VISION DEVELOPMENT IN THE MONOCULAR INDIVIDUAL: IMPLICATIONS FOR THE MECHANISMS OF NORMAL BINOCULAR VISION DEVELOPMENT AND THE TREATMENT OF INFANTILE ESOTROPIA

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ABSTRACT

Purpose: The purpose of this research is to study the vision development in monocular individuals so as to better understand normal binocular vision development and to refine the treatment of infants with infantile esotrophia.

Methods: Thirty-six subjects with one clinically normal eye and one eye with no vision (no light perception or history of enucleation) are studied. In addition to measurement of standard parameters of development such as visual acuity, measurement of motion processing is made by both optokinetic and electrophysiologic techniques.

A comparison is made of vision development among three populations: the monocular population, the normal population, and patients with a history of infantile esotropia.

Such comparison is made to study the relative effects of interruption of binocularity and binocular competition. The monocular population represents individuals who have interruption of binocularity, whereas the infantile esotropia population has both interruption of binocularity and binocular competition.

Results: The OKN data suggest that the monucular population is more similar to the normal population than the esotropia population.

The electrophysiologic data shows a statistically significant difference in the three populations. Motion processing is more fully developed in the monocular population than in the infantile esotropia population when compared to the normal population.

Conclusions:

1. The development of motion processing appears to be particularly vulnerable to abnormal experience during the first year of life.
2. Monocular subjects have a less abnormal motion processing system when compared to patients with infantile esotropia even when monocularity is congenital.
3. The results indirectly support the premise that prealignment alternate

occlusion is of benefit to the patient with infantile esotropia prior to realignment.

4. Development of the motion processing system does not necessarily parallel the development of other binocular functions.

INTRODUCTION

The purpose of this presentation is to study the visual development of the monocular individual in order to better understand normal binocular vision development and to refine the clinician's treatment of infants with strabismus. Visual function is compared in three populations: (1) individuals who either were born with one eye or lost vision in one eye during childhood, (2) individuals with a history of normal binocular vision development, and (3) individuals with a history of infantile esotropia. Visual function is determined by standard clinical examination techniques as well as electrophysiologically. Differences in certain functions of the 3 groups reflect differences in visual development. The results support a rationale for a specific approach to treatment of the infant with strabismus in order to enhance binocular vision development.

STRABISMUS AND ITS RELATIONSHIP TO BINOCULAR VISION—NATURE VERSUS NURTURE

The clinical issues of strabismus and abnormal visual development are so obviously interrelated that a discussion of one requires a thorough understanding of the other. This association is especially important in considering the management of the patient with infantile esotropia. Early and accurate treatment to achieve the sensory goals — no amblyopia and the best possible binocular vision — is advocated on the basis of the clinician's awareness of the presence of a developing, malleable visual system within the patient's first few years of life.

In general, clinicians expect greater success in treating or preventing amblyopia than in preventing a limitation of binocular vision.[1,2] Debate continues whether a potential even exists for normal binocular vision in patients with infantile esotropia.[3,4] At the center of such discussion is a basic philosophic difference regarding the etiology of strabismus itself: Is the limitation of binocular vision in such patients a consequence of an inherent untreatable abnormality, or is this limitation a consequence of negative influences that, if reversed, could result in a return to normal function?

This classic "nature" versus "nurture" controversy as applied to the issue of strabismus and binocular vision has been articulated in the ophthalmic literature for over a century. Worth[5] and Chavasse[6] were the first to discuss in a thorough manner these two opposing views, expanding on earlier works by Javal[7] and Parinaud,[8] respectively. Worth suspected that the cause of

strabismus was congenital as a consequence of a defect in the "fusional facility" within the brain. He hypothesized that in normal development "a desire for binocular vision" maintained eye alignment and that when the "fusional facility" was absent, "the balance of these (muscle) coordinations" was responsible for straight eyes.[5]

Chavasse, on the other hand, regarded the etiology of strabismus as a postnatal event. He felt that binocular vision in normal individuals ensued when a series of "binocular reflexes" developed normally. Some of these reflexes were present at birth, and others were a consequence of experience. He believed that a plasticity existed in this developmental sequencing up to the point of "unconditional fixity." The reflexes were ordered as follows: (1) fixation reflexes responsible for orientation of the eyes and the body to the environment, (2) refixation reflexes responsible for exploring the environment, (3) the accommodation reflex in response to a near object, and (4) the pupil reflex to light. Most important, Chavasse felt that there was a potential for restoring the "binocular refixation reflexes" if "obstacles" to these reflexes were eliminated prior to the onset of "unconditional fixity."[6]

To a certain extent, treatment with surgical or chemodenervation realignment for infantile esotropia has already acknowledged that, at least in part, the Chavassian model for strabismus etiology is correct with respect to the sensory status of these individuals. Most large studies of binocular function in such patients have indicated better binocular function when realignment is achieved prior to the age of 2 years than after the age of 2 years.[3,4,9-11] It is important to note, however, that these studies have shown an *improvement* in, but not *attainment to normal levels* of, binocular visual function. Some clinicians have advocated even earlier realignment, before the age of 6 months, so that even better stereopsis might be achieved.[12] This approach appears to have not only anatomic limitations[13] but also practical limitations about the natural history of the development of eye alignment.[14] If the clinician is cognizant of the developmental issues for binocular vision, he or she is left in the difficult position of doing the very best to enhance binocular vision development while still waiting for anatomic growth and natural history issues to be resolved. Further, by the time esotropia is diagnosed, there already exists some abnormal binocular function that needs to be reversed, if possible, prior to surgery or chemodenervation.[15] Consequently, the importance of *prealignment* management of these patients with infantile esotropia becomes evident.

PREALIGNMENT TREATMENT GOALS FOR INFANTILE ESOTROPIA

Monocular Vision Goals

One common manipulation of the visual system prior to mechanical realignment is the use of occlusion therapy to reverse amblyopia. A patch is worn,

either full-time or part-time, over the eye that has a fixation preference. The fixation pattern is carefully monitored, with the desired outcome being spontaneous alternate fixation. This goal acknowledges the development of vision in each eye and, in particular, the development of visual acuity. By maximizing the visual acuity in each eye, it is felt that there is a greater likelihood of subsequently obtaining excellent eye alignment.[16]

Binocular Vision Goals

A second goal of occlusion therapy focuses more clearly on the Chavassian theory of binocular vision development. Full-time alternate occlusion has been proposed to prevent abnormal binocular interaction prior to therapeutic realignment.[17-19] With such treatment, a patient is temporarily converted to being like a monocular subject. An occlusive patch is worn at all times over one or the other eye; the ratio between the occlusion of the two eyes depends on the clinician's assessment of whether any amblyopia is present. Such treatment eliminates "binocular competition" between the two eyes. Binocular competition refers to the abnormal input to the visual cortex that occurs in certain commonly recognized clinical conditions. These include *strabismus*, where inputs are equal in the two eyes but nonsimultaneous; and when *unequal inputs* are present, such as with significant anisometropia or unilateral media opacity. A temporary interruption of binocular vision by means of alternate occlusion is regarded as a more physiologically acceptable environment for the developing visual system than a circumstance in which abnormal binocular vision, or binocular competition, is also present.[18]

If alternate occlusion is advocated, a key question is whether the potential for binocular vision will tolerate this interruption of binocular input to the visual cortex. Research with rhesus monkeys has shown that temporary interruption can indeed be tolerated and that such occlusion delays the period in which binocular vision can be developed.[15] It is recognized, however, that this treatment goal has a limit as to how long alternate occlusion can be continued before the binocular vision system's potential is lost[20] and permanently impaired cortical function occurs.[21]

THE MONOCULAR MODEL AND ITS RELEVANCE TO STRABISMUS

In this thesis, a special population is examined to better explain the relative roles of binocular competition and interruption of binocularity in normal and abnormal visual development. Thirty-six monocular individuals are studied who, by definition, had an interruption of binocular input to the cerebral cortex. All except 5 either were born with one functioning eye or lost virtually all vision in one eye during the first 6 years of life. The concentration on individuals who lost vision early in life is designed to assess vision developmental issues in this monocular population. The remaining 5 indi-

viduals serve as controls; each had normal visual development as a child and lost all vision in one eye during adulthood. Visual development in all individuals is measured by conventional clinical tests of vision as well as by a new electrophysiologic test that has been shown to be an indicator of early binocular visual experience.

MOTION DETECTION—A MONOCULAR TEST OF BINOCULAR EXPERIENCE

One property of visual function—motion detection— is the most important of all measured visual functions in this study. Its importance is a consequence of its ability to indicate a person's binocular experience during the first few years of life.

OKN Motion Detection

Although this function is not routinely assessed by clinicians, this clinical test has identified interesting differences in the developing infant, the normal adult, and the adult with a history of strabismus or partial visual loss at a young age. It assesses a subject's response to a moving optokinetic nystagmus stimulus. With one eye occluded, the stimulus is moved from a temporal to a nasal (T:N) position as identified from the patient's perspective. As the tester views the subject, a judgment is made whether optokinetic nystagmus (OKN) can be elicited. The tape is then moved in the opposite direction (N:T) and a similar assessment made.

In normal adults, there is a symmetric elicitation of OKN; that is, nystagmus can be induced from both the T:N and the N:T directions. In normal infants younger than 5 months of age, OKN can be elicited in the T:N direction but not in the N:T direction.[22-24] In subjects with a history of infantile strabismus, the response is similar to the immature response of infants, with a significant asymmetric response.[25-28] In adult subjects with a history of disruption of binocularity with partial visual impairment due to monocular cataract, toxoplasma scar, and trauma, OKN asymmetry has been found.[29] These differences in OKN response have been interpreted as an indicator for the presence of a motion detection system whose development is influenced by the early binocular experience of an individual.

In cats, the development of OKN has been linked to the integrity of the nucleus of the optic tract experimentally,[30] and in chickens, OKN has been induced pharmacologically and with directional specificity.[31]

VEP Motion Detection (Motion Processing)

A more recently developed test for motion detection utilizing electrophysiologic measurements has been termed the "motion processing test."[32] This test also is performed monocularly. A stimulus is presented that is interpreted by the visual cortex as having N:T or T:N directional motion. The cortical responses to this stimulus are measured electrophysi-

ologically; this is a very specific form of visual evoked potential (VEP). In adults with normal binocular vision, there is symmetry of response for the two directions.[33] In adults with a history of infantile esotropia, there is an asymmetric response, with the T:N direction more easily detected than the N:T direction.[32,33] In adults with a history of late-onset esotropia, this asymmetry is not present.[34] In normal infants, asymmetry is normally present until the age of 6 months .[33,35] Unlike the OKN test, which involves both sensory (seeing the stimulus) and motor (developing nystagmus in response to the stimulus) functions of the subject, the VEP motion processing test involves the visual pathways exclusively.

The key issue with respect to the function of motion detection is that the characteristics of this visual system are similar in normal infants and in individuals with a history of infantile esotropia. It appears that the expected maturation of the motion detection system does not occur when infantile esotropia is present. Thus, this test can be used as a monocular marker for early binocular experience. However, the type of abnormal binocular experience— whether binocular competition or interruption of binocularity— cannot be ascertained by simple assessment of the motion detection system in the strabismic population, since the strabismic population has components of both competition and interruption of normal binocularity.

The congenital and early-onset monocular model therefore is an important model for differentiating the difference between binocular competition and interruption of binocularity. If this population has an asymmetric motion detection system, then its system is similar to that of adults with infantile strabismus, where an arrest in maturation has occurred. The monocular response would imply that a simple interruption of binocularity impairs maturation of the motion processing system. If the monocular individuals showed motion detection that was more symmetric than the strabismus population, then binocular competition would be implicated, at least in part, for the failure of normal maturation. A motion detection system that is totally symmetric in the monocular population would indicate that this test does not require binocular vision at all for its development.

By understanding the visual development of this monocular population, the rationale for alternate occlusion therapy can then be either supported or refuted. If the monocular population shows a more symmetric development of the motion processing system than the infantile esotropia population, then alternate occlusion makes sense. In essence, alternate occlusion converts the strabismic infant to a monocular— albeit an alternating monocular— state where the detrimental stimulus of binocular competition is eliminated. If the monocular population shows an asymmetric development of motion processing that is more similar to the strabismic population, then binocular competition is not an added detrimental factor and, as such, need not be eliminated with alternate occlusion therapy. If the monocular population shows completely normal development, then reconsideration

must be given for the use of motion detection tests as monocular tests that reflect early binocular experience.

BACKGROUND INFORMATION

KEY DEFINITIONS

Terms that address monocularity, binocularity, development, and function do not have universality of meaning in the existing clinical and basic science literature. To avoid confusion of interpretation, the following definitions are offered for important terms used within this thesis. These definitions have been identified on the basis of the author's intended use within this thesis.

Monocular subject: A person who has vision in one eye only. This study includes persons born with only one eye (congenital unilateral anophthalmos), persons born with one normal seeing eye and one nonseeing microphthalmic eye, and persons with acquired loss of vision in one eye only. The persons with acquired loss either have had one eye enucleated or have demonstrated no light perception in the nonseeing eye.

Binocular subject: A person who has vision in two eyes. The results of previous studies for three types of binocular subjects will be considered in this thesis: normally developing infants, children with a history of infantile esotropia, and normal adults.

Monocular test: An evaluation of visual function performed on one eye only.

Binocular test: A measurement performed with both eyes providing input to the test. Neither eye is occluded. The measured function in general is one which requires that binocular vision — either normal or abnormal — is present. Commonly used binocular tests include the Titmus stereotest and the Worth 4-dot fusion test.

Normal binocular vision: Classically, regarded as vision in which there is simultaneous perception of an object, fusion, and stereopsis.[36] More specifically, normal binocular vision implies both a sensory coordination of a simultaneous percept (bifoveal fixation, bifixation) and a motor coordination (orthophoria). Clinicians traditionally use tests of fusion (Bagolini lenses, Worth 4-dot, troposcope) and of stereopsis (Titmus stereotest, random dot stereogram) to assess for binocular function and assess motor fusion on the basis of the ocular motility examination.

Abnormal binocular vision: Impaired binocular vision; in the presence of a

visual stimulus, there may be either equal inputs in a nonsimultaneous fashion (such as exists with alternating foveal stimulation in an esotropic child with alternating fixation) or unequal inputs, even in the absence of strabismus, which result in images that cannot be fused into a single image. Abnormal binocular vision is measured clinically as abnormal responses to tests of fusion or tests of stereopsis.

Binocular competition: Inhibitory or suppressive interaction between inputs from the two eyes. Binocular competition occurs in the following circumstances: in strabismus where inputs are equal in the two eyes but nonsimultaneous; and when unequal inputs are present with or without associated strabismus, such as with significant anisometropia or with unilateral media opacity.

Full-time alternate occlusion: Therapy to treat binocular competition in which the patient is essentially converted to being a monocular subject. One eye is patched for the waking hours one day, and the other eye is patched for the waking hours on the following day; this cycle is then repeated.

Normal monocular vision: Normal vision provided by one eye that is independent of information from the other eye. Classic parameters for normal monocular vision include 20/20 best correctable acuity, an intact visual field, and contrast sensitivity within the age-specific norms for a given spatial sensitivity.

