Intracortical Connections of Two Functional Subdivisions of the Somatosensory Forepaw Cerebral Cortex of the Raccoon

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The aim of this study was to compare the intrinsic intracortical connectivities of 2 functionally distinct subdivisions of the somatosensory (Sml) forepaw cortex of the raccoon—the somatotopic glabrous skin representation and the more heterogeneous, hairy skin and claw representation of the digits. HRP was injected into one or the other functional subdivision of a particular digit subgyrus of Sml cortex in 10 adult raccoons. The distribution of HRP-labeled neurons and axon terminals in the cortex showed that intrinsic “horizontal” connections exist within and between individual cortical digit zones; the labeling tended to have an oval-shaped configuration that was longer in the mediolateral than in the anteroposterior curvilinear plane. The 2 cortical sectors were found to have different patterns of intracortical projections. The connections of the glabrous skin region of each cortical digit zone were primarily local and confined to that same digit representation. HRP-filled neurons were concentrated near the injection site and decreased in density within the banks and fundi demarcating the injected digit subgyrus; few labeled cells were found in adjoining digit zones. Longer projections to the glabrous subdivision of a particular digit area typically originated from neurons in the heterogeneous subdivision of that same digit area. In contrast, the connections of the heterogeneous region of each digit zone were much more extensive and usually included projections from nonadjacent, as well as neighboring digit zones. The density of HRP-positive neurons declined more gradually with distance from the injection site, and considerable labeling was present in the heterogeneous sectors of adjacent digit zones. The intracortical projections of both functional subdivisions were often, but not always, reciprocal, and the cells of origin tended to be distributed in clusters. The laminar distributions of labeled neurons were similar for both sectors; HRP-filled cells were concentrated more in the supragranular layers, especially in layer III; fewer were found in the infragranular layers, mainly in layer VI and rarely in layer V.

These results show that the intrinsic connections of the

glabrous cortical subdivisions are fairly localized, whereas those of the heterogeneous cortical subdivisions are more diffuse and highly convergent. The differing intracortical connective patterns of the 2 sectors are consistent with their contrasting thalamocortical projection patterns and may contribute to the unique functional properties of neurons located within each sector. Finally, the convergent projections from the heterogeneous cortical regions to a particular glabrous skin region could explain many of the features of Sml cortical reactivation in the raccoon following peripheral nerve transection (Kelahan and Doetsch, 1984).

The representation of the forepaw within the primary somatosensory (Sml) cortex of the raccoon is comprised of 2 functionally distinct subdivisions or sectors (Johnson et al., 1982; Kelahan and Doetsch, 1984; Johnson, 1985). A posteriorly located, rather homogeneous subdivision contains modality-specific neurons that receive input only from the glabrous skin of the digits and have small, somatotopically arranged receptive fields (RFs). Rostral to this sector is a more heterogeneous subdivision, with neurons that have larger, somatotopically less precise RFs located primarily on the hairy skin and claws, but sometimes also involving glabrous skin or deep tissues. This so-called “heterogeneous” region (Johnson et al., 1982) is bounded anteriorly by a “kinesthetic” area—apparently homologous with area 3a in the monkey and cat (Jones and Porter, 1980; Dykes et al., 1986)—that contains neurons responsive to input from muscle and joint receptors (Johnson et al., 1982; Feldman and Johnson, 1985; Johnson, 1985). Located rostral to the kinesthetic area is the “electrically excitable” primary motor (Msl) cortex (Hardin et al., 1968; Ray and Doetsch, 1977).

In the previous paper, Doetsch et al. (1988), reported that the glabrous and heterogeneous subdivisions of the Sml forepaw cortex had different thalamocortical interconnections that could account for the contrasting functional properties of their constituent neurons. The glabrous skin representations were found to receive topographically specific projections from individual subnuclei within the ventral posterior lateral (VPL) nucleus of the thalamus, in agreement with the classical findings of Welker and Johnson (1965). In contrast, the heterogeneous, hairy skin and claw representations typically received convergent projections from several VPL subnuclei, a dorsal kinesthetic region of VPL, and from adjoining thalamic nuclei, specifically the ventral posterior inferior (VPI) nucleus and the posterior (PO) nucleus. The degree of functional homogeneity or heterogeneity characterizing each of the 2 Sml cortical subdivisions may thus

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be explained by the specificity or diversity of their unique thalamocortical inputs.

Several studies have shown that the SmI forepaw cortex of the raccoon undergoes significant functional changes following transection of a cutaneous digital nerve. Neurons located within the glabrous sector of a deafferented cortical digit zone develop “new” RFs on adjoining digits, sometimes within 24 hr following the lesion (Carson et al., 1981; Kelahan et al., 1981; Rasmussen, 1982; Kelahan and Doetsch, 1984). The novel RFs were larger in size and involved mixtures of glabrous and hairy skin or the claws—properties that resemble those of neurons present normally in the heterogeneous cortical regions. Both the temporal and spatial features of cortical reactivation in the raccoon strongly suggest that the primary mechanism of this phenomenon is the unmasking of preexisting anatomical connections, resulting in the emergence of apparently novel inputs to SmI cortex (Kelahan and Doetsch, 1984).

To examine the potential circuitry involved, the strategy (Doetsch et al., 1988) was to study the thalamocortical and possible intracortical connections of the glabrous and heterogeneous subdivisions of SmI cortex that might support functional reactivation. Although the different patterns of thalamic projections to the 2 SmI cortical sectors could account for many of the contrasting properties of these sectors, they do not explain the convergent features that appear within the glabrous subdivision of a deafferented digit zone during cortical reactivation. This suggests that local intracortical connections *between* different digit zones of the SmI forepaw cortex—and especially between the heterogeneous and glabrous cortical regions—may be routes for convergent inputs to these zones. Although very little is known about intrinsic SmI intracortical connections, their existence was demonstrated several years ago by anatomical (Jones and Powell, 1968, 1969) and electrophysiological (Murray and Heath, 1978) methods. No comprehensive study of such projections has been done previously in the raccoon; however, Herron and Johnson (1987) recently showed several examples of interconnections within and between individual digit areas of SmI cortex of this species.

