



INTERNATIONAL ATOMIC ENERGY AGENCY
UNITED NATIONS EDUCATIONAL, SCIENTIFIC AND CULTURAL ORGANIZATION
INTERNATIONAL CENTRE FOR THEORETICAL PHYSICS
I.C.T.P., P.O. BOX 586, 34100 TRIESTE, ITALY, CABLE: CENTRATOM TRIESTE



SMR.853 - 44

ANTONIO BORSELLINO COLLEGE ON NEUROPHYSICS

(15 May - 9 June 1995)

**"The Development of Eye Alignment, Convergence,
and Sensory Binocularity in Young Infants"**

Richard Held
Department of Brain and Cognitive Sciences
Massachusetts Institute of Technology
Cambridge, MA 02139
U.S.A.

These are preliminary lecture notes, intended only for distribution to participants.

MAIN BUILDING STRADA COSTIERA, 11 TEL. 22401 TELEFAX 224163 TELEX 460392 ADRIATICO GUEST HOUSE VIA GRIGNANO, 9 TEL. 224241 TELEFAX 224531 TELEX 460449
MICROPROCESSOR LAB. VIA BEIRUT, 31 TEL. 224471 TELEFAX 224163 TELEX 460392 GALILEO GUEST HOUSE VIA BEIRUT, 7 TEL. 22401 TELEFAX 224559 TELEX 460392

The Development of Eye Alignment, Convergence, and Sensory Binocularity in Young Infants

Frank Thorn,*† Jane Gwiazda,* Antonio A. V. Cruz,‡
Joseph A. Bauer,* and Richard Held*

Purpose. To measure and compare the development of ocular alignment, sensory binocularity, and convergence in infants during the first 5 months of life.

Methods. Healthy infants were tested between 2 and 21 weeks of age. Ocular alignment was measured by the Hirschberg test; convergence was determined by visual examination as an illuminated toy approached an infant's face; and sensory binocularity was measured by preferential looking for fusible versus rivalrous gratings. In experiment 1, we compared the proportion of infants at different ages demonstrating orthotropic ocular alignment with those showing convergence. In experiment 2, we compared the age of onset of convergence to that of sensory binocularity.

Results. Experiment 1: Most infants were orthotropic during the first month, and almost all of the others showed small amounts of exotropia. None of the infants showed accurate convergence until 6 weeks of age. By 4 months of age virtually all were orthotropic and had good convergence. Experiment 2: The onset of sensory binocular fusion occurred at 12.8 ± 3.3 weeks. Full convergence did not occur until 13.7 ± 3.2 weeks, although the first signs of convergence occurred slightly earlier. For individual infants there was a high correlation between the age of onset of sensory binocularity and convergence, and both onsets occurred earlier in girls than in boys.

Conclusions. Ocular alignment did not require the development of binocularity mechanisms, and the development of binocularity mechanisms did not await the onset of good ocular alignment. The relatively sudden onset of binocularity, both sensory (preference for fusion and stereopsis) and motor (convergence) at about 3 months of age and the high correlation between these measures indicate a common causal mechanism that probably involves refinements in striate cortex circuitry. Invest Ophthalmol Vis Sci. 1994;35:544-553.

Normal binocular vision requires orthotropic alignment of the eyes and the binocular mechanisms for disparity-controlled convergence, sensory fusion, and stereopsis. Many studies indicate that these different aspects of binocularity approach adult levels by 4 to 6 months of age.¹⁻⁵ However, differences in data and

interpretation concerning the development of ocular alignment, convergence, binocular fusion, and stereopsis have made it difficult to determine the causal relationships among these components of binocularity.

The most consistent binocularity data are for sensory binocularity. Preferential looking toward binocularly fusible rather than rivalrous stimuli occurs suddenly in individual infants between 6 and 16 weeks of age. Previous studies show that young infants prefer viewing binocularly orthogonal gratings that are seen as rivalrous by adults who have normal binocularity. Older infants prefer the fusible grating.^{3,6,7} Stereopsis tested with preferential looking,^{2,8} motion tracking⁹ or visual evoked potentials^{10,11} also occurs with a sudden onset at this time. The onsets of binocular fusion and stereopsis occur at the same average age^{3,7} and at the

From the *Infant Vision Laboratory, Massachusetts Institute of Technology, Cambridge, Massachusetts; the †New England College of Optometry, Boston, Massachusetts; and ‡Faculdade de Medicina de Ribeirão Preto, USP Dept. Ophthalmologia, Ribeirão Preto, Brazil.

Supported by National Institutes of Health grants 2R01 EY 1191 and SP30-EY02621 and National Institutes of Health Fogarty International Research Fellowship 1 FOS TW04491-01 ICP (S).

Submitted for publication August 7, 1992; revised October 14, 1993; accepted October 22, 1993.

Proprietary interest category: N.

Reprint requests: Frank Thorn, Infant Vision Laboratory, E10-138, Massachusetts Institute of Technology, Cambridge, MA 02139.

same relative age for individual infants within a sample as shown by the high correlation between the two onsets.¹²

The development of convergence is more complex because the convergence response is driven by several cues including accommodation, retinal disparity, and "proximity."¹³ Under some conditions partial convergence can be demonstrated to occur intermittently in infants during the first month. It is believed that this sporadic convergence is triggered by accommodation.^{1,14} According to Aslin and Jackson,^{1,15} very young infants show inaccurate, inconsistent convergence to an approaching object but by 3 to 4 months their convergence is accurate and consistent.^{1,15} Held¹⁶ proposed that this accurate convergence results from the acquisition of disparity control mechanisms within the visual cortex. Using electro-oculograms, Mitkin and Orestova⁴ demonstrated a sudden improvement in convergence between 12 and 15 weeks of age. The age of this sudden improvement matches the age of onset of stereopsis and suggests that retinal disparity plays an essential role in the improvement of accurate convergence.

