Contribution of Thalamic Input to the Specification of Cytoarchitectonic Cortical Fields in the Primate: Effects of Bilateral Enucleation in the Fetal Monkey on the Boundaries, Dimensions, and Gyrification of Striate and Extrastriate Cortex

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ABSTRACT

Bilateral enucleation was performed at different fetal ages during corticogenesis, and the brains were prepared for histological examination. Early-enucleated fetuses (operated prior to embryonic day 77) showed morphological changes at the level of the thalamus and the cortex. In the thalamus, there was a loss of lamination and a decrease in size of the lateral geniculate nucleus. There was a decrease in the size of the inferior pulvinar, but there was no change in the lateral pulvinar.

The border of striate cortex was as sharp in the enucleates as it was in the normal monkeys. In three of the four early enucleates, we observed an interdigitation of striate and extrastriate cortex. In three of the early enucleates, we observed a small island of nonst,riate cortex near the striate border that was surrounded entirely by striate cortex.

Enucleation led to an age-related reduction of striate cortex. This reduction was greater in the operculum than in the calcarine fissure. The reduction of striate cortex was accompanied by an increase in the dimensions of extrastriate visual cortex, so that the overall dimensions of the neocortex remained invariant. The extrastriate cortex in the enucleated animals presented a uniform cytoarchitecture and was indistinguishable from area 18 in the normal animal.

There were changes in the gyral pattern that were restricted mainly to the cortex on the operculum. A deepening of minor dimples as well as the induction of a variable number of supplementary sulci led to an increase in the convolution of the occipital lobe.

These results are discussed with respect to the specification of cortical areas. They demonstrate that the reduction in striate cortex was not accompanied by an equivalent reduction in the neocortex; rather, there was a border shift, and a large volume of cortex that was destined to become striate cortex appears to be cytoarchitectonically normal extrastriate cortex.

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Surgical manipulation of the sensory periphery has been shown to exert an important influence on the development of the cerebral cortex via the thalamic relay nuclei (Van der Loos and Woolsey, 1973; Killackey et al., 1976; for reviews, see O’Leary, 1988; Killackey, 1990). A major challenge is to decipher how this extrinsic control meshes with developmental programs which are intrinsic to the cortex (Rakic, 1988; Kennedy and Dehay, 1993).

In the monkey, fetal removal of the retinæ leads to a drastic reduction in the surface area of the striate cortex (Rakic, 1988; Dehay et al., 1989). There are a number of possible sources of areal reduction of striate cortex follow-
ing enucleation. One is that the areal reduction reflects changes in cell size, because enucleation in rodents (Valverde, 1968) and in monkeys (Dehay, Horsburgh and Kennedy, unpublished observations) has been shown to lead to cortical cell atrophy. A second possibility is that enucleation leads to increased levels of naturally occurring cortical cell death in the developing striate cortex (Finlay and Slattery, 1983; Windrem and Finlay, 1985). A third possibility is that enucleation reduces cell production. This is supported by a large number of studies showing that glomerular cell proliferation (Hamburger and Levi-Montalcini, 1949; Kollias, 1953, 1982; Delong and Sudman, 1962; Currie and Cowan, 1974; Baptista et al., 1990; Sellock et al., 1992; Gong and Shipley, 1995; Dehay et al., 1995). A fourth possibility, which has received much attention over the last few years, is that enucleation leads to a change in the areal specification of immature cortical neurons (Rakic, 1988). This amounts to a respecification of a cortical area; therefore, it is of considerable theoretical interest.

Rakic’s hypothesis postulates that the reduction in surface area of striate cortex is a secondary consequence of the reduction in numbers of ascending fibers from the lateral geniculate nucleus (LGN; Rakic, 1988). Accordingly, the portion of prospective striate cortex that is deprived of its normal input from the LGN, acquires a cytoarchitectonic identity that is distinct from that of striate cortex. This amounts to a developmental change in identity following a respecification. In support of this, Rakic and his collaborators have provided evidence that, in two fetuses enucleated on embryonic day 81 (E81) and E91 (gestation period, 165 days), enucleation appeared to induce regions within and bordering the striate field to acquire a cytoarchitecture combining striate and extrastriate features. This region was referred to as area X (Rakic et al., 1991). However, it has been shown that the reduction of striate cortex following enucleation depends critically upon the age at which the surgical manipulation is carried out (Dehay et al., 1991). Enucleation at E80 and later leads to a reduction in surface area of striate cortex of the order of 10–14%, which is quite modest compared to the reductions of 70% following enucleations prior to E77 (Dehay et al., 1991). However, in these early enucleates, we did not detect regions of area X showing hybrid cytoarchitectonic features that corresponded to the reduction of striate cortex. This would suggest either that respecification does not occur to any great extent or that the expanded extrastriate cortex is indistinguishable from normal area 18.

The aim of the present study was to determine, by using an exhaustive series of tests, whether enucleation does cause a respecification of cortex and to what extent it accounts for the areal reduction of striate cortex. This involved determining whether enucleation causes substantial amounts of cortex destined to become striate cortex to take on the cytoarchitectonic features of extrastriate cortex. If this is the underlying mechanism, then the induced reduction of striate cortex should be accompanied by an expansion of extrastriate cortex. This amounts to a shift in the border between striate and extrastriate cortex. To determine whether this is the case, we made quantitative measurements of the areal dimensions of different cortical regions, including all of the neocortex, the extrastriate visual cortex, and the striate cortex following enucleation at different fetal ages.

A striking feature of the primate visual cortex following early enucleation is the drastic change in cortical folding (Rakic, 1988; Dehay et al., 1989). The developmental determinants of cortical folding remain largely unknown (Welker, 1990). One possibility is that cortical folding permits the cortex to be confined in a restricted volume. Correlating the degree of cortical folding with changes in cortical volume should provide an insight into this interpretation. Another possibility is that cortical folding could serve to minimize distances between densely interconnected areas. Hence, one of the aims of the present study was to provide a description of cortical folding following enucleation and to examine the relationship between induced gyri and the dimensions and locations of cortical fields.

### MATERIALS AND METHODS

Medication prior to surgery consisted of two injections of chlorpromazine (Largactyl; 2 mg/Kg, i.m.) 4 hours before anaesthesia and at the moment of anaesthesia. Before anaesthesia, animals were injected with atropine (1.25 mg, i.m.), dexamethasone (Soludexadron; 4 mg, i.m.). Eight timed, pregnant cynomolgus monkeys (Macaca irus) were prepared for surgery under Ketamine hydrochloride (20 mg/Kg, i.m.) anaesthesia. The monkeys were then intubated, and anaesthesia was continued with halothane in a N2O/O2 mixture (70/30). The heart rate was monitored, and the expired CO2 was maintained between 5–6%. The body temperature was maintained by using a thermostatically controlled heating blanket.

