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7. Other authors have realized the importance of approaching neural coding from the point of view of the organism. In early work, R. Fitzhugh [*J. Gen. Physiol.* **41**, 675 (1958)] discusses real-time decision making. As far as we know, P. I. M. Johannesma [in G. Szekely, E. Lábos, S. Damjanovich, Eds., *Adv. Physiol. Sci.* **30**, 103 (1981); Akadèmiai Kiadò, Budapest] comes closest to our approach.
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11. To ensure that the reconstruction process could be implemented in real time, we required that the filters be causal, for example, $F_1(\tau < 0) = 0$. We calculated the minimum χ^2 causal filters in two ways: (i) The best filter is first calculated without the causality constraint. An explicit formula can be written for this filter in terms of the spike trains and the stimulus

$$F_1(\tau) = \int \frac{d\omega}{2\pi} e^{-i\omega\tau} \frac{\left\langle \tilde{s}(\omega) \sum_j e^{-i\omega t_j} \right\rangle}{\left\langle \sum_{i,j} e^{i\omega(t_i - t_j)} \right\rangle} \quad (3)$$

where $\tilde{s}(\omega) = \langle d\tau \rightarrow \tilde{s}(\omega) = \int d\tau \rangle$. The averages (inside triangular brackets) are over the ensemble of stimuli $s(\tau)$ used in the experiment. This filter can be shifted by a delay τ_{delay} and causality can be imposed by setting the shifted filter to zero at negative times. (ii) χ^2 can be minimized with respect to purely causal functions by expansion of the filters $\{F_n\}$ in a complete set of functions that vanish at negative times. In this method, a delay time must be explicitly introduced that measures the lag between the true stimulus and the reconstruction, so $\chi^2(\tau_{delay}) = \int dt |s(t - \tau_{delay}) - s_{est}(t)|^2$ is minimized. These two methods together ensure that the optimal causal filters are calculated.
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Massive Cortical Reorganization After Sensory Deafferentation in Adult Macaques

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After limited sensory deafferentations in adult primates, somatosensory cortical maps reorganize over a distance of 1 to 2 millimeters mediolaterally, that is, in the dimension along which different body parts are represented. This amount of reorganization was considered to be an upper limit imposed by the size of the projection zones of individual thalamocortical axons, which typically also extend a mediolateral distance of 1 to 2 millimeters. However, after extensive long-term deafferentations in adult primates, changes in cortical maps were found to be an order of magnitude greater than those previously described. These results show the need for a reevaluation of both the upper limit of cortical reorganization in adult primates and the mechanisms responsible for it.

MERZENICH AND HIS COLLEAGUES demonstrated that primary cortical sensory maps in adult animals, like those in infant animals, are capable of reorganization after various peripheral sensory perturbations (*1, 2*). Yet, compared to the massive functional changes that have been found in neonates, in which entire cortical maps may be reorganized (*3*), the changes reported in adults have been relatively small, with an upper limit of 1 to 2 mm along the cortical surface (*1, 2, 4*). Although the finding of any plasticity in primary sensory maps of adult animals was unexpected, the limited extent of the changes suggested they were confined to the projection zones of single thalamocortical axons (*1, 2*). Both the limits of reorganization and the mechanisms responsible must now be reconsidered because of new evidence in adult macaques showing reorganization in the cortex at least an order of magnitude greater than that reported previously.

Tactually elicited neuronal activity was recorded in area SI (*5*) of four cynomolgus monkeys (*Macaca fascicularis*) that had received deafferentations of an upper limb, three unilateral and one bilateral, more than 12 years before the recording session (*6*). All procedures were carried out in accordance with NIH guidelines on the care and use of laboratory animals (*7*). Electrode penetrations were placed approximately 0.75 mm apart across the mediolateral extent of the cortical region that had been deprived of its normal input and less densely in parts of the cortex containing maps of body parts that were unaffected by the deafferentation procedure. We typically recorded activity for each 300-μm advance of the electrode in a penetration.