Base-out prisms placed before the eyes provide retinal disparity cues that induce convergence in adults but do not trigger convergence in infants before 6 months of age.^{1,17} This does not mean that disparity is not an effective convergence cue before this age. However, the disparity induced by a prism is in direct conflict with the information for convergence provided by accommodation and proximity cues. Thus, the prism technique may simply show that disparity cues cannot dominate over competing accommodative and proximity cues until 6 months of age.

Until recently, the literature concerning the temporal development of ocular alignment has also been relatively consistent. Most laboratories using corneal reflections from a fixation light have shown that, when large angle kappas (8° to 10°) are assumed, most infants are approximately orthotropic during the first month.^{1,14,15,18} Data that demonstrated small consistent amounts of exotropia in young infants using a similar technique^{19,20} have since been explained by the infant's large angle kappa.²¹ Recently, Sondhi and colleagues²² and Archer and colleagues,⁵ using the examiner's face as a fixation target, reported that infants up to 2 months of age tend to have very large angles of exotropia ($> 40^\Delta$) and then become orthotropic during the 3rd and 4th months. The cumulative percentage increase in orthotropia with age coincides with that of stereopsis and has led some authors to speculate that there might be a causal relationship between the basic alignment of the eyes and binocular fusion.²³ But, these findings differ sharply from those in which a standard Hirschberg test was used.

Because of their crucial importance in under-

standing the development of binocular mechanisms, we have examined the relationships among the development of eye alignment, convergence, and sensory binocular fusion in young infants. By comparing the presence of orthotropic ocular alignment and convergence in young infants we hope to determine if convergence is delayed until the eyes are aligned (consistent with Sondhi and colleagues²² and Archer and colleagues⁵) or if the eyes are aligned at a much earlier age^{1,14,15,18} and convergence develops according to its own mechanisms. By comparing the development of binocular fusion preference and convergence, both of which involve binocular circuitry, we hope to determine if these two processes develop together in an infant. If they do, this suggests that two similar mechanisms are developing in unison or that the onset of these two functions awaits the development of a shared binocular mechanism.

METHODS

This research followed the tenets of the World Medical Association Declaration of Helsinki. Informed consent was obtained from parents after the nature and possible consequences of the study were discussed. The research was first approved by the Massachusetts Institute of Technology Committee on the Use of Human Experimental Subjects.

Experiment 1

Subjects. Thirty-four healthy infants, who were the product of uncomplicated pregnancies and deliveries, were examined. All births had occurred within 3 weeks of the expected due date. In accord with the previous convention of the laboratory, all ages cited are relative to due date rather than the actual date of birth. This convention is used because grating acuity, the most widely studied visual standard for infants, has been shown to be best predicted by gestational age rather than postparturitional age.²⁴

Each infant was examined during several visits (one to seven visits; mean 3.2 visits) usually on a weekly or biweekly schedule (mean time between visits 1.8 weeks). The mean starting age was 6.6 weeks (range 0 to 12 weeks). Two infants were excluded because they already demonstrated convergence (9 and 11 weeks of age). In this group, 22 infants were girls and 12 infants were boys.

Procedures. **Eye Alignment:** A standard Hirschberg test was performed in a dark room by two experienced examiners, one optometrist (FT) and one ophthalmologist (AC), at a distance of 1 m using a transilluminator. This fixation light was jiggled and flashed to obtain the infant's attention and fixation. It was never directed toward his or her eyes for more

than a 2-second period without jiggling or flashing because young infants' orienting reflex often habituated so that it could be difficult to elicit repeated fixations.

The observer's score sheet had a series of three drawings of a pair of eyes. On each trial for which the observer believed the infant was fixating the target light, he carefully drew the position of the corneal reflections on a pair of eye drawings. Infants' pupils had approximately a 4-mm diameter (between 3.5 and 4.5 mm for six infants whose pupils were measured) and a conversion for the Hirschberg test of $20 \Delta/\text{mm}$ was used.^{21,25-27} Because an infant's angle kappa is normally 8° to 10° ,²¹ we considered decentered corneal reflections to indicate exotropia only when they were more than midway from the pupillary center to the nasal pupillary margin. We believe this method provides an accuracy significantly finer than 0.5 mm per eye ($< 5.7^\circ$ or 10Δ). A comparison of interocular differences is even more accurate ($< 3^\circ$ to 4°). Unmeasured interocular differences in angle kappa might introduce additional uncertainty. However, Barry and colleagues,²⁸ using the first and third Purkinje images of three infrared lights to precisely measure the angle alphas of infants and children, have demonstrated asymmetries of less than 1° in infants. Accordingly, we are confident that our estimates of ocular alignment are accurate to within 10Δ . Such an estimate allows us to measure eye alignment accurately enough to state that alignment is adequate for binocular fusion or coarse stereopsis, but we cannot estimate if the eyes are aligned well enough for fine stereopsis.

The unilateral cover test could resolve the problem of interpreting the Hirschberg test, but it is difficult to perform a cover test on young infants because they normally withdraw from or look at the cover placed before one eye. Examiner FT performed a standard unilateral cover test on 12 unusually cooperative infants between 4 and 8 weeks of age whom he judged to be orthotropic by the Hirschberg test despite a slightly nasalward position of the corneal reflex.

Convergence: An examiner (FT) jiggled an illuminated toy in a dark room approximately 0.5 m from the infant's face until the infant fixated on it. It was then moved slowly toward the bridge of the infant's nose while the examiner observed the infant's eyes. Convergence was classified as none, the first sign of convergence (any bilateral adduction), and full (complete binocular pursuit to within 12 cm of the face). The toy used for a fixation target was a brown rubber pony, the face of which was internally illuminated by the transilluminator. The toy's face was approximately 2 cm in diameter and contained no fine details. The data for the second observer were not included because he often used a different criterion.

Experiment 2

Subjects. Fifty-nine infants (23 girls and 36 boys) were included in this experiment. Fifteen of these also participated in experiment 1. The infants had a mean of 6.5 visits. The mean age for initial testing was 7.5 weeks (range was 1 to 11 weeks). As in experiment 1, all ages are relative to due date.

