The Journal of Neuroscience, January 1, 1997, 17(1):296–307

Postnatal Development of Binocular Disparity Sensitivity in Neurons of the Primate Visual Cortex

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In macaque monkeys, the age at which neurons in the primary visual cortex (V1) become sensitive to interocular image disparities, a prerequisite for stereopsis, is a matter of conjecture. To resolve this fundamental issue in binocular vision development, we measured the responsiveness of individual V1 neurons in anesthetized and paralyzed infant monkeys as a function of the relative, interocular, spatial phase of dichoptic sine-wave gratings. We found that an adult-like proportion of units were sensitive to interocular image disparity as early as the sixth postnatal day, several weeks before the onset age for stereopsis in monkeys. The ocular dominance distributions of cells in infant monkeys were also indistinguishable from those of adults. Thus, at or only a few days after birth, V1 neurons are capable of combining neural signals from the two eyes as in adults and are sensitive to interocular image disparities. However, the monocular spatial-frequency response properties of these disparity-sensitive units were immature, and their overall responsiveness was far lower than that in adults. During the first 4 postnatal weeks, both the spatial frequency response properties and the peak response amplitude rapidly improved, which resulted in a corresponding increase in the absolute sensitivity of individual units to interocular disparity. The results demonstrate that early binocular vision development in monkeys is not constrained by a paucity of disparity-sensitive V1 neurons but, instead, by the relative immaturity of the spatial response properties and the overall unresponsiveness of existing disparity-sensitive neurons.

Key words: postnatal development; binocular disparity; V1 neurons; stereopsis; primates

Our ability to generate a robust, three-dimensional percept of the world based on a pair of two-dimensional retinal images (stereopsis) requires an array of neurons in the visual cortex that can detect interocular image disparities (Marr and Poggio, 1979). In the primary visual cortex (V1) of mature cats and monkeys, signals from the two eyes are linearly combined (Ohzawa and Freeman, 1986a,b; Ohzawa et al., 1996; Smith et al., 1996a,b) and interocular differences in receptive-field position and/or structure (phase) are thought to provide critical disparity cues for both stereopsis and fusional eye movements (Poggio and Fischer, 1977; Ferster, 1981; LeVay and Voight, 1988; Poggio et al., 1988; DeAngelis et al., 1991; Ohzawa et al., 1991; Aslin, 1993; Schor, 1993). However, behavioral studies in primates suggest that some aspects of these basic binocular connections are functionally immature at birth because both newborn humans and macaque monkeys are unable to detect objects embedded in random dot stereograms. In monkeys, stereopsis appears to emerge suddenly at ~4 weeks (O'Dell et al., 1991). Similarly, human infants apparently lack stereopsis before 4 months of age, a developmental age comparable to ~4 weeks in monkeys (Birch et al., 1982; Boothe et al., 1985) but exhibit a rapid onset of stereopsis thereafter. It has been hypothesized that the absence of stereopsis before these ages is attributable to an absence of disparity-sensitive neurons in V1 (Held, 1993).

Unfortunately, there is currently little information on the functional binocular status of individual neurons in infant primates. The ocular dominance distributions of V1 neurons in 2- and 8-d-old infant monkeys indicate that, as in adults, the majority of neurons can be excited by monocular stimuli presented to either eye (Wiesel and Hubel, 1977; LeVay et al., 1980). Likewise, recent anatomical studies suggest that the ocular dominance columns in layer IVC of macaque infants are very much adult-like at birth (Horton and Hocking, 1996) (see also LeVay et al., 1980). However, there have not been any previous attempts to examine directly the disparity sensitivity of cortical neurons in neonates, and there are some indications that cortical binocularity is not adult-like in neonates. Physiologically, there appears to be a greater mixing of left- and right-eye activity in layer IV of 8-d-old monkeys than in adult monkeys or even in infant monkeys just 3 weeks of age (Wiesel and Hubel, 1977; LeVay et al., 1980). The pattern of cytochrome oxidase (CO) in layer IVCβ of newborn rhesus monkeys is qualitatively different from that in adults (Horton and Hocking, 1996), and in infant galagos, a prosimian, the cortical terminal axon arbors of LGN afferents in layer IV can be dramatically larger than the terminal arbors in adults and show different branching characteristics (Florence and Casagrande, 1990). Thus, it is possible that in infant monkeys, the individual axon arbors are immature even though segregation of LGN afferents into eye-specific columns is largely complete at birth. In this respect, intermixing of left- and right-eye signals in layer IV (possibly via intracortical connections) or local imprecision in afferent connections could severely limit or degrade the disparity selectivity of individual cortical neurons outside layer IVC and, thus, be responsible for the absence of stereopsis in neonates.

To investigate the physiological basis for the absence of stereoscopic vision in neonates, we measured the disparity sensitivity of

Received Aug. 8, 1996; revised Oct. 10, 1996; accepted Oct. 15, 1996.

This work was supported by National Institutes of Health Research Grants EY-08128, EY-03611, and RR-07146. We thank V. Sharma and C. Garcia for assistance in experiments and Ron Harwerth for comments on this manuscript.

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Table 1. The age and weight of infant monkeys

Age group	*n*	Age at the start of experiments (d)	Weight (kg)	Age at the end of experiments (d)
1 week	3	6	0.50	8
		7	0.53	9
		10	0.43	12
2 weeks	2	14	0.50	17
		14	0.57	17
4 weeks	2	28	0.71	31
		28	0.58	31
>4 weeks	2	42	0.83	45
		112	3.75	115

individual V1 neurons in infant rhesus monkeys ranging in age from 6 d to 16 weeks.

Some of these results have appeared in abstract form (Chino et al., 1996; Hatta et al., 1996).

MATERIALS AND METHODS

Preparation

The animal preparation and recording methods have been described in detail elsewhere (Smith et al., 1990, 1996a; Chino et al., 1994). Nine infant (see Table 1) and six adult monkeys were anesthetized initially with an intramuscular injection of ketamine hydrochloride (15–20 mg/kg) and acepromazine maleate (0.15–0.2 mg/kg). A superficial vein was canulated, and all subsequent surgical procedures were carried out under sodium thiopental anesthesia. A tracheotomy was performed to facilitate artificial respiration, and the subjects were secured in a stereotaxic instrument. A small craniotomy and durotomy were made over the operculum of V1 to allow tangential electrode penetrations. After all surgical procedures were completed, the animals were paralyzed by an intravenous (i.v.) infusion of pancuronium bromide (a loading dose of 0.1–0.2 mg/kg followed by a continuous infusion of 0.1–0.2 $mg \cdot kg^{-1} \cdot hr^{-1}$) in a 5% dextrose Ringer solution (2.5 $ml \cdot kg^{-1} \cdot hr^{-1}$). The animals were artificially respired with a mixture of 59% N_2O, 39% O_2, and 2% CO_2. The respiration rate was adjusted to maintain the end-tidal CO_2 between 4.0 and 4.5%. The animal's core temperature was held at 37.6°C. Throughout the recording session, anesthesia was maintained by the continuous i.v. infusion of sodium pentobarbital (1–4 $mg \cdot kg^{-1} \cdot hr^{-1}$). The anesthesia level was monitored by observing the EEG, EKG, and heart rate, particularly in response to a periodic paw pad pinch.

Cycloplegia and mydriasis were produced by 1% atropine sulfate, and the animal's corneas were protected with rigid, gas-permeable, extended-wear contact lenses. Retinoscopy was used to determine the contact lens parameters required to focus the eyes on the stimulus screens. The projections of the fovea and the optic disk of each eye were plotted on the tangent screen with the aid of a monocular indirect ophthalmoscope and a path-reversing mirror (Eldridge, 1979).

Recording and stimulation

Tungsten microelectrodes were used to isolate the activity from single cortical neurons, and action potentials were recorded and amplified using conventional technology. For each isolated neuron, the minimum response fields were mapped on the tangent screen and two gimbaled mirrors were used to project the neuron's receptive fields onto the centers of two matched cathode ray tube (CRT) screens (P-31 phosphors). The CRTs had a space-average luminance of 56 cd/m^2. The visual stimuli were drifting sinusoidal gratings. Their orientation, direction of drift, spatial frequency, temporal frequency, contrast, and relative spatial phase could be controlled independently.

