Section 3

Development of the optokinetic system in macaque monkeys

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Abstract

Optokinetic nystagmus in response to horizontal movement of a whole field random dot pattern was measured in infant macaque monkeys from the first week to about 5 months after birth using electrooculography. During monocular and binocular viewing conditions stimulus velocities were varied between 10 and 120 °/s. Monocular stimulation in the temporonasal direction yielded slow phase gain of the optokinetic system which was relatively constant for a given stimulus velocity over the whole period of observation. Gain during nasotemporal stimulation was also clearly present but significantly lower at early stages and increased during further development. This asymmetry of monocular horizontal optokinetic nystagmus (OKN) clearly depended on the stimulus velocity. At lower stimulus velocities (10–20 °/s) OKN was largely symmetrical at 2–5 weeks of age. At higher stimulus velocities (40 °/s) symmetry was reached at about 12 weeks of age or even much later (80–120 °/s). © 1999 Elsevier Science Ltd. All rights reserved.

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1. Introduction

The optokinetic reflex (OKR), a mechanism to stabilize global motion of the environment on the retina can be used to judge an animals ability to react to visual motion. This visual reflex has been thoroughly investigated in a large variety of vertebrates, especially in lateral-eyed afoveate and in frontal-eyed foveate mammals (Tauber & Atkin, 1968). During monocular vision, the OKR in lateral-eyed mammals is largely asymmetric, i.e. the optokinetic response is stronger during motion of the visual world from temporal to nasal than during motion from nasal to temporal (e.g. rat: Hess, Precht, Reber & Cazin, 1985; rabbit: Collewijn, 1965; Dubois & Collewijn, 1979; guinea pig: Hayes & Ireland, 1969; Benassi, Biral & Corazza, 1992). By contrast, frontal-eyed foveate mammals exhibit a largely symmetrical monocular OKR with equally vigorous response during temporal to nasal

and nasal to temporal visual world motion (e.g. cat: Wood, Spear & Braun, 1973; Hamada, 1983; monkey: Koerner & Schiller, 1972; man: Schor & Narayan, 1981; Westall & Schor, 1985; Van den Berg & Collewijn, 1988; Schor, 1993).

Developmental studies in cats (Van Hof-Van Duin, 1978; Atkinson, 1979; Malach, Strong & van Sluyters, 1981) and human infants (Atkinson, 1979; Naegele & Held, 1982; Roy, Lachapelle & Leporé, 1989) have shown that in early childhood monocular OKR is largely asymmetric thus resembling OKR in afoveate animals and becomes symmetrical during the first few weeks to months of life. In cat, there is good evidence from behavioural, anatomical, and physiological data that the appearance of symmetry of OKR coincides with the maturation of a binocular cortical input to the nucleus of the optic tract and dorsal terminal nucleus of the accessory optic system (NOT-DTN), the visuomotor interface in the subcortical OKR pathway (Distler & Hoffmann, 1993). Whether or not this is true also for primates remains to be determined.

Quantitative studies using electrooculography in human infants showed that symmetry of monocular OKR

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is reached for intermediate stimulus velocities (25–34 °/s) at 5–6 months of age, for higher stimulus velocities (48 °/s) at about 6 months of age, whereas symmetry at slow velocities (14 °/s) is not attained for years (Naegele & Held, 1982; Roy et al., 1989). By contrast, observations of the time spent with optokinetic nystagmus (OKN) at medium stimulus velocity (30 °/s) indicate that symmetry may even be reached much earlier at 2–3 months of age (Atkinson, 1979). Furthermore, symmetry of monocular OKR not only depends on stimulus velocity but also on the visibility of the stimulus (e.g. Teller, Succop & Mar, 1993).

Studying the development of the cortical pathway for motion analysis in infant macaques by means of the 2-deoxy-glucose method, we found that the metabolic activity in the associated areas was adultlike at 3 months of age (Distler, Bachevalier, Kennedy, Mishkin & Ungerleider, 1996). It is well known that at least some of these cortical motion analyzing areas project directly to the NOT-DTN, a key structure in the pathway underlying the optokinetic reflex (Hoffmann, Distler & Erickson, 1991; Hoffmann, Distler & Ilg, 1992; Mustari, Fuchs, Kaneko & Robinson, 1994; Lui, Gregory, Blanks & Giolli, 1995). Thus, in search of a behavioural correlate for the developmental time course in cortical areas we studied the optokinetic reflex in baby monkeys ranging from 1 week to about 5 months of age.

There are surprisingly little data available about the development of OKR and motion perception in non-human primates. By quantifying the number of resetting saccades Sireteanu, Katz, Mohn and Vital-Durand (1992) found that monocular OKR is asymmetric at 2 weeks of age, but symmetric at 6 months of age. Measuring the time spent with following eye movements during optokinetic stimulation at high stimulus velocity (50 °/s), Atkinson (1979) found symmetry of OKR at 2–3 weeks of age. A different approach using the preferential looking method indicates that the ability to detect visual motion improves over the first 3 months of life but is not adult-like by the end of this period (Mikami & Fujita, 1992).