In order to compare the ages of onset of convergence and binocular fusion preference, we have included in our data analysis only the infants who completed both tasks after showing neither response on their first visit ($n = 59$). We did not include infants who started the study at an age more than 11 weeks after their expected due date ($n = 11$, first visit between 11.5 and 16 weeks), infants who did not complete one or both tasks because they did not return before the expected onset of binocularity ($n = 2$), infants whose onsets were so late that the parents tired of the study ($n = 5$, discontinued between 22.5 and 29 weeks), and infants who already demonstrated one or both of the binocular responses on their first visit ($n = 4$, first visit between 7 and 11 weeks). The exclusion of these infants should not alter the overall mean onsets significantly but may truncate our distribution of onsets by eliminating primarily infants with very early or very late binocularity onsets. This truncation would be expected to reduce variance of onset age and therefore reduce the correlation between convergence and binocular fusion onsets.

Procedures. **Convergence:** Convergence was tested by one examiner (FT) using the same procedures described in experiment 1. The age of onset for the first sign of convergence was the earliest age at which any bilateral adduction was observed in response to the approaching illuminated toy; the age of onset for full convergence was the earliest age at which complete binocular pursuit to within 12 cm of the face was observed.

Binocular Fusion: Sensory fusion was tested by the fusion-versus-rivalry preferential looking technique.⁶ During this procedure the infants sit on their mothers' laps and wear lightweight goggles containing crossed-polarized filters. They view a screen from a 70 cm distance. Flashing fixation lights are used to bring an infant's attention to the center of a dark 3.6° vertical region bounded on both sides by 17° -horizontal by 27° -vertical screens. One screen side has crossed-polarized superimposed vertical gratings, which are readily fused by normal adults; the other side has non-fusible crossed-polarized orthogonal gratings, a vertical grating viewed by one eye and a horizontal grating viewed by the other, which are not fusible by normal adults. Gratings consisted of a rectangular wave of 0.40 cycles per degree.

The criterion for the onset of sensory binocular

Binocular Development in Infants

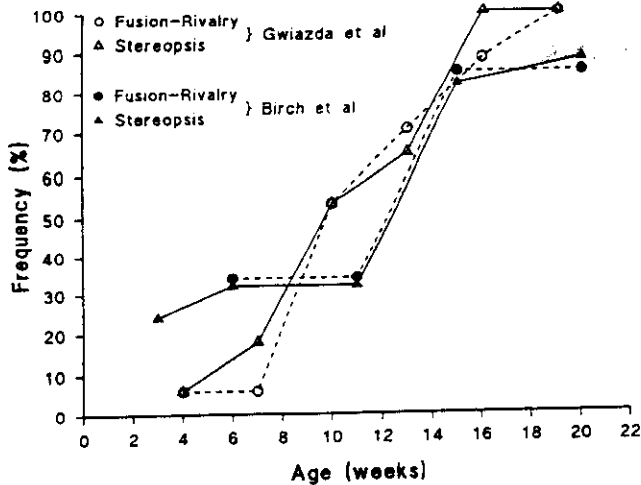


FIGURE 1. Cumulative proportion of infants showing stereopsis and fusion preference as a function of age. Data from Gwiazda and colleagues⁷ ($n = 17$) and Birch and colleagues³ ($n = 9$).

fusion is the age at which an infant first has a looking preference for the binocularly fusible gratings on 12 or more of the 15 trials in one session provided that the infant preferred the fusible gratings on 21 or more of the 30 trials during that session and either the preceding or following session. Both the single session and two session performance levels have been chosen because the probability of reaching either is less than 0.05. The experimenter performing the binocular fusion preferential looking testing (JG) was unaware of the results of convergence testing, and the experimenter performing convergence testing (FT) was unaware of the fusion preference results.

Preference for binocularly fusible versus rivalrous patterns normally switches suddenly from a preference for viewing binocularly orthogonal gratings, that are seen as rivalrous by normal adults, to a preference for the fusible grating^{3,6,7} at about the same age as the onset of stereopsis.^{3,6,7} The similarity in fusion and stereopsis development is shown in Figure 1 using data from Birch and colleagues³ and Gwiazda and colleagues.⁷ The original data from these articles have been grouped into 3-week intervals in the same way that we have grouped our data in experiment 1. In both studies data from individuals show that the onsets of stereopsis and binocular fusion preference occur within 1 week of each other for a majority of the infants. This laboratory generally uses the binocular fusion-rivalry preferential looking test rather than stereopsis because it requires simpler instrumentation and calibration and because it is designed to be unaffected by significant amounts of ocular misalignment even though it is highly correlated with stereopsis. It is also easier to score.

Quantifying the Relationship Between Convergence and Fusion Onset: We have quantitatively related the age of onset of full convergence to that of binocular fusion preference. Such a relationship is usually calculated by means of a linear regression equation. However, a linear regression equation is only valid when relating a dependent variable that was actually measured to an independent variable. Our data involve the measurement of two dependent variables. The simple linear regression function, which assumes that the measurements on the x axis at given points are without significant variance, minimizes variance on the y axis only. This leads to a slope that is always less than it would be if realistic assumptions had been made about variance on the x axis. Therefore, we have calculated a mutual regression function based on the best-fit line of principal axis analysis to compare the age of onset of full convergence to that of binocular fusion preference.²⁹

RESULTS

Experiment 1

The proportion of infants showing orthotropia and convergence is plotted in 3-week intervals in Figure 2. At less than 6 weeks of age, most infants showed orthotropia, but none showed full convergence. The age at which 50% of the infants demonstrated full convergence was 11.9 weeks.

