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Gaze Following Is Accelerated in Healthy Preterm Infants

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Abstract

Gaze following is an essential human communication cue that orients the attention of two interacting people to the same external object. This capability is robustly observed after 7 months of age in full-term infants. Do healthy preterm infants benefit from their early exposure to face-to-face interactions with other humans to acquire this capacity sooner than full-term infants of the same chronological age, despite their immature brains? In two different experiments, we demonstrated that 7-month-old preterm infants performed like 7-month-old full-term infants (with whom they shared the same chronological age) and not like 4-month-old full-term infants (with whom they shared the same postmenstrual age). The duration of exposure to visual experience thus appears to have a greater impact on the development of early gaze following than does postmenstrual age.

Keywords

gaze following, facial expression, emotion, premature, experience, social ability

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Shortly after birth, human infants learn to recognize and communicate with their caregivers. How neural maturation and exposure to a rich social environment interact to build these human-specific social communication skills remains to be elucidated. Studying healthy preterm infants (i.e., those with no risk factors for neurological impairments except prematurity itself) offers unique opportunities to disentangle the roles of neural maturation and exposure to a rich social environment. On the one hand, the richer environment to which preterm infants are exposed, relative to the uterine environment, might accelerate their development. On the other hand, establishment of minimal neural circuitry and sufficient neural maturation might need to occur before the brain is able to process and learn from such an environment.

Most of the studies in which this issue has been examined have been performed in the language-acquisition domain, and their results have been mixed. The loss of response to nonnative features at both segmental levels (i.e., foreign contrast discrimination; Peña, Werker, &

Dehaene-Lambertz, 2012) and suprasegmental levels (i.e., discrimination of a language's rhythmic class; Peña, Pittaluga, & Mehler, 2010) has shown greater dependence on *postmenstrual age* (i.e., the time elapsed since the mother's last menstrual period before the birth date) than on exposure to *ex utero* speech. However, Gonzalez-Gomez and Nazzi (2012) showed that preterm infants' responses to native-language phonotactic regularities depend on the duration of their *ex utero* speech exposure, although the quality of their productions does not. Similarly, Caskey, Stephens, Tucker, and Vohr (2011) reported that preterm infants produced more vocalizations when their parents practiced regular face-to-face interactions with them.

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There is also little consensus with regard to visual-system development. A slight acceleration in visual acuity estimated using behavioral methods was observed in preterm infants compared with full-term infants evaluated at similar postmenstrual age (Van Hof-Van Duin & Mohn, 1986). Using visual evoked responses, Jandó et al. (2012) found earlier development of binocularity in preterm compared with full-term infants, although no acceleration in the reduction of P1 latency was observed in the same preterm infants. Thus, even though the maturation of the early stages of visual perception may follow a fixed timing, binocularity can be accelerated in preterm infants. This conclusion is concordant with the lack of effect of early visual stimulation on synaptic overproduction and pruning in the visual cortex of preterm monkeys (Bourgeois, Jastreboff, & Rakic, 1989).

Neural maturation and exposure to the *ex utero* environment differentially influence various capacities. Such diversity might be related to the heterogeneous maturational calendar of the human brain, which could allow critical periods for learning at different times (Hensch, 2004). Subtle differences in the neural machinery involved in specific types of learning could exist even within the same neural tissue. For example, during infants' acquisition of the native-language phonetic inventory, the loss of sensitivity to foreign phonetic contrasts and the learning of native phonotactic regularities are differentially dependent on biological timing and environmental exposure, as we have found previously (Peña et al., 2012; cf. Gonzalez-Gomez & Nazzi, 2012). Therefore, estimating the influence of these two factors in the different domains of early learning should help to better elucidate the neural mechanisms that underlie human cognitive functions.

In the present study, we focused on preterm infants' ability to follow gaze direction. Only 20% of 3-month-olds follow a caregiver's gaze when the caregiver shifts his or her head and eyes (Scaife & Bruner, 1975). By contrast, 4-month-olds follow the gaze of another person more consistently, but only when the person makes direct eye contact with them before moving his or her eyes (Farroni, Mansfield, Lai, & Johnson, 2003). By 7 months of age, infants tend to show a robust ability to follow the gaze of another person, even when the person's head remains stationary, only eye movement occurs, and the targets are hidden (e.g., Corkum & Moore, 1995; Flom, Deák, Phill, & Pick, 2004).