Using sterile surgical procedures, a midline abdominal incision was made, and a uterotomy was performed. The fetal head was exposed, bilateral eye removal was performed, and the fetus was replaced in the uterus after closing incisions. The mother was returned to her cage and was given an analgesic (Visceralgine; 1.25 mg, i.m.) twice daily for 2 days. In two cases (BB104 and BB34), the fetuses were delivered by caesarian section; otherwise, the fetuses were left until term on E165 (Table 1). The infant and fetal

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**TABLE 1. Dimensions and Relative Proportions of Lateral Geniculate and Pulvinar Nuclei**

<table>
<thead>
<tr>
<th>Case</th>
<th>Age at enucleation</th>
<th>Age at observation</th>
<th>LGN (%)</th>
<th>Lateral pulvinar (%)</th>
<th>Inferior pulvinar (%)</th>
<th>Lateral pulvinar (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BB44</td>
<td>E59</td>
<td>P0</td>
<td>10.7</td>
<td>14.3</td>
<td>13.6</td>
<td>27.9</td>
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<tr>
<td>BB55</td>
<td>E62</td>
<td>P0</td>
<td>11.4</td>
<td>15.3</td>
<td>35.7</td>
<td>26.2</td>
</tr>
<tr>
<td>BB104</td>
<td>E62</td>
<td>E37</td>
<td>5.7</td>
<td>6.8</td>
<td>32.7</td>
<td>23.2</td>
</tr>
<tr>
<td>BB28</td>
<td>E68</td>
<td>P0</td>
<td>7.6</td>
<td>12.5</td>
<td>55.7</td>
<td>23.9</td>
</tr>
<tr>
<td>BB21</td>
<td>E77</td>
<td>P0</td>
<td>9.7</td>
<td>9.9</td>
<td>26.6</td>
<td>35.9</td>
</tr>
<tr>
<td>BB31</td>
<td>E81</td>
<td>P0</td>
<td>12.6</td>
<td>14.3</td>
<td>67.1</td>
<td>34.5</td>
</tr>
<tr>
<td>BB149</td>
<td>E109</td>
<td>P0</td>
<td>19.5</td>
<td>18.6</td>
<td>49.6</td>
<td>43.2</td>
</tr>
<tr>
<td>BB68</td>
<td>Normal</td>
<td>E133</td>
<td>29.6</td>
<td>8.4</td>
<td>39.6</td>
<td>79.7</td>
</tr>
<tr>
<td>BB68</td>
<td>Normal</td>
<td>Three months</td>
<td>34.2</td>
<td>10.2</td>
<td>70.4</td>
<td>53.9</td>
</tr>
</tbody>
</table>

1Values in mm3. LGN: lateral geniculate nucleus; E: embryonic day; P: postnatal day.

2Proportions are expressed as percentages of globus pallidus.
monkeys and three postnatal controls (aged 1–3 months) were anaesthetized with ketamine (20 mg/Kg, i.m.) followed by pentobarbitone (Nembutal; 50 mg/Kg, i.v.) and were perfused through the heart with a 1.25% paraformaldehyde and 1.5% glutaraldehyde solution. After fixation, perfusion was continued with a 10–30% sucrose solution to provide cryoprotection of the brain. Parasagittal sections (60 μm thick) were cut on a freezing microtome, all sections were kept, and at least one in three sections was stained for Nissl substance.

Sections were back projected, and the cortex and thalamus contours were traced out. Areal values of different cortical regions were computed, as were the volumes of visual thalamic nuclei (linear surface measure = length of layer × number of sections × section thickness). To overcome natural variation of brain size, we computed the relative dimensions of cortical regions and thalamic structures. In each animal, the areal dimensions of striate cortex and extrastriate visual cortex were measured, as were the dimensions of the whole of the neocortex. This allowed us to compute the dimensions of these cortical regions as a percentage of the overall neocortex. We measured the volumes of the inferior and lateral pulvinar, the LGN, and the globus pallidus. Relative dimensions of the visual thalamic nuclei were calculated as percentages of the globus pallidus, a structure that is not expected to be directly influenced by enucleation. Linear-regression analysis was used to assess the effects of enucleation on changes of cortical surfaces and thalamic volumes. All operated animals in which quantitative data could be obtained were used to calculate regressions.

If enucleation did cause a respecification of cortex, then the reduction of striate cortex should have been accompanied by an equivalent expansion of the adjacent cortical field. Ideally, one would like to measure striate and extrastriate visual cortex in normal animals and in enucleates. Because the anterior limits of extrastriate visual cortex cannot be rigorously defined on purely histological grounds, it was necessary to use alternative criteria. Therefore, we have defined major cortical gyral landmarks in parasagittal sections that circumscribe the visual cortex. It was important that these landmarks be consistent across animals. In our choice of landmarks, we have included nonvisual cortex rather than running the risk of excluding any visual cortical territory. The bulk of extrastriate visual cortex was confined to the occipital lobe, with some outlying fields in the temporal and parietal lobes. Hence, the cortical territory we have defined consisted of the totality of occipital and temporal lobes and a small fraction of the parietal lobe. We refer to this region as occipital-temporal cortex.

The histological limits of neocortex were easily recognizable and are indicated in Figure 1. The criteria that we have used to demarcate the occipital-temporal cortex are shown in this Figure. In lateral parasagittal sections, the temporal and occipital lobes form a continuous entity, and this lobe is included (Fig. 1, light shading). Medially (39% level), the superior temporal sulcus closes, and the measurements made are posterior to that point. Proceeding farther medially, the superior temporal sulcus becomes progressively shallower, and, at the point of its disappearance (66% level), the dorsal limit of the measured occipital-temporal cortex is placed on the posterior lip of the parietal gyrus. Farther
Normal | Early Enucleate | Late Enucleate

Fig. 2. Visual thalamus. Nissl-stained parasagittal sections showing the major divisions of the visual thalamus at equivalent levels in the three animals. Normal animal: The laminar divisions of the lateral geniculate nucleus (LGN) are clearly visible, and, at more medial levels, the dark staining of the ventrally placed magnocellular layers can be seen. Posterior to the LGN lies the inferior and lateral pulvinar, which is separated by a fiber tract. Early enucleation: The laminar division of the reduced LGN is no longer apparent. At more medial levels, dark staining of the anterior edge probably corresponds to the location of the magnocellular component. The inferior pulvinar is clearly demarcated and is reduced in size. The lateral pulvinar shows dimensions similar to the normal and late enucleate. Late enucleation: The LGN has normal lamination and only moderately reduced dimensions compared to the normal animal. The inferior and lateral pulvinar appears to be normal. Scale bars = 2 mm.

