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Postnatal growth and column spacing in cat primary visual cortex

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Abstract The primary visual cortex (area 17) of cats continues to grow substantially during early postnatal development. To assess the implications of this growth for the organization of visual cortical maps, we analysed both postnatal growth of area 17 and the spacing of ocular dominance columns in the same animals using 2-deoxyglucose autoradiography to label cortical activation patterns. Quantitative analyses of area size and column spacing were performed on flat-mount sections of the cortical hemispheres. Our analysis of the surface area revealed an average increase of the size of area 17 between the third and tenth postnatal weeks by about 51%. About 75% of this increase occurred during the third and sixth postnatal weeks (size increase of 37%). However, the distance between adjacent columns did not exhibit a similar increase but rather remained constant during the same postnatal period. Since cortical growth is not accompanied by an increased spacing of ocular dominance columns, new functional modules must somehow be added during the first postnatal weeks to occupy the enlarging cortical sheet. Possible mechanisms underlying the formation of new modules are discussed.

Keywords Area 17 · Columnar spacing · 2-Deoxyglucose · Postnatal growth · Ocular dominance columns

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Introduction

In the primary visual cortex of the brain, as in other cortical areas, neurons specialized to process particular aspects of the visual input are arranged in complex spatial patterns, called cortical maps, and interact through a dense network of intracortical connections. Recently it was demonstrated that some of these maps, such as orientation preference maps (e.g. Gödecke et al. 1997; Crair et al. 1998) and ocular dominance columns (e.g. Crowley and Katz 2000; Rathjen and Löwel 2000; Crair et al. 2001), can already be visualized in cats and ferrets at a very early postnatal period during which the cortex is still growing. A recent paper by Duffy et al. (1998) has shown that the surface area of primary visual cortex (area 17, V1) of adult cats was more than twice (230%) that of neonatal (1-week-old) kittens, while the shape of area 17 did not change during postnatal development. Such considerable growth should have direct implications for the arrangement of cortical columns and the patchy horizontal connections between these columns (see Schmidt et al. 1999). Prolonged postnatal brain growth might either cause an enlargement of existing cortical modules, probably without significant changes in neuronal circuitry ("balloon-effect"), or, alternatively, indicate a progressive increase in the number of modules and in the complexity of neuronal circuits. In macaque monkeys, V1 size increased by only 16% and the number of cytochrome oxidase blobs occupying V1 remained approximately the same during postnatal maturation (Purves and LaMantia 1993). However, it is presently unknown what happens to the layout of functional cortical maps in cat primary visual cortex as the V1 surface area increases by more than 100% between birth and adulthood.

To address this question, we analysed both postnatal cortical growth of area 17 and the layout and spacing of one of the best-known columnar systems in this area, namely the system of ocular dominance columns. Ocular dominance columns represent the thalamocortical afferents of the left and right eye (LeVay et al. 1978; Löwel and Singer 1987; Anderson et al. 1988), and neurons

located in columns extending through the entire cortical thickness are driven by visual stimulation of the same eye (Hubel and Wiesel 1962; Löwel and Singer 1993). By visualizing functional ocular dominance columns with 2-deoxyglucose we observed a substantial growth of cat area 17 during early postnatal development while the spacing of adjacent ocular dominance columns remained rather unchanged. This suggests that new functional modules are added to occupy the enlarging cortical sheet. Some of these results have been reported in abstract form (Rathjen et al. 1998a, 1998b).

Materials and methods

We used the 2-deoxyglucose (2-DG) technique (Sokoloff et al. 1977; Löwel and Singer 1993) to visualize ocular dominance columns in the primary visual cortex of awake kittens. A total of 23 animals (from 14 litters) from our institutes' colonies was used. The experiments were performed with 3- to 6-week-old animals because (1) ocular dominance columns cannot be labelled with 2-DG at earlier ages (Rathjen and Löwel 2000), and (2) cortical growth slows down considerably after 6 weeks of age in cats (Duffy et al. 1998). The kittens were subjected to a 2-DG experiment while being allowed to move freely around in the laboratory to ensure effective monocular stimulation. The resulting patterns of 2-DG labelled ocular dominance columns were used (1) to determine the size of primary visual cortex (area 17), and (2) to measure the spacing of the domains in the same animals. Some of our experimental animals had already been used in previous studies on the development and spacing of functional ocular dominance columns in strabismic and normally raised kittens (Rathjen and Löwel 2000; Rathjen et al. 2002). Since strabismus had neither an effect on the spacing of ocular dominance columns (Rathjen et al. 2002) nor on the size of area 17 in these animals (see Results), the data of both experimental groups were pooled for final comparative analyses. In addition, we analysed ocular dominance maps from two 10-week-old cats (from the same litter) from already published papers (Löwel and Singer 1992, 1993).