Gaze following is an important first step in social cognition: It has been conceptualized as a primitive orienting response and a precursor of joint attention (e.g., Baron-Cohen, Campbell, Karmiloff-Smith, Grant, & Walker, 1995), and it is predictive of communication skills later in life (Charman et al., 2001). Gaze cues provided by adults have been shown to facilitate learning in infants. Indeed, infants at 4 and 9 months of age have demonstrated

better memory (Reid, Striano, Kaufman, & Johnson, 2004) and improvements in their attention for an object's location and identity (Senju, Csibra, & Johnson, 2008) when provided with gaze cues by experimenters. Adult gaze also facilitates word learning in infants younger than 1 year old by directing the infants' attention to the referent (e.g., Baldwin & Moses, 2001; Morales et al., 2000). Finally, gaze following has been found to be positively correlated with vocabulary in 18-month-olds (Morales, Mundy, & Rojas, 1998).

Because preterm infants are exposed to face-to-face interactions earlier (in terms of postmenstrual age) than infants who are born at term, they may become sensitive to gaze direction sooner as well. To the best of our knowledge, early development of gaze following has not been compared in healthy preterm and full-term infants, although a higher rate of difficulties in social cognition is often reported in preterm infants compared with control populations (e.g., Limperopoulos et al., 2008). Low birth weight and younger gestational age are considered risk factors for social difficulties, hyperactivity, and attentional deficits. However, in most studies, it has been difficult to disentangle the effects of these factors from the effects of other factors that may delay or compromise early parent-infant interactions (e.g., brain lesions or several other nonneurological comorbid conditions that commonly affect preterm infants at birth). In our study, we thus focused on groups of healthy preterm infants who had received rich stimulation very similar to that received by full-term neonates; the preterm and full-term infants differed only in that this stimulation began when the preterm infants' brains were at a more immature stage.

We evaluated how well full-term and preterm infants followed an adult's gaze when cued by head and eye movements (Experiment 1) and by eye movement alone (Experiment 2). We expected that 4-month-old full-term infants would orient to one of two toys targeted by a woman's lateralized gaze when it involved both head and eye movement, and that 7-month-old full-term infants would orient to one of two toys when cued by eye movement alone. We thus predicted that if postmenstrual age is the key factor in gaze following, 7-month-old infants born 3 months prematurely and 4-month-old full-term infants (whose postmenstrual ages are equivalent) should perform similarly. However, if exposure to the *ex utero* world is essential for gaze following, such 7-month-old preterm infants and 7-month-old full-term infants should perform similarly, given their similar time *ex utero*.

Experiment 1

We compared full-term and preterm infants' orientation to one of two similar toys (presented side by side and symmetrically on a screen) when one side was cued by a

