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Effects of prematurity on the development of contrast sensitivity: Testing the visual experience hypothesis

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ABSTRACT

In order to investigate the effects of visual experience on early visual development, the current study compared contrast sensitivity across infants born with different degrees of moderate-to-late prematurity. Here the logic is that at any given postterm age, the most premature infants will have the oldest postnatal age. Given that postnatal age is a proxy for visual experience, the visual experience hypothesis predicts that infants who are more premature, yet healthy, should have higher sensitivity. Luminance (light/dark) and chromatic (red/green) contrast sensitivities (CS) were measured in 236 healthy infants (born −10 to +2 weeks relative to due date) between 5 and 32 weeks postterm age from due date and 8–38 weeks postnatal from birth date. For chromatic CS, we found clear evidence that infants who were most premature within our sample had the highest sensitivity. Specifically, 4–10 additional weeks of visual experience, by virtue of being born early, enhanced chromatic CS. For luminance CS, similar but weaker results were seen. Here, only infants with an additional 6–10 weeks of visual experience, and only at later age points in development, showed enhanced sensitivity. However, CS in preterm infants was still below that of fullterm infants with equivalent postnatal age. In sum, these results suggest that chromatic CS is influenced more by prematurity (and possibly visual experience) than luminance CS, which has implications for differential development of parvocellular and magnocellular pathways.

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1. Introduction

Whether early visual experience in the beginning of life alters visual perception is a question that has garnered much scientific attention, typically in experiments with animals. This literature shows that the experimental *absence* of early visual input clearly disrupts many visual functions, which is generally taken as evidence that early visual maturation requires some form of visual input. Deprivation of either color or motion input disrupts processing for these visual attributes, while processing of other information is intact, suggesting the visual system develops in accordance with the natural statistics of visual input (Cynader & Chernenko, 1976; Pasternak, Merigan, & Movshon, 1981; Sugita, 2004). Another way to address the influence of early visual experience has been to expose a developing animal to a *selective* set of visual inputs. For example, in kittens reared in a visual environment that is biased towards one orientation, the representation of the experienced orientation occupies a larger part of the cortex, suggesting that neurons shifted their preference towards the experienced stimulus (Blakemore & Cooper, 1970; Sengpiel et al., 1998). A third way to address the influence of early visual experience is to measure the effects of *enriched* visual environments. Greenough and colleagues showed that raising animals in enriched cages with changing landmarks and multiple littermates (as compared to unremarkable or impoverished environments) increased cortical synaptic density (Sirevaag & Greenough, 1985, 1987; Turner & Greenough, 1985; Volkmar & Greenough, 1972) and dendritic lengths (Wallace et al., 1992), shaped which synapses were pruned (Greenough & Chang, 1988), and improved behavioral maze performance (Galani, Coutureau, & Kelche, 1998; Mohammed, Jonsson, & Archer, 1986; Mohammed et al., 1990). Altogether, the results from these animal studies of total or partial visual deprivation, selective exposure, and enriched environment support the notion that visual maturation is guided by early visual experience.

Yet, surprisingly, in studies of infant development, it is often assumed that very early visual experience during the early neonatal period has no effect on visual maturation, which is instead driven primarily by genetically-driven biological factors (Clark & Clark, 1976; Kagan, 1984; discussed in Hooks and Chen (2007) and Akerman, Smyth, and Thompson (2002)). Reports of effects of visual experience on visual maturation in *humans* is much harder to come by, as it is not ethical to expose infants to selective environments. Generally, evidence in rare cases of individuals who had congenital visual disorders does support the notion that visual experience is necessary for normal visual development (Birch et al., 1993, 2009), in line with animal studies. However, such evidence

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does not speak to whether visual experience guides visual maturation in an instructive manner. One way to address the influence of early visual experience is to study development in *preterm* infants. Here, the question is whether the additional time spent in the world (by virtue of being born early, which affords them extra visual experience) accelerates visual maturation.

Human infants born prematurely do receive, and can respond to, visual input before term age, and thus there is reason to hypothesize that visual experience shapes maturation during this period. Neuronal cell generation and differentiation at the fovea are complete by 29 weeks gestation (Maldonado et al., 2011; Provis et al., 1985), and the optical quality based on fundus exams of preterms at term age is rather good (Candy, Wang, & Ravikumar, 2009). Pupillary and blink responses to light are present after 25 weeks gestation (Finnstrom, 1972; Robinson, 1966), tracking responses appear after 33 weeks, and pattern preferences are seen after 34 weeks of gestation (Dubowitz, 1979; Dubowitz et al., 1980). Extensive brain development, particularly myelination, is occurring in the last trimester and in the first weeks after term age (Huppi et al., 1998). It is likely then that the visual stimulation before and shortly after term age could have an impact on premature infant's visual and neural maturation, even if spatial vision is quite poor in the first few months (Dobson & Teller, 1978).

The majority of studies on preterm infants that can address this "visual experience" hypothesis have studied infants with low or very low birth weight (under 1500 g) who were born generally under 30 weeks gestation. It is well accepted that this subset of premature infants has a high morbidity of neurological and ocular abnormalities (Atkinson et al., 2008; Birch & O'Connor, 2001; Maalouf et al., 1999; MacKay et al., 2005; O'Connor, Wilson, & Fielder, 2007; O'Connor et al., 2004; Rezaie & Dean, 2002). These infants are also at risk for later visuocognitive impairments during childhood due to ocular or neurological complications arising from their low birth weight or extreme prematurity (Downie et al., 2003; Jakobson, Frisk, & Downie, 2006; MacKay et al., 2005; Pennefather & Tin, 2000). For this reason, the visual experience hypothesis stated above is best addressed using mildly/moderately premature infants born after 30 weeks gestation, who are at lower risk for ocular and brain impairment (Hemgren & Persson, 2004; Vollmer et al., 2003).[1]

To address the visual experience hypothesis, in a previous study, we tested luminance and chromatic contrast sensitivity in healthy premature infants who had normal brain scan results and were born 5–8 weeks prior to term (Bosworth & Dobkins, 2009). In that study, we asked whether preterm infants' contrast sensitivity developmental trajectories *matched* or *exceed* what was expected based on their postterm age.[2] The rationale was that if preterm infants show the same developmental trajectories as fullterm infants when plotted with respect to postterm age, then this scenario would indicate that the preterm infants' additional time since birth (and extra visual experience) did not influence visual development. Conversely, if the visual developmental trajectories of preterms *exceeded* those of age-matched fullterm infants, when matched in postterm age, this would be evidence in favor of the visual experience hypothesis, that is, showing evidence that early experience does influence visual maturation. Results of that study showed that preterms and fullterms, matched for postterm age, performed similarly for luminance (dark/light) contrast sensitivity, but for chromatic (red/green) contrast sensitivity, preterm infants outperformed fullterms. Because luminance and chromatic contrast sensitivities are thought to be mediated by the magnocellular (M) and parvocellular (P) visual pathways, respectively (Lee et al., 1990; Shapley, 1990; Smith et al., 1995), these results suggest that the P pathway is affected by the additional visual experience in preterms to a greater degree than is the M pathway. In support of the notion that P pathway development relies more on visual experience than the M pathway come from studies investigating amblyopic adults who had abnormal visual experience during development. The bulk of those studies report greater deficits in aspects of vision thought to be mediated by the P pathway (Davis et al., 2006; Demirci et al., 2002; but see Zele et al., 2007).

