory maps that follow sensory pairing and other learning paradigms (e.g., Diamond, Armstrong-James, and Ebner, 1993) probably disappear rapidly. Long-term potentiation is the postulated mechanism of changes in synaptic effectiveness in such situations, and long-term potentiation typically dissipates over minutes to hours (Brown, Kairiss, and Keenan, 1990). Of course, a synaptic pathway, once strengthened above threshold, can be maintained via repeated activation, and there may be other mechanisms of maintaining synaptic strength. In either case, the importance of Hebbian mechanisms and NMDA receptors in allowing more active inputs to substitute for less active inputs in even slowly developing and long-lasting adult plasticity is suggested by experiments wherein the reorganization of area 3b of somatosensory cortex after nerve section in monkeys was prevented by blocking NMDA receptors during the recovery period (Garraghty, Muja, and Hoard, 1993). Similarly, reorganization of the hind-limb portion of S1 of adult cats after selective deafferentation was prevented by the continuous infusion of an NMDA receptor antagonist (Kano, Iino, and Kano, 1991). Modulating neurotransmitters such as acetylcholine and norepinephrine may participate in the stabilization process, as depletion of these substances interferes with aspects of developmental plasticity (Bear and Singer, 1986), and acetylcholine depletion prevents some types of adult plasticity (Juliano, Ma, and Eslin, 1991; Webster et al., 1991).

Changes in activity produced by long-standing deprivations or overstimulations probably induce a host of self-regulatory changes in molecular expression that could change the thresholds for synaptic activation. For example, reduced activity as a result of deprivation reduces the expression of metabolic enzymes such as cytochrome oxidase (e.g., Land and Akhtar, 1987; Wong-Riley and Welt, 1980) and succinic dehydrogenase (e.g., Dawson and Killackey, 1987). Long-standing sensory deprivation in monkeys with major reorganization of area 3b (Pons et al., 1991) also resulted in both decreases and increases of different calcium-binding proteins in the somatosensory thalamus (Rausell et al., 1992). These examples suggest that the expression of many neuroregulatory substances depends on levels of neuronal activity, although changes in expression of any particular substance may or may not have a role in plasticity. Levels of production and release of excitatory and inhibitory transmitters may also be regulated by neuronal activity. Most notably, days of continuous whisker stimulation in rats pro-

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duced an increase in the expression of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) in the affected cortex (Welker, Soriano, and van der Loos, 1989). This increase in GABA resulted in a decrease in responsiveness of S1 cortex to normal stimulation of the overstimulated whisker (Welker et al., 1992). Understimulation produced the opposite effect in that the deprived cortex expressed less GABA, and therefore the cortex could be more responsive to weak inputs. There are other examples of activity-related changes in neurotransmitter levels: Median nerve section reduces GABA levels in the deprived cortex of monkeys (Garraghty, Lachica, and Kaas, 1991; see also Rausell et al., 1992), whisker removal has a similar effect on S1 of rats (Land and Akhtar, 1987; Welker, Soriano, and Van der Loos, 1989), and eye removal or eyelid suture depletes GABA in visual cortex of monkeys (Hendry and Jones, 1986). Finally, median and ulnar nerve section in monkeys is followed by a reduction in the neuromodulatory peptide tachykinin in the intrinsic neurons of deprived area 3b (Cusick, 1991).