RESULTS

The age of enucleation was found to be critical for quantitative and qualitative effects on cortex and thalamus.

Thalamic perturbations

Enucleation led to a reduction in the volume of the LGN and the inferior pulvinar. Lamination of the LGN was not apparent following enucleation from E59 and up to and including E81. The two neonates enucleated on E109 and E110 showed normal lamination (Fig. 2).

The earlier the enucleation, the greater the magnitude of LGN reduction (Table 1). The LGN in the neonates enucleated up to and including E77 had a mean volume of 10 mm³ compared to 16 mm³ in the neonates enucleated on E81 and E109. In the 3-month-old control, the LGN had a volume of 34.2 mm³. Linear regression showed that age dependency was significant \( P < 0.04 \).

The relative volumes of the LGN with respect to the globus pallidus (see Materials and Methods) gave a mean value of 25% for neonates enucleated prior to E77, 39% for the E81 and E109 enucleates, and 53.9% for the 3-month-old control. Regression analysis (Fig. 3A) showed that these changes were significant \( P < 0.03 \).

The inferior pulvinar had a mean relative volume of 32% in the neonates enucleated prior to E77 and of 40% in the E81 and E109 enucleates. Regression analysis showed that this effect of enucleation was statistically significant \( P < 0.04 \). Enucleation was not found to affect the volume of the lateral pulvinar (Fig. 3).

Cytoarchitectonics of striate cortex

Area 17 in the primate is characterized by a particularly well-defined laminar cytoarchitecture. A distinctive feature is the subdivision of layer 4 into a number of sublayers, including 4C, 4B, and 4A. The supragranular layers are composed of a thick layer 3 and a layer 2, whereas the infragranular layers possess a pronounced layer 6. Follow-
Following early enucleation, the location of striate cortex with respect to major sulci differed from that in the normal animal. Figure 5 gives the details of the location of striate cortex with respect to normal and induced sulci. Figure 5 also indicates the location of all of the perturbations of striate cortex described in this paper. Changes in the location of striate cortex were more pronounced on the operculum than in the calcarine fissure (Fig. 5). In the normal animal, striate cortex occupies the full width of the operculum. At medial levels, striate cortex stretches from the lip of the parieto-occipital sulcus to a point just posterior to the inferior-occipital sulcus (IOS), so that both banks of the external calcarine sulcus are entirely within the striate field. This configuration is conserved more laterally when the parieto-occipital sulcus runs into the lunate sulcus and, in fact, right up to the most lateral extent of these sulci on the occipital lobe (e.g., up to the 7% level in case BB25; Fig. 5). In the early enucleates, striate cortex on the operculum was considerably shrunken and progressively narrowed as one proceeded laterally. Dorsally, the striate cortex never reached either the parieto-occipital or the lunate sulci. Ventrally, striate cortex failed to reach the IOS, so that the external calcarine sulcus in these animals, contrary to the normal animals, was completely exterior to the striate field. The neonate enucleated at E77 showed a reduced dorsal extent of striate cortex similar to that in the early enucleates. Ventrally, the striate cortex on the operculum in this animal reached the fundus of the external calcarine sulcus. By the 52% level, striate cortex had pulled back from this sulcus. In the early enucleates, striate cortex disappeared from the operculum between the 69-36% level.

Within the striate field, we observed three incidences in early enucleates where there was a restricted perturbation of cytoarchitecture spanning several millimeters. This led to islands of nonstriate cortex in the striate field. This local breakdown in cytoarchitecture was not found after all early enucleations. Therefore, it may not be critically dependent on the age at enucleation, because these anomalies were observed in the fetuses enucleated on E59 and E77 and in one of the two fetuses enucleated on E62. No islands were observed on one of the two E62 fetuses or on the E68 fetus. The largest of these islands was located in the calcarine fissure of the E59 enucleated fetus. It consisted of a region a little over 2 mm in diameter that showed a disturbed formation of cortical layers (Fig. 6A). Layer 4 appeared disorganized, and the cortex was thicker than the surrounding striate cortex; in this regard, the cytoarchitecture of the island differed from that of area 18. Areal measurements showed that the disorganized cortex had a surface area of 3.6 mm²; therefore, it constituted a minute proportion of the missing area 17.

In the E62 enucleate, the island was located in the calcarine fissure, and, in the E77 enucleate, it was located on the operculum. In both cases, the cytoarchitecture of the island differed from that in the E59 enucleate, in that it resembled that of area 18 more closely (Fig. 7). Here, in the E77 animal, the external calcarine and a supplementary sulcus converged at the 44% level, producing an anomalous gyrus. The whole of this gyrus was contained within the striate field. On this gyrus, striate and extrastriate cortices formed a patchwork, and multiple regions of disturbed cortex were present (Fig. 7). In these anomalous cortical regions, layer 4 did not show sublayers, giving these regions a gross resemblance to area 18 in the normal neonate. Multiple minute breaks in layer 4 were observed in this region.
The only other case of disturbed cortical organization was in the neonate that was enucleated on E81. In this animal, several cortical invaginations were observed medially on the operculum (Fig. 6B). Such cortical malformations were not observed in any of the controls or in the other enucleates. The animals enucleated on E109 and E110 showed no cytoarchitectonic perturbations.

Areal dimensions

Striate cortex was reduced in enucleated animals, and the extent of the reduction depended on the age of the fetus when operated (Table 2). Enucleation prior to E77 led to a striate cortex ranging from 215 to 326 mm², and enucleation at E81, E109, and E110 led to a striate cortex ranging from 584 to 865 mm². By plotting the areal dimensions against age of enucleation, it was possible to determine the regression ($P < 0.05$), which showed that the degree of areal reduction depended on the age at enucleation; the younger the fetus, the greater the reduction.