The primary goal of this study was to examine the neural circuitry that could mediate functional reactivation within SmI cortex following peripheral nerve transection. To accomplish this, possible intrinsic intracortical connections of the glabrous and heterogeneous subdivisions of individual SmI cortical digit areas were studied and compared in adult raccoons using the HRP tracer method.

Materials and Methods

Results were obtained from 10 adult raccoons (*Procyon lotor*), using the surgical, electrophysiological, and HRP tracer methods described in the previous paper (Doetsch et al., 1988). Each animal was anesthetized with pentobarbital sodium (30 mg/kg, IP), and the SmI forepaw cortex of both hemispheres was exposed surgically. The responses of small clusters of neurons were recorded with tungsten microelectrodes to identify electrophysiologically the specific digit representations and to determine the boundary between the glabrous and heterogeneous subdivisions of the particular digit zone under study.

A Hamilton syringe was used to make an injection of 36% HRP or a mixture of 36% HRP and 3% wheat germ agglutinin-conjugated HRP into individual cortical digit subgyri of each hemisphere. The injections were made at depths of 1–2 mm below the pial surface and varied in volume from 0.15–0.6 μ l (10 hemispheres) to 0.01–0.04 μ l (10 hemispheres). In the latter cases, the HRP was confined either to the glabrous or heterogeneous sector of the injected cortical digit area. After a survival period of about 48 hr, the raccoon was sacrificed and the brain was prepared for HRP histochemistry using tetramethyl benzidine. Brain

sections reacted for HRP were examined microscopically, and the distributions of HRP-labeled neurons and axon terminals in the cortex were plotted on camera lucida drawings of cortical sections. Further details of the methodology are given in the preceding paper (Doetsch et al., 1988) (see Appendix).

Results

The results disclosed 2 major features of the organization of SmI cortex that have not been described. First, intrinsic “horizontal” interconnections were found to exist within and between individual cortical digit zones. Second, distinct differences were observed in the intracortical connectivity of the glabrous and heterogeneous cortical subdivisions.

HRP injection sites

As described in the preceding paper (Doetsch et al., 1988), the site of an HRP injection typically was found to contain a central core of dense reaction product that was surrounded by a halo zone of HRP diffusion containing more lightly and more uniformly stained neurons and neuropil (Fig. 4A). It was often difficult to distinguish the boundary between the halo zone and adjoining regions of labeled neurons that had actively transported HRP from the core of the injection site. However, the density and uniformity of the labeling was found to decrease, sometimes abruptly and selectively in different cortical layers, with distance from the site of injection. This observation was used as a criterion for determining the approximate border of the halo zone and regions containing retrogradely labeled neurons. Only the results obtained from the *small* (0.01–0.04 μ l) HRP injections are reported here; data from the *large* (0.15–0.6 μ l) injections were used mainly to confirm the basic patterns of the cortical interconnections.

General features of intracortical connections

The HRP injections made into the forepaw region of SmI cortex revealed 2 types of intrinsic cortical interconnections. Projections to the glabrous skin subdivisions of individual cortical digit zones were localized and primarily interconnected different portions of the *same* digit zone. Projections to the heterogeneous subdivisions were much more extensive and interconnected *different* digit areas, as well as disparate parts of the same digit area.

The intracortical connections appeared to be predominantly reciprocal; HRP-filled neurons and axon terminals in SmI cortex overlapped extensively but not completely. While the HRP reaction product contained within neuronal cell bodies was usually clearly evident, the labeling of axon terminals was more difficult to distinguish and was less consistent from one case to another (Fig. 4). Hence, the connections described here are limited to those revealed by the distribution of retrogradely labeled neurons.

Intracortical connections of glabrous skin cortical subdivisions

A *small* (0.01–0.04 μ l) HRP injection made into the electrophysiologically defined glabrous subdivision of a particular cortical digit zone consistently revealed intrinsic projections from different regions of this zone to the site of the injection (Figs. 1–3). Most of these connections were relatively short (1–3 mm), and the cells of origin were confined predominantly to the injected digit area. HRP-filled neurons were concentrated near the injection site and declined in density with distance from this site.

Figure 1. Distribution of labeled neurons in the cortex resulting from a small injection of HRP into the glabrous subdivision of the digit 4 zone of the SmI forepaw cortex. In this and subsequent figures, the core of each HRP injection site is shown in *black* on a lateral surface view of the brain. The *numbered vertical lines* indicate the rostrocaudal levels of the corresponding coronal sections taken through the brain and illustrated in the lower part of the figure. Cortical sulci are designated in *italics*, and functionally or somatotopically different cortical areas are indicated in *bold numbers and letters*. On the coronal sections, the core and the surrounding halo zone of the injection site are shown by the *black and hatched areas*, respectively; the locations of HRP-filled neurons are shown by *dots*. Major sulci and functional areas are identified. See Appendix for all nomenclature and abbreviations. Thickness of sections in this case, 50 μ m; distance between sections illustrated, 1000 μ m, except between sections 101, 131, and 161, 1500 μ m. Labeled cells, constituting the origin of intrinsic projections to the injected cortical site, are located primarily in the injected digit 4 area.

The maximum spread of labeled neurons following HRP injections into the glabrous cortical sectors was more restricted in the anteroposterior dimensions ($\bar{X} \sim 5$ –6 mm, as measured by distances between coronal sections) than in the mediolateral dimensions ($\bar{X} \sim 12$ mm, as estimated by curvilinear measurements of cortical convolutions, Figs. 1–3). Of the anteroposteriorly directed projections to a particular glabrous sector, those originating from regions rostral to the injection site were longer ($\bar{X} \sim 3$ –4 mm) and more numerous, while those from regions caudal to that site were shorter ($\bar{X} \sim 2$ mm) and less dense. The latter fibers, covering small distances, originated from neurons located in the caudal portions of the glabrous sector of the injected digit zone. The longest fibers extended over distances of

about 5–6 mm and arose from cells in the rostral heterogeneous subdivision of the injected digit area.