Reduced activity could also promote several types of neuronal growth that would tend to restore normal activity levels, including the formation of new synapses, extension of dendrites, and the local and even extensive growth of axons and axon arbors. Such structural features of neurons are extremely modifiable during development, but neurons appear to lose morphological plasticity progressively with maturation (Horn, Rose, and Bateson, 1973). Nevertheless, there is evidence that spinal cord damage in adult rats induces increased synaptic turnover in cortex (Ganchrow and Bernstein, 1981), and changes in use of the forelimb correlate with dendrite growth in motor cortex (Greenrough, Larson, and Withers, 1985; Jones and Schallest, 1992). The growth of axons and the formation of new connections can clearly be induced by injury in the developing brain (e.g., Fitzgerald, Woolf, and Shortland, 1990; Rhoades, Belford, and Killackey, 1987), but such growth has been more difficult to demonstrate in adult animals, and there are many situations where there is no apparent sprouting of axons into deprived parts of sensory systems (e.g., Eysel, 1982; Rodin, Sampogna, and Kruger, 1983; Rodin and Kruger, 1984; Rasmusson and Nance, 1986). However, damaged peripheral nerve inputs into the spinal cord can expand into adjacent territories vacated by sectioning dorsal roots or peripheral nerves in adult rats (e.g., Molander, Kinnman, and Aldskogius, 1988; Woolf, Shortland, and Coggeshall, 1992). Similarly, we found that median nerve crush alone induces axonal growth within the deprived zone of spinal cord of adult monkeys (Florence et al., 1993a) (figure 4.10). The nerve crush may induce a growth state, and the lack of evoked activity in the central terminations of the injured axons may allow them to grow into one another's territories. If discorrelations in evoked activity patterns of neurons with different receptive fields have a role in restructuring growth and limiting arbor overlap in adult mammals, as in developing mammals (e.g., Shatz, 1990), then any loss or reduction of evoked activity can be a permissive factor in axon sprouting and growth in the adult nervous system. In adult rats, vibrissae removal is followed by enlargements of the representations of a remaining vibrissa in S1 (Kossut et al., 1988) and by increased expression of growth associated protein (GAP-43) (Dunn-Meynell, Benowitz, and Levin, 1992), suggesting the induction of axonal sprouting.

Presently, there is no clear evidence that any of the reorganizations of sensory representations in adult mammals depend on extensive axon growth; yet there is no obvious alternative explanation for the major reactivations that occur after deafferentation of the complete forelimb (Pons, Garraghty, and Mishkin, 1988) or loss of a hand (Florence et al., in press) in monkeys. In these cases, the long-standing deprivation and reduced activity of central neurons could induce sprouting of nearby axons into deprived tissue, perhaps by the release of some growth factor. Such axon sprouting would seem more likely at the levels of the lower brain stem or thalamus, where distances would be shorter than in cortex. On a smaller scale, a continuous process of neuronal growth and retraction may be important in the maintenance and reshaping of sensory maps throughout life. In an early, innovative study, Rose and coworkers (1960) reported that laminar lesions of visual cortex in adult rabbits, produced by irradiation, resulted in the massive sprouting and growth of axons from normal tissue into the zone of nerve cell loss. The authors suggested that this massive growth was part of the "normal, continuous growth of central neurons."

Perceptual and behavioral consequences of reorganization

Reassignments of neurons in cortical maps from one to another part of a receptor surface could have several different functional consequences. Adding more neu-

rons to the processing circuits for a given part of a receptor surface could enhance the capacity of that circuit. Some evidence is consistent with this view. For example, Recanzone and colleagues (1992 reported that monkeys trained to make a tactile discrimination of the frequency of a vibrating probe on a specific finger improved over time, and the experience increased the size of the cortical representation of that finger. In a similar manner, humans with deafferented zones of skin may express hypersensitivity and increased tactile capacity on skin next to the denervated zone see Wall and Kaas, 1985), and this skin probably has an increased cortical representation. The fact that, with practice, we are capable of improving performance of most sensorimotor tasks implies that the central processing of afferent inputs is not limited initially by receptor elements and that enlarging the neural pool for given inputs can mediate improvements. Reorganizations that follow partial lesions of cortical areas seem to have clear potential for mediating recovery. Partial lesions of cortical maps in humans and monkeys (e.g. Newsome et al., 1985) commonly are followed by perceptual deficits that rapidly diminish over days to weeks. In these cases, normal performance is impaired by reductions in the numbers of neurons in relevant central circuits, and any reassignment of neurons from other circuits to the damaged circuits could lead to improved performance.

There are also reasons to conclude that adding neurons to a network may not always improve performance. If performance is limited by the density of the receptor array, adding more neurons to a processing circuit may produce no improvement. For example, greatly expanding the normally small cortical representations of the back of the hand in monkeys by sectioning cutaneous nerves to the volar hand may not improve tactile acuity because it is already maximal for the low density of receptors on the dorsal hand.

