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Contrast sensitivity threshold measured by sweep-visual evoked potential in term and preterm infants at 3 and 10 months of age

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Abstract

Although healthy preterm infants frequently seem to be more attentive to visual stimuli and to fix on them longer than full-term infants, no difference in visual acuity has been reported compared to term infants. We evaluated the contrast sensitivity (CS) function of term (N = 5) and healthy preterm (N = 11) infants at 3 and 10 months of life using sweep-visual evoked potentials. Two spatial frequencies were studied: low (0.2 cycles per degrees, cpd) and medium (4.0 cpd). The mean contrast sensitivity (expressed in percentage of contrast) of the preterm infants at 3 months was 55.4 for the low spatial frequency (0.2 cpd) and 43.4 for the medium spatial frequency (4.0 cpd). At 10 months the low spatial CS was 52.7 and the medium spatial CS was 9.9. The results for the term infants at 3 months were 55.1 for the low spatial frequency and 34.5 for the medium spatial frequency. At 10 months the equivalent values were 54.3 and 14.4, respectively. No difference was found using the Mann-Whitney rank sum T-test between term and preterm infants for the low frequency at 3 or 10 months or for the medium spatial frequency at 3 or 10 months. The development of CS for the medium spatial frequency was equally fast for term and preterm infants. As also observed for visual acuity, CS was equivalent among term and preterm infants, suggesting that visual experience does not modify the development of the primary visual pathway. An earlier development of synapses in higher cortical visual areas of preterm infants could explain the better use of visual information observed behaviorally in these infants.

Key words
- Contrast sensitivity
- Preterm infants
- Sweep-visual evoked potential
- Visual development
- Visual acuity

Introduction

The task of the visual system is to enable the localization and identification of objects by the organism. The objects are composed of surfaces and are seen against backgrounds. Their localization involves discrimination of luminance, shapes, colors and textures, that is, it involves the ability to see changes in these attributes. During the evolutionary process, human spatial vision has been optimized to detect small changes in the stimuli.

Evolution and neonatal experience are fundamental for the development of a visual system capable of functioning in the environment in which we live (1). Sensitivity to change or contrast sensitivity is thus one of the most important attributes of the visual system (2). In clinical practice, vision is most commonly evaluated in terms of the ability to see the smallest object at the highest contrast. However, this does not take into account the sensitivity to low contrasts. The spatial luminance contrast sensitivity function (CSF) gives us a more complete representation of the spatial processing capacity of the visual system than the measurement of the visual acuity at maximum contrast. Alterations of the CSF related to several pathologies have been found not to affect the visual acuity of infants and children (3-6).

The development of contrast sensitivity is poorly understood (7) and the immaturity of the photoreceptors or of the optics of the eye cannot explain the relation between the capacity of the retina to receive stimuli and contrast sensitivity (8) in infants. Few studies of contrast sensitivity development in infants are available and even fewer investigations dealing with premature infants have been reported.

Visual evoked potentials (VEPs) have been widely used to assess visual functions in infants and children with or without multiple handicaps, with high testability (9,10). A rapid method was developed to obtain VEP spatial vision thresholds. In the sweep VEP method pattern reversal gratings are swept in spatial frequency or contrast magnitude while the response amplitude is estimated online by discrete Fourier analysis and a threshold is obtained by linear interpolation (11). Development of contrast sensitivity and acuity measured by sweep-VEP has been described in term infants by Norcia et al. (12-14) who found two phases in the process. Between 4 and 9 weeks of age, overall contrast sensitivity increased by a factor of 4-5 at all spatial frequencies. Beyond 9 weeks, contrast sensitivity at low spatial frequencies remained constant, whereas sensitivity increased systematically at higher spatial frequencies (13). In another sweep-VEP study (14) the contrast sensitivity obtained for 10-week-old infants reached adult levels for spatial frequencies below 1 cycle per degree (cpd).

Rudduck and Harding (15) used the pattern-reversal VEP to evaluate preterm infants with gestational ages of at least 30 weeks and full-term infants. They found that the pattern VEPs of infants with longer gestation times had higher amplitudes and shorter latencies than those of infants with shorter gestation times, indicating a more complete maturational process.

