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Latent, Manifest Latent, and Congenital Nystagmus

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• **Manifest latent nystagmus (MLN) was identified in 31 patients by accurate eye movement records. All the patients had horizontal tropias, and the nystagmus fast phases were always in the direction of the viewing eye. The slow phases of MLN are decreasing-velocity exponentials while those of the jerk form of congenital nystagmus (CN) are increasing-velocity exponentials. Several subjects who were believed to have latent nystagmus (LN) on clinical examination had small amplitude nystagmus evident by eye movement recording with both eyes open; these were actually cases of MLN. Many patients with MLN are misdiagnosed as having CN. An explanation for MLN and LN is provided based on confusion of egocentric directions between monocular and binocular viewing conditions.**

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Quantitative eye movement recordings have forced a reconceptualization of nystagmus because the literature, based on clinical observation alone, was inadequate and often misleading.[1,2] This is particularly relevant for voluntary,[3] congenital (CN),[4,5] and, the subject of this report, latent nystagmus (LN). The latter, by general usage, is a congenital binocular jerk nystagmus, absent with both eyes fixating, which develops on covering, blurring, or reducing the image brightness in one eye; the fast phase always beats toward the viewing eye.[6-9]

Spanning an interval of several decades, Kestenbaum made major contributions to the understanding of LN, which he described succinctly in his venerated text.[8] He noted LN beating to the left in a boy with right-eye blindness and described cases with alternating strabismus in which the nystagmus fast phases always beat in the direction of the fixating eye. He concluded that the image suppression in the deviated eye was analogous to an occlusion that caused the nystagmus to manifest; the phenomenon was aptly designated "manifest latent nystagmus" (MLN). Kestenbaum also described "superimposed LN" where the neutral zone in CN is shifted by occluding one eye (the shift and consequent changes in the nystagmus were graphically depicted in a previous report[10]); the basic nystagmus in this situation, however, was congenital rather than latent.

Our interest in LN was sparked by the first patient with this diagnosis referred to us for eye movement recording. The amplitude sensitivity of the recording apparatus was less than 0.5°, and we noted jerk nystagmus, not evident clinically, even with both eyes open. The patient had a squint, and the nystagmus fast phases were in the direction of the viewing eye; when the deviated eye was covered, the nystagmus amplitude increased and became apparent clinically. An additional finding was that the nystagmus slow phases were in the shape of a decelerating-velocity exponential. The slow phase configuration in LN had not been described previously, but in the single instance where this could be discerned from a tracing published in the literature, the slow phases were also of decelerating velocity.[11,12] We had not encountered this type of slow phase in other types of primary position nystagmus. The major waveform of CN is an accelerating-velocity exponential slow phase,[4,5] and vestibular nystagmus has a linear (constant-velocity) slow phase. Subsequently, we found decelerating-velocity exponential slow phases in patients referred to us with a diagnosis of CN. They all had a horizontal tropia and their fast phases beat toward the viewing eye; these, indeed, were cases of MLN and not CN. We were thus able to redefine LN as follows: nystagmus not present under binocular viewing conditions that develops in both eyes during monocular viewing; the nystagmus is jerk in type with the fast phase in the direction of the viewing eye and the initiating slow phase a decelerating-velocity exponential. Manifest latent nystagmus is defined as follows: nystagmus present with both eyes open but when only one is being used for vision (ie, the other is suppressed); the nystagmus is jerk-type with the fast phase in the direction of the viewing eye; the initiating slow phase is a decreasing-velocity exponential. In this report we will present, analyze, and discuss the findings of the patients with LN and MLN who have had eye movement recordings in our laboratory.

METHODS

Eye movements were studied using the infrared reflection method of oculography. Position and velocity were measured simultaneously from both eyes using a system with a bandwidth of dc-100 Hz. The eye velocity was measured by electronically differentiating the position signal. The patients were seated in a modified dental chair at the center of a 1.14-m radius arc containing red, light-emitting diodes accurately spaced around it. Each eye was calibrated individually while the other was open but behind cover; this allowed accurate calibration in the presence of a tropia. Binocular recordings were made under both monocular and binocular viewing conditions. When a primary position decelerating-velocity exponential waveform was present, particular attention was directed toward obtaining recordings under both monocular and binocular conditions. The eyes were recorded during fixation at 0° and at various horizontal gaze angles within ±30° of primary position and also during attempted convergence.

Relevant information was obtained from the patients' medical records and our own clinical examinations. This included medical history, visual acuity, strabismus, funduscopy findings, head turn, presence of rotary nystagmus (this cannot be detected by oculography), and ocular dominance.

RESULTS

We found 31 examples of MLN during a 41-month interval covered by this study. The ages of the patients ranged from 6 to 51 years. Each of the 31 patients had a horizontal tropia: 24 patients (77.4%) had an esotropia and seven patients (22.6%) had an exotropia; 17 patients (54.8%) also had a hypertropia. During both monocular and binocular viewing conditions, in each patient there was a horizontal jerk nystagmus with a fast phase beating toward the viewing eye and the slow phase consisting of a decreasing-velocity exponential (Fig 1). Fifteen of the patients (48.4%) exhibited dynamic overshoots in the fast phases of their nystagmus (Fig 2). Also evident in this figure is the amplitude