All animal experiments have been performed according to the German Law on the Protection of Animals and the corresponding US National Institutes of Health regulations (Principles of Laboratory Animal Care, NIH publication No. 86-23, revision of 1985).

Visualization of 2-DG labelled ocular dominance maps

We visualized the complete pattern of ocular dominance columns in the entire area 17 using 2-DG autoradiography as described in detail elsewhere (Löwel and Singer 1993; Rathjen and Löwel 2000). Briefly, a venous catheter was implanted with the animals under either halothane anaesthesia using an inhalation mask (2–4% halothane in a mixture of 70% nitrous oxide and 30% oxygen) or Saffan anaesthesia (15 mg/kg i.m. injectable steroid; Pitman-Moore Ltd., Uxbridge, UK). After full recovery from anaesthesia, one eye was occluded with a black contact lens and 2-deoxy-D-[U-¹⁴C]glucose (specific activity 10.9–11.7 GBq/mmol; Amersham Biosciences, Boulder, CO, USA) was injected intravenously at a dose of 3.7–4.2 MBq/kg. The animals were encouraged to actively explore the laboratory to guarantee effective monocular stimulation. After 45 min, the animals received a lethal dose of pentobarbital, injected intravenously. The brains were removed and the visual cortices flat-mounted prior to freezing the tissue on dry-ice (Freeman et al. 1987; Löwel et al. 1987). Subsequently, 25-µm thick serial cryostat sections (at –17°C) were cut parallel to the cortical surface. The sections were mounted on glass slides, immediately dried on a hotplate and exposed to X-ray film (Agfa Structurix D7) for 3–4 weeks.

Image processing and quantitative analyses

Representative 2-DG autoradiographs of supragranular flat-mount sections of the visual cortical hemispheres were digitized in 8-bit greyscales with a resolution of 20.48 pixels/mm using an image processing system (Imago II, Compulog). Area 17 was delineated on the digitized autoradiographs using the distinct 2-DG activation pattern in that area compared to surrounding cortical regions (see marked regions in Fig. 1; see also Löwel and Singer 1993). After outlining area 17, its size was determined using IDL 5.1 (Research Systems). For this purpose, three representative autoradiographs from each hemisphere were analysed. The spacing of ocular dominance columns was determined by using period statistics, a recently described technique for the 2-dimensional spatial analysis of columnar patterns (Rathjen et al. 2002). Briefly, period statistics detects the typical periodicity length of 2-dimensional patterns while ignoring waveform and absolute amplitudes. In the images, all crossings through the local average along rows and columns of pixels were identified and the distances between all pairs of adjacent negative-slope zero-crossings and all pairs of adjacent positive-slope zero-crossings were calculated in both directions (rows and columns of pixels). This was repeated for rotated versions of the image (rotated in 10° steps up to 170°). Finally, compound histograms were calculated by averaging the histograms obtained from all image rotations. These compound histograms generally exhibit one clear peak at a well-defined distance of subsequent zero-crossings, which was taken as the typical periodicity length of the analysed ocular dominance pattern. For these measurements, one representative autoradiograph from each hemisphere was analysed after establishing that across-section variability within one hemisphere was small compared with the variability across animals (see Rathjen et al. 2002). Furthermore, we calculated correlation coefficients between the weight of the cats and both the size of area 17 and the spacing of ocular dominance columns to determine whether there was a possible influence of body weight on the two parameters during postnatal development.

Results

Size of area 17

In all experimental animals, the primary visual cortex was reliably discernible by its distinctive columnar activation pattern in comparison to the 2-DG labelling in surrounding cortical areas (see also Löwel and Singer 1993). In Fig. 1, the oval-shaped area 17 is outlined with *arrow-heads* in animals of three different ages (3, 4 and 6 weeks of age); within area 17 the *dark grey* columns represent the ocular dominance domains of the open (right) eye and the *light grey* regions represent the domains from the closed (left) eye.