Monocular vision development: The postnatal acquisition of monocular visual functions such as visual acuity (grating acuity, optotype recognition, vernier acuity), contrast sensitivity, and visual field.

Binocular vision development: The postnatal acquisition of binocular vision. Normal binocular vision development implies bifoveal fixation and orthotropia. Abnormal binocular vision development implies an interruption in either the sensory or the motor development of one or both eyes.

Monocular visual function: A measurable function of an eye that is, in itself, indicative of monocular vision and of monocular visual development. Monocular visual function may be normal or abnormal.

Binocular visual function: A measurable function that is indicative of binocular vision and of binocular visual development. Binocular visual function may be normal or abnormal.

Binocular experience: The experience imposed on binocular visual development of binocular vision during the sensitive period; this experience, in

turn, potentially influences the results of both monocular and binocular visual functions. (For example, the binocular experience of a person with a history of untreated infantile esotropia will be reflected in testing of a binocular function such as stereopsis. Additionally, this binocular experience may be associated with measurable abnormalities of a monocular function such as visual acuity and contrast sensitivity.)

Sensitive period: From a developmental standpoint, that portion of time during which normal experience must be present for future development to occur. Additionally, the sensitive period refers to the period in which function is fully developed but still susceptible to loss of function if normal experience is removed. This term does not have universal usage in pertinent literature; the term "critical period" is often used in a similar context.

Infantile esotropia: The clinical entity characterized by an onset of strabismus before 6 months, with esotropia of 30 prism diopters or greater, with no apparent accommodative component, and without any significant difference in the refraction or media clarity of the two eyes; often characterized by alternating fixation, and/or with associated oblique muscle overaction or underaction, dissociated vertical deviation, or positive family history of strabismus. This clinical condition has also been referred to as congenital esotropia,[2] idiopathic congenital esotropia,[37] and essential esotropia.[38]

AN OVERVIEW OF DEVELOPMENT AND THE INFLUENCE OF EXPERIENCE

The Relationship Between Development and Experience

The developmental issue assessed in this thesis is the development of motion detection as a visual function. In and of itself, this visual function has not gained the clinician's attention, since its practical influence in day-to-day activities is poorly understood. As a research marker for early binocular experience, its status in the monocular population may contribute to a better understanding of the mechanism for abnormal binocular vision development associated with infantile esotropia. To better understand the possible responses to monocularity a developing visual system may have, an overview of developmental issues and the potential influences of experience is now presented.

Prenatal development of any given function may result in the function being partially developed, undeveloped, or fully developed at birth. When a partially developed function is enhanced as a consequence of the new "experience" of life, developmentalists refer to this as "facilitation." When an undeveloped function is initiated, the term "induction" is used. When a function is fully developed at birth, the remaining possibilities are for this function to be either maintained or lost. These possibilities are demonstrated graphically in Fig 1.

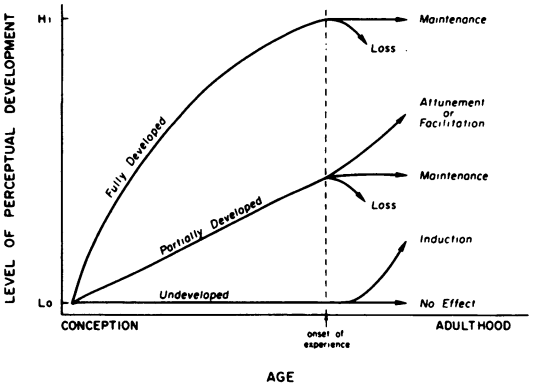

FIGURE 1

Hypothetical growth functions for different forms of pre- and postnatal development (from Aslin,[39] p 48).

The influence of experience can more accurately be described on the basis of a comparison to future development *with* or *without* this experience.[39] Experience is of virtually no significance when maturation occurs with or without the experience. In such a case, development is simply a matter of "maturation." Intermediate forms of experiential influence include "attunement," in which a given experience is essential for a function's complete maturation, "facilitation," in which experience accelerates maturation, and "maintenance," in which experience is required in order to allow a function to continue at a certain level. A diagrammatic representation displays these differences (Fig 2).

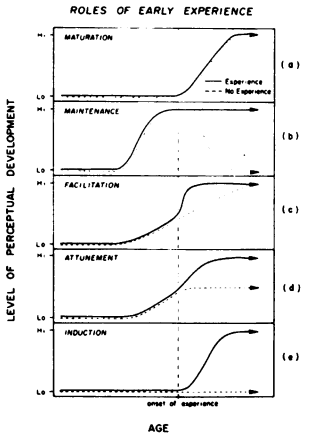

FIGURE 2

Roles of early experience with reference to development in absence of same experience (from Aslin,[39] p 50).

If one now considers symmetric motion detection as the particular perceptual development being assessed, one can compare this development as a consequence of 3 specific experiences. The first experience is that of orthophoria and the second is that of infantile strabismus. The third experience is that of monocularity; in this population, particular attention is given to the age at which monocularity is established. The impact of these 3 experiences on the development of the motion processing system will be compared.

Sensitive Period of Development

The role of experience becomes more complex when the timing of the experience is superimposed on a developing system undergoing further postnatal change. One variable is the timing of the experience in relation to the developmental curve. The period of development in which experience plays an influential role has been termed the "sensitive" period by some[39-42] and the "critical" period by others.[43,44]

Aslin and associates[39] attempted to determine the sensitive period for binocular function by comparing clinical data to mathematical models that would correlate with the visual function. They generated a schematic graph (Fig 3) that depicts the relationship between age of deprivation and the influence on binocular function. The graph implies a greater degree of sensitivity the earlier the insult; data for individuals less than 1 year old were unfortunately not included. Thus, the shape of their graph for the period of time right after birth is incomplete.

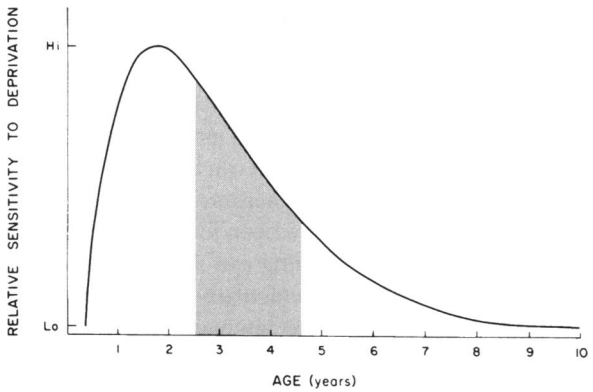

FIGURE 3

Schematic graph representing sensitive period for development of stereopsis. Peak sensitivity to deprivation is within the first few years of life. Shaded area represents a particular patient described in the study (from Aslin,[39] p 54).

Plasticity of a Developing System

In addition to the issue of the critical, or sensitive, period, the influence of experience depends, in part, on the plasticity of a developing system, or its malleability. Can a developing system recover from a detrimental experience, or does the experience arrest development entirely?

One can easily consider these developmental issues for the common abnormal monocular function of amblyopia. Clinicians recognize that an amblyogenic factor is most detrimental when this abnormal experience occurs early in an infant's life. A similar insult to one eye will have entirely different clinical implications at birth, 6 weeks, 6 months, and 6 years of life. The different visual outcomes reflect not only the timing of the insult within the sensitive period but also the plasticity of the visual system at these various times.

An understanding of the binocular vision's sensitive period and plasticity has been more difficult to outline. In part, this difficulty has reflected the difference in the experience of binocular competition as compared with interruption of binocularity. In part, this difficulty has been a methodological error in animal experiments where occlusion with an opaque device has been considered to be the same as suturing of lids,[18] to be discussed further in the section on abnormal binocular vision development.

In summary, development of a particular function can be influenced by the following: (1) a particular experience that can either be detrimental or have a positive influence on development, (2) the sensitive, or critical, period for development of a particular function, and (3) the plasticity of a developing system in response to a particular experience.

NORMAL AND ABNORMAL BINOCULAR VISION DEVELOPMENT

Prenatal Manipulations of Binocular Vision Development

Even before birth, the template for binocular vision is developing. This template has been experimentally interrupted in monkeys and cats by prenatal enucleation of one eye so that a comparison can be made to normal prenatal development and its influences on the anatomy of the visual system. Anatomic abnormalities at many levels have been found when prenatal binocularity is eliminated. First, the remaining eye retains more ganglion cells with their projections to the lateral geniculate nuclei (LGN).[45,46] Second, the LGN shows only two rather than six laminae.[47] Third, the visual cortex receives expanded projections from the remaining eye.[46,48,49]

These prenatal experiments show the importance of the presence of two eyes for the normal development of the pathways subserving binocular vision. Such experiments must be acknowledged particularly in the congenitally monocular population included in this thesis. Unfortunately, one can only

speculate whether similar anatomic changes occur with these individuals as compared to these research efforts, which involve prenatal enucleation.

The Influence of Anatomic Factors on Binocular Vision Development

Postnatal binocular vision development— as presumably prenatal development— does not occur in a vacuum. Other factors that influence binocular development include anatomic constraints, development of vision and of accommodation in each eye, development of eye alignment, and growth of the face. At birth, the distance between photoreceptors is greater than normal; this feature at least in part is responsible for immaturity of both monocular and binocular visual function.[50-52] Retinal immaturity per se is unlikely, however, in itself to limit binocular visual development.[53] Within the visual cortex, the ocular dominance columns, essential for the cortical integration of inputs from the two eyes, are incompletely segregated at birth in both humans and monkeys[54-56] until 6 weeks postnatally.[56] Human anatomic studies have demonstrated an ongoing change in the number of visual cortex synapses until up to 8 months postnatally.[57] The final anatomic issue that has received relatively little attention is the positional relationship between the two orbits and the interpupillary distance. At birth, the angle between the optic axes is 71°; this compares to an adult angle of 68°. As a consequence, retinal disparity is increased, with a subsequent increase in the convergence effort required to maintain bifoveal fixation.[58]

The Influence of Monocular Vision Development on Binocular Vision Development

The development of vision in each eye also plays a role in the development of binocular vision, as evidenced by the clinical testing of stereopsis in which the acuity of one eye is optically degraded with resultant deleterious effects on stereopsis,[59,60] and by the common clinical association between amblyopia and impaired binocular function even when there is no obvious strabismus.[61] When discussing the necessary elements for development of monocular vision, one can easily see the circumlocutory relationship between monocular and binocular development, since each is influenced by the other. Monocular visual functions, including visual acuity, are influenced by issues of eye alignment,[16,61,62] inequality of input (such as anisometropia),[16] and deprivation of input (such as occurs with congenital cataract).[16]

The normal development of visual acuity has been quantified by both electrophysiologic[63-66] and psychophysical[67] techniques. Although the specific values recorded for acuity differ in part as a consequence of the testing modality, each has shown a rapid increase in spatial resolution over the first 6 to 8 months (Fig 4 and 5). Similar, albeit earlier, development of contrast sensitivity has been documented electrophysiologically (Fig 6).[63,68]

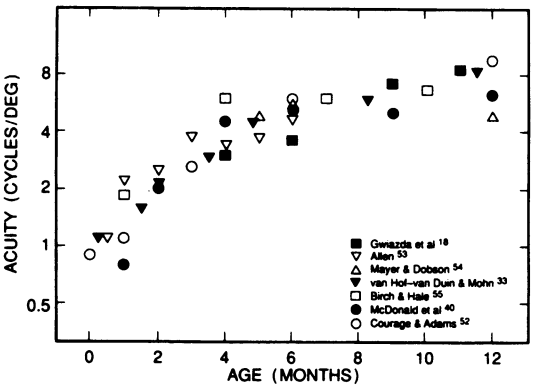

FIGURE 4

Development of grating visual acuity as determined by preferential looking (PL) techniques. Similar acuities are found across 7 studies. Acuities are expressed in cycles per degree. PL techniques rely on infant's interest in and response to grating as preferred object of regard when given choice between it and homogenous target (from Dobson,[67 p139]).

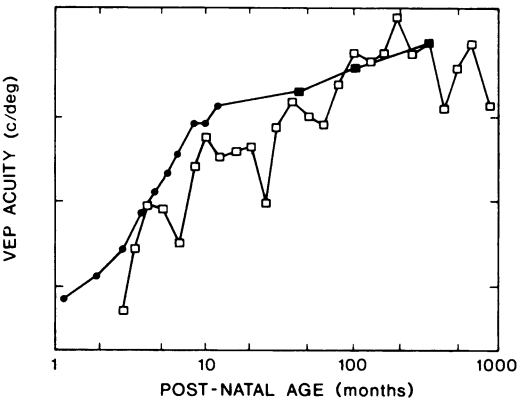

FIGURE 5

Development of grating visual acuity determined by sweep VEP techniques. Consistency of acuities is found in 2 studies, represented by filled symbols versus open symbols. Development is rapid from birth to 8 months; a second, slower growth phase persists through late childhood (from Norcia,[63] p165).

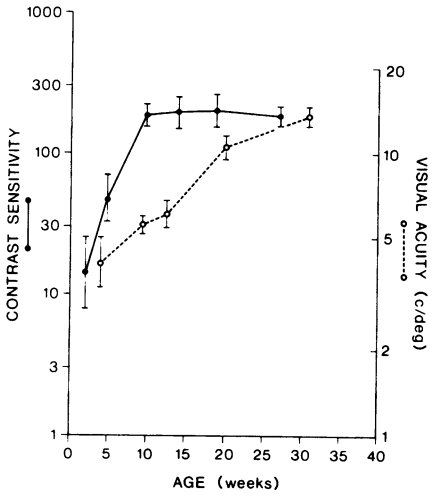

FIGURE 6
Development of contrast sensitivity compared with that of visual acuity, using sweep VEP technology. Development of contrast sensitivity is more rapid (from Norcia,[63] p166).

Accommodation and the associated neurologic reflex of convergence are the next requirement for binocular vision to be considered, since the purely binocular clues for depth perception are enhanced as the distance from object to observer is diminished. The ability of the lens to increase its power is very limited at birth and is improved rapidly over the first 6 months of life[69-72] (Fig 7, left). Convergence, whose function is to maintain bifoveal fixation on an object as its distance to the observer is lessened, increases its accuracy by the age of 6 months[73] (Fig 7, right). The development of vergence, although a factor, does not appear to be the sole limiting factor for the development of binocular vision.[74]

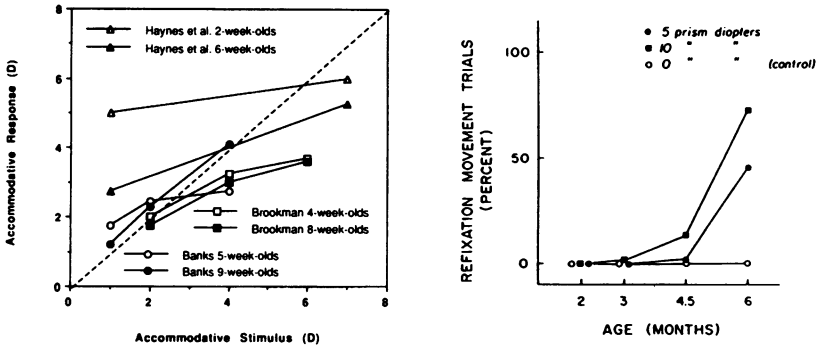

FIGURE 7

Development of accommodation (left) and convergence (right) as determined by retinoscopy in three accommodation studies and by refixation movements elicited by prisms in convergence study. Data from each suggests rapid development of these functions by age of 6 months (from Aslin,[72] pp 31 left, and 34 right).

