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Development of Temporal Response Properties and Contrast Sensitivity of V1 and V2 Neurons in Macaque Monkeys

J. Zheng, B. Zhang, H. Bi, I. Maruko, I. Watanabe, C. Nakatsuka, E. L. Smith 3rd, and Y. M. Chino

University of Houston, College of Optometry, Houston, Texas

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Zheng J, Zhang B, Bi H, Maruko I, Watanabe I, Nakatsuka C, Smith EL 3rd, Chino YM. Development of temporal response properties and contrast sensitivity of V1 and V2 neurons in macaque monkeys. *J Neurophysiol* 97: 3905–3916, 2007. First published April 11, 2007; doi:10.1152/jn.01320.2006. The temporal contrast sensitivity of human infants is reduced compared to that of adults. It is not known which neural structures of our visual brain sets limits on the early maturation of temporal vision. In this study we investigated how individual neurons in the primary visual cortex (V1) and visual area 2 (V2) of infant monkeys respond to temporal modulation of spatially optimized grating stimuli and a range of stimulus contrasts. As early as 2 wk of age, V1 and V2 neurons exhibited band-pass temporal frequency tuning. However, the optimal temporal frequency and temporal resolution of V1 neurons were much lower in 2- and 4-wk-old infants than in 8-wk-old infants or adults. V2 neurons of 8-wk-old monkeys had significantly lower optimal temporal frequencies and resolutions than those of adults. Onset latency was longer in V1 at 2 and 4 wk of age and was slower in V2 even at 8 wk of age than in adults. Contrast threshold of V1 and V2 neurons was substantially higher in 2- and 4-wk-old infants but became adultlike by 8 wk of age. For the first 4 wk of life, responses to high-contrast stimuli saturated more readily in V2. The present results suggest that although the early development of temporal vision and contrast sensitivity may largely depend on the functional maturation of precortical structures, it is also likely to be limited by immaturities that are unique to V1 and V2.

INTRODUCTION

Visual capacities of newborn primates are limited (for recent reviews see Chino et al. 2004; Kiorpes and Movshon 2004b). Visual acuity and spatial contrast sensitivity of infant macaque monkeys become adultlike by the end of the first year of life (Boothe et al. 1988; Kiorpes et al. 2003), but higher perceptual capacities, such as the ability to integrate local information over space (e.g., contour integration), are absent until late in development both in humans (e.g., Kovacs et al. 1999) and monkeys (Kiorpes and Bassin 2003).

An emerging view on primate vision development is that the neural mechanisms that support normal maturation may reflect differential development in at least two parts of our visual brain: *1*) the "low-level mechanisms" [e.g., lateral geniculate nucleus (LGN) and V1] that functionally mature relatively early and *2*) the "mid- or high-level mechanisms" (e.g., visual cortices beyond V1), where functional maturation is progressively delayed in a hierarchical order (Barone et al. 1996; Batardiere et al. 2002; Kiorpes and Movshon 2004b; Zhang et al. 2005).

Neurons in the LGN of infant monkeys have qualitatively adultlike spatial/temporal response properties as early as 1 wk of age, although retinal development limits the contrast sensitivity and the spatial/temporal resolving power of these neurons (Hawken et al. 1997; Movshon et al. 2005). However, "ideal observer analyses" indicated that immaturities in the retina or the LGN during the first several weeks of a monkey's life do not entirely account for the reduced spatial vision and therefore additional limits must be imposed by visual cortex (Kiorpes et al. 2003; Movshon et al. 2005).

The spatial response properties of neurons in monkey V1 are far more mature near birth (Chino et al. 1997; Kiorpes et al. 2003; Rust et al. 2002; Zhang et al. 2005) than previously thought (Blakemore and Vital-Durand 1981). As early as 1 wk of age, V1 neurons are well tuned to stimulus orientation, spatial frequency, and binocular spatial phase disparity and, by 4 wk of age, qualitatively adultlike tuning is present for these response properties (Chino et al. 1997). The center–surround receptive-field (RF) organization of the majority of V1 neurons is adultlike by 2 wk of age. However, the maturation of the RF centers and surrounds of V2 neurons is substantially delayed relative to that in V1 (Zhang et al. 2005). These previous studies have begun to provide evidence for the aforementioned hypothesis of visual system development.

Human infants also have poor sensitivity to temporally modulating stimuli during the first 8 mo of life (roughly equivalent to 8 wk of age in monkeys) (e.g., Dobkins et al. 1999; Rasengane et al. 1997; Swanson and Birch 1991; but see Regal 1981). Normal maturation of "higher-order" temporal vision (e.g., motion integration) is relatively delayed and continues for ≥3 yr, although this ability was reported to be present around 2 mo of age in humans (Dobkins et al. 2004). Infant monkeys, as early as 2 wk of age, appear to be capable of using "global motion information" to control behavior (Kiorpes and Movshon 2004a).

It is not known, however, which neural structures of our visual brain may limit the maturation of temporal contrast sensitivity. Recent studies on LGN development revealed considerable immaturities in their temporal response properties and contrast sensitivity (Hawken et al. 1997; Movshon et al. 2005). However, these investigators concluded that the neural limits imposed on these functions in infant monkeys are likely to reside beyond the LGN, i.e., in V1 or beyond. Very little is known about the normal development of the temporal response properties or the contrast sensitivity of V1 neurons (Rust et al. 2002; Zhang et al. 2005) and absolutely nothing is known

Address for reprint requests and other correspondence: Y. M. Chino, College of Optometry, University of Houston, 505 J. Davis Armistead Bldg., Houston, TX 77204-2020 (E-mail: ychino@uh.edu).

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about the maturation of these response properties in extrastriate neurons. In this study, we examined the temporal frequency tuning, response timing, and contrast sensitivity of V2 neurons at 2, 4, and 8 wk of age and compared them to those in V1 to determine whether V2 and/or V1 neurons are involved in setting limits on the development of temporal contrast sensitivity. Some of the results here were previously presented elsewhere in preliminary form (Nakatsuka et al. 2006).

METHODS

Microelectrode recording experiments were conducted in anesthetized and paralyzed monkeys (*Macaca mulatta*). All experimental and animal care procedures were in compliance with the *Guiding Principles for Research Involving Animals and Human Beings* and were approved by the Institutional Animal Care and Use Committee of the University of Houston.

Subjects

Five 2-wk-old, four 4-wk-old, three 8-wk-old infant monkeys, and four adult monkeys served as subjects. The weight of infant monkeys was between 480 and 600 g in 2-wk-old, 500 and 525 g in 4-wk-old, and 550 and 750 g in 8-wk-old infants. The number of units quantitatively examined in each monkey was 50, 48, 52, 24, and 40 for 2-wk-old; 73, 30, 60, and 55 for 4-wk-old; and 51, 80, and 53 for 8-wk-old infants. The number of units examined in each adult monkey, which varied in weight between 3.9 and 5.75 kg, was 63, 67, 61, and 67.

Preparation

The surgical preparation and recording procedures were described in detail elsewhere (Chino et al. 1997; Smith et al. 1997; Zhang et al. 2005). Briefly, the 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 cannulated and all subsequent surgical procedures were carried out with additional propofol anesthesia ($4-6$ mg $\cdot$ kg^{-1} $\cdot$ h^{-1}, as needed). A tracheotomy was performed to facilitate artificial respiration and, after securing the subjects in a stereotaxic instrument, a small craniotomy and durotomy were made over the lunate sulcus. After all surgical procedures were completed, the animals were paralyzed by an intravenous injection of vercuronium bromide (Norcuron; 0.1 mg $\cdot$ kg^{-1} $\cdot$ h^{-1}) and artificially ventilated with a mixture of 59% N_2O, 39% O_2, and 2% CO_2. Anesthesia was maintained by the continuous infusion of a mixture of propofol (4 mg $\cdot$ kg^{-1} $\cdot$ h^{-1}) and sufentanyl citrate (0.05 μg $\cdot$ kg^{-1} $\cdot$ h^{-1}). Core body temperature was kept at 37.6°C. Cycloplegia was produced by topical instillation of 1% atropine and the animals' 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. Additional spectacle lenses were also used if necessary.