In the mediolateral dimension, the most heavily labeled regions bordered directly on the injection site; the labeling declined in density as it extended into the banks and fundi of the adjacent sulci (Figs. 1–3). HRP-filled cells became scarce beyond the demarcating fundi; the sparse projections from these neurons interconnected the glabrous cortical region of a given digit zone with glabrous regions of adjacent digit zones. No clear evidence of interconnections between nonadjoining digit areas was obtained (Figs. 1–3). The short mediolaterally directed fibers originated from neurons located in the crown and upper banks of the sulci that are part of the glabrous subdivision of the injected

Figure 2. Location of HRP-filled neurons in the cortex following a small injection into the glabrous sector of the digit 3 cortical zone. Section thickness, 40 μ m; distance between sections, 800 μ m. The labeled cells tend to form clusters and are found mainly in the banks and demarcating fundi of the digit 3 area.

digit zone. In contrast, the longer fibers arose from cells in or near regions of the demarcating sulcal fundi; some of these regions may constitute posterior extensions of the heterogeneous sectors into the depths of the subgyral convolutions (Johnson et al., 1982).

No connections were found between the SmI cortical representations of the forepaw digits and the representations of other major body regions, such as the leg or face. Furthermore, no clear evidence was obtained for interconnections between the glabrous subdivisions of the SmI digit cortex and cortical regions located rostral to the heterogeneous sectors, i.e., the kinesthetic area or Msl cortex.

The HRP-filled neurons typically were arranged in multiple clusters or aggregates of varying size and continuity (Figs. 1–4). Most of these clusters included labeled cells in several cortical layers; indeed, the HRP-positive neurons had a characteristic laminar distribution. Short fibers originated from aggregates of neurons in closely adjoining glabrous regions of the crown or sulcal banks of this same zone. These neurons were located primarily in the supragranular layers—many in layer III and fewer in layers II and IV (Fig. 4C). The infragranular layers

contained HRP-positive neurons only occasionally in layer V but considerably more often in layer VI. The longer fibers originated from clusters of cells in or near the fundus of one or both demarcating sulci. These cells were located predominantly in layers VI and III; those in layer VI were often spindle-shaped (Fig. 4E) and sometimes were lightly labeled, especially compared with layer III neurons which usually contained dense HRP reaction product. The glabrous subdivision of a cortical digit zone consistently was found to receive projections from the anterior heterogeneous subdivision of the same digit zone. The neurons giving rise to these fibers were situated preferentially in the supragranular layers (Fig. 4, B, D).

Since the clusters of neurons often involved more than one cortical layer, some of them gave the appearance of neuronal aggregates extending vertically through the cortex (Fig. 4C). However, this cytoarchitectonic feature was variable and depended to some degree on the depth of the cortical injection; with more superficial injections, the clusters of HRP-positive cells were usually restricted to the supragranular cortical layers and thus did not form a complete vertical pattern (not illustrated).

Figure 3. Distribution of labeled neurons in the cortex produced by a small injection of HRP into the glabrous region of the digit 4 cortical area. Section thickness, 40 μ m; distance between sections, 800 μ m. Aggregates of HRP-filled cells are concentrated in the immediate vicinity of the injection site.

Intracortical connections of heterogeneous cortical subdivisions

After small (0.01–0.04 μ l) injections of HRP into the electrophysiologically defined heterogeneous cortical subdivisions, the resulting distribution of labeled neurons revealed a different, more extensive system of horizontal intracortical connections (Figs. 5–7). The characteristic feature of the connections of the heterogeneous regions was that they originated from cortical areas beyond the injected digit zone and involved many more neurons. A given heterogeneous cortical injection site was surrounded by numerous HRP-filled neurons that projected short (1–3 mm) axons into this site (Figs. 5–7). The number of labeled neurons decreased farther away from the injection site, but the labeling extended over distances that were about twice as great in both the anteroposterior and mediolateral planes than those found with injections of glabrous cortical regions.

As with the interconnections of the glabrous cortical sectors, those of the heterogeneous sectors were more limited in maximum extent in the anteroposterior dimensions ($\bar{X} \sim 11$ mm) than in the mediolateral dimensions ($\bar{X} \sim 22$ mm; Figs. 5–7). Among the rostrocaudally oriented projections to a given heterogeneous subdivision, those originating from regions posterior to the injection site were often longer ($\bar{X} \sim 7$ –8 mm) but usually were less dense; those from more anterior regions typically were shorter ($\bar{X} \sim 4$ –5 mm) but more numerous (Figs. 5, 7). In other

words, HRP-filled cells generally were more plentiful and more densely packed rostral than caudal to the injection site. Sometimes gaps were observed in the rostrocaudal distribution of labeling; Figure 7 shows that the HRP labeling in a heterogeneous region was dense anterior and adjacent to the injection site, was interrupted posterior to that site (see sections 241 and 261), and reappeared caudally in the form of several clusters of neurons located within the region of representation of the palmar pads and digit 5 (see sections 281 and 301).

In the anteroposterior plane, the longer but more sparsely distributed fibers arose from neurons in the glabrous sector of the injected digit zone and of adjacent digit zones. The longest of these anteriorly oriented fibers covered distances of about 7–10 mm, originating from cells in or near the representations of the palmar pads (Figs. 5–7). The shorter, more dense fibers arose from the most rostral portions of the heterogeneous regions near the injection site. In contrast to the interconnections of the glabrous cortical sectors, the longest of these posteriorly directed projections had their origin rostral to the heterogeneous regions of SmI cortex, i.e., from neurons located within the kinesthetic area and Msl cortex (see sections 91 and 131 of Fig. 5).