The Influence of Eye Alignment on Binocular Vision Development

The final prerequisite for binocular vision relates to eye alignment. Without bifoveal fixation, binocular visual functions are impaired. Bifoveal fixation can be present only when the eyes are manifestly orthotropic. The natural progression toward orthotropia has been ascertained in a large longitudinal study.[75] Most normal infants are orthotropic by 3 months of age, while some do not achieve this until 6 months of age (Fig 8).[76]

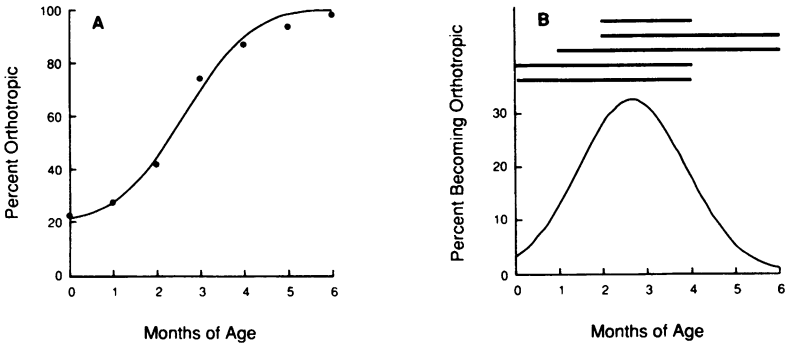

FIGURE 8

Development of orthotropia. A, Percentage of infants with orthotropia at a given age, B, Age distribution for onset of orthotropia. Variation in onset of esotropia, which was confirmed by examination by Archer, is signified by horizontal bars depicting possible time course of onset for given individuals (from Archer,[76] p352).

Development of Specific Binocular Visual Functions

Binocular visual development has been carefully assessed by the research scientist. Its development has been assessed as individual functions, including stereopsis, fusion, and ocular rivalry. Stereopsis relates to the visual system's ability to process information about depth perception as a consequence of simultaneous but slightly disparate images presented to the two eyes. Fusion relates to the visual system's ability to combine similar and perhaps nonidentical information from the two eyes into one image.

Stereopsis: Our understanding of the development of stereopsis was gained in early studies that assessed an infant's response to either real or illusory indicators of depth, or to an infant's ability to reach for an object.[77,78] More recent studies for assessing stereopsis have adapted preferential looking techniques,[73,79,80] eye movement analysis,[81] and VEP techniques.[82-84] Consistent findings, regardless of testing technique, place the development of stereopsis between 2 and 6 months of age. Interestingly, this development is quite abrupt, with little maturation of the system occurring after the age of 6 months (Fig 9).

Fusion: Our understanding of the development of fusion also has been expanded by tests employing preferential looking (PL)[85] and VEP techniques.[82,86] Even though these functions are different than the cortical task for stereopsis, the timing of their development is very similar with the exception of one study, which found fusion to develop earlier than stereopsis.[83] This parallel development has been regarded as a function of the development of the visual cortex.[85]

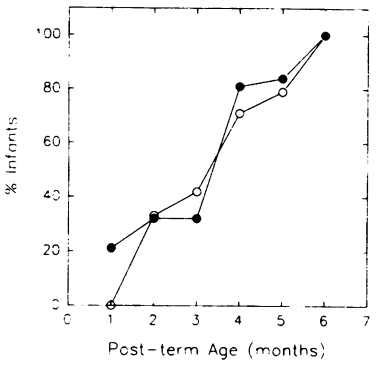

FIGURE 9

Development of stereopsis (closed circles) and fusion (open circles) using (PL) preferential looking techniques that provide one disparate image (stereogram) and one without disparity. Each system develops rapidly within first 6 months (from Birch,[53] p229).

The Relation Between Motion Detection and Binocular Vision Development
Normal Development of Motion Detection:

This function consists of the ability to detect motion from a particular direction with relationship to the eye itself. Normal directional asymmetries exist in infants, with normal symmetries in normal adults.[32,82] A normal infant, when tested monocularly, demonstrates an asymmetry of response to a moving optokinetic target, depending on the direction of target motion. Optokinetic nystagmus is induced when the target is moved in a temporal to nasal direction but is not induced when the target is moved in the opposite direction. Normally, symmetry is demonstrable by the age of 5 months in human infants.[22,23]

The maturation process has been measured electrophysiologically with the motion VEP[87] as well as with quantified OKN testing.[88] The maturation process can be further quantified by varying the parameters of the stimulus; this variation can be for the rate of motion, expressed in the unit of hertz (1 Hz=166 msec), with faster motion detection maturing at an older age or for the size of the stimulus, expressed in cycles per degree (cpd), with smaller stimulus detection maturing at an older age (A.M. Norcia, PhD, and R.D. Hamer, PhD, unpublished data, 1993).

Quantification of Motion Detection—The Asymmetry Index: The characteristics of the motion VEP can be quantified so that the function of motion detection of one individual can be compared with that of another. This "asymmetry index" expresses the relative asymmetry/symmetry of the motion VEP response. An asymmetry index of 1 shows a completely immature response, in which T:N motion processing occurs but N:T motion processing is absent. An asymmetry index of 0 implies symmetry of the response N:T compared to T:N. A high asymmetry index is found in normal infants up to the age of 6 months and in older individuals with a history of abnormal binocular experience in the first 6 months.

Normative Data for the Asymmetry Index: These have been calculated for infants as well as adults (A.M. Norcia, PhD, and R.D. Hamer, PhD, unpublished data, 1993). These data are a compilation of the results of motion VEP testing on 104 children and 21 adults. Four testing stimuli were used: 6 Hz, 1 cpd (6/1); 6 Hz, 3 cpd (6/3); 10 Hz, 1 cpd (10/1); and 10 Hz, 3 cpd (10/3). The number of subjects tested for each stimulus condition was as follows: 6/1: 79 subjects; 6/3: 33 subjects; 10/1: 50 subjects; 10/3: 30 subjects. The graphs of these data depict the development of the motion processing system when the experience is of normal binocular vision. The asymmetry index reaches levels similar to that of adults rapidly for the easiest of testing stimuli and less rapidly for the difficult testing stimuli.

The adult data are plotted as one age for the purposes of simplification; all adults were 20 years or older (Fig 10).

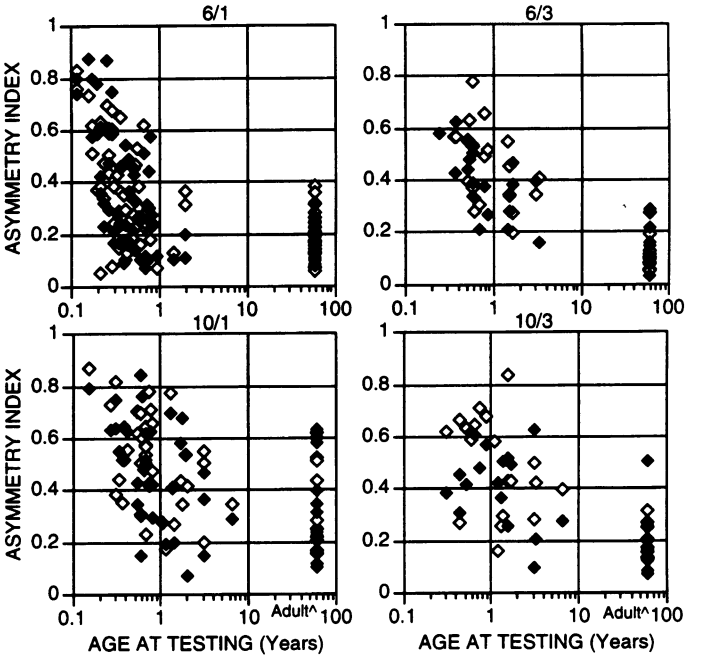

FIGURE 10

Plots of normal development of motion detection quantified by asymmetry index. N= 104 children, 21 adults; not all subjects were tested for all conditions. Age at testing for children shown on log scale . Ages for adults are entered without attention to specific age. Closed diamonds represent right eye data; and open diamonds, left eye data. Results for 4 testing stimuli labeled hertz (Hz)/ cycle per degree (cpd) (from A.M. Norcia, PhD, and R.D. Hamer, PhD, unpublished data, 1993).

Normal binocular vision development is a complex maturational process that commences prenatally. Its development is a story of the maturation of multiple visual functions. Development of binocular vision is codependent with development of eye alignment and of monocular functions. During normal development, the functions of eye alignment, stereopsis, and symmetric motion processing are developing at the same time. The interdependence of the development of each of these functions is well known for some of the relationships, such as the need for eye alignment in order to develop stereopsis[1,89] and normal motion detection.[22] The interrelationships for normal development stereopsis, eye alignment, and motion processing can be diagrammatically represented (Fig 11).[89]

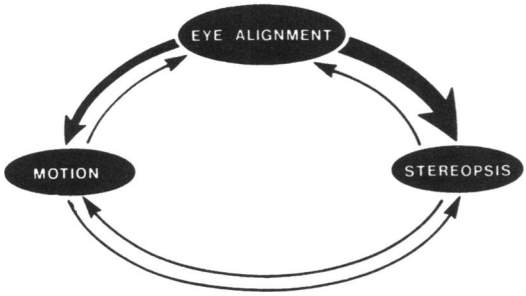

FIGURE 11
Schematic model of developing binocular visual system with interaction between developing motor and sensory elements. Broad arrow connotes hypothesized importance of influence of one function on the other (from Day and Norcia,[89] p286).

Abnormal Binocular Vision Development: Laboratory Models

Abnormal binocular vision development has served as a model for assessing developmental issues, in large part due to the classic experimentation by Wiesel and Hubel,[90-93] in which monocular suturing of kitten lids resulted in a marked reduction of cortical cells that could subsequently be driven by a stimulus presented to the deprived eye. These investigators found the LGN response to be relatively normal, prompting them to suspect the geniculocortical pathways or the cortex itself to be the site of pathology.[91] In anticipation of more extensive physiologic abnormalities as a consequence of doubling the amount of deprivation, the investigators sutured the lids of both eyes over the same time course as the monocularly sutured kittens. To their surprise, the cortical recordings were far more recordable than anticipated.[92,93] The responses had been altered from the norm, but not to the extent associated with unilateral closure. They concluded that "at the cortical level the results of closing one eye depend upon whether the other eye is also closed. The damage produced by monocular closure may therefore not be caused simply by disuse, but may instead depend to a large extent on *interaction* of the two pathways [emphasis added]."[93]

This powerful research and its conclusions provided enthusiasm and a focus for attention for the next generation of vision investigators. As so pointedly discussed by Jampolsky,[18] there unfortunately was a proliferation of laboratory research and conclusions that failed to pay attention to the methodology of the Wiesel and Hubel research. The kitten-lid suture model provided a model for deprivation or diffusion of light to one eye, which resulted in an imbalance of inputs from the two eyes. Enough light could pass through the closed lid to create a diffused image for the "deprived" retina. This was often accepted by others to be equivalent to the model of

occlusion, or absence of any input. The importance of this differentiation was most evident in the clinical model of occlusion for the treatment of amblyopia and in the reverse extrapolation of the occlusion-clinical model into animal studies in which lid suturing was used to simulate occlusion. Lid suturing as a stimulus to the visual cortex is not identical to occlusion of one eye.

Abnormal Binocular Vision and Binocular Competition

This difference between occlusion and diffusion returns to the main focus of this thesis in that the monocular model is analogous to the occlusion model. Vision from only one eye is present. In the deprivation model, vision from both eyes is present; one eye, however, provides a far more degraded stimulus than the other eye.

At the center of abnormal binocular visual development, then, is a difference between the two eyes that is present during the sensitive period for binocular vision development. Commonly, this difference is related to infantile esotropia. The difference between the two eyes is that the object of regard does not simultaneously stimulate the two foveas. Although each fovea is receiving some stimulus, the object of regard stimulates one, a more peripheral object (in relationship to the object of regard) than the other. Other abnormal, unequal inputs relate to anisometropia[59,60] or deprivation such as with a unilateral congenital cataract.[94]

The Role of the Basic Scientist in Delineating Binocular Vision Development

The traditional functions of stereopsis and fusion measured by clinicians have been thoroughly studied using new techniques for analysis. There has been a relative explosion of this developmental information as a consequence of the development of the field of infant vision research over the past 2 decades. Two general types of testing have assessed infant vision. Psychophysical techniques have in large part relied upon preferential looking techniques; the first use of this technique was in the measurement of infant visual acuity.[95] Electrophysiologic assessment has required more extensive investigations for identifying relevant techniques.[96,97]

The Motion Detection System Within the Context of Abnormal Binocular Vision

As previously discussed in the introduction, directional asymmetries for both OKN motion detection[25-28,98] and VEP motion detection exist in patients with a history of infantile esotropia[32,33] or unilateral severe, incomplete visual loss.[29] A quantified expression, or asymmetry index, is a simpler way of comparing the degree of directional asymmetry among specific clinical groups. Such asymmetry indices have been determined for a group of patients with infantile esotropia.[99] These directional asymmetries result in an

asymmetry index that is higher than that in the normal population and that mimics the immature visual system of the infant.[33] The asymmetry indices of patients with infantile esotropia have been plotted (Fig 12) using raw data from subjects reported in this publication.[99] The methodology and personnel responsible for their computations were identical to those used by this author for VEP motion detection and asymmetry index determinations in this thesis.

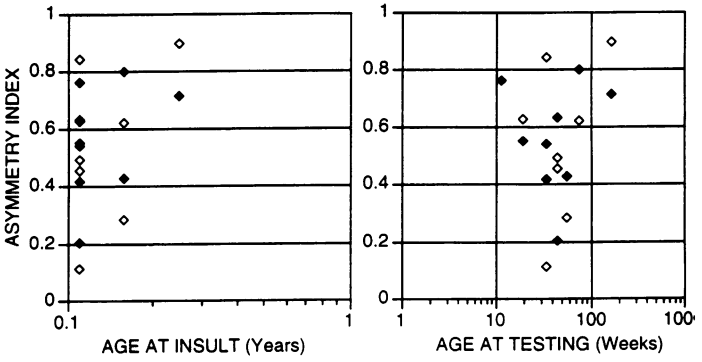

FIGURE 12

Plots of motion detection function in patients with infantile esotropia as quantified by asymmetry index. Data are from 9 children with 17 entry points representing both eyes from 8 individuals and one eye from one patient. Age at insult is defined as age at which esotropia was apparent either by history or by examination by an ophthalmologist. Left, Age at insult (or development of esotropia) is plotted against asymmetry index. Note high values compared with those in Fig 10. Right, Age at testing shows persistence of high values despite older age. Results are for 6 Hz, 1 cpd stimulus (from raw data collected by Jampolsky et al[99]).