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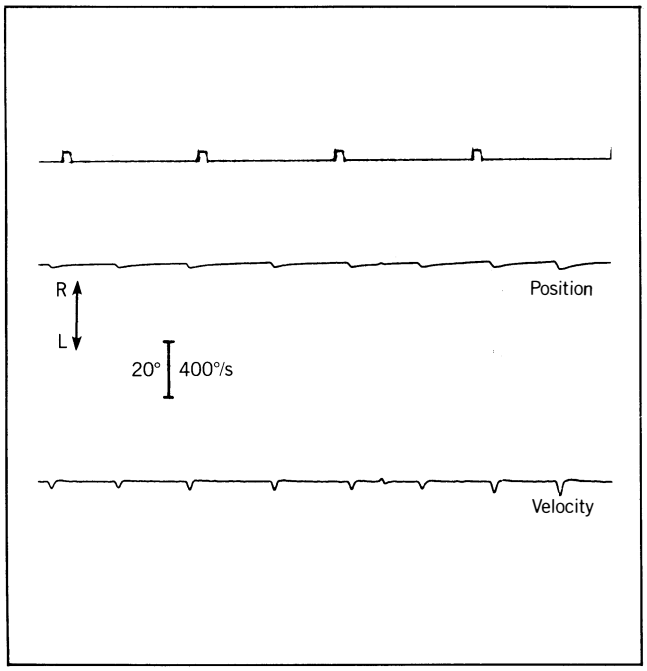


Fig 1.—Eye movement position and velocity in patient with manifest latent nystagmus (MLN) shows characteristic decreasing-velocity exponential slow phase of oscillation; this portion was recorded during occlusion of right eye. In this and subsequent figures, timing marks at top indicate 1-s intervals; R, right; L, left.

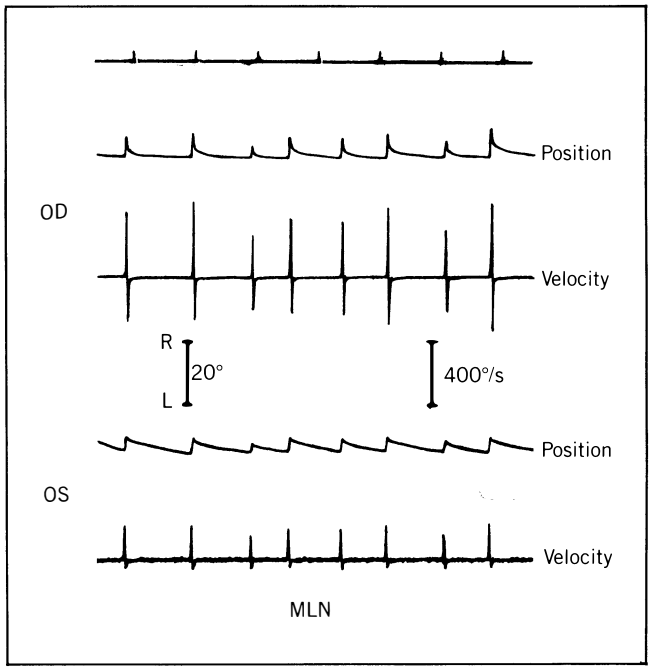


Fig 2.—Simultaneous binocular recording of eye position and velocity of patient with manifest latent nystagmus (MLN). In addition to characteristic decreasing-velocity slow phases, fast phases exhibited dynamic overshoots. Amplitude disconjugacy between two eyes is evident.

Fig 3.—Binocular recording of rightward-beating manifest latent nystagmus (MLN) with OD fixating intermixed with a pendular nystagmus resulting in a dual jerk-right (DJR) waveform. Pendular nystagmus was particularly evident in velocity tracing; MLN was of greater amplitude in fixating OD and ceased entirely at end of tracing, leaving only a pendular nystagmus OD and square wave jerks OS. During this latter transition, OD shifted into an esotropic position.

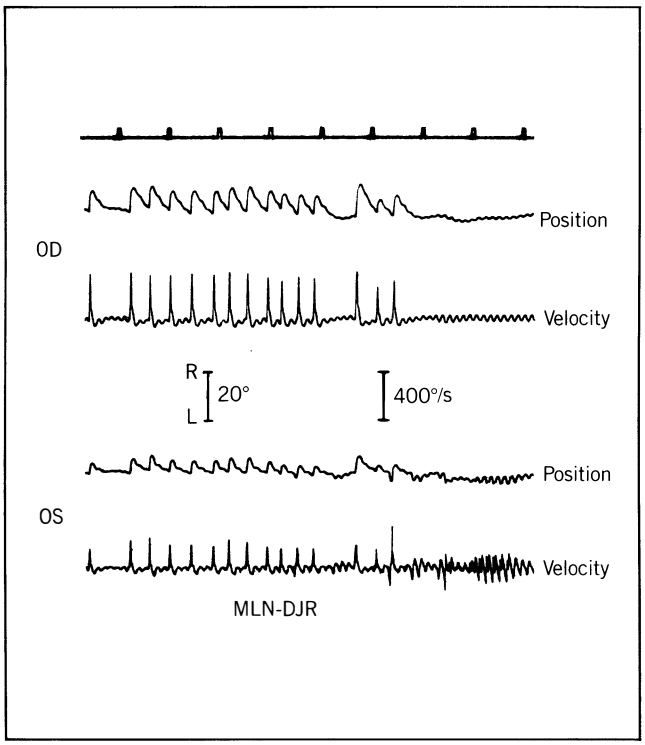
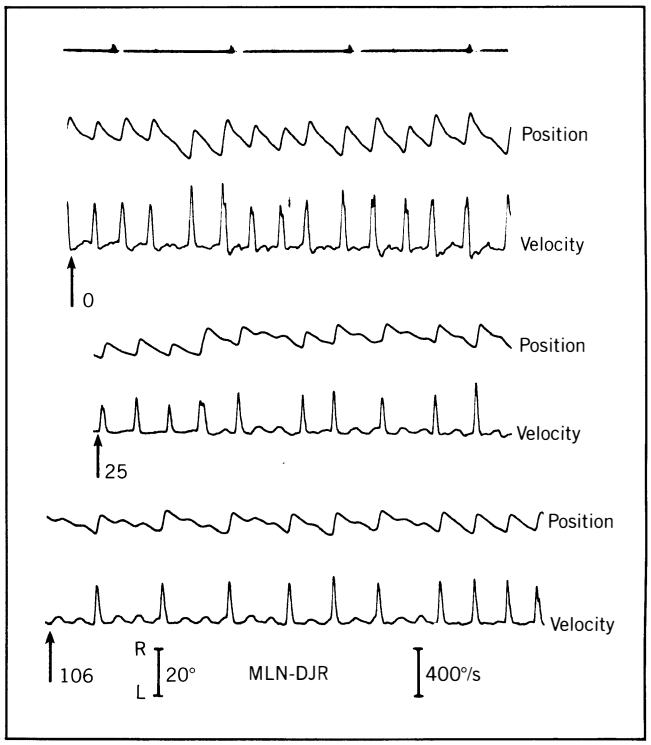