Thus, to achieve a solid quantitative data base about OKR development in infant macaque monkeys we longitudinally tested optokinetic eye velocities with electrooculography applying a broad range of stimulus velocities. Although it would have been very informative we did not vary the spatial frequency of the stimulus to distinguish between contrast frequency and velocity as the critical stimulus parameter for the developmental changes in OKN because experimental sessions with these young monkeys had to be kept short (see also de Graaf, Wertheim, Bles & Kremers, 1990). Nevertheless our data can be compared to a large amount of published work in other species and will serve as the behavioural basis for forthcoming physiological and anatomical studies.

2. Methods

2.1. Subjects

Six newborn and three adult cynomolgous monkeys (*Macaca fascicularis*) were used in the present study. Two infants were born in the breeding colony of IN-SERM, Bron, France, the remaining four infants were born in the breeding colony of Covance Laboratories GMBH, Münster, Germany. All infants were raised by their mothers and only 'borrowed' for the recording sessions. In four of the six animals, optokinetic eye movements could be recorded for up to about 5 months of age on a weekly basis. In the remaining two monkeys the recordings were abandoned at an earlier stage due to lack of cooperation on the infant's or the mother's side. Table 1 summarizes the measured periods for the individual animals. After the completion of the measurements the animals remained at their respective home institution.

All experiments were carried out in accordance with the European Communities Council Directive of 24 November 1986 (S6 609 EEC) and NIH guidelines for care and use of animals for experimental procedures.

2.2. Visual stimulation

The visual stimulus consisted of bright dots of different size projected by a planetarium centered above the animals head into a hemisphere 107 cm in diameter. The stimulus could be moved horizontally in clockwise and counterclockwise direction at stimulus velocities ranging from 10 to 120 °/s thus covering the range of stimulus velocities used in other studies on human and monkey infants. This stimulus proved to be a somewhat less effective optokinetic stimulus when compared to square wave gratings (own unpublished observations on cats and ferrets). We chose this stimulus because it would not drive the optokinetic system into saturation most of the time thus allowing to observe the steady state optokinetic gain in its more linear range. Also it closely resembles the random dot pattern we use for

Table 1
Summary of OKN-testing periods

Animal	Birth	1 meas.	Last meas.
a941	20.11.94	1 wk	8wks
axxx	17.01.95	0.5 wk	10.5 wks
5475	04.06.95	2 wks	18 wks
4191	11.06.95	1.5 wks	17 wks
5247	31.05.95	3 wks	19 wks
5234	14.05.95	5 wks	7 wks
A1	14.10.84	11 yrs	
A2	27.12.84	11 yrs	
A3	02.04.86	10 yrs	

visual stimulation of NOT-DTN neurons in electrophysiological experiments.

2.3. EOG measurements

Eye movements were measured using electrooculography (EOG) because the animals were borrowed only for the sessions and returned to their mothers thereafter. During the sessions, which took place in a room close to the breeding colony, the animals were wrapped in towels and placed snugly into a plastic cylinder. After topical application of local anesthesia, thin (100 μm) bare tip varnish coated Ag/AgCl wire electrodes were acutely attached to the skin at the animal's temples and connected to an EOG amplifier. The signal could be observed on an oscilloscope screen and stored on the disc of a PC computer for off-line computation of frequency histograms of slopes occurring during 100 ms segments of slow eye movements. Steady state optokinetic eye movements were measured during 30 s periods under monocular and binocular viewing conditions. To avoid habituation or charging of the velocity storage integrator, clockwise and counterclockwise stimulation was alternated from trial to trial. A new trial was only started when optokinetic nystagmus and afternystagmus had completely ceased. Slow and fast stimulus velocities were randomly intermingled.

Periods with obvious head movements, flat EOG due to drowsiness, and artifacts due to body movements were excluded from further analysis. The initial jump of OKN was highly variable and only unreliably elicited. To avoid any influence of the animals inattentiveness on our data, we only included steady state optokinetic eye movements in our analysis.

2.4. Control measurements

Control EOG measurements were carried out in three adult cynomolgous monkeys. The monkeys were seated in a primate chair with the head free in the center of a circular arena 170 cm in diameter. Again, the planetarium was mounted above the animals head (Distler, 1996). Otherwise, the same stimulus procedure and data analysis was used as for the infant monkeys.

2.5. Data analysis

Because the EOG signal could not be calibrated we could not calculate the true gain of the optokinetic reflex. Thus, to exclude variations of EOG signal quality between sessions, we have to introduce a normalization procedure, the outcome of which we call *relative gain*. We treated the change in voltage of the EOG signal during slow following eye movements as a qualitative measure of eye velocity (Hoffmann, Distler & Gruesser, 1998). To reach an estimate of steady state eye velocity the eye position signal during constant velocity stimulation was differentiated and slopes smoothed over 100 ms were calculated and displayed in a slope frequency histogram. To obtain a value which allowed to compare OKN performance across velocities the median of this slope distribution was divided by the stimulus velocity applied during its accumulation. To be able to compare these values (median of slopes/stimulus velocity) across different sessions and animals we normalized them in a given session to the maximal value (median of slopes/stimulus velocity) obtained across all velocities in that session. The relative gain was calculated with reference to only 0.95 of this maximal value because in our calibrated coil measurements using the same stimulus conditions gain hardly ever was higher than 0.95. By multiplying the relative gain with the stimulus velocity applied during its measurement we obtained the respective eye velocity estimates (EVE).