Traditional Concepts of Normal and Abnormal Binocular Vision Development Within the Context of Neuroanatomy and Neurophysiology

A child who is undergoing evaluation for binocular function will typically be assessed with tests for stereopsis and tests for fusion. The fusional status is often defined as either "central" or "peripheral" fusion on the basis of response to tests such as the Worth 4-dot test or Bagolini lenses.[2,36] "Suppression" is often used as one label for this abnormal binocularity. What new information can explain terms such as "central" and "peripheral" fusion and "suppression?"

There is no immediately apparent counterpart for suppression or fusion in the neurophysiologic literature. Specifically, there does not appear to be within the retina a neurophysiologic correlate of the clinically ascertained

"central" and "peripheral" separation in fusion. In fact, it appears that there are very limited specific responses by retinal cells regardless of the location within the retina. Projections from the fovea are similar to projections from peripheral retinal cells. What differs is the size range and numbers of receptive fields.[100-102] The absence of anatomic equivalents within the retina implies a more posterior location for the binocular functions of fusion and stereopsis.

The key to understanding the clinical phenomenon of suppression, as well as the key to understanding the difference between binocular competition and interruption of binocularity, may rest with recent work that has carefully identified 4 specific cell types in the visual cortex of the cat. Three specific types are binocular cells, and the fourth group consists of monocular cells. Each has special implications regarding our understanding of the strabismus patient.

The first category of cells has a response only to one eye; these are monocular cells. The three types of "binocular cells" require varying amounts of input from the two eyes, depending on the specific category. The "obligate" or "AND" category requires simultaneous input from both the left and the right eye.[44,103] The "OR" binocular cells can receive excitatory input from either eye in order to function properly. The final category of cells receives excitatory input from one eye and inhibitory input from the other eye.[104,105]

If one examines the impact on the various types of binocular cells by the different experiences of binocular competition and interruption of binocularity, a potential different physiologic activity can be identified. For the purpose of tying this information to its clinical relevance, the experience of binocular competition will be considered as the infantile esotropia population, and the experience of interruption of binocularity will represent not only the strabismic population but also the monocular population. The AND cells are negatively influenced by each condition, since there is no simultaneous stimulation from corresponding receptor fields within the retinas of both eyes. The OR cells would each presumably be dominated by the fixing eye; for the strabismic individual, a preference of fixation would result in the input to the OR cells from predominantly one eye. The monocular individual similarly would have input to the OR cells from just one eye; thus, the OR cells function differently with either of these forms of binocular interruption than with an individual with normal binocular vision. The excitatory/inhibitory cells have the greatest difference between the strabismic and the monocular populations. With the monocular population, either the excitatory or the inhibitory portion of input is present, whereas the opposite input is completely missing. With the strabismic population, each input is represented, although presumably the input from the deviating eye is abnormal when compared with what would be provided by a pair of orthophoric eyes.

It is possible that the clinical characteristics of suppression as a form of binocular function must have representation in some form at the level of these various binocular cells. As the clinician's understanding of the relative roles of each of the binocular cells is enhanced, it may be that traditional understanding of abnormal functions such as suppression will allow a more effective means for returning function toward a normal existence.[94]

An additional consideration of the neuroanatomic correlates for vision and its development is the conceptual organization of the visual pathways into "streams" of cells that subserve different functions of vision.[106] Streams are identified as "parvocellular" or "magnocellular" on the basis of neurophysiologic and neuroanatomic research in monkeys.[107-111] Each stream appears to serve unique functions of vision. The parvocellular stream loosely defined appears to be responsible for "static stereopsis," with sensitivity to fine stereopsis cues[112] in representation at the fovea,[113] spatial sensitivity for high frequencies,[114] and color perception.[115] The magnocellular stream loosely defined appears to be responsible for "motion stereopsis," with sensitivity to a broader disparity range,[116] with parafoveal representation,[113] a broad range of spatial frequency sensitivity,[114] and poor color sensitivity.[115] Thus, these two streams appear in part to be responsible for the separation of specific binocular visual functions neuroanatomically.

THE MONOCULAR MODEL OF VISION DEVELOPMENT

The monocular child has been assessed in the past as providing further understanding to strabismus and its etiology. Helveston and associates[117] reviewed the histories of five patients who had enucleations prior to the age of 4 months. Each developed a head turn, preferred fixation in adduction, and abduction nystagmus following enucleation of one eye. The investigators proposed that this oculomotor abnormality was in some way related to the developing visual system and that their clinical findings supported Chavasse's reflexogenic theory of strabismus etiology. They recognized the unique qualities of these patients and cautioned clinicians to be aware of the potential complication of "unilateral esotropia" with early enucleation.

Another approach to the monocular child has been to assess the oculomotor system of the monocular child. Ciancia[118] and Harcourt[119] in 2 separate studies found 22 children, each with one "blind" eye, with nystagmus in the good eye; esotropia was not a constant feature. It is important to note that these studies made no distinction between a *diffusion* stimulus such as a congenital cataract and an absence, or *occlusion*, stimulus. The significance, however, in terms of this thesis is that each investigator recognized that the oculomotor system was influenced by unique aspects of complete or partial loss of vision in one eye during visual development.

Asymmetries of the optokinetic response[120] have been assessed in early-acquired monocular patients as well as in individuals with severe incom-

plete visual loss[29] and compared with persons with normal binocular vision and strabismus. These studies, as this thesis, assessed, therefore, the motion detection system. Because of the similarities with these studies, their methodology and conclusions are now reviewed.

In the first study, the investigators assessed OKN in three populations: 36 normal individuals older than 6 years of age; 27 patients with a history of strabismus; and 36 monocular subjects who had had enucleation between 5 months and 5 years of age. The strabismus population was further divided into early- and late-onset strabismus by using 24 months as the distinguishing age. OKN was measured with a large screen that subtended an area 105° by 84° at the testing distance of 10 cm. Testing was performed monocularly. Videotapes were made of the subjects' eye movements and analyzed for OKN. Asymmetry "scores" were calculated in a fashion similar to the asymmetry index of this thesis, in which a high score indicated persistence of a T:N bias and a low score indicated a symmetric response directionally. Only the early-onset strabismus patients had asymmetry scores statistically different from those of the normal subjects. The investigators concluded that abnormal binocular competition created a persistence of directional asymmetries in humans. They found a difference between the early-onset strabismus population and the enucleate population, concluding that "the disruption of visual development produced by enucleation is not equivalent to that produced by strabismus."[120]

In the second study, the investigators assessed OKN in a single population of 6 adults who had had severe but incomplete visual impairment in one eye during infancy; unlike the previously mentioned study, these 6 subjects therefore represented a population in which binocular competition had been present during development of the motion detection system. OKN was measured with a full-field OKN drum, and eye movement velocities were determined with electro-oculography and digital computer. The investigators concluded that the altered motion processing was a consequence of altered early binocular experience.[29]

In this thesis, the difference between the strabismus population and the enucleate or monocular population is assessed in a different manner than the in previously cited studies. Although both optokinetic symmetry measurements and motion processing are monocular tests that reflect binocular visual function, the OKN response has a sensory as well as a motor component. With motion processing analysis, the integrity of the visual pathways is the sole consideration. As a purely sensory test, the results may then be interpreted to reflect function of the visual pathways exclusively.

It is interesting to speculate what the results of this current study might show. One possible outcome would be that the monocular subjects have high asymmetry indices. This finding would be consistent with the findings in patients with early-onset strabismus, implying that interruption of binocular vision is a sufficiently abnormal experience to result in this asymme-

try. If this result were found, it would indicate a fundamental difference in VEP motion processing and OKN testing results.[120] Another possible outcome would be that the asymmetry index was lower than the strabismus population but higher than the normal population; in this case, one could conclude that binocular competition was an additive abnormal experience. The final possibility would be that the asymmetry index was completely normal; in this case, one might conclude that the motion processing system does not need binocular vision for its development.

METHODS

PATIENT SELECTION

Three general types of monocular subjects were recruited for this study. The first group consisted of individuals born with one clinically normal eye and one eye with no vision. This was regarded as the most ideal type of monocular individual, since no form of binocular vision was ever experienced postnatally.

The second group of monocular subjects obtained monocular status after some period of binocular vision and before reaching visual maturity; that is, after birth but before the age of 6 years. Some form of binocular vision was present in all of these individuals during the accepted time frame for not only the development of binocular vision but also the plasticity of the binocular system. This second group was subsequently divided into three categories on the basis of the type of binocular experience. One category had normal binocular visual development until vision was suddenly and completely lost in one eye. The second category had a known period of normal binocular vision, followed by a specific insult resulting in severe but incomplete visual loss (abnormal binocular vision), followed by complete loss of vision in one eye. The final category had an assumed period of normal binocular visual development, followed by an assumed period of abnormal binocular vision, followed by enucleation of one eye.

The third group of subjects lost vision in one eye after visual maturity had occurred. Presumably, each of these individuals had normal binocular visual development.

Monocular subjects were recruited from a group of 75 general ophthalmologists and 12 pediatric ophthalmologists by verbal and/or written communication from the author. The office records of a busy ocularist were also reviewed by the author, with appropriate individuals contacted through their referring ophthalmologist. Advertisements were posted at 3 area colleges and at one school of optometry for further recruitment.

The majority of subjects lived within a radius of 50 miles from the author. A special effort was made to recruit congenitally monocular individuals, since these individuals represented the most ideal circumstance to test the author's hypothesis. One of these individuals traveled a distance of 3,000

miles, another a distance of 800 miles, two a distance of 500 miles, and one a distance of 250 miles.

Patient selection criteria were confirmed by the author, who performed a thorough clinical history and examination of each patient after an explanation of the research project and its purposes was given to the individual and an informed consent for participation obtained.

CLINICAL HISTORY AND EXAMINATION

Definition of Developmentally Significant Events

Since this thesis concentrates on developmental issues, four important dates were established: (1) date of birth, (2) age at the time of insult, (3) age at the time of complete loss of vision in one eye, and (4) age at the time of testing.

Age at insult was defined as the time at which normal binocular vision development was known to be arrested. For the patients with a congenital absence of a functioning eye, the age at insult was the same as the date of birth. The author fully acknowledges the potential that prenatal development of the visual pathways might have been abnormal, but is unable to more accurately date the age at insult other than as a congenital abnormality.

The age at insult for trauma-related and for infection-related loss of vision was defined within the limits of available historical data. Confirmation of this date with the referral source was made when possible.

The age at insult for subjects with retinoblastoma was the most difficult date to assign accurately. Criteria for dating this insult were photographic documentation of leukocoria with the child fixing on the camera, observation of leukocoria by a parent, or observation of leukocoria by a physician. When at least two of these three criteria were met, the earliest observation was recorded as the age at insult.

Complete loss of binocular vision was defined as the age at which no perceivable vision was present as a consequence of either enucleation of one eye or loss of all vision (no light perception). This judgment was made either by history or by confirmation with medical records. The age at insult and the age of complete loss of vision were identical in the congenital group, in 5 subjects with trauma, and in one retinoblastoma subject who was evaluated for left-sided epiphora at 6 months of age and incidentally found to have a large retinoblastoma in the right eye. This patient demonstrates the difficulty in defining the age at insult in the retinoblastoma group.

The age of the individual at testing was determined by the date of testing and the patient's date of birth. This age was noted, since the data from the monocular subjects were to be compared with developmental data from individuals with normal visual development in which the age of testing was the key variable.

The presence of significant family history, including a history of strabismus, was ascertained because of previous reports that questioned the influence of family history of strabismus on the development of motion detection abnormalities.[121,122]

Clinical Examination Methodology

Each patient underwent a clinical examination that included an assessment in the seeing eye of best corrected visual acuity by standard Snellen testing, confrontation visual field, pupil examination, and refraction. A fundus examination of the healthy eye was also performed. When a microphthalmic, phthisical, or nonseeing fellow eye was present, it was examined to confirm the absence of light perception.

Best Visual Acuity: The best corrected visual acuity of the sound eye was determined clinically in an age-appropriate fashion. Standard Snellen letter optotypes were used on subjects able to recognize letters, and Allen picture optotypes were used for young children unable to recognize letters. Distance acuity measurements with corrected refractive error were attempted on all subjects; a near card with Allen pictures was used for one child (MC, category IV) who did not respond to distance testing.

Cycloplegic Refractive Errors: These were obtained from clinical records of each subject by the author or by the referring ophthalmologist.

The Fundus Examination: This was performed on the functioning eye at the time of clinical examination. Each patient's assessment included at least one examination with the benefit of dilating drops.

Head Turn: The subject or relatives were questioned whether a head turn had been observed in the past. An observation was made at the time of clinical examination whether there appeared to be a noticeable head turn as the subject sat in the examination chair and responded to tests such as assessment of visual acuity. The subjects were not observed for head turn during navigation about the examination room.

Pupil Examination and Confrontation Visual Fields: These were performed with standard clinical techniques.

Longitudinal Examinations

Two individuals (CM and DE) were studied longitudinally. CM was examined at 4 months, 10 months, 1 year 11 months, and 3 years. DE was examined at 2 years 9 months and at 3 years 9 months. All clinical tests and motion detection tests were performed on each visit within the limits of the age of testing.

Categories of Individuals

Five categories of monocular subjects were selected. These categories differ from each other from the standpoint of visual developmental issues.

Category I: The congenitally monocular subject represents the most

ideal form of subject, in whom there is a complete postnatal absence of binocular experience. Nine individuals are included in this group. Five were born with unilateral anophthalmos, and three were born with extreme unilateral microphthalmos in which no vision was ever felt to have been present. One had a blind congenitally deformed eye enucleated at the age of 6 years; further historical details were not available except that the individual was certain that no vision was ever present.

Category II: This is the monocular subject with a concurrent abrupt and complete loss of vision at a specific time during visual development. Five individuals, each of whom sustained trauma, are included in this category. The difference in category I and category II individuals developmentally is that category II individuals had a period of normal binocular visual development prior to the injury.

Category III: This is the monocular subject with a well-defined period of normal binocular development, with an insult at a specific time to one eye, followed by a period of abnormal binocular vision with subsequent complete loss of vision in the eye. Five individuals, three with trauma and two with infection, are included in this category.

Category IV: This is the monocular subject with a probable period of normal binocular development who subsequently had abnormal binocular competition or interruption and who at a specific time had definitive complete interruption of binocularity. This category includes 12 individuals, each of whom had a retinoblastoma.

Category V: This is the monocular subject with normal visual development whose binocular vision was interrupted as an adult. Five individuals, three of whom sustained trauma and two of whom had adult-onset tumors, are included in this category. Each patient had complete loss of vision in one eye.

The patient selection criteria regarding early binocular experience are summarized in Tables I through V.

TABLE I: HISTORY AND PHYSICAL EXAMINATION DATA FOR CATEGORY I SUBJECTS (CONGENITAL LY MONOCULAR)

PATIENT	PATHOLOGY	AGE AT TEST	VISUAL ACUITY	REFRACTION	FUNDUS	FAMILY HISTORY STRABISMUS	HEAD TURN
KW	anophthalmos OS	10 mo	CSM	+2.00	WNL	no	no
CM	anophthalmos OS	4 mo 10 mo 1 yr 11 mo 3 yr	20/25	+1.25	WNL	no	no
JP	microphthalmos OD	3 yr 5 mo	20/25	+0.75	WNL	yes	no
JM	anophthalmos OS	4 yr	20/25	+1.75	WNL	no	no
MB	anophthalmos OS	6 yr	20/25	+1.00	WNL	no	no
SG	microphthalmos OD	7 yr 6 mo	20/20	pl=+0.50x90 q	WNL	no	no
ER	anophthalmos OS	10 yr	20/20	=0.50=+.025x90	borderline optic nerve	no	no
TP	microphthalmos OD	40 yr 2 mo	20/20	-0.75=+4.50x25	WNL	yes	no
JM	deformity OS	62 yr	20/20	+2.25=+0.25x30	WNL	yes	no

CSM, central, steady, maintained WNL, within normal limits.