The discrepancy between the observations of the two examiners can be accounted for as follows. The

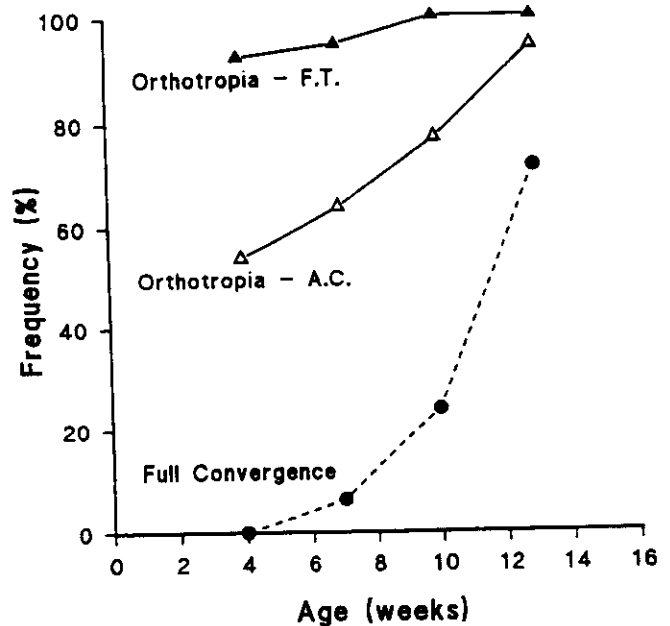


FIGURE 2. Proportion of infants demonstrating orthotropia according to two examiners and demonstrating full convergence, as a function of age.

two examiners judged about the same total amount of nasal decentration of the corneal reflection for almost all infants. Often this was about halfway from the pupil center to the nasal margin of the pupil because of the infant's large angle kappa. If both reflections were less than half way from the pupil center our criterion for orthotropia was reached. If one was closer to the pupil center and the other closer to the nasal margin of the pupil, then it was judged that the reflections were asymmetrical and that an exotropia occurred. Thus, the difference between an orthotropia and a small exotropia involved a subtle measurement difference (usually within our measurement error range). One observer accepted symmetry of corneal reflections more often than the other (for infants less than 1 month of age, 93% versus 56%). It should be noted that both corneal reflections always fell within the pupillary margins for both observers, indicating that exotropias were never more than 30Δ .

During the 80 subject visits when an infant was seen by both examiners, they agreed that the infant was orthotropic 62 times and exotropic two times. Examiner FT judged exotropia only twice when examiner AC judged orthotropia, but examiner AC judged exotropia 14 times when examiner FT judged orthotropia. During 32 visits the infant was too uncooperative for one of the examiners to make a judgment. On these visits, the successful examiner showed the same proportion of orthotropic judgments as when both examiners were able to make successful judgments. One infant was judged to have intermittent esotropia on all four of his visits.

The unilateral cover test was performed successfully on 10 of the 12 infants tested between 4 and 8 weeks. In each case, the infant's fixation did not move when one eye was covered, indicating that the infants were indeed orthotropic.

Experiment 2

Figure 3 shows cumulative onset functions for binocular fusion preference and the two criteria for convergence (first sign of convergence and full convergence) with each data set being fit by a Gaussian integral. The three best-fit functions are very similar with the same slope.

There were no positive responses before 5 weeks of age. The mean onset for binocular fusion preference was 12.8 ± 3.3 weeks. Fusion preference is preceded by the first indication of convergence (mean 12.1 ± 3.2 weeks) and followed by the onset of full convergence (mean 13.7 ± 3.2 weeks). These onsets for binocular fusion are slightly later than in previously published studies^{3,4,7} and these convergence onsets are significantly later than those in experiment 1. This discrepancy is partially explained by the fact that

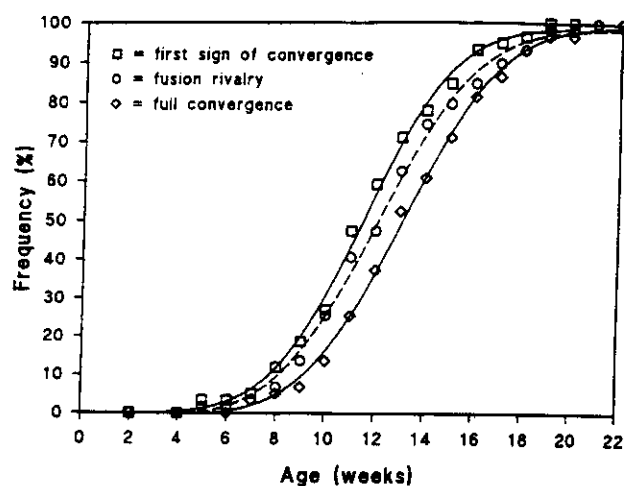


FIGURE 3. Cumulative proportion of infants showing the onset of partial and full convergence and binocular fusion-rivalry preference, as a function of age.

most studies calculate the population onset age as the age when 50% of the infants achieve a particular behavior. Because the distributions for the data in this experiment are positively skewed normal distributions, the 50% achievement criteria occurs earlier than the means (fusion preference 12.1 weeks, first sign of convergence 11.4 weeks, and full convergence 13.1 weeks). This age of onset estimate is 0.6 to 0.7 weeks earlier than the calculated means. The other identifiable factor is that, through chance differences in scheduling, most of the infants in experiment 2 were boys, whereas most of those in experiment 1 were girls (see below).

For individual infants both the preference shift from rivalry to fusion and from no convergence to full convergence occurred during a brief period, normally less than 2 weeks. For 53% of the infants, the first sign of convergence was full convergence pursuit. Although the onset of fusion occurs only 1 week before full convergence, the difference is statistically significant (paired $t = 2.43$, $P = 0.018$ two-tailed).

The similar onset functions for the group as a whole are reflected in the individual data. The onsets for sensory fusion and full convergence for the individual infants showed a significant correlation ($r = 0.59$, $P < 0.0001$), as shown in Figure 4. The magnitude of this correlation is somewhat limited by a narrow distribution of onset ages (SD 3.1 weeks). The principal axis best-fit line for this scatter plot is $C = 0.941(F) + 1.668$, where C is onset age of full convergence, and F is onset age of fusion preference, both in weeks of age. The slope of this best-fit line is not significantly different from 1.0. The age of onset of the first sign of convergence also demonstrated a significant correlation with the age of onset of binocular fusion ($r = 0.54$, $P < 0.0001$).