Recording and visual stimulation

Tungsten-in-glass microelectrodes were used to isolate the activity from individual cortical neurons. Action potentials were extracellularly recorded and amplified using conventional technology. A typical penetration for V1 recording began several millimeters posterior to the lunate sulcus and about 1.5 cm from the midline and ended when the electrode tip entered the white matter. The tangential penetrations for V2 recording (the angle of deviations from the perpendicular penetration was about 20°) were typically started right behind the blood vessel running along the lunate sulcus and also about 1.5 cm from the midline. The penetration ended when the electrode tip exited V2. All receptive fields were located within 5.0° of the center of the projected fovea.

For each isolated neuron, the receptive fields for both eyes were mapped and its ocular dominance was initially determined using handheld stimuli (Hubel and Wiesel 1962). Responses to drifting sine-wave gratings (3.1 Hz, 80% contrast) were measured to determine the orientation and spatial frequency tuning functions for each unit. The visual stimuli were generated on a monochrome monitor (VRG) with ultrashort persistence (frame rate = 140 Hz; 800 × 600 pixels, screen size = 20 × 15° at 114 cm and mean luminance = 50 cd/m^2). Recorded action potentials were digitized at 25 kHz and sampled at a rate of 140 Hz (7.14-ms binwidths) and complied into peristimulus time histograms (PSTHs) that were equal in duration to, and synchronized with, the temporal cycle of the grating (TDT data-acquisition system). Cells were classified as simple or complex on the basis of the temporal characteristics of their responses to a drifting sine-wave grating of the optimal spatial frequency and orientation (Skottun et al. 1991).

Following the determination of the preferred orientation, direction of drift, and optimal spatial frequency of each neuron, we determined its receptive-field center size. Specifically, the center of the receptive field was found by locating the position where the largest response was evoked by a 0.5° grating patch; responses were measured as a function of the diameter of the optimized circular grating patch that was positioned at the RF center. The measured area response functions were fitted with following formula (Cavanaugh et al. 2002): $R(x) = K_cL_c(x)/[1 + K_sL_s(x)]$, where $L_c(x) = [w_c \times \mathrm{erf}\,(x/w_c)]^2$, $L_s(x) = [w_s \times \mathrm{erf}\,(x/w_s)]^2$, and where x is the stimulus diameter, K_c and K_s are the gains of the center and surround, and L_c and L_s are the summed squared activities of the center and surround mechanisms. The spatial extents of the center and surround components are represented by w_c and w_s. During curve fitting, we always constrained functions so that $w_c < w_s$. Based on the area-response function of each unit, we determined the extent and size of the RF center, defined as the smallest circular grating that produced the maximum response.

After optimizing stimulus orientation/direction, spatial frequency, and size for each unit, we examined its temporal frequency tuning, visual latency, and contrast sensitivity.

Data analysis

TEMPORAL FREQUENCY TUNING. We obtained temporal frequency response functions by presenting seven temporal frequencies ranging from 0.8 to 51.2 Hz in octave steps. To determine each cell's optimal temporal frequency, temporal resolution, and tuning bandwidth, we fit our temporal frequency tuning data with a function of the following form (Movshon et al. 2005)

$$G(m_0) = m_1\exp[-(m_0/m_2)^2]/[1 + (m_3/m_0)^{m4}] \quad (1)$$

where m_0 is the temporal frequency, m_1 is a scaling constant, m_2 is the characteristic temporal frequency, m_3 sets the corner frequency of the low-frequency limb of the function, and m_4 sets the slope of the low frequency limb. We defined the characteristic temporal frequency as the frequency at which the response of the "core" of the temporal impulse function falls to 1/e of its maximum (Movshon et al. 2005) and temporal resolution as the frequency at which the response falls to 1/10th of the peak firing rate on the fit function. The bandwidth was calculated by the following formula: $\log_2 TF_2 - TF_1$, where TF_2 is the high temporal frequency at which responses became 50% of the peak firing rate and TF_1 is the low temporal frequency at which responses became 50% of the peak firing.

VISUAL LATENCY. Latency measurement was made for two different stimulus conditions in each unit, i.e., with drifting gratings for this study and with stationary gratings for a separate study (Zhang et al.

2006). We first optimized stimulus orientation, spatial frequency, and size for each unit. If a unit was a simple cell, we determined the optimal spatial phase of the unit with stationary counterphase gratings. For stimulation with drifting gratings (contrast = 80%) optimized for spatial frequency, orientation/direction, size, and spatial phase, temporal frequency was set at 3.1 Hz and drifted for 640 ms. For stimulation with optimized stationary gratings, the stimulus was turned on and off for a period of 640 ms.

Optimized gratings (drifting or stationary) were presented 100 times and responses of neurons were recorded. PSTHs were constructed from these 100 spike trains (duration = 640 ms) with a binwidth of 1.0 ms (unlike in all other measurements in which binwidth was 7.14 ms) and onset latency was computed from the histogram. For this, "noise" preceding responses to stimulus onset was calculated by counting spontaneous activity for a period of 250 ms and was described by a Poisson distribution. Visual latency was determined by measuring the time between stimulus onset and the time at which the unit's response significantly exceeded the background noise distribution over three consecutive bins (i.e., exceeded a level corresponding to a probability of $P = 0.01$)—more specifically, the time between stimulus onset and the time at which the unit's response exceeded the first of the three "significant" consecutive bins. The average latencies for drifting and stationary gratings were nearly identical for V1 and V2 neurons of all ages. *Peak latency* was determined from the averaged spike train by measuring the time between stimulus onset and the time at which a unit's responses reached 95% of its peak firing to minimize potentially high variability (jitter) in locating "peak" responses (Bair et al. 2003) (Fig. 4*A*). *Time-to-peak* was determined by measuring the time required for a unit's responses to reach 95% of its peak firing rate after the response level rose above noise (Fig. 4*A*).

CONTRAST SENSITIVITY. With optimized drifting gratings, we plotted the response amplitude of each unit as a function of stimulus contrast. We fit contrast response data with the following hyperbolic function

$$G(C) = R_m C^n / (C_{50}^n + C^n) \quad (2)$$

where R_m is maximum response, C_{50} is semisaturation contrast, and n is the slope of the function. We constrained our fits by including "zero data points," i.e., forcing data points that are ±2 SE below the noise (mean spontaneous activity) to zero. *Contrast threshold* was operationally defined as the contrast at which the fit function intersected the response level of 2 SE above the noise (Fig. 7*A*). There were substantial numbers of V1 and V2 neurons in 2- and 4-wk-old infants that did not have spontaneous activity. For such units, contrast threshold ("hard threshold") was defined as the contrast at which the fit function intersected "0" discharge.

All data used for the quantitative analysis of temporal tuning and contrast sensitivity were derived from fit functions using least-squares fit. The goodness of fit was assessed by computing the percentage of variance in data that was accounted for. Specifically, the sum of squared deviations from the mean (i.e., the total variation) and the sum of the squared deviations between the data and the predictions (i.e., the residual variation) were computed. Then the residual variation was subtracted from the total variation, which was divided by the total variation to express the variance accounted for as a percentage of the total variation. Mean goodness-of-fit (r) values for the temporal frequency tuning functions for V1 and V2 neurons were ≥0.90 (except for 0.89 for V2 in 4-wk-olds) and median r values were >0.95 (except for 0.91 for V2 in 4-wk-olds and adults). Mean r values for contrast response functions were ≥0.95 and median values were >0.97 for all infants and adults.

Statistical significance level was tested for group differences with one-way ANOVA for population means and Kruskal–Wallis tests for median values unless specified otherwise because some of our data did not meet strict criteria for "normal distribution." Also, unless specified otherwise, each significance level indicates the results of *both* tests, i.e., if a significance level was not reached in one of the two tests, the result was considered not to be significant.

Histology

At the end of each penetration, small electrolytic lesions (5 μA, 5 s, electrode negative) were made at three points along the track for later reconstruction. Experiments were terminated by administering an overdose of sodium pentobarbital (100 mg/kg) and the animals were killed by perfusion through the heart with an aldehyde fixative. Frozen sections were stained for Nissl substance and cytochrome oxidase. The laminar distribution of individual units was estimated from recording depths and electrode tracks. Our sampling was in general uniform and similar in all subject groups.