TABLE II: HISTORY AND PHYSICAL EXAMINATION DATA FOR CATEGORY II SUBJECTS (ABRUPT AND COMPLETE VISION LOSS)

PATIENT	PATHOLOGY	AGE AT INSULT	AGE AT TEST	VISUAL ACUITY	REFRACTION	FUNDUS	FAMILY HISTORY STRABISMUS	HEAD TURN
RB	injury OS	8 mo	33 yr	20/15	+0.25	WNL	no	no
KM	injury OD	23 mo	33 yr 1 mo	20/15-	-4.50	WNL	no	right
PW	injury OD	4 yr	27 yr 10 mo	20/20-	-3=+1.00x80	WNL	no	no
PA	injury OS	4 yr	36 yr 9 mo	20/15-	+0.25	WNL	no	no
TC	injury OD	5 yr 7 mo	16 yr 1 mo	20/15	+1.25	WNL	yes	no

TABLE III: HISTORY AND PHYSICAL EXAMINATION DATA FOR CATEGORY III SUBJECTS (ABRUPT INCOMPLETE VISION LOSS FOLLOWED BY COMPLETE VISION LOSS)

PATIENT	PATHOLOGY	AGE AT INSULT	AGE NO VISION	AGE AT TEST	VISUAL ACUITY	REFRACTION	FUNDUS	FAMILY HISTORY STRABISMUS	HEAD TURN
MC	infection OS	6 mo	12 mo	36 yr 6 mo	20/20	+0.25=0.75x180	WNL	no	no
BN	infection OS	8 mo	15 mo	26 yr 3 mo	20/20+	-4.75	WNL	no	no
RT	injury OD	22 mo	4 yr	5 yr	20/25+	+0.50	WNL	no	no
TN	injury OS	5 yr	7 yr	15 yr	20/20+	+1.00	WNL	no	no
MB	injury OS	6 yr	6 yr 3 mo	30 yr 2 mo	20/20	-0.25	WNL	no	no

TABLE IV: HISTORY AND PHYSICAL EXAMINATION DATA FOR CATEGORY IV SUBJECTS (ENUCLEATION PRECEDED BY PERIOD OF ABNORMAL BINOCULAR VISION)

PATIENT	PATHOLOGY	LEUKOCORIA	ENUCLEATION	AGE AT TEST	VISUAL ACUITY	REFRACTION	FUNDAS	FAMILY HISTORY STRABISMUS	HEAD TURN
MO	RB OD	2 mo	6 mo	2 yr 2 mo	20/50	=1=+0.75x90	WNL	no	right turn
IR	RB OD	6 mo	6 mo	13 yr	20/20+	+0.75=+ fl.00x160	WNL	no	no
LC	RB OS	6 mo	11 mo	7 yr 10 mo	20/25+	+2.50=+0.50x180	WNL	no	no
KL	RB OD	6 mo	11 mo	9 yr 9 mo	20/20	-0.50=+0.50x90	WNL	no	no
TS	RB OS	6 mos	23 mo	2 yr 8 mo	20/20	+.25=+0.50x80	WNL	no	no
DE	RB OS	12 mo	13 mo	2 yr 9 mo					
				3 yr 9 mo	20/20-	+1.25	WNL	no	no
RF	RB OD	15 mo	18 mo	7 yr 3 mo	20/20	+0.50	WNL	no	right turn
GH	RB OS	18 mo	20 mo	8 yr 5 mo	20/20	-1.50	WNL	no	no
PS	RB OD	18 mo	23 mo	2 yr 2 mo	20/25	+1.00	WNL	no	no
EB	RB OD	2 yr	3 yr	27 yr 5 mo	20/15-	-3.00=+0.50x170	WNL	no	left turn
MC	RB OD	2 yr 1 mo	2 yr 2 mo	2 yr 10 mo	20/30	+1.25=+0.25x180	nasal RB	no	no
EL	RB OS	3 yr	3 yr	3 yr 7 mo	20/15	-0.25	WNL	no	no

TABLE V: HISTORY AND PHYSICAL EXAMINATION DATA FOR CATEGORY V SUBJECTS (LOSS OF VISION AS ADULT)

PATIENT	PATHOLOGY	AGE AT PATHOLOGY	AGE NO VISION	AGE AT TEST	VISUAL ACUITY	REFRACTION	FUNDAS	FAMILY HISTORY STRABISMUS	HEAD TURN
MB	injury OS	20 yr	immed	20 yr 1 mo	20/15	+0.25	WNL	no	no
SK	injury OS	28 yr	immed	36 yr 11 mo	20/15	-10.75=1.25x100	WNL	no	no
PP	tumor OS	35 yr	38 yr	45 yr 2 mo	20/20	-1.75=+0.75x3	WNL	yes	no
RP	tumor OD	56 yr	immed	66 yr 2 mo	20/15-1	+1.50 sph	WNL	no	no
RK	injury OD	63 yr	immed	73 yr 4 mo	20/20-1	+1.00=+0.50x90	WNL	no	no

The demographic data presented in Tables I through V can be summarized as follows. The age at the time of testing ranged from 4 months to 73 years, 4 months. In 17 patients, the right eye had either been enucleated or had no vision. In 19 patients, the left eye was the nonfunctional eye. The etiologies for complete monocular visual loss were tumor (N=14), trauma (N=11), congenital (N=9), and infection (N=2). Thirty of the 36 patients

had no known family history of strabismus. Five of the 36 patients had a family history of strabismus. One subject was an adopted child, and family history was not available.

Distance acuity measurements with corrected refractive error were obtained for 34 of 36 patients, near quantified acuity for one young child, and judgment of fixation pattern only for the youngest tested subject. All acuities were in the normal age-matched range of acuities.[123] The distribution of the refractive errors was as follows: 15 patients were hyperopic, with a range of +0.25 to +2.00; 9 patients were hyperopic astigmatic with a range from +0.25=+.50x180 to +2.50=.50x180; 5 patients were myopic, with a range from -0.25 to -4.75; 6 patients had myopic astigmatism, with a range from -0.50=+0.50x90 to -10.75=+1.25x100 and -0.75=+4.50x100; 1 patient had an astigmatic error of plano=+0.50x90. Thirty-four patients had completely normal results on fundus examination, including assessment of optic nerves, maculae, vessels, and retinas. One patient (MC, born 2/6/90) with one eye previously enucleated for retinoblastoma had a small retinoblastoma in the nasal midperiphery of the remaining eye. One patient (ER, born 7/16/83) with congenital unilateral anophthalmos had a borderline-sized optic nerve in the seeing eye; his visual acuity was 20/20, and the refractive error was +0.50=+0.25x90.

Excluded from the tables were selection criteria that confirmed normal pupils and confrontation visual fields in all subjects. The presence of a nasal retinoblastoma in MC, category IV, was not detected with confrontation visual fields. This patient was 2 years, 3 months at the time of testing.

OKN METHODOLOGY

Optokinetic Nystagmus Symmetry/Asymmetry

An assessment was made clinically by the author as to the status of symmetry of nystagmus induced by an optokinetic tape. The length of the tape was 47 inches, with an alternating pattern of vertically oriented black and white stripes 3/4 inch in width. The optokinetic tape was held at a testing distance of 2 1/2 to 3 and moved first in a T:N direction. If OKN was induced, the tape was then moved in a N:T direction. If OKN was not induced, repeated attempts in both directions were made. If OKN was recognized with motion of the tape in both directions, a "symmetric" response was entered in the clinical data. If OKN was recognized in only one direction, multiple attempts were made to induce nystagmus in the opposite direction before entering an "asymmetric" response in the database. When nystagmus could not be induced, an entry of "no nystagmus" was made. This entry was made only after multiple attempts, in order to eliminate lack of cooperation as a factor. Although no attempt was made to quantify the speed of motion of the OKN tape, an attempt was made to be consistent in this speed from subject to subject.

VEP METHODOLOGY

Steady-state VEP

A general description of this type of VEP and its interpretation is presented to familiarize the reader with its choice in this thesis:

A steady-state VEP involves the presentation of multiple stimuli at such a rapid rate that the brain does not return to a baseline function but rather remains in an activated "steady state." The stimulus presented is moved back and forth at a constant rate between two positions. The electric potential generated can be measured in terms of its amplitude, or strength of the potential, as well as its phase, or timing, characteristics. In a steady-state VEP, the stimulus will generate a signal only at the frequency of the stimulus and at this frequency's harmonics, or multiples; for example, with an 8-H stimulus, responses may be seen at 8 Hz and at its harmonics (eg, 16, 24, 32 Hz). Each harmonic is labeled as, for example, the first (F1, 8 Hz), second (F2, 16 Hz), or third (F3, 24 Hz), harmonic. These complex signals are filtered from background EEG noise by a process known as spectrum analysis.[102] The specific harmonics generated depend on the type of stimulus. With an "on-off" stimulus, both even- and odd-numbered harmonic multiples are seen. An "on-off" stimulus remains in one place but is not present at all times. With a "reversal" stimulus, only the even-numbered harmonics appear. A reversal stimulus is present at all times but shifts its position. The resultant steady-state VEP is demonstrated in Fig 13.

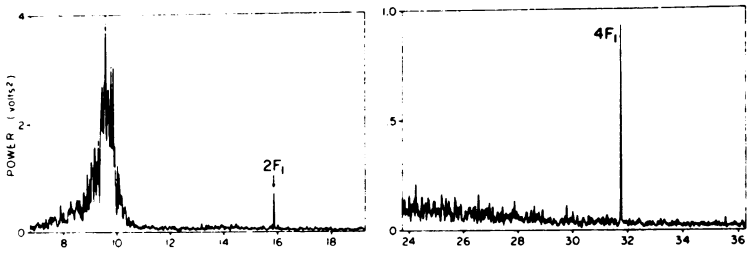

FIGURE 13

Steady-state VEP measurement using spectrum analysis. EEG activity is present at all frequencies, but VEP activity is responsible for peaks at 16 and 32 Hz. These consecutive peaks represent harmonics of the stimulus presented at 8 Hz. The broad peak between 8 and 13 Hz is the alpha-EEG activity, (from Regan,[102]).

The specific harmonics that are detected may be a function not only of the type of stimulus but also of the subject's response. This feature is the basis for understanding the motion-processing VEP. Thus, with a subject who is able to see both the N:T and T:N portion of the motion-processing stimulus, a reversal stimulus is perceived and only even-numbered harmonics appear. If an asymmetric ability to process motion is present, then the stimulus behaves like an on-off stimulus and both even and odd-numbered harmonics appear.

For comparative purposes, diagrams termed polar plots representing steady-state motion VEPs are shown in Fig 14. Each subject has a diagrammatic representation of the amplitude and the phase for the first (F1) asymmetric component and the second (F2) symmetric component of the harmonic. The normal adult shows a significant response only at the even harmonic, F2 (symmetric component). The normal infant has a larger F1 asymmetric component, and the phase (or direction of the vectors) is 180° out of phase when the left eye is compared with the right eye. This "bow tie" appearance has been cited as the hallmark for an asymmetric response.[33] A similar asymmetric response is found in an adult who had a history of early-onset esotropia.

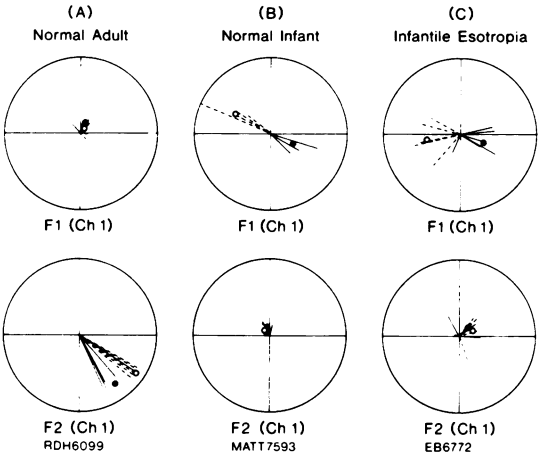

FIGURE 14

Steady-state VEP data comparing phase and amplitude of motion-processing trials in normal adult, normal infant, and adult with history of infantile esotropia. Top polar plot represents first harmonic, asymmetric component (F1), and bottom polar plot represents second harmonic, symmetric component (F2). All plots are from channel 1 (Ch 1). Right eye data are represented by solid lines; left eye data are represented by dashed lines. Mature adult has strong F2 symmetric component. Infant has a strong F1 asymmetric component. Adult with history of infantile esotropia also has strong F1 asymmetric component (from Norcia et al,[33] p438).

VEP Interpretation: Raw data from the VEP was subjected to Fourier analysis to define the amplitude and phase for each harmonic of a given stimulus. Using statistical criteria, the information obtained on multiple trials with the stimulus was scored with a computer.[124] An "asymmetry index" then was calculated with the information provided by the VEP.

The "asymmetry index" is calculated as a comparison of the relative balance of asymmetric to symmetric components of the VEP. The F1 first harmonic is the dominant asymmetric component, and the F2 second harmonic is the dominant symmetric component. As a fraction, this is expressed as the amplitude of the first harmonic responses divided by the sum of the first and second harmonic responses (F1/ F1+F2). This index theoretically ranges from 0 for a completely symmetric response to 1 for a completely asymmetric response. The higher the asymmetric index, the greater the portion of asymmetric response.

VEP Procedure: Motion VEPs were performed by independent specialists in a dedicated laboratory facility. The motion VEPs were recorded with a fully alert subject sitting either in a parent's lap or by himself or herself (Fig 15). Testing was performed in a darkened room in which only the video monitor screen was illuminated. The infant's attention was attracted to the video monitor screen by the use of a small toy held by one of the testers. The stimulus was then presented on the screen (Fig 16); the duration of the entire trial was 10 seconds. The subject's fixation was constantly assessed during the trial to ensure that attention on the stimulus was maintained. The distance between the subject and the screen was 100 to 138 cm; at 138 cm, the screen is 10° wide and 7.5° high. If fixation effort was lost by the subject, the trial was interrupted by the observing tester, who pressed a button. The trial was then automatically reset to its criteria at 0.5 to 1 sec prior to the button press. When fixation was reestablished, a second button press restarted the stimulus at this point. The new data then replaced the potentially inaccurate data due to loss of fixation in the data collection.