Normally the cortical representations of body parts are organized into highly topographic maps (*8, 9*) (Fig. 1). In macaques, the upper limb representation in SI is always bordered by the representation of the trunk medially and the face laterally (*10*). In the region of the border of the face and hand representations, which is located opposite the tip of the intraparietal sulcus (*8*), the face map contains the representation of the chin

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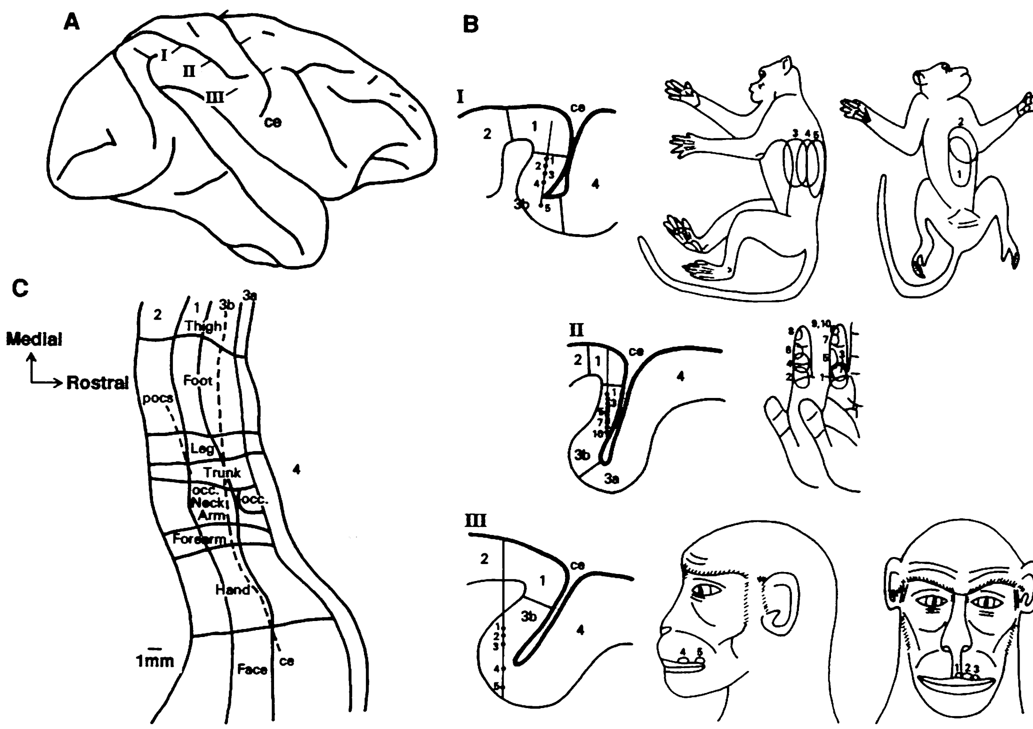

Fig. 1. (**A**) Lateral brain view indicating location of the three parasagittal sections (I through III) illustrated on the right. (**B**) Three parasagittal sections through SI of a normal animal showing electrode tracks (vertical lines) and recording sites (dots). Numbered recording sites (not all are identified by a numeral because of a lack of space) correspond to numbered receptive fields on the body part shown to the right of the parasagittal section. As recording sites traverse the caudal bank of the central sulcus through area 3b, receptive fields on both the trunk (I) and face (III) shift laterally away from ventral midline, while those on the digits (II) shift distally. (**C**) Flattened map of SI showing normal somatotopy. Body part borders are marked by horizontal lines, areal borders by vertical lines, and central and postcentral sulci by dashed vertical lines. The following abbreviations are used: ce, central sulcus, pocs, postcentral sulcus, and occ., occiput. Figure modified from (*8*).

