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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.

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.