Motion VEPs were measured monocularly using a vertical sine-wave stimulus that is moved back and forth at 6 or 10 Hz (Fig 16). The spatial frequency was either 1 or 3 cpd. When cooperation was limited, testing was performed only at 1 cpd. The use of multiple testing conditions with variations in the temporal frequency of stimulus motion and the spatial frequency was to allow a more accurate determination of the level of maturation of the motion processing system, since complete maturation occurs at different ages for different stimuli (A.M. Norcia, PhD, R.D. Hamer PhD, unpublished data, 1993). Multiple trials for each testing condition were performed within the limits of the patient's cooperation and attention. The testing conditions were introduced in order of ascending complexity of stimulus, with 6 Hz, 1 cpd introduced first, then 6 Hz, 3 cpd, then 10 Hz, 1 cpd, and finally 10 Hz, 3 cpd. Each condition was given up to 10 individual trials for analysis by the computer.

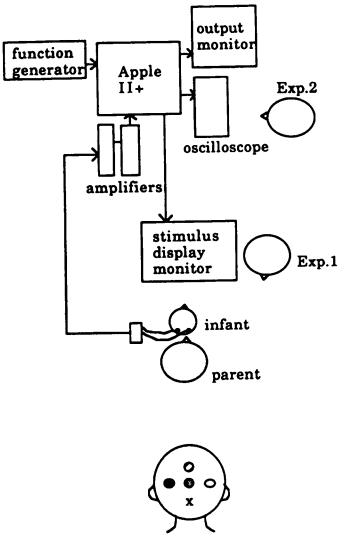

FIGURE 15

Schematic representation of testing apparatus (top) and electrode placement on subject's scalp (bottom). In top, experimenters 1 and 2 are represented as Exp 1 and Exp 2. In bottom, electrode placement is with one channel over left hemisphere, one over right hemisphere, and ground electrode superiorly placed. Inion is represented by "x" (from Skoczenski,[125 p 39]).

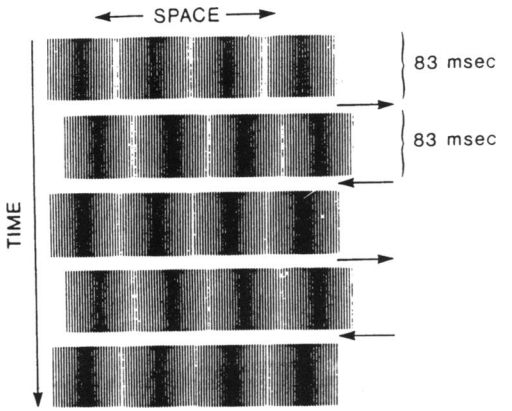

FIGURE 16

Stimulus for motion VEP. Vertical sinusoidal grating was displayed on video monitor. Grating with spatial frequency of 1 or 3 cpd was presented at temporal frequencies of 6 or 10 H. Grating was moved back and forth a distance of one fourth of cpd width. A 6-Hz stimulus (83 msec x 2) is illustrated in this figure (from Jampolsky et al[99]).

RESULTS

OKN SYMMETRY/ASYMMETRY

Twenty-four of 36 subjects (67%) were found to have symmetry of response to the OKN tape. Three of 36 subjects (8%) had an asymmetric response in which only T:N motion of the OKN tape elicited nystagmus. In 9 of 36 individuals (25%), no nystagmus could be induced with motion of the OKN tape in either direction.

The 9 congenital monocular individuals were the most difficult subjects in whom to induce an OKN response. Seven of 9 (78%) of these individuals had no nystagmus. The only individuals in category I that could be judged were the two oldest subjects in this category; their responses were symmetric responses.

All 15 individuals in categories II, III, and V were judged to be symmetric.

Of the 12 individuals in category IV, 7 (58%) were symmetric, 3 (25%) were asymmetric, and 2 (17%) had no nystagmus.

MOTION PROCESSING RESULTS

Testing Success Rate

Testing of each of the 36 subjects produced data reflecting the amplitude and phase of the response to stimuli presented in multiple trials. In 32, (89%) of the 36, a complete set of data with responses to all 4 stimulus conditions was obtained. In one subject (category IV, PS), only the 6/1 stimulus could be tested. In another 2 (category I, ER and category II, TC), all stimuli were tested except the 10/1 condition. In one subject who was tested on 4 separate occasions (category I, CM), testing was achieved on one to three stimuli. In each of the four subjects with an incomplete database, testing was limited by the degree of cooperation.

Representative Individual Data Sets

The electrophysiologic data were subjected to Fourier analysis that analyzed and divided the VEP into symmetric and asymmetric components. These components are then diagrammed on a polar plot for each testing channel (N=2). Each plot represents a specific testing stimulus. Thus, for any individual testing stimulus (such as 6 Hz, 1 cpd), a symmetric (F2) and an asymmetric (F1) polar plot is produced for each of the two channels. Four plots are produced for each stimulus; or 2 channels each with 2 harmonics. Two representative subjects (ER, category I and MB, category V) are portrayed with polar plots to illustrate how the raw data were used to calculate the asymmetry index (Figs 17 and 18).

Figure 17 plots data from one recording channel for MB, category V, who suddenly lost all vision in the left eye at the visually mature age of 20 years. The upper panel plots the first harmonic response (asymmetric com-

ponent) recorded at the stimulus frequency of 6 Hz, 1 cpd. The lower panel plots the second harmonic response (symmetric component) for the same stimulus. Each vector on the plot indicates the amplitude and phase from a single 10-sec trial. The open circle indicates the average response over the combined trials. This patient shows a large and statistically significant symmetric component and a small and statistically not significant asymmetric component. A significant response is composed of individual trial vectors having similar phase (timing) relationships with the stimulus. This can be seen in the lower panel, where each individual trial vector has a similar amplitude and phase. Nonsignificant results are composed of individual trial vectors that have a random phase distribution. Statistical significance of the responses was determined by the Rayleigh test,[126] which determines whether a particular distribution of phase angles is random. This statistic ranges from 0 for completely random data to 1.0 for data sets where each entry has the same phase angle. For MB, the amplitude of the symmetric component (lower panel) was 0.65 μV, depicted by the circle that extends approximately 0.65 of the plot's radius, which represents 1.00 μV. The amplitude of the asymmetric component was 0.05 μV. The asymmetry index considers what proportion of the total response (derived from the sum of the two components, eg 0.7 μV) is represented by the asymmetric component (0.05/0.70=0.07). This asymmetry index is close to zero, indicating a highly symmetric motion VEP response consistent with the patient's history of normal binocular vision development preceding his acquired monocular state. The asymmetry index for this channel, testing stimulus 6 Hz, 1 cpd, is then averaged with the asymmetry index calculated from the other channel to obtain the average asymmetry index (see Table X) for the testing stimulus 6 Hz, 1 cpd.

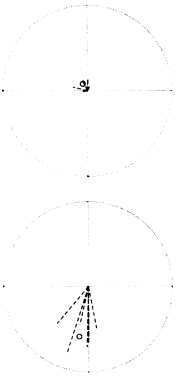

FIGURE 17

Polar plot from MB, category V. Subject lost vision in left eye as adult. Top represents first harmonic, asymmetric component F1; bottom represents second harmonic, symmetric component, F2. Symmetric component is strong, indicative of mature motion processing system. Asymmetric component is negligible.

Figure 18 plots the data for subject ER, category I, a congenitally monocular patient. The data were recorded at 6 Hz, 1 cpd, as for the previously described individual, MB. For subject ER, significant responses are present for both the symmetric and asymmetric components. The amplitude of the asymmetric component was 0.32 μV, depicted by the open circle. The amplitude of the symmetric component was 0.36, depicted by the open circle. The asymmetry index is 0.32/0.68, or 0.47, for this channel. This asymmetry index is greater than the asymmetry index for the individual MB.

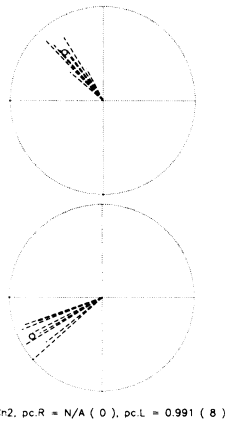

FIGURE 18

Polar plots from ER, category I, congenital monocular individual. Top plot represents first harmonic, asymmetric component F1, and bottom plot represents second harmonic, symmetric component F2. Both components have significant response. In comparison to MB in Fig 17, these plots represent a greater degree of asymmetry.

All further asymmetry indices of individuals will be reported as an average of the calculations for each of the two channels. Each testing stimulus will have its own asymmetry index. All of the results are obtained with statistically significant data as defined by the Rayleigh test.[126]

Motion VEP Asymmetry Results

Asymmetry Index as a Function of Age at Insult, Loss of Vision, and Age at the Time of Testing: A series of graphs depict the asymmetry indices for each testing stimulus of the monocular subjects. The asymmetry index is plotted against 3 criteria: age at insult (Fig 19), age at loss of vision (Fig 20), and age when tested (Fig 21). For each testing stimulus, there is a gradual reduction in the asymmetry index with older age at insult and with age at loss of vision. This gradual reduction in the asymmetry index is at a more gradual slope when compared with data for the normal population (Fig 10).

No significant pattern is present in the graph plotting asymmetry index against age when tested. This differs from normative data, where the age of testing reflects the key developmental marker; a more significant effect on development for the monocular individuals— who in large part were older than the normal population sample— is the age at insult or the age of complete loss of vision. Since the age at insult was defined in this study in a conservative manner, it is this criterion that is used in most of the graphs representing data from the monocular population and the strabismus population.

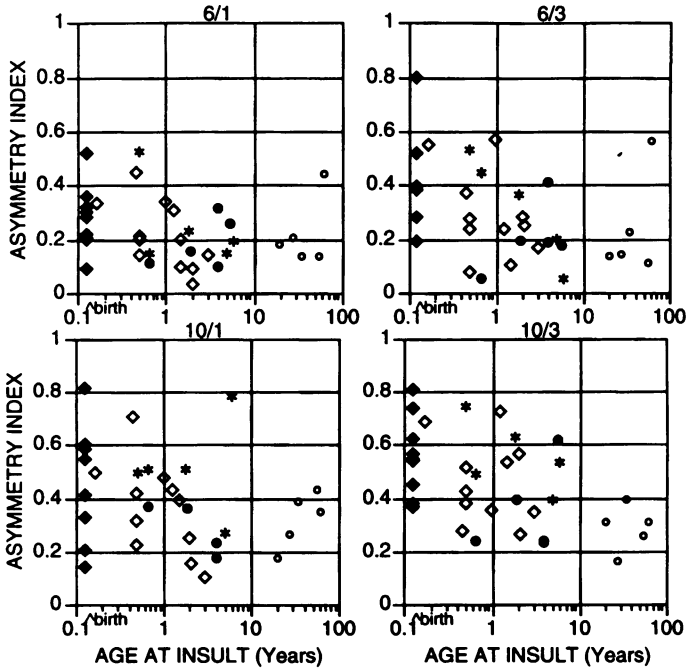

FIGURE 19

Plots of asymmetry indices for all monocular subjects by age at insult. Data are from 36 individuals. Categories of patients are represented as follows: I, closed diamond; II, closed circle; III, asterisk; IV, open diamond; V, open circle. Results are plotted for 4 testing stimuli labeled as Hz/cpd. As with normative data, there is reduction in asymmetry index, as insult occurs at older age. This reduction occurs at younger age for simplest testing stimulus, 6/1, and is prolonged with increasing complexity of stimulus.

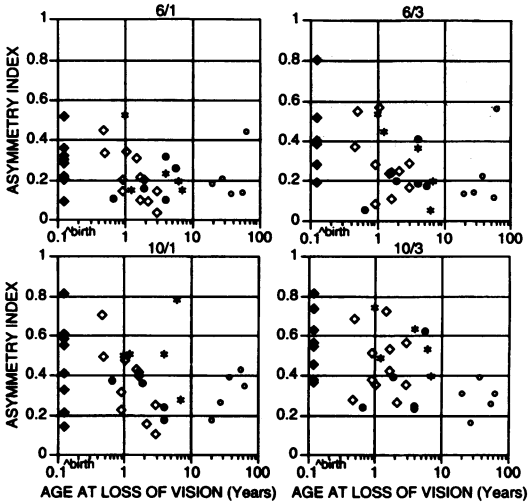

FIGURE 20

Plots of asymmetry indices for all monocular subjects by age at loss of all vision. Data are from 36 individuals. Categories are represented is as follows: I, closed diamond; II, closed circle; III, asterisk; IV, open diamond; V, open circle. Results are plotted for 4 testing stimuli labeled as Hz/cpd. Results are comparable to data represented in Fig 19.

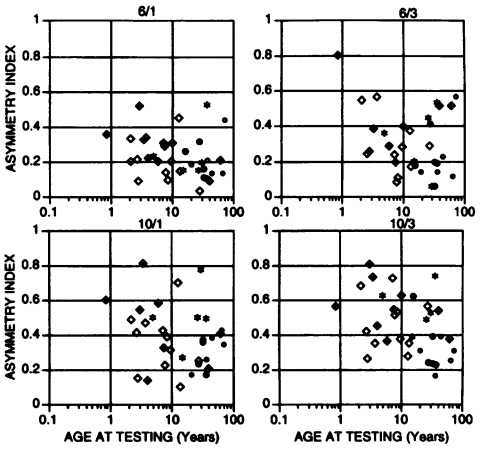

FIGURE 21

Plots of asymmetry indices for all monocular subjects by age at testing. Data are from 36 individuals. Categories are represented as follows: I, closed diamond; II, closed circle; III, asterisk; IV, open diamond; V, open circle. Results are plotted for 4 testing stimuli labeled as Hz/cpd. Results fail to show significant relationship between asymmetry index and age at testing as exists with Fig 10.

Database for Each Individual, Organized by Category: Tables VI through X depict all asymmetry indices of all individuals (N=36).

The VEP asymmetry index is listed for each stimulus (6 Hz, 1 cpd, or 6/1; 6 Hz, 3 cpd, or 6/3; 10 Hz, 1 cpd, or 10/1; 10 Hz, 3 cpd, or 10/3) tested on each individual. When the data for an individual are incomplete for the entire set of stimuli, the nonavailability (na) is indicated in the appropriate column.

Statistical data from each of the individual categories are presented for each table to include N for each testing stimulus, the mean for each stimulus, and the standard deviation and standard error for each stimulus.

Two individuals were tested on multiple occasions (CM, category I and DE, category IV). Only one data set is included for each of these individuals in Table I. The selected data set represents the most recent testing session. Longitudinal data from these 2 patients are presented in Table XI.