Dobson and Teller (16) discuss the fact that spatial visual acuities assessed behaviorally are lower than those obtained from VEPs during the first 6 months of life. They consider the fact that different pathways are involved in the two techniques and attribute the difference in thresholds, in part, to the fact that the behavioral thresholds require the retrieval of a larger amount of information than the electrophysiological measurement. The longer processing pathway could explain losses of signals from high spatial frequencies due to their demodulation or loss.

Children born prematurely are at risk of impairment of visual functions (17-20) even in the absence of other neurological signs of impairment (21,22). Some studies have evaluated the spatial resolution of visual stimuli and its development in preterm infants. Kos-Pietro et al. (23) did not find differences between term and preterm infants in visual acuity assessed by the steady-state pattern-reversal VEP. These investigators suggested that the visual experience may not be the most relevant factor for visual acuity development in the preterm infants. Baraldi et al. (24) compared the visual acuity of term and preterm infants at equal gestational ages using two visual acuity tests, one performed by forced-choice preferential look (FPL) and

the other by reversal-pattern VEP. The preterm infants showed better visual acuity assessed by FPL than the term infants. No difference was detected in the VEP test.

The VEP-measured spatial resolution reflects the visual pathway processing of the information up to the level of the primary visual area, processed by the retina and geniculo-striate pathway; it indicates that the visual pathway is able to resolve the stimulus information (11). The responses may reflect pre-cortical and/or cortical activity. Since the VEP-measured spatial resolution is closely similar in term and preterm infants, the higher visual acuity presented by preterms when measured with behavioral methods could be due to processing at higher neural levels. Visual acuity corresponds to one point of the CSF, the point at which the highest spatial frequency threshold is achieved with the highest luminance contrast. Given that this point is higher in preterms, it is relevant to find out if the CSF of preterms is uniformly higher than that of term children or if it is equal for lower and intermediate spatial frequencies, diverging only at the higher end. The aim of our study was to answer this question by measuring the contrast sensitivities in term and preterm infants at 3 and 10 months of age in order to determine whether the longer visual experience of preterm infants affects the development of the CSF.

Subjects and Methods

Subjects

The subjects were 16 healthy infants with normal fundi in the ophthalmologic evaluation and without any evidence of systemic or neurological disease after thorough clinical evaluation and laboratory tests. They were referred to this study by the University Hospital of the University of São Paulo (HU-USP). Informed consent was obtained from the parents of all infants. The study was approved by the HU-USP Ethics Committee. The infants were grouped as term infants (N = 5) if their gestational age was above 37 complete weeks. Infants born prior to 37 weeks of gestation were considered to be preterm (N = 11) in accordance with the World Health Organization (WHO) (25) (Table 1). Infants were tested at 3 and at 10 months. Six volunteers with 20/20 Snellen visual acuity composed the adult control group.

Measurement of visual acuity

Stimuli and apparatus. The electrophysiological correlates of contrast sensitivity were measured by means of visually evoked potentials, using the NuDiva version of the sweep-VEP system (12,26). The stimuli were vertical sine wave gratings of 0.2 and 4.0 cpd displayed on a high-resolution video monitor (Dotronix Model EM2400-D788), with a mean luminance of 159.5 cd/m^2 comprising a visual angle of 33.6 x 25º at the test distance of 50 cm, used for the infants, and 16.8 x 12.5º of visual angle at the distance of 100 cm, used for adults. In each session, a sequence of ten levels of contrast was pre-

Table 1. Characteristic of term, and preterm infants who participated in the study.