Most studies, including our previous study, investigated a group of preterm infants, collapsed across a considerable range in the severity of prematurity, and compared the two groups of preterms vs. fullterms. Collapsing across a wide range of gestational lengths would create a heterogeneous subject population, possibly obscuring true effects of prematurity. This may explain why some results from previous studies are mixed in terms of whether the visual development of premature infants was the *same* as fullterms when matched on postterm age (Dobson, Mayer, & Lee, 1980; Kos-Pietro et al., 1997; Mirabella et al., 2006; Oliveira et al., 2004) or *exceeded* fullterms when matched in postterm age (Norcia et al., 1987; Roy et al., 1995; Roy, Lachapelle, & Lepore, 1989; Sokol & Jones, 1979; Tsuneishi & Casaer, 2000; van Hof-van Duin & Mohn, 1986). It stands that if visual experience has an effect on visual maturation, then greater prematurity could have greater acceleration effects upon visual maturation. To investigate this, the current study is a follow-up to Bosworth and Dobkins (2009), with a larger sample of preterm infants over a wider range of gestational ages and comparing groups of infants born at different degrees of prematurity. Specifically, we compared groups of infants born at 32, 34, 38, and 40 weeks gestation (i.e., born 8, 6, 2, and 0 weeks premature). In doing so, the current study asked whether effects of visual experience are additive, such that the more visual experience an infant has (within the healthy mildly or "late" preterm period), the greater the impact on visual sensitivity. Moreover, like the previous study, we attempted to circumvent potential confounds of neurological insult by testing only healthy "late" preterm infants who were born no more than 9 weeks premature. This moderate-to-late preterm range currently accounts for more than 70% of all preterm births and is the fastest growing population of birth rates in the United States over the past two decades (Davidoff et al., 2006).

2. Method

2.1. Subjects

2.1.1. Subject populations

Infants were recruited by mass mailings of 3000–4000 letters sent each month to new parents residing in San Diego County, and parents who were interested called our laboratory to schedule testing. Because we employed red/green isoluminant stimuli, we excluded infants with a greater than 50% chance of colorblindness, for example, male infants whose maternal grandfather was known to be colorblind. To further ensure that all our infants were generally healthy, inclusion criteria included: at the time of birth, no indication of hypoxia or fetal stress; less than 2 days of assisted ventilation in the NICU after birth; and, between birth and while enrolled in our study, no history of surgery, hospitalizations,

[1] Approximately 20% of infants born at 30 weeks gestation or less have abnormal cranial ultrasound results, whereas infants born over 30 weeks have only a 1% incidence of abnormal brain scans, and infants born at 32 weeks or older have a 0.1% incidence (Harris et al., 2007). Thus, the population of preterm infants born over 30 weeks is significantly healthier. It is this population that appeals to us as a means to address hypotheses about whether visual maturation is guided by "pre-programmed" biological maturation or visual experience, in the absence of confounding brain impairment.

[2] This age has many terms such as postconceptional, adjusted, and postterm age, which are equivalent descriptions, with the former being used to emphasize the length of the gestational period and the latter being used to emphasize the "adjusted" postnatal age, or the age the preterm infant would be if they were born at term (at 40 weeks gestation). We use postterm age to represent, conceptually, the infant's "biological" age.

Table 1
Infants were binned within four "birth groups", which we refer to as −8, −6, −2, or 0 weeks. Pre/post maturity is defined as the number of weeks between birthdate and due date, with negative values meaning infants were born early and positive values meaning they were born late.

Birth group	Count (N = 236)	Prematurity		Postterm age		Postnatal age		Birth weight (lbs)	
		Average	Range	Average	Range	Average	Range	Average	Range
−8	31	−7.95 (0.9)	−10.0 to −7.0	16.3 (7.0)	5.0–27.7	24.3 (7.2)	12.2–37.6	4.19 (0.7)	2.13–5.0
−6	53	−5.58 (0.7)	−6.9 to −4.1	15.7 (6.1)	6.3–28.7	21.1 (6.0)	12.4–33.9	4.85 (0.9)	3.13–6.3
−2	53	−2.10 (0.8)	−3.9 to −1.0	17.2 (7.4)	6.6–31.8	19.2 (7.3)	7.8–33.9	6.92 (1.3)	4.11–9.6
0	99	0.14 (0.7)	−0.9 to 2.1	18.1 (6.5)	7.6–31.7	17.7 (6.4)	7.9–32.0	7.86 (1.1)	5.2–10.4

retinopathy of prematurity, convulsions, neurological abnormalities or brain lesions.

A total of 285 infants were tested, and 49 infants (29 preterms and 20 fullterms) were excluded because of an insufficient number of trials or the data were too noisy (i.e., unable to fit a psychometric function) due to sleepiness, fussiness, teething, or illness. Of the infants who were not able to complete testing, the majority of fullterms were older than 6 months, and most preterms were younger than 2 months. Thus, a total of 236 infants contributed data to this study (presented in Table 1). Gestational length was determined by parental report of due date (in comparison to birth date), typically based on the first ultrasound, or on the last menstrual period.[3] In order to increase the likelihood of a healthy sample, the inclusion criterion was that the gestational length was greater than or equal to 30 weeks. Infants in our sample ranged from 30 weeks (10 weeks early) to 42 weeks (2 weeks late) gestation. Note that 16% of the preterm infants and 38% of the fullterm infants in the current study were also included in an earlier report comparing preterms to fullterms (Bosworth & Dobkins, 2009), in order to balance ages across subject groups.