Fig 4.—Segments taken from different portions of a recording in patient with both manifest latent (MLN) and pendular nystagmus. Waveforms varied from intermixed (dual jerk-right [DJR]) to one or other predominating. Numbers at beginning of segments indicate time in seconds elapsed from time zero.



disconjugacy sometimes found in MLN.

As with all biological processes, there was often variability in the amount of curvature (deceleration) of the slow phases from beat to beat. The overwhelmingly predominant shape in the patients designated as having MLN was a decreasing-velocity exponential, although occasional runs of beats may have been less curved or virtually linear. Some of the figures in this article will exhibit large variations in slow phase decelerations. These figures were selected to illustrate aspects of MLN other than slow phase waveform, and the few beats illustrated should not detract from our assertion that the basic slope was a decelerating-velocity exponential. Also, the slow phases of an occluded (or cortically suppressed) eye can be extremely variable due to superimposed drifts in this open-loop (ie, no visual feedback) condition.

Seventeen (54.8%) of the 31 patients had CN in addition to the MLN. This was established in 14 (45.2%) patients by the presence of a clinically observable rotary nystagmus in primary position and in three (9.7%) patients by pendular nystagmus in addition to the MLN (Fig 3 and 4). These figures demonstrate the intrasubject variability when the waveforms of both MLN and pendular nystagmus coexist; this was *not* a case of periodic alternating nystagmus. The types may be admixed or one may predominate at various times. When both are present, the waveform is dual jerk[3] and mimics the dual jerk waveform of CN with the important difference that the LN form has a decreasing-velocity slow phase on which the pendular oscillation rides.

None of the 31 patients had overt neurological disease, but four (12.9%) had retrolental fibroplasia; all four had CN in addition to the MLN. The CN was pendular in two patients with hypertropia (one with an esotropia and the other an exotropia), and the CN was rotary in the other two who had esotropia but no hypertropia. There was no statistically significant correlation between the presence of hypertropia and CN, both occurring in 17 (54.8%) of the 31 patients with MLN.

Three patients were referred to us with a specific clinical diagnosis of LN. Primary position nystagmus was not noted during clinical examination, but in each the eye movement recording demonstrated MLN during binocular viewing with the fast phases beating toward the viewing eye (the viewing eye can easily be checked since its occlusion would cause reversal of the existing MLN direction, whereas occlusion of the other [suppressed] eye would not); as with the entire group, these three patients had horizontal tropias. We have not seen a case of "true" LN where there was no recordable nystagmus during binocular viewing. We will be using the term LN, however, to denote the presence of jerk nystagmus beating toward the viewing eye with a decreasing-velocity slow phase consequent to occlusion of one eye, present in our 31 patients in one or both directions. The latter is depicted in Table 1 with the breakdown of the directionality of MLN. Sixteen subjects had bidirectional MLN, indicating that either eye was used for fixation. Fifteen (48.4%) subjects had unidirectional MLN, meaning they would only fixate with a single eye under binocular viewing conditions. Seven of these 15 exhibited the appropriate LN when the preferred eye was covered, but eight did not. During binocular viewing, in two of the 16 subjects with bidirectional MLN, the nystagmus always beat to the side of the adducting eye when gaze was directed to either side of the midline (ie, jerk right in left gaze and jerk left in right gaze).

In one subject with bidirectional MLN, the nystagmus was uniocular in each direction. Only the fixating eye oscillated, whereas the nonfixating suppressed eye (or the eye behind cover) was motionless. A second recording session with this same patient disclosed little or no MLN,

Table 1.—Directionality of Latent and Manifest Latent Nystagmus in 31 Subjects

	Manifest Latent Nystagmus	
Latent Nystagmus	**Unidirectional (JR/JL)**	**Bidirectional (JR/JL/Add)***
Unidirectional	8 (4/4)†	. . .
Bidirectional	7 (5/2)	16 (5‡/9/2)

*Preferred direction. JR indicates jerk-right; JL, jerk-left; Add, adduction.
†LN direction = MLN direction.
‡One subject's nystagmus was uniocular in each direction (ie, only in eye being used); eye behind cover, or being suppressed, was motionless.