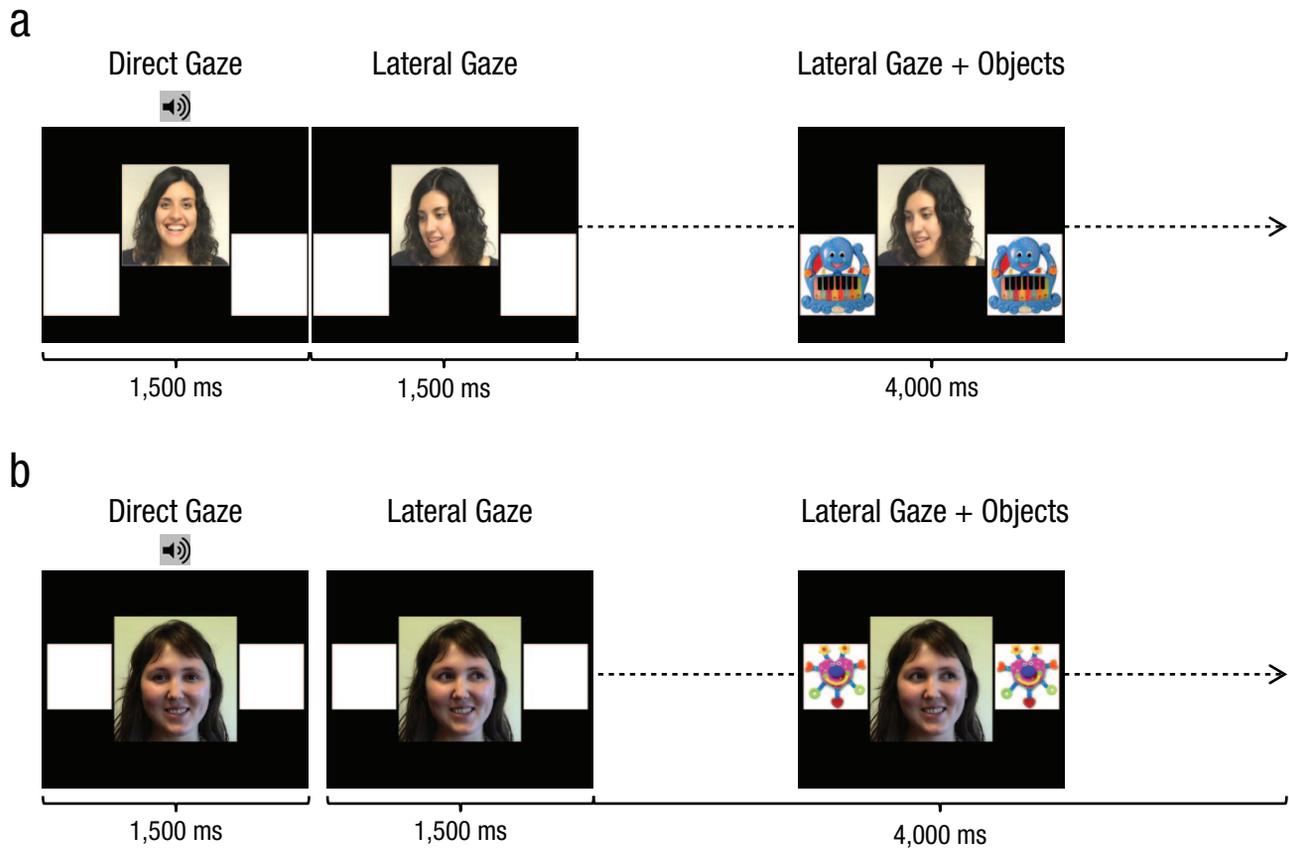


Fig. 1. Examples of stimuli used in Experiments 1 and 2. In Experiment 1 (a), a video of a woman directing her gaze toward the infant was presented for 1,500 ms. The woman then made a peek-a-boo-like gesture, while making vocalizations, and directed her gaze to the infant again for 1,000 ms. Then, a still picture of the same woman was shown for 1,500 ms. In this picture, her gaze and her head were directed toward one of two empty white panels. Next, videos of moving toys were projected simultaneously on the left and right white panels for 4,000 ms. Experiment 2 (b) was similar, but in this experiment, the still picture showed only the woman's gaze (and not her head) as being directed toward one of the empty white panels. To make the conjunctiva clearly visible when only the eyes moved, the woman directed her gaze to the left or the right region by following a horizontal movement parallel to the floor. The empty white panels were therefore displayed near the regions where the woman's eyes indicated that her gaze was directed.

woman's head and eye movement (Fig. 1a). We measured gaze with an infant-adapted eye-tracking system that recorded gaze every 20 ms.

Method

Participants. We tested four groups of healthy infants (see Fig. 2): full-term 4-month-olds (FT4), full-term 7-month-olds (FT7), preterm 7-month-olds (PT4), and preterm 10-month-olds (PT7). The preterm infants were born 2.5 to 3 months (8 to 10 weeks) early. Thus, the FT4 and PT4 infants had different chronological ages (4 and 7 months, respectively) but equivalent postmenstrual ages (~13 months); the FT7 and PT7 infants also had different chronological ages (7 and 10 months, respectively) but equivalent postmenstrual ages (~16 months). To facilitate comparison between the preterm and full-term groups, we designate the preterm infants according to the

chronological age of the corresponding full-term groups, rather than according to the preterm infants' own chronological age. In other words, PT4 infants had more visual experience than FT4 infants, and PT7 infants had more visual experience than FT7 infants.

