In human primary visual cortex, parvalbumin (PV) is expressed by Cajal–Retzius cells in layer 1 by 20 weeks of gestation (20W), but its immunoreactivity is mostly lost by term. PV immunoreactivity in layers II–VI mainly develops later, from 26 to 34W, following an approximately 'inside-outside' sequence in a series of bands. PV-positive perikarya appear in layer V by 20W, but only in small numbers. They increase in number and staining intensity by 26W. By 30W a band of densely labelled somata and neurite occupies layers IVC–VI. By 34W a second, less dense, band of cell bodies and neurite appears in IVB and IVCa, separated from the deep band by IVc which is cell-sparse and almost fibre-free. Between 38 and 40W, a third minor band consisting mainly of fibres is seen in layer IVA. Reactive cell bodies form clusters, and the neuropil staining is mosaic-like. PV-positive neurons are of two main types: large with a wide dendritic arbor, and smaller with simpler dendrites. However, a few have characteristics of pyramidal cells, and a few others resemble glial cells. The laminar pattern of PV-immunoreactive somata in human striate cortex is established by term, rather than postnatally as in most mammals, implying that PV may be involved in neuronal development in prenatal human striate cortex.

Introduction

The neuronal roles of calcium-binding proteins, which are capable of buffering intracellular calcium, have been emphasized in recent years. Calbindin (CB) and parvalbumin (PV) are the most extensively studied molecules of this family in the central nervous system (Kleinschmidt et al., 1987; Mattson and Kater, 1987; Celio, 1990; Kater and Mills, 1991; Andresson et al., 1993; Kawaguchi and Kubota, 1993; Spitzer, 1994). CB and PV are expressed in different subpopulations of GABAergic inhibitory interneurons: they are excellent markers for characterizing different types of these neurons and are useful for detecting alterations in cortical interneurons in pathological conditions in man and in animal models (Celio, 1986, 1990; DeFelipe et al., 1989, 1993; Freund et al., 1990; Kobayashi et al., 1990; Demeulemeester et al., 1991; Akil and Lewis, 1992; Williams et al., 1992; Andresson et al., 1993; Fonseca et al., 1993; Leifer and Kowall, 1993; Blümcke et al., 1994; Ferret et al., 1994; Anderson et al., 1995; Yan et al., 1996). Their differential localization in the mammalian visual system may be associated with separate signal channels from the retina through the lateral geniculate nucleus (LGN) to the visual cortex (Casagrande, 1994). In primates, including man, there is a differential distribution of CB and PV in interneurons, which may be related to functional segregation in visual cortex, as they are correlated with the distribution of cytochrome oxidase (CO). For example, CB somata in primary visual cortex of monkey and man surround the CO-rich 'puffs' (Celio et al., 1986; Hendry and Carder, 1993; Yoshioka and Hendry, 1995). Dense PV reactivity closely matches CO expression in layer IV and in the 'blobs' in layer III (Johnson and Casagrande, 1995). In the primate LGN, CB and PV are expressed by different geniculo-cortical relay cells. PV neurons and neuropil are localized primarily in the main layers which are highly CO-reactive, whereas CB is principally restricted to the CO-pale koniocellular layers (Blümcke et al., 1994; Casagrande, 1994; Johnson and Casagrande, 1995).

Study of the development of CB and PV has provided important information concerning structural and functional maturation of cortical neurons (Enderlin et al., 1987; Stichel et al., 1987; Jones and Hendry, 1989; Huntley and Jones, 1990; Hendrickson et al., 1991; Akil and Lewis, 1992; Mizu et al., 1992; Soriano et al., 1992; Alcantara et al., 1993; Hogan and Berman, 1993, 1994; Lund and Lewis, 1993; Alcantara and Ferrer, 1994; del-Rio et al., 1994; Spatz et al., 1994; Anderson et al., 1995). In the primate primary visual cortex, PV cell bodies appear with the onset of visually evoked activity, while labelling of the neuropil correlates with the completion of thalamocortical connections. In contrast, the expression of CB correlates with the prenatal arrival of axons from the LGN, and its disappearance from most neuronal cell bodies coincides with the loss of cortical plasticity and the reduction in synapse and dendritic spine numbers (Hendrickson et al., 1993). In the monkey prenatal cortex, the genesis and elimination of dendritic spines of layer III pyramidal cells are coincident with the formation and reduction of axonal cartridges or 'candles' from PV-immunoreactive chandelier cells, suggesting plasticity of local circuitry between cortical interneurons and pyramidal cells during development (Anderson et al., 1995).

