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The growth of cat cerebral cortex in postnatal life: a magnetic resonance imaging study

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Abstract

To follow up the development of an individual brain over time and to measure its growth we have analysed the brains of individual cats from postnatal day 12 to adulthood using magnetic resonance imaging. From the anatomical images, four parameters were calculated: anteroposterior extent of the telencephalon, brain volume, neocortical surface area and neocortical volume. The development of the anteroposterior extent was similar in all cats. It increased between the 3rd and 6th postnatal week from 33 to 37.5 mm ending up ≈40 mm in adulthood. The brain volume showed greater variability. On average, the volume increased from 11.5 to 16.5 cm^3 in the same period. Adult values were ≈19 cm^3. Considerable interindividual variability was observed in neocortical surface area. In one cat, it expanded from 12.5 to 26 cm^2 between days 14 and 41. In another cat, this area expanded from 16 to 24.5 cm^2 between days 12 and 40. On average, the surface area expanded by 34% between the 3rd and 6th week. Adult values ranged from 27 to 30 cm^2. Neocortical volume increased from 2.9 to 4.1 cm^3 between the 3rd and 6th postnatal week and to 4.5–5.2 cm^3 in adulthood. The asymmetry between the hemispheres in both neocortical surface area and volume was <3% in all animals for most of the observation period. Comparison of the neocortical surface measurements with data on postnatal growth of cat primary visual cortex obtained by 2-deoxyglucose autoradiography indicates that the primary visual cortex grows at the same speed and amounts to ≈15% of the entire neocortical surface area throughout development.

Introduction

It is well known that the brain of all mammalian species grows substantially during postnatal development. The human brain, for example, increases in weight from an average of 350 g in newborns to 1400 g in adult males (Pakkenberg & Voigt, 1964; Dekaban & Sadowsky, 1978). Similarly, in cats, the volume of the neocortex increases from ≈1000 mm^3 at birth to 4500 mm^3 in adulthood (Villablanca *et al.*, 2000a) and the surface area of primary visual cortex of adult cats is more than twice (230%) that of neonatal (1-week-old) animals (Duffy *et al.*, 1998). Despite this pronounced increase in brain tissue relatively little attention has been paid to this phenomenon and nearly nothing is known about the functional consequences of this growth. In addition, because previous analyses, at least in animals, have relied on interindividual comparisons of animals of different age nothing is known about individual brain sizes and growth rates. Since the advent of noninvasive imaging techniques it is possible to follow up the development of an individual brain over time and to quantitatively measure its growth. We have therefore performed a longitudinal study and analysed the brains of individual cats from our colony from postnatal day (PND) 12 to adulthood using magnetic resonance imaging (MRI) techniques. We measured four parameters from the anatomical MRI images: maximal anteroposterior (AP) extent, total brain volume, neocortical surface area and neocortical volume. Finally, we compared the surface measurements of the neocortex as a whole with data on the postnatal growth of cat primary visual cortex which we previously obtained by 2-deoxyglucose autoradiography (Rathjen *et al.*, 2003) in animals of the same colony. The aim was to analyse whether primary visual cortex grows to a greater extent than the neocortex as a whole, as previously described for the rat primary somatosensory cortex (Riddle *et al.*, 1992). Some of these results have been reported in abstract form (Rathjen *et al.*, 1998a,b; Struif *et al.*, 1999; Engelmann *et al.*, 2000).

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Materials and methods

The postnatal growth of the cat brain was visualized in a longitudinal study by magnetic resonance imaging (MRI). Imaging was focused on brain growth in the early postnatal period between weeks 2 and 6 (PW 2–6), complemented by selected measurements in adult animals. We have analysed the brains of five cats from our institute's colony. Using a 4.7-Tesla horizontal bore magnet (Bruker Biospin GmbH, Ettlingen, Germany), four animals were analysed starting at PND 12 (cat A), 14 (cat B), 17 (cat C) and 23 (cat D), and then imaging was repeated weekly until PND 40 (cat A), 48 (cat B), 46 (cat C) and 43 (cat D). Using a 3-Tesla magnet (Bruker Biospin GmbH, Ettlingen, Germany), imaging was repeated on PND 375 in cat C and on days 77

TABLE 1. Measurements of cat brain and body weight during development

Cat	PND	AP extent (mm)	Brain volume (cm^3)	Neocortical surface area left (cm^2)	Neocortical surface area right (cm^2)	Neocortical volume left (cm^3)	Neocortical volume right (cm^3)	Body weight (g)
A	12	30.6	9.99	16.34	16.03	2.32	2.37	221
	19	32.9	11.68	–	–	2.84	2.90	259
	27	35.1	14.47	23.29	22.70	3.46	3.50	285
	33	36.0	15.26	24.60	23.93	3.65	3.63	310
	40	36.9	16.69	24.73	24.65	–	–	400
B	14	30.4	6.90	11.98	13.26	–	–	222
	20	32.9	10.70	19.08	19.45	2.69	2.71	240
	28	35.5	–	–	–	–	–	256
	34	36.5	14.17	23.42	23.69	3.59	3.65	290
	41	37.9	15.98	25.76	25.83	4.06	4.04	400
	48	38.2	16.47	27.43	27.55	–	–	490
C	17	32.1	10.54	18.62	18.44	2.49	2.53	228
	25	34.5	13.16	22.66	22.45	3.09	3.12	257
	32	36.5	14.57	25.27	25.31	3.61	3.65	270
	38	–	16.42	26.85	26.59	3.90	3.84	350
	46	38.2	16.67	29.32	29.17	4.16	4.13	500
	375	40.6	19.24	29.48	29.31	4.60	4.56	4020
D	23	33.8	12.35	22.18	21.75	3.09	3.11	370
	29	34.8	14.42	25.85	25.21	3.62	3.65	460
	37	36.6	16.25	28.44	27.76	4.16	4.17	530
	43	36.8	16.77	–	–	–	–	660
	77	–	18.52	30.12	29.79	5.02	5.07	1510
	211	40.8	19.15	30.13	29.96	5.14	5.20	3870
E	290	–	18.65	26.89	27.32	4.64	4.78	3400

PND, postnatal day. AP extent, maximal extent between frontal and occipital pole of the telencephalon. Brain volume, brain volume excluding cerebellum. Neocortical surface area and Neocortical volume left/right, neocortical surface area and volume of the left and right hemisphere starting at the Sulcus rhinicus anterior/posterior.

and 211 in cat D. For comparison, the brain of one additional animal (cat E) was analysed only in adulthood (PND 290). Cats B and C were littermates while cats A, D and E were from different litters. From the anatomical MRI images, four parameters were calculated (AP extent of the telencephalon, brain volume, neocortical surface area and neocortical volume, see Table 1) and their postnatal development compared in the different animals.