Twenty-one infants (7 PT4, 4 PT7, 6 FT4, and 4 FT7) were excluded from the analysis because they did not complete the experimental protocol. Twelve infants (5 preterm, 7 full-term) were excluded because of fussiness, sleepiness, or nonspecific discomfort. Six infants (4 preterm, 2 full-term) were excluded because of insufficient eye signal quality (i.e., the iris color was too light or an eyelid opening was too small). Finally, 3 infants (2 preterm, 1 full-term) were excluded because of technical failure during the experiments. Our final sample included 20 FT4 infants (10 boys, 10 girls), 23 FT7 infants (10 boys, 13 girls), 19 PT4 infants (12 boys, 7 girls), and 19 PT7 infants (10 boys, 9 girls). We used the number of participants in

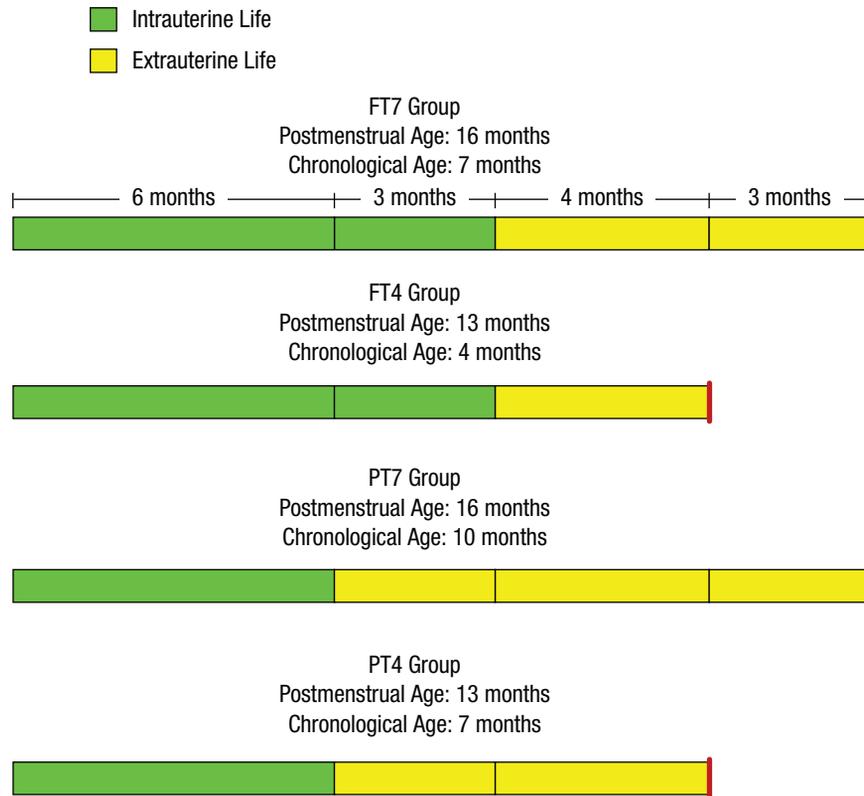


Fig. 2. Postmenstrual and chronological ages of the full-term (FT) and preterm (PT) groups in this study. The horizontal rectangles indicate the duration of intra- and extrauterine life. The time of testing is indicated by a red vertical line placed at the right extreme of each horizontal bar. Note that infants in the FT7 group had a postmenstrual age similar to that of infants in the PT7 group (16 months) and simultaneously a chronological age similar to that of infants in the PT4 group (7 months).

previous similar studies to determine our desired sample size (Peña, Mehler, & Nespor, 2011; Peña et al., 2012).

The preterm infants were born between 29 and 31 weeks of gestational age (wGA; $M = 29.2$ wGA, $SD = 1.2$), and the full-term infants were born between 38 and 42 wGA ($M = 39$ wGA, $SD = 1.2$). At birth, all infants (a) had Apgar scores of 7 or higher at 1 and 5 min; (b) had normal weight, size, and cranial perimeter for their gestational age; (c) demonstrated normal otoacoustic emissions; and (d) had neuropsychiatric scores corresponding to their gestational ages. The preterm infants had retinal development, auditory brainstem-evoked responses, and brain ultrasonography results that were normal for their gestational age. (In both experiments reported here, all infants lived in households where Spanish was the only language spoken, were of lower-middle socioeconomic class, and exhibited normal clinical outcomes at assessments during their first 2 years of after birth.)