Cortical synapses and dendritic spines in the human brain develop and mature through stages of proliferation, overproduction, and subsequent attrition, as in other species (Huttenlocher et al., 1982; Michel and Garey, 1984; Huttenlocher and de Courten, 1987; Bourgeois and Rakic, 1993). Structural refinement and plasticity in late gestation or early postnatal life are critical for the functional maturation of neural systems, but are not well understood in man due to methodological limitations. Perinatal study of molecules such as calcium-binding proteins may provide insight into the mechanisms of plasticity of human vision. We have examined the development of PV in the human primary visual cortex (V1, striate cortex, or area 17 of Brodmann, 1909) in the second half of gestation by means of immunocytochemistry.

Materials and Methods

Four fetal and two neonatal human brains were studied. Their ages were estimated from maternal history, body and brain weight, and crown-rump length at 20, 26, 30, 34, 38 and 40 weeks (W) of gestation. Three fetuses (20–30W) were obtained in therapeutic termination of pregnancy (the two youngest being elective terminations, the other because of maternal malignant disease), and one (34W) from an accident-induced abortion. The other two brains were from one slightly premature (38W) and one fullterm (40W) case of neonatal death from non-neurological causes. The 38W case was born with a thoracogastroschisis and died on the second day after birth; the brain was normal according to

Q. L. Cao, X. X. Yan, X. G. Luo and L. J. Garey

1Department of Anatomy and Neurobiology, Hunan Medical University, Changsha, Hunan 410078, People's Republic of China and 2Department of Anatomy, Charing Cross and Westminster Medical School, London W6 8RF, UK

3Present address: Department of Anatomy and Neurobiology, University of California, Irvine, CA 92717, USA

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Figure 1. Developmental change of the laminar distribution and numerical density of PV-immunoreactive somata in fetal human striate cortex at different ages (W = weeks of gestation). Each column represents the number of cells in a 50 \( \mu \)m deep, 1 mm wide strip of cortex parallel to the pial surface. Cortical layers are indicated on the horizontal axis. CP, cortical plate.

Morphometric analyses were performed in the upper and lower banks of the calcarine sulcus in the striate cortex and at the border between the primary and the secondary visual areas. With the aid of an image analysis system, the numerical density of positive cells in horizontal 50 \( \mu \)m deep strips through the cortical layers beneath 1 mm of pial surface was calculated in each brain (Fig. 1). Soma sizes of 20–200 neurons in each brain (20 for 20W, 100 for 26W and 200 for the others) were measured by moving the slide in a series of regular scans (Fig. 2).

Results
We have described the laminar differentiation of the human striate cortex elsewhere (Yan et al., 1992). In cresyl violet preparations the cortical mantle at 20W consists of the subplate (SP), superficial to which is the cortical plate (CP), the deep part of which has already differentiated into layers V and VI, and the rest of which will form the future layers III-IV, and, most superficially, the marginal zone (MZ) or layer I (Figs 3 and 4A). At 26W, layers V and VI are more distinct and CP is wider and more densely cellular in its upper and lower portions, the latter of which will form the future layers II-IV, and, most superficially, the marginal zone (MZ) or layer I (Figs 3 and 4A). At 26W, layers V and VI are more distinct and CP is wider and more densely cellular in its upper and lower portions, the latter of which will form the future layers II-IV, and, most superficially, the marginal zone (MZ) or layer I (Figs 3 and 4A).

