Lesion-induced plasticity in the second somatosensory cortex of adult macaques

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ABSTRACT We have reported that elimination of the representation of any body part in the primary (i.e., postcentral) somatosensory cortex of the adult macaque selectively eliminates the representation of that same body part in the second somatosensory area SII. We now report that, although removal of the entire postcentral hand representation does indeed leave the SII hand representation unresponsive to somatic stimulation initially, 6–8 weeks later this cortex is no longer silent. Instead, most or all of the region that had been vacated by the hand representation is now found to be occupied by an expanded foot representation. This massive somatotopic reorganization, involving more than half the areal extent of SII, exceeds that previously observed in the postcentral cortex after peripheral nerve damage and may reflect a greater capacity for reorganizational changes in higher order than in primary sensory cortical areas.

In macaques, the sensory surface of the body is represented in a map-like fashion in the primary somatosensory cortex, or postcentral strip (consisting of the cytoarchitectonic areas 3a, 3b, 1, and 2), and in an adjoining field within the lateral fissure known as the second somatosensory area, or SII. There has been little reason to suspect that elimination of the postcentral strip would have any effect on the somatotopic representation in SII, since it was believed that the major determinant of each well-defined somatosensory cortical map was the precisely organized somatotopic projection that it received directly from the thalamus. However, we have found that removal of the postcentral strip eliminates the somatosensory representation in SII, indicating that the cutaneous activation of neurons in SII is in fact critically dependent on a projection to it from the postcentral cortex rather than on a direct projection from the thalamus (1). This evidence raises the following questions. What happens to the neurons in SII that are initially deactivated after removal of the postcentral representations of specific body parts? Do these neurons continue to remain unresponsive to tactile stimulation or, after sufficient time, do they become responsive once again? And if the latter, do they come to again represent the body part whose postcentral representation was removed or do they come to represent instead body parts whose postcentral representations were left intact? To answer these questions we recorded somatic activity in SII several hours after and several weeks after removal of the postcentral hand representation. The results demonstrate that under these circumstances, and at some time between the two recording periods, SII undergoes massive topographic reorganization.

Single- and multiunit activity was recorded from SII in 11 hemispheres of seven macaques (five *Macaca mulatta* and two *Macaca fascicularis*) anesthetized with a mixture of halothane and nitrous oxide. Staggered electrode penetrations were placed 0.5–1.0 mm apart, and neuronal responses were sampled at 100- to 200-μm intervals through the depth of SII,

yielding a recording-site density of ≈2.3 mm² across the entire extent of SII. Receptive fields of neurons at the recording sites were determined by applying light tactile stimulation at various locations on the contralateral body surface and then by exploration with higher-amplitude stimulation, as described elsewhere (1, 2). Recordings were obtained in 4 intact hemispheres, in 3 hemispheres in which the postcentral hand representations had been removed 18–48 hr earlier, and in 4 hemispheres in which the same representations had been removed 6–8 weeks earlier (Fig. 1). [Some of these data formed part of the earlier report (1) describing the functional dependency of SII on the postcentral strip.] Small electrolytic marking lesions (10 μA for 10 sec) were placed at strategic recording sites to aid in later reconstruction of the mapping data. The partial ablations of the postcentral cortex were performed by aspiration with aseptic microsurgical technique while the animals were deeply anesthetized with Nembutal. Postmortem histological examination confirmed that the ablations and electrode tracks were located as planned. Maps of SII were then reconstructed (Fig. 2 *A* and *B*) as described in detail elsewhere (2, 3).

Consistent with other reports (4, 5), our recordings from SII of intact hemispheres revealed a systematic representation of the body surface extending 9–12 mm in the rostro–caudal dimension. The normal somatotopy of SII is illustrated in Fig. 2*C*, which shows consistent features of its organization—such as location, distribution, and areal extent of the representations of various body parts. Note that receptive field topography starts with the head representation rostrally in SII and proceeds to the representations of the hand and arm before ending with those of the leg and foot caudally. In addition, there is a rough somatotopic progression from the ulnar to the radial portion of the hand across the parietal operculum (Fig. 2*C*). Typically, more than half the tissue in SII is devoted to the representation of the hand. In contrast, the representation of the foot ordinarily occupies <15% of SII (4). The representations of the trunk, arm, and leg likewise constitute relatively small percentages of the total body map in SII. We did not attempt to estimate the percentage of SII normally occupied by the representation of the head, because the precise electrophysiological delineation of the border between the postcentral and SII head representations was beyond the scope of this experiment; the location of the border in Fig. 2 is based instead on cytoarchitectonic criteria.