Despite the massive reduction of striate cortex, the overall dimensions of the neocortex did not differ significantly between early and late enucleates (Table 2). This was compatible with the possibility that cortex that was destined to become striate cortex had taken on a nonstriate cortex cytoarchitecture, i.e., that there had been a border shift. A more stringent test of this was to compare the overall dimensions of the visual cortex (extrastriate plus striate cortex), which were provided by the measurement of the occipital-temporal cortex. Again, this was not affected by the age at enucleation, giving a mean value of 2,506 mm² in the four fetuses enucleated between E59 and E68 and 2,427 mm² in the E81, E109, and E110 enucleates. These findings fit with the possibility that, if there had been a border shift in the early enucleates, then there should have been an expansion of the extrastriate visual cortical areas. In fact, this was found to be the case. The dimensions of the extrastriate visual cortex were estimated by subtracting striate cortex from the occipital-temporal cortex (Table 2, column 4). This returned a mean area of $2,197$ mm² for the extrastriate visual cortex in the early enucleates (E46, E61, E62, and E68) and $1,718$ mm² for the late enucleates (E81, E109, and E110).

The controls were 1–3 months old, and, at these ages, some postnatal cortical expansion would have occurred (O’Kusky and Colonnier, 1982). This prevented us from comparing absolute values in normal animals and enucleates in Table 2. More importantly, we needed to eliminate the possibility that variations of overall brain size were masking significant changes. To overcome these difficulties, we have calculated changes in the relative dimensions of striate, extrastriate, and occipital temporal cortex (Table 3).

In the four cases of early enucleation (prior to E77), striate cortex had a mean value of 6.9% of the total neocortex, whereas, among the three late enucleates (E81, E109, and E110), it had a mean value of 16%. In the normal animals, striate cortex had a mean value of 18%. Plotting the percentage value of striate cortex against age at enucleation gave a statistically significant linear regression ($P < 0.01$). According to the border-shift hypothesis, the overall dimensions of the occipital-temporal cortex should remain a constant proportion of the neocortex following enucleation despite the reduction in the dimensions of striate cortex. Indeed, this was found to be the case (Fig. 8A).

Extrastriate visual cortex (i.e., occipital-temporal cortex minus striate cortex) in the early enucleates (E59, E62, E62, and E68) constituted 52% of the neocortex compared to 47.9% in the late enucleates (E81 and E109) and to 46.4% in the normal animals (Table 3). The linear regression (Fig. 8B) showed that the expansion of the extrastriate cortex...
Fig. 5. Parasagittal sections through the occipital lobe showing the limits of striate cortex with respect to the sulci pattern. Medial is to the left, and numbers refer to percentage distance of the section from the midline. Layer 4C of striate cortex is outlined in red. CAL, calcarine; IOS, inferior occipital sulcus; LAT CAL, lateral calcarine; LS, lunate sulcus; OT, occipital-temporal sulcus; A–H, supplementary sulci in the enucleate cases.
Figure 5 (Continued.)
following early enucleation was statistically significant ($P < 0.03$).

If the reduction of striate cortex was largely due to a border shift, then one would predict that late enucleated animals (where there was only a modest striate cortex reduction) would have values for extrastriate visual cortex similar to those in the normal animals. In fact, this was the case ($P = 0.24$).

Enucleation led to a more pronounced reduction of striate cortex on the operculum than in the banks of the calcarine fissure (Table 4). On the operculum, the normal striate cortex had a mean value of 508 mm$^2$, which was reduced to a mean value of 54 mm$^2$ in the early enucleates. In the calcarine fissure, the mean value for striate cortex was 653 mm$^2$ in the normal animals and 254 mm$^2$ in the early enucleates. Regression analysis showed that the age-related reduction was significant in both the operculum and the calcarine fissure ($P < 0.05$). Striate cortex in the calcarine fissure constituted an average value of 80% of the total striate cortex in the early enucleates and 55% in the normal animals.

The results thus far have shown that there was a border shift when the operculum and calcarine fissure data were pooled. Could it be that the border shift was restricted to the operculum, where the reduction was much greater? To determine if this was the case, we investigated whether there was an expansion of extrastriate cortex in both cases. A gross measure of the extrastriate cortex on the operculum can be obtained by subtracting both the striate cortex on the operculum and the total cortical surface measured in the calcarine fissure from the occipital-temporal cortex. When opercular extrastriate visual cortex was calculated as a percentage of neocortex, it was found to constitute a mean value of 41% in the early enucleates and of 35% in the late enucleates (Table 4). Regression analysis showed that the expansion of the opercular extrastriate cortex correlated significantly with the age at enucleation ($P < 0.04$). A measure of extrastriate visual cortex in the calcarine fissure can be obtained by subtracting calcarine striate cortex from the total calcarine cortex. Expressed as a fraction of the total neocortex, the calcarine extrastriate cortex constituted 7% of the neocortex in the early enucleates and 3.7% in the late enucleates. Regression analysis showed that this expansion in the calcarine sulcus correlated significantly with the age at enucleation ($P < 0.05$).

Note that what we have identified as extrastriate cortex was very different in terms of visual areas in the operculum and the calcarine fissure. This invalidated a quantitative comparison between the two. Dorsally (i.e., the opercular measure), it included visual areas V1, V2, V3, V3A, V4, V5, and the temporal and the parietal visual area (Zeki, 1980; Van Essen et al., 1986; Maunsell and Van Essen, 1987; Colby et al., 1988; Gattass et al., 1988). In the calcarine fissure, the extrastriate area corresponded to a more restricted number of visual areas and was mainly composed of V2 and V3 (Gattass et al., 1988).

**Cytoarchitectonics of peristriate cortex**

Surrounding the reduced striate cortex in the enucleate, there was a cortical region that showed a well-developed layer 4 and a prominent layer 3 containing large pyramidal cells. The cytoarchitectonics of this peristriate cortex resembled that of area 18 in the normal animal. Figure 9 shows a low-power view of the occipital lobe taken from equivalent levels in a normal animal and in an early enucleate (E59). In the enucleate, striate cortex on the operculum was confined to a small region on the occipital pole. The uniformity of the peristriate field can be seen in the high-power views shown in Figure 10, which shows that the cytoarchitectonics of area 18 in the posterior bank of the lunate sulcus of the normal animal are comparable to those shown by the cortex in the lunate sulcus of the operated animal and in the peristriate cortex on the operculum.