All animal experiments have been performed according to the German Law on the Protection of Animals and the corresponding European Communities Council Directive of 24 November 1986 (86/609/EEC). The study was reviewed and approved by the responsible governmental authorities (reference number 53.2–42502/2–220 IFN MD, Regierungspräsidium Dessau).

Animals and anaesthesia

The animals were anaesthetized with isoflurane using an inhalation mask [1.2–2.2% isoflurane (Hoechst AG, Frankfurt am Main, Germany) in a mixture of 70% carbogen and 30% nitrous oxide]. In addition, the adult animals received an initial dose of ketamine hydrochloride (5 mg/kg; Ketanest, Parke-Davis GmbH, Berlin, Germany) mixed with xylazine hydrochloride (0.3 mg/kg; Rompun, Bayer AG, Leverkusen, Germany), injected intramuscularly. The animal's head was fixed with an incisor bar and ear plugs.

Image acquisition

Magnetic resonance imaging was performed on a 4.7-Tesla BRUKER BioSpec 47/20 scanner with a horizontal bore of 21 cm diameter (72 mm access for imaging), equipped with self-shielded gradients (BGA-12, 200 mT/m, minimal rise time 200 μs). T2-weighted images in both the frontal and sagittal plane were obtained using a Rapid Acquisition Relaxation Enhanced Sequence (RARE; Hennig *et al.*, 1986) with the following parameters: recovery time (TR), 5000 ms; echo time (TE), 20 ms; field of view, 46–70 mm (according to head size); matrix size, 256 × 256. The slice thickness was consistently 1.5 mm. T2-weighted contrast and image quality obtained with standard parameters available at that field strength proved superior to T1-weighted images. Because the small-bore 4.7-Tesla scanner had an accessible inner diameter of only 72 mm cats older than PW 7 were examined using a 3-Tesla BRUKER MedSpec 30/60 head scanner, equipped with self-shielded gradients (SK-330; 30 mT/m, minimal rise time 150 μs) and a custom-made surface coil (inner diameter 180 mm). In these cases, higher quality images were obtained using a T1-weighting sequence. We acquired T1-weighted images in both the frontal and sagittal plane using a 3-dimensional Modified Driven Equilibrium Fourier Transform Sequence (MDEFT; Lee *et al.*, 1995) with the following parameters: recovery time (TR), 16 ms; echo time (TE), 6 ms; tau, 550 ms; field of view, 80–128 mm (according to head size); matrix size in plane, 256 × 256. The phase encoding steps in the z-direction were 64 or 96 and the effective slice thickness was 1 mm. Image reconstruction by Fourier transform increased image size in the z-direction in cases where the number of phase-encoding steps did not equal a power of two. Thus the interpolated slice thickness of volumes acquired with 96 phase-encoding steps in the z-direction was 0.75 mm.

Data analysis

Quantitative analyses of the anatomical magnetic resonance images were performed manually using NIH-Image on a Macintosh G3 Power PC. Four parameters were calculated to quantify the postnatal growth of the cat brain: (i) the maximal AP extent of the telencephalon; (ii) the total brain volume excluding the cerebellum; (iii) the neocortical surface area; and (iv) the neocortical volume (Fig. 1). Although two different scanners and sequences were used for acquiring images from cats younger and older than PW 7 the properties of interest (grey matter/white matter contrast, distinction of cortical surface from cerebrospinal fluid) are accessible with similar accuracy with both image types so that the contrast mechanism is not relevant for our analysis of the image data. In the following, the four analysed parameters are described in detail.

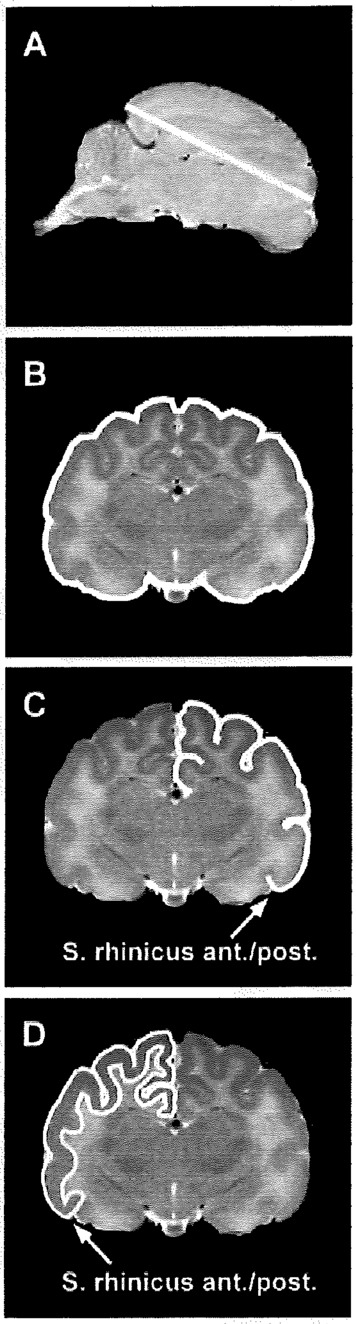

FIG. 1. The four parameters measured to quantify the postnatal growth of the cat brain. (A) The AP extent was determined as the maximal length between the frontal and occipital pole of the telencephalon. (B) The total brain volume excluding the cerebellum was determined by measuring the area of consecutive slices and multiplying them by the slice thickness. (C) To determine the surface area of the neocortex (starting at the Sulcus rhinicus anterior/posterior), the length along the gyri and sulci of both hemispheres on consecutive slices was multiplied by the slice thickness, adding the surface area of the first and last slice. (D) The neocortical volume of both hemispheres (starting at the Sulcus rhinicus anterior/posterior) was determined by measuring the area of the grey matter on consecutive slices and multiplying by the slice thickness.

The AP extent was measured on sagittal images as the maximal length between the frontal and occipital pole of the telencephalon (line selection, Fig. 1A). The total brain volume excluding the cerebellum was determined on frontal images by measuring the area of consecutive slices (polygon selection, Fig. 1B) multiplied by the effective/interpolated slice thickness (0.75–1.5 mm). The sum of all single slice volumes revealed the total volume. The brainstem was included in the measurements until the cerebellum occurred on the images. This roughly corresponds to a virtual cut through the brainstem after the pons. The surface area of the neocortex was determined for both left and right hemispheres on frontal images. Starting at the Sulcus rhinicus anterior/posterior, the surface length along the gyri and sulci was measured in consecutive slices (segmented line selection, Fig. 1C) and multiplied by the effective/interpolated slice thickness (0.75–1.5 mm). The total neocortical surface area was calculated as the sum of all single values plus the surface area of the first and last slice. Similarly, the neocortical volume was determined for both left and right hemispheres on frontal images. Starting at the Sulcus rhinicus anterior/posterior, grey matter area was determined on consecutive slices (polygon selection, Fig. 1D) and multiplied by the slice thickness. The results of all measurements are given in Table 1.