Because the preterm infants in our study were not ill, they were able to benefit from a rich and complex experience from birth onward. During the neonatal period before the study, they were clinically examined at least six

times a day outside the incubator and were fed and stimulated by parents through a kangaroo procedure, a medical protocol that involves skin-to-skin contact between the mother or father and their newborn. These infants were discharged from the hospital at around 34 wGA with clinical recommendations for feeding and care at home. Ethical approval for this experiment was obtained from the Sóltero del Río Hospital Ethics Committee. All parents provided informed written consent.

Stimuli and apparatus. All visual stimuli were displayed on a 17-in. eye-tracker monitor (Tobii 1750; Tobii Technology, Stockholm, Sweden) with a screen size of $1,024 \times 768$ pixels and 16-bit color depth. The tracker automatically recorded each infant's binocular eye fixations at a sampling rate of 50 Hz. Videos and pictures of two adult women were the stimuli for this experiment. On each trial, videos and pictures of one of the women, chosen randomly, were displayed over a central region. To the lower left and lower right of the face stimuli, pictures of toys were presented symmetrically in regions delimited by white areas that remained visible

throughout each trial. All images used in the study were in color. Infants were positioned at a distance of 60 cm from the monitor. At this distance, the central region for facial stimuli subtended a $13.0^\circ \times 12.2^\circ$ area, and the left and right regions for toys each subtended an $8.9^\circ \times 9.7^\circ$ area. The toy regions were located 6.74° away from the midpoint of the horizontal axis (see Fig. 1a). Any differences in expression or other features in the left-facing and right-facing versions of the women in the pictures and videos were eliminated by digital manipulation to create mirror images.

Procedure. Testing occurred in a soundproof booth. Infants sat on their parent's laps in front of the eye-tracker monitor. Parents wore a mask so they could not see the stimuli. First, binocular gaze calibration was performed by using fixations of longer than 100 ms on five centered points and on the four corners of the monitor, where visual attractors were successively presented.

The experiment consisted of 20 trials. The start of each trial was signaled by the simultaneous presentation of a sound and a visual attention grabber in the central panel for 1,000 to 2,000 ms. Once the infant's gaze was centered, a video of a woman directing her gaze toward the infant was presented in the center of the monitor for 1,500 ms. The woman then made a peek-a-boo-like gesture and directed her gaze to the infant again for 1,000 ms. Then, a still picture of the same woman was shown for 1,500 ms. In this picture, her gaze and her head were directed toward one of the empty white panels. In half of the trials, the woman in the video directed her gaze to the left side; in the other half, she gazed to the right. The direction was chosen at random for each trial. Next, videos of moving toys were projected simultaneously on the left and right white panels for 4,000 ms, and the woman's face continued to be displayed. Across the 20 trials, each woman displayed 10 different peek-a-boo-like gestures. The test was stopped any time infants manifested discomfort.

Data acquisition and analysis. Infants' binocular gaze was recorded every 20 ms throughout the experiment. The gaze analysis was focused on square areas of interest specifically covering the female face and toys (i.e., the center area and lateralized white areas). We use the term *first gaze* to refer to the first fixation after the lateralized gaze cue. We expected that our analysis would reveal a preference by infants to direct their first gaze to the cued white panel, because their attention to it should have been enhanced if they were able to use this gaze cue (McCall, 1971; Rigato, Menon, Farroni, & Johnson, 2013). We also measured the latency of the first gaze and the total looking time on the targeted side. We predicted that analysis of these variables might reveal faster and prolonged visual exploration of the stimuli

cued by the adult's gaze (Gredebäck, Johnson, & von Hofsten, 2010).

We thus analyzed five gaze variables over the regions of interest:

- *Frequency of first-gaze direction:* the numbers of times that the first fixation exceeding 100 ms fell on the left and right white regions after the woman lateralized her gaze;
- *First-gaze latency:* the time between the onset of the woman's lateralized gaze and the onset of the infant's first fixation over one of the lateralized regions;
- *Total looking time:* the total duration of the infant's gazes toward each of the lateralized panels;
- *Number of fixations:* the number of fixations lasting longer than 100 ms that were directed to the left and right panels;
- *First-gaze duration:* the duration of the first gaze over one of the lateralized panels.