Our analyses of the size of area 17 at different postnatal ages revealed a substantial growth during early postnatal development. Both strabismic and normally raised animals showed a significant increase in surface area with increasing age (Spearman rank correlation coefficients: strabismic animals $r_s=0.672$, $P<0.01$; normal animals $r_s=0.662$, $P<0.01$). Since there were no significant differences in the size of area 17 between strabismic and normally raised animals in any of the investigated age groups (Mann-Whitney U -tests, all $P>0.1$), the data were pooled for further analyses. Figure 2A,B shows the combined results for the size measurements of area 17 (number of hemispheres $n=39$).

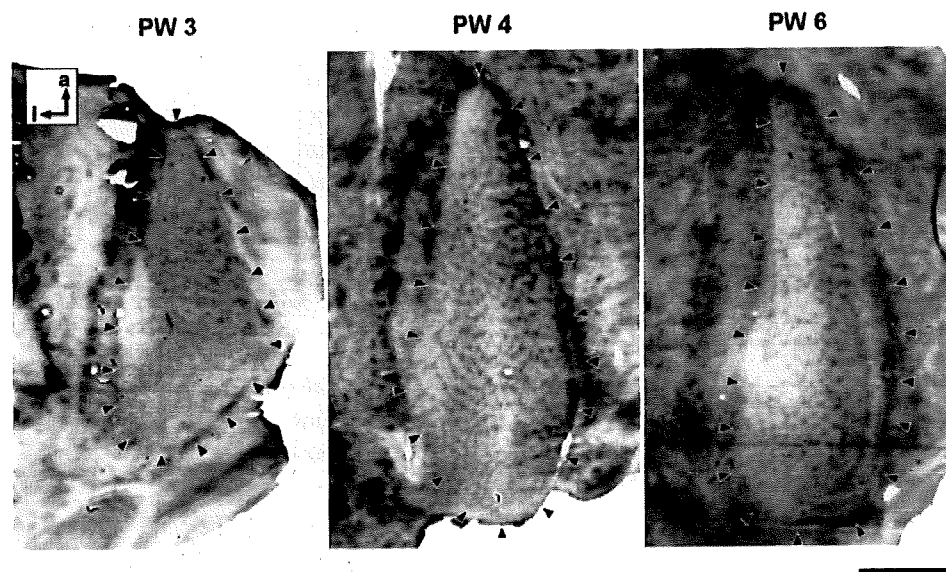


Fig. 1 2-Deoxyglucose (2-DG)-labelled ocular dominance columns in kitten visual cortex. 2-DG autoradiographs of supragranular flat-mount sections of unfolded left hemispheres from kittens aged 3–6 weeks. Primary visual cortex (area 17, *arrowheads*) is reliably discernible by its distinct activation pattern compared to surrounding cortical regions. *Dark grey* domains in area 17 represent the

ocular dominance domains of the open eye, *light grey* regions represent those of the closed eye. In the illustrated examples, the size of area 17 increases from 247 mm² in the 3-week-old animal (PW 3) to 438 mm² in the 4-week-old kitten (PW 4) and 490 mm² in the 6-week-old kitten (PW 6). *a* anterior, *l* lateral, PW postnatal week. Scale bar 1 cm