Results

Using magnetic resonance imaging we visualized the postnatal growth of individual cat brains between PND 12 and adulthood. Throughout the early postnatal period (PW 2 until the end of PW 6) measurements were repeated weekly in four animals (cats A–D). In addition, anatomical MRI images were obtained in adulthood in three cats (cats C–E). Using a 4.7-Tesla magnet in early development and a 3-Tesla magnet in animals older than PW 7 (see Materials and methods), we acquired complete series of images in the frontal and sagittal plane.

Examples of our imaging data showing both a sagittal (Fig. 2) and a frontal image series (Fig. 3) are illustrated. Data are from cat B at PND 20. In the figures, every second 1.5-mm-thick MRI slice is displayed. Contrast between grey and white matter was sufficient to clearly delineate cortex, cerebellum, various brainstem nuclei (Fig. 2) and di- and mesencephalic regions (Fig. 3).

Brain growth was substantial in all cats during postnatal development. This growth is visible with the naked eye in longitudinal MRI-image series from single animals. In Fig. 4, sagittal images of the brain (close to the midline) of cat B at the ages of PW 3, 4, 5 and 6 are displayed. The pronounced postnatal brain growth is also visible in frontal sections (slice taken close to the Commissura medialis) obtained from the brain of another animal (cat D) at PW 3 and 30 (Fig. 4, right).

To quantify brain growth and to compare postnatal development in different animals we calculated four parameters from the anatomical MRI images: (i) AP extent of the telencephalon; (ii) brain volume; (iii) neocortical surface area; and (iv) neocortical volume (for details see Materials and methods section). AP extent, brain volume, neocortical surface area and neocortical volume grew substantially during postnatal development in all cats (Table 1).

AP extent

The development of AP extent was rather similar in all cats. Figure 5 shows the individual AP extents for the examined cats (cats A–D) at

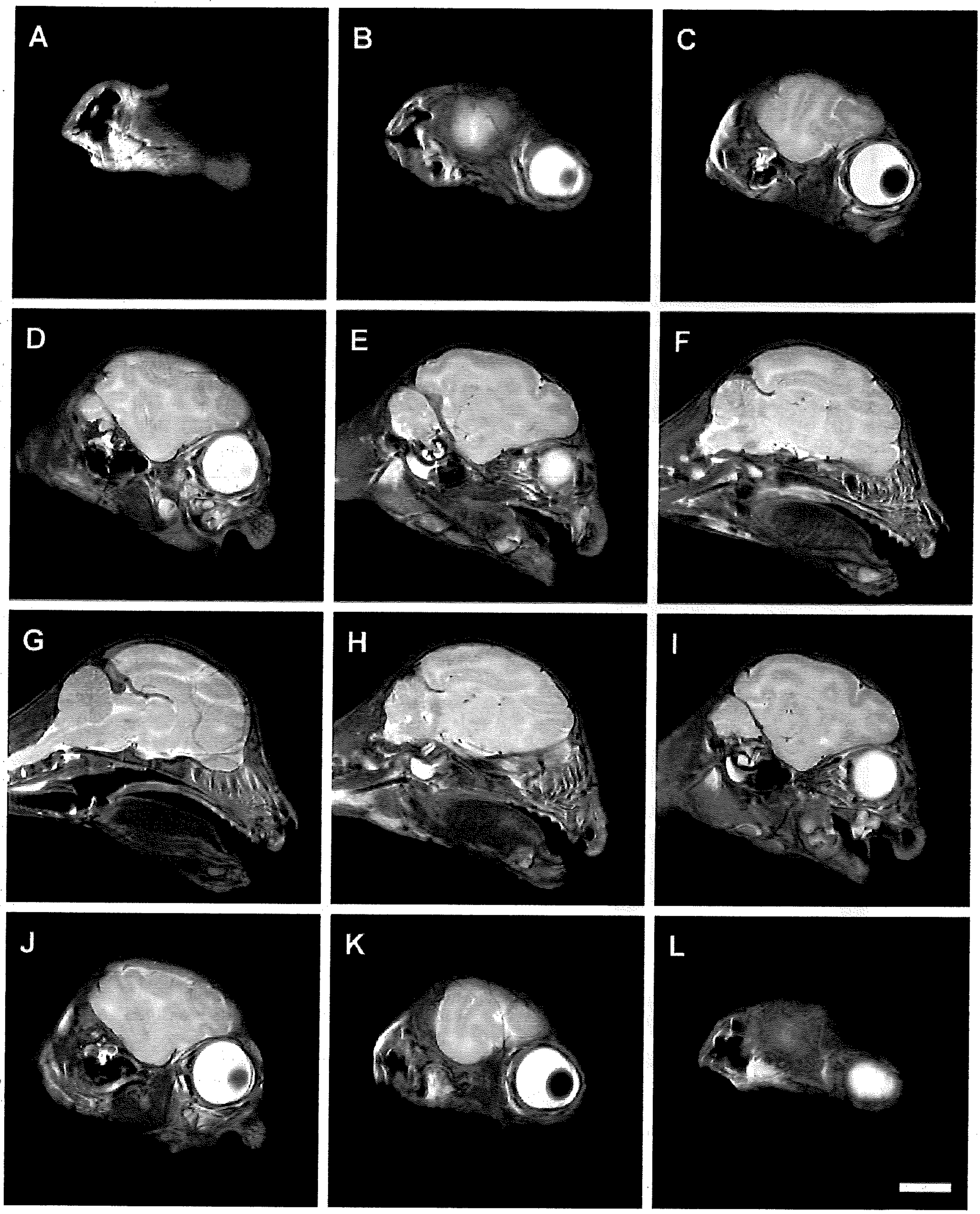

FIG. 2. Magnetic resonance imaging of the brain of cat B at PND 20. Every second slice of a series in the sagittal plane is shown. The slice thickness is 1.5 mm, the gap accordingly also 1.5 mm. Anterior is always to the right and posterior to the left. Scale bar, 1 cm.