RESULTS

We quantitatively analyzed the temporal frequency response functions, visual latencies, and contrast sensitivities of 284 neurons in V1 and 332 neurons in V2 of 12 infant monkeys. Comparison data were obtained from 76 V1 neurons and 182 V2 neurons in four adult monkeys. The data from simple and complex cells were combined for the subsequent analyses because there were no significant differences in any of the response properties of interest between the cell types. All data from different experiments were derived measures from respective fit functions and are summarized in Table 1.

Temporal frequency tuning

As early as 14 days of age, the temporal frequency response functions of V1 and V2 neurons measured with high-contrast (80%) sine-wave gratings exhibited qualitatively adultlike tuning. The temporal tuning functions had distinct band-pass profiles (operationally defined as "band-pass" if the low-frequency responses of a neuron dropped to one half of its peak amplitude such that we could measure a unit's bandwidth) and the overall shape of these tuning curves did not show major changes during development (Fig. 1). Despite the band-pass profiles of representative units in Fig. 1, the median optimal temporal frequency of V1 and V2 neurons was nearly an octave lower at 2 wk of age compared with those in adults (Table 1). Temporal resolution was lower at 2 and 4 wk of age in V1 and at all infant ages in V2 (i.e., as late as 8 wk of age). Also note that at 2 wk of age, responses of the representative V2 unit were strikingly low for all temporal frequencies.

The population data in Fig. 2 demonstrate that the optimal temporal frequency, characteristic temporal frequency, and temporal resolution of V1 neurons were significantly lower at 2 and 4 wk of age than at 8 wk or in adults (Fig. 2, *A–C*) ($P < 0.01$). However, there were no differences between 8-wk-old infants and adults in any of these measures ($P > 0.8$). Similar results were previously reported by Rust et al. (2002), although the average temporal resolutions of their infants and adults, measured using the same criteria as those in this study, were lower by a factor of 3.0 than in this study.

In V2, the mean optimal frequency, characteristic temporal frequency, and temporal resolution were significantly lower even at 8 wk of age than in adults (Fig. 2, *E–G*) ($P < 0.01$). These contrasting results in V1 and V2 at 4–8 wk of age suggest that the rate of the maturation of temporal frequency tuning in V2 is slower than that in V1.

TABLE 1. *Summary of mean, median, and sample size in 2- (2W), 4-(4W), and 8-wk-old (8W), and adult monkeys*

	2W			4W			8W			Adult		
	Mean ± SE	Median	*n*	Mean ± SE	Median	*n*	Mean ± SE	Median	*n*	Mean ± SE	Median	*n*
						A. V1						
TF, Hz	5.09 ± 0.33	3.70	114	4.90 ± 0.25	4.60	88	7.77 ± 0.59	6.15	82	8.86 ± 0.42	8.35	76
TR, Hz	19.85 ± 1.17	16.30	114	17.25 ± 0.99	15.30	88	27.15 ± 1.69	25.50	82	33.98 ± 1.87	31.80	76
TC, Hz	11.67 ± 0.73	9.15	114	9.92 ± 0.63	8.94	88	15.63 ± 1.05	14.57	82	19.91 ± 1.33	17.91	76
BW, oct	3.08 ± 0.12	3.04	114	2.77 ± 0.09	2.69	88	2.90 ± 0.12	2.86	82	3.42 ± 0.12	3.35	76
OL, ms	60.36 ± 1.75	61.00	76	54.59 ± 2.44	51.00	57	49.08 ± 1.82	50.00	45	44.15 ± 1.39	42.77	71
PL, ms	87.73 ± 1.57	84.50	76	78.91 ± 2.67	75.00	57	69.15 ± 1.77	71.10	45	63.79 ± 1.50	63.00	71
Time to peak, ms	33.32 ± 1.26	31.50	76	29.09 ± 1.90	24.00	57	25.94 ± 1.34	26.00	45	24.74 ± 0.59	24.30	71
Threshold, %	8.63 ± 0.60	6.71	114	8.45 ± 0.63	6.80	100	7.30 ± 0.76	5.16	60	4.91 ± 0.40	3.81	76
R_{max}, ips	25.27 ± 2.86	16.46	93	25.46 ± 2.48	19.46	90	26.75 ± 3.01	21.26	56	30.90 ± 4.03	22.09	74
C_{50}, %	24.59 ± 1.56	20.07	93	24.82 ± 1.32	23.74	90	26.67 ± 1.89	23.00	56	20.61 ± 1.02	18.55	74
n	3.05 ± 0.19	2.56	93	2.99 ± 0.22	2.28	90	2.45 ± 0.19	2.19	56	1.95 ± 0.12	1.60	74
						B. V2						
TF, Hz	5.23 ± 0.31	4.50	100	6.09 ± 0.31	5.15	130	6.67 ± 0.37	5.60	102	9.93 ± 0.42	8.65	182
TR, Hz	18.76 ± 1.04	15.90	100	22.35 ± 1.21	17.90	130	22.78 ± 1.19	18.90	102	38.42 ± 1.75	30.95	182
TC, Hz	10.73 ± 0.64	8.43	100	13.03 ± 0.77	10.58	130	12.99 ± 0.71	11.24	102	22.53 ± 1.10	17.92	182
BW, oct	2.92 ± 0.12	2.87	95	2.84 ± 0.11	2.70	125	3.09 ± 0.12	2.98	101	3.32 ± 0.10	3.01	181
OL, ms	65.64 ± 2.71	66.00	54	62.95 ± 1.79	58.00	106	54.22 ± 1.32	52.00	67	47.34 ± 1.36	45.90	126
PL, ms	88.85 ± 2.52	92.00	54	72.87 ± 2.60	77.00	106	67.85 ± 1.65	64.80	67	63.21 ± 1.45	62.00	126
Time to peak, ms	32.10 ± 1.51	32.00	54	29.02 ± 1.03	28.00	106	23.56 ± 1.10	23.20	67	22.73 ± 0.58	22.00	126
Threshold, %	10.70 ± 1.12	7.86	64	8.94 ± 0.72	7.06	127	8.11 ± 0.89	4.79	81	5.58 ± 0.35	4.82	156
R_{max}, ips	10.73 ± 0.99	8.12	56	20.04 ± 1.73	16.47	119	23.51 ± 2.38	18.44	78	29.84 ± 2.14	21.46	153
C_{50}, %	19.51 ± 1.52	18.82	56	22.93 ± 1.46	19.83	119	25.79 ± 1.59	22.31	78	23.90 ± 1.18	20.12	153
n	3.61 ± 0.36	2.43	56	3.40 ± 0.27	2.37	119	2.84 ± 0.26	2.13	78	2.15 ± 0.09	1.85	153

The temporal frequency tuning bandwidths for both V1 (Fig. 2*D*) and V2 (Fig. 2*H*) neurons did not change systematically over age ($P > 0.1$). All V1 neurons, infants or adults, exhibited a "band-pass" profile. This result is different from the previous studies reporting that a substantial proportion of V1 neurons, particularly simple cells, exhibited "low-pass" tuning profiles (e.g., DeValois et al. 2000; Saul et al. 2005). However, we encountered more V2 neurons that exhibited "low-pass" tuning profiles at 2 (5%) and 4 wk (4%) than at 8 wk (1%) or in adults (0.6%). These differences were not statistically significant (chi-square test, $P > 0.1$).

To capture how the overall temporal frequency tuning of V1 and V2 neurons changed as a population of developing neurons, the temporal tuning profile was created for each infant age by calculating the mean (±SE) response amplitude for each temporal frequency (Fig. 3). At 2 wk of age, roughly equivalent to 2 mo of age in humans for spatial contrast sensitivity (Boothe et al. 1988), the average temporal response function had a clear band-pass tuning profile for both V1 and V2. However, the relative reduction in response amplitude for the lowest temporal frequency (0.8 Hz) was substantially less than the low-frequency roll-off in older infants or in adults.