2.1.2. Using birth groups to test the visual experience hypothesis

In our analyses, we grouped infants into four "birth group" categories based on how early or late they were born relative to expected due date (with a negative value meaning they were born early and a positive value meaning they were born late). We did this by first sorting the infants by prematurity, starting with the most preterm infant at −10 weeks preterm, and then creating 3-week bins. This yielded four birth group categories: −10 to −7 weeks (mean = −8.0 weeks); −7 to −4 weeks (mean = −5.6 weeks); −4 to −1 weeks (mean = −2.1 weeks); and −1 to +2 weeks (mean = +0.1 weeks). See Table 1 for the exact range values. For simplicity, we refer to these four birth groups as "−8, −6, −2 and 0" weeks. There were 31, 53, 53, and 99 infants in each group, respectively. Our goal was to test the "visual experience" hypothesis by comparing visual sensitivity across the different birth groups. We attempted to keep the different birth groups matched in both the average and range of postterm age at test date to match them in "biological" age (i.e., age since conception). Because the average postterm age was very similar across birth groups (16.3, 15.7, 17.2, and 18.1 weeks of age, respectively, $F(3,233) = 0.37$; $p = 0.77$), the infants in the most premature birth group ("−8 weeks") were necessarily of the oldest *postnatal* age and presumably had the most visual experience within our sample. The mean postnatal ages for the birth groups were 24.3, 21.1, 19.2, and 17.7 weeks, respectively, which was significantly different ($F(3,233) = 7.96$; $p < 0.0001$).

2.2. Apparatus and stimuli

Luminance (light/dark) and chromatic (red/green) stimuli were presented on an Iiyama Vision Master Pro 510 monitor (1024 × 768 pixels, 100 Hz) powered by a Dell Dimension computer, and viewed at a distance of 38 cm. Stimuli were horizontally oriented sinusoidal gratings (moving upward or downward) with a spatial frequency of 0.27 cycles/degree and a temporal frequency of 4.2 Hz. These parameters were chosen because they are near the peak of the contrast sensitivity functions for young infants (e.g., Atkinson, Braddick, & Moar, 1977; Banks & Salapatek, 1978; Dobkins, Anderson, & Lia, 1999; Hartmann & Banks, 1992; Rasengane, Allen, & Manny, 1997). The stimuli subtended 11° by 11°, and were centered 15° to the left or right of the middle of the video monitor. The mean chromaticity of the gratings and the background was CIE = 0.486, 0.442. The mean luminance of gratings and the background was 20 cd/m^2. Contrast of stimuli is described in terms of *cone contrast*, i.e., the amount of response modulation produced in the long- and medium-wavelength-selective cones in the eye (see Dobkins, Anderson, & Lia, 1999 or Gunther & Dobkins, 2002 for methodological details).

2.2.1. Determining red/green isoluminance

The red/green chromatic stimulus in the main experiment was presented at the mean isoluminance value obtained from 22 adults, using standard motion photometry (Dobkins & Teller, 1996b; Rydberg et al., 1994; Teller & Lindsey, 1993). In the motion photometry, adults fixated on a small dot in the center of a moving red/green grating and adjusted the luminance contrast in the grating until the percept of motion was least salient. Each adult subject's isoluminance point was determined from the mean of 25 trials. The stimulus conditions for the motion photometry procedure were identical to those employed in the main experiments (i.e., same size, orientation, spatiotemporal frequency). As previously discussed (e.g., Dobkins & Teller, 1996b), the justification for using the adult mean isoluminance value in our infant experiments is based on previous experiments demonstrating that infant and adult mean isoluminance points are highly similar for red/green stimuli (Bieber, Volbrecht, & Werner, 1995; Brown et al., 1995; Dobkins, Anderson, & Kelly, 2001; Maurer et al., 1989; Morrone, Burr, & Fiorentini, 1993; Pereverzeva et al., 2002; Teller & Lindsey, 1989). Moreover, Brown and colleagues argue quantitatively that the variability of isoluminance points across infant subjects is comparable to the variability across adult subjects, when measurement error is taken into account. In previous studies, we have calculated that the amount of luminance error likely to exist in our red/green stimuli is below luminance contrast threshold for infants (see Dobkins & Teller, 1996b).

[3] There will be some error in our postterm age calculation, based on parental report of due dates, however, this error has been reported to be small, on the order of ±2 days. This is based upon obstetrical studies that compare the known gestational dates of infants conceived via in vitro fertilization (defined as day from oocyte retrieval in IVF pregnancies) vs. the gestational dates using ultrasound technology (which is based on data from a large number of spontaneous pregnancies). These studies show that, in the first trimester, ultrasound dating is off from the actual gestational age within a range that has a standard deviation of 2.30–2.45 days across studies (Sladkevicius et al., 2005; Tunon, Eik-Nes, Grottum, Von During, & Kahn, 2000).

2.3. Obtaining contrast sensitivities

For each infant, a luminance and chromatic contrast threshold was obtained using Forced-Choice Preferential Looking (FPL) with the method of constant stimuli (Teller, 1979; see Dobkins & Teller, 1996a, 1996b for details), which relies on the fact infants prefer to look at a patterned stimulus on one side of a display rather than a blank, homogeneous field on the opposite side. An adult experimenter held the infant 38 cm away from the front of the stimulus monitor in the view of a video camera aimed at the infant's face. On each trial, a grating stimulus appeared on the left or right side of the video monitor, and the experimenter used cues such as the infant's head turning and gazing behavior to judge the left vs. right location of the stimulus. Typically, five contrast values (1.25–25% cone contrast) were presented for each luminance and chromatic conditions, with these conditions and contrast levels randomized across trials. Stimuli remained present on the video monitor until the experimenter made the left/right judgment, which was typically less than 2 s. The experimenter's answer was entered into the computer by pressing keys on the keyboard and computer beeps provided feedback as to whether the experimenter was correct. Because the mean luminance and chromaticity of the stimulus is the same as that of the background, when the contrast in the stimulus is at or below "contrast threshold", it blends into the background and cannot be seen. Data from each infant was obtained over the course of 2 or 3 days within a 1-week period. The infant's age was calculated as the average of the first and last visits. On average, 80.9 (±29) and 82.7 (±29) trials were obtained across infants, respectively, for chromatic and luminance conditions. The number of trials for luminance ($F(3,233) = 1.55$; $p = 0.20$) and chromatic ($F(3,233) = 1.69$; $p = 0.17$) conditions did not differ across birth groups. For each infant, a psychometric curve was fit to the chromatic and luminance data using Weibull functions and maximum likelihood analysis (Watson, 1979; Weibull, 1951). Threshold was defined as the contrast yielding 75% correct performance. Contrast sensitivity (CS) was computed as the inverse of threshold $*$ 100, and then logged since log, but not linear, sensitivity data conform to normal distributions (Graham, 1989).