A window discriminator provided standard pulses that were accumulated by a PDP-11/73 computer. The neuron's responses were sampled at a rate of 100 Hz (10 msec binwidths) and compiled into peristimulus time histograms (PSTHs) that were equal in duration to, and synchronized with, the temporal cycle of the grating stimulus. The amplitude and phase of the temporal response components in the PSTHs were determined by Fourier analysis.

To facilitate comparisons of the relative effectiveness of different stimuli, the potential impact of short-term variations in the responsiveness of cortical neurons was minimized by collecting the data using a multihistogram technique (Henry et al., 1973; Movshon et al., 1978). In all experiments, the stimuli were presented multiple times in a randomly ordered sequence for relatively short periods (e.g., 10 cycles of a sine-wave grating were drifted across the receptive field). During a given experiment, the re-randomized stimulus sequence was usually repeated three to six times, producing PSTHs for each stimulus that represented the neuron's response to 30–60 stimulus cycles. One or two blank stimuli (i.e., zero contrast control) were included in each repeat of the re-randomized sequence to provide a measure of the neuron's maintained firing rate.

To identify recording sites, small electrolytic lesions were produced at two to three sites along the electrode track (5 μA, 5 sec). At the end of the recording experiments, an overdose of sodium pentobarbital (100 mg/kg, i.v.) was administered to induce a deep level of anesthesia, and the animals were killed by a perfusion through the heart with an aldehyde fixative (2% paraformaldehyde followed by 2% paraformaldehyde and 10% sucrose). The brain was removed and stored overnight in 30% sucrose at 4°C.

Response analysis and experimental design

Monocular properties. Cells were classified as simple or complex cells based on established criteria (Skottum et al., 1991). The optimal orientation and orientation bandwidth were measured from the unit's orientation response function obtained with a near-optimal spatial frequency (drift rate 3.1 Hz, contrast 30–50%). Direction selectivity was calculated by the following formula: direction selectivity index = $(P - N)/P$, where P is the response amplitude for stimulus drift in the preferred direction and N represents the response for the opposite direction. At the optimal orientation, a spatial frequency response function was measured so as to determine the cell's optimal spatial frequency and spatial resolution (defined as the highest spatial frequency that produced a reliable response above the mean noise level). Spatial frequency bandwidth was determined by measuring the full width of the tuning functions at one-half of the peak firing rate in octaves.

Binocular properties. Ocular dominance of each unit was determined qualitatively (Hubel and Wiesel, 1962) and quantitatively (Chino et al., 1994). The sensitivity of cortical units to binocular disparity was assessed by quantifying the cell's response as a function of the relative interocular spatial phase of optimal dichoptic gratings (Fig. 1*a*) (Freeman and Robson, 1982; Ohzawa and Freeman, 1986a,b; Chino et al., 1994; Smith et al., 1996a). Responses were collected for 16 dichoptic grating pairs that had different relative interocular phases, ranging from 0° to 360° in 22.5° steps. Monocular stimuli for each eye and one blank control were included in the parameter file. For descriptive and analytical purposes, a single cycle of a sine wave was fitted to each neuron's phase-tuning function using an algorithm based on a residual root mean square error criterion (Ohzawa and Freeman, 1986a). The amplitude of the fitted sine wave was used to calculate the degree of binocular interaction [binocular interaction index (BII) = amplitude of the fitted sine wave ÷ the average response amplitude]. A signal-to-noise ratio (S/N = amplitude of the fitted sine wave ÷ the residual mean square error of the fit) was also calculated to determine the relative strength of the sinusoidal signal in the phase-tuning curve (see Fig. 1*b*).

RESULTS

Extracellular single-unit recordings were made from 376 neurons in the nine infant monkeys and from 240 units in the six adult monkeys. In each subject, the electrode traversed all cortical layers of the operculum at similar angles to the surface, and we attempted to study every isolated unit in each penetration. The receptive fields of all units were located between 1.5° and 4.0° from the center of the fovea.

Ocular dominance distribution

The relative ability of monocular stimuli presented to the left and right eyes to excite a V1 neuron was measured qualitatively using hand-held stimuli (Hubel and Wiesel, 1962) and quantitatively by comparing the monocular response amplitudes for optimal stimuli (Chino et al., 1994). As reported in 2- and 8-d-old monkeys

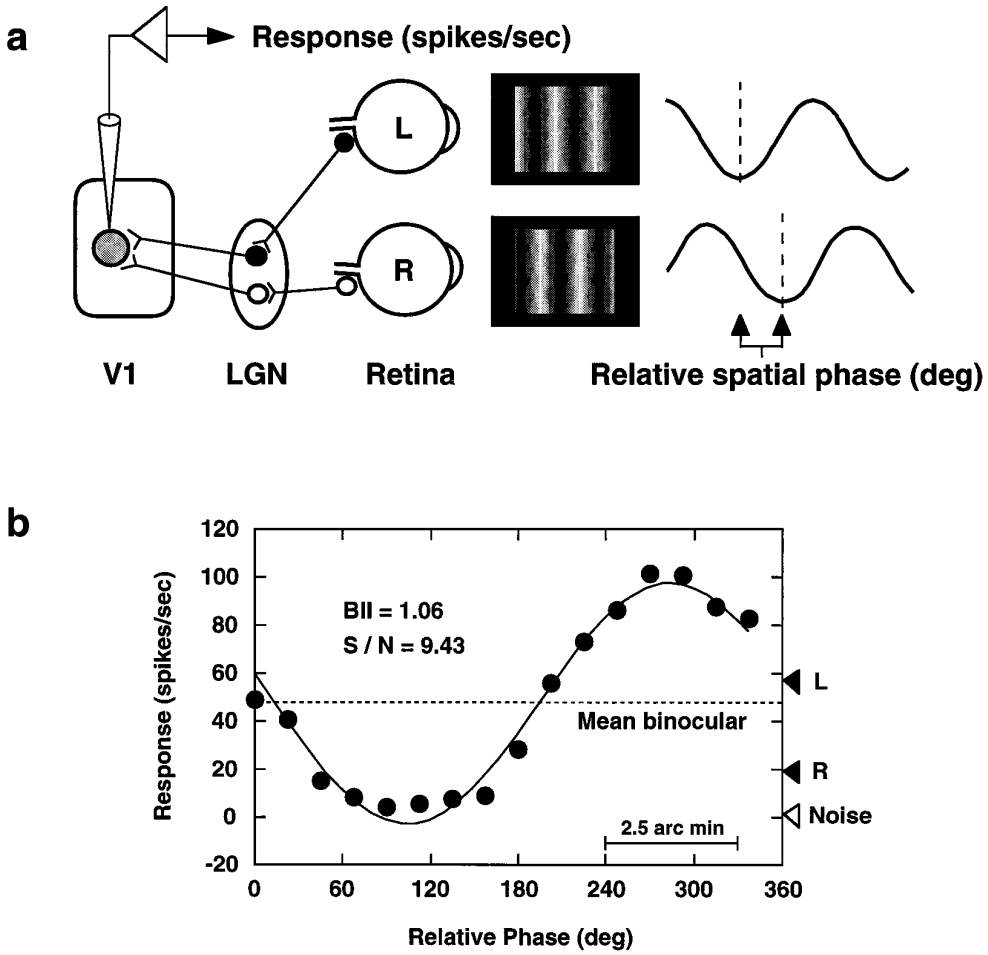

Figure 1. *a*, Diagram illustrating the methods used to measure the disparity sensitivity of V1 neurons in infant and adult monkeys. *Left*, Recording setup. Extracellular single-cell recordings were made with a tungsten microelectrode in the operculum of V1 in anesthetized and paralyzed rhesus monkeys. *Right*, Visual stimulation methods. A pair of identical sinusoidal gratings (corresponding to the cell's optimal orientation and spatial frequency) were drifted in the unit's preferred direction (temporal frequency 3.12 Hz; contrast 30–50%), and the relative interocular spatial phase was systematically varied between 0° and 360° in 22.5° steps. *b*, An example of an interocular phase-tuning function for a simple cell in an adult monkey. The tuning function was obtained by plotting the fundamental Fourier response amplitude (F1) as a function of the relative interocular spatial phase differences. The phase-tuning function was fit with a single cycle of a sine wave. The binocular interaction index (*BII*) was calculated by taking the ratio of the amplitude of the fitted sine wave over the average response amplitude. A signal-to-noise ratio (*S/N*) was determined by dividing the amplitude of the fitted sine wave by the residual mean square error of the fit (Ohzawa and Freeman, 1986a; Smith et al., 1996a). Monocular response levels for the left (*L*) and right (*R*) eyes are indicated by the *filled triangles*. The mean binocular responses is indicated by the *dotted line*. The cell's maintained firing rate is shown by the *open triangle* (*Noise*). The scale bar shows the angular displacement corresponding to a 90° phase shift for sine wave gratings of the unit's optimal spatial frequency (6 c/d).