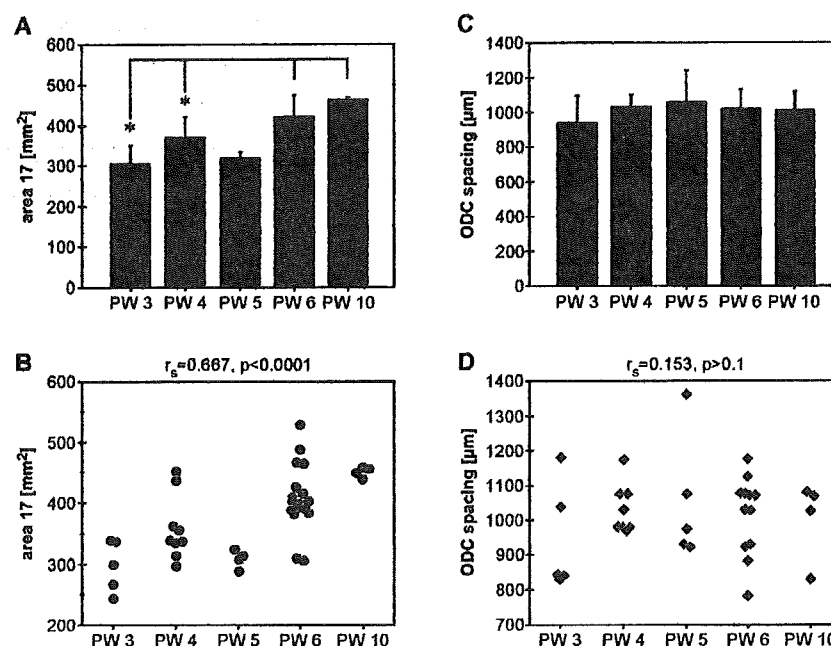


Fig. 2A–D Analysis of the size of area 17 and the spacing of ocular dominance columns (ODC) in kittens at postnatal week (PW) 3–10. **A** Mean surface area of cat area 17 for the five investigated ages (PW 3, PW 4, PW 5, PW 6 and PW 10). For 3- and 4-week-old kittens, the primary visual cortex is significantly smaller than for 6- and 10-week-old kittens (selected Mann-Whitney *U*-tests, $*P < 0.05$; see Results for further details). Error bars represent SD. **B** Scattergram of the same dataset as in A, illustrating the pronounced inter-individual variability. Note that there is a strong and

significant increase of the surface area of area 17 with increasing age (Spearman rank correlation coefficient $r_s = 0.667$, $P < 0.0001$). **C** Mean spacing of ODC for the same five investigated ages. There are no significant differences between the age groups (Mann-Whitney *U*-tests, $P > 0.1$). Error bars represent SD. **D** Scattergram of the same dataset as in C, illustrating the considerable inter-individual variability. Note that there is no significant increase of the spacing of ODC with increasing age ($r_s = 0.153$, $P > 0.1$)

Average surface area (\pm SD) increased from $300 \pm 42 \text{ mm}^2$ in 3-week-old kittens ($n=5$) to $453 \pm 8 \text{ mm}^2$ in 10-week-old animals ($n=4$). At 4–6 weeks of age, area 17 exhibited the following sizes: 4 weeks ($n=9$) $361 \pm 52 \text{ mm}^2$, 5 weeks ($n=4$) $311 \pm 15 \text{ mm}^2$, and 6 weeks ($n=17$) $412 \pm 56 \text{ mm}^2$. The data thus demonstrate an average increase of 51% in the size of area 17 between the third and tenth postnatal week (Fig. 2A,B). Interestingly, most of this increase in size, namely about 75%, had already occurred at the end of the sixth postnatal week (size increase of 37%).

The scattergram in Fig. 2B illustrates that there is a large inter-individual variability in the measured area sizes of the different age groups. The observed decrease of area size in 5-week-old animals is most likely attributable to this pronounced inter-individual variability and to the small number of animals (only two) analysed in that age group.

Despite this pronounced inter-individual variability, there was a significant age-dependent increase of the size of area 17. On performing Mann-Whitney *U*-tests, the differences between the younger and older age groups proved significant (postnatal week PW 3 versus PW 10, PW 4 versus PW 6, PW 4 versus PW 10, $P < 0.05$; PW 3 versus PW 6, $P < 0.005$). The significant postnatal growth of area 17 was also verified by the Spearman rank correlation coefficient $r_s = 0.667$ ($P < 0.0001$).

Spacing of ocular dominance columns

The evaluation of the periodicity of ocular dominance columns using period statistics demonstrated that the distance between the columns remained rather constant in the order of 1 mm during the investigated postnatal period (Fig. 2C,D). Individual spacing values (\pm SD) were the following: 3 weeks (number of hemispheres $n=5$) $940 \pm 157 \mu\text{m}$, 4 weeks ($n=8$) $1032 \pm 70 \mu\text{m}$, 5 weeks ($n=5$) $1052 \pm 183 \mu\text{m}$, 6 weeks ($n=12$) $1013 \pm 112 \mu\text{m}$, and 10 weeks ($n=4$) $1005 \pm 116 \mu\text{m}$. Figure 2D illustrates the pronounced inter-individual variability of ocular dominance column spacings at all analysed ages. By performing Mann-Whitney *U*-tests, no significant differences between any of the age groups (3–10 weeks) could be detected (all $P > 0.1$). The absence of an age-dependent effect on column spacing was also confirmed by the Spearman rank correlation coefficient $r_s = 0.153$ ($P > 0.1$).