The shape of the average temporal tuning functions of V1 and V2 neurons did not substantially change after 4 wk of age and were not different from those in adults. However, the optimal temporal frequency, the temporal resolution, and the

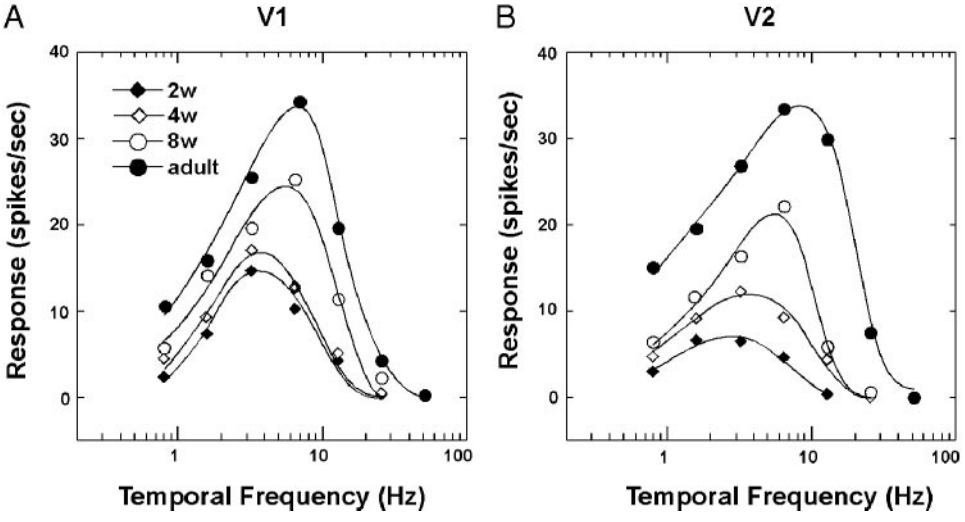

FIG. 1. Development of temporal frequency tuning functions in macaque monkeys. Representative tuning functions of primary visual cortex (V1, *A*) and visual area 2 (V2, *B*) at 2, 4, and 8 wk of age and in adults. High-contrast (80%) sine-wave gratings optimized for orientation, spatial frequency, size, and direction of drift for each unit were used as stimuli.

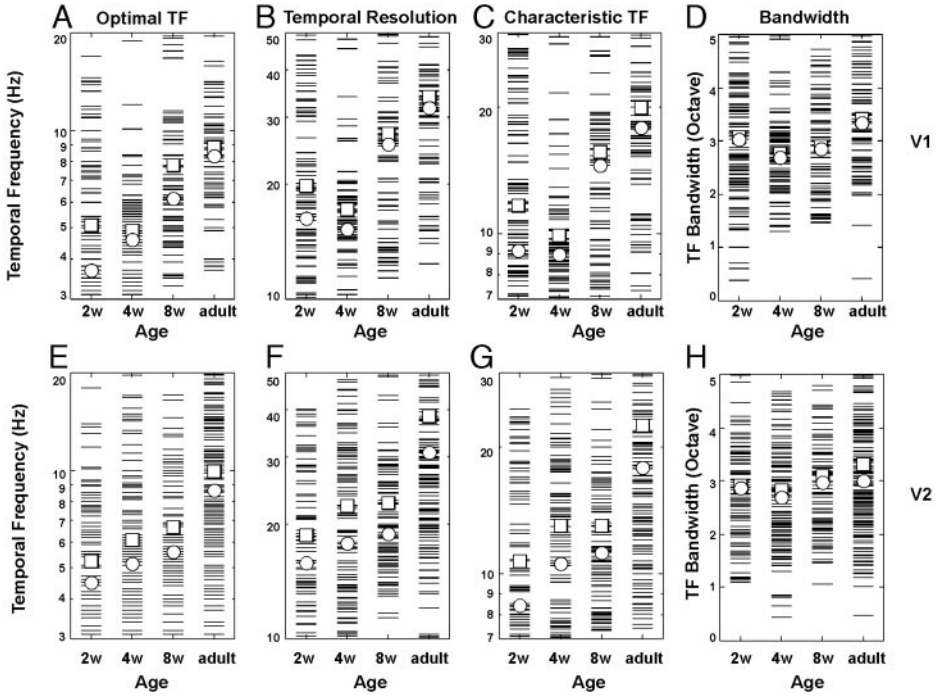

FIG. 2. Development of the temporal response properties of V1 (*top row*) and V2 neurons (*bottom row*). Population data on the optimal temporal frequency (*A* and *E*), temporal resolution (*B* and *F*), characteristic temporal frequency (*C* and *G*), and bandwidth (*D* and *H*) are illustrated in each panel. Horizontal lines indicate data from individual units. Mean (square) and median values (circles) are also indicated. Single line may represent a value for multiple units.

bandwidth determined from these average functions showed the age-dependent changes that were similar to those obtained by averaging comparable values of individual units (compare Figs. 2 and 3).

Response timing

Onset latency was determined for each unit from its average spike train by measuring the time between stimulus onset and the time at which unit's responses significantly exceeded the noise level over three consecutive bins (Maunsell et al. 1992) (Fig. 4*A*). The shortest onset latency recorded for V1 neurons in our adult monkeys was about 20 ms, which is consistent with the previously reported shortest latency for macaque V1 measured with a similar method (Maunsell et al. 1992). The onset latency of V1 and V2 neurons was significantly longer at 2 and 4 wk of age than in 8-wk-old infants or adults ($P < 0.01$), whereas the latency for 8-wk-old infants was not different from that in adults ($P > 0.1$). Similar results in V1 were previously reported by Rust et al. (2002), although the average latencies in their study, measured with the same method as that in this study, were roughly 20 ms longer in both infants and adults than onset latencies in this study. Also note that at all infant ages fewer neurons had onset latency <40 ms compared with that of adults (Fig. 4*B*). V2 neurons of infants had similar delays in onset latency except that their latency was significantly longer at 8 wk of age than that in adults ($P < 0.01$).

Peak latency was determined from the averaged spike train by measuring the time between stimulus onset and the time at which a unit's responses reached 95% of its peak firing to minimize potentially high variability (jitter) in locating the "peak" response (Bair et al. 2003) (Fig. 4*A*). Both in V1 and V2, the peak latency was substantially longer at 2 and 4 wk of age compared with that in adults ($P < 0.01$) (Fig. 5*A*). The variability in peak latencies (e.g., the range) was larger in V2

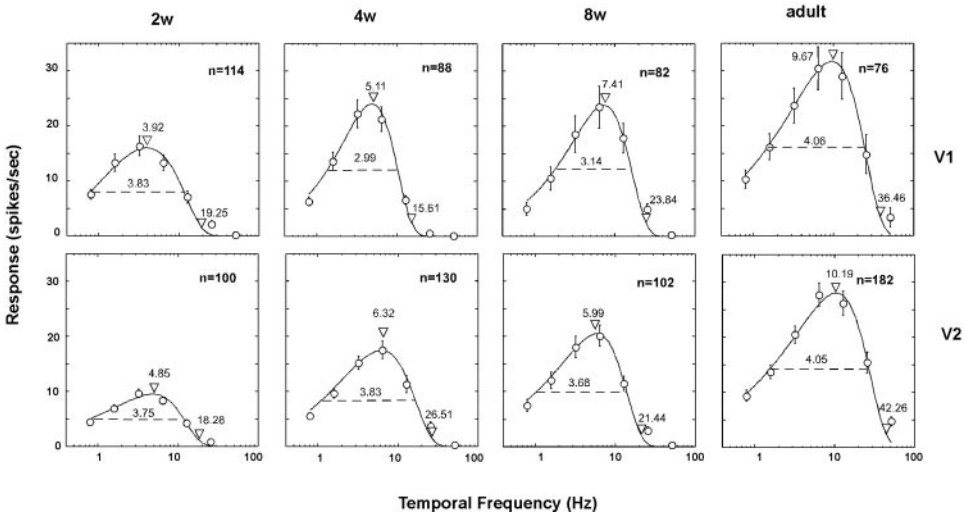

FIG. 3. Mean (±SE) temporal response functions of V1 and V2 neurons in infants and adults. Firing rate of individual units was averaged for different temporal frequencies. Optimal temporal frequency and temporal resolution are derived from fit functions and indicated by open triangles. Dotted lines with numbers indicate the bandwidth in octaves.

