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OKN, perceptual and VEP direction biases in strabismus

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Abstract

The present study quantified nasalward/temporalward biases in monocular optokinetic nystagmus (MOKN) and perceived velocity in patients with either early onset esotropia, late onset esotropia and in normals. MOKN was measured with low spatial frequency, small-field gratings drifting at 9.4°/s. MOKN bias was quantified as the ratio of nasalward slow-phase velocity divided by the sum of temporalward and nasalward slow-phase velocities ($N/(N+T)$). Observers also rated the perceived velocity of gratings moving in nasalward and temporalward directions (3 or 9.4°/s) using a two interval forced choice task. MOKN and perceived velocity biases were correlated negatively in both early onset and late onset groups in the perceptual task—nasalward moving targets were rated as slower than temporalward targets, but in the MOKN task, slow-phase gain was higher for nasalward than for temporalward targets. Oscillatory-motion, visual evoked potentials (VEPs), were recorded in response to 1 c/deg gratings undergoing apparent motion at 10 Hz in a subset of the observers. VEP direction biases were quantified by calculating the ratio of first harmonic response amplitudes to the sum of first and second harmonic amplitudes. Significant correlations were found between the direction biases obtained on all three measures. Perceived velocity and MOKN bias measures were also correlated negatively. Patients with early onset esotropia (infantile esotropia) had larger biases than late onset esotropes or normals on each measure and the biases were more frequently bilateral in the early onset patients. The pattern of results is consistent with early critical periods for the mechanism(s) underlying MOKN, perceived velocity and cortical responsiveness. A single site model for all three asymmetries is unlikely, at least in simple form, because of the negative correlation between MOKN and perceived velocity biases and because of the differences in relative magnitude between the perceptual and MOKN biases.

Keywords: Motion perception; Optokinetic nystagmus; Strabismus; Velocity; Visual evoked potentials

1. Introduction

Patients with a history of early interruption of binocularity such as occurs in infantile esotropia exhibit a complex of directional biases in their oculomotor, perceptual and cortical evoked responses. Oculomotor biases are manifested as asymmetries of monocular optokinetic nystagmus (MOKN) and monocular smooth pursuit eye movements. Characteristically, there is reduced slow phase velocity of the MOKN response to temporally directed motion [1–8]. A similarly directed asymmetry of smooth pursuit eye movements has been also reported in patients with early onset strabismus [9–13].

Monocular directional asymmetries in visual evoked potential responses to oscillatory apparent motion (MVEPs) have been documented in normal infants and in infantile esotropia [14–17]. The MVEP response pattern is consistent with biases of motion responsiveness for nasalward versus temporalward motion in each eye, although the exact direction of the bias is ambiguous. The oscillatory motion VEP in late onset strabismus, while not completely normal, does not generally show the 180° phase shift between eyes that is the signature of nasalward/temporalward asymmetries seen in early infancy and early onset strabismus [18].

While consensus exists with regard to the presence of MOKN and pursuit asymmetries, the same cannot be said of perceptual asymmetries. Schor and Levi [19] evaluated horizontal motion sensitivity in a number of observers with strabismus and amblyopia and did not

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find directional biases despite abnormal OKN. They did however find specific losses of directional selectivity. Tychsen and Lisberger [13] reported that nasally directed stimulus motion was perceived as faster than temporally directed motion in observers with infantile esotropia. Roberts and Westall [5] were unable to confirm these perceptual biases in their population despite significant MOKN asymmetry. Hartmann et al. [7] using a motion nulling paradigm concluded that perceptual biases were either non-existent or considerably smaller than eye movement biases. Kommerell [4] using optokinetic stimuli and magnitude estimation noted a normal velocity discrimination threshold in one subject who had early onset strabismus and marked asymmetry of smooth pursuit. Hague, Shallo-Hoffmann [20] reported elevated thresholds for detection of nasally directed motion when compared with the temporal direction in observers with early onset esotropia, the opposite direction to that described by Tychsen and Lisberger [13]. More recently, Shallo-Hoffmann et al. [21] reported elevated thresholds for nasalward motion in the chronically deviated eye and elevated temporalward thresholds in the habitually fixating eye (non-alternating infantile esotropia).