To assess the asymmetry of the eye movements, we calculated an asymmetry index (ASI) by simply dividing the difference between the optokinetic responses (medians of slopes; see above) to temporonasal (tn) and nasotemporal (nt) stimulation by the stronger of the two: $ASI = (tn - nt)/tn$ for $tn > nt$, and $ASI = (tn - nt)/nt$ for $tn < nt$. An ASI of 1.0 indicates no reaction in nasotemporal direction and thus total asymmetry whereas an ASI of 0 indicates equal reaction in both directions and thus symmetry. Measurements where the slow phase of OKN pointed against the stimulus direction received an ASI greater than 1.

3. Results

The OKN performance of the infant monkeys very much depended on the degree of attention. For example, monkey 5475 as a rule performed very well whereas in other cases more time between trials had to be allowed to regain the animal's attention. Therefore, to minimize variability, we measured two complete velocity tunings for each viewing condition (binocular, left eye only, right eye only) per weekly session and then averaged the data. In addition, the sequence of the viewing conditions was altered from one weekly session to the next.

In the very young animals optokinetic eye movements were easiest elicited at 20 and 40 °/s, whereas 10 °/s appeared to be very difficult to follow smoothly. At older ages, high stimulus velocities (80 °/s) were also quite effective although the highest velocity tested (120 °/s) remained difficult to stabilize even for adults.

3.1. Binocular measurements

To test if any of the animals showed asymmetric optokinetic eye movements during binocular vision,
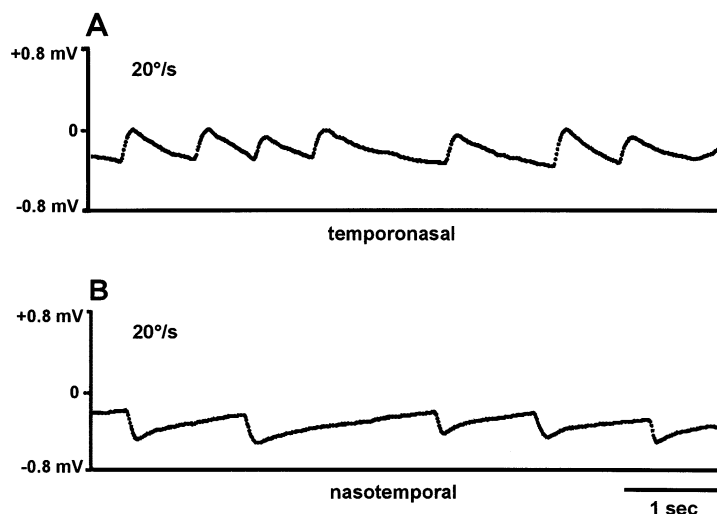
Fig. 1. An example of an EOG record of optokinetic eye movements of a 6 day old macaque during monocular stimulation at 20 °/s. (A) Stimulation in temporonasal direction. (B) Stimulation in nasotemporal direction. The record gives EOG voltage (ordinate) over time of stimulation (abscissa).

each weekly session contained binocular measurements. In no case did we see any systematic or significant asymmetry of slow eye movements between clockwise and counterclockwise stimulus movement in this condition.

3.2. Monocular measurements

In all animals and in all sessions, both the left and the right eyes were tested. With this procedure, we never saw any indication of a stronger or more symmetric as compared to a weaker or more asymmetric eye in any of our animals. However, one of the animals (axxx) differed from the other monkeys in two respects: (1) with the exception of the lowest stimulus velocity tested the relative gain was very low during the first 2–3 weeks of life followed by a steep increase in both temporonasal and nasotemporal direction; (2) very often nasotemporal stimulation elicited stronger responses than temporonasal stimulation. For these reasons, the animal was not included in the cumulative analyses shown below.

In all other animals already at the earliest age tested (at 3 days after birth), optokinetic eye movements could be elicited both in temporonasal and in nasotemporal direction. However, the optokinetic response in nasotemporal direction was clearly weaker and less reliable and depended even more on the attention of the animal. Figure 1 shows the EOG record of a 6 day old infant monkey tested monocularly during temporonasal (A) and nasotemporal (B) stimulus movement at 20 °/s.

To quantify the development of the slow phase optokinetic eye movements, we calculated the relative gain and from that the eye velocity estimate (EVE) (see methods). Figure 2 gives the eye velocity estimates pooled over all animals across the different age groups at the various stimulus velocities tested. Responses to temporonasal (left columns) and nasotemporal (right columns) stimulation are plotted separately. In the very young age groups (1–2 and 3–4 weeks), the optokinetic response in temporonasal direction is clearly present but highly variable especially at higher stimulus velocities. With increasing age, the range of scatter as indicated by the speckled rectangles and vertical bars decreases. At 5–8 weeks of age, EVE in the temporonasal direction has reached its final state for all velocities but 80 °/s and especially 120 °/s. By contrast, the optokinetic response to nasotemporal stimulation is rather low and hardly depends on stimulus velocity in the early age groups as indicated by the flat velocity tuning. In nasotemporal direction, EVE continues to increase for stimulus velocities between 40 and 120 °/s until the end of our observation period. This indicates that the decrease of asymmetry of OKN during development (see below) is mainly the result of the increase in response during nasotemporal stimulation.