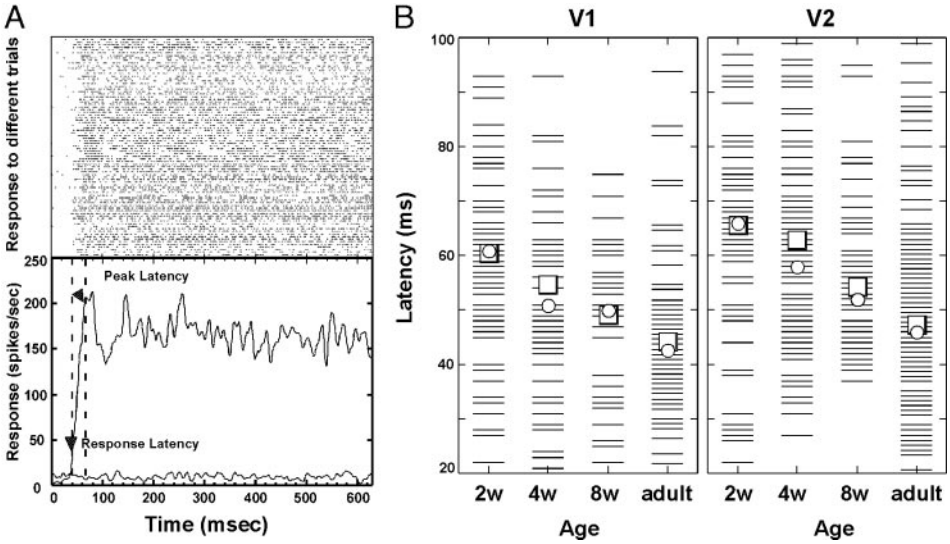

FIG. 4. Development of response timing of V1 and V2 neurons in infants and adults. *A*: methods to measure the onset latency, peak latency (time required for response to reach 95% of the peak), and time-to-peak (peak latency minus onset latency). *Top*: plot of spikes (individual dots) during a stimulus cycle (640 ms) for 100 trials. *Bottom*: responses as a function of time in peristimulus time histogram (PSTH). *B*: population data for the onset latency of V1 and V2 of infants and adults. Each horizontal line signifies an individual neuron, open squares indicate mean values, and circles signify median values. Single line may represent a value for multiple units.

at 2 and 4 wk of age because more units exhibited longer peak latencies.

The time required for a unit's responses to reach 95% of its peak firing rate after the response level rose above noise (i.e., *time-to-peak*) was longer and more variable at 2 wk of age in both V1 and V2 than in 8-wk-old infants or adults ($P < 0.01$) (Fig. 5*B*). However, only V2 neurons showed a significantly slower time-to-peak at 4 wk of age ($P < 0.01$). These results suggest that the normal maturation of cortical connections that determine the overall response timing may be slower in V2 than in V1.

In our adult monkeys, the temporal resolution of V1 and V2 neurons was in general negatively correlated with their onset latencies (Fig. 6). However, this correlation between latency and resolution in V1 and V2 was weaker in infants than in adults. For this analysis, the characteristic temporal frequency was used to characterize a unit's temporal resolving power (Movshon et al. 2005).

Contrast sensitivity

To examine the development of contrast sensitivity, we fit the responses of each neuron for different contrasts with a hyperbolic function (Albrecht and Hamilton 1982; Geisler and Albrecht 1997; Sclar et al. 1990) (Fig. 7*A*). As in other experiments, stimulation was confined to the receptive-field center of each unit. *Contrast threshold* was operationally defined as the contrast at which the fit function intersected the response level of ±2 SE above noise. As previously reported for V1 neurons of 1- and 4-wk-old infants (Rust et al. 2002) there were considerable numbers of V1 and V2 neurons in 2- and 4-wk-old infants that did not have spontaneous activity. For such units the threshold contrast was defined as the contrast at which the fit function intersected "0" discharge ("hard threshold"). C_{50} is the *semisaturation contrast* that indicates the overall sensitivity of a unit to stimulus contrast (i.e., the location of the hyperbolic function on the contrast axis); n is the *exponent* that signifies the steepness of the function; and R_m is the *maximum response* that signifies the firing rate at which the unit's responses saturate.

There was a relatively large percentage of both V1 and V2 neurons that exhibited values of $C_{50} \geq 100\%$, with no sign of response saturation at the highest contrast used in this study (80%) (Fig. 7*B*). Consequently, the measurement of R_{max} was either not possible or, if measurable, the determined values were exceptionally high and thus these units were not included in the subsequent population analysis of C_{50}, R_{max}, and n.

Figure 8*A* illustrates the contrast response functions of representative V1 and V2 neurons for infants and adults, i.e.,

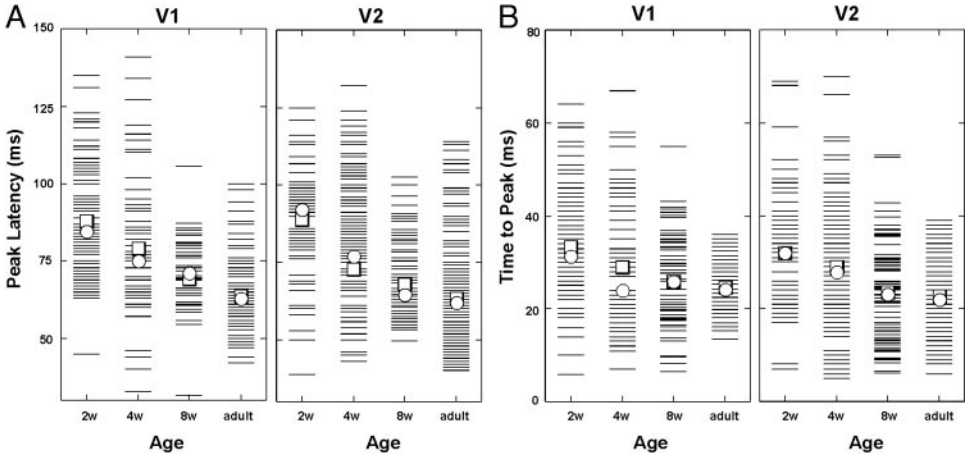

FIG. 5. Development of response timing of V1 and V2 neurons in infants and adults. *A*: population data for the peak latency of infants and adults (see Fig. 4*A*). *B*: population data for the time-to-peak in infants and adults. Each horizontal line signifies an individual neuron, open squares indicate mean values, and circles signify median values. Single line may represent a value for multiple units.

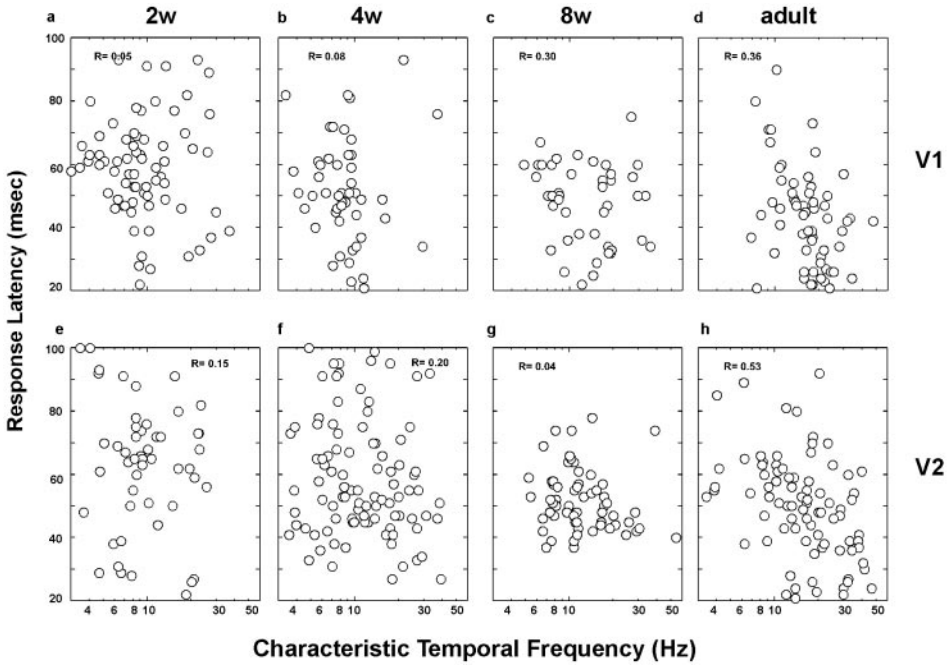

FIG. 6. Relationship between onset latency and characteristic temporal frequency of individual neurons in infants and adults. Note that the moderate negative correlations found in V1 of 8-wk-old infants ($R = 0.30$) and adults ($R = 0.36$) and the large correlation in V2 ($R = 0.53$) of adults are largely absent in infants. R values are correlation coefficients.

neurons that exhibited the threshold, C_{50}, n, and R_{max} that were closest to the respective average value for each population. The most obvious immaturity was the elevated threshold of the V1 and V2 neuron in 2- and 4-wk-old infants and lower R_m of the V2 neuron in all infants including 8-wk-old.