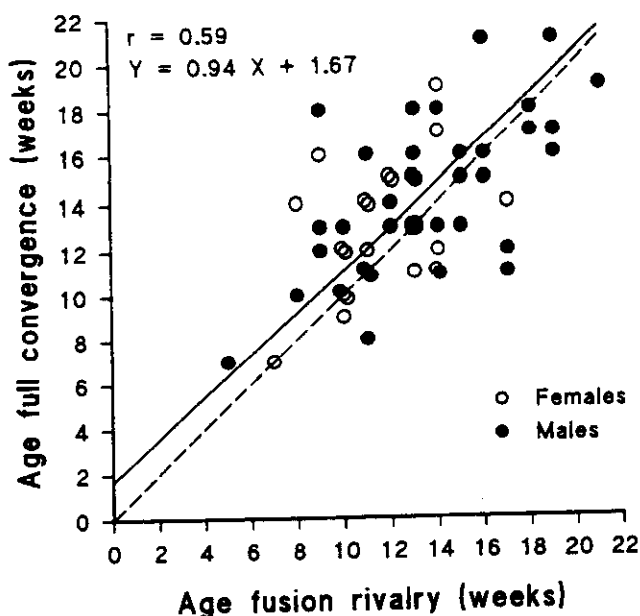


FIGURE 4. Scatter plot for age of onset of full convergence and binocular fusion-rivalry preference for all 59 infants in experiment 2. Open circles, girls; filled circles, boys.

As in earlier studies,^{7,50} girls have an earlier mean onset age than boys for binocular fusion preference (11.6 versus 13.5 weeks). The mean onset of full convergence also occurred earlier in girls (13.0 versus 14.2 weeks). A two-dimensional analysis of variance shows that girls have a significantly earlier onset than boys for these binocular measurements ($F[1,57] = 4.329$, $P = 0.042$) and that fusion preference occurs significantly earlier than convergence ($F[1,57] = 6.584$, $P = 0.013$). However, there is no significant interaction effect between gender and the visual task ($F[1,57] = 0.838$, $P = 0.364$). The lack of an interaction suggests that a subject's gender does not induce a significant difference between the ages of onset of the two tasks even though t tests show that girls precede boys by a highly significant amount for binocular fusion ($t = 2.26$, $P = 0.014$ one-tailed) and a not quite significant amount for convergence ($t = 1.44$, $P = 0.078$ one-tailed).

DISCUSSION

Our data show that the onset of convergence and sensory fusion can neither be the cause nor the result of good eye alignment because most infants' eyes are orthotropic or very close to orthotropic during the first month. On the other hand, the close link between convergence and sensory fusion onsets is unmistakable. The two onsets occur at about the same time and the correlation between the two onsets is highly significant. This suggests a common causal factor, which we

believe is the onset of functioning fusion and disparity mechanisms in the central visual system.¹²

Factors in Judging Ocular Alignment

Our ocular alignment data are similar to those in most previous studies.^{1,14,15,18} However, our examiners considered the differentiation between orthotropia and small angles of exotropia to be the most difficult judgment that they performed. The four major sources of uncertainty or error in making these judgments are: the large angle kappa of infants, the absence of convergence, difficulty in judging when an infant is looking at a fixation target, and the infant's arousal level. All of these factors can increase the likelihood that aligned visual axes will be judged as exotropic.

The basic factor confounding the interpretation of an infant's ocular deviation is the angle kappa. We might expect the reflection of a light on a subject's cornea to be centered in the pupil when the subject fixates the light, but this is rarely the case. The corneal reflection is usually displaced relative to the optical axis or pupillary center by an amount denoted as angle kappa. Slater and Findlay²¹ showed (using photographs of corneal reflections during monocular viewing) that the mean empirical angle kappa of neonates is 8° , consistent with the 8.5° angle kappa calculated on anatomical considerations. This finding implies that, based on the Hirschberg test, neonates would appear to have a 30Δ exodeviation when their eyes are perfectly aligned on a distant target.

The lack of convergence shown by young infants can add to the illusion of an exodeviation, because an infant must be tested with a relatively near target. We have tested as far away as we deemed practical (1 m). If the interpupillary distance of an infant is assumed to be about 40 mm, this viewing distance would add 4Δ exo to a nonconverging infant's apparent exodeviation. The nearer viewing distances (25 cm to 50 cm), that are commonly used in testing infants, also add to the appearance of an exodeviation (16Δ and 8Δ , respectively).

The calibration of a zero point for the Hirschberg test is very difficult because we can never be certain of precisely where an infant is fixating. We believe the primary reason that our two observers did not always agree with each other is that infants do not always look at the fixation light. For example, if an infant looked directly at the fixation light on each of three fixation trials, each eye would have a corneal reflection decentered nasally by about 8° from the center of the pupil. If the infant looked just 8° to the side of the fixation light on one trial, the corneal reflection would be centered in one eye and 16° nasal in the other eye, and this infant would be categorized as having an intermittent small-angle exotropia. Thus, judgments of when

the infant is fixating the light or off to the side are crucial. Photographic or video records of the Hirschberg test appear to provide a more accurate measurement of eye alignment than simple direct viewing as used in our study.^{1,14,15,18-20} These techniques provide a hard copy of the infants' looking behavior and therefore allow for repeated precise measurements. But, the key factor causing inaccuracies in using the Hirschberg test on infants is the judgment of where the infant is looking and this must be made by an observer. The unilateral cover test can resolve the problem of interpreting the Hirschberg test when fixation and the size of the angle kappa are uncertain. For the ten infants under 8 weeks of age on whom the unilateral cover test was successfully performed, the infants were indeed orthotropic even though large angle kappas made the interpretation of the Hirschberg test difficult.