The mediolaterally oriented projections to the heterogeneous sector of a particular digit zone arose predominantly from heterogeneous regions of the same zone and of neighboring digit areas (Figs. 5–7). Each injection site was surrounded by exten-

Figure 4. Photomicrographs showing a representative HRP injection site within SmI cortex, varying patterns of labeling, and different morphologies of HRP-filled neurons in the cortex. *A*, Typical HRP injection made in the heterogeneous subdivision at the border of the digit 3 and digit 4 cortical zones of the left hemisphere (see Fig. 5); scale, 1 mm. *B*, Loosely clustered groups of HRP-filled neurons in layers II–IV of the heterogeneous region of the digit 2 cortical area following the injection illustrated in Figure 4*A*; scale, 0.25 mm. *C*, Small, vertically oriented cluster of labeled neurons extending through cortical layers II–V of the glabrous sector of the digit 2 cortical zone resulting from the injection shown in Figure 4*A*; scale, 0.2 mm. *D*, Small group of HRP-filled pyramidal cells located deep in layer III of the heterogeneous subdivision of the digit 2 cortical zone following the injection of Figure 4*A*; scale, 50 μ m. *E*, Two HRP-positive, spindle-shaped neurons located in cortical layer VI near the fundus of the postcruciate sulcus between the heterogeneous regions of the digit 4 and digit 5 cortical areas resulting from the injection of Figure 4*A*; scale, 50 μ m.

sive regions of HRP-filled neurons that gradually declined in density with distance from this site. Short fibers originated from cells located in adjacent parts of the injected heterogeneous sector; longer fibers arose from neurons in more distant portions of the same heterogeneous subdivision or from neurons in het-

erogeneous (and glabrous) regions of adjacent digit areas. The longest fibers arose from cells that were located at least 10 mm medial or lateral to the injection site and originated from heterogeneous portions of nonadjoining digit zones. In one case, the heterogeneous cortical region representing the claw and hairy

Figure 5. Location of HRP-positive neurons in the cortex following a small injection into the heterogeneous sector at the border of the digit 3 and digit 4 cortical areas (see Fig. 4A). Section thickness, 50 μ m; distance between sections, 2000 μ m. There is widespread labeling of cells in the injected digit 3 and digit 4 areas, extending anteriorly into the region of the kinesthetic area and Msl cortex, and posteriorly into the region of the palmar pad zone. Clusters of labeled neurons are also distributed mediolaterally with respect to the injection site and are present in the noninjected cortical areas representing digits 2 and 5.

skin of both digits 4 and 3 was found to receive projections from neurons in the cortical zones for digits 2 and 5, as well as those for digits 4 and 3 (Fig. 5). Thus, the mediolaterally directed projections to the heterogeneous cortical sectors were considerably longer than those of the glabrous sectors and interconnected somatotopically different representations within the Sml forepaw cortex. Consistent with the glabrous cortical subdivi-

sions, no projections to the heterogeneous subdivisions of the forepaw digits were found to originate from Sml cortical representations of other major body parts such as the leg or face.

As with the glabrous cortical regions, neurons projecting to the heterogeneous regions typically were arranged in clusters of varying configurations (Figs. 4–7). The laminar distribution of labeled neurons resembled that observed with the injections of

Figure 6. Distribution of labeled neurons in the cortex resulting from a small HRP injection into the heterogeneous subdivision of the digit 4 cortical zone. Section thickness, 50 μm ; distance between sections, 1000 μm . Note the extensive labeling of groups of cells throughout the anterior heterogeneous regions of the digit 4 and digit 3 areas and the decrease in HRP-positive cells posteriorly near the pad zone.

the glabrous sectors: Most HRP-filled cells were located in the supragranular layers II–IV, with the greatest number in layer III. The infragranular layers contained very few labeled cells in layer V but more in layer VI, especially within demarcating fundi. The neuronal clusters sometimes formed vertically ori-

ented aggregates that crossed the boundaries of cortical cell layers (Fig. 4C).

If the 2 major functional subdivisions were compared by flattening the cortex into a 2-dimensional plane and viewing it from above, each injection site would appear to be surrounded

Figure 7. Location of HRP-filled neurons in the cortex following a small injection into the heterogeneous sector of the digit 4 cortical area. Section thickness, 50 μ m; distance between sections, 1000 μ m, except between sections 131 and 161, 1500 μ m. Clusters of labeled cells are present throughout the digit 4 zone and extend posteriorly into the pad zone. There is a gap in labeling at the transition from the digit 4 area to the pad area (sections 241 and 261).

by clusters of neurons projecting their axons into that site. These neurons would be distributed in an oval-shaped pattern, with its long axis directed in the mediolateral plane. Both the major and minor axes of this oval pattern would be about 2 times longer for injections in the heterogeneous cortical subdivisions than for injections in the glabrous subdivisions. From this perspective, it is clear that the mediolaterally oriented projections extended over greater distances than the anteroposteriorly directed projections. Thus, the most extensive projections to each glabrous sector may originate from neurons within heterogeneous regions located both medially and laterally near the fundi of demarcating triradiate sulci (Johnson et al., 1982), as well as

heterogeneous regions located rostral to that sector. Finally, this approach confirms that each heterogeneous region contains an extensive network of convergent projections that may interconnect somatotopically different digit and palmar pad representations within SmI cortex and may include projections from the kinesthetic area and Msl cortex as well.

Discussion

The forepaw digit representations within the 2 functional subdivisions of SmI cortex of the raccoon were found to contain "horizontally projecting," intracortical connections that generally were more extensive in the mediolateral plane than in the

anteroposterior plane. The glabrous and heterogeneous cortical subdivisions had characteristically different patterns of interconnectivity. The intracortical connections of the glabrous sectors were relatively short and were confined mostly to the same digit zone and its associated heterogeneous sector. The neurons giving rise to these fibers tended to form clusters and were concentrated in cortical layers III and VI. In contrast, the intracortical projections of the heterogeneous cortical subdivisions were longer and interconnected regions between, as well as within, individual digit areas. The cells giving rise to these intracortical fibers also formed clusters and were located primarily in cortical layers III and VI. The intracortical projections to the heterogeneous regions originated more anteriorly—sometimes from portions of the kinesthetic area and MsI cortex—and from more lateral and medial cortical regions than did the projections to the glabrous sectors. Finally, the interconnections within SmI cortex of *both* functional subdivisions were confined to the forepaw representation and did not involve the representations of other major body parts such as the leg or face.