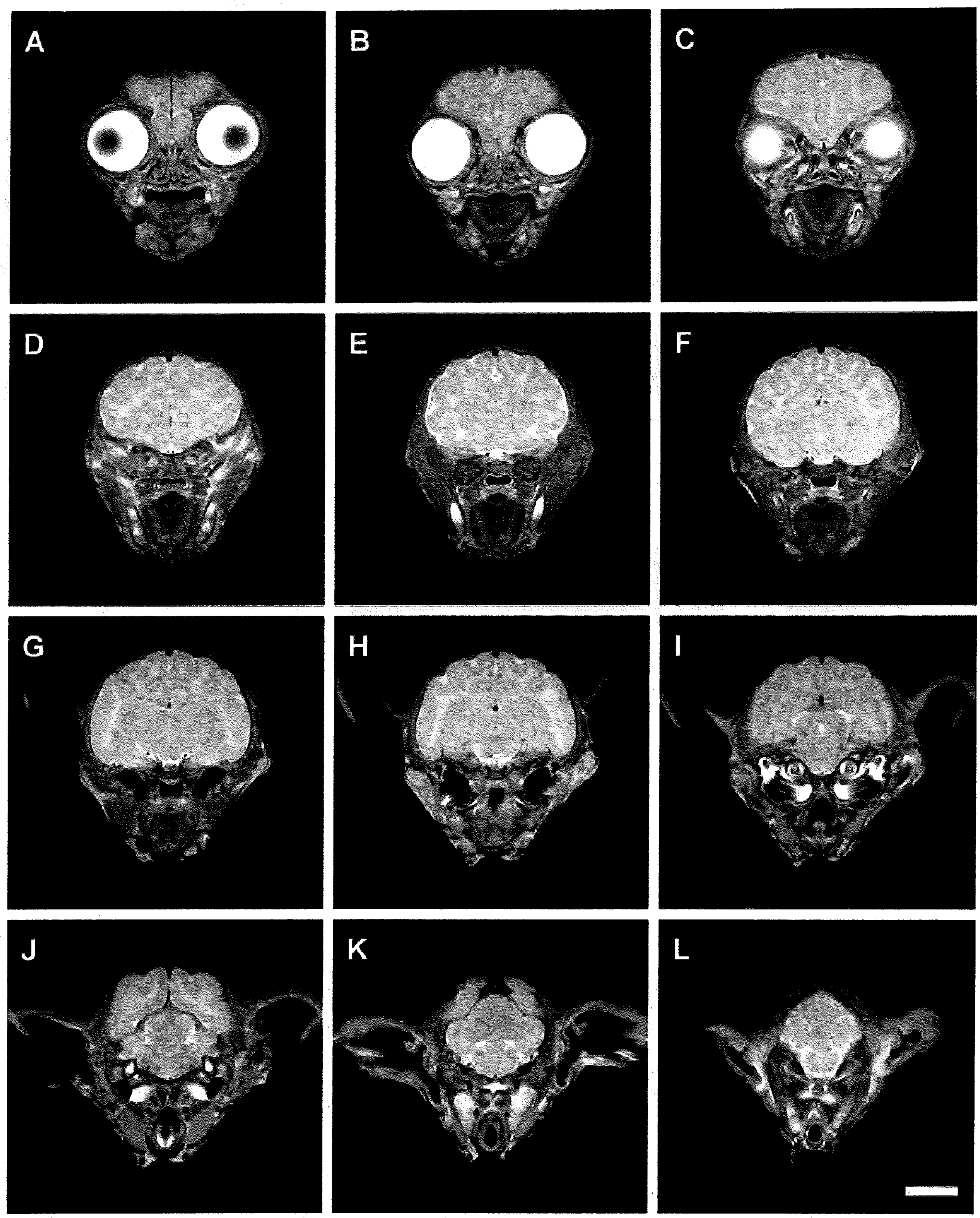

FIG. 3. Magnetic resonance imaging of the brain of cat B at PND 20. Every second slice of a series in the frontal plane is shown. The slice thickness is 1.5 mm, the gap accordingly also 1.5 mm. Scale bar, 1 cm.