2.4. Data analyses

As a first step, we plotted and conducted a regression on log contrast sensitivity vs. log postterm age, separately for the different birth groups. Here the logic is that at any given postterm age, the most premature birth group will have the oldest postnatal age. Given that postnatal age is a proxy for visual experience, the "visual experience" hypothesis predicts that the most premature birth group should have the highest sensitivity.

To more directly quantify the effects of birth group (and thereby investigate the "visual experience" hypothesis), we conducted two analyses of covariance (ANCOVA's) on log CS values, with birth group (−8, −6, −2, and 0 weeks) as the independent variable and log postterm age as the covariate. Note that even though postterm age range and averages did not vary significantly across birth groups (see above, and Table 1), we thought it best to remove variance due to postterm age within each birth group by treating it as a covariate. ANCOVA's were performed separately for luminance and chromatic contrast sensitivity, because the distribution of variance was greater for the former. Two-tailed Student *t*-tests were used to test differences between birth groups. Normality of data, using Kolmogorov–Smirnov tests, and homogeneity of variance, using Levene's test, for each luminance and chromatic CS and each subject group, were verified before statistical analyses.

Given that the results of our ANCOVA's supported the visual experience hypothesis, we next quantified the *extent* of effects of additional time outside the womb. To this end, for each of the three birth groups that could be considered moderately or mildly premature (i.e., the −8, −6 and −2 week groups), we asked if contrast sensitivity was predicted from postnatal age. We did this by, first, using data from 65 of the 99 infants in the "0 week" birth group who were born ±4 days from their due date to predict what contrast sensitivity should be for a given postnatal age, fitting a regression line of "Log Contrast Sensitivity vs. Log Postnatal Age". These 65 infants were chosen because they represent a near exact estimate of expected CS given a certain postnatal age. The postnatal ages of this "exact fullterm" subgroup ranged from 7.9 to 30.0 weeks. (Likewise, because these infants were born within 4 days of their due date, postterm age range was nearly identical to postnatal age range, i.e., from 7.5 to 29.8 weeks.) Once we had the equation relating CS to age obtained from "exact fullterms", we calculated each infant's predicted CS based on his or her postnatal age. Then, we subtracted their *predicted* CS from their *actual* CS and converted this difference into a linear percentage. The extent to which these values fall below 100% indicates how much lower each infant's sensitivity was than predicted based solely on his or her postnatal age.

3. Results

3.1. Linear regression for postterm age

Fig. 1 plots log contrast sensitivities (CS) as a function of log postterm age, separately for the four different birth groups (−8, −6, −2, and 0 weeks). Data points for each infant are plotted separately for luminance (1A) and chromatic (1B) stimuli. The same data are presented in terms of postnatal age in Fig. 2. As expected, contrast sensitivity increased over the age range tested, as evidenced by Pearson correlation coefficients being significantly different from zero (all p values $\leqslant 0.004$, presented in Table 2). Most relevant to the current study, assuming postnatal age is a proxy for visual experience, the "visual experience" hypothesis predicts that the lines for the −8, −6, −2 and 0 week groups should fall in order from the highest to lowest, respectively. Generally, this is observed in Fig. 1. Chromatic CS was highest in the −8 week birth group, followed by the −6 week birth group, and then roughly equal sensitivities for the −2 and 0 week birth groups. A similar, albeit much weaker, pattern is seen for luminance CS, primarily for older ages.

For luminance CS, the −8 week birth group had the highest slopes. If it really is the case that the slope for luminance CS is steeper for the most preterm birth group, as seen in Fig. 1, it suggests that they underperform the other birth groups *early* in development (approximately under 10 weeks, based on the intersection of the preterm and fullterms at this age, see Fig. 1) and then outperform the other birth groups later in development (over 10 weeks of age). To determine if this pattern was supported statistically, we compared the −8 week birth group with the 0 week birth group, separately for two age groups: $\leqslant$10 weeks (mean ages 8.8 and 8.9 weeks, respectively) and $\geqslant$11 weeks (mean age 20.15 and 20.36 weeks, respectively). While there was no significant difference in Luminance CS between the −8 and 0 week birth groups at the younger postterm age (mean CS: 0.84 vs. 1.00; $t(29) = 0.93$; $p = 0.36$, 2-tailed t test), the −8 week birth group was superior at the older postterm age (mean CS: 1.66 vs. 1.40; $t(99) = 2.27$; $p = 0.025$). These difference effects at early vs. later points in development suggest that it may take time for the effects of visual experience to overcome some early disadvantage of being premature, an issue we return to in Section 4.

3.2. Linear regression for postnatal age

Fig. 2 plots all individual data as a function of postnatal age. Based on the intersection of the lines for all birth groups, prematurity