Finally, an infant's arousal level can influence eye alignment. Rethy³¹ used the Hirschberg test to measure eye alignment in sleeping neonates. He judged 37% of his premature and 43% of his full-term sleeping infants to be orthotropic with the remainder showing 15° to 35° of exodeviation. He believed that this tendency toward exotropia approximates the anatomical position of the eyes at rest, noting that when the neonates awoke their exotropic eyes would often assume an orthotropic position. By 3 weeks of age most infants showed an orthotropic alignment during testing due, he believed, to increased wakefulness, accommodative convergence, and stronger fixation behavior.

Using a Face as a Fixation Target

Recently, a group used a very different technique for measuring the ocular alignment of young infants.^{5,22,32} The examiner held the infant on his or her arm with the head in the examiner's hand so that the infant could fixate on the face of the examiner. The examiner then used the corneal reflection of his or her own face, which appears as a dark silhouette against a light background. Thus, rather than judging the position of a small light spot on the cornea tested from a 0.4- to 1.0-m viewing distance, the examiner judged the position of a large dark area against a slightly lighter background from a 0.2 to 0.25 m viewing distance. The rationale for this technique was that infants attend to a face better than to a light. However, our examiners found the task of judging the position of their own reflection from an infant's cornea to be far more difficult than the Hirschberg test.

Nixon and colleagues,³² using the novel technique described above, report that 58% of 1031 testable newborn infants were orthotropic and 39% exotropic. Sondhi and colleagues,²² using the same technique,

found that 30% of 2271 newborns were orthotropic and that almost all the others were exotropic. These proportions remained constant through 6 weeks of age. There was then a rapid increase in orthotropia to 75% at 3 months and 97% at 6 months. Archer and colleagues,⁵ again using the same technique on 3316 newborn infants, found that fewer than 25% were orthotropic with 72% showing an exotropia. At 3 months, 75% were orthotropic and at 6 months 97% were orthotropic. We do not know why Nixon and colleagues³² found a much higher percentage of orthotropic neonates, because this study involved the same group of experimenters using the same technique as the two subsequent studies. In Archer and colleagues'⁵ study moderate exotropias (defined as a corneal reflection falling more than halfway to the limbus from the pupillary center) were seen in 52% of newborn infants and 30% of 1-month-old infants. If the infant's pupillary diameter is 4 mm, the horizontal width of the infant's cornea from limbus to limbus is 10 mm, and we assume 20Δ/mm angular deviation, then this deviation amounts to 40Δ to 100Δ of exodeviation, which most examiners would consider a large-angle deviation, and is in direct contradiction to all the other studies cited.^{1,14,15,18}

Because of the large samples used in these studies,^{5,22} the findings have received considerable attention. Thus, it is important to try to understand why they differ from our findings and those of so many others. A large angle kappa and a lack of convergence for a near viewing distance can account for about a 45Δ exodeviation. However, if the infant is alert and fixating on the examiner's eyes, the corneal reflections would be approximately symmetrical and the examiner would interpret this as orthotropia with a large angle kappa. We think the unusual confounding factor, when using the examiner's face as the fixation target, is that the facial features on which the infant fixates change with age. Infants younger than 2 months of age tend to fixate on the largest high contrast feature of the head, namely the hair line and the silhouette of the head.³³⁻³⁶ In Archer and colleagues'⁵ procedure, the room lighting comes from behind the examiner so that features of the face are especially dim relative to the silhouette of the examiner's hair. If Archer and colleagues'⁵ young infants fixated on the lateral hairline and silhouette, then the examiner would be 15° to 20° (26Δ to 35Δ) eccentric to the line of sight and would conclude that the infant was highly exotropic. By 4 months of age, infants act more like adults, spending most of their time looking at the features of the face³³⁻³⁶ with special attention on the eyes.³⁷

It is surprising that the cumulative distribution of the age of orthotropia onset from Archer and col-

leagues'⁵ study is so similar to the cumulative distribution of the age of onset of stereopsis and binocular fusion^{3,6-8,23} and convergence (Figs. 1, 3) if Archer and colleagues' data are due to a mechanism as seemingly unrelated as the change in an infants' strategy for facial scanning. A portion (about 15Δ) of the reduction they show in exotropia during the 3rd and 4th month can be explained by the onset of consistently accurate convergence. The similarity in the development of facial scanning and binocularity may be explained by the findings of Kleiner and Banks.³⁸ They have shown that the proportion of time that 2-month-old infants look at a drawing of a face versus a competing pattern is related to the phase spectrum of facial features rather than the contrast spectrum of the pattern. It is the phase spectrum of borders within a picture or drawing, not the contrast spectrum, that allows adults to recognize faces and other objects although an altered contrast spectrum may degrade the visibility of the face or object.

Our laboratory has demonstrated that vernier acuity, which measures sensitivity to phase changes within a pattern, develops in parallel with stereopsis and binocular fusion preference.³⁹ In fact, vernier acuity is similar to stereopsis and binocular fusion in that girls develop it at an earlier age than boys.⁴⁰ We have hypothesized that vernier acuity develops parallel to binocularity because it also depends on the development of the visual cortex. Thus, the serendipitous parallel development of binocular mechanisms and eye alignment as described by Archer and colleagues⁵ may represent the development of mechanisms within the visual cortex both as they relate to fusion-induced convergence and to the phase-sensitive mechanisms needed for adultlike facial scanning.

Eye Alignment Versus Sensory Binocularity

Most young infants are within a few prism diopters of orthotropia even though functional binocular mechanisms do not develop until about 3 months of age. Thus, it is clear that binocular mechanisms are not necessary for good ocular alignment in early infancy. The question of whether good ocular alignment is necessary for the development of binocularity is not as clear. We know that surgically induced exotropia in kittens⁴¹ and infant monkeys⁴² during the critical period for susceptibility to abnormal visual experience causes a loss of cortical binocularity and therefore a loss of the mechanisms required for fusion-induced convergence. However, the critical period for the development of sensory binocularity in humans with strabismus does not start at birth but at about 6 months of age.^{43,44} In addition, Birch and Stager⁴⁵ have shown that infants who become strabismic have as high a probability of developing stereopsis before

strabismus onset (between 3 and 5 months of age) as do normally developing infants. Thus, it may be that good ocular alignment is not necessary for the development of the neural mechanisms underlying binocularity, although the maintenance of these binocular mechanisms requires good alignment.⁴⁵ Because good eye alignment exists in most young infants, this is difficult to test.