This trend is also evident if the development is inspected on the basis of the relative gain. In Fig. 3, the relative gain of responses to temporonasal (left columns) and nasotemporal (right columns) stimulation are plotted separately to emphasize the different developmental course. Also, the development of the responses is shown separately for the different stimulus velocities tested. For each plot a set of regression functions were tested (using the program GB-Stat®), the one with the highest correlation is plotted. Two results are clearly demonstrated by that figure: first, the response to temporonasal stimulation is almost constant during the observation period as indicated by the low slope of the linear regression line. By contrast, the

responses to nasotemporal stimulation are very low in young animals and increase especially over the first 5–12 weeks of life, depending on the stimulus velocity as indicated by the reciprocal X and Y regression. Second, stimulation at different velocities leads to different levels of response gain with low stimulus veloc-

ities eliciting eye movements with higher gain than higher stimulus velocities.

Table 2 gives the mean relative gain values and one standard deviation of all animals. Vertical columns give the gain values at different velocities at certain ages in weeks (w), horizontal columns give the values at a
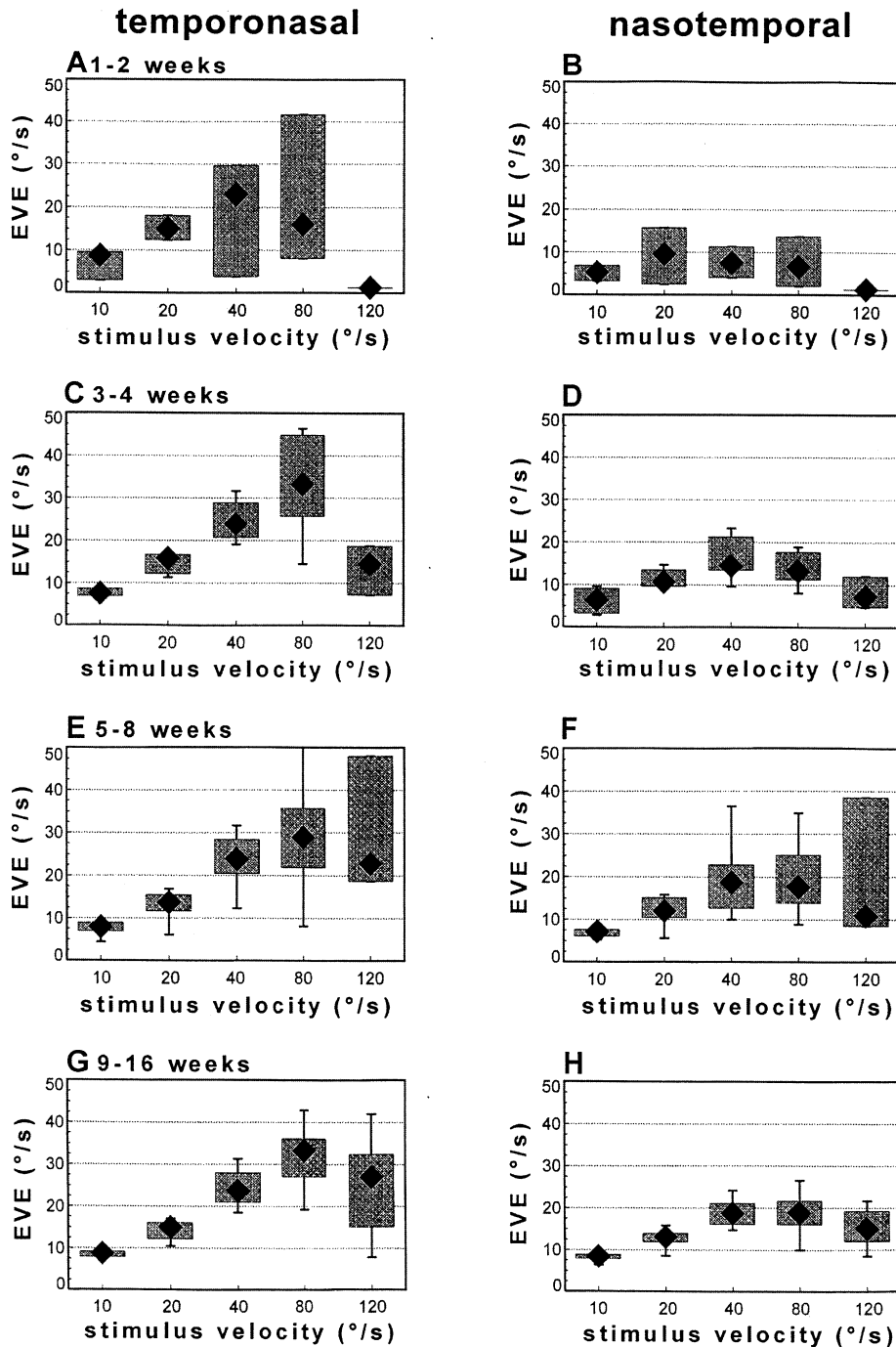