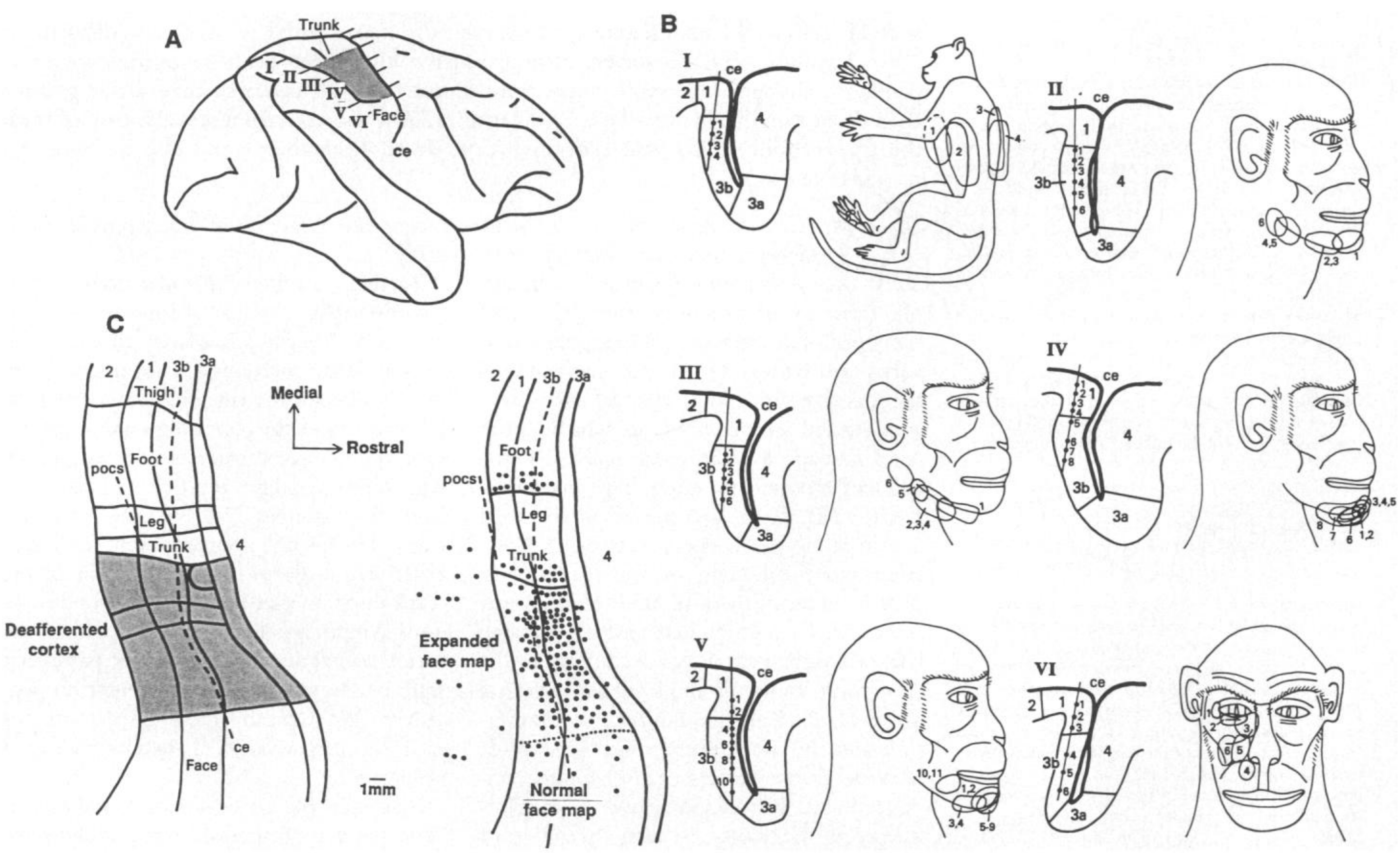

Fig. 2. (**A**) Lateral brain view showing the portion of the postcentral cortex that was deprived of its normal inputs by the deafferentation procedure ("deafferented zone" marked by shading) and the locations of the six parasagittal sections (I through VI) illustrated on the left. (**B**) Sections I and VI show receptive field data from the cortex medial and lateral, respectively, to the deafferented zone. The normal receptive field progression from ventral midline to lateral body parts across the trunk and face was encountered as the electrode traversed the caudal bank of the central sulcus through area 3b (compare with Fig. 1). Sections II through V show the portion of the face represented across the deafferented zone. In section II, located immediately adjacent to the trunk representation, recording sites were still responsive to stimulation of the face. Also, the normal sequence of receptive fields from the ventral midline (chin) to the lateral parts of face (lower jaw) was apparent as recording sites traversed area 3b, as was the mirror reversal of this sequence in area 1 (sections IV through VI). (**C**) Two flattened maps of SI, the first showing the deafferented zone (marked by shading), and the second the recording site density in the animal illustrated (CM3). Other conventions as in Fig. 1.

and lower jaw and the hand map contains the representation of the thumb. The entire upper-limb representation extends lateromedially for 10 to 14 mm, from the lateral tip of the intraparietal sulcus to the lateral tip of the postcentral sulcus, where the trunk representation is normally found.

The area of the cortex deprived of its normal input by the deafferentation procedure, which we refer to as the deafferented zone, included the SI maps of the fingers, palm, remaining upper limb, neck, and occiput (Fig. 2) (*8*). Our recordings unexpectedly revealed that this entire zone responded to stimulation of the face. In the animal illustrated in Fig. 2, we were able to obtain vigorous neuronal responses to light stimulation of the face in 124 recording sites distributed throughout the deafferented zone. Furthermore, none of the sites we tested was unresponsive.

Virtually identical findings were obtained in the three other animals. All 320 sites tested in the deafferented zone in the four animals were activated by face stimulation. An additional 90 and 51 recording sites located lateral and medial, respectively, to the deafferented zone revealed the expected normal topography of face and trunk (*8, 10*). Thus, in all cases, the medial border of the expanded face representation abutted the normal representation of the trunk. There was no apparent elevation of response thresholds at any of the recording sites across the new face map as compared to those across the normal face map; in both, a slight deflection of facial hairs was sufficient to obtain a vigorous neuronal response.