Convergence Versus Eye Alignment and Sensory Binocularity

Convergence involves ocular alignment and sensory binocularity because the function of convergence is to align the eyes for different viewing distances using binocular information. Ocular alignment is important for fusional convergence because fusional convergence cannot be expressed if the eyes deviate excessively, even if the necessary retinal disparity control mechanisms exist in the brain. Similarly, stereopsis and binocular fusion cannot normally be expressed if the ocular deviation is excessive or if convergence does not allow bifixation at a near distance. Our data indicate that convergence depends on mechanisms similar to those of sensory fusion and stereopsis. These similarities include the gender difference in which girls develop earlier than boys. Thus, just at the time binocular mechanisms require reinforcement as they enter into their critical period, fusional convergence is initiated to provide this fine control of ocular alignment at all viewing distances.

Cortical Control Mechanisms

The visual cortex, as well as other cortical areas of postnatal infant primates, continues to develop along a number of parameters including neuron size, neuropil density, dendritic spine density, and the number of synapses.^{46,47} Although these quantitative changes imply functional change during the postnatal period, they do not lend themselves to an analysis of the functional neural refinements expected to be associated with visual refinement. The ocular dominance columns of the striate cortex provide a model system for visualizing refinement of columnar circuitry. In the newborn rhesus macaque, ocular dominance columns are readily identified in layer 4 of the striate cortex but the boundaries between adjacent columns are highly blurred. This indicates a diffuse lateral geniculate nucleus input to layer 4 that crosses the functional borders that must be maintained for proper binocular function.⁴⁸ In effect, the information from the two eyes is mixed together at their entrance into the striate cortex so that the interocular comparison needed for retinal disparity comparison would be scrambled.^{16,23}

By 2 months of age the boundaries between adjacent columns are sharply delineated and the monkey's stereopsis can approach adult levels. In humans, ste-

reopsis suddenly develops in individual infants at an average age of 3 months, consistent with a refinement of the ocular dominance boundaries.⁴⁹ At the same time infants stop preferring a pattern containing orthogonal gratings to the two eyes and start to look preferentially at binocularly fusible gratings. Shimojo and colleagues⁶ suggest that in the young infant the orthogonal gratings may be integrated into a preferred grid pattern and that only when the information from the two eyes is segregated within layer 4 of the striate cortex can the two gratings be disengaged so that one can be suppressed by the other through binocular rivalry. At that time the fused (or summed) parallel gratings would suddenly be preferred to the rivalrous pattern.

The parallel between the development of vernier acuity and the sensory binocular functions is expected if vernier acuity also depends on a refinement of cortical columns (though not ocular dominance columns). In this case, precise relative monocular position sense (or spatial phase) rather than a precise relative interocular positional sense between the two eyes develops rapidly at about the same age. This refinement of the positional sense appears to underlie the mature facial scanning behavior of the 3- and 4-month-old infant that allows an examiner and parents to observe the infant looking directly at their face.

Conclusions

Most infants are orthotropic at 1 month of age; almost all the others are just slightly exotropic. Thus, the results of this study indicate that early infantile ocular deviations cannot delay the development of binocularity mechanisms, nor can the binocular mechanisms that develop at about 3 months of age have an effect on the initial alignment of the eyes. The relatively sudden onset of binocularity, both sensory (preference for fusion and stereopsis) and motor (fusional convergence), at about 3 months of age and the high correlation between these measures suggest a common causal mechanism. We hypothesize that this important benchmark involves the refinement of circuits in the cerebral cortex, especially those of the ocular dominance columns.

Key Words

infants, ocular alignment, binocular fusion, convergence, binocular vision

References

1. Aslin RN. Development of binocular fixation in human infants. *J Exp Child Psychol.* 1977;23:133-150.
2. Held R, Birch EE, Gwiazda J. Stereoacuity in human infants. *Proc Natl Acad Sci USA.* 1980;77:5572-5574.
3. Birch EE, Shimojo S, Held R. Preferential-looking assessment of fusion and stereopsis in infants aged 1 to 6 months. *Invest Ophthalmol Vis Sci.* 1985;26:366-370.
4. Mitkin A, Orestova E. Development of binocular vision in early ontogenesis. *Psychologische Beiträge.* 1988;30:65-74.
5. Archer SM, Sondhi N, Helveston EM. Strabismus in infancy. *Ophthalmology.* 1989;96:133-137.
6. Shimojo S, Bauer J, O'Connell KM, Held R. Pre-stereoptic binocular vision in infants. *Vision Res.* 1986;26:501-510.
7. Gwiazda J, Bauer J, Held R. Binocular function in human infants: correlation of stereoptic and fusion-rivalry discriminations. *J Pediatr Ophthalmol Strab.* 1989;26:128-132.
8. Birch EE, Gwiazda J, Held R. Stereoacuity development for crossed and uncrossed disparities in human infants. *Vision Res.* 1982;22:507-513.
9. Fox R, Aslin RN, Shea SL, Dumais ST. Stereopsis in human infants. *Science.* 1980;207:323-324.
10. Braddick O, Atkinson J, Julesz B, Kropfl W. Cortical binocularity in infants. *Nature.* 1980;288:363-365.
11. Petrig B, Julesz B, Kropfl W, Baumgartner G, Anliker M. Development of stereopsis and cortical binocularity in human infants: Electrophysiological evidence. *Science.* 1981;213:1402-1404.
12. Held R. Development of binocular vision and stereopsis. In: Regan D, ed. *Binocular Vision.* London: Macmillan; 1991:171-178.
13. Kruger PB, Pola J. Stimuli for accommodation: Blur, chromatic aberration and size. *Vision Res.* 1986;26:957-971.
14. Slater AM, Findlay JM. Binocular fixation in the newborn baby. *J Exp Child Psychol.* 1975;20:248-273.
15. Aslin RN, Jackson RW. Accommodative-convergence in young infants: development of a synergistic sensory-motor system. *Can J Psychol.* 1977;33:222-231.
16. Held R. Normal visual development and its deviations. In: Lennerstrand G, von Noorden G, Campos E, eds. *Strabismus and Amblyopia.* London: Macmillan; 1988:247-257.
17. Parks MM. Growth of the eye and development of vision. In: Liebman S, Gellis S, eds. *The Pediatrician's Ophthalmology.* St. Louis: CV Mosby, 1966:15-25.
18. Hershenson M. Visual discrimination in the newborn. *J Comp Physiol Psychol.* 1964;58:270-276.
19. Wickelgren L. Convergence in the human newborn. *J Exp Child Psychol.* 1967;5:74-85.
20. Wickelgren L. The ocular response of human newborns to intermittent visual movement. *J Exp Child Psychol.* 1969;8:469-482.
21. Slater AM, Findlay JM. The corneal reflection technique and the visual preference method: Sources of error. *J Exp Child Psychol.* 1975;20:240-247.
22. Sondhi N, Archer SM, Helveston EM. Development of normal ocular alignment. *J Pediatr Ophthalmol Strab.* 1988;25:210-211.
23. Held R. Two stages in the development of binocular vision and eye alignment. In: Simons K, ed. *Infant Vision: Basic and Clinical Research.* New York: Oxford University Press. In press.