Herron and Johnson (1987) recently obtained connectional data from several cases of HRP injections into the SmI forepaw cortex of the raccoon that are basically in agreement with the results of the present study. Although these investigators did not distinguish electrophysiologically between the glabrous and heterogeneous sectors, they concluded that intrinsic connections exist between disparate digit areas of SmI cortex. The cells of origin were found to be located primarily in layer III of the sulcal cortical regions that may form posterior extensions of the heterogeneous cortex (Johnson et al., 1982).

Intracortical connections in the raccoon and other species

The intracortical connections of the SmI forepaw cortex may be divided into 2 major types: those linking different parts of the *same* functional cortical region and those interconnecting entirely *different* cortical regions. The first type includes the intrinsic connections that were confined either to the glabrous cortical sectors or to the heterogeneous sectors. The second type involves the connections between the glabrous cortical regions and the heterogeneous regions.

Connections of the first type, between somatotopically different (heterotopic) parts of the *same* functionally or cytoarchitecturally defined cortical area, are present in other species (Jones and Powell, 1968, 1969; Jones et al., 1978; Murray and Heath, 1978; Bowker and Coulter, 1981). The results of some anatomical tracer studies, for example in the monkey, indicate that the cells of origin or the axon terminals of such fibers may form elongated strips or bands extending in a mediolateral direction through the injected cortical area for distances up to 5 mm or more (Jones et al., 1978; Bowker and Coulter, 1981). In the raccoon, oval-shaped patterns of clustered, intracortically projecting neurons were found in the digit representations of each functionally distinct subdivision; although these oval cell distributions were more extensive in the mediolateral than in the anteroposterior plane, they did not resemble the elongated bands found in the simian brain. This result suggests that the interconnections between heterotopic cortical regions are more restricted and punctate in the raccoon than in the monkey. Whether clusters of labeled neurons in the raccoon SmI cortex formed truly continuous strip-like aggregates could not be determined in the present study because cortical sections were cut in only one plane, and all consecutive serial sections were not analyzed. In any case, heterotopic projections—although they

obviously exist—have not been emphasized in the literature, and the extent to which they interconnect distant regions within the body representations of SmI cortex in different species is not clear.

Projections of the second type, between 2 functionally distinct cortical regions, were found in SmI cortex of the raccoon to interconnect the glabrous and heterogeneous sectors of the cortical digit zones. Dense interconnections were typically observed between the glabrous and heterogeneous representations of the same digit. This pattern of projections resembles the extensive, somatotopically corresponding (homotopic) interconnections between functionally or cytoarchitecturally *different* cortical areas that have been found in other species (Jones et al., 1978; Bowker and Coulter, 1981; Kaas, 1983; Cusick and Kaas, 1984). Such interconnections often have been described as homotopically precise. For example, small cortical regions representing the fingertips in areas 3b and 1 of the monkey are reported to be reciprocally and selectively interconnected (Kaas, 1983; Cusick and Kaas, 1984). On the other hand, as previously discussed, injections of a tracer into a single cytoarchitectonic area can produce mediolaterally oriented strips of labeling in one or several neighboring cytoarchitectonic areas (Jones et al., 1978; Bowker and Coulter, 1981). In the raccoon, no evidence was obtained for strictly homotopic interconnections between the glabrous and heterogeneous cortical regions; instead, convergent projections from several digit representations of one functional subdivision to a single digit representation of the other subdivision were common. The latter findings are not consistent with the idea of exclusively homotopic connections between functionally separate cortical areas and must be reconciled experimentally and conceptually in future work.

Anatomical and functional significance of intracortical connections in the raccoon

The differential intracortical projection patterns of the glabrous and heterogeneous subdivisions support the idea that these subdivisions are functionally separate cortical regions. However, despite their connectional and physiological differences (Johnson et al., 1982; Kelahan and Doetsch, 1984; Johnson, 1985; Doetsch et al., 1988), the 2 regions are difficult to distinguish on the basis of cytoarchitectonic criteria (Johnson et al., 1982). Some obvious variations in cytoarchitecture may be seen between the subgyral crowns that contain the glabrous skin representations and the walls or fundi of adjacent sulci that may contain posterior extensions of the heterogeneous, hairy skin and claw representations (Johnson et al., 1982). The cortex of the subgyral crowns is considerably thicker and is characterized by cell laminae that are more highly differentiated and by a cell-sparse layer V that is especially wide and more distinct compared with the cortex forming the fundi and banks of the tri-radiate sulcus. However, it is unclear whether these differences reflect functionally significant cytoarchitectonic features or whether they can be accounted for simply by the infolding of cortical tissue and variations in the density of thalamocortical projections. In the anterior, smooth gyral regions of the SmI digit areas, where the electrophysiologically defined glabrous and heterogeneous subdivisions meet, it was impossible to distinguish the 2 subdivisions histologically with confidence.

Although significant physiological differences among cortical fields are often correlated with cytoarchitectonic differences, exceptions to this “rule” are fairly common. In general, distinct variations in functional properties are considerably more fre-

quent than clear changes in cytoarchitecture. Thus, a given cytoarchitectonic area may contain several distinct subsets of neurons whose properties vary with respect to different physiological parameters—RF somatotopy, submodality sensitivity, or dynamic response characteristics such as firing frequency and adaptation rate. For example, the spatial segregation of slowly adapting neurons in area 3b of the cat (Dykes et al., 1980) and monkey (Sur et al., 1984) appears to be uncorrelated with any distinguishable cytoarchitectonic border. Other instances of cytoarchitectonic and functional independence include the presence of 2 forepaw representations within SmI cortex (area 3b) of the rat (Chapin and Lin, 1984) and the squirrel (Sur et al., 1978) and the existence of neurons with bilateral RFs in the hindpaw representation but not in the forepaw representation of area 3b in the cat (Doetsch and Towe, 1976). In this context, clear cytoarchitectonic differences between SmI cortical representations of glabrous and hairy skin surfaces of the forepaw have been reported for only one species, the prosimian potto (Fitzpatrick et al., 1982). Further study is required to determine whether physiological variations within SmI cortex of the raccoon correspond to distinct cytoarchitectonic or myeloarchitectonic differences.