Fig. 2. Development of estimated eye velocity (EVE) during monocular stimulation in temporonasal (left columns, A, C, E, G) and nasotemporal direction (right columns, B, D, F, H). The dark diamonds indicate the median of the data points of all animals, the speckled rectangles represent the scatter of the data (25–75 % range), the vertical bars indicate the 10–90 % range. Ordinate: estimated eye velocity EVE (°/s), abscissa: stimulus velocity (°/s). The data were combined in the following age groups: 1–2 weeks (A, B), 3–4 weeks (C, D), 5–8 weeks (E, F), 9–16 weeks (G, H).
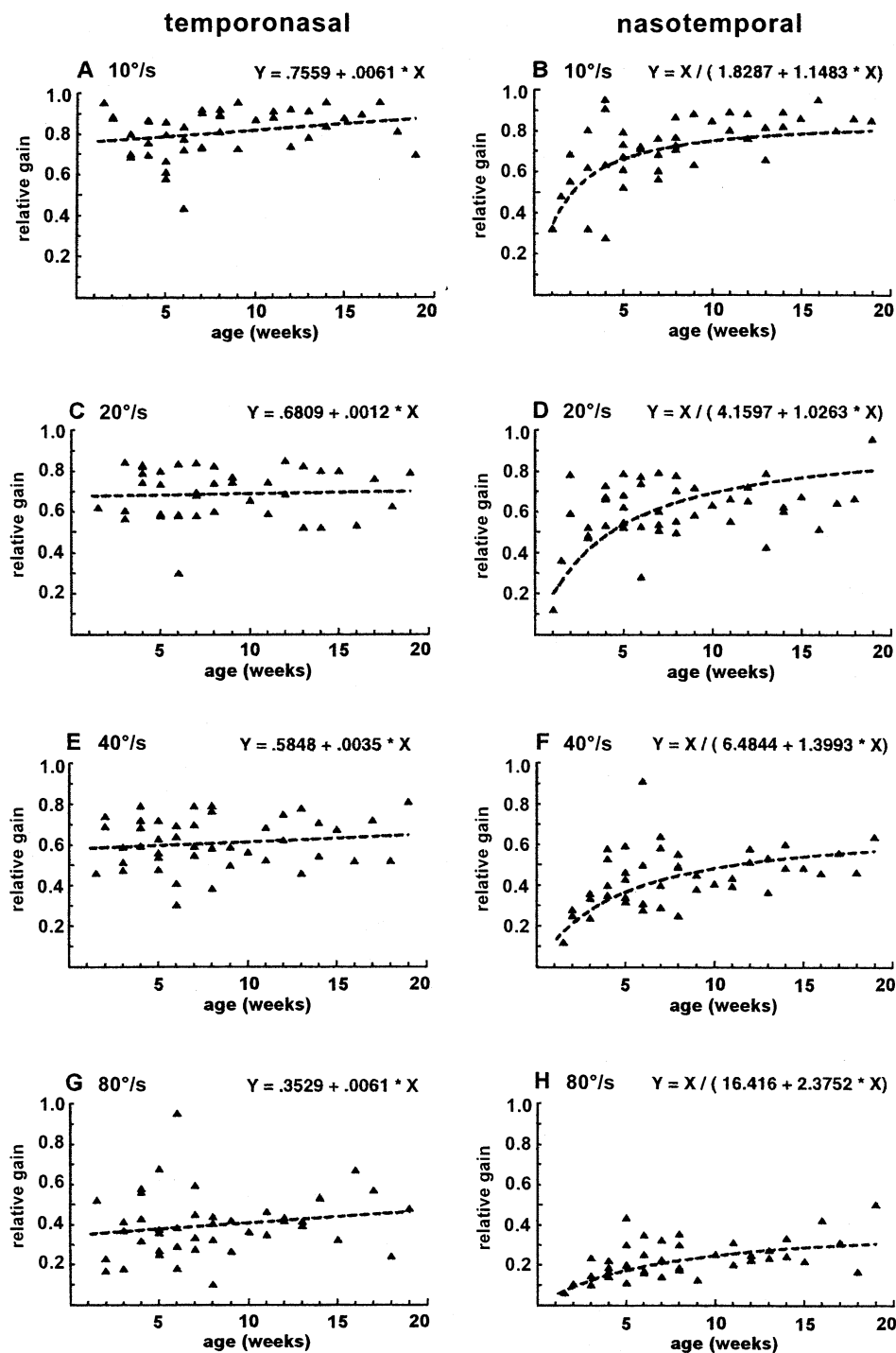
Fig. 3. Development of the relative gain of the slow phase of OKN in response to temporonasal (left column) and nasotemporal (right column) stimulus direction. The velocities tested are shown in different plots: A, B: 10 °/s, C, D: 20 °/s, E, F: 40 °/s, G, H: 80 °/s. Ordinate: relative gain, abscissa: age (weeks).

certain velocity (10–120 °/s) and a certain direction (temporonasal tn or nasotemporal nt) across the age groups. Significant differences between the relative gain of the response to temporonasal and nasotemporal stimulation at a certain velocity and a certain age are indicated by asterisks.