The present work examines the relationship between sensory and oculomotor biases. In the first experiment, data on MOKN and perceived velocity biases from a large, population-based study, the co-operative amblyopia classification study (CACS) was analyzed retrospectively [22]. In a follow-up experiment on a smaller sample, the relationships between MOKN, perceived velocity bias and monocular oscillatory-motion VEPs were examined.

2. Methods

2.1. Observers

In the CACS sample (Experiment 1), data were collected from 200 patients with either early onset ($n = 50$) or late onset esotropia ($n = 150$). Sixty-nine clinically normal observers also participated. Patients were classified retrospectively as having had early onset strabismus if they reported a history of symptoms of (or treatment for) strabismus starting during the first year of life. Patients with a reported onset of strabismus or treatment between 1 and 9 years of age were classified as 'late onset'. Ocular histories were obtained from medical records and from histories obtained from the patient or parents. Sixty-nine percent of the early-onset group and 89% of the late onset group were amblyopic (acuity worse than or equal to 6/12 in one eye). Additional details of these two patient groups can be found in Schor et al. [23]. In the follow-up experiment (Experiment 2), data were collected from 16 normal observers, 11 observers who were known to have strabismus with onset after age one and in 18 observers whose onset was prior to 1 year (16 of 18 had a onset prior to 6 months as determined from the patients' ophthalmic chart).

2.2. Apparatus and Procedures

Common methods were used in Experiment 1 and 2 to measure slow-phase velocity of small field MOKN and the perceived velocity of gratings moving in nasalward and temporalward directions. Only the second study measured the symmetry of the oscillatory-motion visual evoked potential (MVEP). All measurements were made monocularly with refractive corrections in place.

2.3. Monocular Optokinetic Nystagmus (MOKN)

Eye movements made in response to a horizontally moving vertical sinusoidal grating were recorded using an Applied Science Laboratories Eye-Trac Model 210 limbus tracker. The gratings were displayed on a 15 in diagonal Princeton Max-15 monitor (60 Hz non-interlaced with 31 kHz horizontal raster scan). The field size was $14.3 \times 11.1°$, viewed at 100 cm. In Experiment 1, a low spatial frequency grating was moved either leftwards or rightwards at 9.4°/s. The spatial frequency of the grating was scaled with visual acuity; for LogMar acuities better than 20/100 (Snellen Equivalent), the spatial frequency was 1 c/deg. For acuities between 20/100 and 20/600, 0.5 c/deg was used and below 20/600, 0.25 c/deg was used. In Experiment 2, the spatial frequency was fixed at 1.06 c/deg at a velocity of 9.4°/s to yield a constant temporal frequency of 10 Hz (recall that $TF = SF*V$). No fixation marks were used. Observers were instructed to keep grating in focus, to keep their eyes centered on the screen and to not follow individual stripes (so-called 'stare' nystagmus).

2.4. Psychophysical velocity discrimination

Observers were asked to judge the relative velocity of high contrast sine wave gratings (1 c/deg) presented on the Princeton Max-15 monitor. The velocities tested centered around a reference velocity of 3°/s in Experiment 1 and 9.4°/s in Experiment 2. Field size was $14.3 \times 11.1°$ when viewed at 1 m. Observers were instructed to fixate an 0.5° fixation mark placed at the center of the screen. An adaptive version of the method of constant stimuli was used; on each trial the observer was first shown a sinusoidal grating moving at a standard velocity followed by a second grating moving at the test velocity. The observer was then asked to judge which target moved faster, the standard which always moved in the same direction, or the test which could move in either direction. The direction of the test

grating was randomized so that direction-related biases could be evaluated separately for each direction. Probit curves were used to determine the point of subjective equality (50% point) between test and reference velocities. Additional details for the psychophysics can be found in Schor et al. [23].

2.5. MOKN and perceptual bias estimates

MOKN bias was estimated by dividing the nasalward slow-phase velocity by the sum of the nasalward and temporalward slow-phase velocities ($N/N+T$). A value of 0.5 indicates no bias while values greater than 0.5 indicates higher slow-phase velocity in response to the nasalward direction of stimulus motion (temporal to nasal motion in the visual field).