Binocular Development in Infants

24. Birch EE, Spencer R. Monocular grating acuity of healthy preterm infants. *Clin Vision Sci.* 1991;6:331-334.
25. Brodie SE. Photographic calibration of the Hirschberg test. *Invest Ophthalmol Vis Sci.* 1987;28:736-742.
26. DeRespinis PA, Naidu E, Brodie SE. Calibration of Hirschberg test photographs under clinical conditions. *Ophthalmology* 1989;96:944-949.
27. Ruttum MS, Shimshak KJ, Chesner M. Photographic measurement of the angle of strabismus. In: Campos EC, ed. *Strabismus and Ocular Motility Disorders*. Houndmills: Macmillan; 1990:155-160.
28. Barry JCAP, Effert R, Burhoff A, Reim M, Kaupp A. Dependence of angle alpha on age and axial length assessed with Purkinje reflection pattern evaluation. ARVO Abstracts. *Invest Ophthalmol Vis Sci.* 1993;34:862.
29. Sokal RR, Rohlf FJ. *Biometry*. San Francisco: WH Freeman; 1969:526-532.
30. Bauer J, Shimojo S, Gwiazda J, Held R. Sex differences in the development of binocularity in human infants. ARVO Abstracts. *Invest Ophthalmol Vis Sci.* 1986;27:265.
31. Rethy I. Development of the simultaneous fixation from the divergent anatomic eye-position of the neonate. *J Pediatr Ophthalmol.* 1969;6:92-96.
32. Nixon RB, Helveston EM, Miller K, Archer SM, Ellis FD. Incidence of strabismus in neonates. *Am J Ophthalmol.* 1985;100:798-801.
33. Salapatek P. Pattern perception in early infancy. In: Cohen LB, Salapatek P, eds. *Infant Perception: From Sensation to Cognition*. New York: Academic; 1975:133-148.
34. Maurer D, Salapatek P. Developmental changes in the scanning of faces by young infants. *Child Dev.* 1976;47:522-527.
35. Haith MM, Bergmann T, Moore MJ. Eye contact and face scanning in early infancy. *Science.* 1977;198:853-855.
36. Hainline L. Developmental changes in visual scanning of face and nonface patterns by infants. *J Exp Child Psychol.* 1978;25:90-115.
37. Zusne L. *Visual Perception of Form*. New York: Academic; 1970.
38. Kleiner KA, Banks MS. Stimulus energy does not account for 2-month-olds' face preference. *J Exp Psychol Human Percept Perform.* 1987;13:594-600.
39. Shimojo S, Birch EE, Gwiazda J, Held R. Development of vernier acuity in infants. *Vision Res.* 1984;24:721-728.
40. Held R, Shimojo S, Gwiazda J. Gender differences in the development of human visual resolution. ARVO Abstracts. *Invest Ophthalmol Vis Sci.* 1984;25:220.
41. Hubel DH, Wiesel TN. Binocular interaction in striate cortex of kittens reared with artificial squint. *J Neurophysiol.* 1965;28:1041-1059.
42. Crawford MLJ, von Noorden GK. Concomitant strabismus and cortical eye dominance in young rhesus monkeys. *Trans Ophthalmol Soc UK* 1979;99:369-374.
43. Banks M, Aslin RN, Letson RD. Sensitive period for the development of human binocular vision. *Science.* 1975;190:675-677.
44. Hohmann A, Creutzfeldt OD. Squint and the development of binocularity in humans. *Nature.* 1975;254:613-614.
45. Birch EE, Stager DR. Monocular acuity and stereopsis in infantile esotropia. *Invest Ophthalmol Vis Sci.* 1985;26:1624-1630.
46. Huttenlocher PR, de Courten C, Garey LJ, van der Loos H. Synaptogenesis in human visual cortex: Evidence for synapse elimination during normal development. *Neurosci Lett.* 1982;33:247-252.
47. Lund JS, Boothe RG, Lund RD. Development of neurons in the visual cortex (area 17) of the monkey (*macaca nemestrina*): A Golgi study from fetal day 127 to postnatal maturity. *J Comp Neurol.* 1977;176:149-188.
48. LeVay S, Wiesel TN, Hubel DH. The development of ocular dominance columns in normal and visually deprived monkeys. *J Comp Neurol.* 1980;191:1-51.
49. Hickey JL, Peduzzi JD. Structure and development of the visual system. In: Salapatek P, Cohen L, eds. *Handbook of Infant Perception*. New York: Academic; 1987:1-42.