Patient	Gestational age (weeks)	Apgar 1st min	Apgar 5th min	Weight (g)
Preterm				
1	35	8	9	1490
2	34	2	8	1770
3	27	5	7	1215
4	36	7	10	1885
5	29	6	8	990
6	28	3	8	1100
7	32	6	8	1895
8	32	7	9	1200
9	37	8	9	2865
10	32	7	10	1855
11	32	9	10	1025
Term				
1	39	9	10	3230
2	40	7	8	2280
3	39	8	9	3700
4	40	9	10	3170
5	40	9	10	3890

sented at the rate of 1 frame per second, with ten pattern reversals at each contrast. The reversal rate was 6 Hz. VEP recordings were obtained with EEG electrodes (Grass Gold Disc Electrodes, E6GH, West Warwick, RI, USA) attached to the scalp with electrode cream and cotton pads (Webril II, São Paulo, SP, Brazil). A headband (3M Coban Self-Adherent Wrap 1581, São Paulo, SP, Brazil) was used to keep the electrodes in place. The EEG was recorded from two bipolar placements (O_1 and O_2), 2-3 cm to the left and right of a common reference electrode (O_z) placed 1 cm above the inion on the midline (26). A ground electrode was placed 2-3 cm above O_z according to the ISCEV protocol (12). The EEG was amplified with a Neurodata Acquisition System (West Warwick, RI, USA) (12C-4-23 - gain = 10,000; -3dB cutoff at 1 and 100 Hz).

Procedure. When the child was alert and looking attentively at the video monitor, the experimenter activated the contrast stimulus sequence. The EEG was simultaneously recorded from the two channels and filtered in real time (sampling rate = 397 Hz) to isolate the VEP. The recordings were digitized and a discrete Fourier transform (DFT) was applied to measure amplitude and phase over a 1-Hz band centered on the second harmonic of the visual stimulation frequency. The test was performed binocularly in a darkened room. Throughout each trial small toys hanging in front of the video monitor were moved by the experimenter to attract the child's attention and to maintain its fixation approximately at the center of the screen.

Analysis. Sweep-VEP correlates of contrast sensitivity were estimated using an automated algorithm. This algorithm performs a linear fit of the data relating the sweep-VEP second harmonic amplitude to linear contrast. For each spatial frequency the threshold contrast is considered to be the value of the extrapolation of this function to zero amplitude. A signal-to-noise ratio of 2:1 at peak amplitude for individual trials and 3:1 for the average was required. A threshold was obtained for each channel. Three to 12 repetitions of the sweep-VEP were run until at least three whose highest contrast peaks met the signal-to-noise ratio with a constant phase could be chosen for averaging (27). The final contrast sensitivity estimates are reported as percent (%).

Results

Contrast thresholds were obtained for all infants. The mean (± SD) contrast threshold of the preterm infants at 3 months was 55.4 ± 7.8% for the low spatial frequency (0.2 cpd) and 43.4 ± 7.4 for the medium spatial frequency (4.0 cpd). At 10 months the low spatial contrast threshold was 52.7 ± 5.1% and the medium spatial contrast threshold was 9.9 ± 4.1%. The results for the contrast thresholds of the term infants at 3 months were 55.1 ± 6.8 for the low frequency and 34.5 ± 12.1% for the medium spatial frequency. At 10 months the equivalent values were 54.3 ± 5.2 and 14.4 ± 3.7% (Figure 1). The adult contrast thresholds to low and medium spatial frequencies were 24.6 ± 9.1 and 1.9 ± 0.7%, respectively. A statistically significant difference was found between all infant groups and adults for low spatial frequency ($P = 0.008$) and for medium spatial frequency ($P \leq 0.001$; Figure 1).

The development of contrast sensitivity was different for each spatial frequency evaluated, both for term and preterm infants. Only 5 preterm and 2 term infants were evaluated at 3 and 10 months. A greater improvement in sensitivity was found for the medium spatial frequency ($P = 0.004$) compared to the low spatial frequency (Figure 2). No statistically significant difference was found between the term and preterm contrast thresholds for any situation: low spatial frequency at 3 months ($P = 0.858$) and 10 months ($P = 0.571$) and medium spatial frequency at 3 months ($P = 0.390$) and at 10 months ($P = 0.857$).