While each heterogeneous cortical region exhibits some characteristic features of somatosensory koniocortex, the status of this region as a single functional area is open to question. As discussed in the preceding paper (Doetsch et al., 1988), the heterogeneous sector might consist of several subregions, each with its own distinct functional characteristics and separate thalamocortical inputs. More detailed cytoarchitectonic, connectional, and electrophysiological studies are required to examine this possibility.

Since the functional microstructure of the heterogeneous SmI cortex in the raccoon is not understood, homologous regions of SmI cortex in other species are difficult to identify. The heterogeneous cortical regions of the raccoon may constitute a unique specialization of cortical tissue within area 3b or a distinct border zone between areas 3b and 3a. However, it is more likely that this region is common to other mammals and is simply enlarged in the highly tactile raccoon. Cortical areas with similar functional or anatomical features in other species may include anterior or medial portions of the forepaw sensorimotor cortex in the cat (Welt et al., 1967; Towe et al., 1968; McKenna et al., 1981) and a convergent "border zone" surrounding the forelimb "core zone" of SmI cortex in the monkey (McKenna et al., 1982). Other regions of particular relevance are the perigranular or dysgranular zones surrounding or intermingled with the granular portion of SmI cortex in the rat (Chapin and Lin, 1984; Welker et al., 1984). The granular cortical areas in the rat, like the glabrous cortical regions in the raccoon, contain neurons that are modality specific and have small somatotopic RFs (Chapin and Lin, 1984; Welker et al., 1984); these areas receive dense thalamic projections predominantly from VPL (Killackey, 1973; Donoghue et al., 1979). In contrast, the dysgranular cortical areas, like the heterogeneous regions in the raccoon, contain neurons that have larger, less somatotopic RFs and sometimes display convergent, multimodality sensitivities (Chapin and Lin, 1984; Welker et al., 1984). The dysgranular areas receive relatively modest thalamic projections, primarily from regions adjoining VPL and including portions of the posterior (PO) nucleus (Herkenham, 1980; Lu and Lin, 1986); they receive corticocortical projections from the neighboring granular zones, from area 3a, and from MSl cortex (Akers and Killackey, 1978; Chapin and Woodward, 1982). Although the dys-

granular SmI cortical zones in the rat and the heterogeneous cortical regions in the raccoon obviously share some important features, whether these areas are truly homologous remains to be determined.

In any case, it is clear that there are convergent projections within and between the heterogeneous and glabrous sectors of SmI cortex in the raccoon and that such heterotopical interconnectivity exists in SmI cortex of other species as well. Indeed, horizontal intracortical connections appear to be a feature shared by other sensory areas—for example, visual cortex (Rockland and Lund, 1983; Matsubara et al., 1987)—and therefore must be incorporated into current concepts of cortical organization.

Physiological role of cortical interconnections

Until recently, concepts of cortical organization were dominated by the idea of vertical information processing within independent functional units or modules, originally referred to as "columns," that were believed to comprise the sensory cortex (Mountcastle, 1957). The discovery that extensive reciprocal connections exist within and between somatic cortical areas forced a modification of this view to include the idea of horizontal information processing, involving interactions between the proposed cortical columns. In this scheme, the fundamental role of all cortical interconnections may be to modulate or integrate patterns of neuronal activity in neighboring or distant modules. Within SmI cortex, convergent horizontal inputs to a given aggregate of neurons could endow a subset of those neurons with RFs and dynamic response properties that are more complex than those of layer IV neurons, whose characteristics are primarily determined by their dominant input from a specific thalamic nucleus, such as VPL. The most significant modulatory effects would thus be exerted on neurons located in the supragranular and infragranular layers.

The short intrinsic interconnections between heterotopic portions of the same cortical field could modify local patterns of neuronal activity that are determined predominantly by input from the same thalamic nucleus. The horizontal projections may exert selective excitatory influences on adjoining neuronal aggregates or they may have inhibitory effects, perhaps mediated by GABA-ergic neurons (Jones, 1981, 1986). These inputs could modulate the vertical flow of information and alter the response properties of projection neurons located in cortical laminae above or below the thalamic recipient layer IV (Uhr and Chapin, 1983). Differences in physiological characteristics as a function of depth within SmI cortex have been described in several species. For example, in the monkey (Whitsel et al., 1972; Sur et al., 1985), cat (Doetsch and Towe, 1976; McKenna et al., 1984), and rat (Chapin, 1986), the RFs and functional properties of many neurons located in the supra- and infragranular layers are more complicated than those of neurons in granular layer IV. Increases in RF size have been observed also for neurons in the deeper layers of SmI cortex in the raccoon (G. S. Doetsch, unpublished observations). Thus, intrinsic intracortical connections may contribute to laminar variations within a cortical module and to the functional uniformity or diversity within a given cortical field.

The longer corticocortical interconnections between homotopic or heterotopic portions of separate cortical fields could modulate or integrate distant patterns of neuronal activity that are determined primarily by inputs from entirely different thalamic nuclei. The long projections appear to have excitatory synaptic effects on distant neurons (Zarzecki, 1986). Although

of a cortical digit zone could mediate the appearance of new and diverse responses following peripheral nerve transection. Injury-induced unmasking of input from the heterogeneous regions to the glabrous subdivision of a cortical digit area may then explain why neurons in that area develop convergent functional properties similar to those of neurons located in the heterogeneous regions. Nerve transection may physiologically unmask inputs by disinhibition or facilitation, thus allowing the influence of normally subthreshold connections—particularly those from the heterogeneous to the glabrous subdivisions—to be actively expressed as new responses in SmI cortex. Unmasking may involve the suppression of GABA-mediated intracortical inhibition; administration of GABA antagonists has been shown to cause expansion of the RFs of individual neurons within SmI cortex of the raccoon (Kelahan and Doetsch, 1984) and cat (Hicks and Dykes, 1983; Dykes et al., 1984). Finally, the possibility that physiological unmasking may occur also in VPL of the thalamus and in the dorsal column nuclei cannot be excluded.