For a trial to be considered valid, the infant's first gaze had to have been preceded by a central gaze fixation that exceeded 200 ms in duration. The mean of each gaze variable for correct and incorrect responses was computed separately for the left and right panels. A response was coded as correct when the infant followed the adult's gaze direction and his or her gaze fell on the cued region of interest. To account for individual differences in visual behavior, we normalized the values for all five variables before statistical analysis. That is, each variable related to one side was divided by the sum of the same variable for both sides. For instance, the proportion of correct first-gaze direction was calculated by taking the number of trials in which the first gaze was directed toward the correct side and dividing that number by the total number of trials in which the first gaze was directed toward either the correct or the incorrect side. The normalized values for all five variables were subjected to multivariate analyses of variance with group (PT4, PT7, FT4, or FT7) as a between-subjects factor. In post hoc pairwise comparisons, we used the Bonferroni test to compare every combination of groups.

Results

Each preterm and full-term infant contributed between 14 and 20 trials, and an average of 14.7 trials per infant (between 6 and 8 per side) was used to compute mean variable values. A significant group effect was observed in the proportion of correct first-gaze direction, $F(3, 77) = 4.08, p < .010, \eta^2 = .137$ (see Fig. 3a; FT4: $M = .501, SD = .127$; FT7: $M = .607, SD = .134$; PT4: $M = .615, SD = .174$; PT7: $M = .655, SD = .145$). Post hoc analysis showed that

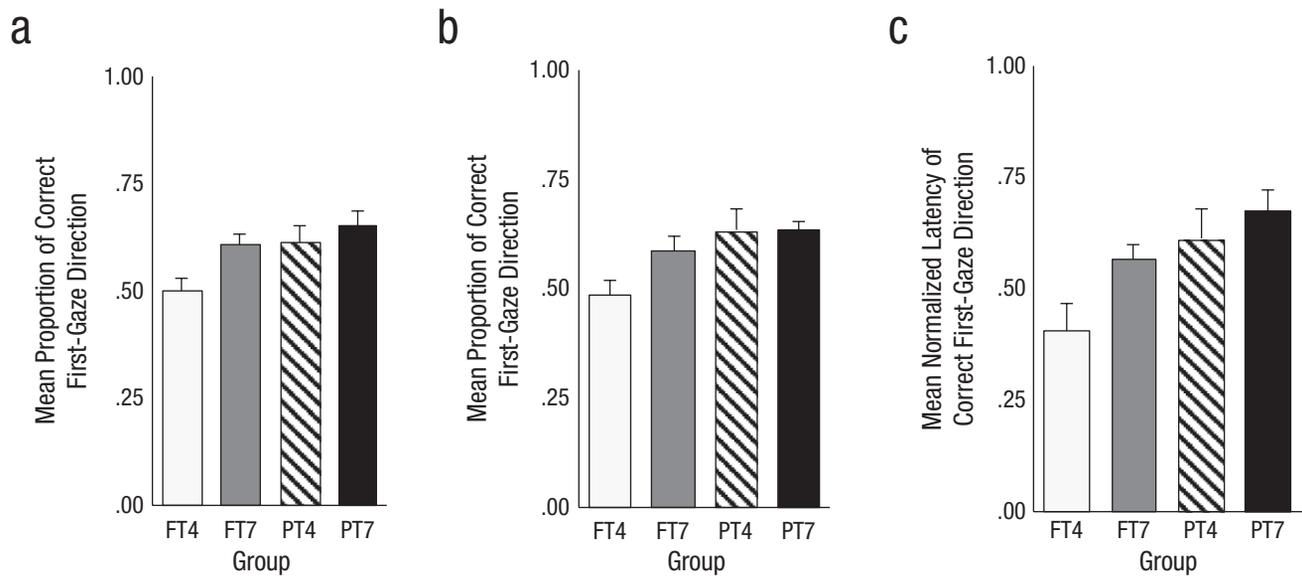


Fig. 3. Experimental results. The graphs in (a) and (b) show the mean proportion of correct first-gaze direction as a function of infant group in Experiments 1 and 2, respectively. The graph in (c) shows the mean normalized latency of correct first-gaze direction (normalized by the latency across correct and incorrect trials) as a function of infant group in Experiment 2. On the y-axes, .5 indicates the chance level of performance. Error bars indicate 1 *SEM*. See Figure 2 for explanation of the group designations.

both PT4 and PT7 infants behaved like FT7 infants, following gaze direction significantly more often than the FT4 infants. This difference was significant for each of those three groups ($p < .010$ for FT4 vs. PT7, and $ps < .05$ for FT4 vs. PT4 and FT4 vs. FT7). There were no significant group differences for the other variables, and no gender differences were found.