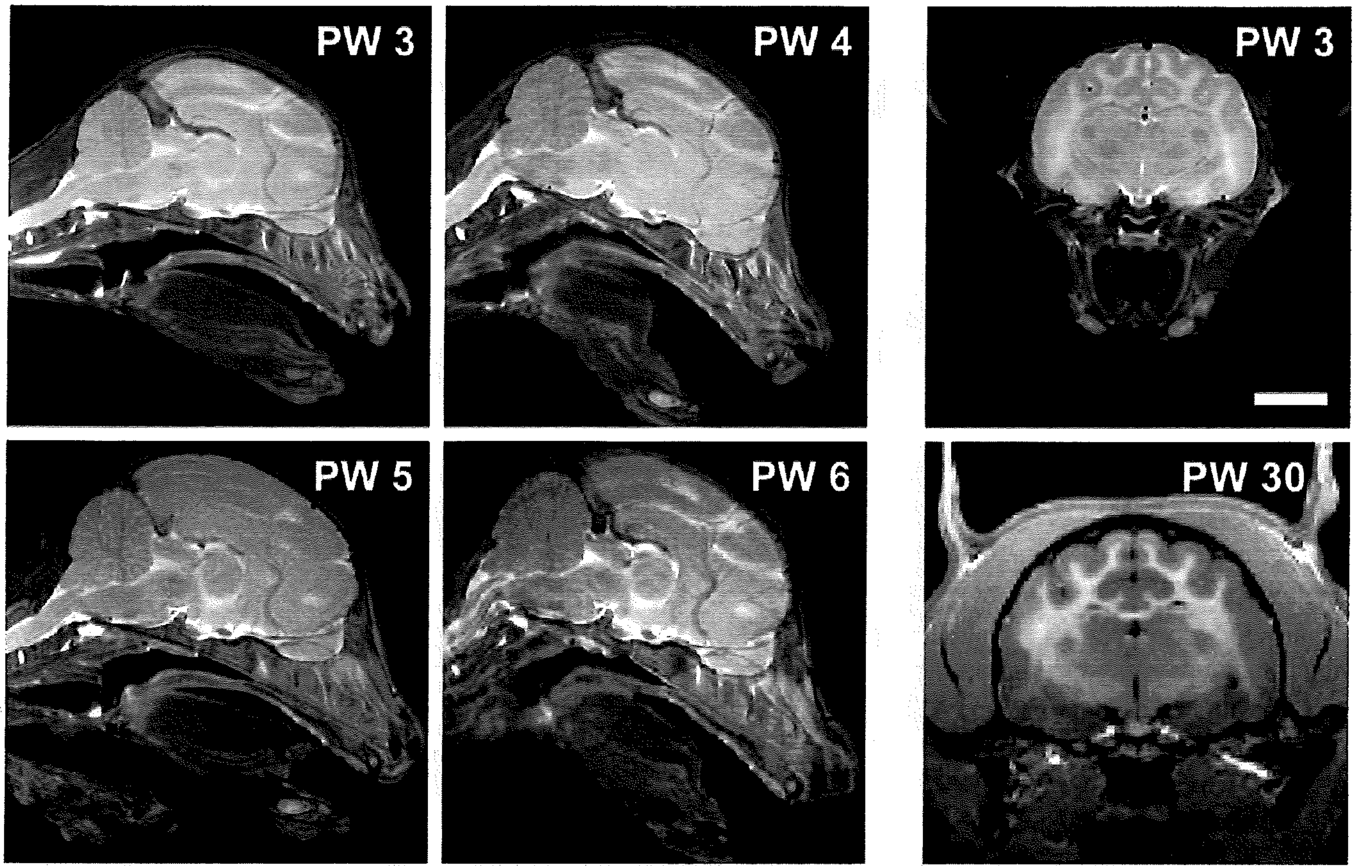

FIG. 4. Magnetic resonance imaging of the developing brain of cats at various postnatal dates. (Left) Sagittal sections (medial, close to the midline level) of the brain of cat B at the age of 3, 4, 5 and 6 weeks (PW 3–6). Anterior is always to the right and posterior to the left. (Right) Frontal sections through the brain of cat D at PW 3 and 30. Note that the brain grows substantially after birth. Scale bar, 1 cm.

the different postnatal days (see also Table 1). The AP extent was ≈30.5 mm in PW 2 animals and increased to 36.9–38.2 mm in PW 6–7 cats. In adulthood, AP extent measured 40.6 mm (cat C) and 40.8 mm (cat D). Thus, most of the measured postnatal increase in AP extent (23%) occurred between PW 2 and 6.

Brain volume

Figure 6 illustrates the postnatal development of brain volume in cats A–E at different postnatal days. In contrast to the AP extent, brain volume showed greater interindividual variability during early development (see also Table 1). This was especially evident in the early measurements of cats A and B. While cat A had a brain volume of 9.99 cm^3 at an age of 12 days, the brain volume of cat B measured only 6.90 cm^3 at postnatal day 14. These differences, however, decreased during the following weeks. On PND 40/41, cat A had a brain volume of 16.69 cm^3 and cat B had a volume of 15.98 cm^3. Thus, between PW 2 and 6, brain volume increased by ≈67% in cat A and by ≈132% in cat B. The adult values ranged between 18.65 and 19.24 cm^3 (average 19.01 cm^3).

Neocortical surface area

Figure 7 illustrates postnatal development of neocortical surface area for both left and right hemispheres of cats A–E. As for brain volume, there was considerable interindividual variability in both area size and growth rates during the early postnatal period (see also Table 1). In cat A, neocortical surface area (one hemisphere) expanded from 16.34 cm^2 (left hemisphere) and 16.03 cm^2 (right hemisphere) at PND 12 to 24.73 cm^2 (left) and 24.65 cm^2 (right) at PND 40, accounting for an average increase of ≈53% in 28 days. By contrast, in cat B neocortical surface area expanded between PND 14 and 41 from 11.98 cm^2 (left) and 13.26 cm^2 (right) to 25.76 cm^2 (left) and 25.83 cm^2 (right), accounting for an average increase of ≈105% in 27 days. Thus, the growth rate of neocortical surface area of cat B was twice as large as that of cat A during the same postnatal period (PW 2–6). Adult values ranged from 26.89 cm^2 (left hemisphere of cat E) to 30.13 cm^2 (left hemisphere of cat D) (average 28.83 cm^2). Interestingly, cat C reached adult values of neocortical surface area in PW 7 (average 29.25 cm^2 at PND 46 compared to 29.40 cm^2 at PND 375; see Table 1 and Fig. 7) when its body weight was <1/8th of its adult value (500 g compared to 4020 g; see Table 1).

Neocortical volume

The development of neocortical volume was rather similar in all cats. Figure 8 illustrates the individual volumes for the examined cats (cats A–D and E) at the different postnatal days (see also Table 1). Neocortical volume (one hemisphere) ranged between 2.32 cm^3 and 2.71 cm^3 in PW 2–3 animals and increased to 4.04–4.16 cm^3 in PW 6–7 cats. In adulthood, neocortical volume measured 4.56 cm^3 (right hemisphere of cat C at PND 375), 5.20 cm^3 (right hemisphere of cat D at PND 211) and 4.78 cm^3 (right hemisphere of cat E at PND 290). Thus, unlike neocortical surface area, for which most of the

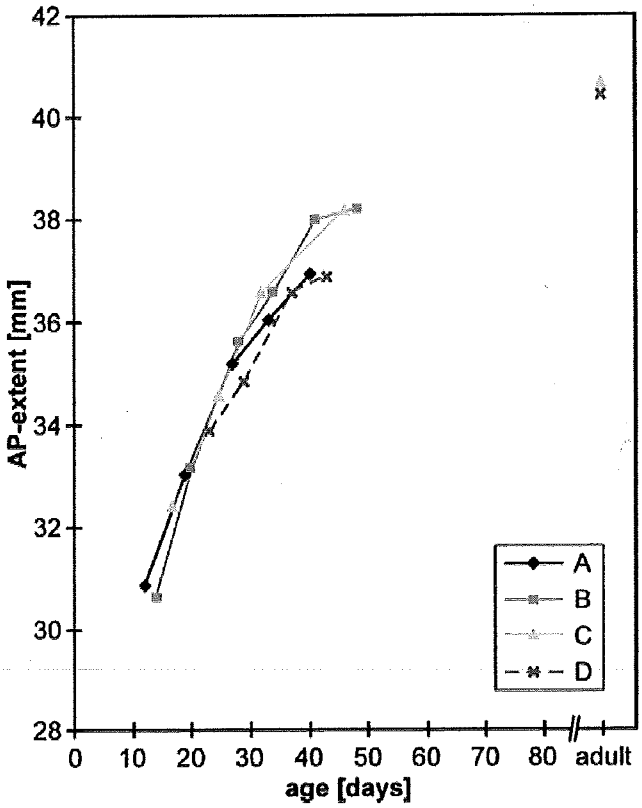

FIG. 5. Postnatal increase in the AP extent of the telencephalon. The AP extent of cats A–D is shown for each of the investigated postnatal days. Data for cats older than 6 months are binned as adult. Note that in all cats the AP extent grew at a similar rate.