The distribution of contrast threshold for our population of V1 and V2 neurons in Fig. 8*B* demonstrates that at 2 and 4 wk of age, contrast threshold was significantly higher than that in adults ($P < 0.01$). However, contrast threshold was elevated but not significantly higher at 8 wk of age compared with that in adults ($P > 0.1$). The average contrast threshold of V2 neurons for our adult monkeys was similar to that reported by Levitt et al. (2001).

The mean or median R_m valueof V1 neurons did not change over age ($P > 0.1$). However, the R_m of V2 neurons at 2 and 4 wk of age, excluding "nonsaturating" units described earlier, was significantly lower than that in adults, indicating saturation at lower response levels (Fig. 9*A*). Also, the median R_m values of V2 neurons, but not mean R_m, in 8-wk-old infants were significantly lower than those in adults ($P < 0.01$).

In both V1 and V2, the slope of the contrast response function was generally steeper in 2- and 4-wk-old infants than that in adults, i.e., exhibited significantly greater n values than those in adults ($P < 0.01$) (Fig. 9*B*). Also, this trend continued for n values of V2, but not V1, neurons at 8 wk of age ($P < 0.01$). The observed steeper slopes of infant neurons are related

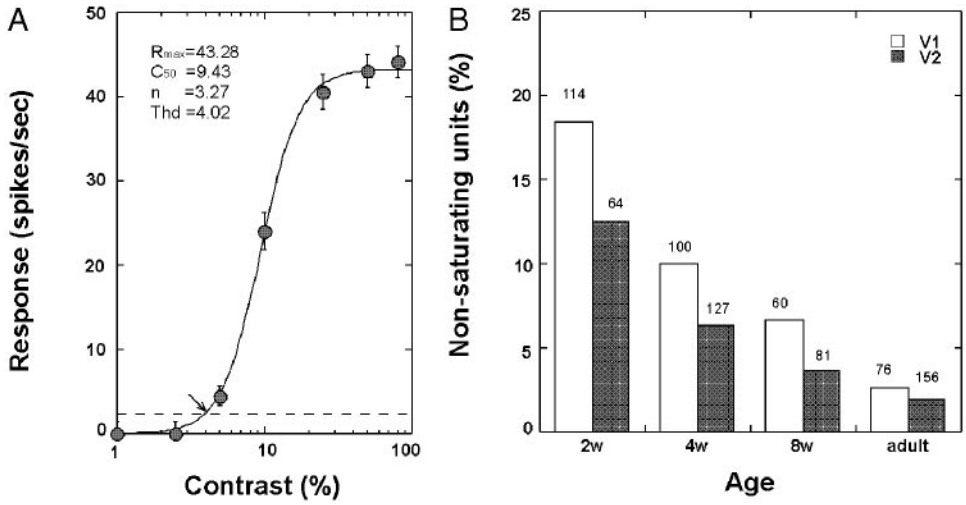

FIG. 7. *A*: methods to measure contrast sensitivity of V1 and V2 neurons in infants and adults. Responses of each unit for different contrasts were fit with a hyperbolic function (Albrecht and Hamilton 1982). We constrained our fits by introducing "zero data points", i.e., forcing data points that are ± 2 SE (dotted line) below the noise (mean spontaneous activity) to zero. Contrast threshold (Thd) was operationally defined as the contrast at which the fit function intersected the response level of 2 SE above noise (an arrow). C_{50} is the semisaturation contrast that indicates the overall sensitivity of a unit to stimulus contrast (i.e., the location of the hyperbolic function on the contrast axis); n is the exponent that signifies the steepness of the function; and R_m is the maximum response that signifies the firing rate at which the unit's responses saturate. *B*: proportion of V1 (open bars) and V2 (filled bars) neurons that did not exhibit measurable saturation at the highest contrast (operationally defined as neurons with $C_{50} > 100\%$) (Albrecht and Hamilton 1982). Number on *top* indicates the sample size.

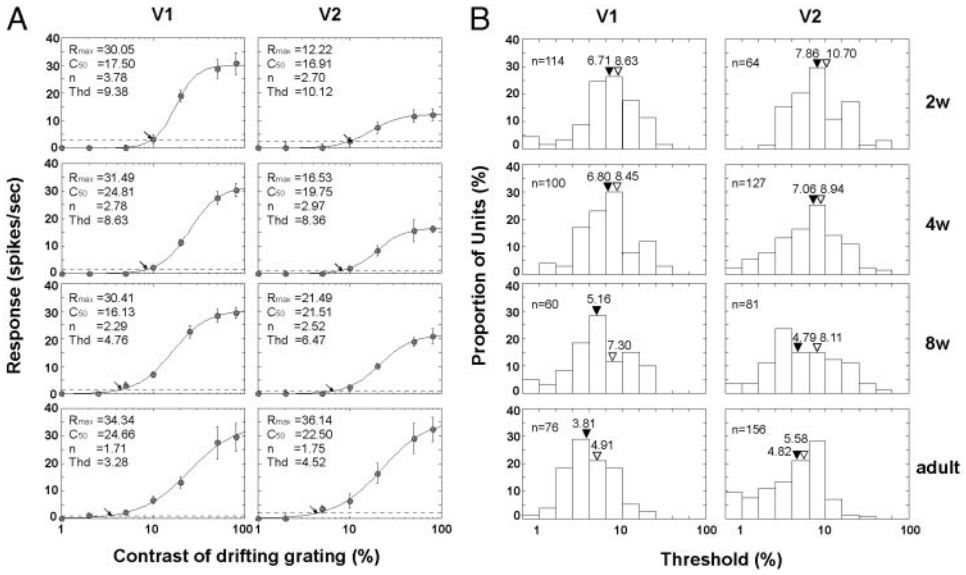

FIG. 8. Development of contrast sensitivity of V1 and V2 neurons in infants and adults. *A*: contrast response functions of representative V1 and V2 neurons in infants and adults. Units with Thd, C_{50}, n, and R_{max} values that are closest to population means were selected. Arrows indicate the location of contrast threshold in the fit function. Dotted line indicates the response level of 2 SE above noise. *B*: distributions of contrast threshold of V1 (*left*) and V2 (*right*) neurons in infants and adults. Mean (open triangles) and median (filled triangles) are shown for each group.

to higher prevalence of neurons in infants with large n values (e.g., >3.0).

The average or median C_{50} did not significantly change over age in V1 or V2 (Fig. 10*A*). This result appears to be closely associated with the observed elevated threshold, steeper slope of contrast response functions, and/or reduced R_m, in many neurons of 2- and 4-wk-old infants (Fig. 8*A*). In a related matter, we also found that the correlation between C_{50} and contrast threshold of individual neurons are not necessarily very strong in infants or adults except for V2 neurons at 2 wk of age (Fig. 10*B*), although both are excellent measures of their overall responsiveness to stimulus contrast.

DISCUSSION

The key findings of this study are that the temporal response properties and contrast sensitivity of V1 and V2 neurons were immature during the first 4 wk of life but become mostly adultlike by 8 wk of age. However, the optimal temporal frequency and temporal resolving power of V2 neurons did not reach the adult level even at 8 wk of age. The important question, then, is whether these cortical immaturities reflect the functional development of LGN neurons (Hawken et al. 1997; Movshon et al. 2005) and, if so, whether the known LGN immaturities are amplified in visual cortex.