Experiment 2

The results of Experiment 1 suggested that preterm infants, even those at the chronological age of 7 months, were able to follow an adult's gaze when it involved simultaneous movement of the head and eyes. In Experiment 2, we explored whether eye movement alone was sufficient to evoke the same behavior.

Method

Participants. We tested healthy infants in age groups identical to those described for Experiment 1. Seventeen infants (6 PT4, 4 PT7, 5 FT4, and 2 FT7) were excluded because they did not complete the experimental protocol. Eight infants (5 preterm, 3 full-term) were excluded because of fussiness, sleepiness, or nonspecific discomfort. Seven infants (4 preterm, 3 full-term) were excluded because of difficulties with continuous recording of the eye signal. Finally, 2 infants (1 preterm, 1 full-term) were excluded because of technical failures. Our final sample

included 21 FT4 infants (9 boys, 12 girls), 22 FT7 infants (11 boys, 11 girls), 18 PT4 infants (9 boys, 9 girls), and 20 PT7 infants (9 boys, 11 girls). The preterm infants were born between 29 and 31 wGA. The full-term infants were born between 38 and 42 wGA. Sample-size criteria and infants' clinical and epidemiological profiles were similar to those in Experiment 1.

Stimuli and procedure. Figure 1b displays some still images from a trial. The same apparatus, stimuli, and procedure from Experiment 1 were used; however, in the still pictures, only the direction of the eyes was lateralized; the head was stationary. At a distance of 60 cm, the white squares subtended a $7.5^\circ \times 7.7^\circ$ area, 7.63° away from the midpoint of the horizontal axis.

Data acquisition and analysis. Data acquisition and analysis were the same as in Experiment 1.

Results

Each infant contributed between 14 and 20 trials, and an average of 14.5 trials per infant (between 6 and 8 per side) was used to compute mean variable values. Analysis of the proportion of correct first-gaze direction again revealed a significant group difference, $F(3, 77) = 4.61$, $p < .005$; $\eta^2 = .135$ (see Fig. 3b; FT4: $M = .485$, $SD = .159$; FT7: $M = .584$, $SD = .174$; PT4: $M = .634$, $SD = .197$; PT7: $M = .635$, $SD = .085$). A significant group difference

was also found for first-gaze latency, $F(3, 77) = 3.77$; $p < .014$; $\eta^2 = .127$ (see Fig. 3c; FT4: $M = .406$, $SD = .274$; FT7: $M = .563$, $SD = .156$; PT4: $M = .611$, $SD = .285$; PT7: $M = .676$, $SD = .212$). A crucial observation was that PT4 infants behaved like FT7 and PT7 infants, but not like FT4 infants. Pairwise comparisons showed that the proportion of correct first-gaze direction was significantly lower in FT4 infants compared with PT4 ($p = .027$), PT7 ($p = .020$), and FT7 ($p = .044$) infants. Moreover, first-gaze latency was significantly shorter in FT4 infants than in PT4 ($p = .049$), PT7 ($p < .001$), and FT7 ($p = .031$) infants. Analysis of the other variables revealed no other significant group or gender differences. Longer latencies in the successful groups (i.e., those who followed the woman's gaze significantly more often than predicted by chance) suggest that (a) eye direction might have been more difficult to notice in the absence of the head-direction cue and (b) the FT4 infants might have disregarded eye movement cues and randomly oriented their gaze to the left or right side.