Perceived velocity biases were calculated by dividing the temporalward matching speed by the sum of the temporalward and nasalward speeds ($T/(T+N)$). If the patient requires a lower test velocity than the standard to accept the match, the perceived speed of the test is higher than that of the standard—that is a lower test velocity is perceptually equivalent to a higher reference velocity. If the nasalward perceived speed as faster than the temporalward speed, this ratio will be greater than 0.5. If perceived speed controls MOKN slow-phase gain, we would expect a positive correlation between the two measures.

2.6. MVEP Recording

MVEPs were measured monocularly in response to a 1 c/deg vertical sinusoidal gratings displayed on a video monitor ($18.6 \times 25°$, viewed at 70 cm) with a space average luminance of 80 c/deg/m^2 and a Michelson contrast of 80%. The gratings were square wave alternated between two positions separated by 90° of spatial phase. The temporal rate of stimulation (positional jitter) was 10 Hz (20 changes of direction per second). Responses were measured from five derivations (O_1, O_z, O_2, vs. F_z and $O_z - O_1$ and $O_z - O_2$) and the EEG was digitized at 450 Hz over a 1–100 Hz pass band (-6dB). The data reported here are average values for the three occipital leads referenced to the frontal lead which produced larger response amplitudes than the two bipolar derivations.

The EEG was subjected to spectral analysis to extract the amplitude and phase of the evoked response at the first five harmonics of the 10 Hz stimulus frequency. A Recursive Least Squares adaptive filter [24] was used. The filter calculated the amplitude and phase in 0.5 s intervals and the ten values in each 5 s trial were coherently averaged to obtain a mean amplitude and phase for that trial. These mean values were then coherently averaged over all trials obtained in a given condition. The first (F_1) and second (F_2) harmonics were the largest and most consistently recordable response components and the remaining analysis was confined to these components.

2.7. MVEP bias measure

The degree of asymmetry of the MVEP was quantified by comparing the relative proportion of F_1 (asymmetric component) and F_2 (symmetric component) amplitudes. An asymmetry index was calculated by dividing the F_1 amplitude by the sum of F_1 and F_2 amplitudes. The asymmetry index ranges between zero and one, with higher values corresponding to greater degrees of asymmetry. A direction for the VEP bias cannot be assigned, due to the ambiguity of response polarity inherent in the AC-coupled steady-state VEP.

3. Results

3.1. Comparison of direction biases across diagnostic groups

Using separate within-observer analyses of variance (ANOVA) we analyzed the magnitude of MOKN, perceived velocity and MVEP biases in the normal, early onset and late onset diagnostic groups for both experiments. Fig. 1a plots the cell means for the MOKN bias measures obtained in Experiment 1. An ANOVA performed on the bias measure indicated that there was a significant main effect of diagnosis ($F_{2,266} = 23.7$; $P < 0.0001$), no main effect of eye ($F_{2,266} = 0.005$; $P = 0.94$) and no interaction with preferred or non-preferred eye and diagnosis ($F_{2,266} = 1.1$; $P = 0.33$). Both early onset and late onset groups had significantly abnormal nasalward MOKN biases.

Cell means for the MOKN bias measures obtained in Experiment 2 are plotted in Fig. 1b. There was a significant difference between the groups ($F_{2,42} = 49.7$, $P = < 0.0001$), a difference between eyes (non-preferred eyes had a larger bias; ($F_{2,42} = 9.4$ $P = 0.004$) but no interaction between diagnosis and eye tested (preferred or non-preferred: $F_{2,42} = 0.457$; $P = 0.64$). There was a significant difference between normals and early onset strabismus ($P = < 0.0001$; Fisher's PLSD) and late onset and early onset strabismus ($P = < 0.0001$) but no significant difference between normals and late onset strabismus ($P = 0.13$).