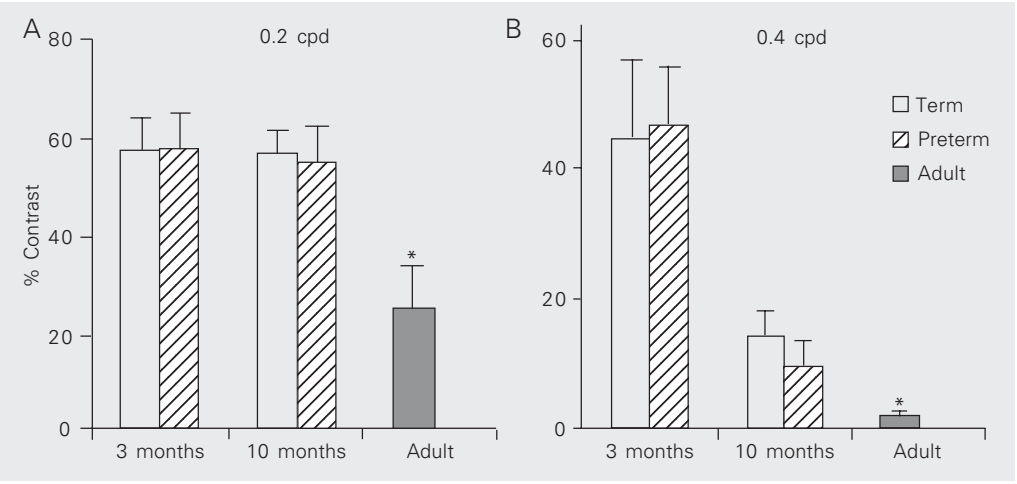

Figure 1. Contrast thresholds of term and preterm infants at 3 and 10 months of age and of adults. Data are reported as means ± SD. No significant difference was found between term and preterm infants but both differed significantly from adults for low spatial frequency (P = 0.008; A) and for medium spatial frequency (P ≤ 0.001; B; Mann-Whitney rank sum T-test).

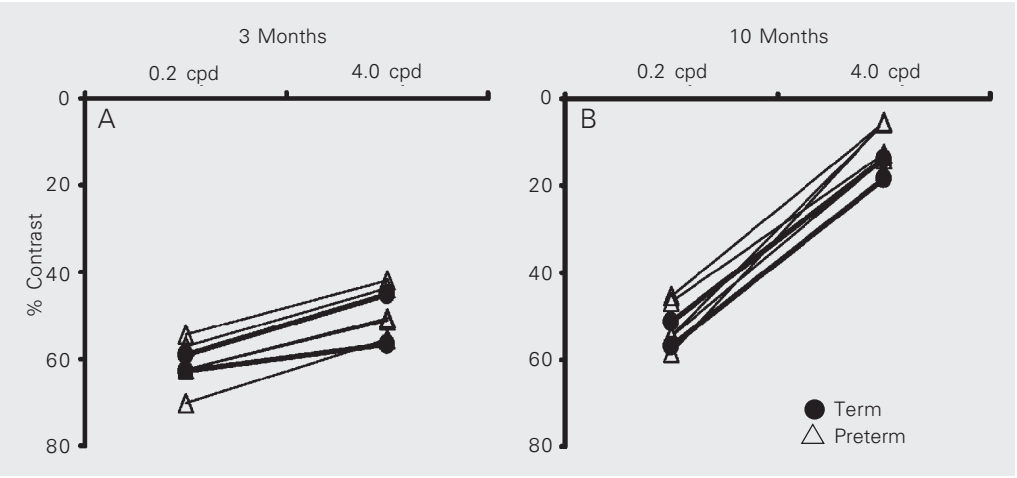

Figure 2. The development of contrast sensitivity thresholds for low and middle spatial frequencies at 3 months (A) and 10 months (B) in term and preterm infants. The middle spatial frequency contrast threshold developed faster in both groups (P = 0.004; Mann-Whitney rank sum T-test). Preterm subjects are plotted with thin lines and term infants are plotted with thick lines.

Discussion

The measurement of visual development of term and preterm infants is important because the visual system of infants of the same age but with different periods of visual experience can be compared. This could help to elucidate aspects of visual development that still remain unknown.