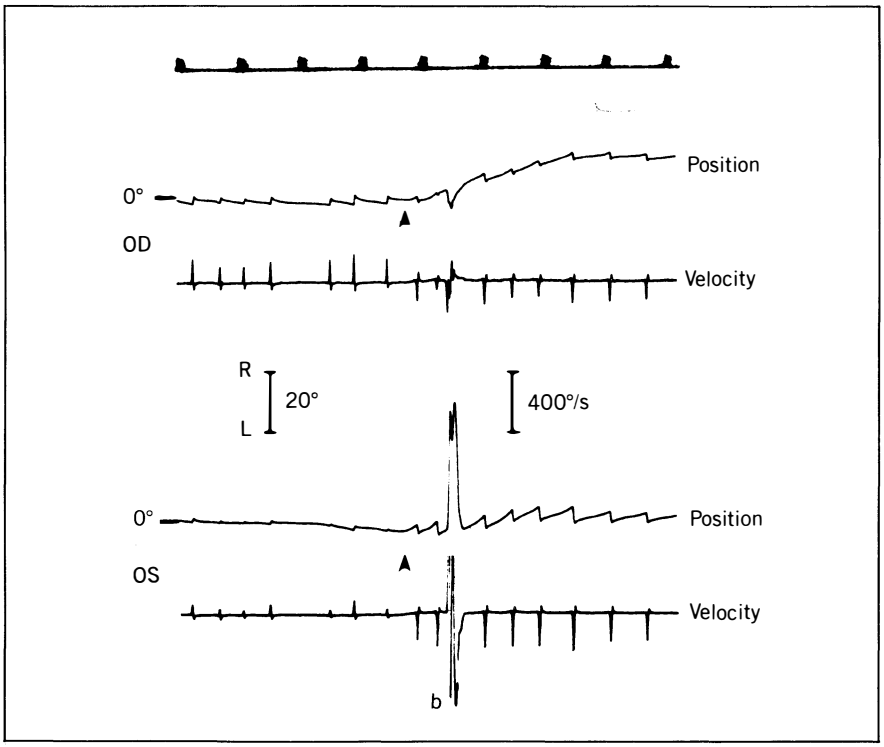


Fig 5.—Simultaneous binocular recording of eye position and velocity of patient showing transition from jerk-right manifest latent nystagmus to jerk-left latent nystagmus on covering OD (arrow). Blink is indicated at b. See text for details.

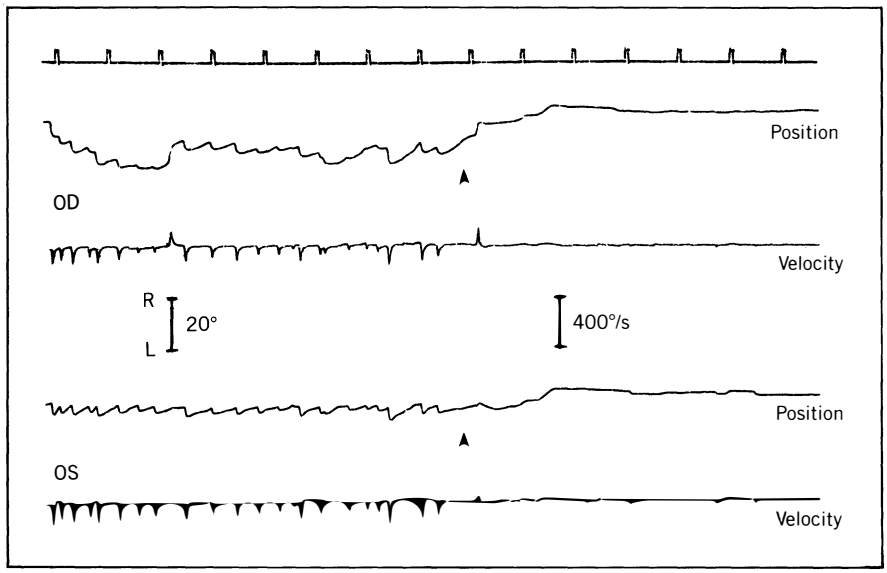


Fig 6.—Simultaneous binocular recording of eye position and velocity in patient showing effects of "looking" with OS and then (at arrow) "looking" OU. After arrow, both eyes remained open but only jerk-left manifest latent nystagmus was observed.

