Optokinetic Asymmetry in Esotropia

Joseph L. Demer, M.D., Ph.D.
Gunter K. von Noorden, M.D.
Houston, Texas

ABSTRACT

Laboratory evidence suggests that the interruption of binocularity produced by early onset strabismus inhibits normal development of cortical inputs to the brainstem optokinetic pathway, producing an asymmetry in monocular optokinetic responses. It has been proposed that this optokinetic asymmetry can be useful in evaluating the presence of binocular vision.¹

We studied 134 strabismic and 16 orthotropic patients to determine the clinical prevalence of asymmetric optokinetic responses. Cooperative children and adults were tested. For each subject, the observer made a judgment about the presence or absence of symmetry in the nasally directed versus temporally directed monocular optokinetic responses to motion of a hand-held drum.

Clinical evidence of significantly greater nasally than temporally directed optokinetic responses was observed in 58% of esotropic patients who developed strabismus before the age of 6 months; in 22% of esotropic patients with onset between 6 and 12 months of age; in 9% of esotropic patients with onset between 12 and 24 months of age; and in only 5% of esotropic patients with onset of esotropia after the age of 24 months. No asymmetry was observed in any of the exotropic patients or in the hypertropic patient and was present in only 6% of orthotropic patients. Statistical analysis indicates that in this population the finding of monocular optokinetic asymmetry in an esotropic patient implies an 85% chance that the onset of esotropia occurred in the first 6 months of life. Quantitative electro-oculographic recording demons-

FROM Texas Children's Hospital, Cullen Eye Institute and Clayton Neurology Laboratory, Baylor College of Medicine, Houston, Texas.

Sharon Congdon performed the electro-oculographic recordings reported here. This research was supported by grants from the National Eye Institute EY-06394 and EY-02520, and the Clayton Foundation for Research.

Reprint requests should be addressed to Joseph L. Demer, M.D., Ph.D., Jules Stein Eye Institute, University of California at Los Angeles, 10833 Le Conte Avenue, Los Angeles, California 90024.

INTRODUCTION

Monocular, horizontal optokinetic tracking in normal human infants under the age of 3 months is asymmetric and characterized by more vigorous following of nasally directed stimuli than temporally directed stimuli,¹ While this asymmetry disappears after the age of about 6 months,² the asymmetry reportedly persists in those experiencing reduced binocularity as a result of early-onset strabismus.³ An attempt to determine the clinical prevalence of such an asymmetry in patients with clinical evidence of asymmetric optokinetic responses to motion of a hand-held drum.

286

NOVEMBER/DECEMBER 1988, VOLUME 25, NUMBER 6
humans have had limited clinical relevance. Most of the studies noted above have involved very small numbers of subjects having diverse pathologies, limiting the generality of the results. The study by Mein involved 120 subjects, but the great majority of these were preselected for the presence of dissociated vertical deviation.9 One study has evaluated monocular optokinetic asymmetry in a large number of strabismic children.10

In the present study we used a hand-held optokinetic drum to establish the prevalence of monocular optokinetic nystagmus asymmetry in a large pediatric ophthalmology practice, as well as to relate this finding to other clinical characteristics. The overall goal was to determine the usefulness of clinical optokinetic testing in the diagnosis and management of pediatric ophthalmology patients. Limited use of quantitative eye movement recording was performed in the laboratory to confirm the clinical tests.

SUBJECTS AND METHODS

We studied 134 strabismic and 16 orthotropic patients. Patients included cooperative children of ages 3 years or more, and adults. Ocular histories were obtained from patients, their parents, or referring physicians. The age of onset of strabismus was verified by direct examination by the authors or referring ophthalmologists, or by family photographs, if possible, but was frequently available only from histories given by parents. All subjects underwent a complete visual and ocular motility examination, including visual acuity testing, cycloplegic refraction, measurement of ocular alignment by prism-cover testing, and evaluation of ductions and versions. Stereopsis was evaluated using the Titmus or Lang tests in subjects able to cooperate. The presence of latent nystagmus, dissociated vertical deviation, and oblique muscle overaction was evaluated using standard criteria.11 In particular, latent nystagmus was considered to be a conjugate, jerk nystagmus present only upon covering of one eye and having the slow phase directed toward the covered eye.