3.2. Perceived velocity

Cell means for the perceived velocity bias measure ($T/T+N$) are plotted in Fig. 1c, for Experiment 1. As in the case of the MOKN data, both early onset and late onset groups had abnormal perceived velocity biases. The main effect of diagnosis was significant at the

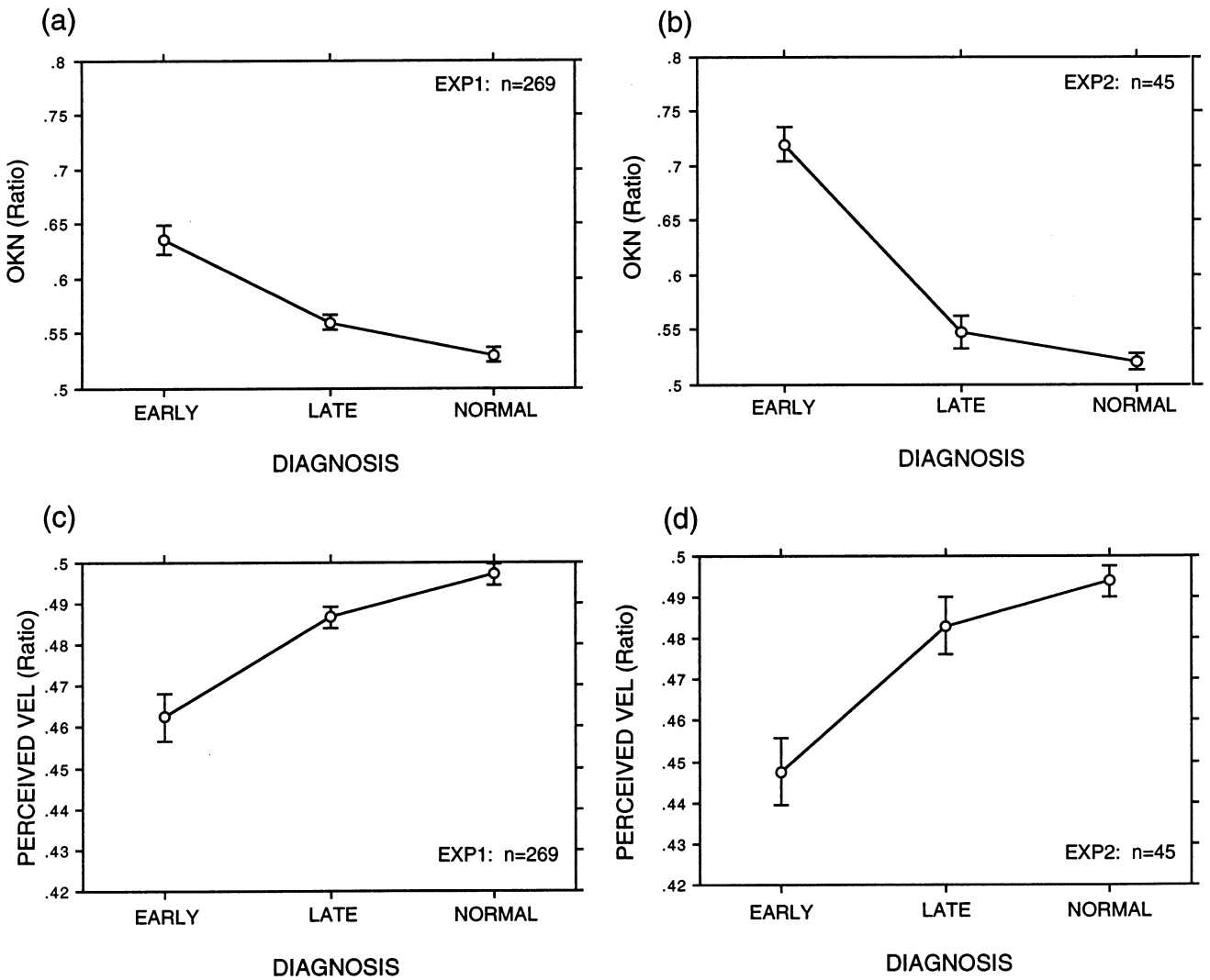

Fig. 1. (a) The ratio of nasalward eye-speed to the sum of nasalward and temporalward eye-speed is plotted for early (n = 50), late (n = 150) and normal (n = 69) observers from Experiment 1. Early onset patients show the larger nasalward biases (ratios greater than 0.5) than do late onset patients who in turn have larger biases than do normals. (b) The ratio of nasalward eye-speed to the sum of nasalward and temporalward eye-speed is plotted for early (n = 18), late (n = 11) and normal observers (n = 16) from Experiment 2. Early onset patients show larger nasalward biases (ratios greater than 0.5) than do late onset patients who did not differ significantly from normals. (c) The ratio of temporalward matching speed to the sum of nasalward and temporalward matching speeds is plotted for early (n = 50), late (n = 150) and normal observers (n = 69) of Experiment 1. Early onset patients show larger biases (ratios less than 0.5) than do late onset patients who in turn have larger biases than do normals. The bias is such that temporalward motion is rated as faster than the standard. (d) The ratio of temporalward matching speed to the sum of nasalward and temporalward matching speeds is plotted for early (n = 18), late (n = 11) and normal observers (n = 16) observers of Experiment 2. Early onset patients show larger biases (ratios less than 0.5) than do late onset patients who do not differ from normals. The bias is such that temporalward motion is rated as faster than the standard, as in (c).