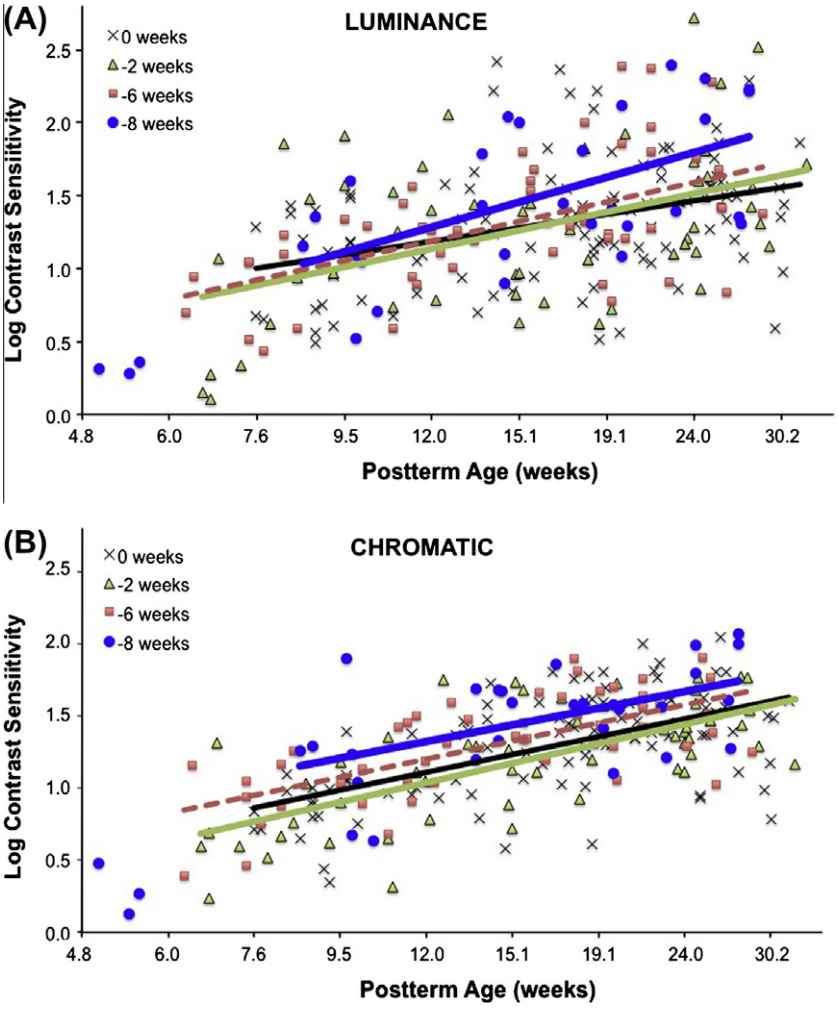

Fig. 1. Log cone contrast sensitivity values for all 236 infants. Each infant provided a single data point for luminance (A) and chromatic (B) contrast sensitivity. Data are shown separately for the four different birth groups: −8, −6, −2, and 0 weeks, indicating how preterm infants were relative to due date, with the 0 week group representing the fullterm infants. Linear regression lines are plotted for each birth group. Note that for the −8 week group, the youngest three infants are excluded from the regression line, because no infants of those ages exist for the other groups.

appears to have a detrimental effect before 25 weeks postnatal age, but after that age, we see the −8 week group *outperform* fullterms. That is to say, at younger ages, biological maturation has a greater impact on CS than postnatal age and, by proxy, visual experience. Later, when infants have had more than 25 weeks of experience outside the womb, differences in biological immaturity may no longer matter. Thus, the steeper slopes reflect accelerated development which overcomes the greater biological immaturity.

3.3. ANCOVA results

To more directly statistically analyze the effects of birth group, we conducted an ANCOVA on log luminance and log chromatic CS values, with birth group (−8, −6, −2, and 0 weeks) as the independent variable and log postterm age as the covariate. Group means for luminance and chromatic CS (adjusted for the covariate log postterm age) as a function of birth group are presented in Fig. 3. In line with the visual experience hypothesis, for chromatic CS, there was a significant main effect of birth group ($F(3,231) = 4.72$; $p = 0.003$), which is driven by the two most premature birth groups (−8 and −6 weeks) having higher chromatic CS than the other two birth groups (−2 and 0 weeks). This was confirmed with planned comparisons, showing that chromatic CS was significantly better for the −8 than the 0 week birth group ($t(128) = 2.55$; $p = 0.01$, by about 1.5-fold) and better in the −6 than the 0 week birth group ($t(150) = 3.17$; $p = 0.002$, by about 1.3-fold). By contrast, there was no difference in chromatic CS between the −2 and 0 week birth group ($t(150) = -1.12$; $p = 0.27$). For luminance CS, there was no main effect of birth group ($F(3,231) = 1.11$; $p = 0.35$), however, there was a visible trend for higher luminance CS in the more premature birth groups, which mirrors the effects seen in the regression analysis of Fig. 1. In sum, the results of this analysis provide clear support for the "visual experience" hypothesis for development of chromatic CS, whereas the support for effects of experience on luminance CS is much less obvious.

3.4. Quantifying the extent of visual experience effects for chromatic CS

The results of our regression analyses and ANCOVA are consistent with the idea that postnatal age (a proxy for visual experience) affects CS. Next, we asked whether postnatal age can provide a *complete* account of chromatic CS by comparing preterm infants' CS to what would be expected from fullterm infants matched in postnatal age. To this end, for each infant in the three preterm birth groups (−8, −6 and −2 weeks), we calculated their *predicted* CS based on their postnatal age (using data from "exact fullterm" infants, see Section 2). We then subtracted their

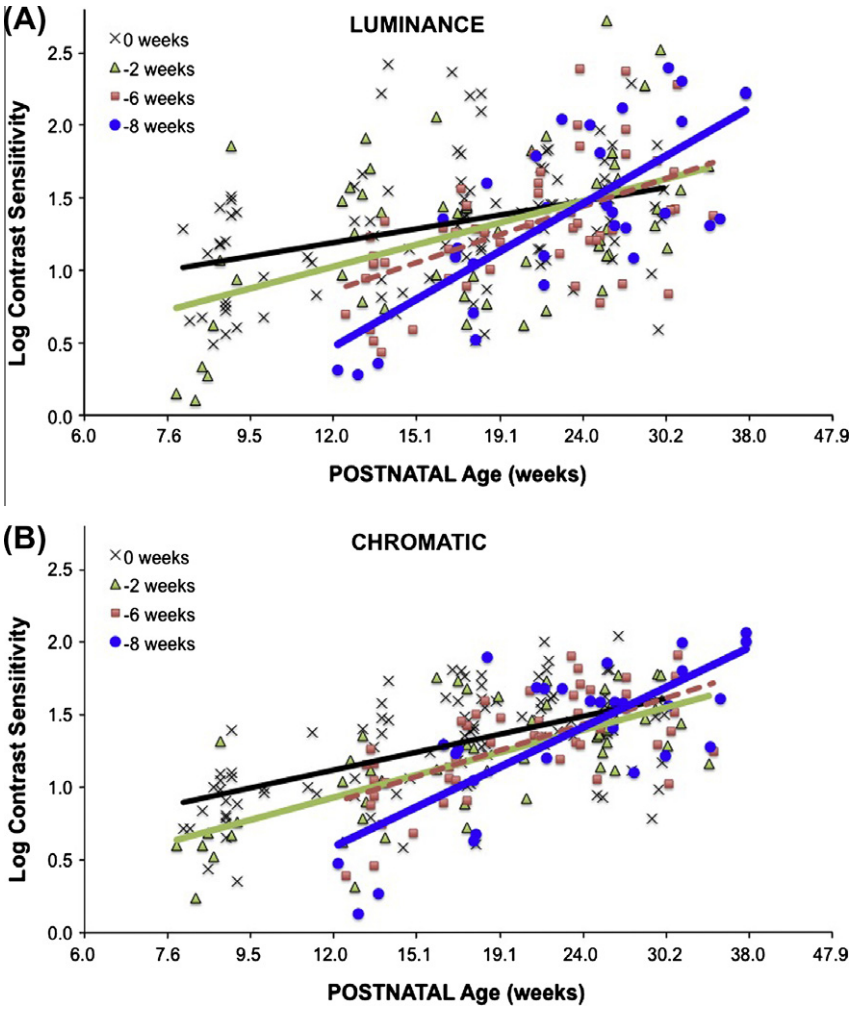

Fig. 2. Details are the same as for Fig. 1, with the exception that the same log contrast sensitivity data are plotted as a function of postnatal age (weeks since birth). The youngest three infants who were excluded from the regression lines in Fig. 1 are now included, as they are within a comparable age range of the other groups. Regression coefficients are comparable with and without those infants.