PV Immunoreactivity in the Marginal Zone (Layer I)
The first elements of the human visual cortex to express PV in
large amounts were Cajal–Retzius cells (Huntley and Jones, 1990; Meyer and González-Hernández, 1993) in MZ, the prospective layer I, but they had mostly lost their reactivity by term. At 20W many moderately stained cell bodies with short, irregular processes were seen in MZ. Most were unipolar or bipolar, but some were already multipolar (Fig. 3A). By 26W, PV-reactive cells in MZ had increased in soma size and staining intensity, but not in numerical density (Figs 1 and 3B). By 30W, positive cells in layer I were fewer and less reactive (Figs 1 and 3C), but positive fibres running parallel to the pial surface were numerous. They originated from cells in layer I and others in deeper layers (Fig. 3C). After 30W, the numbers of both reactive cells and fibres in layer I declined (Fig. 1), and the remaining cells had small somata and few processes (Fig. 3D,E). By term almost no positive somata or fibres remained (Fig. 3F).

Differentiation of PV-Immunoreactive Somata in Layers II–VI

In area 17 of the youngest brain (20W), a few small, round, weakly stained perikarya were identified in layer V (Fig. 1). Most had no visible processes or were unipolar (Fig. 4B,C). No immunoreactive perikarya were detected in other parts of the cortex, except in layer I. By 26W, many weak to moderately immunoreactive bipolar cells had appeared in layers V and upper VI (Fig. 1); a few were multipolar with short, often unbranched, processes (Fig. 4D,E). By 30W, PV-immunoreactive perikarya formed a single cellular band from deep IVC to upper VI, densest in V (Figs 1 and 5A,B). Cells in this band sent processes to more superficial layers, some of which branched to form horizontal parallel fibres in layer I (Fig. 3C). Sometimes the cells were organized in clusters tangentially across the cortex (Fig. 5D). There were denser and more darkly stained neurons in primary than secondary visual cortex (Fig. 5E) with complex dendritic arbors (Fig. 5F). A few small PV-immunoreactive somata and scattered positive fibres were encountered in the white matter.

**Figure 2.** Distribution of cross-sectional areas of PV-immunoreactive somata in fetal human striate cortex at different ages (W = weeks of gestation).

**Figure 3.** Parvalbumin (PV) labelling in layer I of prenatal human striate cortex. By 20 weeks (W) of gestation (A), a number of small unipolar and bipolar cells some thick fibres are lightly to moderately stained, both mainly in the upper half of the layer. By 26W (B), the staining intensity of the somata and fibres and the number of fibres are increased, but the number of somata is unchanged. By 30W (C), positive somata are reduced in number and staining intensity, but thin fibres are richly distributed throughout layer I, most densely in the deep part. Later, a progressive loss of reactive somata and fibres is seen until at 40W both are scarce. (D) 34W; (E) 38W; (F) 40W. Layer I is indicated by broken lines. Bar = 25 μm.
from 30W. By 34W, the number of PV neurons had increased further throughout the cortex (Fig. 1). They were mostly in two bands, the deep one from layers IVC to upper VI, as at 30W, and the upper one, with fewer cells, in IVB and the upper part of IVC (IVCa). Between the two bands was IVCB, where only a few small, faint somata were observed. Cells in layers II and III were small and sparse (Figs 1 and 5A), whereas some in deeper layers had large somata (Fig. 6B–D). The laminar pattern of positive somata was maintained from 34W onward (Figs 1, 7, and 8), but the clustering of positive cells was heightened. The clusters were more easily identified in calcarine cortex than in the peripheral portions of area 17: they were vertically congruent in both cellular bands, in IVB/IVCa and V/VI. Their diameter was 100–300 μm, and the centre to centre distance of adjacent clusters was 300–600 μm (Fig. 8A). Positive cells had undergone further morphological differentiation (see below).