**Border of striate cortex**

The border of striate cortex in the enucleates showed a number of irregular features. The morphology of the normal striate border is shown in Figure 11A. The dense layer 4C and the thinner layer 4A turned in towards each other in a characteristic tuning-fork pattern to meet the less dense layer 4 of area 18. In some cases, following early enucleation, the border of the reduced striate cortex was found to be associated at medial levels with a supplementary sulcus (for example, the dorsal border at the 94 and
Fig. 7. Local perturbation of striate cortex on operculum. A–D: Photomicrographs of adjacent sections showing an anomalous gyrus entirely contained within the striate cortical field. On the gyrus, there is a mosaic of striate and extrastriate cortex. A′–D′: Drawings of sections showing the limits of striate cortex (red lines). Scale bar = 1 mm.
84% levels in case BB95; the 69% level in case BB104; the 68, 60, 52, and 44% levels in case BB21; the ventral border at the 69% level in case BB104; and the 57 and 48% levels in case BB28; see Fig. 5). When the striate border in the enucleate was associated with a supplementary sulcus in this way, its resemblance to the normal border was maximal (Fig. 11B). In the enucleate, there was a reduction of cortical thickness as one passed from striate to extrastriate cortex that was similar to the reduction found in the normal animal (see Figs. 10, 11, 13A). In the reduced striate cortex, there were instances of abnormal undulations of the cortex on either side of the border that could obscure the reduction of cortical thickness that occurred at the border as one passed from striate to extrastriate cortex (Fig. 11C,D).

The truncation of layers 4C and 4A of the reduced striate cortex was as abrupt in the enucleate as it was in the normal animal, and this contributed largely to the sharpness of the border. However, we saw two instances where layer 4 of the extrastriate cortex abutting the border of the reduced striate cortex had a less clearly defined lamination (illustrated in Fig. 11C). Elsewhere in the enucleates, layer 4 of the extrastriate cortex was sharply defined, even when there were no induced sulci and where cortical undulations disrupted the border (shown in Fig. 11D).

Two-dimensional reconstructions of area 17 in the normal animal showed that the contour of this area was smooth and continuous. This contrasted with the ragged striate border in the early enucleates, which is shown in Figure 12. Reconstructions in enucleates showed the striate cortex on the operculum as an elongated protrusion. In Figure 12, an indentation of striate cortex can be seen. This was a prominent feature following early enucleation and was never observed in the normal animal. An example of indentation is shown in Figure 13A. Here, a break appeared in the striate cortex, so that a ventral sliver of striate cortex protruded out into the surrounding extrastriate cortex. Note that, despite the fact that this tongue of striate cortex was reduced to only several hundred microns across, it maintained an appropriate lamination almost right up to its tip. This intriguing disruption of the striate cortex of case BB28 can be followed in the low-power drawing in Figure 5.

The dorsal wedge of striate cortex continued to narrow as one progressed laterally on the cortex (going from the 86% to the 48% level in Fig. 5), reached a minimum width at the

---

**TABLE 2. Dimensions of Cortical Regions**

<table>
<thead>
<tr>
<th>Case</th>
<th>Age at enucleation</th>
<th>Age at observation</th>
<th>Striate cortex</th>
<th>Occipital-temporal cortex</th>
<th>Extrastriate visual cortex</th>
</tr>
</thead>
<tbody>
<tr>
<td>BB46</td>
<td>E59</td>
<td>P0</td>
<td>326.3</td>
<td>4,610.0</td>
<td>2,631.7</td>
</tr>
<tr>
<td>BB65</td>
<td>E02</td>
<td>P0</td>
<td>284.8</td>
<td>4,095.3</td>
<td>2,332.8</td>
</tr>
<tr>
<td>BB104</td>
<td>E02</td>
<td>E157</td>
<td>315.5</td>
<td>3,134.6</td>
<td>1,874.5</td>
</tr>
<tr>
<td>BB28</td>
<td>E08</td>
<td>P0</td>
<td>315.5</td>
<td>4,662.0</td>
<td>2,533.2</td>
</tr>
<tr>
<td>BB21</td>
<td>E77</td>
<td>P0</td>
<td>512.5</td>
<td>3,478.8</td>
<td>2,079.7</td>
</tr>
<tr>
<td>BB35</td>
<td>E81</td>
<td>P0</td>
<td>711.2</td>
<td>4,407.3</td>
<td>2,570.8</td>
</tr>
<tr>
<td>BB49</td>
<td>E109</td>
<td>P0</td>
<td>865.7</td>
<td>5,231.3</td>
<td>2,888.6</td>
</tr>
<tr>
<td>BB39</td>
<td>E110</td>
<td>P0</td>
<td>548.2</td>
<td>3,800.1</td>
<td>1,928.7</td>
</tr>
<tr>
<td>BB34</td>
<td>Normal</td>
<td>E133</td>
<td>674.7</td>
<td>3,608.7</td>
<td>1,989.9</td>
</tr>
<tr>
<td>BB65</td>
<td>Normal</td>
<td>Three months</td>
<td>1,132.5</td>
<td>6,703.3</td>
<td>3,709.6</td>
</tr>
<tr>
<td>BB70</td>
<td>Normal</td>
<td>Two months</td>
<td>959.3</td>
<td>5,259.6</td>
<td>2,970.9</td>
</tr>
<tr>
<td>BB75</td>
<td>Normal</td>
<td>One month</td>
<td>1,388.3</td>
<td>7,299.9</td>
<td>4,279.8</td>
</tr>
</tbody>
</table>

1. Values in mm.
2. Extrastriate visual cortex: occipital-temporal cortex minus striate cortex.

---

**TABLE 3. Relative Proportions of Cortical Regions**

<table>
<thead>
<tr>
<th>Case</th>
<th>Age at enucleation</th>
<th>Age at observation</th>
<th>Striate cortex (%)</th>
<th>Occipital-temporal cortex (%)</th>
<th>Extrastriate visual cortex (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BB46</td>
<td>E59</td>
<td>P0</td>
<td>7.1</td>
<td>57.0</td>
<td>53.7</td>
</tr>
<tr>
<td>BB65</td>
<td>E02</td>
<td>P0</td>
<td>7.0</td>
<td>57.0</td>
<td>53.7</td>
</tr>
<tr>
<td>BB104</td>
<td>E02</td>
<td>E157</td>
<td>6.9</td>
<td>53.4</td>
<td>50.0</td>
</tr>
<tr>
<td>BB28</td>
<td>E08</td>
<td>P0</td>
<td>14.7</td>
<td>59.8</td>
<td>52.8</td>
</tr>
<tr>
<td>BB21</td>
<td>E77</td>
<td>P0</td>
<td>15.9</td>
<td>57.5</td>
<td>49.5</td>
</tr>
<tr>
<td>BB35</td>
<td>E81</td>
<td>P0</td>
<td>16.5</td>
<td>55.2</td>
<td>46.3</td>
</tr>
<tr>
<td>BB49</td>
<td>E109</td>
<td>P0</td>
<td>16.4</td>
<td>54.6</td>
<td>44.2</td>
</tr>
<tr>
<td>BB34</td>
<td>Normal</td>
<td>E133</td>
<td>16.8</td>
<td>54.6</td>
<td>44.2</td>
</tr>
<tr>
<td>BB65</td>
<td>Normal</td>
<td>Three months</td>
<td>16.8</td>
<td>54.6</td>
<td>44.2</td>
</tr>
<tr>
<td>BB70</td>
<td>Normal</td>
<td>Two months</td>
<td>18.1</td>
<td>56.1</td>
<td>46.3</td>
</tr>
<tr>
<td>BB75</td>
<td>Normal</td>
<td>One month</td>
<td>19.0</td>
<td>58.6</td>
<td>40.0</td>
</tr>
</tbody>
</table>

1. Proportions are expressed as percentage of neocortex for striate cortex and occipital-temporal cortex minus striate cortex for extrastriate visual cortex.
2. Extrastriate visual cortex: occipital-temporal cortex minus striate cortex.