Temporal tuning

Figure 11*A* compares the relative development of the temporal resolution of LGN neurons estimated from the published data on the characteristic temporal frequency of P- and M-cells (Movshon et al. 2005) with the characteristic temporal frequency of V1 and V2 neurons obtained in this study. Data from infants were normalized to values of 1.0 for adults. Comparing the data from multiple studies may not provide ideal results for a number of reasons. The LGN and cortical recording experiments were conducted for different animals in different laboratories and thus methodological differences may potentially confound comparisons. For example, in the LGN experiment, "integration time" was used as a measure of visual latency

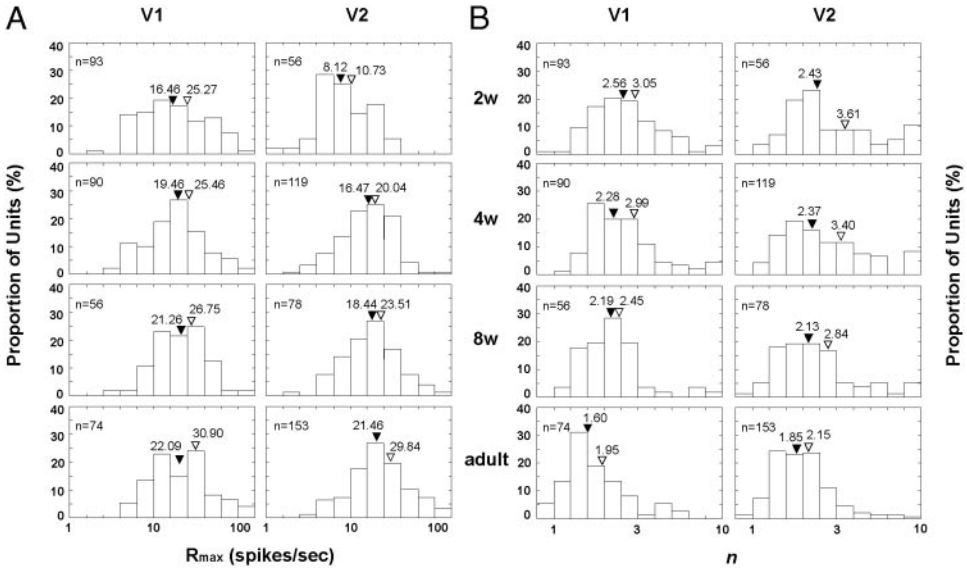

FIG. 9. Development of R_{max} and n of V1 and V2 neurons in infants and adults. *A*: distributions of R_{max} of V1 (*left*) and V2 (*right*) neurons in infants and adults. Mean (open triangles) and median (filled triangles) are shown for each group. *B*: distributions of n of V1 (*left*) and V2 (*right*) neurons in infants and adults. Mean (open triangles) and median (filled triangles) are shown for each group.

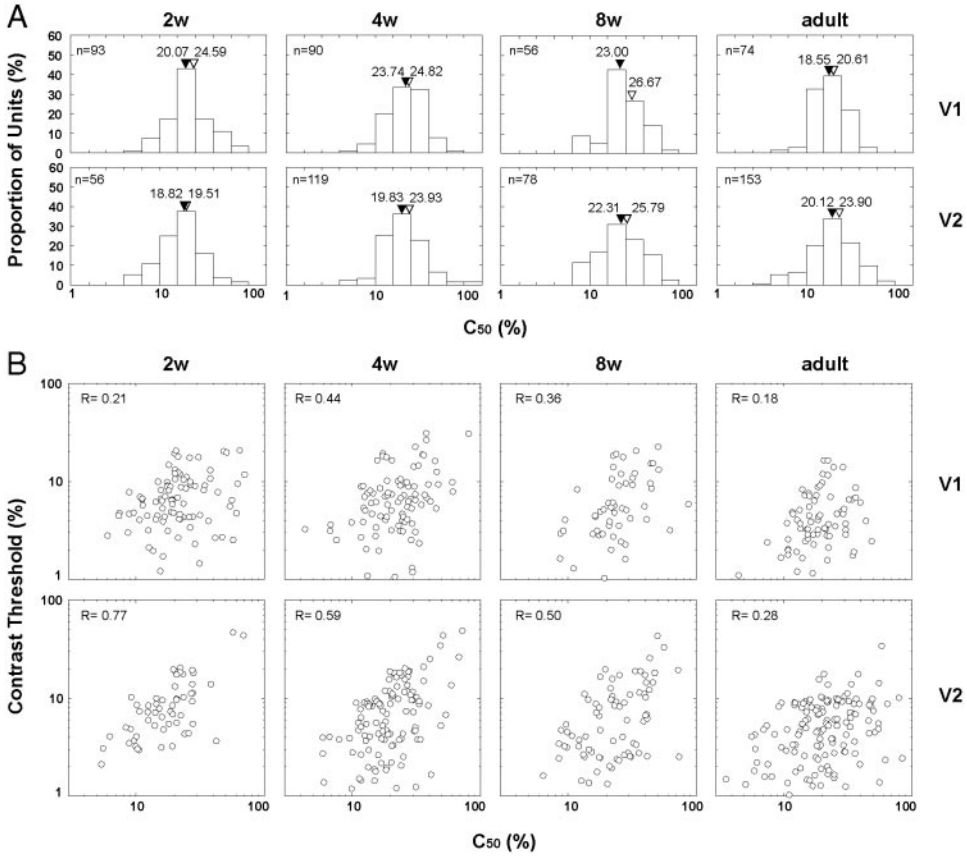

FIG. 10. *A*: distributions of C_{50} of V1 (*top*) and V2 (*bottom*) neurons in infants and adults. Mean (open triangles) and median (filled triangles) are shown for each group. *B*: scatterplots of C_{50} as a function of contrast threshold of individual V1 and V2 neurons in infants and adults.

(Movshon et al. 2005), whereas in this study we directly determined onset latency from each cell's average spike train. Also comparing cortical responses to LGN P- and M-cells is potentially confounded because of uneven convergence of these two inputs on individual cortical neurons (e.g., Maunsell and Gibson 1992; Maunsell et al. 1999; Nealey and Maunsell 1994; Nowak and Bullier 1995, 1997). Moreover, the ages of infant monkeys in these studies were different and the "adult monkeys" in the LGN study were 24 wk old or "older" (unspecified), whereas our adult monkeys were ≥18 mo old.

Despite these limitations, a relatively clear picture emerges as to the relative timing of the functional maturation of the LGN, V1, and V2. The temporal resolutions of LGN neurons at 1 and 4 wk of age and V1/V2 neurons at 2 and 4 wk of age are similar and about one half of their respective adult values. Thus the low temporal resolving power of V1 neurons in 2- and 4-wk-old monkeys found in this study may largely reflect limits imposed by the precortical structures, i.e., the LGN (Hawken et al. 1997; Movshon et al. 2005) and the retina (Hendrickson 1992; Packer et al. 1990).