$P < 0.0001$ level ($F_{2,266}$) = 19.5. There were no significant effects involving eye. Fig. 1D, plots the derived bias measures for perceived velocity in Experiment 2. The within observers ANOVA indicated a significant effect of diagnostic group ($F_{2,42} = 17.7$, $P < 0.0001$), a non-significant effect of eye dominance ($F_{2,42} = 1.8$, $P = 0.18$) and no interaction between eye dominance and diagnosis ($F_{2,42} = 2.34$; $P = 0.10$). The normal observers had significantly lower velocity biases than the early onset group ($P < 0.0001$; Fisher's PLSD) as did the late onset group ($P = 0.001$). There was a trend for the normal observers to have lower velocity biases than the late onset group ($P = 0.075$).

3.3. Correlation of MOKN and perceived velocity

There were significant negative correlations between MOKN and perceptual biases within the early onset and late onset groups in Experiment 1, but not in the normal group. Combining across all observers in Experiment 1, the correlations between MOKN and perceived velocity $r = -0.40$ and $r = -0.29$, in the

non-preferred and preferred eyes, respectively ($P < 0.0001$). The slopes of the regression lines were all less than 1—MOKN biases were relatively greater than perceived velocity biases. However, these biases were opposite those seen in the MOKN data; temporalward motion was seen as faster than nasalward motion. For Experiment 2, simple regressions between the MOKN and velocity bias measures for each eye (all observers included) showed a strong correlation between these measures ($r = -0.413$, $P = 0.0048$ for the preferred eye; and $r = -0.614$, $P = < 0.0001$ for the non-preferred eye. As was seen in Experiment 1, the correlations between MOKN and perceived velocity biases were negative and the slopes of the regression line were less than unity. Correlations were not significant within groups, as they were in the larger samples of Experiment 1.

3.4. MVEP biases across diagnostic groups

Fig. 2 plots the group mean asymmetry indices for the VEP for preferred (filled symbols) and non-preferred eyes (open symbols). Note that a value of 0.0 corresponds to equal amplitudes for nasalward and temporalward motion. As with MOKN and velocity perception biases, we found statistically significant differences between the different patient groups on this measure ($F_{2,42} = 19.35$; $P = < 0.0001$), with no effect of eye dominance ($F_{2,42} = 2.641$, $P = 0.1079$) and no interaction between diagnosis and eye dominance ($F_{2,42} = 1.21$; $P = 0.30$). There were lower asymmetry indices in the normal group compared to both early ($P < 0.0001$) and late onset ($P = 0.016$) groups. The late onset group also had a lower level of bias than did the early onset group ($P = 0.0029$)

The MVEP does not contain absolute direction information and thus direct correlation with MOKN and velocity perception biases was not possible. Since the MOKN and perceived velocity biases were predominantly unidirectional, it is their magnitude that is of interest in a correlation analysis. We therefore used the absolute value of the difference between the calculated bias and 0.5. This allowed direct correlations to be performed between all variables based on the magnitude of bias, ignoring direction.

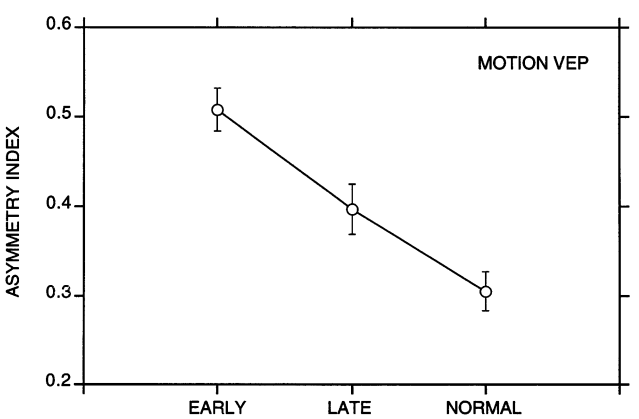

Fig. 2. MVEP bias for normal, late onset and early onset observers for preferred (filled symbols) and non-preferred eyes (open symbols). Early onset patients have significantly higher levels of MVEP bias than do either normal or late onset observers.