Not all of the face, however, was represented in the reorganized region; rather, stimulation of only a relatively small portion of the face, from the chin to the lower jaw, was found to activate neurons in this zone. At the same time, the pattern of reorganization in this new part of the face map was not random but highly systematic. As in normal face maps (Fig. 1), the midline of the face, in this case the chin, was represented caudally in area 3b (that is, near the border of areas 1 and 3b), whereas progressively more lateral parts of the face, in this case the lateral parts of the lower jaw, were represented in progressively more rostral parts of area 3b (that is, toward the border of areas 3b and 3a). Normally, the representation of the chin and lower jaw is located immediately adjacent to the hand representation. Consequently, it appeared as though each point on the normal face map along the original border of the hand and face representations had been stretched medially into a line approximately 10 to 14 mm long, the length of the deafferented zone. This resulted in the apparent stretching of the entire chin and lower jaw map [at least in areas 3b and 1 (*5*)] onto a cortical sheet 10 to 14 mm long, until the expanded face representation met the normal trunk map (*11*). These findings extend the previously proposed upper limit (*4, 12*) for reorganization in adult primates by an order of magnitude and leave open the possibility that the limit is even greater.

What mechanisms could account for such massive cortical reorganization in mature animals? In earlier studies on the effects of peripheral deafferentations in adult primates, the deafferentations were relatively restricted, involving small parts of the hand (*1, 2*) or visual field (*13*), and the deafferented zone came to represent the sensory surfaces mapped along the zone's lateral and medial edges, with each of these two representations expanding toward the deafferented zone's center. Furthermore, the occupation of the deafferented zone by these new inputs was often incomplete, with small islands of tissue remaining unresponsive to stimulation of any body part (*1, 2, 4*). Because of those features and the spatial limit of reorganization, which was generally in the range of 1 to 2 mm, it was reasonable to relate the filling in of the map to the mediolateral arborization of single thalamocortical axons (*1, 2*), which is also in the range of 1 to 2 mm (*14*). Because of the spatial extent of such arborization, neurons at a given cortical site could receive overlapping thalamic projections from two populations of axons, one representing a dominant skin region and the other an adjacent, nondominant skin region; if so, then loss of the former would allow neuronal activation by the latter, either immediately or after a delay. Although such a mechanism may suffice for the limited changes described previously, it is insufficient to account for the extensive reorganization reported here.

An alternative possibility is that preexisting inputs from face representations in cortical areas outside SI came to activate the deafferented zone. Such a possibility seems remote, however, because all connections of these areas with SI are between somatotopically matched representations (*15*), a circumstance that should impose the same constraints on reorganization as the somatotopically matched thalamocortical projections. If the reorganization we found took place exclusively at the cortical level (*1, 2, 4*), then the only alternative to the immediate or delayed unmasking (*16*) of preexisting thalamocortical or corticocortical projections would be the sprouting of new projections across the deafferented zone. Yet there is no evidence to date of even limited sprouting of sensory terminals in the neocortex after peripheral nervous system injury in adult mammals.

These considerations lead us to propose that much of the functional reorganization we observed was a reflection of changes that had taken place subcortically and were then simply relayed to the cortex (*17*). Body part maps are represented within a much smaller neural space in the brain stem than in the thalamus, and in the thalamus than in the cortex, reflecting the extensive divergence that occurs along pathways connecting the brainstem, thalamus, and cortex (*18*); as a result, reorganization over a relatively small distance at the brain stem or thalamic levels would be reflected as much larger changes at the cortical level (*19*). Thus, if projections to or from brain stem nuclei representing the face were to have synapsed onto all or most of the brain stem or thalamic cells that had previously represented the upper limb, then the entire upper limb representation in the cortex would likewise have come to represent the face. Furthermore, axonal sprouting after deafferentation has been reported to occur in the spinal cord (*20*), making it more plausible that such changes could also be taking place at higher subcortical stations.

Our finding of extensive reorganization after peripheral deafferentation raises many additional questions. For example, why was the deafferented zone not occupied by an expanded trunk as well as by an expanded face representation (*21*)? Did the expanded face representation mediate tactile perception, and could it serve as a substitute for the normal face representation? Was the neural activity in the expanded representation relayed to higher order cortical and subcortical stations? Answers to such questions about mechanism and function could lead to harnessing the immense reorganizational capability of the adult nervous system for therapeutic purposes (*22*).

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