TABLE VI: OKN RESULTS AND MOTION VEP ASYMMETRY INDICES FOR CATEGORY I SUBJECTS (CONGENITALLY MONOCULAR)

PATIENT	PATHOLOGY	AGE AT INSULT	AGE AT TEST	OKN	6/1	6/3	10/1	10/3
KW	anophthalmos OS	congenital	10 mo	nn	.37	.81	.62	.58
CM	anophthalmos OS	congenital	3 yr	nn	.53	NA	.56	.82
JP	microphthalmos OD	congenital	3 yr 5 mo	nn	.33	.40	.82	.75
JM	anophthalmos OS	congenital	4 yr	nn	.23	NA	.15	.46
MB	anophthalmos OS	congenital	6 yr	nn	.21	.29	.60	.38
SG	microphthalmos OD	congenital	7 yr 6 mo	nn	.30	.21	.34	.56
ER	anophthalmos OD	congenital	10 yr	nn	.31	.41	NA	.64
TP	microphthalmos OD	congenital	40 yr 2 mo	s	.10	.53	.22	.50
JM	deformity OS	congenital	62 yr	s	.22	.53	.42	.39

OKN: s=symmetric; a=asymmetric; nn=no nystagmus

Statistical summary category I:	6/1	6/3	10/1	10/3
N:	9	7	8	9
Mean:	.29	.45	.47	.57
SD:	.12	.20	.22	.15
SE:	.04	.07	.08	.05

TABLE VII: OKN RESULTS AND MOTION VEP ASYMMETRY INDICES FOR CATEGORY II SUBJECTS (ABRUPT AND COMPLETE VISION LOSS)

PATIENT	PATHOLOGY	AGE AT INJURY	AGE AT TEST	OKN	6/1	6/3	10/1	10/3
RB	injury OS	8 mo	33 yr	s	.11	.06	.38	.24
KM	injury OD	23 mo	33 yr 1 mo	s	.16	.20	.36	.40
PW	injury OD	4 yr	27 yr 10 mo	s	.32	.41	.24	.25
PA	injury OS	4 yr	36 yr 9 mo	s	.10	.19	.18	.24
TC	injury OD	5 yr 7 mo	16 yr 1 mo	s	.26	.18		.62

OKN: s=symmetric; a=asymmetric

Statistical summary category II:	6/1	6/3	10/1	10/3
N:	5	5	4	5
Mean:	.19	.21	.29	.35
SD:	.10	.13	.10	.17
SE:	.04	.06	.05	.08

TABLE VIII: OKN RESULTS AND MOTION VEP ASYMMETRY INDICES FOR CATEGORY III SUBJECTS (ABRUPT INCOMPLETE LOSS WITH SUBSEQUENT COMPLETE LOSS OF VISION)

PATIENT	PATHOLOGY	AGE AT INSULT	AGE NO VISION	AGE AT TEST	OKN	6/1	6/3	10/1	10/3
MC	infection OS	6 mo	12 mo	36 yr 6 mo	s	.52	.53	.49	.73
BN	infection OS	8 mo	15 mo	26 yr 3 mo	s	.14	.44	.50	.48
RT	injury OD	22 mo	4 yr	5 yr	s	.23	.36	.50	.62
TN	injury OS	5 yr	7 yr	15 yr	s	.14	.19	.27	.39
MB	injury OS	6 yr	6 yr 3 mo	30 yr 2 mo	s	.19	.05	.77	.52

OKN: s=symmetric; a=asymmetric

Statistical summary category III:	6/1	6/3	10/1	10/3
N:	5	5	5	5
Mean:	.24	.31	.50	.55
SD:	.16	.19	.18	.13
SE:	.07	.09	.08	.06

TABLE IX: OKN RESULTS AND MOTION VEP ASYMMETRY INDICES FOR CATEGORY IV SUBJECTS (ENUCLEATION PRECEDED BY PERIOD OF ABNORMAL BINOCULAR VISION)

PATIENT	PATHOLOGY	LEUKOCORIA	ENUCLEATION	AGE AT TEST	OKN	6/1	6/3	10/1	10/3
MO	RB OD	2 mo	6 mo	2 yr 2 mo	a	.34	.56	.50	.70
IR	RB OD	6 mo	6 mo	13 yr	a	.46	.38	.72	.29
LC	RB OS	6 mo	11 mo	7 yr 10 mo	s	.15	.09	.24	.52
KL	RB OD	6 mo	11 mo	9 yr 9 mo	s	.21	.29	.33	.39
TS	RB OS	6 mo	23 mo	12 yr 8 mo	a	.23	.25	.43	.44
DE	RB OS	12 mo	13 mo	3 yr 9 mo	a	.35	.58	.49	.36
RF	RB OD	15 mo	18 mo	7 yr 3 mo	s	.32	.25	.44	.74
GH	RB OS	18 mo	20 mo	8 yr 5 mo	s	.11	.12	.41	.54
PS	RB OD	18 mo	23 mo	2 yr 2 mo	nn	.21	NA	NA	NA
EB	RB OD	2 yr	3 yr	27 yr 5 mo	s	.04	.30	.27	.58
MC	RB OD	2 yr 1mo	2 yr 2 mo	2 yr 10 mo	nn	.10	.26	.17	.28
EL	RB OS	3 yr	3 yr	13 yr 7 mo	s	.15	.18	.12	.36

OKN: s=symmetric; a=asymmetric: nn=no nystagmus

Statistical summary category IV:	6/1	6/3	10/1	10/3
N:	12	11	11	11
Mean:	.22	.30	.37	.47
SD:	.12	.16	.17	.16
SE:	.04	.05	.05	.05

TABLE X: OKN RESULTS AND MOTION VEP ASYMMETRY INDICES FOR CATEGORY V SUBJECTS (LOSS OF VISION AS ADULTS)

PATIENT	PATHOLOGY	AGE AT PATHOLOGY	AGE NO VISION	AGE AT TEST	OKN	6/1	6/3	10/1	10/3
MB	injury OS	20 yr	immediate	30 yr 1 mo	s	.17	.12	.16	.30
SK	injury OS	28 yr	immediate	36 yr 11 mo	s	.19	.12	.25	.15
PP	tumor OS	35 yr	38 yr	42 yr 2 mo	s	.12	.21	.37	.38
RP	tumor OD	56 yr	immediate	66 yr 2 mo	s	.12	.10	.42	.24
RK	injury OD	63 yr	immediate	73 yr 4 mo	s	.43	.55	.33	.30

OKN: s=symmetric; a=asymmetric

Statistical summary category IV:	6/1	6/3	10/1	10/3
N:	5	5	5	5
Mean:	.21	.22	.31	.27
SD:	.13	.19	.10	.08
SE:	.06	.08	.05	.04

Longitudinal Data: Fig 22 represents asymmetry indices for two individuals who were tested on more than one occasion. The database for the longitudinal testing is included in Table XI.

TABLE XI: OKN RESULTS AND MOTION DETECTION RESULTS OF LONGITUDINAL TESTING

PATIENT	PATHOLOGY	AGE AT INSULT	AGE AT ENUCLEATION	AGE AT TEST	OKN	6/1	6/3	10/1	10/3
CM (category I)	anophthalmos OS	congenital	congenital	4 mo	nn	.85	NA	NA	NA
			10 mo		nn	.52	NA	NA	NA
			1 yr 11 mo		nn	.63	NA	.71	NA
			3 yr		nn	.53	NA	.56	.82
DE (category IV)	RB OS	12 mo	13 mo	2 yr 9 mo	a	.28	.40	.43	.40
				3 yr 9 mo	a	.35	.58	.49	.36

NA, not applicable; OKN, optokinetic nystagmus; OKN: s=symmetric; a=asymmetric: nn=no nystagmus

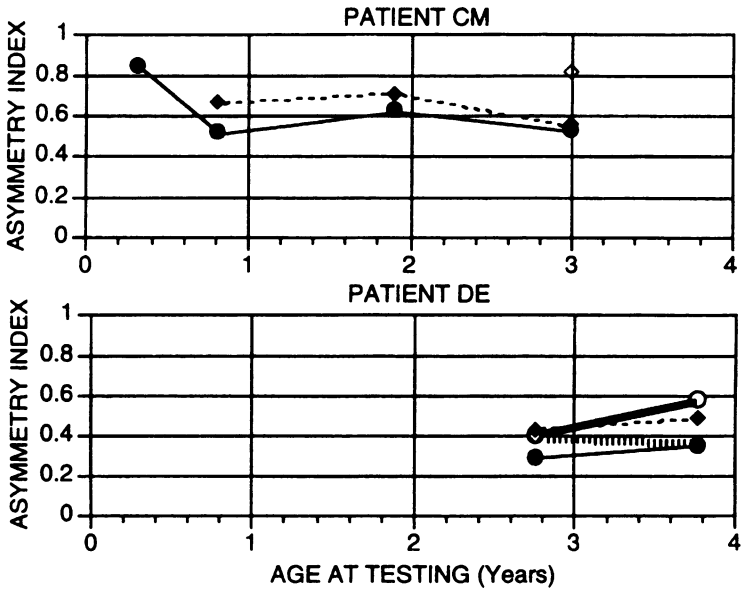

FIGURE 22

Plots of asymmetry indices from 2 subjects, CM (category I) and DE (category IV). Results of 4 testing sessions for CM and 2 testing sessions for DE are shown. Results are plotted for 4 testing stimuli labeled as hertz (Hz)/cycle per degree (cpd). Testing stimuli are delineated as thin solid line for 6/1, thick solid line for 6/3, dotted line for 10/1, and striped line for 10/3. Incomplete database is present for CM.

Comparison of Results From Monocular Individuals and Infantile ET Individuals

Figure 23 compares the individual asymmetry indices of the monocular individuals (N=36) to those of the infantile esotropia patients previously reported by Jampolsky et al.[99] At first glance, the obvious difference between the two populations (left graph) would appear to reflect a younger age of insult and, hence, higher asymmetry index, for the esotropic population. When the graph is restricted to those individuals in both groups with an age of onset less than 1 year (right graph), there are clearly lower asymmetry indices in the monocular population.

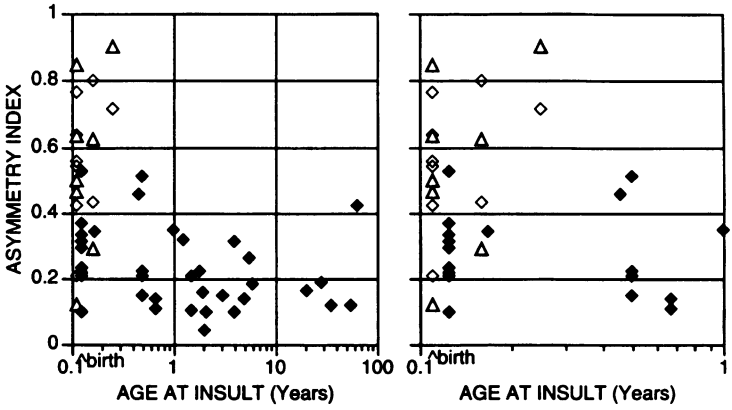

FIGURE 23

Comparison of infantile esotropia patients[99] and monocular subjects' asymmetry indices. Testing stimulus is 6 Hz, 1 cpd. Age of insult is age at which binocular vision was lost, either by establishing monocularity or by developing strabismus. Left, all monocular individuals (N=36) are represented by closed diamond. For esotropic population, each subject (N=9) has entry for right eye (open diamond) and for left eye (open triangle) when significant data were obtained. For comparable age at insult, asymmetry index is higher in infantile esotropia population. Right, expanded portion of graph for purpose of illustrating only subjects 1 year or less at age of insult (N=18 for monocular population, N=9 for esotropic population).

Figure 24 compares the means of the asymmetry indices of the monocular population with those of the infantile esotropia patients previously reported by Jampolsky and associates.[99] An analysis of variance shows a significant difference ($P<.0001$) among the 7 groups (the normal population, 5 monocular categories, and the infantile esotropia population[99]). A Scheffe's S post hoc analysis shows no significant difference among the 5 monocular

categories, but each of the 5 monocular categories was significantly different from the infantile esotropia population.

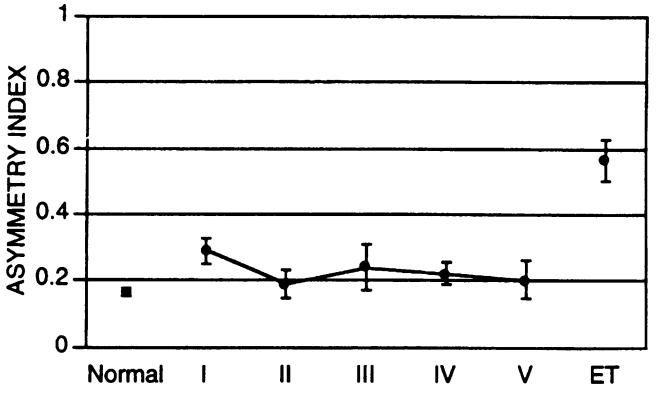

FIGURE 24
Comparison of infantile esotropia patients[99] and monocular individuals' mean asymmetry indices. Testing stimulus is 6 Hz, 1 cpd for all subjects. Vertical bar represents standard error. Normal values represent data shown in Fig 10 (A.M. Norcia, PhD and R.D. Hamer, PhD, unpublished data, 1993). Esotropia values represent data shown in Fig 12 (from Jampolsky et al[99]).

Comparison of Results Among Different Categories of Monocular Subjects
It was acknowledged in the patient selection criteria that the monocular population would have differences in early visual development. These differences reflect the status of binocular vision development. For category I subjects, no postnatal binocular experience was present. For category II subjects, assumed normal binocular experience was present until a specific insult occurred, which immediately resulted in a monocular status; no binocular competition was present. For category III subjects, normal binocular experience was present until a specific insult occurred, which resulted in incomplete visual loss in one eye. Thus, binocular competition was present in these individuals until all vision in one eye was subsequently lost. For category IV subjects, the most ambiguous historical details among the various monocular categories are present. Each of these subjects presented with a clinical picture in which binocular competition was present; the onset of this competition could only be approximated by a review of historical or photographic information. Presumably, a period of normal binocular vision preceded the period of abnormal binocular vision. For category V subjects, normal binocular vision was fully developed prior to the onset of monocular visual loss. Do any of these experiential differences influence the motion detection system as measured by the asymmetry index?

A two-way analysis of variance was performed to assess the effects of monocular category and testing condition (stimulus size and frequency) on the asymmetry index. Five of the 36 patients had incomplete data sets and were therefore excluded from this analysis. The main effect of testing condition was significant ($P=.0001$); the main effect of category was significant ($P=.02$). The interaction between testing condition and monocular category was not significant ($P=.50$).

As might be expected, the mean asymmetry index was greater for each increasingly more complex stimulus, with 6 Hz, 1 cpd the least complex and 10 Hz, 3 cpd the most complex.

The mean asymmetry index was lowest in categories II and V. Category V represented visually mature individuals, which would be expected to have low asymmetry indices approaching the normal population. Category II represents those individuals with no binocular competition; their abnormal binocular experience was limited to interruption of binocularity. The relatively higher mean asymmetry indices are present in categories I (with no binocular experience whatsoever), III (with a period of binocular competition that was well defined), and IV (with a period of binocular competition that was less well defined, Fig 25).

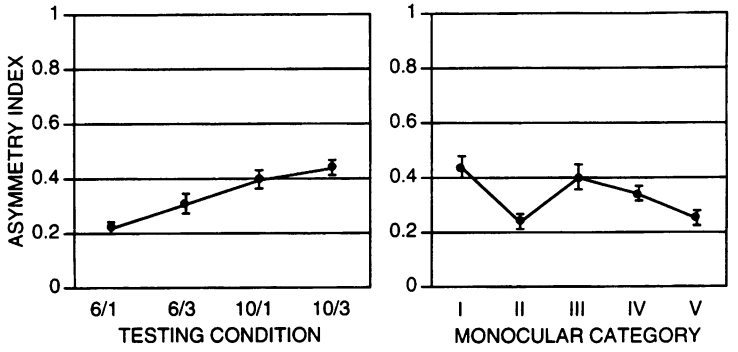

FIGURE 25

Effects of monocular category and testing condition, mean asymmetry indices. Vertical bars represent standard error. Left: testing; for each data point of testing condition, all 5 monocular categories are included. Right: category; for each data point of category, all 4 testing conditions are included.