**PV-Immunoreactive Fibres in Prenatal Human Striate Cortex**

Immunoreactive puncta representing transversely sectioned fibres were visible in the neuropil, but no pattern was observed before 30W when they were mainly in layer V, congruent with the band of reactive somata (Fig. 5B,E). By 34W, two highly reactive neuropil bands were found, the deep one in layer V and upper VI and a new, lighter band in IVB-IVCa. Between them was a band in IVCB with only a few small, faint cells but no positive puncta (Fig. 6A,D). The neuropil staining patterns in the two oldest cases were similar, but an additional band of fibres appeared in deep III and IVA containing a mosaic-like pattern of small zones with little immunoreactivity (Figs 7A,D and 8A,C). Non-immunoreactive perikarya were surrounded by PV-positive perisomatic baskets (Fig. 6C,D). We did not, however, detect the PV-immunoreactive axon 'candles' described elsewhere (see Discussion). The cell and neuropil bands and the mosaics in layers III and IV ended at the border of areas 17 and 18, whereas the deep band in V/VI crossed the border (Fig. 8B).

The distribution of long, positive fibres was generally parallel to that of reactive somata and puncta. They were sparse in the two youngest brains (Fig. 4B–E), but from 30W long fibres were observed in the cortex, densest in layers V and upper VI and randomly oriented. The next densest layer was I, where the fibres were mostly horizontal. In the middle cortical layers the fibres were predominantly vertical and originated from the cells with large somata in the infragranular layers. Many dense fibres were present in lower VI and the subcortical white matter from 30W onward, mainly from positive cells in the deep cortical layers (Figs 5B, 6A, 7A,C, and 8F).

**Morphological Maturation of PV-Immunoreactive Neurons**

Most PV neurons displayed characteristics of non-spiny non-pyramidal cells when they were mature enough to determine. At 26W positive neurons already had different sizes and shapes (Figs 2, 4D,E, and 5F). By 34W there were two major types. One had a large soma (greatest diameter 15–23 μm) and a complex, wide, usually multipolar, dendritic arborization, usually with three or more primary dendrites. Sometimes, their axon could be traced for several hundred micrometres (Figs 7B,D and 8D–F). These large cells made up 11–23% of the total population of PV neurons at 34W and later (Fig. 2). At term they were mainly in layer IVC. The other major type was more numerous (75–85% of the total) and had a smaller soma (greatest diameter 8–17 μm).
Figure 5. PV immunoreactivity in 30W visual cortex. In a section counterstained with cresyl violet (A) all layers of the adult striate cortex are identifiable, and PV-positive somata are distributed as a band in layer V and the neighbouring IVc and VI. Positive cells in deep cortical layers send ascending processes to the superficial layers (B); some reach layer I and branch to form parallel fibres (arrowhead in C) running in the lower part of layer I. PV-reactive neurons are sometimes organized in clusters (indicated by arrowheads in D). (E) The primary visual cortex (V1) contains more densely packed PV neurons in the cellular band than the secondary visual cortex (V2). (F) High power view showing PV cells of different shapes and sizes, and the highly reactive neuropil in layer V. Cortical layers are indicated with numbers (1–6 = I–VI), letters (sublayers) and broken lines. Bar = 100 μm in (A–D), 25 μm in (E, F).

and a simpler dendritic tree with fewer, less branched primary dendrites with smaller arborizations. These small cells were found in all layers except I, and occasionally the white matter, but were more frequent in IV–VI (Figs 1, 2, and 6–8).

Lightly to moderately stained PV-reactive pyramidal cells were occasionally encountered (<5%) in layer V of the four oldest cases. They were relatively small (<10 × 15 μm). Like the non-pyramidal neurons, no dendritic spines were visible on their soma or dendrites (Fig. 8E).

Finally, we encountered a few positive cells (<1%) in the two neonates with medium to large somata and numerous rough-surfaced, extensively branched processes, rather like astrocytes (Fig. 7B) or oligodendrocytes (Fig. 7C). Their nature is unknown and, apart from glial cells, might be PV-containing neurogliaform neurons (Jones, 1975), or a transient neuronal form.