3.3. Asymmetry of monocular OKR

The development of symmetrical OKN depended on the stimulus velocity. In very young animals (< 4 weeks), the optokinetic response showed little asymmetry (ASI < 0.3) for low stimulus velocities ranging from

10 to 20 °/s, and high asymmetry (ASI = 0.8) at 80–120 °/s. With increasing age, lower stimulus velocities elicited more and more similar responses to temporonasal and nasotemporal stimulation, whereas at higher stimulus velocities the response to nasotemporal stimulation remained weaker for a longer period of time (see also Table 2). Assuming an artificial threshold for 'near symmetry' of 0.2, symmetry is reached for 10 °/s at about 2–3 weeks of age (Fig. 4A), for 20 °/s at about 4–5 weeks of age (Fig. 4B), for 40 °/s at about 14 weeks (Fig. 4C), and for 80 °/s or higher, symmetry was not reached during our testing period (Fig. 4D).

4. Discussion

The present study shows that infant macaques can show a remarkably strong and symmetrical optokinetic response to monocular stimulation already a few days after birth. Quite early on after birth the response to temporonasal stimulation is more reliable and becomes adult-like within the first month, whereas the strength of the response to nasotemporal stimulation is on average weaker and continues to improve until several months after birth. Symmetry is therefore reached at different ages depending on stimulus velocity. It is difficult to directly compare our data with those of Atkinson (1979) because of the different methods employed. Whereas Atkinson (1979) assessed response strength only qualitatively by judging the time spent with OKN, we have a quantitative comparison between the relative gain in the two directions from the EOG measurements. This may explain why Atkinson (1979) found symmetry of OKN at 50 °/s at 3 weeks of age, whereas in our data symmetry at 40 °/s is reached only at about 4 months of age.

4.1. Comparison with studies in human infants

Infant monkey visual system development closely mimics human infant visual system development when the 'weeks to months rule' is applied to the temporal dimension, so that 4 weeks in the monkey are equivalent to 4 months in the infant (Boothe, Dobson & Teller, 1985). This relation holds true for most parameters of spatial vision, including binocular interactions (Wiesel & Hubel, 1974; Chino, Smith, Hatta & Cheng, 1997) and stereoacuity, a product of binocular vision which has been recently investigated (O'Dell & Boothe, 1997).

In the human infant, eye movements are present from birth but less mature than in monkey. Steady fixation, pursuit of a slow moving object, saccades and elements of OKN have been described (for review see Hainline, 1993). Specifically, OKN has been studied in detail with the goal that it could constitute a convenient probe to test the integrity and normal development of motion processing pathways. Just like monkeys, human infants are born with a weaker response to monocular nasotemporal stimulation. Response to such a stimulation increases over the first 3–6 months of life when it becomes similar to the response to temporonasal stimulation (symmetrical) (Atkinson, 1979; Naegele & Held, 1982). It constitutes a clinically significant sign because the lack of symmetrization is usually indicative of a defect or lag of major visual functions. Three observations have led investigators to link the symmetrization of OKN to the development of binocular vision and stereopsis. One is based on anatomical and physiological data from studies in the cat (see below), the second one is the close temporal coincidence between the two events. The third one is the common observation that early onset strabismus, accompanied by a maldevelopment

Table 2
Relative gain of slow phase eye movements: means all cases[a]

Age (weeks)	1–2	3–4	5–6	7–8	9–11	12–14	15–19	Adult
Velocity								
10°/s tn[b]	.70 ± .32	.75 ± .12	.70 ± .13	.84 ± .13**	.85 ± .10	.84 ± .14	.84 ± .13	.80 ± .12
10°/s nt	.51 ± .17	.73 ± .19	.68 ± .13	.71 ± .12	.80 ± .13	.80 ± .10	.86 ± .08	.72 ± .15
20°/s tn	.75 ± .14**	.74 ± .16**	.63 ± .20	.71 ± .13*	.69 ± .13	.69 ± .15	.70 ± .12	.83 ± .10
20°/s nt	.42 ± .26	.57 ± .16	.60 ± .20	.62 ± .13	.63 ± .10	.63 ± .14	.71 ± .13	.77 ± .13
40°/s tn	.46 ± .28*	.61 ± .14**	.55 ± .17*	.64 ± .16**	.58 ± .12**	.64 ± .14*	.63 ± .12**	.66 ± .11
40°/s nt	.17 ± .09	.40 ± .15	.45 ± .17	.45 ± .16	.41 ± .04	.51 ± .09	.51 ± .09	.58 ± .12
80°/s tn	.26 ± .20**	.41 ± .14***	.39 ± .21*	.39 ± .14**	.37 ± .08**	.45 ± .06***	.41 ± .17	.33 ± .09
80°/s nt	.06 ± .05	.17 ± .07	.25 ± .11	.24 ± .11	.22 ± .08	.25 ± .06	.28 ± .13	.33 ± .10
120°/s tn	.03 ± .04	.12 ± .05	.20 ± .11*	.20 ± .08*	.17 ± .10	.26 ± .05***	.19 ± .15	.16 ± .05
120°/s nt	.02 ± .03	.08 ± .03	.12 ± .10	.10 ± .02	.13 ± .06	.15 ± .02	.13 ± .07	.14 ± .05

[a] Significance levels Mann–Whitney U-test:* $P \leq .05$; ** $P \leq .01$; ***$P \leq .001$.