Thus, our group data indicate that the spacing of ocular dominance columns stays constant at around 1 mm between the third and tenth postnatal week whereas the size of primary visual cortex increased by more than 50% during the same observation period. To further confirm that cortical growth is not accompanied by an increased spacing of ocular dominance columns we compared ocular dominance spacing and the size of area 17 in individual animals. Figure 3A illustrates the direct correlation of the two parameters and shows that larger primary visual cortices do not contain wider ocular dominance column spacings (Spearman rank correlation

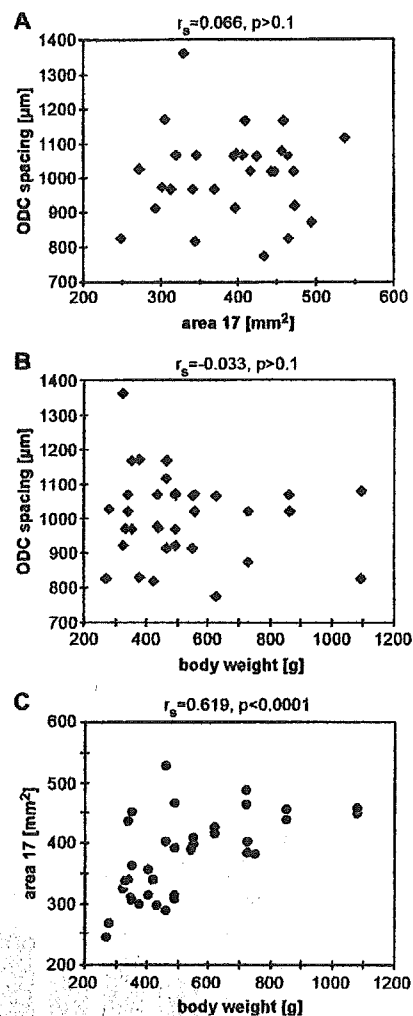


Fig. 3A–C The spacing of ocular dominance columns (ODC) displayed as a function of the size of area 17 (A), as a function of the body weight of the experimental animals (B), and the size of area 17 as a function of body weight during development (C). **A** There is no increase in the spacing of ODC with increasing size of area 17 (Spearman rank correlation coefficient $r_s = 0.066$, $P > 0.1$). **B** There is also no increase in the spacing of ODC with increasing body weight of the cats ($r_s = -0.033$, $P > 0.1$). Thus, neither larger areas 17 nor heavier cats necessarily have more widely spaced ocular dominance domains indicating that ODC spacing is largely independent of both area size and body weight of the animals. **C** There is an increase of the size of area 17 with increasing body weight in the experimental animals. Thus, heavier (and older) cats tend to have larger primary visual cortices ($r_s = 0.619$, $P < 0.0001$).

coefficient $r_s = 0.066$, $P > 0.1$). There is also no significant correlation within the age groups with the most entries (PW 4 $r_s = 0.600$, $P > 0.1$; PW 6: $r_s = -0.201$, $P > 0.1$). Furthermore, the number of flat-mount sections was rather similar in the different age groups indicating that cortical flat-mounts of the animals were not compressed differently during the flattening procedure.

Figure 3B shows that there is also no significant correlation between the body weight of our experimental

animals and column spacing (Spearman rank correlation coefficient $r_s = -0.033$, $P > 0.1$). These data indicate that the spacing of ocular dominance columns is largely independent of both area size and body weight of the animals.

Finally, we checked whether there might be a correlation between body weight and the size of area 17, since on average both parameters increase with increasing age. As illustrated in Fig. 3C, there is a significant correlation ($r_s = 0.619$, $P < 0.0001$) between the size of area 17 and body weight during development, as already shown for the size of area 17 and age (see Fig. 2B). We also analysed the relationship between the size of area 17 and body weight within the age groups with the most entries (4 and 6 weeks). There was no weight-dependence of the size of primary visual cortex within either of those age groups. This observation was confirmed by calculating Spearman rank correlation coefficients: For 4-week-old cats the coefficient was $r_s = -0.183$ ($P > 0.1$); for 6-week-old cats the coefficient was $r_s = 0.128$ ($P > 0.1$). These data indicate that the size of area 17 is largely independent of the body weight within a particular age group.