An important difference in the development of temporal frequency tuning between V1 and V2 was that at 8 wk of age, the optimal and temporal resolution of V2 neurons remained significantly lower (60% adult) than that in adults, whereas the near-adult values (80% adult) were reached in V1 at this age (see Fig. 2 and Table 1). Thus the rate of

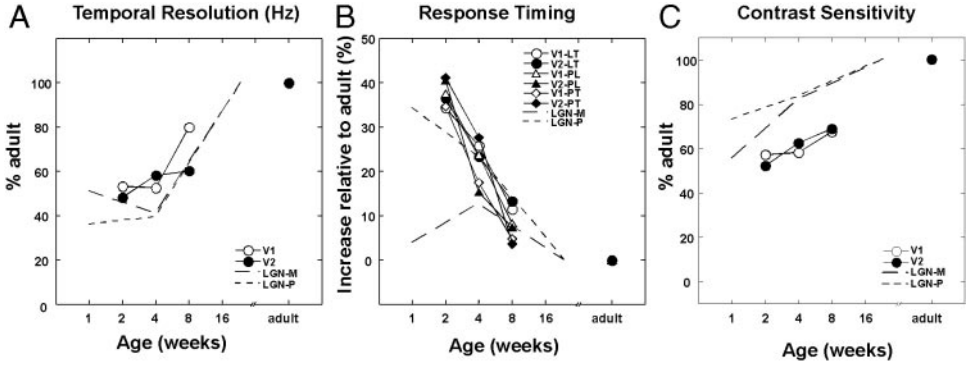

FIG. 11. Comparisons of the development of the temporal response properties and contrast sensitivity of the lateral geniculate nucleus (LGN), V1, and V2 neurons. *A*: relative maturation of temporal resolution in infant V1 and V2, LGN P- and M-cells (Movshon et al. 2005). Data from infants were normalized to value of 1.0 in adults. *B*: relative maturation of onset latency (LT), peak latency (PL), and time-to-peak (TP) of V1 and V2 neurons and the integration time of LGN P- and M-cells (Movshon et al. 2005) in monkeys. Increases relative to adults (%) were plotted for each age group. *C*: development of average contrast sensitivity in V1 and V2 and LGN P- and M-cells (Movshon et al. 2005) in monkeys. Data from infants were normalized to value of 1.0 in adults.

maturation of temporal frequency responses is slower in V2 than in V1.

The impact of the observed immature temporal response properties of V1 and V2 neurons on visual capacities of infant monkeys is difficult to assess because there are no published data on the early development of temporal vision in monkeys. However, the temporal resolving power in human infants estimated by psychophysical methods (Dobkins and Teller 1996; Dobkins et al. 1999; Rasengane et al. 1997; Regal 1981; Swanson and Birch 1990) and with P-VEP recording (e.g., Morrone et al. 1996) are known to be relatively poor during the first 4–8 mo of life (roughly equivalent to 4–8 wk of age in monkeys). Direct comparisons between our single-unit data in infant monkeys and psychophysical or VEP observations in human infants may not be optimal or may even be misleading for a number of reasons, including major differences in stimulus conditions between this and human studies. However, our data suggest that the early perceptual development of temporal vision in human infants is likely to be limited by similar immaturities in the temporal response properties of subcortical and cortical neurons.

Response timing

To make similar comparisons on response timing, the integration time of LGN neurons (Movshon et al. 2005) and visual latencies of V1 and V2 neurons in infants are compared with those in adults (Fig. 11*B*). For this comparison, we plotted the magnitude of delays (percentage increases in latency) in infants relative to that in adults. At 2 wk of age, the onset latency of V1 and V2 neurons was longer by approximately 4% relative to the adult latencies, whereas the integration time of LGN neurons in infants was increased by about 20% (10–30%) from the adult values. Thus the relative slower onset latency found in V1 and V2 arise because of longer latencies in the LGN and substantial immaturities unique to the functional connections beyond the LGN.

Another important immaturity in response timing was that the time required for a unit's responses to reach 95% of its peak firing rate from stimulus onset (peak latency) or from the time when the cell's responses significantly exceeded noise (time-to-peak) was far longer (Fig. 11*B*) and more variable (Fig. 5) in V1 and V2 of 2- and 4-wk-old infants than that in adults. These delays were greater in V2 than in V1.

A potential consequence of these immaturities in the response timing of cortical neurons may be that the feedforward signals from V1 and/or V2 to individual neurons of higher-order visual areas are slower and more variable in infant monkeys than in adults. As a result, this may influence how precisely higher-order visual neurons can integrate relatively weak signals from V1/V2 over a large distance during the first 4 wk of the monkey's life. The neural basis of relatively slower development of perceptual tasks that require precise integration of input signals is thought to be localized in higher-order visual areas (Kiorpes and Movshon 2004b; Kiorpes and Bassin 2003). Our data suggest that the neuronal limits on these tasks may begin earlier in the cortical hierarchy.

Contrast sensitivity

The summary diagram in Fig. 11*C* compares the relative development of contrast sensitivity of LGN neurons (Movshon et al. 2005) with that of V1 and V2 neurons of this study. The contrast sensitivity of V1 and V2 neurons was lower at 2 and 4 wk of age compared with that of LGN neurons. Interestingly the time course of contrast sensitivity development in V1 and V2 paralleled that of the LGN, particularly P-cells, although it is important to keep in mind that the convergence of P and M inputs to individual V1 neurons is known to be quite uneven (Maunsell and Gibson 1992; Maunsell et al. 1999; Nealey and Maunsell 1994; Nowak and Bullier 1995, 1997). Considered together, the contrast sensitivity development of V1 and V2 neurons largely reflects that of the LGN and the retina, although considerable additional immaturities are present in V1 and V2.

Behavioral consequences of the observed immaturities of contrast sensitivity in cortical neurons are not entirely clear because the behavioral assessment of contrast sensitivity for infant monkeys younger than 10 wk of age is not possible or not overly reliable (Kiorpes and Movshon 2004a,b). However, the observed 40–50% reductions in contrast sensitivity of V1 and V2 neurons during the first 4 wk of monkey's life are likely to have a large impact on their behavioral contrast sensitivity.

Slower functional development in V2

The basic connections and structural organization of the LGN, V1, and extrastriate visual areas are qualitatively adult-like by birth (Burkalter et al. 1993; Coogan et al. 1996; Horton and Hocking 1996; Rakic 1976, 1977). According to an emerging view of visual system development, however, the functional maturation of the primate visual system appears to proceed at a slower rate in higher-order visual areas (Barone et al. 1996; Batardiere et al. 2002; Kiorpes and Movshon 2004b; Rodman and Consuelos 1994; Rodman et al. 1993; Zhang et al. 2005). Some of the data in this study (such as temporal frequency tuning) and previous findings from our laboratory are consistent with this view of functional development (Table 2). We previously found that the RF surround of V1 neurons is

TABLE 2. *Earliest age when responses become indistinguishable from adults*

Property	V1			V2		
	2W	4W	8W	2W	4W	8W
Orientation direction						
Orientation bandwidth (1)	*			*		
Directional bias (2)		*			*	
Center–surround						
Surround size (3)		*				
Surround suppression (3)		*				
Center size (3)			*			*
Contrast						
Contrast threshold (3, 4)			*			*
Temporal						
Response latency (4)			*			
Optimal temporal frequency (4)			*			
Temporal resolution (4)			*			
Spatial						
Optimal spatial frequency (1)						
Spatial resolution (1)						
Firing rate						
Mean peak firing rate (1, 3, 4)						

(1) Chino et al. (1997). (2) Hatta et al. (1998). (3) Zhang et al. (2005). (4) This study.

mature by 4 wk of age, whereas in V2, the RF surround size and surround suppression are not adultlike even at 8 wk of age. These observations suggest that the intrinsic long-range connections in V2 and/or the feedback connections from higher-order visual areas that are thought to support the RF surround (Angelucci et al. 2002; Bair et al. 2003; Schwabe et al. 2006) mature later in development.

Table 2 also shows that the temporal response properties of individual V1 neurons mature relatively earlier than their spatial frequency response properties. This is consistent with the previous findings in human infants that temporal vision generally develops earlier than spatial vision (e.g., Hartman and Banks 1992; Norcia 2004). However, adultlike orientation selectivity is present in both V1 and V2 neurons as early as 2 wk of age or earlier (Chino et al. 1997; Wiesel and Hubel 1974). The cortical circuits required for the orientation selectivity of individual cortical neurons are thus present very early in life and are functioning at birth more or less as in adults. These results are consistent with the perceptual studies reporting that human neonates can discriminate the orientation of static lines (e.g., Atkinson et al. 1988; Slater and Kirby 1998).

Overall our results show that the developmental time course substantially varies for the different response properties of visual cortical neurons and that this variability in development appears to reflect the maturational status of many cortical circuits that mediate specific neuronal response properties. A general rule, however, appears to be that the functional maturation of the primate visual system is slower in higher-order visual areas than in V1.

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Present addresses: I. Maruko, Department of Ophthalmology, Fukushima Medical University, Fukushima, Japan; I. Watanabe, Department of Ophthalmology, Kawasaki Medical University, Kurashiki, Okayama, Japan; C. Nakatsuka, Department of Ophthalmology, Okayama University School of Medicine, Okayama, Japan.

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