(Wiesel and Hubel, 1977; LeVay et al., 1980), the ocular dominance distributions for V1 neurons in all of our infant monkeys, including those studied at 6 d of age, were indistinguishable from those of adults (Fig. 2).

Development of disparity sensitivity

Both simple and complex units exhibited clear sensitivity to interocular image disparity only a few days after birth. The basic data set obtained for a simple cell from a 6-d-old infant is illustrated in Figure 3. This unit was relatively well tuned to monocular stimulus orientation, direction of movement (Fig. 3*a*), and spatial frequency (Fig. 3*b*). Moreover, its binocular phase-tuning function (Fig. 3*c*) was adult-like. Specifically, the binocular response amplitude of this simple cell was greater than the dominant monocular response amplitude (*R*) for relative interocular spatial phase disparities between ~140° and 320° and peaked at a disparity around 180°, i.e., the cell exhibited binocular facilitation. The binocular response amplitude decreased systematically, approaching the noise level for phase values 180° away from the optimum (i.e., binocular suppression). Thus, the tuning function was reasonably fit with a single cycle of a sine wave. This cell's binocular response characteristics were qualitatively similar to those of the adult simple cell illustrated in Figure 1*b*. The BII and S/N for the simple cell in Figure 3*c* were 0.76 and 2.74, respectively. Cells like this one with BII values $\geq$ 0.3 are typically regarded as "disparity-sensitive cells" (Ohzawa and Freeman, 1986a,b; Chino et al., 1994; Smith et al., 1996a).

Figure 4 illustrates the variety of interocular phase-tuning functions found in our 1-week-old monkeys. As in adults (Smith et al., 1996a), the degree of binocular phase tuning, as reflected by the BII values and the relationship between the cell's dominant monocular response amplitude and its peak binocular response, varied from cell to cell. However, all of the major characteristics of disparity-tuning functions in adults were also found in our 1-week-old monkeys. For example, the simple cell in Figure 4*a* exhibited well balanced monocular responses and a robust phase-tuning function (BII = 1.13, S/N = 5.44). Its binocular responses were dominated by synergistic interactions between left- and right-eye inputs. The unit in Figure 4*b* responded primarily to right-eye stimulation, but it showed a high degree of modulation in its tuning function (BII = 0.73, S/N = 3.86). Facilitatory interactions were also prevalent in the binocular responses of this unit. Units that were driven only by one eye under monocular stimulus conditions also showed clear binocular interactions (Fig. 4*c*,*d*). For example, the units in Figure 4, *c* and *d*, were excited only through one eye but showed robust binocular interactions that were primarily suppressive in nature. We also encountered one truly monocular simple cell (Fig. 4*e*), i.e., the response amplitudes of the cell were the same for monocular and binocular stimulus conditions.

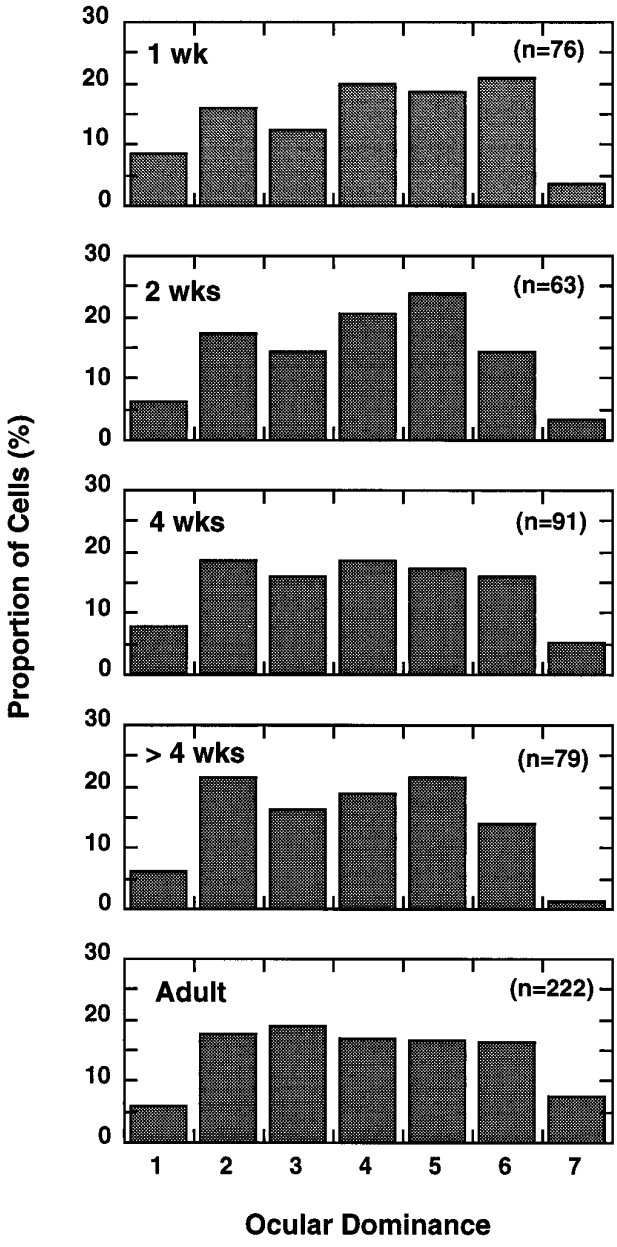

Figure 2. Ocular dominance distributions of V1 units in infant and adult monkeys. A neuron's ocular dominance was determined by traditional qualitative methods (Hubel and Wiesel, 1962) and confirmed by comparing the monocular response amplitudes for optimal stimuli (Chino et al., 1994). Ocular dominance *1* represents cells driven exclusively by the contralateral eye; *7*, cells driven exclusively by the ipsilateral eye; *4*, cells driven equally by both eyes; *2–3*, *5–6*, binocularly activated units dominated by the contralateral or ipsilateral eyes, respectively.

As in adults, the complex cell population studied in the 6-d-old monkeys (Fig. 4*f–j*) exhibited a greater variety of binocular interactions than that found for simple cells. The degree of binocular interactions varied greatly even among binocular complex cells with relatively balanced ocular dominance. For some complex cells, clear instances of phase-dependent, synergistic, and antagonistic binocular interactions could be observed (e.g., Fig. 4*f*,*g*). However, as in adults, the binocular responses of many complex cells were relatively independent of the phase disparity, but for these cells comparisons of the binocular and dominant monocular