Discussion

The results of the present study show that cat primary visual cortex grows considerably during early postnatal life: the size of area 17 increases from 300 to 453 mm², and thus by about 51%, between the third and tenth postnatal week. The majority of this increase (about 75%) occurs until the end of postnatal week 6. Interestingly, however, the spacing of adjacent ocular dominance domains remains in the order of 1 mm during the same postnatal period.

Our data on cortical growth are in good agreement with a previous study by Duffy et al. (1998). In that study, monoclonal antibodies CAT-301 or SMI-32, which label distinct patterns of neurons in area 17, were used to visualize cat primary visual cortex. Postnatal growth was measured on stained tangential sections from unfolded and flattened hemispheres after perfusing the animals with 2% paraformaldehyde. The size of area 17 increased from 169 mm² in 1-week-old kittens to 392 mm² in adult cats. Thus extent of the area in adult cats was more than twice that of neonatal (1-week-old) kittens, whereby 84% of the total postnatal growth occurred between postnatal weeks 1 and 6 (Duffy et al. 1998). The observation of a rapid increase in visual cortical surface area until the end of postnatal week 6 is supported by our results as well. Interestingly, however, surface areas as measured on the 2-DG autoradiographs in the present study were generally larger (by about 15%) than the values given by Duffy et al. (1998). The most likely explanation for this size difference is that the perfusion and post-fixation used by Duffy et al. (1998) caused some tissue shrinkage. In contrast, in the present study, only native tissue was used so that measured sizes of area 17 should closely resemble *in vivo* area sizes. This interpretation is supported by another study in which the size of cat area 17 was

reconstructed from stained serial frontal sections corrected for tissue shrinkage (Takács et al. 1992). In this study, the surface area of area 17 of 6-week-old kittens was 387 ± 71 mm² (mean \pm SD) and therefore only slightly smaller than the 412 ± 56 mm² obtained for 6-week-old animals in the present study.

The considerable growth of primary visual cortex during early postnatal development, when cortical columns and patchy horizontal connections are already present and maturing, raises the question about the consequences of the size increase in area 17 for the layout of the connections and functional maps. Assuming an isotropic expansion of visual cortex, the 51% increase in the surface area between the third and tenth postnatal week translates into a 23% (linear) increase in column spacing. The present group data do not, however, support such an increase in the spacing of ocular dominance columns with increasing age. Furthermore, there were no significant differences in column spacing between any of the five investigated age groups. Nevertheless, given the pronounced inter-individual variability of spacing values, one could argue that individual animals might have shown an increase in column spacing with increasing age. This suggestion would be supported if the larger surface areas contained wider column spacings, though, in fact, this never occurred in any single age group (see Fig. 3A). Finally, the number of flat-mount sections was rather similar in the different age groups indicating that cortical flat-mounts of the younger animals have not been compressed more during the flattening procedure than those of older cats.

There is only one study in the literature in which ocular dominance maps were visualized longitudinally in single animals over a period of about 6 weeks during early postnatal development (between postnatal weeks 3–9; Sengpiel et al. 1998). Optically recorded maps in cat area 17 were compared before and after the induction of a squint angle (exotropia) at PW 3–4. In that study, there were no obvious changes in the pattern of ocular dominance columns during early postnatal development as assessed by 2-dimensional cross-correlation analysis. However, magnification of the initial ocular dominance maps by 20% revealed cross-correlation coefficients that increased from recording session to recording session (four of five kittens), yielding a stronger correlation of the last recorded map with the expanded mapping than with the original map that was obtained before the induction of squint (Sengpiel et al. 1998). The authors interpreted these observations as evidence for a modest expansion of ocular dominance columns due to the growth of area 17 (balloon-effect). However, since all pattern features influence the result of the cross-correlation analysis, direct conclusions on the development of the spacing of ocular dominance columns cannot be drawn.