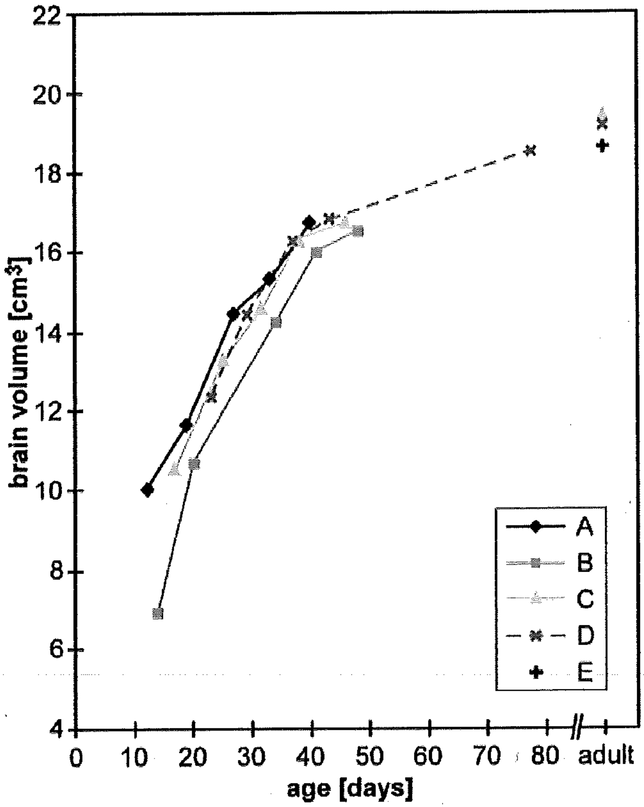

FIG. 6. Postnatal increase in the brain volume (excluding cerebellum). The brain volume of cats A–E is shown for each of the investigated postnatal days. Data for cats older than 6 months are binned as adult. Note the interindividual variability in the brain volume especially at the beginning of the measurements at an age of ≈2 weeks.

measured postnatal increase occurred between PW 2 and 6, neocortical volume continued to increase into adulthood.

To analyse this phenomenon in more detail, we additionally plotted the ratio of neocortical surface area to neocortical volume over time. As illustrated in Fig. 9A, this ratio declines with age. Evaluating the entire data set, this decline proved to be significant (Spearman rank correlation coefficient $r_s = -0.746$, $P = 0.0021$). The analyses for individual animals showed clear tendencies for three of the four cats followed throughout development (cat A, $r_s = -0.500$, $P = 0.4795$; cat B, $r_s = -1.000$, $P = 0.1573$; cat C, $r_s = -0.829$, $P = 0.0639$; cat D, $r_s = -1.000$, $P = 0.0455$). Because neocortical volume divided by neocortical surface area equals neocortical thickness, the plot thus demonstrates that the average neocortical thickness increases with increasing age (from an average of 1.36 mm in cat C at PND 17 to 1.72 mm in cat D at PND 211). In contrast, the ratio of brain volume to neocortical volume stayed rather constant over time in the majority of animals (Fig. 9B). Calculating the Spearman rank correlation coefficient for the entire data set revealed no significant changes ($r_s = -0.428$, $P = 0.0693$). The analyses for individual animals showed variable trends (cat A, $r_s = -0.200$, $P = 0.7290$; cat B, $r_s = -0.500$, $P = 0.4795$; cat C, $r_s = 0.029$, $P = 0.9491$; cat D, $r_s = -0.900$, $P = 0.0791$).

Brain symmetry

The analysis of neocortical surface area furthermore revealed that values of left and right hemispheres were rather similar (see Fig. 7 and Table 1) indicating that left and right hemispheres grow at the same rate during postnatal development. In cats A, C and D, neocortical surface area was slightly larger in the left than in the right hemisphere. The difference was, however, <3% during the entire observation period. In contrast, in cats B and E the right hemisphere was consistently larger but differences were <2% for most of the observation period (see Table 1).

The analysis of neocortical volume revealed that values of left and right hemispheres were rather similar (see Fig. 8 and Table 1), again indicating that left and right hemispheres grow at the same rate during postnatal development. In cats A, B, D and E neocortical volume was slightly larger in the right than in the left hemisphere. The difference was, however, <3% during the entire observation period. In contrast, in cat C the left hemisphere was minimally larger but again differences were not consistent and always <1.6% throughout the observation period (see Table 1).

Taken together, there was no pronounced and no consistent hemispheric asymmetry in neocortical surface area and neocortical volume at any investigated age.

Comparison between neocortical and visual cortical surface area

Since we have previously analysed the postnatal growth of cat primary visual cortex (Rathjen *et al.*, 1998a,b, 2003), we wondered whether neocortical and visual cortical surface area grow at the same rate or whether there are differences in growth during early postnatal development. To this end, we compared the present MRI surface measurements with our previous data obtained by analysing the size of primary visual cortex (area 17) on 2-deoxyglucose autoradiographs containing

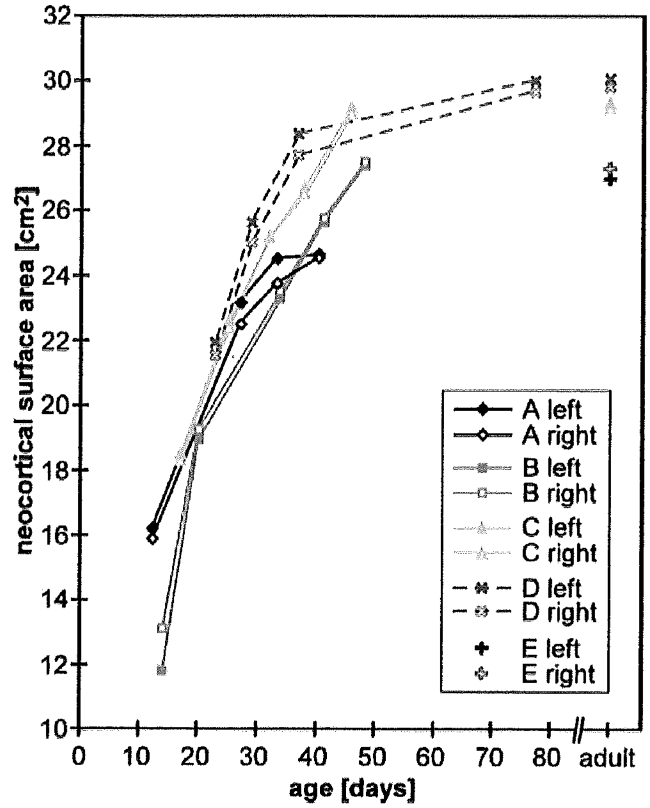

FIG. 7. Postnatal increase in neocortical surface area. The neocortical surface area for both hemispheres of cats A–E is shown for each of the investigated postnatal days. Data for cats older than 6 months are binned as adult. Note the interindividual variability in the neocortical surface area throughout development. Note in addition that the asymmetry between the hemispheres is consistently low.