MOKN bias and MVEP asymmetry were significantly correlated in both the preferred eye ($r = 0.554$, $P = < 0.0001$) and in the non-preferred eye ($r = 0.382$, $P = 0.0096$). Perceived velocity bias and MVEP asymmetry were significantly correlated in the non-preferred eye ($r = 0.574$, $P = < 0.0001$) but not in the non-preferred eye ($r = 0.134$, $P = 0.3874$). Note that these correlations are necessarily positive since the direction information was removed from the MOKN and velocity measure by the use of absolute values.

3.5. Concordance of biases in the two eyes

In each experiment, the normal group's 95% confidence limits for the bias measures were used to determine the percentages of patients in the early onset and late onset groups who were abnormal. In Experiment 1, MOKN bias was bilateral in 30% of the early onset cases (15 of 50) and in 9% (14 of 150) late onset cases. A bias was present in one or both eyes in 60% of the early onset patients and in 33% of the late onset group. For the perceived velocity measure, 12% of the early onset group were biased bilaterally, compared to 2% in the late onset group.

In Experiment 2, seventeen observers (94.4%) had a significantly abnormal MOKN bias in the preferred eye and 16 observers (88.9%) were abnormal in the non-preferred eye. Sixteen observers in this group (88.9%) had significantly abnormal MOKN in both eyes while 17 observers had significant biases in at least one eye. In the late onset group three of the 11 observers had significant biases (27.3%) in the preferred eye and two observers (18.2%) had a significant bias in the non-preferred eye. No subject had a significant bias in both eyes, although five observers had significant biases in one eye.

In the early onset group seven of 18 observers (38.9%) in the preferred eye and eleven (61.1%) in the non-preferred eye had significant perceived velocity biases when compared to the normal group. Although only five observers (27.8%) had a significant bias in both eyes, thirteen (72.2%) had a significant bias in one or both eyes. By contrast, significant biases did not occur in bilaterally in the late onset group. Rather, they were confined to the preferred eye, with five of 11 observers (45.5%) having biases (not all these biases were in the same direction, however).

The MVEP was significantly abnormal in four of 18 (22.9%) of preferred eyes and seven of 18 (38.9%) of

non-preferred eyes in the early onset group. Only two observers (11.1%) had significant differences from the norm in both eyes. Ten early onset observers (55.6%) were abnormal in at least one eye. In the late onset group there were no significant abnormalities in the preferred eye and significant anomalies in three of 11 (27.5%) non-preferred eyes in this group. No late onset observer had significant bilateral abnormalities.

4. Discussion

4.1. MOKN asymmetries

Patients with a history of early onset strabismus (infantile esotropia) frequently showed significant directional biases in their MOKN. Overall, 70% of our early onset observers (47 of 68) had a significantly abnormal MOKN in one eye or both eyes. Moreover, the MOKN bias was bilateral in 46% of patients overall (and in 17 of 18 patients in Experiment 2). By contrast, only 34% of the late onset patients (55 of 161) had a significant bias in one or both eyes and the abnormality was bilateral in only 9%.

Demer and von Noorden [3] reported the prevalence of significant MOKN asymmetry to be 52.5% in patients who developed strabismus in the first year of life and 8.7% in observers with onset of strabismus between 12 and 24 months of age. They [3] considered a patient to have an MOKN asymmetry if it was definitely present upon direct observation of the patient's eyes, but they did not report whether the asymmetry was present in one or both eyes or if there was a difference between preferred and non-preferred eyes. Bourron-Madiguier et al. [25] used the EOG to record MOKN. They reported a higher prevalence of asymmetric MOKN in all groups than did [3]—92% in observers with onset of strabismus before 6 months, 64% with onset between 6 and 12 months, 33% between 12 and 24 months and 23% with onset of strabismus after 24 months. Furthermore, they observed a greater prevalence of bilateral MOKN asymmetries in patients with early onset esotropia. Among the early onset esotropes (0–1 year) 76% had bilateral nasalward MOKN asymmetries and 12% had unilateral asymmetries. Among patients with onset of esotropia after 1 year of age, only 9% were asymmetric bilaterally and 14% were asymmetric unilaterally. It would thus seem that the presence of bilateral MOKN asymmetry is a strong indicator of onset of strabismus before 6–12 months of age.