Instead of improving performance, adding new neurons to central circuits sometimes may degrade capacity. Neurons with reorganized inputs may maintain their original output and effector targets so that errors are made and misperceptions occur. Hand areas of cortex, when activated by the foot or face, may continue to signal stimuli on the hand. Partial deafferentations of skin regions commonly result in mislocalizations of tactile stimuli (see Wall and Kaas, 1985). For example, Ramachandran, Rogers-Ramachandran, and Stewart, (1992) recently reported that patients with forelimb amputations felt tactile stimuli on the face as being both on the face and on the missing forelimb. The fact that most amputees have phantom sensations of missing limbs Melzack, 1990) suggests that central representations of limb inputs are being activated and continue to mediate the perception of the missing limb. Similarly, phantom auditory perception (tinnitus) distresses a large portion of individuals with inner ear pathological processes; one postulated cause of tinnitus is that decreased input from the periphery causes plastic changes in synaptic weights within the central auditory system, and false sensations result (Jastreboff, 1990).

Conclusions

Over the last 15 years, the plasticity of sensory and motor representations in the brains of adult mammals has been extensively studied, and a number of major conclusions are now supportable.

1. We know that sensory representations, especially at the cortical level, are normally quite dynamic. Receptive field sizes and locations are modified rapidly by natural stimuli outside the classical receptive field, attention and other modifications of the behavioral state, within-field stimuli, learning, and sensory pairing. Most of these modifications are rapidly reversible and thus differ from the more persistent reorganizations of sensory maps in adults that are reminiscent of developmental plasticity. However, if the sensory bias is long-term, the neural change may be enduring.

2. Reorganizations of sensory maps are produced by manipulations that alter patterns of sensory and other neural activity. The most obvious reorganizations follow partial removal or deactivation of afferent drive by nerve section, receptor surface damage, or central lesions. Alterations are also produced by prolonged localized sensory stimulation, sensory experience, and electrical stimulation of sensory maps. More active inputs appear to expand and substitute for less active inputs.

3. Reorganizations have been demonstrated in the somatosensory, auditory, visual, and motor systems at both cortical and subcortical levels, and in a wide range of mammalian species. Thus, the capacity for reorganization seems to be a fundamental characteristic of the adult nervous system, and plasticity may be possible throughout the nervous system. Nevertheless, the most dramatic examples of reorganization are at the cortical level, and changes at early stages of processing may be quite limited.

4. Changes in sensory representations that occur within minutes or hours suggest the rapid potentiation of previously existing synapses. Possible mechanisms include the reduction of afferent drive of off-focus inhibition, the potentiation of synapses via correlated presynaptic and postsynaptic activity, and the involvement of NMDA glutamate receptors, as well as the enhancement of weak activation via the release of neuromodulators. Many of the rapid changes in organization dissipate rapidly as well when premanipulation conditions return.

5. Other modifications in map structure take days to weeks and possibly longer to emerge. These slowly emerging changes are compatible with synaptic and membrane receptor turnover and selection, axon and dendritic growth, and reductions and increases in the production of neurotransmitters and neuromodulators. Most map changes likely depend on a number of rapidly and slowly emerging mechanisms.

6. The reversibility of slowly emerging map changes in somatosensory cortex produced by nerve crush with nerve regeneration suggests that the basic anatomical framework for map organization is relatively stable and that structural organizations that emerge during development tend to persist.

7. Maps at different levels of sensory systems may differ in the way they represent a sensory surface. Thus, local modifications in one map may have widespread consequences in the map at the next level. In addition, maps at higher levels express greater change as a result of accumulating the effects of modifications at earlier levels.

8. There is only limited evidence on the behavioral consequences of map reorganization. Changes in sensory maps could lead to improvements in sensorimotor skills, compensations for sensory losses and impairments, and recoveries of lost abilities following central nervous system damage. Reorganizations could also produce misperceptions and perceptual errors. Modification in sensory systems may mediate all of these behavioral changes.

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