Fig. 2*D* illustrates the altered somatotopy in SII of a hemisphere in which the postcentral representation of the hand was removed 24 hr earlier (see Fig. 1). Note that in both location and extent, the representations of the head, trunk, arm, leg, and foot appeared to be entirely normal (compare with Fig. 2*C*). By contrast, the portion of SII that would be expected to represent the hand was completely unresponsive even to high-amplitude stimulation of the hand or of any other body part, with the exception of one or two small zones of

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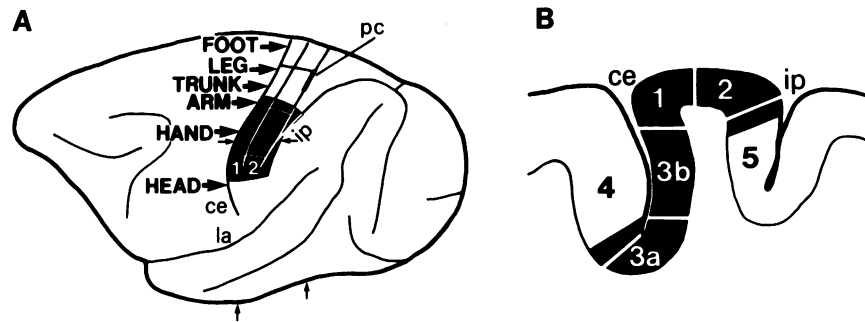
FIG. 1.   (A) Dorsolateral view of a macaque brain, showing the approximate location of the representations of various body parts in the postcentral somatosensory strip. Areas 3a and 3b are located inside the central sulcus (see *B*) and, therefore, are not visible in this view, but their representations parallel those shown for areas 1 and 2. The small horizontal arrows indicate the location of the parasagittal section illustrated in *B*. The small vertical arrows indicate the rostro–caudal extent of the SII region. (B) Parasagittal brain section through the hand representation of the postcentral strip (see *A*) illustrating the location of the cytoarchitectonic areas (3a, 3b, 1, and 2) that were removed. Abbreviations: ce, central sulcus; ip, intraparietal sulcus; la, lateral sulcus; and pc, postcentral sulcus. Numbers designate cytoarchitectonic areas.

tissue responsive to light tactile stimulation of the hairy (i.e., dorsal) surface of the hand. The receptive fields of the neurons in these small zones were always centered on the forearm (i.e., never confined to the hand), suggesting that the source of their input was the postcentral forearm representation, some of whose neurons also have receptive fields that extend onto the dorsum of the hand. Findings essentially duplicating those illustrated in Fig. 2*D* were obtained in the two other cases studied within 48 hr of removing the postcentral hand representation.

A very different result was obtained in the hemispheres that were studied 6–8 weeks after such removals. In each of these chronic cases, the cortex in SII that from its location would be expected to represent the hand turned out to be highly responsive, surprisingly, to stimulation of the foot, not of the hand. Indeed, the foot representation underwent massive expansion from an area constituting only 5–12% of SII in each of the four intact hemispheres to an area constituting 55–75% of SII in each of the four hemispheres with chronic lesions of the postcentral hand representation (Fig. 2*E*). Thus, the areal extent of the foot representation in the hemispheres with lesions appeared to equal the combined area of the hand and foot representations in the intact hemispheres. This filling of an initially unresponsive region extended for more than half the total area of SII, for a distance of as much as 5 mm in the rostro–caudal dimension. Responses to somatic stimulation were noted across the entire extent of SII, and no unresponsive regions could be detected.

Whether the representations of other body parts also underwent postoperative expansion in SII is unclear. There was no obvious increase in the representation of either the head or arm, each of which, like the foot representation, is also normally located immediately adjacent to the representation of the hand in SII. For the head and arm representations, however, their failure to expand may reflect encroachment of the lesion into the head and arm representations of the postcentral strip (see Fig. 1), because of our deliberate extension of the lesion slightly past the estimated borders of the postcentral hand representation to ensure its entire removal. At the same time, evidence for enlargement of the SII representations of the trunk and leg—i.e., body parts whose representations in the postcentral strip were clearly spared—was also only minimal. Indeed, since the expansion of the foot representation was almost exactly equal to that of the former hand representation, it seems unlikely that the representation of any other body part could have expanded to a significant degree.