Dubowitz et al. (28) showed that in the first weeks of life, probably up to the first month, when the infants are not visually attentive, the VEP recordings consist of long-latency potentials that have been suggested to represent the visual activity of extra-geniculate projections from mesencephalic and nonspecific thalamic nuclei, rather than from the direct and specific retino-geniculo-cortical visual pathways. After this period and coinciding with responsive smiling, the VEP consists of a short-latency potential, which has been attributed to activity in the retino-geniculo-striate pathway (28,29). Long-latency responses are also present in children with delayed visual maturation and in children with cortical blindness. The age of the infants that participated in the present study and their good attention to visual stimuli indicate that our recordings reflect a cortical response. Another aspect indicative of a cortical response in our VEP recordings is the relatively high temporal rate of stimulation that we used. At this rate the thalamic responses, which appear at a simulation frequency of

about 1 Hz, are excluded (29).

We found no difference in the contrast sensitivity of term and healthy preterm infants using the sweep-VEP. This result agrees with the previously reported lack of difference between term and preterm infants for visual acuity, measured by the reversal pattern VEP response (16). Since we measured differences in contrast sensitivity processed by the visual pathway at the level of the primary visual cortex, our result suggests that the primary visual cortex processing of term and preterm infants is closely similar.

The longer visual experience of preterm infants did not result in a lower contrast threshold (or higher contrast sensitivity) in the early period of life, but it could provide a background for faster development. However, our measurements at the end of the first year of life did not indicate this. The present results show that the development of contrast sensitivity does not differ between term and preterm infants for the spatial frequencies that were tested. This has also been found for visual acuity (24). The present results do not confirm the conclusion by Norcia et al. (14) that 10-week-old infants reached adult contrast sensitivity thresholds for low spatial frequencies. Our data indicate that the development of contrast sensitivity is much slower in both term and preterm infants, for low than for middle spatial frequencies, with no difference in thresholds between 3 and 10 months for the 0.2 cpd stimulus. At this age, the thresholds for low spatial frequencies are much higher than for adults, but for the middle frequency tested there was a large change showing thresholds approaching the adult value. This indicates a high development age for the CSF in consonance with what happens to visual acuity.

It is well known that visual development is experience-dependent. These preliminary results on contrast sensitivity, in association with other studies of spatial resolution (23,24) performed on term and preterm infants, suggest that the longer period of visual experience of preterm infants does not affect the capacity of the visual system to resolve spatial stimuli. The experience of preterm infants probably affects the synapses of the cortical visual areas that process visual information at higher levels and in the visual association cortex. According to Diamond (30), the higher cortical areas are more receptive to environmental richness than other cortical areas, with corresponding effects on behavior.

Experience during the critical period is necessary to guarantee the normal development of the visual pathways and their functions and it is well known that interruptions of sensory experience during this period may lead to impairment of visual function (31). The length of exposure to visual experience should affect the development of synapses in the association cortex in order to enable the subject to use optimally the inputs of visual information. In newborn infants deprived of pattern vision by cataracts, it has been shown that visual acuity was not better than at birth at the time of cataract removal, regardless of the age of the infants (1 week to 9 months). However, 1 h of visual input was sufficient to improve visual acuity significantly, showing that visual acuity depends on patterned visual input, which promotes rapid visual acuity development (32).

The present results show that the additional experience of preterm infants compared to term infants does not improve contrast sensitivity measured by VEP, excluding this level of processing as a possible beneficiary of this experience, at least within three months after the onset of visual experience. Perhaps differences could have appeared at earlier ages. A possibility exists that differences between preterm and term infants can be found in behavioral measurements of contrast sensitivity, as shown for visual acuity by Baraldi et al. (24) and as suggested by Diamond's studies (30).

The questions touched upon here are also relevant to amblyopia, which is a condition

arising from deprivation of patterned vision, as opposed to the situation of the premature infant, who is exposed to patterned stimuli for a longer time than term infants.

The additional visual exposure due to prematurity does not allow the infants to see much more, but may improve the processing and use of what they see.

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