DISCUSSION

VISION DEVELOPMENT IN THE FUNCTIONING EYE

Although the "results" section is organized to highlight the important data regarding motion detection, a brief discussion of the data from the patient selection criteria deserves mention in light of previous reports on function

of the seeing eye in individuals with early-acquired monocularity.

The clinical history and examination fulfilled several purposes in terms of interpretation of this study. It defined the age range in which monocularity was established in relationship to the sensitive window for visual development.

As can be evidenced by the data, it appears that monocular acuity, refraction, and confrontation visual fields were not influenced by the loss or absence of one eye and confirms that the remaining eye was normal on standard clinical examination techniques.

Previous animal studies have suggested that a rearrangement of function may result in "supernormal" vision in the remaining eye.[127,128] "Supernormal" vision relates to an individual's ability to define a linear break (vernier acuity) that subtends an angle smaller than the receptive field size for foveal cells. One postulated mechanism for this improved function was felt to be a shrinking of the receptive field size, and thus an enhancement of resolution potential.[129]

Studies of human early-acquired enucleates have revealed inconsistent conclusions regarding the function in the remaining eye. In particular, vernier acuity has been found to be normal in one such study[130] and supernormal in another.[131] Contrast sensitivity has been found to be enhanced, perhaps on the basis of reorganization of the visual pathways.[132]

One aspect of the function of the remaining eye that previous investigators have studied relates to the presence or absence of a head turn. Presumably, this adaptation to monocularity results in a more balanced field of vision than if the head were held perfectly straight. One exception to this interpretation would be if there were an oculomotor drive for an abnormal head posture, such as in the esotropic monocular individuals reported by Helveston and associates[117]; these patients developed nystagmus except in adduction.

In this study, 32 of 36 individuals (89%) demonstrated no clinically noticeable head turn. Three subjects (8%) with a history of right eye enucleation at ages 6 months, 18 months, and 23 months demonstrated a right head turn. One patient with a history of right-eye enucleation and with concurrent left Duane's syndrome demonstrated a left head turn. The mechanism for her head turn was felt to be a consequence of Duane's syndrome, since the side of her enucleation would have predicted, if any, a turn in the rightward direction. Interestingly, the presence of her head turn would imply that she had developed, to some extent, binocular visual function prior to the development of a vision-threatening retinoblastoma.

The relative absence of abnormal head posturing in the present sample conflicts with a previous report of head turns in association with enucleation.[133] In part, this difference could simply reflect that a different task—and therefore a different visual need—was being requested. In the series where head turns were so frequently found, the subjects were requested to

navigate down a hallway. An adaptive head position would in that circumstance be beneficial for sampling all of the environment, or using a more representative visual field for navigational purposes. In the testing of visual acuity, the monocular individual's task is one of resolution in which foveal function, rather than full extent of visual field, is of greater importance.

DEVELOPMENT OF OKN RESPONSE: IMPLICATIONS

Definition of Sensitive Period for OKN Motion Detection

The assessment of motion detection systems with OKN is consistent with the study of Reed and associates[120] in that the acquired monocular population can be characterized in large part as having more symmetric OKN than the infantile esotropia population. It is of interest that the 3 categories (II, III, and V) that had a period of well-defined normal early binocular visual experience (with the timing of this known interruption of development as young as 6 months) included no individuals with an asymmetric response. This is consistent with normative data for humans in which OKN symmetry is established by the age of 5 months.[22-24]

Another implication of the symmetric response in this population with a known normal 6 months of vision is that once established, the motion detection system appears to remain intact despite future insult. Even in category III, where a period of known binocular competition existed, there is no clinically apparent reversal to a more immature, asymmetric response. This would suggest that the sensitive period for the OKN form of motion detection is limited to the first 6 months and that at this age, the system's maturation is complete without residual plasticity.

Analysis of Subjects With Asymmetry of OKN

In category IV, 3 of 12 subjects (25%) had an asymmetry of the OKN response. Of all subjects in the study, this was the only category in which this immature, asymmetric form of response is seen. In these 3 individuals, leukocoria had been present since 2, 6, and 12 months of age, respectively. Presumably, each of these individuals had a time where binocular competition was present, arresting normal maturation of this function in a way that such arrest occurs in patients with infantile esotropia. One must note, however, that 3 other individuals in category IV who were 6 months of age at insult developed a symmetric OKN response. The most logical explanation for the different functions in these two groups with apparent matching of the age at insult is that one can only guess to what degree binocular competition and binocular interruption were present in any individual. The natural history for growth of the retinoblastoma is simply not well enough defined to make this distinction. One can, however, postulate that the 3 asymmetric individuals had a greater preponderance of competition and that the 3 symmetric individuals had a greater preponderance of interruption. One

additional factor that was not present historically in any of these 6 children would be if strabismus had been present in conjunction with the retinoblastoma; then, asymmetry might be expected on the basis of strabismic binocular competition. This explanation is weakened by the clinical expectation that strabismus would not be likely until vision was significantly reduced.

Analysis of Congenital Monocular Subjects' OKN Responses

The OKN response in the congenital monocular individuals was noteworthy in that no nystagmus could be induced in 7 of the 9; the two oldest patients in this category demonstrated symmetry. In one respect, the absence of *any* asymmetric response supports the theory that it is binocular competition that is responsible for an arrest of maturation of the motion detection.

This argument is weakened by the difficulty in obtaining *any* OKN response. Initially, it was suspected that this difficulty occurred because of the young age of many individuals in category I. However, there appears to be another factor, as evidenced by an age comparison to other categories. Of all 9 individuals from all categories who were 4 years or age or younger at the time of testing, 4 of 4 category I subjects and 2 of 5 category IV subjects had no nystagmus. Of the 27 individuals older than 4 years at the time of testing, 3 of 5 category I subjects had no nystagmus, but none of the remaining 22 patients in other categories of the same age had this OKN ambiguity. It thus appears that there is a unique deficit in OKN generation in the congenitally monocular population.

One possible explanation for the difficulty in obtaining any OKN, regardless of the direction of motion, is that a prenatal modification in neural pathways occurred as a consequence of the altered development manifest as congenital monocularity. A differential influence of prenatal enucleation in cats on axonal growth for specific ganglion cells has been found.[134] On electrophysiologic measurements, the axons for the X cells were unaltered in comparison to normal binocular cats. The Y cells had abnormal arborization. Unfortunately, the studies did not address the arborization pattern for the W cells. These are the cells that particularly project to the nucleus of the optic tract, which is integrally involved in the OKN pathways.[136] If these cells are in some way altered by prenatal events leading to congenital monocularity, then the neuroanatomic and neurophysiologic basis for the OKN response might be lost entirely. Furthermore, the Y cells in cats are thought to be related to the M cells in primates; the M cells form the basis of the cortical motion pathways.[136] Thus cortical input to the NOT may also be selectively depressed.

It is also possible that an OKN response might have been elicitable under more robust testing circumstances than a simple clinical OKN tape. This possibility, however, does not eliminate the potential significance of absence of OKN with conventional testing in the congenital monocular subjects.

DEVELOPMENT OF MOTION PROCESSING: IMPLICATIONS

Development of Motion Detection in Monocular Individuals

The normative data for asymmetry indices (see Fig 10) demonstrate that motion processing reaches adult levels at an early age. With the least sensitive stimulus (6 Hz, 1 cpd), the development appears to change dramatically within the first year of life, reaching adult levels by 5 to 8 months of age. Developmental changes persist into the first few years of life with more sensitive stimuli.

In the monocular subjects, there is a relationship between the asymmetry index and the age at insult. For the early-acquired monocular subjects, and in particular categories II and III, this relationship reflects 2 factors—the period of normal binocular vision prior to the insult and the effect of the experience of monocularity. To a first approximation, the monocular patients appear to have an arrested form of normal development.

The influence of the experience of monocularity can be more completely assessed with the longitudinal data on subjects CM and DE (see Fig 22). Neither individual had a pronounced reduction of the asymmetry indices for particular testing conditions.

The congenitally monocular subjects offer a different perspective on the experience of congenital monocularity. Data for subject TP suggest that there may be a prolonged maturational process with monocularity. For the testing conditions of 6 Hz, 1 cpd and 10 Hz, 1 cpd, his asymmetry indices are within the normal range. For the testing conditions of 6 Hz, 3 cpd and 10 Hz, 3 cpd, his asymmetry indices are outside the normal range. Data for subject JM data similarly support maturation to a normal level for the simpler 6 Hz, 1 cpd, with values outside the normal range for the more complex stimuli.

The fact that the magnitude of residual—motion asymmetry correlates with the age at insult suggests that normal binocular vision is required for proper development of motion-processing mechanisms. Therefore, indices of motion asymmetry can be properly thought of as an alternative indicator of the history of binocular vision development, as previously suggested.[99]

The congenital monocular subjects (category I) provide the greatest possibility of isolating monocularity as a developmental issue and, in so doing, isolating the factor of interruption of binocularity from binocular competition. It is appropriate, therefore, to assess these 9 individuals by plotting their asymmetry indices at the time of testing against age-matched normal individuals (Fig 26).

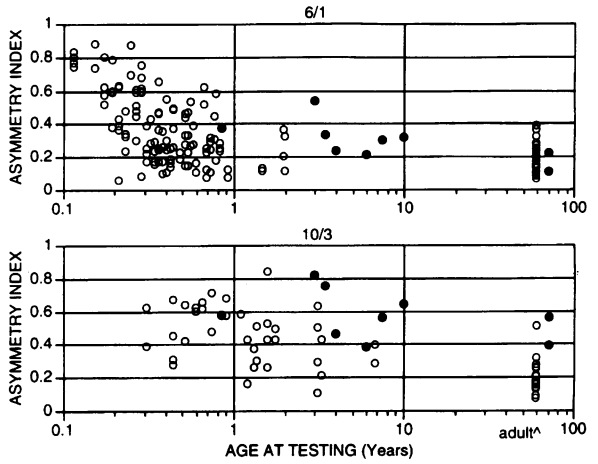

FIGURE 26

Asymmetry index of category I congenital monocular individuals compared to normative data by age at testing. Stimulus is labeled as Hz/cpd for 6/1 and 10/3 stimuli. Congenital subjects; closed circles; normals; open circles. Congenital monocular subjects have asymmetry indices that are higher than those of age-matched normal individuals, especially for 10/3.

Comparison of the Experience of Monocularity With the Experience of Infantile Esotropia on Development of Motion Detection

The clinical implications of this thesis are most supported by a review of the comparison of the monocular experience to the strabismus experience during development of motion detection. These data are presented in Figs 23 and 24. It is important to note that for each of these populations, the asymmetry index is plotted as a function of the age at insult. Fig 24 provides a comparison of the mean asymmetry index for each monocular category and the esotropic population, asserting that difference in asymmetry index is statistically significant.

The asymmetry index is higher in the strabismic population than in the monocular population or in the normal infant. One can conclude that binocular competition is more negative an experience than interruption of binocularity. The importance of this conclusion will be further elucidated in the next 2 sections.

Definition of the Sensitive Period for Motion Detection by VEP Testing

The graph calls attention to the fact that, by definition, the infantile esotropia population will have a very limited range for not only the age at insult but also the duration of any normal binocularity. There is a persistence of this high asymmetry index in untreated patients[99] as well as a failure to return to

normal levels even when treatment is rendered.

The influence of strabismus per se on asymmetry index later in development has shown that a later onset of strabismus does not result in a high asymmetry index.[137] This would suggest again that the motion detection system has an early, limited period of development in which an abnormal experience such as strabismus or monocularity can influence its development.

Implications for the Management of Infantile Esotropia

From a developmental perspective, the motion detection system is less abnormal when binocular interruption is present alone than when binocular competition is present in conjunction with interruption of normal binocularity. This would support the concept that alternate occlusion is of benefit in eliminating binocular competition preoperatively, since it eliminates competition, leaving the less deleterious interruption in place prior to realignment.

Two potential issues deserve further exploration. For such intervention to be effective, the motion detection system must have some degree of plasticity in order to restore a more normal development. For such treatment to be safe, such intervention must have no discernible side effect for the motion detection system or for other developing visual functions.

Jampolsky and associates[99] have studied motion processing in 14 infants with infantile esotropia using a VEP Technique similar to that used in this study. The age at onset of strabismus ranged from birth to 12 weeks. VEP motion studies were consistent with infantile esotropia in that the average asymmetry index was 0.58 compared with the age-matched norm of 0.28. The VEPs were repeated after a period of alternate occlusion of at least 5 weeks' duration. The asymmetry index on average decreased to 0.43 ($P<.012$); individually, there appeared to be a more consistent decrease of the asymmetry index in the dominant eye. A control group with no occlusion failed to show a corresponding decrease in asymmetry that one might expect if the decrease simply reflected a maturational process. An earlier study from the same institution had shown an improvement in the motion processing function after patients with strabismus and alternating fixation were surgically straightened at a young age.[138] Although that study affirmed the plasticity of the motion processing system, the alternate occlusion study implies that binocular competition is detrimental to the motion processing maturation and that interruption of binocularity by means of alternate occlusion results in a reduction of the asymmetry index.

As previously discussed in the introduction, the effects of alternate occlusion have been assessed by researchers.[19,21,99] Clearly, there is a limit to the amount of time alternate occlusion can be performed. Indeed, there are both research and clinical experience to suggest that alternate occlusion can be safely performed.

Implications for Other Binocular Functions and for the Nature Versus Nurture Controversy

The function of motion detection has been defined as a function that provides information about early binocular experience. One must recognize, however, that motion detection itself is not a binocular function. To conclude that an improvement in motion detection by elimination of binocular competition will result in improved binocular function assessed by other means may be inaccurate. It will be important in future studies to correlate recovery of motion symmetry with changes of other forms of binocular visual function.

What can be concluded, however, is that there is plasticity of the developing visual systems that is influenced by binocular experience. This plasticity is very much in agreement with Chavasse's belief that abnormal binocular visual development can be reversed toward a more normal developmental sequence.

CONCLUSIONS

1. The development of motion detection appears to have a sensitive period, which is particularly vulnerable to abnormal experience within the first year of life and which extends into the second or third year. Attainment of a normally developed motion system as quantified by the VEP asymmetry index requires normal binocular vision; without this experience, motion detection will develop incompletely, leaving persistent neonatal directional biases. Both the experience of monocularity and the experience of infantile esotropia impair normal development of binocularity and the motion detection function.

2. The monocular population shows a less abnormal motion processing system when compared with patients with infantile esotropia, even when monocularity is congenital. This difference in development is considered to reflect the deleterious effects of binocular competition, as seen in the untreated strabismus patient, compared with simple interruption of binocularity, as seen in the monocular individual.

3. The results support indirectly the premise that prealignment alternate occlusion is of benefit to the patient with infantile esotropia prior to realignment. The likely mechanism for this benefit is that alternate occlusion eliminates binocular competition, leaving the patient with the less debilitating experience of interrupted binocularity.

4. The development of the motion detection system does not necessarily parallel the development of other binocular functions, but it is nonetheless a function reflective of early binocular experience.

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