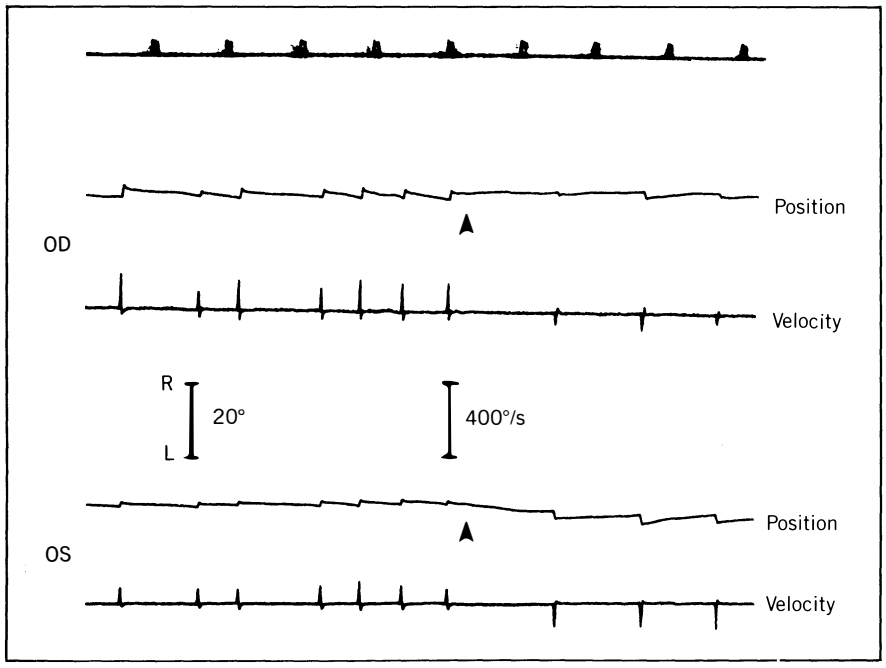


Fig 7.—Simultaneous binocular recording of eye position and velocity shows curious effect of darkness in patient who had only jerk-right manifest latent nystagmus in light. Darkness (at arrow) caused spontaneous reversal of drift and thus reversal of direction of MLN.

even in the fixating eye. The patient reported that she has nystagmus ("eye shaking") only when she is under prolonged emotional stress.

The transition from MLN to LN in the opposite direction on covering the fixating eye is demonstrated in Fig 5 in a subject with an exotropia. During binocular viewing, the subject fixated with the right eye and the nystagmus beat in the rightward direction. The amplitude of the nystagmus was greater in the fixating right eye than in the exotropic left eye. At the instant of covering the right eye, the conjugate leftward drift (slow phase) reversed and the rightward drift of the jerk-left nystagmus commenced. The covered right eye moved into an exotropic position aided by enhanced rightward slow phases. During the transition after the occlusion, the phoria-induced drifting in both eyes transiently masked the nature of the slow phases.

The waveform of a patient with an esotropia who preferred to fixate with the left eye is depicted in Fig 6. The drift in the nonfixating right eye obscured the shape of the slow phases. At the arrow, the patient was instructed to "look with both eyes." The left eye became slightly esotropic and the right eye took up fixation, yet no MLN occurred. Another patient with only unidirectional MLN showed a curious reversal of conjugate drift, and thus of MLN, in darkness (Fig 7).

During uniocular viewing, the amplitude of the nystagmus in the viewing and covered eyes was equal in 23 subjects (74.2%), greater in the viewing eye in seven subjects (22.6%) and in the nonviewing eye in only one subject (3.2%).

The relationships between the magnitudes of LN and MLN between the left and right eyes and between jerk-right and jerk-left nystagmus are summarized in Tables 2 to 4. Though most patients had amplitude conjugacy between the two eyes (Table 2), in only 16 patients was the magnitude of jerk-right LN equal to that of jerk-left, and in only seven patients did this equality hold for MLN (Table 3). The comparison between the relative amplitudes in each eye and the direction of MLN is shown in Table 4. Conjugacy is predominant, but when there was a difference in the magnitudes of the nystagmus in each eye, the nystagmus was greater in the eye that was abducting during the fast phases.

The correlations among uniocular amblyopia, ocular dominance, and consistent head turn during binocular viewing appears in Table 5 for those patients with unidirectional MLN. Four of the five patients with uniocular amblyopia had nystagmus beating in the direction of the fixating eye and eight out of ten in the direction of the dominant eye. All five patients with a leftward head turn had jerk-right MLN, and three of the four with a rightward head turn had jerk-left MLN. There was no statistically significant correlation between head turn direction and eye dominance or amblyopia (Table 6). In eight of the 15 patients with a head turn, the nystagmus amplitude decreased (to zero in two) when the viewing eye was placed in adduction by the head turn; six decreased with the viewing eye in abduction; and one had increased nystagmus with the head turn that placed his viewing eye in abduction (Table 7).

COMMENT

None of our patients had LN in the strict sense (latent vera). The three patients who did not appear to have nystagmus clinically during binocular viewing did have small amplitude nystagmus readily visible on oculography. Since the termination of our study, we recorded one additional case in which LN was the clinical diagnosis but in which nystagmus was evident with both eyes open during the eye movement recording. The reports in the literature of LN showing eye movement recordings have utilized nonquantitative insensitive recording techniques. There is a distinct question as to whether true LN exists. In an informal poll of laboratories using sensitive recording equipment, we received only one acknowledgment that a single case of true LN was indeed recorded (K. J. Ciuffreda, OD, oral communication, May 1978). Thus, it would appear that true LN (latent vera) does exist but must be exceedingly rare. It would appear in binocular and uniocular oculography as depicted in idealized form in Fig 8. The closest phenomenon to true LN that we observed was in patients with uniocular MLN in whom we were able to show LN on occlusion of the eye that the patient did not spontaneously view with; this was present in seven cases (Table 1).

The 31 subjects described all had MLN. Twenty-two of those subjects were referred to us with a clinical diagnosis of CN but were identified, instead, as having MLN because of a decreasing-velocity exponential slow phase rather than the increasing-velocity exponential characteristic of CN. During the time interval of this study, we recorded approximately 136 patients with CN. Thus, the 22 MLN cases referred as CN suggest that 14% of the population of patients with a clinical diagnosis of CN actually have MLN. This might be suspected by the presence of a horizontal tropia, which was universal in our 31 patients and has been reported as occurring in only 16% of patients with CN.[13] Kornhuber, with Jung, reported a 95% incidence of horizontal tropia in patients with "LN."[11,14] The fact that they reported 74 patients with LN suggests strongly that most of the patients probably had MLN. Anderson[15] reported a horizontal tropia in 16 of 17 cases of "LN."