Table 2
Slopes and *R* squared coefficients for each of the four birth groups.

Birth group	Luminance				Chromatic			
	Slope		R^2		Slope		R^2	
	Postterm age	Postnatal age	Postterm age	Postnatal age	Postterm age	Postnatal age	Postterm age	Postnatal age
−8	1.71[a]	2.67	0.53	0.35	1.15[a]	2.75	0.55	0.56
−6	1.29	1.93	0.25	0.30	1.25	1.80	0.44	0.44
−2	1.26	1.51	0.20	0.24	1.35	1.55	0.46	0.49
0	0.92	0.95	0.12	0.14	1.23	1.23	0.34	0.34

[a] When comparing slopes for postterm age, we felt it necessary to remove the three youngest infants from the regression line because no such ages existed in the other groups. When these infants are included in the regression line, the slopes increase to 2.05 and 1.74 for luminance and chromatic, respectively.

predicted CS from their *actual* CS. To facilitate ease of understanding, these difference scores were converted into linear "percentage of predicted" scores, with values *less* than 100% indicating that contrast sensitivity is *lower* than would be predicted based solely on postnatal age. The mean percentage of predicted scores were 78%, 80% and 74% for the −8, −6 and −2 week birth groups, respectively, for chromatic CS. In sum, chromatic CS was approximately 80% of what would be expected from a fullterm infant of the same postnatal age, indicating that postnatal age cannot provide a full account of contrast sensitivity, an issue we return to in Section 4.

4. Discussion

The current study compared development of contrast sensitivity in mildly/moderately preterm infants born no more than 10 weeks prematurely to that of fullterm infants. The results from the current study and our previous study (Bosworth & Dobkins, 2009) both support the conclusion that chromatic CS is enhanced more than luminance CS in the preterm group, presumably because of additional environmental exposure by virtue of more time outside the womb. With an increased size in the number of infants by more than double in the current study (102 infants to 236

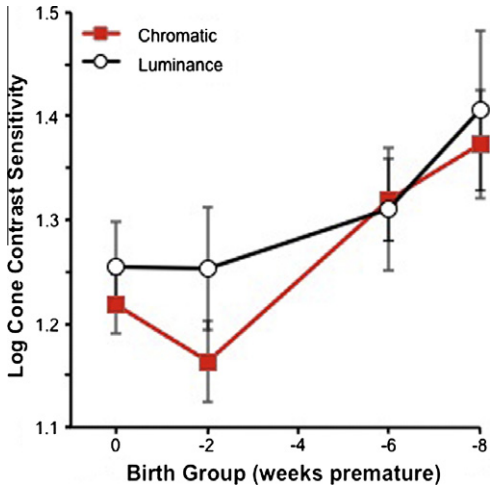

Fig. 3. Least squared log cone contrast sensitivity means, for each birth group, adjusted for the covariate postterm age (average age = 15.7 weeks postterm) for luminance (*black line*) and chromatic (*red line*) stimuli. The postnatal age for each birth group differed as follows: 17.7, 19.2, 21.1, and 24.3 weeks. Error bars denote standard error of the means.

infants), here we further asked whether the *amount* of additional environmental exposure was correlated with contrast sensitivity, by comparing infants with different gestational lengths. In sum, with respect to *chromatic* CS, the results of the current study provide clear evidence for effects of visual experience, demonstrating increasing sensitivity with greater prematurity. For *luminance* contrast sensitivity, advantageous effects of prematurity are weaker, and appear later in development. Yet, for both chromatic and luminance stimuli, the premature group still lagged behind their postnatal age-matched peers in contrast sensitivity. This means that both biological factors related to extrauterine environmental exposure and experiential factors must interact in controlling development of contrast sensitivity. Below, we discuss our findings with respect to previous studies of contrast sensitivity in preterm infants, separately for chromatic and luminance CS.

4.1. Chromatic contrast sensitivity

To date, the current study and our previous study (Bosworth & Dobkins, 2009) are the only ones to compare chromatic CS across infants that differed in prematurity. In line with the results of the previous study, the current study found that for chromatic CS, preterm infants outperformed fullterms by about 1.3–1.5-fold. Both the regression analysis (Fig. 1) and the ANCOVA performed on group means (Fig. 3) indicated that infants born between 30 and 36 weeks gestation (i.e., the two most premature birth groups, −8 and −6 weeks) had significantly higher chromatic CS than infants born between 36 and 42 weeks gestation (i.e., the other two less premature birth groups, −2 and 0 weeks). In sum, the current study indicated that 4–10 additional weeks of visual experience enhanced chromatic CS, however, less than 4 additional weeks did not. It is possible that we were unable to detect the effects of 1–4 additional weeks partly due to errors in estimation of gestational age (based on errors in estimating due dates), which would affect infants born near term date to a greater extent than infants born at more extreme deviations from due date. Regardless, the results of the current study corroborate those of our earlier Bosworth and Dobkins (2009) study, showing small but consistent positive effects of visual experience on early development of chromatic CS. However, note that both the current and the previous studies showed that preterm infants' contrast sensitivity was still lower than would be predicted based solely on their postnatal age, performing with a contrast sensitivity that was approximately 80% of what would have been expected at their postnatal age, had they been born on time. Thus, while visual experience plays a substantial role in chromatic CS development, it is not the full account. There are several possible reasons for this, including the possibility that preterm infants may receive less visual input than fullterm infants matched in postnatal age (because they sleep longer hours and/or because they shut their eyes more in waking hours). Other reasons stemming from health complications of being premature may also contribute as well. Finally, biological and experiential factors may be interactive, producing an outcome that is neither strictly driven by visual experience nor genetically-driven biological maturation. Interestingly, results are consistent with recent studies showing that very preterm children exhibited significantly better at color deficiency tests for than term controls (O'Reilly et al., 2010; Pitchford et al., 2011).