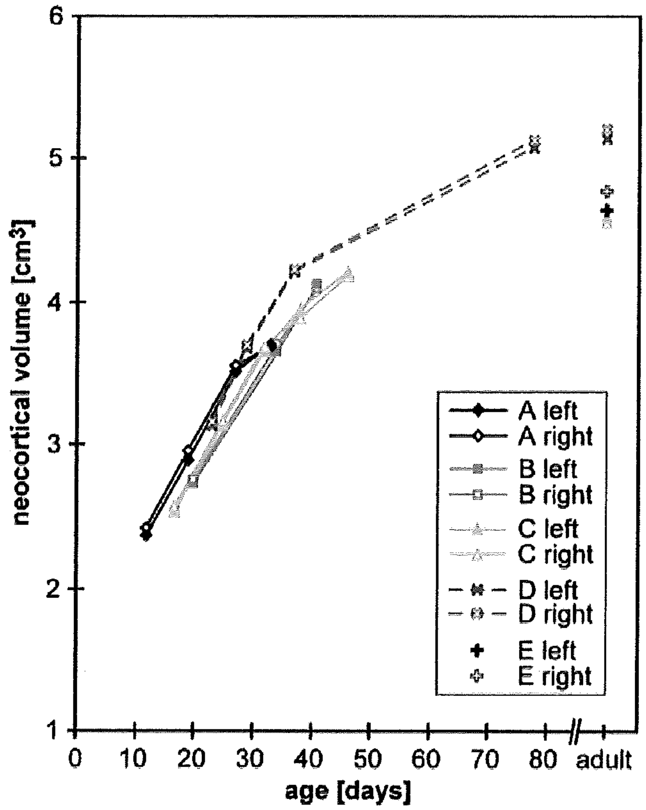

FIG. 8. Postnatal increase in neocortical volume. The neocortical volume for both hemispheres of cats A–E is shown for each of the investigated postnatal days. Data for cats older than 6 months are binned as adult. Note the consistently low asymmetry between the hemispheres.

patterns of ocular dominance columns (Rathjen *et al.*, 1998a,b, 2003). Figure 10 illustrates this comparison between neocortical and visual cortical growth. The data of single hemispheres of each postnatal age were averaged and fitted with a logarithmic curve. Comparison of the two curves shows that the surface area of the entire neocortex and that of area 17 grows at approximately the same rate. Moreover, the size of primary visual cortex amounts to ≈15% of total neocortical surface area throughout development so that its relative share of neocortical area remains rather constant during the investigated postnatal period.

Discussion

The cat brain grows substantially during early postnatal life. Because our experimental animals showed a considerable interindividual variability, it is important to analyse individual brains to determine real growth rates especially during the first postnatal weeks. The noninvasive technique of magnetic resonance imaging is the method of choice for this approach.

The smallest amount of variability could be detected for the AP extent, which expanded more or less steadily for all four investigated cats at an average of 14% between PW 3 and 6. Concerning the brain volume, there were greater differences especially between the measurements at the end of PW 2. During the following weeks, however, the brain volumes of the cats adjusted to one another. The brain volumes increased between PW 3 and 6 by ≈43%. The neocortical volumes showed a rather small variability especially at the beginning of the measurements with an average increase of ≈41% between PW 3 and 6. The most prominent variability could be observed in adulthood where the neocortical volume between the smallest and the greatest hemisphere differed by 14%.

The neocortical surface area showed the greatest interindividual variability, in particular during early postnatal development. In cat A, there was an increase of 53% between PND 12 and 40 while, in cat B, surface area increased nearly twice as much (105%) in the same postnatal period (between PND 14 and 41). This interindividual variability does not seem to be correlated with body weight because body weight of cats A, B and C was nearly identical at their first MRI session but their neocortical surface areas varied by 42% (between 11.98 cm^2 in cat A and 18.62 cm^2 in cat C). In adulthood, body weights varied by 16% while neocortical surface area varied by only 11%. We do not yet have a good explanation why initial interindividual variability seems to be greater than that of adulthood. On average, cat neocortical surface area grew ≈34% (range 30–37%) between PW 3 and 6. For cats C and D, which were also investigated as adults, the neocortical surface areas were within adult size at PW 6 (97 and 95%, respectively). In terms of percentage of adult size, the parameters AP extent (93, 90%), brain volume (86, 87%) and neocortical volume (87, 82%) lagged behind the surface area of the neocortex at this age.

As our magnetic resonance images clearly show, gyrification was already rather pronounced even at PW 3 (Fig. 4). In line with this, the ratio of neocortical surface area to neocortical volume decreased over time, indicating that neocortical thickness increases with increasing

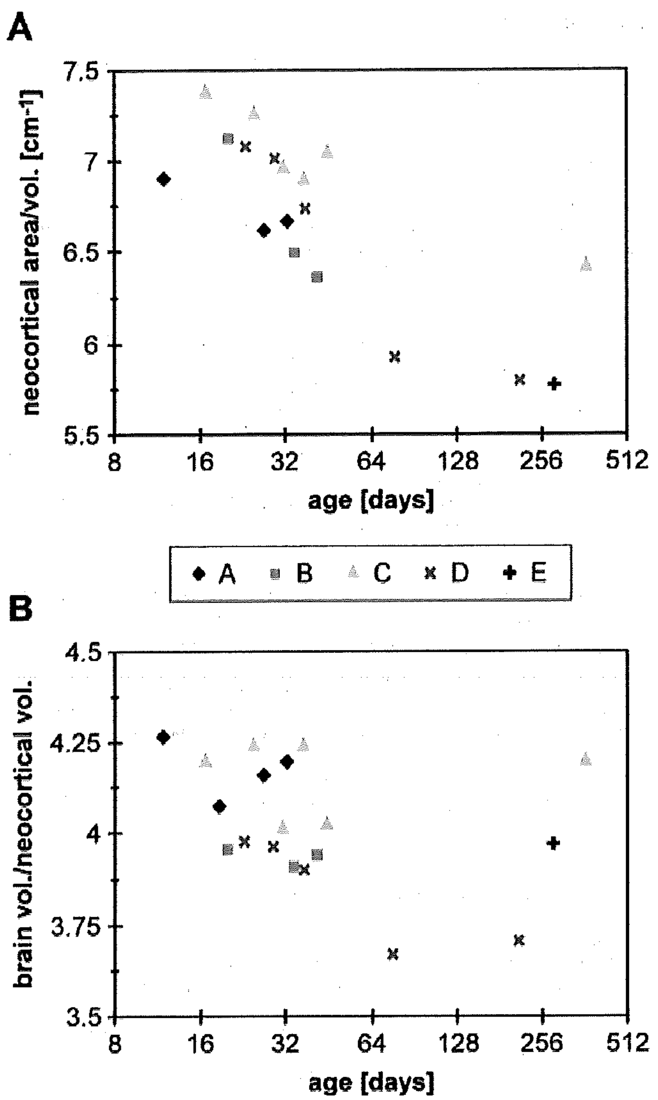

FIG. 9. Ratio plots illustrating growth relations of the neocortex. (A) Ratio of neocortical surface area to neocortical volume over time in cats A–E. This ratio declines significantly with age (Spearman rank correlation coefficient for the entire data set: $r_s = -0.746$, $P = 0.0021$). The plot thus demonstrates that the average neocortical thickness increases with increasing age. (B) Ratio of brain volume to neocortical volume. This ratio stays rather constant over time with nonuniform trends within individual animals (Spearman rank correlation coefficient for the entire data set: $r_s = -0.428$, $P = 0.0693$). Note the logarithmic scales ($\log_2$) of the horizontal-axes for clearer illustration.