Appendix

Nomenclature and abbreviations

Cortical sulci

Ans	ansate
Cen	central
Cru	cruciate
Cor	coronal
Pc	postcruciate
Ss	suprasylvian
Tri	triradiate

Functional cortical areas

I–5	forepaw digits 1–5
F	face
HL	hindlimb
MsI	primary motor
P	palmar pads

References

- Akers, R. M., and H. P. Killackey (1978) Organization of cortico-cortical connections in the parietal cortex of the rat. *J. Comp. Neurol.* 181: 513–538.
- Bowker, R. M., and J. D. Coulter (1981) Intracortical connectivities of somatic sensory and motor areas: Multiple cortical pathways in monkeys. In *Cortical Sensory Organization, Vol. 1, Multiple Somatic Areas*, C. N. Woolsey, ed., Humana, Clifton, NJ.
- Carson, L. V., A. M. Kelahan, R. H. Ray, C. E. Massey, and G. S. Doetsch (1981) Effects of early peripheral lesions on the somatotopic organization of the cerebral cortex. In *Clinical Neurosurgery*, Vol. 28, P. W. Carmel, ed., pp. 532–546, Williams & Wilkins, Baltimore.
- Chapin, J. K. (1986) Laminar differences in sizes, shapes, and response profiles of cutaneous receptive fields in the rat SI cortex. *Exp. Brain Res.* 62: 549–559.
- Chapin, J. K., and C.-S. Lin (1984) Mapping the body representation in the SI cortex of anesthetized and awake rats. *J. Comp. Neurol.* 229: 199–213.
- Chapin, J. K., and D. J. Woodward (1982) Cortico-cortical connections between physiologically and histologically defined zones in the rat SI and MI cortices. *Soc. Neurosci. Abstr.* 8: 853.
- Cusick, C. G., and J. H. Kaas (1984) Cortical and thalamic connections of the representations of the digits of the hand in areas 3b and 1 of squirrel monkeys. *Soc. Neurosci. Abstr.* 10: 498.
- Doetsch, G. S., and A. L. Towe (1976) Response properties of distinct neuronal subsets in hindlimb sensorimotor cerebral cortex of the domestic cat. *Exp. Neurol.* 53: 520–547.
- Doetsch, G. S., K. W. Johnston, C.-S. Lin, and G. P. Standage (1988) Thalamic connections of two functional subdivisions of the somatosensory forepaw cerebral cortex of the raccoon. *J. Neurosci.* 8: 1873–1886.
- Donoghue, J. P., K. L. Kerman, and F. F. Ebner (1979) Evidence for two organizational plans within the somatic sensory-motor cortex of the rat. *J. Comp. Neurol.* 183: 647–664.
- Dykes, R. W., D. D. Rasmussen, and P. B. Hoeltzel (1980) Organization of primary somatosensory cortex in the cat. *J. Neurophysiol.* 43: 1527–1546.
- Dykes, R. W., P. Landry, R. Metherate, and T. P. Hicks (1984) Functional role of GABA in cat primary somatosensory cortex: Shaping receptive fields of cortical neurons. *J. Neurophysiol.* 52: 1066–1093.
- Dykes, R. W., P. Herron, and C.-S. Lin (1986) Ventroposterior thalamic regions projecting to cytoarchitectonic areas 3a and 3b in the cat. *J. Neurophysiol.* 56: 1521–1541.
- Feldman, S. H., and J. I. Johnson (1985) The kinesthetic cortical area anterior to primary somatic sensory cortex in the raccoon (*Procyon lotor*). *Anat. Rec.* 211: 60A–61A.
- Fitzpatrick, K. A., M. Carlson, and J. Charlton (1982) Topography, cytoarchitecture, and sulcal patterns in primary somatic sensory cortex (SmI) of the prosimian primate, *Perodicticus potto*. *J. Comp. Neurol.* 204: 296–310.
- Hardin, Jr., W. B., N. Arumugasamy, and H. D. Jameson (1968) Pattern of localization in the “precentral” motor cortex of raccoon. *Brain Res.* 11: 611–627.
- Herkenham, M. (1980) Laminar organization of thalamic projections to rat neocortex. *Science* 207: 532–535.
- Herron, P., and J. I. Johnson (1987) Organization of intracortical and commissural connections in somatosensory cortical areas I and II in the raccoon. *J. Comp. Neurol.* 257: 359–371.
- Hicks, T. P., and R. W. Dykes (1983) Receptive field size for certain neurons in primary somatosensory cortex is determined by GABA-mediated intracortical inhibition. *Brain Res.* 274: 160–164.
- Hyvarinen, J., and A. Poranen (1978) Movement-sensitive and direction and orientation-selective cutaneous receptive fields in the hand area of the post-central gyrus in monkeys. *J. Physiol. (Lond.)* 283: 523–537.
- Iwamura, Y., M. Tanaka, and O. Hikosaka (1980) Overlapping representation of fingers in the somatosensory cortex (area 2) of the conscious monkey. *Brain Res.* 197: 516–520.
- Iwamura, Y., M. Tanaka, M. Sakamoto, and O. Hikosaka (1983) Converging patterns of finger representation and complex response properties of neurons in area 1 of the first somatosensory cortex of the conscious monkey. *Exp. Brain Res.* 51: 327–337.
- Johnson, J. I. (1985) Thalamocortical organization in the raccoon: Comparison with the primate. *Exp. Brain Res. Suppl.* 10: 294–312.
- Johnson, J. I., E.-M. Ostapoff, and S. Warach (1982) The anterior border zones of primary somatic sensory (SI) neocortex and their relation to cerebral convolutions, shown by micromapping of peripheral projections to the region of the fourth forepaw digit representation in raccoons. *Neuroscience* 7: 915–936.
- Jones, E. G. (1981) Anatomy of cerebral cortex: Columnar input-output organization. In *The Organization of the Cerebral Cortex*, F. O. Schmitt, F. G. Worden, G. Edelman, and S. G. Dennis, eds., pp. 199–235, MIT Press, Cambridge, MA.
- Jones, E. G. (1986) Connectivity of the primate sensory-motor cortex. In *Cerebral Cortex, Vol. 5: Sensory-Motor Areas and Aspects of Cortical Connectivity*, E. G. Jones and A. Peters, eds., pp. 113–174, Plenum, New York.
- Jones, E. G., and R. Porter (1980) What is area 3a? *Brain Res. Rev.* 2: 1–43.
- Jones, E. G., and T. P. S. Powell (1968) The ipsilateral cortical connections of the somatic sensory areas in the cat. *Brain Res.* 9: 71–94.
- Jones, E. G., and T. P. S. Powell (1969) Connections of the somatic sensory cortex of the rhesus monkey. I. Ipsilateral cortical connexions. *Brain* 92: 477–502.
- Jones, E. G., J. D. Coulter, and S. H. C. Hendry (1978) Intracortical connectivity of architectonic fields in the somatic sensory, motor and parietal cortex of monkeys. *J. Comp. Neurol.* 181: 291–348.
- Kaas, J. H. (1983) What, if anything, is SI? Organization of first somatosensory area of cortex. *Physiol. Rev.* 63: 206–231.
- Kelahan, A. M., and G. S. Doetsch (1984) Time-dependent changes in the functional organization of somatosensory cerebral cortex following digit amputation in adult raccoons. *Somatosens. Res.* 2: 49–81.
- Kelahan, A. M., R. H. Ray, L. V. Carson, C. E. Massey, and G. S. Doetsch (1981) Functional reorganization of adult raccoon somatosensory cerebral cortex following neonatal digit amputation. *Brain Res.* 223: 151–159.