[b] tn, temporonasal; nt, nasotemporal stimulation; significance levels are marked between tn and nt values at the same velocity.

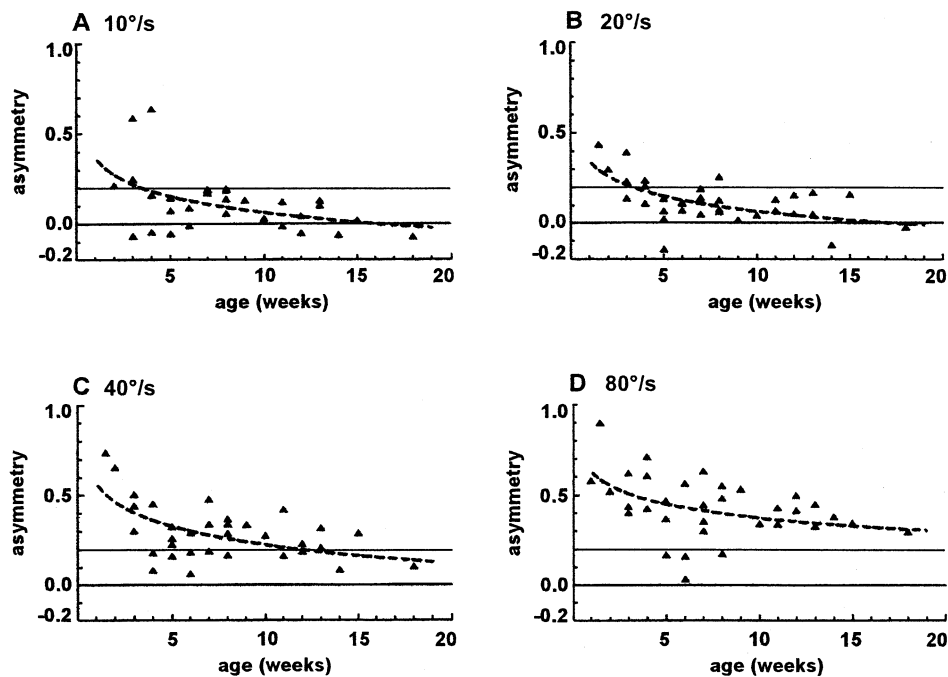**A 10°/s**

B 20°/s

C 40°/s

D 80°/s

Fig. 4. Development of symmetry of monocular OKN tested with different stimulus velocities and plotted against age. For each plot data were taken across all animals. A, 10 °/s; B, 20°/s; C, 40°/s; D, 80°/s. Ordinate: asymmetry index, abscissa: age (weeks).

of binocular vision is usually characterized by an arrest or a gross deficit of monocular OKN in response to nasotemporal stimulation (Tychsen & Lisberger, 1986). However, this point is controversial and some authors have claimed that only a proportion of early strabismic patients showed asymmetrical monocular OKN (Wattam-Bell, Braddick, Atkinson & Day, 1987), or have made shallow unilateral visual deprivation the primary cause of the lack of symmetrization (Shawkat, Harris, Taylor, Thompson, Russell-Eggitt & Kriss, 1995).

In any case, many authors have pointed out a close relation between infantile esotropia and a deficit of motion processing expressed by a lack of sensitivity or inadequate pursuit and saccades (Tychsen & Lisberger, 1986; Kapoula, Bucci, Eggert & Garraud, 1997; Fawcett, Raymond, Astle & Skov, 1998). Furthermore, clear deficits of smooth pursuit eye movements and/or OKN have been described in monkeys and in humans after lesions located either in the occipital cortex, in the posterior parietal cortex or in the region of the frontal eye field (Lynch & McLaren, 1983; Zee, Tusa, Herdman, Butler & Gücer, 1986; Thurston, Leigh, Crawford, Thompson & Kennard, 1988; Rizzo & Hurtig, 1989; Jacobs, Shawkat, Harris, Kriss & Taylor, 1993; Morrow & Sharpe, 1995; Heide, Kurzidim & Kömpf, 1996; Keating, Pierre & Chopra, 1996; Lekwuwa & Barnes, 1996).

As a consequence, OKN is used in the clinic to assess the physiological condition of both the subcortical and cortical motion specific pathways and the oculomotor plant (Van Hof-Van Duin & Mohn, 1983; Buquet &

Charlier, 1996; Prechtl, Einspieler, Cioni, Bos, Ferrari & Sontheimer, 1997).

4.2. Comparison with data in subprimate mammals

In the present study, we have shown that in monkey, already shortly after birth monocular OKN can be elicited reliably not only in temporonasal but also, albeit weaker, in nasotemporal direction. This clearly differs from data in the cat where at 3 weeks of age only OKN in temporonasal direction can be elicited, whereas optokinetic response to nasotemporal stimulation first occurs at 4 weeks of age (Van Hof-Van Duin, 1978; Malach et al., 1981). Over the following weeks OKN remains asymmetric until about 6 months of age.