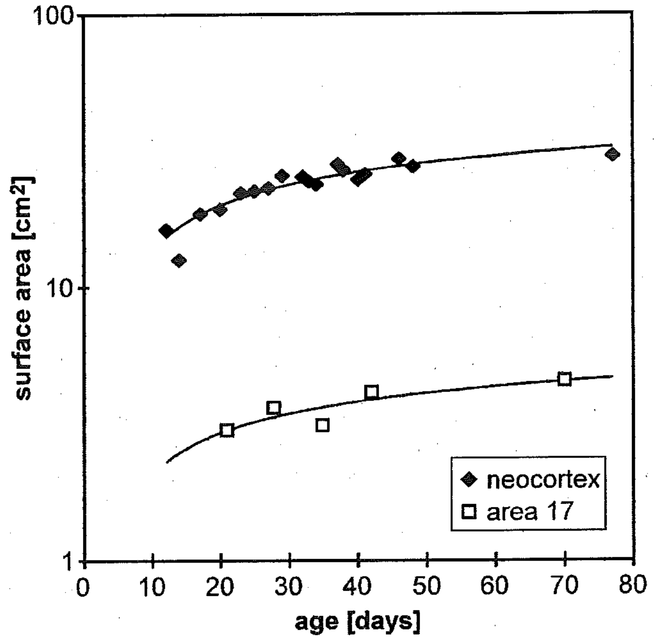

FIG. 10. Comparison between the postnatal growth of neocortical and primary visual cortical (area 17) surface area in early postnatal life. The data for the hemispheres of each postnatal age were averaged and fitted with a logarithmic curve. The primary visual cortex amounts to ≈15% during development (data on visual cortex from Rathjen *et al.*, 2003).

age. Furthermore, the ratio of brain volume to neocortical volume stays rather constant over time (Fig. 9). Taken together, these observations strongly suggest that brain growth during the investigated postnatal period can largely be ascribed to general growth as opposed to gyrification which most probably is prominent during earlier (presumably prenatal) developmental phases.

The comparison between neocortical and visual cortical surface area (see Rathjen *et al.*, 1998a,b, 2003) showed that, on average, the primary visual cortex amounts to ≈15% of the total neocortical surface area during early postnatal life (Fig. 10). Thus the primary visual cortex of cats seems to grow at a similar rate to that of the entire neocortex, indicating an isotropic expansion of primary visual cortex and neocortex. This is in contrast to observations in the somatosensory system. In rats, primary somatosensory cortex (S1) grows to a somewhat greater extent than the neocortex as a whole (Riddle *et al.*, 1992). One suggestion was that the apparently greater growth of S1 compared to the rest of the neocortex might be explained by greater metabolic and/or electrical activity of this cortical region. Because it has been shown previously that cat V1 is very metabolically active during postnatal development (Chugani *et al.*, 1991) this explanation may not hold true for the visual system. One has to keep in mind, however, that our area 17 data were from different animals than the MRI data. Given the pronounced interindividual differences in neocortical size and growth rates we cannot exclude the presence of differential growth between area 17 and the rest of the neocortex in individual animals with the present data set. Alternatively, the greater proportionate growth of S1 might be caused by a greater proportionate growth of the body surface as opposed to the retina.

Concerning the growth rates, the data presented here can be compared with a recently published study by Villablanca *et al.* (2000a,b). In this study, the volume of the neocortex was measured in cats at 11 time points during development (fetal day 59 to adult) using series of frontal sections processed for cytochrome oxidase histochemistry or stained with thionin. The results of this study showed that neocortical volume expands rapidly and reaches adult values around postnatal day 45. In the two animals that we followed longitudinally into adulthood this was, however, not the case and neocortical volume continued to increase. Villablanca *et al.* (2000a) further showed that the neocortical volume is significantly lower in adult cats (aged 295–565 days, except for one cat examined at PND 2190) than in animals at an age of 60 or 180 days. Such a decrease in grey matter volume has also been described for primates including man (e.g. Jernigan *et al.*, 1991; Pfefferbaum *et al.*, 1994). Because our study focused on the early development and growth of the brain it contains only limited measurements in older animals. In the two animals (cats

C and D) that we followed over an observation period roughly comparable to the study of Villablanca *et al.* (2000a), neocortical volume was, however, larger at the older ages (PND 375 compared to PND 46 and PND 211 compared to PND 77). Although we thus could not observe a decrease in neocortical volume, we might just have missed the 'shrinkage period' due to our sparse measurements in older animals.

Our imaging data show that there is only a slight asymmetry between the hemispheres. In three cats, the left neocortical surface area was consistently larger during the investigation period. The other two cats showed consistently larger surface areas in the right hemisphere. On average, however, all observed differences were <2%. Concerning the neocortical volume, four cats had a slightly larger right hemisphere with differences <3% during the entire observation period. In the other cat, however, the left hemisphere was slightly larger on average but again differences were not consistent and always <1.6%. Thus the nonsignificant tendency for generally larger right hemispheres (0.4–3.6% in 7 of 11 age groups) as reported by Villablanca *et al.* (2000a) could not be confirmed in our study with individual animals.

Similarly, our visual cortical surface measurements revealed no consistent left–right asymmetries (Rathjen *et al.*, 2003). While differences between the sizes of left and right area 17 amounting to up to 24% could be observed in a subset of the animals (5 from 15), (i) the differences were not consistent (three times the left, and twice the right area 17 was larger), and (ii) in the majority of animals (10 out of 15), size differences were <5%.

Large size differences between left and right hemisphere have been reported previously for the major somatic representations in rat neocortex. Within individual rats, the magnitude of lateral differences averaged 7.9% for the whisker pad representation and 15.4% for the furry buccal pad (Riddle & Purves, 1995). Because such variations are likely to be reflected in somatosensory performance, the absence of consistent left–right asymmetries in visual cortical surface area suggests a more 'symmetric' performance in this modality, i.e. that visual stimuli in the left and right visual hemifield are perceived more similarly.

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Abbreviations

AP extent, maximal anteroposterior extent of the telencephalon; MRI, magnetic resonance imaging; PND, postnatal day; PW, postnatal week.

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