Seventeen of our 31 patients with MLN also had a coexisting CN. In three the CN was horizontal pendular, and in 14 it was rotary. Anderson[15] noted that approximately 15% of his patients had primary position rotary

Table 2.—Conjugacy of Latent (LN) and Manifest Latent (MLN) Nystagmus

|N|	LN	MLN	LN and MLN
|RE| = |LE|	25	23	22
|RE| > |LE|	3	5	3
|RE| < |LE|	2	2	1
Uniocular	1	1	1

Table 3.—Directional Magnitudes of Latent (LN) and Manifest Latent (MLN) Nystagmus

|N|	LN	MLN	LN and MLN
|JR|* = |JL|	16	7	6
|JR| > |JL|	5	6	4
|JR| < |JL|	2	3	1
NA	8	15	8

*JR indicates jerk-right; JL, jerk-left; NA, not applicable.

Table 4.—Conjugacy and Directionality of Manifest Latent Nystagmus (MLN)

	MLN		
|N|	JR*	JL	JR and JL
|RE| = |LE|	17	18	12
|RE| > |LE|	7	1	1
|RE| < |LE|	1	3	...
NA	6	9	...

*JR indicates jerk-right; JL, jerk-left; NA, not applicable.

Table 5.—Amblyopia and Eye Dominance in Manifest Latent Nystagmus (MLN)

	Total Patients	JR	JL
Amblyopia			
RE	...	...	...
LE	**5**	4	1
None	**10**	5	5
Dominance (VA*)			
RE	**10**	8	2
LE	...	...	...
None	**5**	4	1
Head turn			
Right	**4**	3	1
Left	**5**	5	0

*VA indicates visual acuity; JR, jerk-right; JL, jerk-left.

Table 6.—Amblyopia, Dominance, and Head Turn*

Head Turn	No. of Patients	Dominant Eye			Amblyopic Eye		
		R	0	L	R	0	L
R	6	3	3	...	...	4	2
L	7	6	...	1	...	4	3
R and L	2	...	2	...	...	2	...
Total	**15**	**9**	**5**	**1**	**0**	**10**	**5**

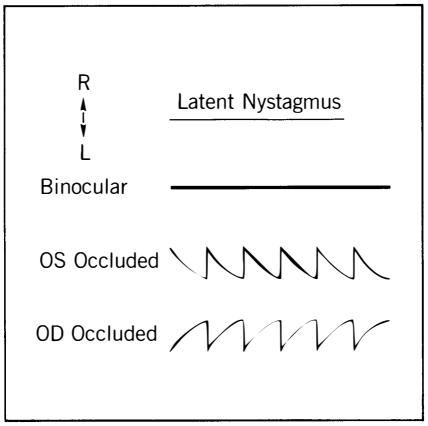
*R indicates right; L, left.

Table 7.—Head Turn and the Magnitude of Manifest Latent Nystagmus

With Preferred Head Turn*	No. of Patients	Head Turn		
		R	L	R and L
|N|↓/0, VE_{Add}	6/2	3/2	1	2
|N|↓, VE_{Abd}	6	1	5	...
|N|↑, VE_{Abd}	1	...	1	...
Total	**15**	**6**	**7**	**2**

*VE indicates viewing eye; Add, adduction; Abd, abduction; R, right; L, left.

Fig 8.—Latent nystagmus shows no nystagmus under binocular viewing conditions and nystagmus under monocular viewing conditions beating in direction of viewing eye and having characteristic decreasing-velocity slow phase.



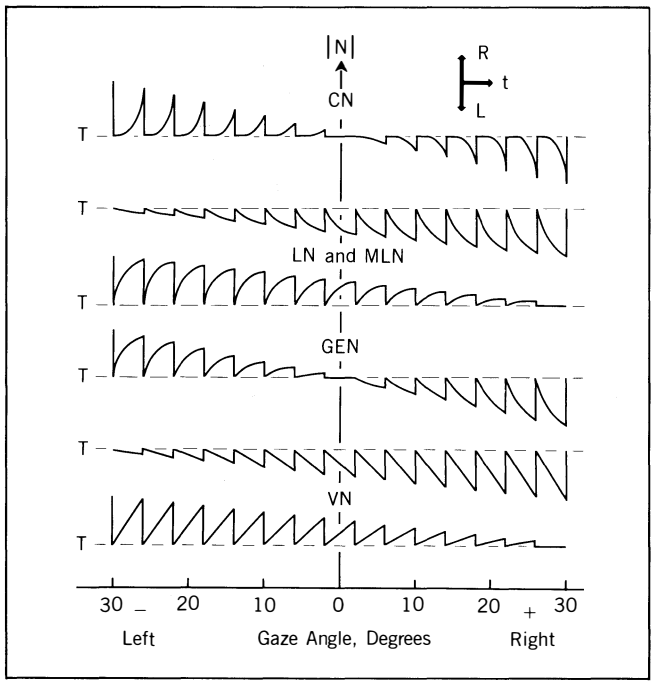


Fig 9.—Variation with gaze angle of magnitude |N| of congenital (CN), latent and manifest (LN and MLN), gaze-evoked (GEN), and vestibular (VN) nystagmus. Note also slow phase differences and fact that fast phases are foveating.