Optokinetic nystagmus was clinically evaluated in all patients using a hand-held drum 10 cm in diameter and 26 cm high, marked with vertical stripes alternating every 45° of circumference with stylized animal figures. The drum was held about 30 cm from the patient's eyes and rotated at approximately 20 revolutions/min, corresponding to an angular velocity directly ahead of the patient of 38/sec. Testing was performed monocularly with the right and left eyes. An optokinetic response was considered to be an evoked jerk nystagmus with slow phase in the direction of motion of the stimulus stripes, which stopped and started in synchrony with the stimulus. The response was judged qualitatively based on the velocity of the slow phases and frequency of quick phases and was recorded in narrative form. Responses were required to be unequivocally asymmetrical to be designated as such; doubtful cases were considered to be symmetrical. The presence or absence of latent nystagmus was not considered as a modifying factor in classification of symmetry of the optokinetic response.

The clinical evaluation method of optokinetic nystagmus was validated in two ways. In ten patients, testing was performed in duplicate by the authors acting as independent observers, who were found to agree in their assessment of the presence or absence of optokinetic asymmetry in nine of ten cases.

As additional validation, in two patients having clinical evidence of optokinetic asymmetry, confirmatory quantitative electro-oculographic measurements were performed. Calibration was obtained for saccadic targets 15° to the left and right of center. The stimulus for quantitative optokinetic measurements was a full-field, vertically striped drum surrounding the patient 70 cm from the eyes. The optokinetic drum was sinusoidally rotated by a servomotor under the control of a PDP 11/73 digital computer; the rotation was at 0.1 or 0.2 Hz, and various velocity amplitudes. Smooth pursuit was quantitatively tested using a small laser spot target projected on a screen and deflected in a sinusoidal pattern by mirror galvanometers under computer control. A frequency of 0.2 Hz was employed for pursuit testing. Eye movements were recorded using bi-temporally placed Ag/Ag-Cl electrodes with digital sampling at 200 Hz. Slow phase eye velocities were extracted using an automated technique described elsewhere.12

Confidence intervals were constructed for the prevalence of clinical optokinetic asymmetry using the normal approximation to the binomial distribution valid for large samples.13 A similar method was also used for comparing the prevalence of asymmetry among various groups.13

RESULTS

Data on the frequency of clinical monocular optokinetic asymmetry in 150 patients are summarized in the Table. It may be seen from the Table that optokinetic asymmetry is rare in orthotropic patients and was not found in any of the esotropic patients or the single hypertropic patient. Among all of the 120 esotropic patients, however, the frequency of optokinetic asymmetry was 32.5%.

Information concerning the age of onset of esotropia was available for 101 patients. When categorized according to age of onset, a striking pattern emerges that is illustrated in Figure 1, which is a histogram of the frequency of clinical monocular optokinetic asymmetry. It may be seen from Figure 1 that 58.0% (55% confidence interval 44% to 72%) of esotropic patients with onset before 6 months of age exhibit monocular optokinetic asymmetry, significantly greater than the 22.2% (confidence interval 0% to 49%, p<0.0001) of those with onset between 6 and 12 months. This in turn is significantly greater than the 8.7% (confidence interval 0% to 22%) frequency of monocular optokinetic asymmetry seen in esotropic patients with onset from 12 to 24 months of age, or the 5.3% (confidence interval 0% to 16.5%) frequency in those with onset over 24 months. There was no significant difference in the frequency of asymmetry between the latter two groups. Clinical monocular optokinetic asymmetry was present in five of 19 (26.3%) of esotropic patients.
TABLE
Clinical Monocular Optokinetic Asymmetry

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Symmetric</th>
<th>Asymmetric</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Number</td>
<td>Number</td>
</tr>
<tr>
<td></td>
<td>of Patients (%)</td>
<td>of Patients (%)</td>
<td>of Patients (%)</td>
</tr>
<tr>
<td>Orthotropia</td>
<td>15 (93.8)</td>
<td>1 (6.2)</td>
<td>16 (10.7)</td>
</tr>
<tr>
<td>Esotropia</td>
<td>81 (67.5)</td>
<td>39 (32.5)</td>
<td>120 (80.0)</td>
</tr>
<tr>
<td>Onset 0 to 6 mos.</td>
<td>21 (42.0)</td>
<td>28 (58.0)</td>
<td>50 (33.0)</td>
</tr>
<tr>
<td>Onset 6 to 12 mos.</td>
<td>7 (77.8)</td>
<td>2 (22.2)</td>
<td>9 (6.0)</td>
</tr>
<tr>
<td>Onset 12 to 24 mos.</td>
<td>21 (91.3)</td>
<td>2 (8.7)</td>
<td>23 (15.3)</td>
</tr>
<tr>
<td>Onset &gt;24 mos.</td>
<td>18 (94.7)</td>
<td>1 (5.3)</td>
<td>19 (12.7)</td>
</tr>
<tr>
<td>Onset ?</td>
<td>14 (74.7)</td>
<td>5 (25.3)</td>
<td>19 (12.7)</td>
</tr>
<tr>
<td>Exotropia</td>
<td>13 (100.0)</td>
<td>0 (0.0)</td>
<td>13 (8.7)</td>
</tr>
<tr>
<td>Hypertropia</td>
<td>1 (100.0)</td>
<td>0 (0.0)</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Total</td>
<td>110 (73.3)</td>
<td>40 (26.7)</td>
<td>150 (100.0)</td>
</tr>
</tbody>
</table>