---

**A) Occipital-temporal cortex**

**B) extrastriate visual cortex**

---

Fig. 8. Regression plot of the effect of age of enucleation on occipital-temporal cortex as a percentage of total neocortex (A) and on extrastriate visual cortex as a percentage of neocortex (B). A: The relative size of the occipital-temporal cortex is not found to be influenced by enucleation, and the values of the control animals fall within the range of the operated animals. B: There is a correlation between the age of enucleation and the relative size of the extrastriate visual cortex (see text) in which the earlier the enucleation, the larger the visual field (P < 0.03). Note that adult values overlap the values of the late enucleation. Open circles, enucleates; Solid circles, mean of the normal values (normal values were provided for reference and were not used for constructing the regression).
TABLE 4. Dimensions and Relative Proportions of Cortical Regions on the Operculum and in the Calcarine

<table>
<thead>
<tr>
<th>Case</th>
<th>Age at enucleation</th>
<th>Age at observation</th>
<th>A17 calc.</th>
<th>A17 operc.</th>
<th>A17 calc./A17 total (%)</th>
<th>Dorsal extrastriate visual cortex (%)</th>
<th>Extrastriate visual cortex in calcarine (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BB24</td>
<td>E59</td>
<td>P0</td>
<td>249.9</td>
<td>77.3</td>
<td>76.3</td>
<td>43.5</td>
<td>6.5</td>
</tr>
<tr>
<td>BB85</td>
<td>E62</td>
<td>P0</td>
<td>243.9</td>
<td>60.0</td>
<td>74.9</td>
<td>41.6</td>
<td>5.2</td>
</tr>
<tr>
<td>BB104</td>
<td>E217</td>
<td>E17</td>
<td>159.4</td>
<td>56.0</td>
<td>86.1</td>
<td>39.6</td>
<td>5.3</td>
</tr>
<tr>
<td>BB28</td>
<td>E88</td>
<td>P0</td>
<td>271.6</td>
<td>44.0</td>
<td>57.3</td>
<td>37.4</td>
<td>5.3</td>
</tr>
<tr>
<td>BB24</td>
<td>E77</td>
<td>P0</td>
<td>285.8</td>
<td>218.6</td>
<td>57.1</td>
<td>37.4</td>
<td>4.2</td>
</tr>
<tr>
<td>BB35</td>
<td>E81</td>
<td>P0</td>
<td>390.2</td>
<td>321.0</td>
<td>54.9</td>
<td>35.5</td>
<td>4.2</td>
</tr>
<tr>
<td>BB49</td>
<td>E109</td>
<td>P0</td>
<td>475.4</td>
<td>392.3</td>
<td>54.7</td>
<td>36.1</td>
<td>3.2</td>
</tr>
<tr>
<td>BB20</td>
<td>E110</td>
<td>P0</td>
<td>323.5</td>
<td>224.7</td>
<td>60.0</td>
<td>33.2</td>
<td>3.1</td>
</tr>
<tr>
<td>BB34</td>
<td>Normal</td>
<td>E133</td>
<td>353.3</td>
<td>321.4</td>
<td>52.4</td>
<td>34.8</td>
<td>3.5</td>
</tr>
<tr>
<td>BB68</td>
<td>Normal</td>
<td>Three months</td>
<td>682.9</td>
<td>480.3</td>
<td>51.6</td>
<td>34.4</td>
<td>3.2</td>
</tr>
<tr>
<td>BB70</td>
<td>Normal</td>
<td>Two months</td>
<td>529.9</td>
<td>428.4</td>
<td>50.3</td>
<td>34.4</td>
<td>4.4</td>
</tr>
<tr>
<td>BB75</td>
<td>Normal</td>
<td>One month</td>
<td>786.9</td>
<td>616.5</td>
<td>55.3</td>
<td>32.6</td>
<td>3.5</td>
</tr>
</tbody>
</table>

65% level, and then widened again before disappearing laterally to the 48% level. This example illustrates an important point: We never observed a case where a piece of striate cortex was completely detached from the bulk of striate cortex; instead, there was always a neck of striate cortex connecting such protrusions to the striate field. In the eight cases of enucleation altogether, there were four instances of indentation: two on the operculum (following enucleation at E59 and E68) and two in the calcarine (following enucleation at E59 and E62). An example of indentation in the internal calcarine is shown in Figure 13B.

Sulcal pattern

In the normal animal, the only fully formed sulcus on the operculum was the external calcarine; however, it was not present in all cases (Fig. 5). When it was present, it began medially just ventral and posterior to the IOS and ran for a
Fig. 10. High-power views of peristriate cortex in normal (A) and early-enucleate (B–F) animals. A: Area 18 in the lunate sulcus of the normal animal. B: Extrastriate cortex from the posterior bank of the lunate sulcus. C: Extrastriate cortex bordering a supplementary sulcus. D: Extrastriate cortex on the operculum. E: Reduced striate cortex. F: Extrastriate cortex in the external calcarine sulcus. Scale bar = 1 mm.
variable distance rostrally on the lateral surface before disappearing into a shallow dimple in the vicinity of the foveal representation. The course of the external calcarine followed the ventral limb of the calcarine fissure. In fact, the external calcarine disappeared when the underlying calcarine fissure terminated (33 and 35% levels, respectively, in normal cases BB25 and BB3; 42% level in case BB35).