Discussion

Our results demonstrate that the duration of exposure to visual experience has a significantly greater impact on the development of early gaze following than does postmenstrual age. In Experiments 1 and 2, PT4 infants behaved like FT7 infants; these two groups had been exposed to the *ex utero* environment for equivalent amounts of time. Both groups tended to first orient their gaze toward the toy indicated by the woman's gaze direction. This behavior was not observed in the FT4 infants, who looked randomly to either side, and so there were significant differences between PT4 and FT4 infants, despite the fact that they shared the same postmenstrual age.

The acceleration of gaze following observed in preterm infants in the current study is consistent with results reported for development of binocularity (Jandó et al., 2012), learning of phonotactic regularities (Gonzalez-Gomez & Nazzi, 2012), and early vocalizations (Caskey et al., 2011). However, our findings contrast with prior findings regarding language-discrimination capacities (analysis of the rhythmic properties of the native language—Peña et al., 2010; acquisition of the native phonetic repertoire—Peña et al., 2012) and neonatal memory for the mother's voice (deRegnier, Wewerka, Georgieff, Mattia, & Nelson, 2002). They also contrast with numerous clinical observations indicating that neurocognitive development of healthy preterm infants is guided mainly by neural maturation (deRegnier, 2008).

These discrepancies highlight the developmental asynchronies in the human brain that affect learning. A

particular cognitive system must be able to respond to external stimulation if a learned pattern of response is to be established. Previous studies have shown that when preterm infants are as young as 29 weeks of gestation, they can discriminate external stimuli, such as phonemes (Draganova et al., 2005; Mahmoudzadeh et al., 2013), demonstrating that perceptual mechanisms are functional as early as this age. However, other stimulus-dependent learning may require the development of other neural circuitry, such as circuits involving γ -aminobutyric acid (GABA) interneurons. These neurons reach their final location later than pyramidal neurons. This delayed development may postpone any type of learning, as is proposed by window-of-opportunities, or critical-periods, hypotheses.

Gaze perception in adults engages occipitotemporal areas along the dorsal visual stream from visual area V5/MT (middle-temporal) to the posterior temporal region (Pelphrey, Morris, Michelich, Allison, & McCarthy, 2005). The visual dorsal pathway is known to be particularly vulnerable in preterm infants (Atkinson & Braddick, 2007). It is therefore surprising to find an acceleration of gaze following in preterm infants, especially considering that preterm infants are typically delayed in detecting reversal of dot motion compared with full-term control infants (Birtles, Braddick, Wattam-Bell, Wilkinson, & Atkinson, 2007). Biological motion perception might rely on specific circuits of the V5/MT area that favor face motion processing, as suggested by neuropsychological dissociations (Vaina, Lemay, Bienfang, Choi, & Nakayama, 1990) and the early development of biological motion perception in neonates of several species (Simion, Regolin, & Bulf, 2008; Vallortigara, Regolin, & Marconato, 2005).

To some extent, vulnerability to lesions and sensitivity to the environment might be two sides of the same coin, in that both are dependent on the maturational state reached at around term (Taylor, Jakobson, Maurer, & Lewis, 2009). Area V5/MT myelination matures quickly around the time of full-term birth (Flechsig, 1920) and receives direct retinthalamic projections that bypass V1 (Warner, Kwan, & Bourne, 2012). As maturation progresses, the balance between the direct route to the MT area and the V1-MT pathway is shifted such that the latter becomes favored (Warner et al., 2012). Additional studies that test infants' perception of biological motion and of reversal of dot motion using the same method are necessary to further clarify these points.

Longitudinal studies would also be needed to determine whether earlier gaze-following capacity in preterm infants is in any way predictive of later social communication abilities, given their higher risk of autism (Mahoney, Minter, Burch, & Stapel-Wax, 2013). The study of healthy

preterm infants is essential for understanding human cognitive development because it helps to differentiate the effects of environmental sensitivities, neural maturation, and neural vulnerability on closely related cognitive capacities.

Author Contributions

M. Peña developed the study concept. M. Peña and G. Dehaene-Lambertz contributed to the study design. M. Peña and D. Arias performed the testing and data collection. M. Peña performed the data analysis. M. Peña and G. Dehaene-Lambertz interpreted the data. M. Peña and G. Dehaene-Lambertz drafted the manuscript. All authors approved the final version of the manuscript for submission.

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Declaration of Conflicting Interests

The authors declared that they had no conflicts of interest with respect to their authorship or the publication of this article.

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