One possible explanation for the seemingly selective expansion of the foot representation in SII is that much of the SII hand representation is specialized for receiving and processing information from glabrous skin (4). Thus, when deprived of

normal inputs from the postcentral glabrous hand representation, this vacated tissue in SII may be more receptive to inputs from the glabrous foot representation than from the representation of hairy body parts. One way to test this possibility is to record from SII in hemispheres with chronic postcentral removals of the representations of all body parts except those of the hairy and glabrous hand and foot. Since such a lesion would deactivate only hairy body part representations in SII (1), a differential expansion of the representations of the hairy parts of the hand and foot would provide evidence that zones of SII are specialized for processing information from one type of skin region. Such a test could yield valuable hints regarding ontogenetic mechanisms of map formation.

Since the topographic reorganization illustrated in Fig. 2*E* did not occur within the first 48 hr after the lesion of the postcentral hand representation, this reorganization was clearly not the result of an immediate unmasking of preexisting inputs. Other explanations for the effect, therefore, must be considered, including some mechanism that would yield delayed unmasking of preexisting inputs (6, 7) or axonal sprouting of new inputs (8), as well as the possible modulation of such mechanisms by differential sensory stimulation of intact representations (9).

Whatever the explanation for the reorganization, the present findings have important implications regarding the site and extent of cortical plasticity in adult monkeys. The first evidence of cortical topographic reorganization in the somatosensory system of adult monkeys was obtained in primary somatosensory cortex after nerve cuts, nerve crushes, and digit amputations (10–13). These studies left open the possibility that the changes measured in cortex were a reflection of changes occurring at subcortical levels. The present findings of somatotopic reorganization in SII following selective lesions in the postcentral strip, taken in conjunction with the fact that SII is dependent for its somatic activation upon projections from the postcentral strip rather than on a direct projection from the thalamus (1), provide compelling evidence that plasticity after injury in the somatosensory system of adult primates can occur within the cerebral cortex itself. As for the extent of the changes, the reorganization found in the hand representation of primary somatosensory cortex extended over a distance of 0.5–2 mm (10–13). Also, small unresponsive zones of 1–2 mm² were found within the primary hand representation months after denervation of as few as two adjacent digits of the hand (13). By contrast, the topographic reorganization in SII after removal of the entire postcentral hand representation covered a distance of as much as 5 mm and left no detectable zones of unresponsiveness. This comparison raises the possibility that higher-order areas of somatosensory cortex have a greater capacity for plasticity after injury than do primary areas. Furthermore,