4.2. Luminance contrast sensitivity

With regard to luminance CS, although the results of the current ANCOVA performed on group means did not support the visual experience hypothesis, when we performed a *post hoc* analysis on infants between 11 and 31 weeks of postterm age, luminance CS was significantly better in the most premature infants (−8 week birth group) than in the least premature infants (0 week birth group). This trend can be seen in Fig. 3. This was also seen in the regression analysis of Fig. 1, where it appeared that the youngest and most premature birth group (−8 weeks) performed worse than the least premature birth groups but outperformed them later on after 10 weeks of postterm age. In our previous study of preterm vs. fullterm infants (Bosworth & Dobkins, 2009), we saw a very similar trend for the luminance CS data, in that only at later time points in development (around 20–30 postterm weeks) did the preterm infants outperform the fullterm infants. In sum, the results from both the current and previous study suggest that there may be small effects of visual experience on luminance CS, but that they are smaller than those observed for chromatic CS, and may only be observable at later time points. Two reasons are suggested for this. First, it is possible that luminance CS is primarily driven by pre-programmed biological maturation. Secondly, it is possible that luminance CS is negatively affected by prematurity (and obscures the effects of visual experience) early on in development.

To date, studies measuring contrast thresholds report that contrast sensitivity is unaffected (Kozeis et al., 2012; Mirabella et al., 2006) or impaired (Dowdeswell et al., 1995; Larsson, Rydberg, & Holmstrom, 2006; O'Connor et al., 2002; O'Connor, Wilson, & Fielder, 2007) by prematurity in samples that include infants with very low birth weights (⩽1500 g), typically born under 32 weeks gestation, which is much more premature than the sample in the current study.[4] To our knowledge, there have been two other preferential looking studies that have measured visual sensitivity as a function of gestation length, in *mildly/moderately* preterm infants, both of which provided some evidence for effects of visual experience. van Hof-van Duin and Mohn (1986) measured visual acuity in fullterm infants and preterm infants who were born less than or greater than 31 weeks gestation. They found the rate of development was slightly faster in the more premature infants, which was

[4] In the Mirabella et al. (2006) study, although contrast thresholds were unaffected by prematurity, premature infants did show significantly higher amplitudes in VEP responses to suprathreshold gratings at low spatial frequencies. In another study, also using the sweep VEP method to measure contrast thresholds, Oliveira et al. (2004) compared preterm infants (born between gestational ages 27–36 weeks) and fullterm infants of the same *postnatal* age (at 3 months) and found the two groups to be very similar, suggesting that postnatal experience accounts well for contrast sensitivity.

supported by regression line slopes of 1.0 and 1.2 for log age–log acuity functions in the less-preterm and more-preterm infants, respectively. The mean acuity was also consistently higher in the preterm infants compared to fullterm infants, when matched in postterm age. These results indicate that a period of several weeks of extra-uterine experience before the expected term date, in the absence of neural or ocular complications, is accompanied by a slightly faster rate of visual maturation, with a tendency for greater acceleration with longer periods of prematurity.

In another preferential looking study, Shepherd, Fagan, and Kleiner (1985) compared acuity and contrast sensitivity in fullterm and preterm infants with a mean age of 3 weeks postterm. The authors divided the preterm infants into two groups: those born before with approximately 6 weeks of postnatal experience vs. infants born after 36 weeks gestation, with only 0.7 week of postnatal experience at the time of test. Hence, while the two preterm groups were tested at a similar postterm age, the more premature group had about 5 weeks more postnatal experience. Results showed that acuity was the same in fullterms and these two preterm groups, indicating that the extra time outside the womb did not accelerate development of spatial resolution. However, the more premature group had *higher* luminance CS, although statistics were not reported on this. (From their figure, at approximately 0.12 cycles/degree, the contrast threshold was about ~8% for the more preterm group vs. ~12% for the less preterm group.) The results from these two studies, along with the current study, provide some (albeit weak) evidence for the effects of visual experience on luminance CS.

4.3. Differential effects on magnocellular vs. parvocellular pathway development

The current study measured luminance and chromatic CS with the notion that they are differentially related to the magnocellular (M) and parvocellular (P) subcortical pathways, respectively. Specifically, M neurons are more sensitive than P neurons to luminance contrast, and conversely, P neurons are more sensitive than M neurons to red/green chromatic contrast (Lee et al., 1990; Shapley, 1990; Smith et al., 1995). However, it is important to note that although the P pathway may be the sole mediator of chromatic CS, both the M and P pathways are likely to mediate luminance CS (see Lennie & D'Zmura, 1988; Merigan & Maunsell, 1993; Skottun, 2000, for reviews). As such, our results clearly support the notion that the P pathway is enhanced by extra visual experience, but two interpretations are possible about the roles that M and P pathways play in the weaker effects we observed upon luminance CS. *One*, perhaps *only* the P pathway is affected by prematurity, resulting in enhanced chromatic CS and some smaller enhancement of luminance CS, due to P pathway "spill-over" effects onto luminance CS. In other words, the benefits seen in both luminance and chromatic CS could solely be due to P pathway changes. *Alternatively*, a more straightforward interpretation is that both M and P pathways are affected by prematurity, with the P pathway affected to a greater degree.

Interestingly, another study, while not using luminance and chromatic, instead tested development of M and P pathways in preterm and fullterm infants using signatures seen visually evoked potentials, with the N1 component reflecting the P pathway response, and the P1 reflecting the M pathway response (Hammarrenger et al., 2007). They tested at two different spatial frequencies (2.5 and 0.5 cycles/degree), at four contrasts (4%, 12%, 28%, and 95%), across a range of postterm ages. The results of their study showed that preterm birth had little effect on the waveform patterns to the P-specific stimuli, while those to the M-specific stimuli were delayed. They interpret this to mean that the development of P pathway is not affected, while it appeared to disrupt development of the M pathway. While this does not mirror the conclusions of the current study, it should be noted that the preterm infants in Hammarrenger et al. (2007) were more premature (born <30 weeks gestation and very low birth-weight) than the preterm infants tested in our current and previous study. Because of this, they admit that the detriments observed in their study could be due to undetected neurological complications in some of their preterms. Thus, it is likely the detrimental effects of extreme prematurity may negate any accelerated maturation conferred by extra visual experience. If there are, in fact, detrimental prematurity effects, there are two scenarios that could reconcile the results of both our studies and those of Hammarrenger et al. First, it could be that the M and P pathways are *equally* insulted by prematurity complications, and that the P pathway is more affected by extra visual experience. Secondly (and conversely), it could be that the M and P pathways are *equally* affected by extra visual experience, and that the M pathway is more insulted by prematurity complications (in line with the general notion that the M pathway is more vulnerable to biological insults and genetic abnormalities, see Atkinson & Braddick, 2011). Either way, we would expect the P pathway to be less negatively affected by prematurity than the M pathway, which is true in both our studies and the Hammarrenger study. Then, one only need to assume that the insults from prematurity are more prominent in very premature infants, to explain the differences between Hammarrenger et al. (a detriment in the M, but not the P pathway) and our studies (an enhancement in the P pathway, and no detriment in the M pathway). In fact, we do see a slight detriment in the M pathway at early points in development in the most premature birth group (−8 weeks, see Fig. 1), which is further in line with these notions.