Discussion
Previous studies on the development of PV-immunoreactive neurons in the cerebral cortex have been undertaken in rodents (Enderlin et al., 1987; Celio, 1990; Soriano et al., 1992; Alcantara et al., 1993; del-Río et al., 1994), cats (Stichel et al., 1987; Demeulemeester et al., 1991; Alcantara and Ferrer, 1994; Hogan and Berman, 1994), and primates (Blümcke et al., 1990, 1994; Celio, 1990; Hendrickson et al., 1991; Blümcke and Celio, 1992; Spatz et al., 1994; Johnson and Casagrande, 1995). Our observations add data on the prenatal development of PV in the human striate cortex, which shows broad similarities to that in other mammals, especially non-human primates, though certain species differences emerge. A major difference between man and monkey is the presence of positive cells in human infragranular layers, which never show high PV reactivity during development in the monkey (Enderlin et al., 1987; Hendrickson et al., 1991; Alcantara et al., 1993; Alcantara and Ferrer, 1994; del-Río et al., 1994; Hogan and Berman, 1994; Spatz et al., 1994).

In man, Cajal-Retzius cells are the first to express PV in large numbers, starting before 20W, reaching a maximum at 26–30W, with most then losing PV reactivity by term. Transient expression of CB and PV in Cajal-Retzius cells has been observed.
Figure 6. PV immunoreactivity in the striate cortex of a 34W fetus. (A) A section lightly counterstained with cresyl violet; positive neurons are now distributed throughout the cortex, mostly in two bands, a deep one occupying layers V and upper VI, and an upper one in IVB and IVcB. The deep band contains more cells and richer neuropil than the upper. Between the bands, IVcB (arrowhead) is free of neuropil staining and sparsely cellular. (B, C) PV labelling in layers II and V. Most somata are relatively small but some, in deeper layers, are larger. There is a honeycomb-like appearance in the neuropil, with immunonegative perikarya (*) outlined by well-stained fibres. This is also illustrated in layer IV (D). Laminar labelling as in Figure 5. Bar = 100 μm in (A), 25 μm in (D), 10 μm in (B, C).
Figure 7. Morphology and distribution of PV-reactive somata and fibres in the striate cortex at 38W. (A) In a section lightly counterstained with cresyl violet, three bands of cell bodies and neuropil are seen in layers V and upper VI, lower IVB and IVc, and IVa. The first two consist of both perikarya and fibres, and the last one mainly of fibres. Two light bands located in the upper half of IVB and IVc are indicated by triangles. The upper one contains immunoreactivity-free mosaics. (B–D) Different types of PV neurons. Large neurons with wide dendritic arbours are indicated by arrowheads. Most other small reactive somata belong to another type of cell with smaller somata and simpler dendritic trees. Two cells in (B) and (C), indicated by arrows, represent additional types of cortical PV cell, possibly an astrocyte and an oligodendrocyte respectively (see text). Laminar labelling as in Figure 5. Bar = 150 μm in (A), 25 μm in (B–D).
Figure 8. PV immunoreactivity in full term (40W) neonatal human visual cortex. (A) In a section lightly counterstained with cresyl violet, the laminar distribution pattern of positive somata and neuropil in striate cortex is similar to that in the 38W neonate illustrated in Figure 5. (B) The cell and neuropil bands in layer IV end at the border between areas 17 (V1) and 18 (V2), but the dark band in layer V crosses the border. (C) Clusters of positive cell bodies (open arrows) in layers IV-VI and the dark and light (arrowheads) bands of labelled cells and neuropil in cortex in the banks of the calcarine sulcus. (D-F) Types of PV-positive neurons; arrowheads in (D) indicate neurons with wide dendritic arbors, one with a visible axon (right). A positive pyramidal-like neuron is indicated by an arrow in (E). Other neurons are of the small type. Laminar labelling as in Figure 5. Bar = 150 \mu m in (A-C), 25 \mu m in (D-F).
in monkeys (Huntley and Jones, 1990; Hendrickson et al., 1991), rats, and cats (Enderlin et al., 1987; Stichel et al., 1987). Meyer and González-Hernández (1993) defined two populations of Cajal-Retzius cells, polymorphic and persisting, in the prenatal human cortex. The former differentiate before 18W, mature at 26W, and then disappear after 30W, a similar time-course to those in our study. The regression layer I PV neurons starts soon after the arrival of PV-positive fibres from the infragranular layers, implying a role of PV in the differentiation of cortical neurons (see below).