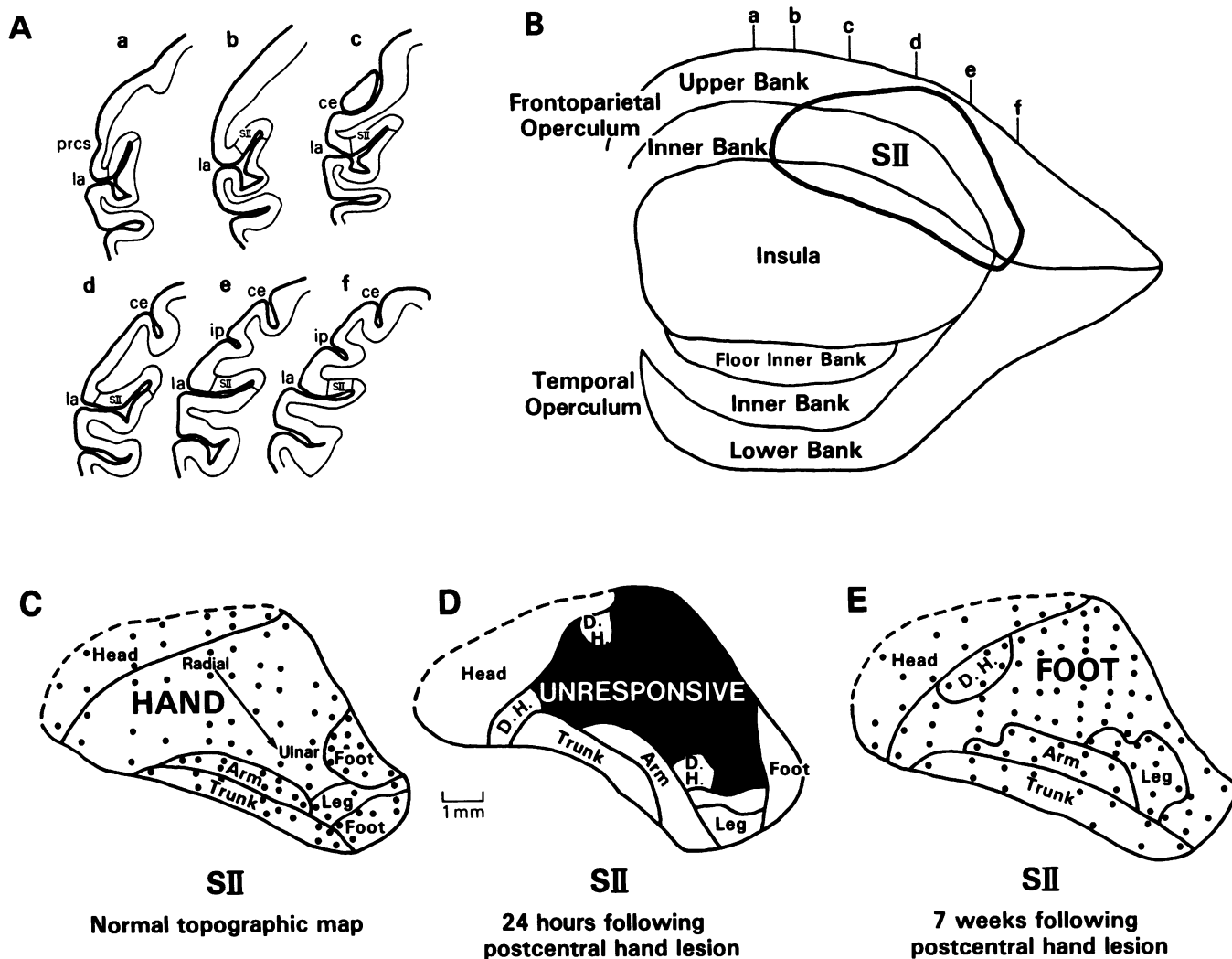
FIG. 2. A rostro–caudal series of coronal sections (sections a–f) taken through SII and adjoining cortical areas. (*B*) Flattened map of the lateral sulcus reconstructed from the sections shown in *A* (for detailed description of methods, see refs. 2 and 3). Note the location of SII as determined both cytoarchitectonically and electrophysiologically. (*C–E*) Enlargements of a flattened view of the SII region as shown in *B*, reconstructed from coronal sections of selected cases. (*C*) A somatotopic map of the SII region as determined from recordings in an intact hemisphere. Note the large amount of tissue devoted to the representation of the hand. In the intact hemispheres, some receptive fields for the hand included hairy and glabrous skin, and these two representations, therefore, are not differentiated as they are in *D* and *E*. Dashed lines in *C–E* indicate the approximate border between the postcentral and SII head representations, based solely on cytoarchitectural evidence. All other borders are based on both electrophysiological and cytoarchitectural criteria. Dots indicate recording sites on which the maps are based. (*D*) A somatotopic map of the SII region obtained 24 hr after removal of the postcentral hand representation (see Fig. 1). Note total absence of somatic activity from sites in the expected location of the hand representation in SII (compare with *C*). Note also the seemingly normal location and extent of the representations of body parts other than the hand. Density of recording sites was similar to that in *C* and *E*. Results duplicating those illustrated in *D* were obtained in two other cases studied within 48 hr after surgery. (*E*) A somatotopic map of the SII region obtained 7 weeks after removal of the postcentral hand representation (see Fig. 1). Note the expansion of the representation of the foot into the expected location of the hand representation (compare with *C*). Results similar to those illustrated in *E* were obtained in three other cases studied from 6 to 8 weeks after their operations. D.H., dorsal hand. Other abbreviations are as in Fig. 1.

since cortical processing pathways appear to be organized in analogous fashion in all the sensory modalities (1, 4, 14, 15), the present findings suggest that all higher-order sensory areas in adults may be capable of an unsuspected degree of plasticity after injury.

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