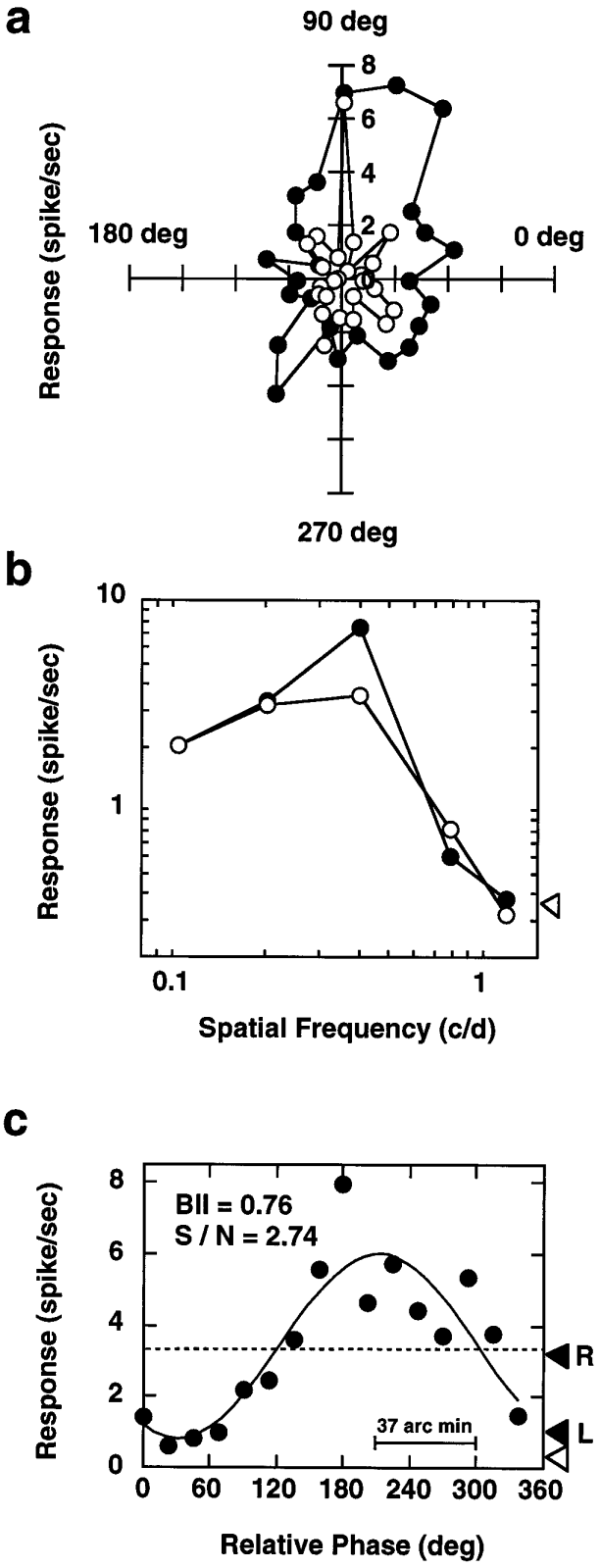

Figure 3. An example of monocular and binocular responses from a simple cell in a 6-d-old monkey. *a*, Polar plots of orientation response functions for the left (*open circles*) and right (*filled circles*) eyes. F1 amplitudes were plotted as a function of the direction of stimulus movements. *b*, Spatial frequency response functions for the left (*open circles*) and right (*filled circles*) eyes. *Open triangle* indicates the cell's maintained firing rate. *c*, Binocular phase-tuning function for the same simple cell. The format and conventions are as in Figure 1*c*.

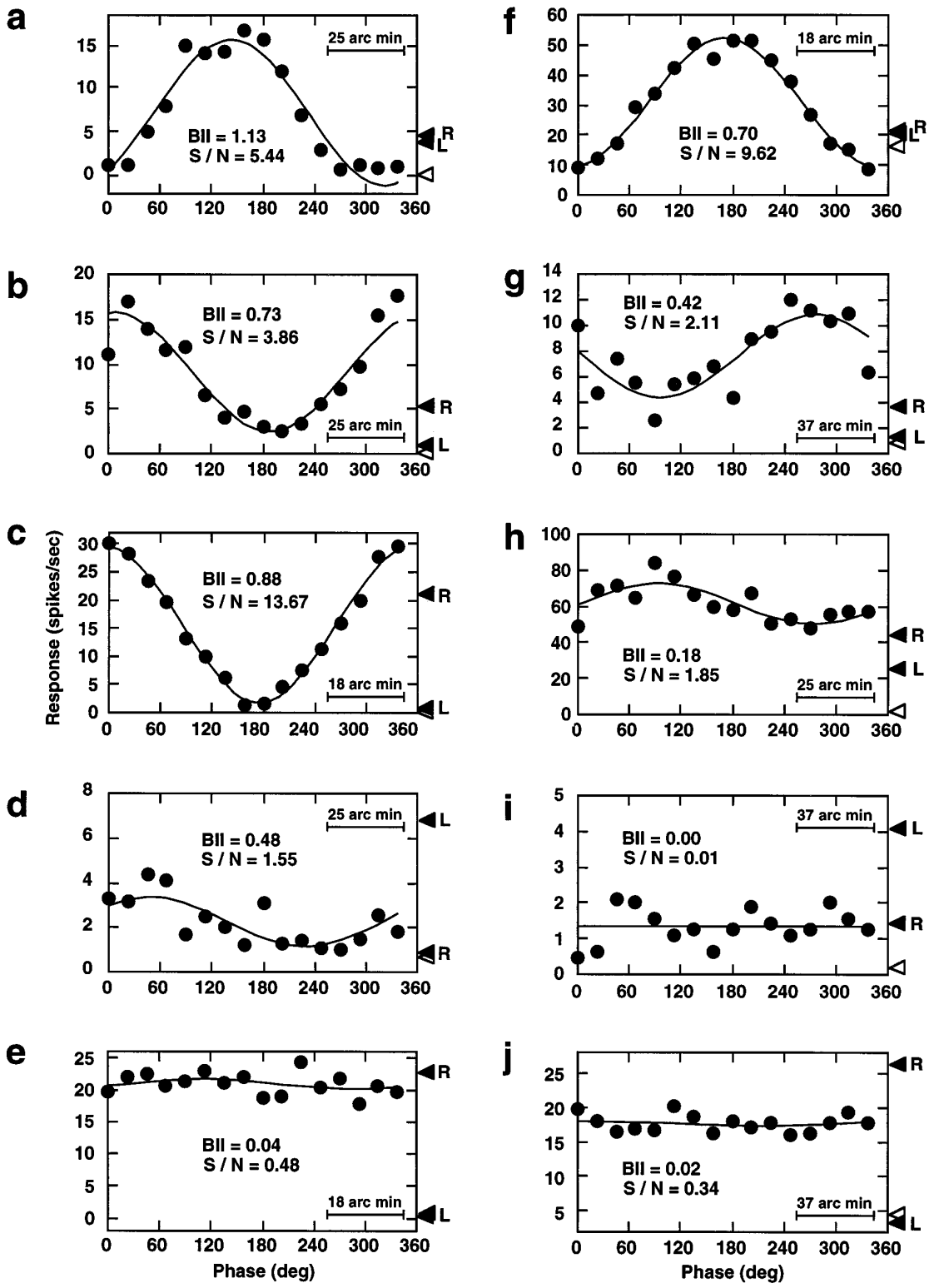

Figure 4. Binocular phase-tuning functions for five representative simple cells (*a–e*) and five representative complex cells (*f–j*) from 1-week-old monkeys. The F1 amplitudes for simple cells and the mean response amplitudes for complex cells were plotted as a function of the relative interocular phase differences. The format and conventions are as in Figure 1*c*.

response amplitudes often provided clear evidence of either binocular facilitation (Fig. 4*h*) or suppression (Fig. 4*i*); also, many complex cells that appeared to be excited by only one eye exhibited non-phase-specific suppression for dichoptic stimuli (Fig. 4*j*).