The emergence of PV neurons in layers II–VI in human area 17 follows an approximately inside-outside sequence, similar to that in other mammals, though the time-courses differ. In non-humans the differentiation of PV starts either just before or after birth (Enderlin et al., 1987; Stichel et al., 1987; Hendrickson et al., 1991; Akil and Lewis, 1992; Alcantara et al., 1993; Alcantara and Ferrer, 1994; del-Rio et al., 1994; Hogan and Berman, 1994; Spatz et al., 1994; Anderson et al., 1995).

The differentiation of PV-immunoreactive neurons in visual cortex may be correlated with the onset of visually driven activity and activation of cortical inhibitory GABAergic interneurons (Hendrickson et al., 1991; Alcantara et al., 1993; Alcantara and Ferrer, 1994; del-Rio et al., 1994). The former theory does not explain the prenatal emergence of PV somata in human striate cortex, though the latter one is possible as the differentiation of PV in man is relatively late compared to the establishment of cortical lamination and the expression of GABA (Sauer et al., 1983; Yan et al., 1992). An alternative explanation might be that man has a relatively long gestation, resulting in the visual cortex undergoing stages of development prematurely that begin postnatally in non-human species. Spontaneous potentials (Spitzer, 1994) could already be active in the visual pathway in the late human fetus, and may trigger the expression of molecules such as PV. On the other hand, there is evidence that CB and PV neurons have N-methyl-D-aspartate (NMDA) receptors that may play a role in neuronal plasticity (Kawaguchi and Kubota, 1993), be highly significant during maturation of the nervous system (Tsumoto et al., 1987), and be relevant to humans at birth when the eyes are already open.

We have demonstrated two main types of PV cells, large and small non-pyramidal neurons, in the human striate cortex, in agreement with observations in non-humans, particularly the monkey (Blümcke et al., 1990; Hendrickson et al., 1991; Akil and Lewis, 1992; Alcantara et al., 1993; Alcantara and Ferrer, 1994; Conde et al., 1994; Anderson et al., 1995). The morphological features of large PV neurons in perinatal human striate cortex are similar to the class of wide arbor basket interneurons in adult monkey cortex defined by PV immunocytochemistry and Golgi preparations (Lund and Lewis, 1993; Conde et al., 1994).

PV fibre systems in mammalian cerebral cortex could have multiple origins. One is from intrinsic PV neurons, including basket, chandelier, and bitufted cells, and we found immunonegative perikarya outlined by reactive fibres in layers IV–VI rather like PV-positive pericellular baskets (Stichel et al., 1987; DeFelipe et al., 1989, 1993; DeFelipe and Jones, 1991; Hendrickson et al., 1991; Akil and Lewis, 1992; Alcantara et al., 1993; Alcantara and Ferrer, 1994; Conde et al., 1994; Anderson et al., 1995). In contrast, PV-reactive 'candles' (Akil and Lewis, 1992; Alcantara et al., 1993; Lund and Lewis, 1993; Alcantara and Ferrer, 1994; Conde et al., 1994; del-Rio et al., 1994; Anderson et al., 1995) were not detectable in our material, even by term. This may be because the candle system lags behind the basket system, an effect enhanced by the large PV neurons appearing more mature than the small ones at the end of gestation. There is coincident formation and elimination of dendritic spines on layer III pyramidal cells and the appearance and attrition of PV-positive candles in the monkey prefrontal cortex, suggesting a dynamic refinement of intracortical circuitry between the projection cells and GABAergic interneurons (Akil and Lewis, 1992; Anderson et al., 1995). In the human visual cortex, the formation of synapses and dendritic spines starts prenatally but is only completed after birth (Huttenlocher et al., 1982; Michel and Garey, 1984; Huttenlocher and de Courten, 1987), and this may explain why PV-positive candles are not detectable at birth in man.