To try to explain this difference, we have to look at the neuronal substrate underlying the optokinetic reflex. In all mammals investigated to date, a common pathway has been identified (rat: Cazin, Precht & Lannou, 1980; Precht & Strata, 1980; Cazin, Lannou & Precht, 1984; rabbit: Collewijn, 1975a,b; guinea pig: Lui, Giolli, Blanks & Tom, 1994; cat: Hoffmann & Schoppmann, 1975, 1981; Grasse & Cynader, 1984; ferret: Klauer, Sengpiel & Hoffmann, 1990; opossum: Volchan, Rocha-Miranda, Picanço-Diniz, Zinsmeisser, Bernardes & Franca, 1989; wallaby: Hoffmann, Distler, Mark, Marotte, Henry & Ibbotson, 1995; monkey: Kato, Harada, Hasegawa, Igarashi, Koike & Kawasaki, 1986; Hoffmann, Distler, Erickson & Mader, 1988; Kato, Harada, Hasegawa & Igarashi, 1988; Schiff, Cohen & Raphan, 1988; Hoffmann & Distler, 1989; Cohen,

Schiff & Buettner-Ennever, 1990; Mustari & Fuchs, 1990; Hoffmann et al., 1991; Hoffmann et al., 1992;). The key structure in this pathway is the pretectal nucleus of the optic tract together with the dorsal terminal nucleus of the accessory optic system (NOT-DTN) serving as the sensorimotor interface. Retinal slip neurons in the NOT-DTN are characterized by their direction selective response to ipsiversive stimulus movement, i.e. retinal slip neurons in the left NOT-DTN prefer leftward movement, those in the right NOT-DTN prefer rightward movement. In nonprimate species, they receive direct retinal input almost exclusively from the contralateral eye (Ballas, Hoffmann & Wagner, 1981; Klooster, Want & van der Vrensen, 1983). Retinal slip neurons project to the inferior olive, the nucleus praepositus hypoglossi, the dorsolateral pontine nucleus, and the nucleus reticularis tegmenti pontis (Aas, 1989; Mustari et al., 1994; Buettner-Ennever, Cohen, Horn & Reisine, 1996). The information is then transmitted to the vestibular nuclei and via climbing fibers to the flocculus of the cerebellum. Projections to the nuclei innervating the extraocular muscles close the loop (for review see Simpson, Giolli & Blanks, 1988). In some but not all of the mammals investigated, an additional cortical input to the NOT-DTN has been identified (rat: Schmidt, Zhang & Hoffmann, 1993; guinea pig: Lui et al., 1994; cat: Schoppmann, 1981, 1985; ferret: Klauer et al., 1990; monkey: Hoffmann et al., 1991; Hoffmann et al., 1992; Lui et al., 1995). Studies in cats with cortical lesions (Wood et al., 1973; Grasse, Cynader & Douglas, 1984) or with defective binocular vision (Cynader & Hoffmann, 1981; Hoffmann, 1983; Distler & Hoffmann, 1996) have indicated that at least in this species the cortical loop transmits binocular information as well as information about high velocity stimuli to the NOT-DTN. This has been confirmed in a developmental study. At 3 weeks of age, almost all NOT-DTN cells in kittens were exclusively driven by the contralateral eye. At this age, no cortical input to the NOT-DTN can be identified neither physiologically nor anatomically. At 4 weeks of age, however, the majority of the NOT-DTN cells receives an additional input from the ipsilateral eye, i.e. they are binocular. At this age, for the first time, their velocity tuning curves show clear optima, including responses to high velocities. This is also the age when a functional cortical input to the midbrain can first be identified (Plummer & Behan, 1989; Norita, Stein & McHaffie, 1991; Distler & Hoffmann, 1993) and, for the first time, a reliable optokinetic response to nasotemporal stimulation is present (Van Hof-Van Duin, 1978; Malach et al., 1981).

If we extrapolate the interpretation of the cat data to the monkey, we would have to postulate that already shortly after birth the NOT-DTN contains binocular neurons which would then be responsible for the optokinetic responses in both horizontal directions during monocular viewing. One possible anatomical substrate for this binocular convergence in infant monkeys could be provided by the strong bilateral retinal projection to the NOT-DTN present already at birth (Kourouyan & Horton, 1997). Data about the development of the cortical input to the NOT-DTN in monkeys are not available yet. If, like in cat, the cortical loop to the midbrain matures only some time after birth, one can propose the following hypothesis: The direct retinal input from both eyes to primate NOT-DTN is able to drive the system moderately symmetrically early in postnatal life. As the cortical input becomes functional, the role and importance of the retinal input is gradually reduced until the system is clearly dominated by the cortical input in adulthood (Hoffmann et al., 1988). Since binocular convergence by retinal input from both eyes is present in this model already at birth, no abrupt qualitative change in the symmetry of OKR would be expected at the time when the cortical input becomes functional. Thus, only the gradual developmental changes observed in OKR with respect to eye velocity and symmetry would still need to be explained by gradual maturation of the cortical areas and/or their projection to the NOT-DTN.

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