The prevalence of interocular phase tuning in infants and adults was compared by plotting the cumulative proportions of cells at each BII and S/N value for both the simple and the complex cell populations (Fig. 5). Simple cells showed gener-

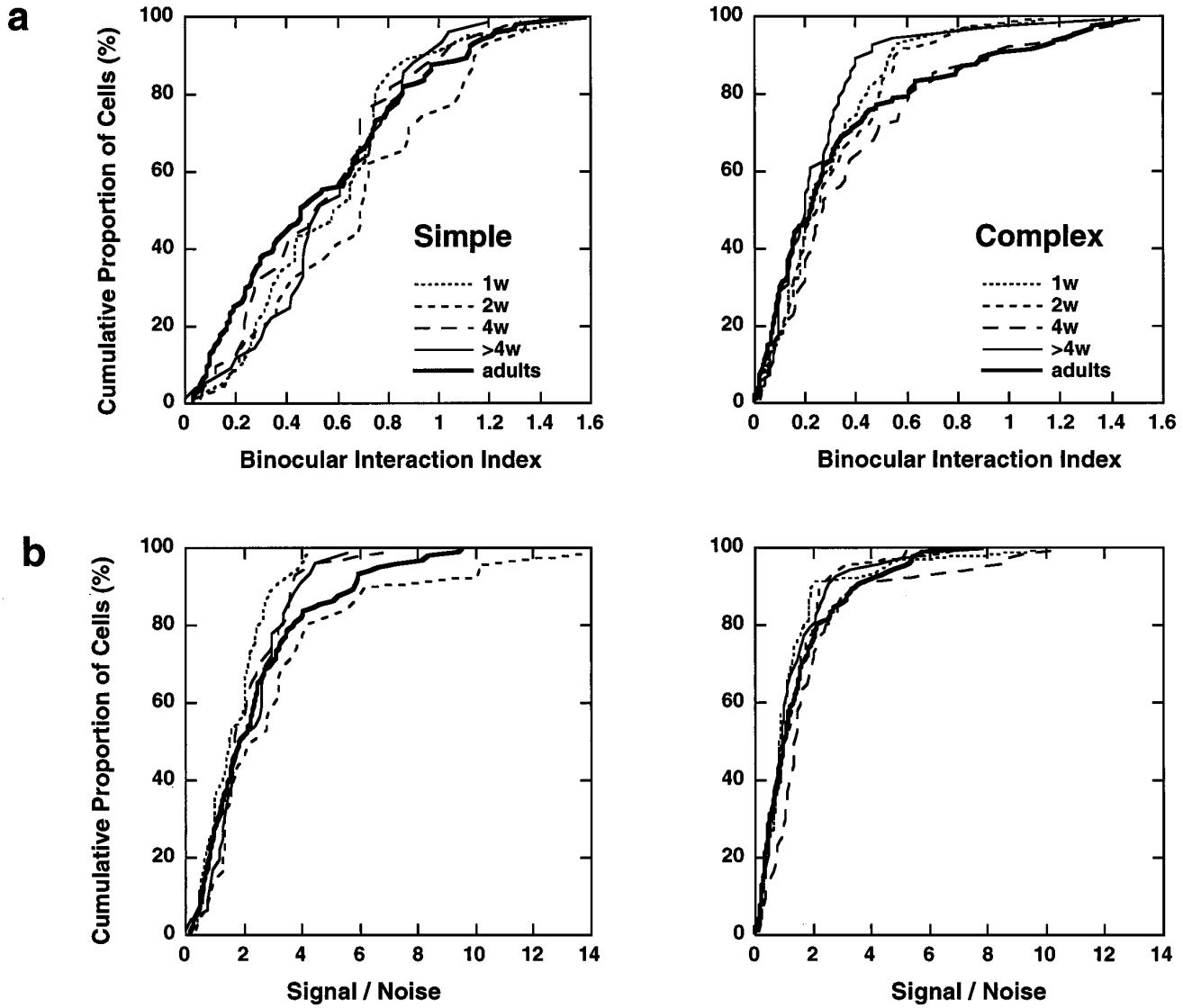

Figure 5. Development of disparity sensitivity in monkey V1. *a*, Cumulative proportions of cells at each BII value for simple (*left*) and complex cells (*right*) in V1 of infant and adult monkeys. *b*, Cumulative proportion of cells at each S/N value for simple (*left*) and complex cells (*right*). No significant differences were found between any of the infant and adult groups (Kruskal–Wallis test, $p > 0.1$).

ally higher BII values than complex cells for all age groups (Fig. 5*a*). More important, the distributions of the BII (Fig. 5*a*) and S/N values (Fig. 5*b*) for our young infant monkeys did not differ significantly from those obtained in adults (Kruskal–Wallis test, $p > 0.1$). Thus, as in adults, >70% of simple cells and 40% of complex cells in 1-week-old monkeys were disparity-sensitive (i.e., BII ≥ 0.3).

Because cells with preferred orientations near vertical are well suited for detecting the horizontal disparity cues that are required for stereopsis (see, for example, Orban, 1991), we examined the distribution of BII values as a function of the preferred stimulus orientation. The scatterplots in Figure 6 demonstrate that in both infants and adults the degree of modulation in a cell's disparity-tuning function was independent of the cell's preferred orientation; and specifically, a normal proportion of phase-sensitive cells preferred near-vertical orientations in all of our infant groups. Thus, in very young infant monkeys a normal complement of V1 units is well suited for detecting horizontal disparity cues.

Monocular spatial properties

The experiments thus far have indicated that early binocular vision development in primates does not appear to be constrained by either a paucity of disparity-sensitive V1 neurons or qualitative differences in the nature of cortical binocular interactions. In adults, the overall ability to signal small changes in retinal disparity is known to vary with a neuron's spatial frequency-tuning characteristics (Norcia et al., 1985; Ohzawa and Freeman, 1986a,b; Ohzawa et al., 1996; Smith et al., 1996a,b). Thus, the absolute sensitivity and/or selectivity of individual cells in infants to retinal disparity and the emergence of stereopsis could be strongly influenced by the monocular spatial response properties of individual V1 units. Therefore, we determined the sensitivity of individual neurons to stimulus orientation, direction of stimulus drift, and spatial frequency as a function of age.

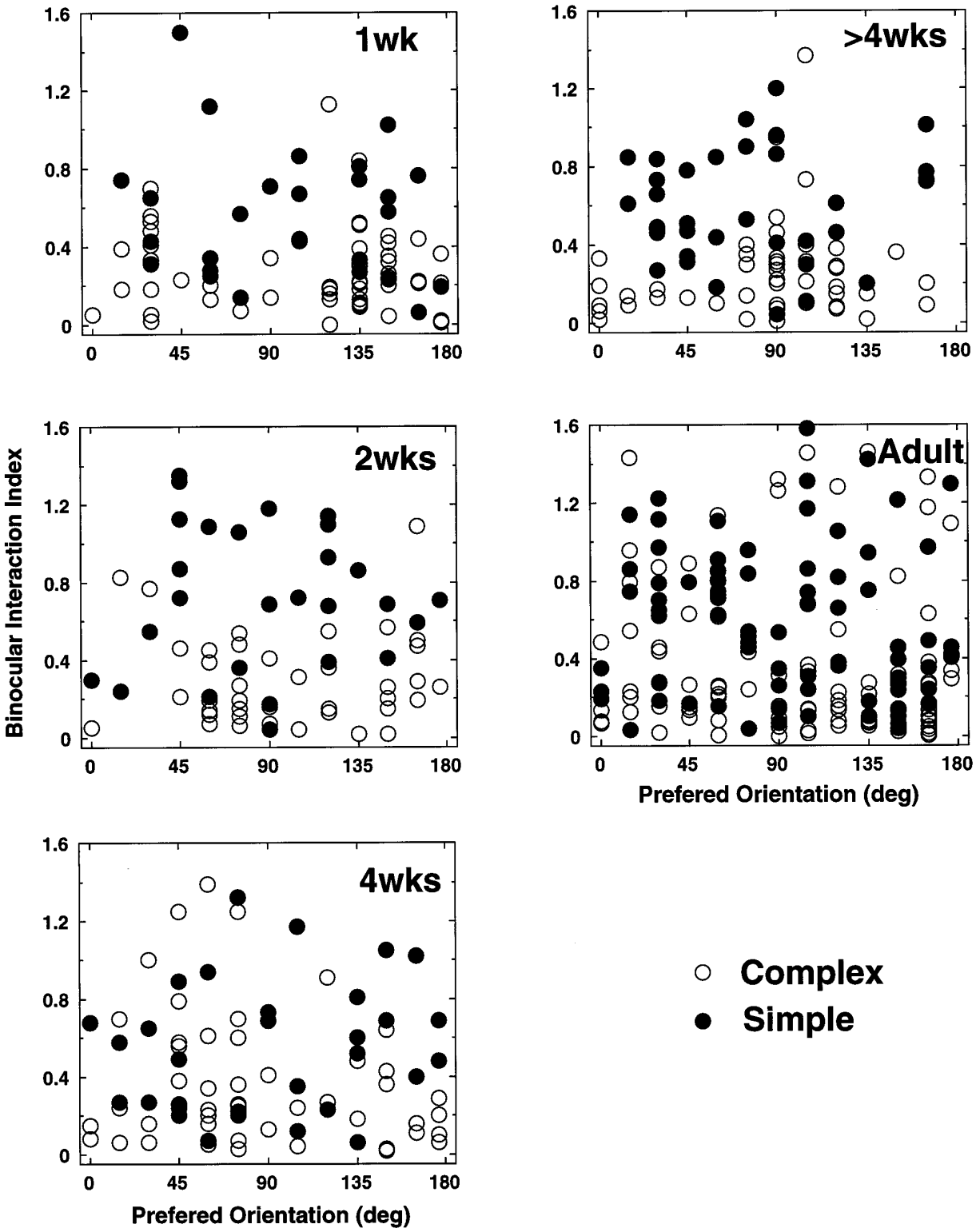

Figure 6. Scatterplots illustrating the binocular interaction index as a function of the preferred orientation for individual simple (*filled circles*) and complex cells (*open circles*). No systematic differences were found between any of the age groups.