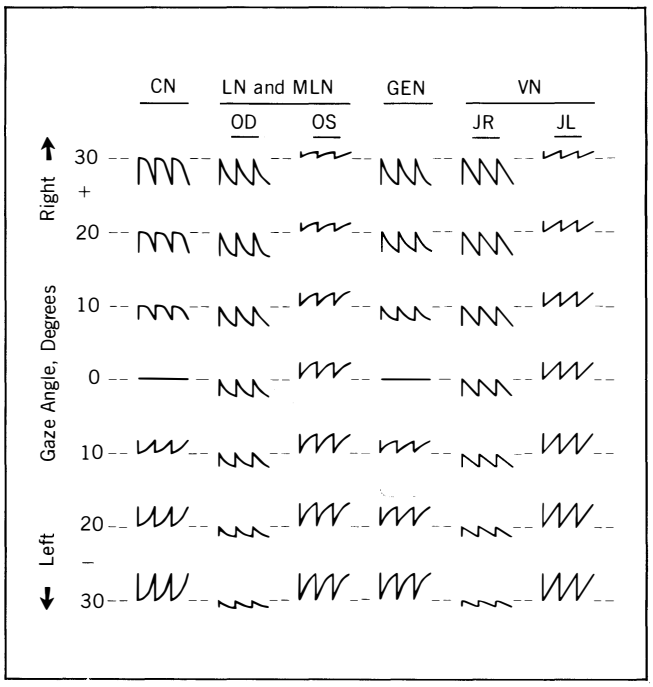


Fig 10.—Illustration of what eye movement recordings would look like for congenital (CN), latent and manifest (LN and MLN), gaze-evoked (GEN), and vestibular (VN) nystagmus. Three beats of each type of nystagmus at each gaze angle are shown. Subheadings under LN and MLN (OD and OS) indicate viewing eye, and under VN (JR [jerk-right] and JL [jerk-left]) indicate direction of nystagmus. Note slow phase differences, variation over gaze angle, and fact that fast phases are foveating.

Fig 11.—Simultaneous binocular recording of eye position and velocity of esotropic patient shows transition in latent nystagmus direction (from jerk-left to jerk-right) and in gaze direction on reversal of cover (arrows). Gaze direction change is accomplished by enhanced fast phases and diminished slow phases.

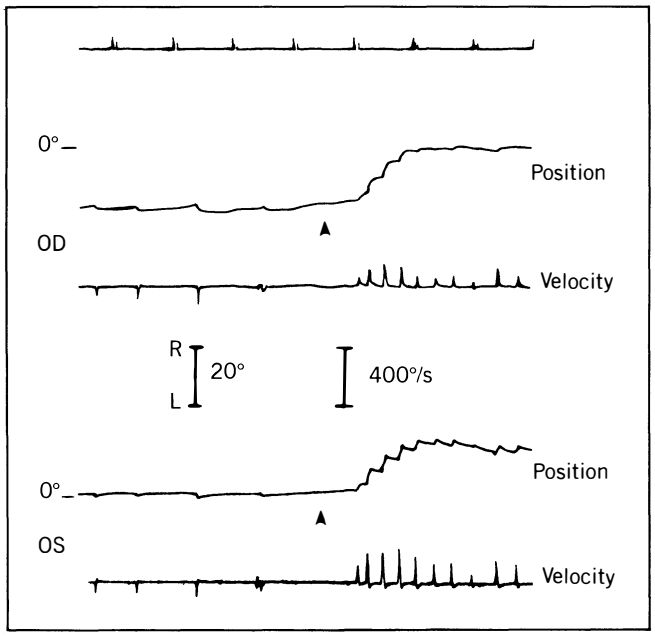
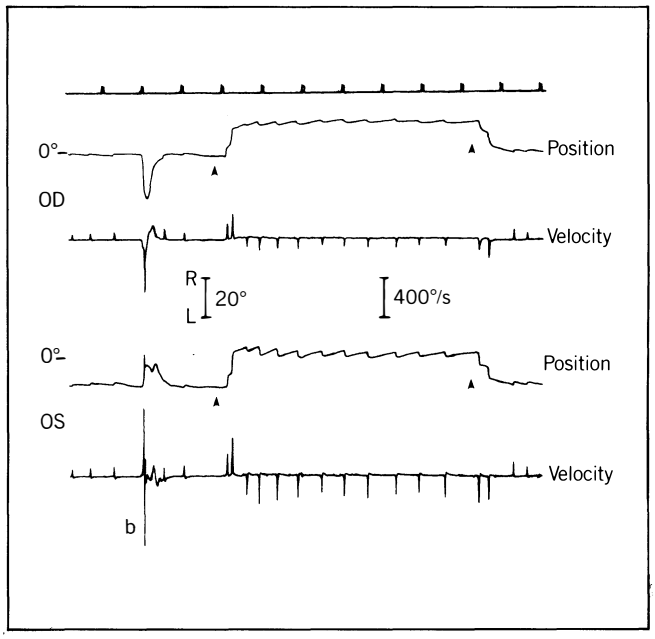


Fig 12.—Simultaneous binocular recording of eye position and velocity of exotropic patient shows transitions in latent nystagmus direction (from jerk-right to jerk-left and back to jerk-right) and in gaze direction on successive reversals of cover (arrows). Gaze direction changes are accomplished by saccades and enhanced slow phases. A blink is indicated at b.