The M vs. P pathway differentiation implicated in our current and previous (Bosworth & Dobkins, 2009) and well as in the Hammarrenger et al. (2007) study is generally in line with results from previous studies that have investigated the effects of abnormal early visual experience on M and P pathway development. In *humans*, the bulk of the data report greater deficits in aspects of vision thought to be mediated by the P pathway (deficits for high spatial frequency stimuli: Bradley & Freeman, 1981; Hess & Howell, 1977; Levi & Harwerth, 1977, and deficits for red/green chromatic stimuli: Davis et al., 2006; Demirci et al., 2002; but see Zele et al., 2007). Corroborating the human results, studies of visually deprived *animals* have reported that morphological changes are greater within the P layers, compared to the M layers, of the LGN (Hendrickson et al., 1987; LeVay, Wiesel, & Hubel, 1980 and see von Noorden, Crawford, & Levacy, 1983 for greater P disruption in the LGN of a single human). And, within primary visual cortex, greater effects of deprivation have been noted within the P-pathway recipient (4C-beta) lamina than the M-pathway recipient (4C-alpha) lamina (Hendrickson et al., 1987).

In sum, studies of early visual deprivation in animals and humans are generally consistent with the notion that P pathway development, more so than the M pathway development, requires normal visual experience. On the flip side of the coin, the results of the current study suggest that development of chromatic CS within the P pathway is affected by visual experience. Because contrast sensitivity is thought to be determined by the sensitivities of neurons at or before the level of primary visual cortex (Boynton et al., 1999; Hawken & Parker, 1990; Palmer, Cheng, & Seidemann, 2007), this suggests that the locus of visual experience effects could likewise be at or before the level of primary visual cortex. Accordingly, the change could be at the level of subcortical P neurons themselves or on the P representation at the level of visual cortex.[5]

[5] At the cortical level, past layer 4 of V1, P cell signals certainly mingle with M pathway signals (see Dobkins & Albright, 2003 for review), however, the mingling is not entirely complete, and thus it seems reasonable to propose a "P pathway representation" in cortex.

4.4. Alternative explanation

An alternative explanation for improved CS of the preterm infants compared to fullterm infants could be that with greater environmental exposure, infants' control of head, neck and eye movement improves. This might facilitate preferential looking judgment of infant's saccades by the tester. This improvement in motor control is suggested by a study showing faster latency of fixation shifts to highly visible targets in preterm infants at 4–6 weeks postterm age, a younger age than that used in the present study (Atkinson, 2000). However, even if improved head and eye movement control is part of the effect of increased environmental exposure, it cannot explain the difference between chromatic and luminance CS found in the current study. Thus, we suggest that the environmental exposure effect is greater for chromatic CS than for luminance CS, and that this may represent greater sensitivity to exposure in the P rather than the M pathway. Such differences might reflect the relative maturity of the two systems at the age of testing.

Another alternative is that perhaps the preterm infants are more alert, and for whatever reason, this impacts chromatic CS more than luminance CS. Early behavioral evidence does not support enhanced alertness and orienting (Gorski, Davison, & Brazelton, 1979; Kopp et al., 1975; Leijon, 1982; Palmer et al., 1982) or preferential looking behavior (Baraldi et al., 1981; Dubowitz et al., 1980, 1983; Morante et al., 1982) in preterms. However, recent advances in sleep research do show preterm infants have longer periods of alertness and wakefulness (Davis & Thoman, 1987; Holditch-Davis et al., 2004; White-Traut et al., 2002).

4.5. Conclusion

The current study provides evidence for effects of visual experience, demonstrating increasing visual sensitivity with greater prematurity (in the absence of health complications) for chromatic CS, evident at a very early age, and smaller effects for luminance contrast sensitivity appear a few weeks later in infancy. It is worth noting that prematurity does represent a risk, at any gestational age, due to disruption of other facets. As reviewed above, infants with very low birth weight under 1500 g are at risk for retinopathy of prematurity and neurological damage. Neurological and behavioral outcome of preterms worsens with lower gestational age at birth (Hack, Friedman, & Fanaroff, 1996; McCormick, Workman-Daniels, & Brooks-Gunn, 1996). Prematurity disrupts other aspects such as sleep patterns, endocrine rhythms and feeding, and imposes stress on infant–maternal relationships. Most notably, attention is disrupted in school-aged children who were very premature (reviewed in depth in Atkinson and Braddick (2012)). Although that may seem conflicting with the current results, which shows positive effects, it is possible that even mildly preterm infants may be worse in other perceptual and cognitive domains, and the improvement seen here may be related to visual attention, acceleration of retinal factors, or changes in synaptogenesis in the LGN or cortex. Importantly, an improvement in contrast sensitivity does not necessarily mean it confers a behavioral advantage for the infants, it only indicates that these infants are being affected by the precocious visual experience.

Finally, because we did not describe the statistical properties of the visual experience of our subjects, we cannot know whether the presumed effects of visual experience are "instructive" (i.e., shaping development in a way that is meaningful based on the statistics of the environment). Our studies tested only a single spatiotemporal frequency, and thus it is yet determined whether the observed effects generalize across a broad range of stimulus parameters. Studies that investigate the potential effects of additional visual experience in late preterms might be more likely to reveal positive results if stimulus properties which are readily experienced are tested. Moreover, tasks that are more limited by low-level sensory processing levels are probably less likely to change due to visual experience, as compared to other tasks such as position discrimination or vernier acuity that depend on higher cortical function (Geisler, 1984; Levi & Klein, 1985; Levi, Klein, & Aitsebaomo, 1985; Skoczenski & Norcia, 1999; Wilson, 1986).

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