Orientation/direction selectivity

The polar plots in Figure 7*a* show that although selectivity to stimulus orientation and drift direction was quite reasonable even in our youngest monkeys, the degree of orientation tuning appeared to be subnormal during the first 4 postnatal weeks. The orientation selectivity of individual units was quantified by measuring the full bandwidth of the tuning function at one-half the peak response amplitude. The average orientation selectivity was significantly broader at 6 d of

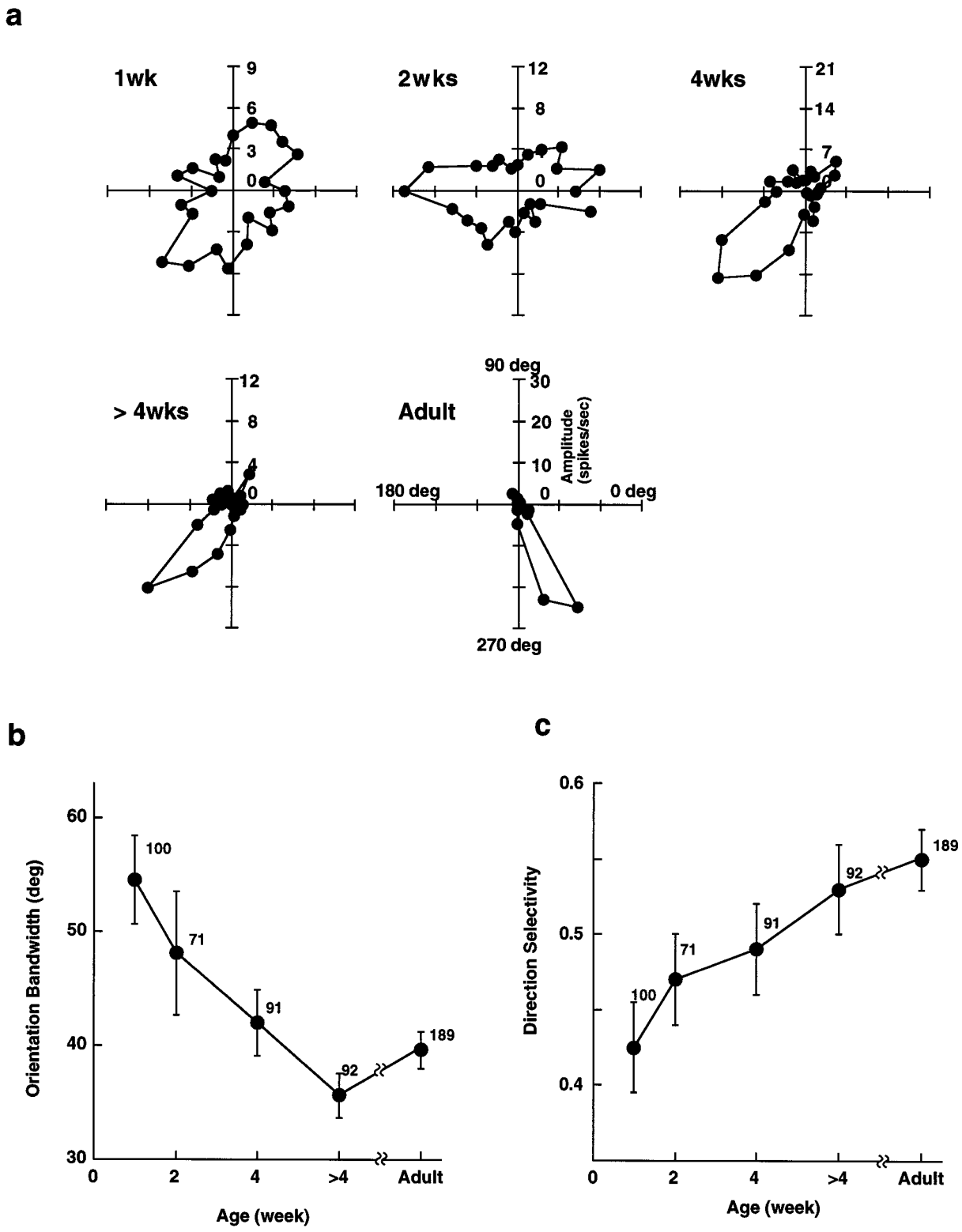

Figure 7. Orientation and direction selectivity of V1 neurons in infant and adult monkeys. *a*, Polar plots of responses as a function of stimulus orientation and drift direction in a representative unit from each age group. Response amplitudes were represented by the distance from the origin, and the angular position represents the direction of the grating's drift. *b*, The mean ± SE orientation bandwidth as a function of age. Orientation bandwidth for each unit was calculated from its orientation response function at half-maximal response amplitude. *c*, The mean ± SE direction selectivity as a function of age. A direction selectivity index was calculated by the formula: $DI = P - N/P$, where P is the response amplitude for the cell's preferred direction of stimulus drift and N represents the response to the opposite direction.