Small indentations on the cortical surface of the normal animal accommodate the underlying structures and cytoarchitectonic fields. We need to describe these indentations or dimples in the normal animal because they become major induced sulci in the early enucleates. The opercular surface also accommodated the calcarine fissure dorsally, where a shallow dimple runs parallel and posterior to the lunate sulcus (as mentioned by Polyak, 1957). This is indicated in Figure 5 by the solid arrowheads in the normal newborns (cases BB25 and BB3) and in the two late enucleates (cases BB35 and BB20). A second dimple was associated with the striate border. It was found near and parallel to the lunate sulcus (see Fig. 5, open arrowheads at the 40, 33, 28, and 26% levels in case BB25 and at the 54, 41, and 29% levels in case BB3).

In the early enucleates, there were a variable numbers of supplementary sulci on the operculum (Fig. 5). Except for case BB28, where there was a slight accentuation of the gyrification in the calcarine fissure, there was no morphological change in the sulcal pattern of cortex buried in the calcarine fissure. The external calcarine was present in all cases and in all of the early enucleates (except for case BB28) and extended much farther anteriorly than in the normal animal. In some instances, the external calcarine ran into the IOS (see Fig. 5, case BB104, 28% level).

The shallow dimple running parallel to the lunate sulcus and immediately above the upper part of the calcarine fissure (Fig. 5, solid arrowhead in the normal animal) became much more pronounced and was a consistent feature in all of the early-enucleated animals (Fig. 5, labelled A). Because of the shrinking of striate cortex in the enucleate, sulcus "A" was situated in extrastriate cortex, whereas it was located in striate cortex in the normal animals. Sulcus A took a homologous course to the dimple, running along the dorsal limb of the calcarine fissure, and disappearing at the lateralmost limit of the calcarine fissure. Other supplementary sulci (as many as five) were found in the enucleates.

Sulci in the enucleates that are homologous to major sulci in the normal animal (e.g., the external calcarine and the IOS) showed a number of abnormalities. These included discontinuities that were displayed by the inferior temporal sulcus and that spanned the full medial-lateral extent of the cortex in the normal animal, terminating at lateral levels in cases BB95, BB104, and BB21. Another typical abnormality was the fusion of major sulci, which is demonstrated by the merger of the external calcarine and IOS at the 28% level in case BB104. The border of the reduced striate cortex was associated often, but not always, with a deep sulcus in the extrastriate cortex near to it (see Fig. 5, 94 and 84% levels in case BB95; 69% level in case BB104; 57 and 48% levels in case BB28; 68, 60, 52, 44, and 38% levels in case BB21).
**DISCUSSION**

The present study provides evidence that the age-related reduction of striate cortex following enucleation is accompanied by a reduction in the size of the LGN and by an expansion of extrastriate cortex. Although the cortical changes occur both in the calcarine fissure and in the operculum, the magnitude of the reduction of striate cortex is nearly five times greater on the operculum than it is in the calcarine fissure. The reduction of striate cortex on the operculum is associated with an increase in cortical folding and with occasional instances of an unusually interdigitated striate border. Cortex surrounding the reduced striate cortex showed no cytoarchitectonic disturbances; it was homogeneous and was morphologically indistinguishable from normal area 18.

In a study of this kind, the small number of animals results in having only one animal per age group, and variations in brain size limit the observations to the most pronounced effects of enucleation. Nevertheless, the present results show conclusively that, in the early-enucleated animals, the overall dimensions of the neocortex and occipital-temporal cortex are comparable to those in normal animals. This indicates a shift in the position of the border between striate and extrastriate cortex and suggests that cortex that was destined to become striate cortex has acquired the cytoarchitectonics of area 18.

**Disruption of the striate border**

The striate border in the early enucleates is comparable to the normal animals in terms of cytoarchitectonic precision. However, the interdigitation of the border as well as the holes in striate cortex in the vicinity of the border suggest that border formation is disrupted in the early enucleate.

**Specification of cortex**

Rakic has referred to cortex that would normally become striate cortex and that, subsequent to enucleation, takes on an alternative cytoarchitecture as area X (Rakic, 1988; Rakic et al., 1991). He has suggested that such cortex is hybrid, in that it incorporates cytoarchitectonic features that are characteristic of both area 18 and striate cortex and that can be considered to be a novel cortical area. Quantification of the areal dimensions in the present results show that, in fact, such reorganized cortex is very rare; it would correspond to the hole in striate cortex shown in Figure 6A and perhaps to the one instance of a small piece of extrastriate cortex with a poorly defined layer 4 bordering...
Fig. 12. Two-dimensional reconstruction of striate cortex in normal (A) and enucleate (B) animals. Dark shading, opercular striate cortex; light shading, striate cortex in the calcarine fissure.
Fig. 13. Interdigitation of striate and extrastriate cortex. A: An example of a 2,400-μm-long interdigitation of striate and extrastriate cortex on the operculum. Note that the layering and the borders of this extremely narrow finger of cortex look remarkably normal. This was found in all early enucleates and was more frequent in cortex representing the central visual field. Arrowheads indicate the striate border. B: A rare example of interdigitation in calcarine. Scale bars = 1 mm.

Striate cortex (Fig. 11C). The holes that were found accounted for only a minute portion of the missing striate cortex. The largest hole had a surface area of 3.6 mm² and was observed in the E59 enucleate. In this animal, this corresponds to just under 0.6% of the missing striate cortex.

The present results show that the cortical region that fails to acquire striate status develops the morphological characteristics of area 18. This would suggest that without instruction from the LGN, cortex on the occipital pole follows a default developmental program that generates an area 18 cytoarchitecture.

A characteristic feature of striate cortex in the primate is that it has nearly twice the number of neurons per unit area than any other portion of the cerebral cortex, including the adjacent area 18 (Rockel et al., 1980). The greater number of neurons per unit area of striate cortex is the consequence of a higher proliferative activity of the ventricular zone giving rise to area 17 (Dehay et al., 1993). In the present results, cortex that was originally destined to become striate cortex acquired the cytoarchitectonics of normal area 18, suggesting that the reduction of numbers of LGN afferents might lead to a reduction in the total number of neurons produced by the cortical germinal zones of striate cortex, which is in line with evidence that afferent fibers exert a mitogenic control (Hamburger and Levi-Montalcini, 1949; Kollros, 1953; Delong and Sidman, 1962; Currie and Cowan, 1974; Kollros, 1982; Baptista et al., 1990; Selleck et al., 1992; Gong and Shipley, 1995; Dehay et al., 1995). The neocortex of the late enucleates showed a tendency to be larger than that in the early enucleate (Table 2) both for animals perfused at birth and for the two fetuses (cases BB104 and BB34; note that the frontal lobes in case BB20 were damaged during extraction of the brain, so that total neocortex was not available in this animal). Interanimal variability led to the conclusion that this tendency was not statistically significant. However, this finding does support the possibility that thalamic afferents may regulate early neurogenesis, when the size of the precursor pool is related to the future dimensions of the cortex (Dehay et al., 1991). Altogether, these results suggest that the change of fate of
striate cortex does not occur in the immature cortical plate; rather, it occurs in the precursors at the level of the ventricular zone (Kennedy and Dehay, 1995).