Taken together, there is no clear evidence that the considerable postnatal growth of cat area 17 is accompanied by a corresponding increase in the spacing of ocular dominance columns. This suggests that the average spacing between ocular dominance columns represents a

constant geometric quantity that may be important for cortical map development. Support for the idea of constant columnar spacings comes from analyses of the development of long-range horizontal connections in cat area 17 (Galuske and Singer 1996). It was shown that the distance between reciprocally interconnected patches of neurons did not change significantly between the end of the second postnatal week and adulthood so that the mean patch period remained rather constant during this period (postnatal day P12 937 μm , P21 894 μm , P26 928 μm , P50 933 μm , adult 824 μm).

Since the spacing of adjacent columns seems to remain rather constant during postnatal development, the question arises as to what happens to the layout of cortical maps in a growing area 17. One hypothesis is that new functional columns must be added during postnatal development to occupy the enlarging cortical sheet. Emergence of new columns can, in principle, be achieved in two ways: (1) by the formation of new columns, or (2) by the segregation of existing columns. Since neurogenesis, neuronal migration, and the ingrowth of thalamocortical afferents into the cortex have come to an end by the third postnatal week in cats (LeVay et al. 1978; Luskin and Shatz 1985; Shatz and Luskin 1986), the formation of completely new columns is rather unlikely, and cortical enlargement is thought to be based on the elaboration of dendritic and axonal elements and the addition of myelin (e.g. Haug et al. 1976).

Columns that develop by the segregation of large columns, however, should preserve the connections of their parent column so that the already established networks of both thalamocortical afferents and horizontal circuitry should be maintained during this reorganization process. But how could a growth-related expansion and segregation of existing columns take place? Such a scenario would imply that large columns just about to segregate co-occur with small columns that have just split up. Evidence for this idea comes from the above mentioned study by Galuske and Singer (1996) concerning the development of long-range horizontal connections and showing that the variability of patch size within the maturing neuronal network is initially very high and decreases during postnatal development. The properties of the period statistics (i.e. the calculation of the typical periodicity length of an area, see Materials and methods) do not, however, allow us to determine whether there is a similar decrease in the variability of the spacing of ocular dominance columns during early postnatal development.

Is there any other experimental evidence for an expansion and segregation of columns during early postnatal development of the visual cortex? While Sengpiel et al. (1998) had indications for a modest expansion of ocular dominance domains, they did not observe the appearance of new domains. It is, however, possible that there are spatial and/or temporal discontinuities in the growth of area 17. Firstly, the superficial part of area 17 that is accessible to optical imaging is rather small compared to the entire area. Secondly, only the representation of the central visual field can be

visualized, so that layout differences could exist between central and more peripheral representations of the visual field. Interestingly, in this context, the kitten's visual field is increasing at the same time during which most of the observed postnatal growth of area 17 takes place (Sireteanu and Maurer 1982). At an age of 2 weeks, kittens are able to orient monocularly toward stimuli at 45° in the temporal and 15° in the nasal visual field. During the following weeks the performance of the animals improves and the periphery is added. Adult performance is not reached before the age of 6 weeks when kittens can orient toward stimuli at 90° in the temporal and 45° in the nasal visual field. The delay in orienting toward the periphery is not likely to be caused by a motor deficit, since already the youngest animals turned spontaneously at least 90° to the side, but is more likely caused by the postnatal maturation of the neural visual system (Sireteanu and Maurer 1982). This maturation includes the retina, the superior colliculus, and the projections from the cortex. As an example, the cat retina is immature at birth and its central regions mature before its peripheral regions (e.g. Johns et al. 1979).

Due to the previous evidence, and given that there is a temporal gradient in the development of the visual field, one might imagine that a similar gradient does also exist in the development between the central and peripheral area 17. Such a maturational gradient was indeed proposed recently to explain differences in the degree of thalamocortical segregation between the peripheral and central visual field representation in monocularly deprived cats (Schmidt et al. 2002). After induction of monocular deprivation at around eye-opening, afferents of the normal eye overlap completely with afferents of the deprived eye in the peripheral visual field representation of these cats. In contrast, domains of normal and deprived eye afferents are clearly segregated in the central visual field representation, at least in hemispheres ipsilateral to the normal eye. This could be taken as evidence for a delayed maturation and thus for a relatively higher vulnerability of peripheral than of central parts of area 17 to the effects of early monocular deprivation during development (Schmidt et al. 2002).