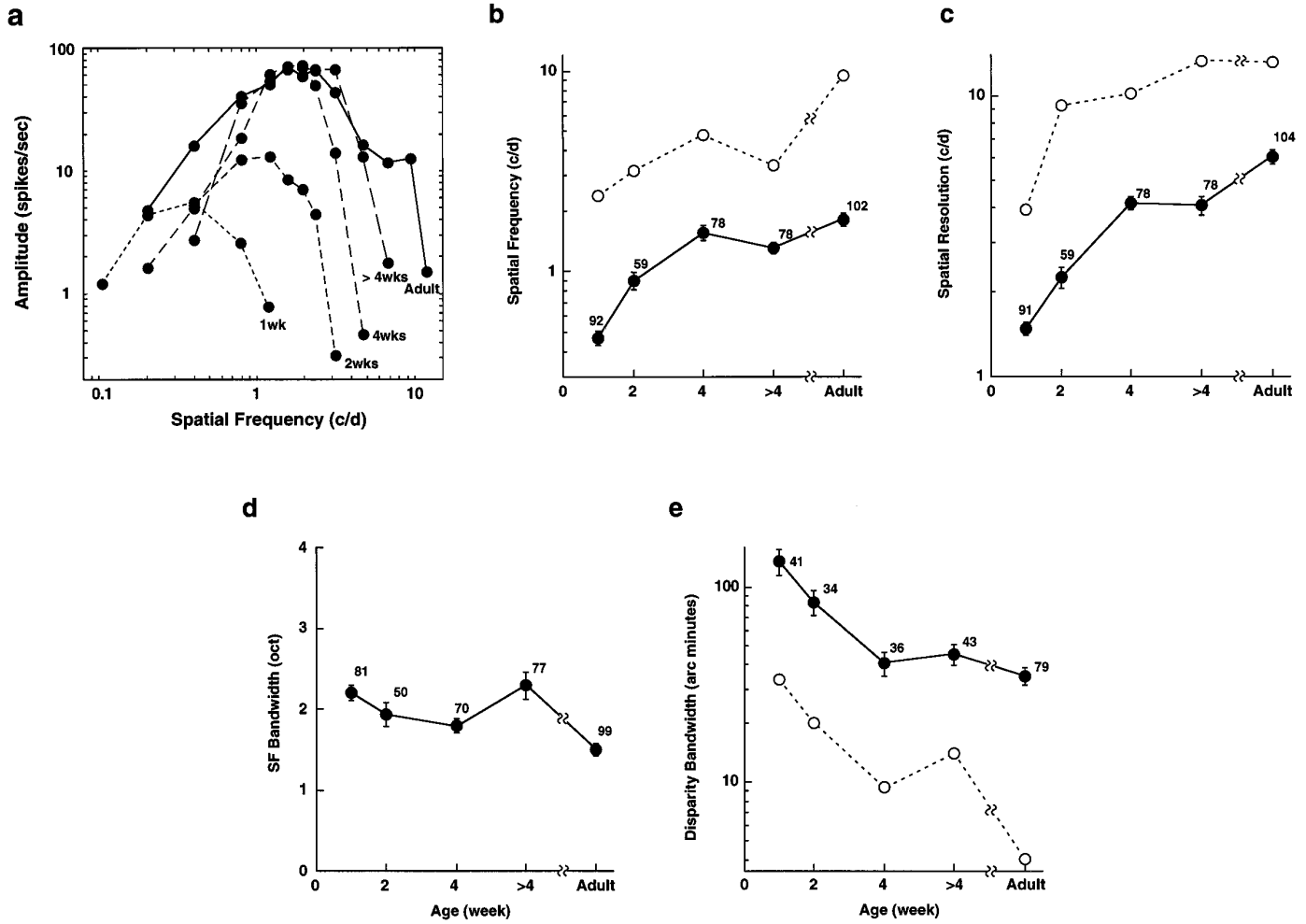

Figure 8. Development of spatial frequency tuning of V1 neurons in infant monkeys. *a*, Spatial frequency response functions for representative units from each age group. *b*, The mean ± SE optimal spatial frequency as a function of age. The data points connected with a *dotted line* illustrate the responses of the best performing cells for each age group. *c*, Mean spatial resolution as a function of age. The data for the best performing cells are connected with the *dotted line*. *d*, The mean ± SE spatial frequency bandwidths as a function of age. Bandwidth was calculated by the formula: BW (octave) = $\log_2 f_2/f_1$, where f_2 and f_1 represent the high and low spatial frequencies, respectively, at which the response dropped to half-maximal amplitude. *e*, The mean ± SE disparity bandwidth of all disparity-sensitive units (*filled circles*) and the five best-performing cells (*open circles*) as a function age. Bandwidth was calculated by the formula: BW (arc min) = 60/optimal spatial frequency (c/d) × 0.5. The formula was based on the fact that in a typical disparity-sensitive unit, a 180° phase shift would change the cell's response from maximum binocular facilitation to maximum binocular suppression.

age; however, it rapidly improved during the first 4 weeks (Fig. 7*b*). Similarly, direction selectivity showed a comparable increase during the same developmental period (Fig. 7*c*).

Spatial frequency

The representative spatial frequency response functions in Figure 8*a* illustrate the major changes that occurred in spatial tuning during early development. As anticipated, the representative unit from a 1-week-old monkey showed a very low optimal spatial frequency (0.4 c/d) and a low spatial resolution (1.2 c/d). However, the tuning function had a clear low spatial frequency roll-off (as in >90% of the units in 1-week-old monkeys) and, thus, the bandwidth can be calculated by determining the high and low spatial frequencies at which the response amplitude dropped to half-maximum. In addition, the peak response amplitude at 1 week was substantially lower than that for the adult unit. Both the optimal spatial frequency and the spatial resolution rapidly increased during the next 3–4 weeks and, over several months, there was a steady but slow improvement. The population data indicate that during the first 4 weeks the mean optimal spatial frequency (Fig. 8*b*) and spatial resolution (Fig. 8*c*) increased by >1 octave. However, only minor changes were found in the average bandwidth for the spatial frequency-tuning functions (Fig. 8*d*).

Because the absolute spatial scale for a cell's interocular phase-tuning function varies with its optimal spatial frequency (Freeman and Ohzawa, 1992), the absolute bandwidth of the binocular phase-tuning curves also decreased sharply during the first 4 weeks (Fig. 8*e*). The mean disparity function bandwidth for the 5 cells that had the highest optimal spatial frequencies improved from 40 arc min at 6 d of age to 9 arc min at 4 weeks and then gradually improved to 4 arc min for adults. The disparity tuning bandwidths for the monkeys at or older than 4 weeks of age are comparable to those previously reported for "tuned excitatory" neurons in adult V1 (Poggio and Talbot, 1981; Livingston and Hubel, 1987). These results illustrate that a cell's ability to detect a small absolute displacement between the two retinal images greatly improves during the first 4 weeks.

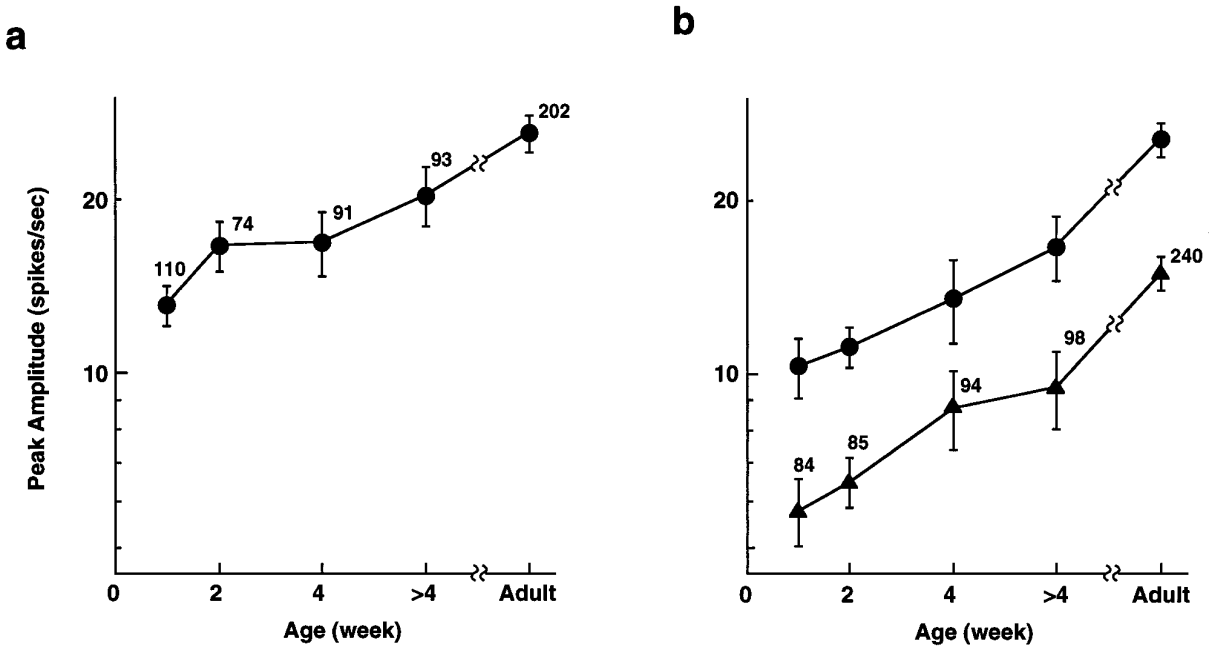

Figure 9. Responsiveness of V1 units in infant and adult monkeys. *a*, The mean ± SE peak response amplitude obtained under monocular conditions as a function of age. *b*, The mean ± SE peak response amplitude obtained for the optimal binocular (*circles*) and monocular (*triangles*) stimulus conditions during the binocular phase-tuning experiments.

Responsiveness of V1 units

In young infants, the overall responsiveness of the average neuron was exceedingly poor before 4 weeks of age (Fig. 9). However, the peak response amplitude rapidly increased, particularly during the first 4 weeks. Interestingly, the average monocular amplitude for a cell's dominant eye measured during the binocular experiments (Fig. 9*b*) nearly tripled between the age of 1 week and adulthood, whereas that obtained during the monocular experiments (Fig. 9*a*) increased only twofold. This difference may reflect a greater degree of contrast adaptation or response fatigue among infant units during the binocular experiments (Ohzawa and Freeman, 1986a; Smith et al., 1996a), which may reduce the already weak responses of units in 1-week-old monkeys.