**Larger reduction of striate cortex on the operculum**

It has been known for some time that, in the normal animal, intraocular injections of synaptic tracers or injections into the LGN lead to more intense cortical labelling in the calcarine than in the central representation on the operculum (Tigges et al., 1977; Livingstone and Hubel, 1988). Similarly, the ocular dominance columns have been shown to have a higher frequency and density in the calcarine than in the operculum (LeVay et al., 1985). One interpretation of these results is that the density of retinal innervation is higher for central visual representation both in the LGN and in the striate cortex (Malpeli and Baker, 1975; Myerson et al., 1977). Although these findings have been contested (Wassle et al., 1989), they have been confirmed by other studies (Perry and Cowey, 1985; Silveria et al., 1989; Azzopardi and Cowey, 1993). These findings suggest that, in the retinogeniculostriate pathway, there is a progressive increase in the volume of tissue devoted to central vision at each level. Similar findings have been reported in the somatosensory cortex of the star-nosed mole (Catania, 1995). This principle is referred to as **central magnification** (as opposed to peripheral scaling, where the peripheral receptors are thought to project to a constant volume of central tissue).

The reduction of striate cortex following enucleation shows that its dimensions are at least partially determined by its afferent input. Killackey has referred to this as **afferent specification** (Killackey, 1990). However, the concept of central magnification suggests that there are certain limitations to afferent specification mechanisms, because it suggests that central development may not be dictated solely by peripheral input. The principle of central magnification suggests that there is an early determination of the cortical volume allocated to central and peripheral representation of the visual field that is independent of the number of inputs.

One possibility that needs to be considered is that the greater susceptibility of the central striate field to enucleation itself could be a consequence of central magnification. If the number of LGN fibers contacting a unit volume of the foveal representation in the cortex is much less than in the periphery, then a uniform decrease in fiber density could lead to a failure to reach a threshold value leading to the much larger reductions observed in the central representation.

**Thalamic perturbations**

The presence of the retina is critical for the normal development of the thalamus. Enucleation at all ages leads to a reduction in the size of the LGN and the inferior pulvinar while apparently sparing the lateral pulvinar. Furthermore, up to and including E81, the presence of the eyes is necessary for the normal lamination of the LGN.

The reduction of the inferior pulvinar confirms an earlier observation of a reduction in size of this nucleus in human congenital anophthalmia (Hasler and Wagner, 1965). Bender (1983) has shown that visual activation of the inferior pulvinar depends on the topographical projection from striate cortex and not on ascending projections. This suggests that the inferior pulvinar provides a relay for an alternative route for striate cortex to exert an influence on extrastriate cortex (Ungerleider et al., 1985; Cusick et al., 1993). The sparing of the lateral pulvinar and the reduction of the inferior pulvinar suggest that the reduction of this nucleus might be a secondary consequence to the reduction of striate cortex, reflecting the functional differences of these two nuclei.

Following early enucleation, the massive loss of neurons in the LGN (Rakic and Williams, 1986) and the inferior pulvinar (present findings) takes place some 15 days after proliferation of LGN neurons (Rakic, 1977); thus, it is largely the consequence of increased levels of normal cell death (Williams and Rakic, 1988). This contrasts with the more modest loss of LGN cells following enucleation in the postnatal mouse (Cullen and Kaiserman-Abramof, 1984), which could be due to the enucleation having been carried out too late in the mouse or to a species difference related to the more convergent organization of the retinothalamic pathway in the primate (Perry et al., 1984).

**Induction of abnormal gyri and sulci**

The functional necessity for cortical folding can be considered in simple mechanistic terms as solving the problem of packing the extended cortical surface into the restricted volume of the cranial vault (Welker, 1990). The consequences of early enucleation show that this is only a very partial explanation of cortical folding. In the early enucleate, the occipital-temporal cortex is the same size as in the late enucleate, yet it shows an increase in cortical folding, possessing up to eight deep supplementary gyri. Two of these supplementary gyri are the exaggeration of small dimples, which, in the normal animal, accommodate the underlying calcarine fissure. The other supplementary gyri would appear to have no homology in the normal animal.

It has been speculated that gyral formation correlates to cortical fields and that areal boundaries tend to coincide with cortical folds (Welker, 1990). This fits the frequent observation that connections are most common between neighbouring areas (Young, 1992), so that gyration may serve to ensure minimum trajectories for connections between areas (Welker, 1990). In the fetal monkey, the phase of rapid gyration at E100–120 coincides with the formation of cortical pathways linking the visual areas. Striate cortex and area V2 are equivalent in size, and both are considerably larger than the other visual areas; therefore, striate cortex and area V2 must be the most intensely interconnected visual cortical areas. In the normal cortex, the retinotopographic representation in striate cortex and in area V2 is such that corresponding points in the two areas are in register on the operculum and on the posterior bank of the lunate sulcus (Gattass et al., 1981); thus, the axonal trajectories have to traverse only a few millimeters. In the early enucleate, the large changes in the dimensions of striate and extrastriate cortex disrupt the appropriate topographical relationship between cortical surfaces, which, in turn, may generate the unusual gyral pattern in these animals. We can conclude from the perturbed gyration following early enucleation that, in normal development, gyri formation serves largely to accommodate cortical connectivity.

**CONCLUSIONS**

The variability in the induced changes in gyral pattern as well as the disruption of the striate border suggest that
multiple factors, including LGN afferents, contribute to determining the dimensions and contours of cortical fields. The findings in the enucleate are relevant to our understanding of the mechanisms specifying cortical areas. Phylogenetic considerations have led to the suggestion that adaptation in more complex mammals leads to an increase in cortex surface and multiplication of numbers of areas (Jerison, 1973; Haug, 1987; Kaas, 1987). The fact that the total neocortical volume is affected very little by removal of the sensory periphery raises the possibility that the dimensions of neocortex are governed by mechanisms, which are mainly intrinsic to the developing cortex. This contrasts with the dimensions and cytoarchitectonics of striate cortex, which come under mainly extrinsic control via the thalamic afferents.

ACKNOWLEDGMENTS
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LITERATURE CITED