FIGURE 1: Histogram showing the prevalence of clinical monocular optokinetic nystagmus (OKN) asymmetry in esotropic patients with various ages of onset of strabismus. The asterisks indicate statistically significant differences in prevalence between adjacent columns, and the error bars indicate 95% confidence intervals for mean prevalence. Thus, there was a significantly greater prevalence of asymmetry in esotropic patients with onset before the age of 6 months than those with onset between 6 and 12 months, and those in turn had a significantly greater prevalence than those with later onset.

Having an uncertain onset of strabismus.

Of the 30 patients known to have dissociated vertical deviation, 29 were esotropic and one was orthotropic. Monocular optokinetic asymmetry was present in 19 of these 30 patients (63.3%). Fifteen of these 19 patients with asymmetric optokinetic nystagmus had onset of esotropia before the age of 6 months, one between 6 and 12 months, and three had unknown onset.

Of the 22 patients known to have latent nystagmus, all were esotropic and 19 had onset under the age of 6 months. Sixteen of the 22 patients had asymmetric monocular optokinetic responses and 11 of these 16 patients also had dissociated vertical deviation. However, two patients with both latent nystagmus and dissociated vertical deviation had symmetrical optokinetic responses, and five esotropic patients with latent nystagmus but no dissociated vertical deviation had symmetrical optokinetic responses.

Eighteen patients were known to have had amblyopia in one eye. In five of these patients the monocular optokinetic asymmetry was present only in the amblyopic eye, and the response in the sound eye was symmetric. In three of these patients the optokinetic asymmetry was present in both eyes, while in nine patients the optokinetic asymmetry was absent. In the remaining monocularly amblyopic patient, the asymmetry was present only in the sound eye and not in the amblyopic eye.
Quantitative electro-oculographic recording of optokinetic responses and foveal smooth pursuit for small targets was performed in two amblyopic patients exhibiting clinical optokinetic asymmetry in the amblyopic eye, but not in the sound eye. In one patient, aged 15 years, cooperation and fixation were inadequate to obtain interpretable records. The other patient was able to cooperate for adequate recording. She was a 10-year-old girl with a history of esotropia documented by ophthalmological examination at age 3 months, as well as treated ambyopia in the right eye, now with subnormal binocular vision following strabismus surgery. On clinical monocular optokinetic nystagmus testing, she was found to have asymmetrically reduced temporal as opposed to nasal slow phase velocity for the right eye only; the optokinetic response was judged to be symmetrical for the left eye and also under binocular conditions. There was no latent nystagmus.

Quantitative optokinetic testing was performed using a full-field, sinusoidal stimulus with frequency 0.1 Hz, amplitude 40°/sec. Response gain is defined to be eye velocity divided by stimulus velocity. Gain was calculated separately for rightward and leftward slow phases and is equal to the slope of the linear regression relating stimulus velocity and response velocity. The monocular optokinetic response for the right eye is seen in Figure 2A, and shows an asymmetrically low gain (eye velocity divided by stimulus velocity) of 0.28 for temporally directed slow phases to the right, compared with 0.55 for nasally directed slow phases to the left (32.8% asymmetry). The monocular optokinetic response for the left eye is seen in Figure 2B, showing a lesser degree of asymmetry; gain for temporally directed slow phases to the left was 0.34, while gain for nasally directed slow phases to the right was 0.45 (12.8% asymmetry). The response to binocular optokinetic stimulation is seen in Figure 2C, showing a gain of 0.44 for slow phases to the right and 0.49 for slow phases to the left (5.6% asymmetry). Despite the asymmetry of the optokinetic responses, the foveal smooth pursuit responses were remarkably symmetrical under monocular and binocular conditions. Smooth pursuit was tested for a small lighted target moving sinusoidally in the horizontal plane, with
Optokinetic Asymmetry

FIGURE 2D: Similar to A, but showing monocular foveal smooth pursuit in the formerly amblyopic right eye of the same patient. In contrast to the asymmetric full field optokinetic response in A, gains for nasally and temporally directed pursuit are nearly equal, reflecting a minimal asymmetry of 1.6%.