4.2. Perceived velocity biases

The perceptual bias was not as great in magnitude as the MOKN bias, as indicated by the shallow slopes of the regression lines. Combining across Experiments 1 and 2, 57% of early onset patients and 37% of late onset patients were abnormal in one or both eyes. Perceived velocity was less often bilateral than was MOKN (16% of early onset patients vs. 46% and 2% vs. 9% of late onset patients). The specific percentages of patients judged to be abnormal depends upon the criterion used—we used the 5% tail of the normal observer distribution. The criterion doesn't affect the overall conclusion: perceived velocity biases may be detected both in early and in late onset strabismus but these biases are more likely to be bilateral and more severe when found in association with early onset strabismus.

Abnormalities of perceived velocity were first reported by Tychsen and Lisberger [13] in two observers with early onset strabismus. They noted that nasally directed motion was perceived as faster than temporally directed motion of the same stimulus speed. Roberts and Westall [5] were unable to confirm this finding, although different stimuli and subject populations and the small magnitude of the perceived velocity bias, especially compared to MOKN may help to explain the conflicting reports. Moreover, stimulus parameters may influence the magnitude of the perceived velocity bias. It is known, for example that both the MVEP asymmetry [15] and the MOKN asymmetry [26,27] vary with the spatio-temporal parameters of the stimulus. It is probable that the same holds for the perceived velocity bias.

More recently, Hague et al. [20] and Shallo-Hoffmann et al. [21] have reported direction biases in thresholds for discriminating stationary from moving gratings. The targets were eccentrically viewed, near threshold grating patches. In a small group of patients, Hague et al. [20] reported lower thresholds for temporally directed motion in early onset patients, but not in late onset patients. The present results agree in the sense that our higher perceived velocity for temporalwards motion is consistent with a lower threshold in this direction, but they differ in that perceived velocity biases were present in both early and late onset groups. Shallo-Hoffmann et al. [21] found in a larger sample of infantile esotropes that the direction of best threshold depended on whether the habitually fixating or non-fixating eye was tested. Thresholds were lower for temporalward motion in the non-fixating eye but were lower for nasalward motion in the fixating eye. We did not see an effect of preferred vs. non-preferred eye in our perceived velocity measures. The perceived velocity task and the motion threshold task may tap different mechanisms and it is unknown whether foveal viewing produces different effects than eccentric viewing.

The direction discrepancy between our perceived velocity findings and those of Tychsen and Lisberger [13] may be due to differences in stimulus-evoked eye movements occurring during the perceptual rating task. If

OKN is elicited by the gratings we used, it is likely to be of higher velocity for nasalward vs. temporalward targets. Heidenreich and Turano [28] have found that perceived velocity is reduced during slow eye movements in the direction of the eye movement. Perceived velocity may be lowered due to a reduction in retinal slip velocity in the direction of a following eye movement. It is possible that grating targets such as those used in the present study may have elicited eye movements that were not being elicited by Tychsen and Lisberger's small line targets.

If stimulus evoked eye movements account for the inverse relationship between MOKN and perceptual bias directions, this must be due to a failure of fixation to suppress the OKN response during the velocity rating task—an additional type of abnormality [29]. Interestingly, both early and late onset esotropes have comparable and, if anything, slightly lower than normal OKN gain in the nasalward direction (data not shown), yet early onset patients differ from late onset patients in their underestimation of nasalward speed. In this case, it seems less likely that the abnormality in nasalward perceived velocity would be directly related to stimulus induced OKN. On the other hand, in the temporalward direction there are clear differences in MOKN gain that might account for the increasing magnitude of the perceptual bias via the effect reported by Heidenreich and Turano [28]. Careful measurement of eye movements during perceptual rating tasks (c.f. [21]) and a comparison of small and large field targets appear to be a necessary next step in resolving the question of the relationship between perceptual and oculomotor biases.