- Killackey, H. P. (1973) Anatomical evidence for cortical subdivisions based on vertically discrete thalamic projections from the ventral posterior nucleus to cortical barrels in the rat. *Brain Res.* 51: 326–331.
- Lu, S. M., and C.-S. Lin (1986) Cortical projection patterns of the medial divisions of the nucleus posterior thalami in the rat. *Soc. Neurosci. Abstr.* 12: 1434.
- Matsubara, J. A., M. S. Cynader, and N. V. Swindale (1987) Anatomical properties and physiological correlates of the intrinsic connections in cat area 18. *J. Neurosci.* 7: 1428–1446.
- McKenna, T. M., B. L. Whitsel, D. A. Dreyer, and C. B. Metz (1981) Organization of cat anterior parietal cortex: Relations among cytoarchitecture, single neuron functional properties, and interhemispheric connectivity. *J. Neurophysiol.* 45: 667–697.
- McKenna, T. M., B. L. Whitsel, and D. A. Dreyer (1982) Anterior parietal cortical topographic organization in macaque monkey: A reevaluation. *J. Neurophysiol.* 48: 289–317.
- McKenna, T. M., A. R. Light, and B. L. Whitsel (1984) Neurons with unusual response and receptive-field properties in upper laminae of cat SI cortex. *J. Neurophysiol.* 51: 1055–1076.
- Mountcastle, V. B. (1957) Modality and topographic properties of single neurons of cat's somatic sensory cortex. *J. Neurophysiol.* 20: 408–434.
- Murray, H. G., and C. J. Heath (1978) The spread of connections within cat primary somatic sensory cortex. *Brain Res.* 141: 160–164.
- Rasmusson, D. D. (1982) Reorganization of raccoon somatosensory cortex following removal of the fifth digit. *J. Comp. Neurol.* 205: 313–326.
- Ray, R. H., and G. S. Doetsch (1977) Observations on the pyramidal system of the North American raccoon (*Procyon lotor*). *Soc. Exp. Biol. Med.* 2: 2 (abstr.).
- Rockland, K. S., and J. S. Lund (1983) Intrinsic laminar lattice connections in primate visual cortex. *J. Comp. Neurol.* 216: 303–318.
- Sur, M., R. J. Nelson, and J. H. Kaas (1978) The representation of body surface in somatosensory area I of the grey squirrel. *J. Comp. Neurol.* 179: 425–449.
- Sur, M., J. T. Wall, and J. H. Kaas (1984) Modular distribution of neurons with slowly adapting and rapidly adapting responses in area 3b of somatosensory cortex in monkeys. *J. Neurophysiol.* 51: 724–744.
- Sur, M., P. E. Garraghty, and C. J. Bruce (1985) Somatosensory cortex in macaque monkeys: Laminar differences in receptive field size in areas 3b and 1. *Brain Res.* 342: 391–395.
- Towe, A. L., D. Whitehorn, and J. K. Nyquist (1968) Differential activity among wide-field neurons of the cat postcruciate cerebral cortex. *Exp. Neurol.* 20: 497–521.
- Uhr, J. L., and J. K. Chapin (1983) Contribution of thalamo-cortical and corticocortical connections to receptive field properties in the rat Sml cortex. *Soc. Neurosci. Abstr.* 9: 250.
- Warren, S., H. A. Hamalainen, and E. P. Gardner (1986) Objective classification of motion- and direction-sensitive neurons in primary somatosensory cortex of awake monkeys. *J. Neurophysiol.* 56: 598–622.
- Welker, W. I., and J. I. Johnson, Jr. (1965) Correlation between nuclear morphology and somatotopic organization in ventrobasal complex of the raccoon's thalamus. *J. Anat.* 99: 761–790.
- Welker, W., K. J. Sanderson, and G. M. Shambes (1984) Patterns of afferent projections to transitional zones in the somatic sensorimotor cerebral cortex of albino rats. *Brain Res.* 292: 261–267.
- Welt, C., J. C. Aschoff, K. Kameda, and V. B. Brooks (1967) Intracortical organization of cat's motor sensory neurons. In *Neurophysiological Basis of Normal and Abnormal Motor Activities*, M. D. Yahr and D. P. Purpura, eds., pp. 255–293, Raven, New York.
- Whitsel, B. L., J. R. Roppolo, and G. Werner (1972) Cortical information processing of stimulus motion on primate skin. *J. Neurophysiol.* 35: 691–717.
- Zarzecki, P. (1986) Functions of corticocortical neurons of somatosensory, motor, and parietal cortex. In *Cerebral Cortex, Vol. 5: Sensory-Motor Areas and Aspects of Cortical Connectivity*, E. G. Jones and A. Peters, eds., pp. 185–211, Plenum, New York.