Frequency 0.2 Hz, and amplitude 20 and 40°/sec. The monocular pursuit response for the right eye is seen in Figure 2D; gain for temporally directed slow phases to the right was 0.64, while gain for nasally directed slow phases to the left was 0.62 (1.5% asymmetry). This high degree of asymmetry was typical of all of the pursuit responses. Other recordings, not shown, demonstrated the absence of latent nystagmus, which can also be inferred by the passage through the origin of the regression lines in Figures 2A and 2B. Latent nystagmus, if it had been present, would have been observed to produce a significant positive or negative offset in the y-intercept of the regression lines.

Discussion

In the present study, the directional symmetry of monocular, horizontal optokinetic nystagmus was evaluated using a widely available clinical instrument, the hand-held optokinetic drum. The data in Figure 1 demonstrate a clear influence of the age of onset of esotropia on the frequency of clinical asymmetry of monocular optokinetic responses, confirming in a large pediatric ophthalmology practice the observations of others. In particular, asymmetric reduction in the velocity of temporally directed slow phases relative to nasally directed slow phases was present in 58% (95% confidence interval 44% to 72%) of esotropic patients with onset of strabismus under the age of 6 months. This was significantly higher than the prevalence of this finding in esotropic patients with later onset. There was, in turn, a significantly greater prevalence of monocular optokinetic asymmetry in patients with onset of esotropia under the age of 12 months than in patients with an older onset of esotropia. In the present study, the prevalence of asymmetry was 22% (confidence interval 0% to 49%) for patients with onset of esotropia between 6 and 12 months, and 9% (confidence interval 0% to 22%) for patients with onset between 12 and 24 months, and 5% (confidence interval 0% to 16%) for patients with onset of esotropia after 24 months of age. The maximum values of confidence intervals for the prevalence of monocular optokinetic asymmetry found in the present study for each age range of onset are significantly lower than found in the study of Bourron-Madignier et al. From the data of these investigators, one can calculate a 92% prevalence of monocular optokinetic asymmetry in patients with onset of esotropia under 6 months of age, 64% prevalence in patients with onset from 6 to 12 months of age, 33% prevalence in patients with onset from 12 to 24 months of age, and 23% in patients with onset of esotropia after 24 months of age. The higher prevalence reported by these authors may reflect differences in the patient population under investigation. In the present study, monocular optokinetic asymmetry was not observed in patients having exo- or hyperdeviations, and was found in only one orthotropic patient.

Application of Bayes' statistical theorem permits our data on the prevalence of clinical monocular optokinetic asymmetry to be used for making conclusions about the age of onset of esotropia in other patients. Assuming the prevalence of early onset esotropia that was observed in this study (42% of all esotropic patients), the finding of clinical monocular optokinetic asymmetry in an esotropic patient implies an 85% likelihood that the onset of strabismus was before the age of 6 months. This information may be useful in predicting the likelihood of achieving binocularity following surgical re-alignment and may indicate the need for increased vigilance in monitoring for the development of other manifestations of the infantile esotropia syndrome, such as dissociated vertical deviation. It has been reported that transient monocular optokinetic asymmetry may be observed in orthotropic patients under the age of 18 months, only to resolve between 1 and 2 years of age. Since the data here were obtained in patients aged 3 years or more, the clinical significance of the finding of monocular optokinetic asymmetry is established only for patients in this age group. However, it is not uncommon for the clinician to be faced with the management of an esotropic child over the age of 3 years for whom no reliable history is available concerning the onset of strabismus. In this situation, the finding of monocular optokinetic asymmetry can be a helpful clue to the onset of the disorder. It should be stressed that the finding of monocular optokinetic asymmetry does not imply a certainty that esotropia is of onset less than 6 months of age, nor does the absence of such asymmetry necessarily rule this out.

The present findings should be interpreted with some caution, since parental reporting was used to determine the age of onset of strabismus in most cases. Such reporting is
probably reliable enough to assign patients to the stated
categories of age of onset when large angle, manifest
strabismus is present. Since lay persons may overlook
subtle or intermittent esotropia, it is conceivable that the
low incidence of clinical optokinetic asymmetry observed in
patients having the reported onset of esotropia over the age
of 12 months may in fact be due to an earlier onset of
strabismus than reported. Our findings may thus be
consistent with the hypothesis that clinical optokinetic
asymmetry develops only in esotropic children having an
onset of strabismus before 1 year of age. Occult strabismus
of early onset may be the cause of the rare cases of
optokinetic asymmetry observed in children with reported
later onset esotropia.