DISCUSSION

The major finding of this study is that the binocular connections for encoding binocular disparity information are operating in a qualitatively normal manner in primate V1 only a few days after birth, if not at birth. Our results dovetail nicely with the recent anatomical findings that an adult-like cytoarchitecture exists in the visual cortex of newborn monkeys (Purves and LaMantia, 1993; Horton and Hocking, 1996). The present results also indicate that the differences in the disparity-encoding characteristics of V1 neurons between infants and adults are associated primarily with differences in absolute spatial scale.

Disparity sensitivity in V1 and the onset of stereopsis

The presence of disparity-sensitive V1 units in our 1-week-old monkeys fulfills a critical requirement for fusion and stereopsis, two of the most fundamental properties of binocular vision. Thus, the reported absence of stereopsis in monkeys before 4 weeks of age is not attributable to the lack of disparity detectors in V1 (Birch, 1993; Held, 1993; Shimojo, 1993). It is possible that stereopsis exists in neonates, but the current behavioral testing methods are not sensitive enough to detect their stereoscopic vision. On the other hand, there are a number of other reasons why stereopsis may not emerge until several weeks after birth. For example, the apparent onset delay may be caused by an immaturity in the higher-order cortical neurons that extract local disparity information from V1 neurons (Hubel and Wiesel, 1970; Maunsell and Van Essen, 1983; Burkhalter and Van Essen, 1986; Fellerman and Van Essen, 1986; Hubel and Livingston, 1987; Poggio et al., 1988; Roy et al., 1992) or by inadequate development of fusional vergence eye movements at birth (Aslin, 1993; Schor, 1993). Currently, no data relevant to either of these important alternatives exist for monkeys.

With our experimental methods, we could not measure *absolute* interocular disparities and, thus, we did not determine whether the population of neurons in infant monkeys exhibited the full ranges of optimal disparities found in adults (i.e., crossed, uncrossed, and zero disparities) (Poggio, 1995). In very young infants, *all* V1 cells could be selective for "zero" disparity or the same fixed crossed and uncrossed disparity, which would contribute to the absence of stereopsis. However, this is an unlikely possibility. For such restricted binocular properties to exist, *all* receptive fields would have to be precisely aligned on the horopter or for some fixed depth from the horopter. This would be an exceptionally difficult challenge for the processes regulating innate neuronal connections and one that is not in agreement with current anatomical findings (Florence and Casagrande, 1990; Pospichal et al., 1994). Even if all V1 units were selective for some range of either crossed or uncrossed disparities, it is unlikely that this situation would prevent stereopsis. Humans that apparently lack one pool of these "stereodetectors" can perform quite well on standard tests of stereopsis (Jones, 1977). One simply has to position binocular convergence appropriately to take advantage of the remaining pool.

The ocular dominance distributions obtained from infant monkeys in this and other studies (Wiesel and Hubel, 1977; LeVay et

al., 1980) strongly suggest that neurons tuned to crossed, uncrossed, and zero optimal disparities are probably present at birth. In adult monkeys (Poggio and Fisher, 1977) and cats (Fischer and Kruger, 1979; Ferster, 1981; LeVay and Voigt, 1988), the optimal disparities of individual units can be predicted from their ocular dominance. Cells with balanced ocularities typically have their optimum disparity near the fixation plane, whereas cells dominated by the contra- and ipsilateral eyes exhibit optimal responses for far and near disparities, respectively. Because the anatomical basis for ocular dominance columns in V1 is adult-like at birth (Horton and Hocking, 1996) and the ocular dominance distributions of infant units (Fig. 2) are indistinguishable from those of adults, it is more likely that all of the functional disparity classes of V1 units are present at or shortly after birth.

Monocular spatial properties

The data from the monocular experiments suggest that the onset of stereopsis may be constrained by an immaturity in the spatial response properties of individual V1 neurons. We demonstrated that before 4 weeks of age, nearly all simple and complex cells were selective for orientation and movement direction, which indicates that the basic mechanisms required for orientation/direction selectivity are functional near birth (Wiesel and Hubel, 1977; Wiesel, 1982). However, the abnormally broad tuning of V1 units shortly after birth (Fig. 7) also indicates cortical immaturity, which may contribute to the poor binocular performance of monkeys soon after birth. It is a matter of long-standing debate as to how orientation and direction selectivity of individual cortical cells emerge in adult monkeys and cats (Das, 1996). Regardless, the lower orientation/direction selectivity of V1 neurons in infants may arise because of abnormal spatial (Hubel and Wiesel, 1962; Ferster et al., 1996) and/or temporal (Saul and Humphrey, 1992; Reid and Alonso, 1995) summation of geniculate signals, which may be associated with the immature afferent LGN axon arbors (Florence and Casagrande, 1991; Pospichal et al., 1994) and the irregular CO patterns found in Layer IVC of neonates (Horton and Hocking, 1996). However, an immaturity in intracortical inhibitory (Sillito et al., 1980; Pei et al., 1994) and/or excitatory neuronal networks (Nelson and Katz, 1995; Somers et al., 1995) may not be ruled out as an additional factor.

We also found that before the onset for stereopsis, the average V1 neuron was tuned to relatively low spatial frequencies (Fig. 8*a–c*). The lower optimal spatial frequencies exhibited by individual units in young infants probably reflect in large part a limit imposed by immaturity in precortical structures, particularly the retina (Jacobs and Blakemore, 1988; Packer and Hendrickson, 1990). However, the spatial resolution of some LGN units in neonates appears to be significantly higher than that of V1 units in our study (J. Movshon, personal communication) and, thus, spatial and/or temporal imprecision in convergence of afferent signals also could have influenced the spatial frequency response characteristics of V1 neurons. Regardless of the underlying mechanism, immaturity in the spatial frequency response characteristics of individual neurons appears to severely limit the early development of disparity sensitivity in V1. Interestingly, the rapid improvement in spatial resolution and the concomitant increase in the cells' sensitivity to angular disparities achieved toward the end of fourth postnatal week coincides with the onset age of stereopsis in monkeys (O'Dell et al., 1991).

Responsiveness of V1 cells in neonates

Under both monocular and binocular conditions, the peak firing rates of V1 units in 1- and 2-week-old monkeys were substantially lower than those in adults (Fig. 9). The overall lower response amplitude is an additional factor that may have reduced the effectiveness of cortical disparity processing in infants. These lower response rates may have been caused by a reduction in the excitatory drive of afferent inputs, reflecting perhaps an immaturity in the photoreceptor outer segments (Parker et al., 1990) and/or the aforementioned LGN axon arbors in layer IVC. Although there is currently very little data on the normal development of intrinsic cortical connections in monkeys, a recent report (Lund and Levitt, 1996) and our preliminary study suggest that the long-range horizontal connections within V1 may also be immature, which could additionally contribute to the overall sluggishness of V1 responses (Rockland and Lund, 1983; Katz and Callaway, 1992; Nelson and Katz, 1995).

The rapid improvement in the responsiveness of V1 neurons during the first 4 weeks of life is also likely to contribute to the sudden onset of stereopsis in young monkeys. An interesting possibility is that when the responses of disparity-sensitive V1 neurons exceed a certain "threshold" binocular amplitude, they may become capable of signaling higher-order cortical neurons of the nature and magnitude of binocular retinal image disparity. Regardless, it is clear that in terms of the change in cell's absolute firing rate per unit of angular disparity, the increase in responsiveness together with the improvement in spatial resolution greatly increases absolute sensitivity to small interocular differences in image disparity.

Conclusions

The binocular signal convergence and disparity tuning of V1 neurons shortly after birth are qualitatively similar to those of adults. These results suggest that the neural connections for producing disparity-sensitive neurons are largely determined by prenatal processes. Although these binocular neural connections functionally emerge without an extensive amount of normal visual experience, the binocular properties of V1 neurons are highly vulnerable to discordant binocular input at the earliest stages of postnatal development because these disparity-encoding mechanisms begin to operate at or near birth and the primary visual cortex exhibits a high degree of plasticity during early development (Chino et al., 1994; Smith et al., 1996c).

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