According to the hypothesis of a temporal gradient, the central parts of area 17 could develop during the first 3–4 postnatal weeks and undergo a more pronounced cortical growth than the peripheral parts of area 17, which would, according to their functional activation, develop and expand more fully in the following weeks. Thus, more space could be made available for the rearrangement of connections in active brain regions, corresponding to the idea of an active brain growth in contrast to a passive brain growth in which the rearrangement of connections is only a consequence of cortical growth (see Aboitiz 1996). In the former scenario, the expansion and segregation of columns could take place in both the spatial and temporal domains. The overall shape of area 17 does not, however, have to change (see Duffy et al. 1998). Since only central parts of area 17 are accessible for optical imaging, column

expansion and segregation in the periphery cannot be visualized with current techniques.

Several studies have indeed shown that such an anisotropic cortical growth does exist. In the visual system, blobs appear to grow about twice as much during postnatal development as does V1 as a whole (a 39% increase in blob cross-sectional area versus a 16% increase in the area of V1 as a whole; Purves and LaMantia 1993). In rat somatosensory cortex, the barrels and barrel-like modules grow to a greater extent than does the surrounding inter-barrel cortex or the primary somatosensory cortex as a whole (Riddle et al. 1992). Recently, it was shown that in star-nosed moles the tactile fovea is greatly over-represented in somatosensory cortex in early development compared to the adult (Catania 2001). Even the addition of new modules as a consequence of postnatal growth has already been observed. In the mouse olfactory bulb the number of processing units (glomeruli) is steadily increased during postnatal development. However, this situation differs from the visual cortex because neurogenesis plays a major role on the receptor side in the olfactory but not in the visual system (Pomeroy et al. 1990; LaMantia et al. 1992).

Concerning module number, a different concept may be implemented in the macaque monkey visual cortex. The number of blobs per unit area decreases by about 18% during postnatal development, while the surface area of the primary visual cortex increases by about 16% (Purves and LaMantia 1993). As a consequence, the number of blobs remains approximately the same during maturation, which should correspond to an increase in blob spacing (not determined; balloon-effect). However, since the postnatal growth of 16–18% in monkey V1 (Purves and LaMantia 1993; Duffy et al. 1998) translates to only about 8% increase in linear measurements, this enlargement might either not require a columnar segregation scenario or the scenario is in place already before birth (for a correlation between developmental phases see Robinson and Dreher 1990).

A possible explanation for why the columnar spacing should remain constant during postnatal development is the interaction of multiple feature maps. In primary visual cortex, several spatially periodic maps such as those for ocular dominance, spatial frequency and orientation are superimposed, and display specific spatial relationships with each other (e.g. Crair et al. 1997; Hübner et al. 1997; Löwel et al. 1998; Kim et al. 1999). The specific arrangement of the different functional systems is thought to ensure that all possible combinations of stimulus features are represented at least once in any given region of the visual cortex to avoid functional blind spots in the visual field. Indeed, a recent study has indicated that visual cortical maps are optimized for uniform coverage (Swindale et al. 2000). Any distortion of the spatial relationships between ocular dominance, spatial frequency and orientation maps by shifting or mirror-inverting the maps led to a decline of coverage uniformity. It would be interesting to know whether distortions caused by an isotropic expansion of all maps would also cause a

decline of coverage uniformity. In that case, the maintenance of a constant columnar spacing could be crucial to ensure a uniform representation of the combined feature maps throughout visual cortex and thus to ensure undisturbed perception within the entire visual field.

In summary, the present study provides evidence that the postnatal growth of cat area 17 is not accompanied by an increased spacing of ocular dominance columns. As a consequence, new functional columns must somehow be added during postnatal development to occupy the enlarging cortical sheet. Thus, our study may be taken as a tentative support for the anisotropic hypothesis of cortical development. Further investigations are needed to decide whether the proposed delay in maturation between central and peripheral visual field representations is implemented in cat primary visual cortex. In this context, the improvement of methods to detect local differences in the pattern of orientation and ocular dominance columns may be helpful (Kaschube et al. 2000, 2002). In the future, functional magnetic resonance imaging, which so far has achieved visualization of orientation maps in restricted regions of superficial cat area 18 (Kim et al. 2000), will hopefully allow us to detect columns within the entire visual cortex and to follow up their development in the same animal over time.

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