Clinical asymmetry of monocular optokinetic response
was not observed in all of the patients who had onset of
esotropia before the age of 6 months. A similar finding was
noted in the clinical optokinetic study of Bourron-Madigier
et al. This result does not permit the conclusion that
asymmetry is absent in these patients, however, since the
hand-held optokinetic drum is a qualitative and probably
relatively insensitive test of optokinetic function. The
clinical criterion we employed for a diagnosis of optokinetic
asymmetry was strict, requiring the presence of
unequivocally reduced temporal as opposed to nasal slow
phase velocity. The reliability of this approach is indicated
by the 90% level of agreement achieved when patients were
evaluated by two independent observers.

In one patient with infantile esotropia in whom
quantitative electro-oculographic measurements were
compared with clinical evaluation of optokinetic nystagmus,
the quantitative study confirmed the presence of nasal-
temporal asymmetry in the formerly amblyopic eye. How-
ever, the quantitative measurements also showed a lesser
degree of asymmetry during monocular testing of the
follow eye, despite symmetrical responses during binocular
stimulation. This implies that while the hand-held
optokinetic drum can reliably detect gross asymmetry in
the monocular optokinetic response, the method may miss
subtle degrees of asymmetry. Quantitative eye movement
recordings in all patients would thus be required to
determine the true prevalence of monocular optokinetic
asymmetry, compared with the "clinical" prevalence, as
reported here.

Quantitative eye movement recordings of monocular
optokinetic and foveal smooth pursuit responses in the
infantile esotropia patient also revealed dissociation
between these two types of responses. The asymmetry was
evident only in the optokinetic responses, not in the pursuit
responses. In this patient, at least, the monocular asy-
metry thus appears to be due to asymmetrical response to
peripheral retinal motion information, rather than to
foveal motion information. Tychsen et al demonstrated
monocular pursuit asymmetry in adults with history of
infantile strabismus using a constant velocity pursuit
stimulus. Although reduction in the stimulus field size has
been reported to increase the observed monocular
optokinetic asymmetries in amblyopic patients,

have reported this is an inconsistent finding and that the
opposite trend may occasionally be present. Since foveal
pursuit and optokinetic nystagmus have different proper-
ties and neural substrates, further study of the dif-
ferential influence of early onset esotropia on these ocular
motor functions might be expected to yield insight into the
mechanisms of strabismus. Flynn has reported that ves-
tibulo-ocular reflex suppression also frequently exhibits a
monocular directional asymmetry in patients with early
onset esotropia. This phenomenon, while not the focus of
the current report, deserves further investigation and
correlation with monocular optokinetic asymmetry.

In the present study, clinical monocular optokinetic
asymmetry was found to be associated with latent nystag-
us, amblyopia, and dissociated vertical deviation. How-
ever, these findings were by no means invariably linked.
Further, in amblyopic patients, the asymmetry was some-
times found in the amblyopic eye, sometimes in the non-
amblyopic eye and was sometimes absent. The discordance
of the findings associated with the congenital esotropia
syndrome suggests that these clinical manifestations
may all be due to a common cause that makes each of them
likely but not inevitable. This raises questions for theories
that explain latent nystagmus and strabismus as being
directly caused by monocular optokinetic asymmetries.
The common cause for the observed abnormalities may well
be interrupted binocular interaction during a critical
developmental period. Sensitive binocular sensory testing
of patients having early onset of strabismus may provide
additional insight into the pathogenesis of this disorder.

REFERENCES

1. Atkinson J: Development of optokinetic nystagmus in human
infant and monkey infant: An analogue to development in
kittens, in Freeman RD (ed): Developmental Neurobiology of
2. Naegle JR, Held R: The postnatal development of monocular
monocular optokinetic nystagmus to peripheral binocular
4. van Hof-van Duin J, Mohn G: Monocular and binocular
optokinetic nystagmus in humans with defective stereopsis.
5. Tychsen L, Hurtig R, Scott WE: Pursuit is impaired but the
vestibulo-ocular reflex is normal in infantile strabismus.
Arch Ophthamal 1985; 103:536-539.
6. Tychsen L, Lisberger SG: Maldevelopment of visual motion
processing in humans who had strabismus with onset in
7. Bourron-Madignon M: Unilateral congenital organic
amblyopia and manifest latent nystagmus, in Kaufmann H
(ed): Transactions of the 16th Meeting. European
Strabismological Association. Giessen, European
8. Kommerell G: The pathophysiology of infantile strabismus, in
Kaufmann H (ed): Transactions of the 16th Meeting of the
European Strabismological Association. Giessen European