4.3. MVEP asymmetries

Motion VEP asymmetries in early onset strabismus have been described previously [14,16–18]. In the present study, the MVEP was significantly more biased in the early onset group compared to either the normal or late onset groups. The late onset group also had a higher level of bias than did the normals. The same overall pattern of results was found by Hamer et al. [18] for similarly selected patient groups.

Of the early onset observers, only 11.1% had significant MVEP abnormalities in both eyes, while 55.6% were abnormal in one or both eyes. None of the late onset observers were abnormal in both eyes and three of 11 (27.5%) were abnormal in one eye the non-preferred eye. The low percentage of abnormality on the VEP measure is in part due to the wide range and high standard deviation of the normal observers (mean 0.293, s.d. = 0.139 for the preferred eye and mean 0.316, s.d. = 0.108 in the non-preferred eye).

4.4. Correlations between variables.

All of the pairwise correlations between MOKN, perceived velocity and MVEP measures were correlated except for the MVEP and perceived velocity bias measures from the preferred eye. Kommerell et al. [17] did not find a correlation between the MVEP asymmetry and the MOKN asymmetry in eight patients with infantile esotropia. The lack of correlation in the Kommerell et al. [17] study could have been due to the use of a qualitative rating scale of observed MOKN generated by a tape, rather than an objective, slow-phase gain measure derived from an eye-tracker. Alternatively, Kommerell et al. [17] restricted their analysis to infantile esotropia patients, while in the present study, the correlation was made across a much larger population with a wider range of MOKN and MVEP asymmetries.

What can be said about the causal relationships between the MOKN, perceived velocity and MVEP measures? The three measures could become correlated through a disruption of the development of a common site, such as visual cortex or through disruption of multiple sites at a common time during separate critical periods. Early deprivation of binocular input in the monkey (through alternate-day monocular exposure) results in a persistent MOKN asymmetry and asymmetric local field potentials in striate cortex [30]. Asymmetries at the level of striate cortex could also influence perceived velocity. Alternatively, there could be more than one mechanism operating across the three study measures. Each mechanism would have to have its own developmental asymmetry that was susceptible to disruption by strabismus. If these mechanisms had contemporaneous critical periods, asymmetries of the different types would be correlated through an insult at a common time, rather than at a common place.

A simple model of perceptual bias leading to oculomotor bias appears to be untenable, given the negative correlation between MOKN gain and perceived velocity, combined with differences in the magnitude of these biases. The MVEP results cannot be interpreted in terms of absolute direction, so it is unclear which direction of motion produces the largest VEP response.

Other oculomotor biases, such as latent nystagmus (LN) could play a role in correlating MOKN, perceptual judgements and MVEP responses. Tychsen and Lisberger [13] discounted LN as a factor in their experiments since perceived velocity was higher for nasalward motion, in spite of lowered retinal slip velocity in this direction caused by LN. Moreover, Shalo-Hoffmann et al. [21] have reported a series of patients with significant perceptual biases who did not have LN. In the population studied in Experiment 1, LN (observed with a visuoscope) occurred in relatively few patients 18%–20% of patients in the early and late onset groups respectively [23]. We repeated the analyses shown in

Fig. 1a and c for the MOKN and perceived velocity bias measures, excluding the patients who had LN. These ratios differed by 1.5%, at most. Furthermore, if LN were a factor in the present experiments, we would expect higher levels of bias at 3°/s rather than at 10°/s since LN velocity would proportionately larger relative to the lower velocity. However, average biases were less at 3°/s than at 10°/s (compare Fig. 1b and d). In the case of the VEP, Norcia et al. [14] were not able to induce asymmetries in normal observers by having them execute eye movements designed to simulate LN (see also discussion in [31]) and Zhai et al. [32] found that VEP asymmetry was not increased when the eye was viewing in abduction versus adduction, in spite of differences in LN.

The MOKN, MVEP and velocity perception biases may each show variation over the spatio-temporal surface and as a result choice of the optimal stimulus parameters becomes significant. A comparison of the spatio-temporal tuning of the three measures may be a particularly sensitive way to determine if they share the same substrate.

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