Another source of cortical PV fibres is extrinsic, e.g., from the LGN. In the thalamo-receptive layer IV, PV-positive asymmetric synapses (excitatory) are found, in addition to symmetric (inhibitory) synapses (Jones and Hendry, 1989; DeFelipe and Jones, 1991). We noticed an increase of neuropil staining and the presence of a mosaic-like pattern in layer IVA by birth. The change probably reflects an increase of PV-positive LGN axons, in addition to dendrites and axons of cortical PV interneurons. In the primate, the magnocellular layers of LGN project to IVCa and parvocellular layers to IVCB and IVA (Hendrickson et al., 1978; Florence and Casagrande, 1990; Peters and Sethares, 1991; Casagrande, 1994) and both contain PV-reactive relay neurons (Blümcke et al., 1994; Johnson and Casagrande, 1995). A relatively slow development of PV-reactive cell bodies and neuropil in IVCB compared to IVCa was observed in the macaque (Hendrickson et al., 1991), and is confirmed in our study in man. Hendrickson et al. (1991) suggested that this delay could be due to a late appearance or maturation of geniculate input to IVCB, late expression of PV in geniculocortical axons to IVCB, or late expression of PV in IVCB interneurons. These suggestions, particularly the first two, seem to be also true in human striate cortex, where IVCB has the highest PV-reactive neuropil staining in the adult, but still only a few small positive neurons (Blümcke et al., 1990). Furthermore, it is of interest that in humans PV neuropil intensity in IVB/IVCa, and even in deep III and IVA, has reached an adult level, but that in IVCB it is still extremely low at birth compared to that at maturity. This notion, together with the observation of a higher CO reactivity in magnocellular than parvocellular layers in LGN in newborn monkeys, suggests that large LGN neurons make an earlier structural and functional connection to the cortex than small LGN neurons in both monkey and human (Kennedy et al., 1985; Blümcke et al., 1990; Hendrickson et al., 1991; Blümcke and Cello, 1992; Wong-Riley et al., 1993; Casagrande, 1994; Spatz et al., 1994).

There are striking periodic distribution patterns of PV immunoreactivity in the human striate cortex before birth. These include cell clusters and neuropil mosaics. This organization is linked to CO 'blobs' and structural/functional segregation in mature visual cortex (Blümcke et al., 1990, 1994; DeFelipe and Jones, 1991; Blümcke and Cello, 1992; Casagrande, 1994; Spatz et al., 1994; Johnson and Casagrande, 1995). A relation of the PV patchiness to ocular dominance or other functional columnar organization in neonatal human striate cortex is unlikely, since an irregular arrangement of PV-labelled cell bodies and neuropil has also been noted in premature monkey striate cortex and rat parietal cortex at a time when functional cortical columns are not thought to be established (Hendrickson et al., 1991; Alcantara and Ferrer, 1994). Furthermore, CO 'puffs', which can be regarded as functional cytoarchitectonic units, are not clear in human striate cortex until the fourth postnatal month (Wong-Riley, 1989; Horton,
1990; Wong-Riley et al., 1993). Likewise, functional parameters of human vision, including stereoauity, are all relatively poor before 4-6 months (Boothe et al., 1985; Brown, 1990).

Nevertheless, co-localization of PV and CO in layer IV, and the similarity of cortical and LGN patterns in primates from birth to adulthood (Kennedy et al., 1985; Blümcke et al., 1990; Horton, 1990; Hendrickson et al., 1991; Wong-Riley et al., 1993; Spatz et al., 1994; Johnson and Casagrande, 1995) suggest that PV patches in prenatal cerebral cortex might be immature precursors of future functional modules.

Notes

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Address correspondence to L.J. Garey, Department of Anatomy, Charing Cross and Westminster Medical School, London W6 8RF, UK.

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