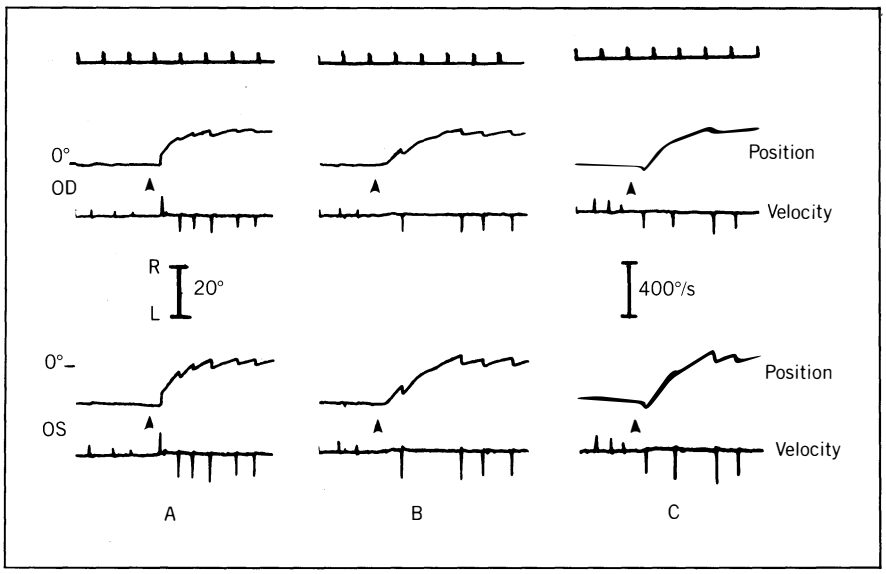


Fig 13.—Simultaneous binocular recordings of eye position and velocity of exotropic patient shows transitions in latent nystagmus direction (from jerk-right to jerk-left) and in gaze direction on reversal of cover (arrows). Gaze direction changes are accomplished by a saccade and enhanced slow phase in A and by enhanced slow phases and diminished fast phases in B and C.

Table 8.—Dynamics of Latent Nystagmus (LN) Direction Changes*

Eye Initially	Gaze Position		LN Direction				Gaze Direction Change†	Gaze Change due to
			Initial		Final†			
	Initial	Final	Sϕ	Fϕ	Sϕ	Fϕ		
Occluded	ET	O	T	N	N	T	T	↑TFϕ w/o NSϕ ↑TFϕ and ↓NSϕ
Viewing	O	ET	N	T	T	N	N	↑NFϕ w/o TSϕ ↑NFϕ and ↓TSϕ
Occluded	XT	O	T	N	N	T	N	↑NSϕ and ↓TFϕ NFEM and ↑ NSϕ NFEM and NSϕ
Viewing	O	XT	N	T	T	N	T	↑TSϕ and ↓NFϕ TFEM and ↑ TSϕ TFEM and TSϕ

N indicates nasal; T, temporal; Fϕ, fast phase; Sϕ, slow phase; ↑, enhanced; ↓, diminished; ET, esotropia; XT, exotropia; w/o, without; FEM, fast eye movements (saccades) that are *not* Fϕ.
†Columns relating required gaze direction changes to LN directions.

nystagmus and Kornhuber,[14] with Jung,[11] reported a 38% incidence in their series. Anderson and Kornhuber and Jung noted a high incidence of alternating hyperphoria prompting Kornhuber and Jung to describe a "characteristic syndrome" of LN, horizontal tropia, primary position rotary nystagmus, and alternating hyperphoria. Seventeen of our 31 patients with MLN had a vertical tropia, but this did not correlate with the coexistence of a rotary CN.

Both LN and MLN are regarded as congenital forms of nystagmus. Although Anderson[15] suggested that difficult labor and deliveries were frequent in his patients, Kornhuber,[14] with Jung[11] found a frequent familial occurrence and believed that a genetic disorder was more likely than early life brain damage. Of particular relevance in this regard is that four of our patients with MLN had retrolental fibroplasia and each had a coexisting CN. Manifest latent nystagmus has not been reported previously as occurring secondary to retrolental fibroplasia.

Despite the fact that CN, MLN, and presumably true LN may be congenital or secondary to an early life visual defect, and may even coexist in the same patient, this should not justify the common practice of lumping these different nystagmus forms together simply as "congenital nystagmus." This is misleading, functionally incorrect, and, as with most oversimplifications, serves to impede progress in the uncovering of the underlying mechanisms of these different motor instabilities. The waveforms of CN represent classical high-gain instabilities of a closed-loop feedback system; the waveform of LN (MLN) is that of a passive slow movement off target corrected by a saccade.

In addition to the distinct differences in the slow phase waveforms of MLN and the jerk form of CN (the former decelerating and the latter accelerating in velocity), we found another waveform difference between these two nystagmus types. More than 48% of our patients with MLN exhibited dynamic overshoots[16] of their fast phases (Fig 2), whereas none of more than 150 CN patients recorded in our laboratory had dynamic overshoots. The function of dynamic overshoots in general is uncertain as is their significance in the fast phases of MLN. The fast phases of all forms of nystagmus thus far studied are corrective, meaning that they serve to bring the fovea on or toward the target following slow phases that carry the eye away from the target.

Manifest LN and CN also differ in their variations over a range of gaze angles (Fig 9 and 10). These figures illustrate schematically these differences between CN and MLN as well as the gaze-paretic variety of gaze-evoked nystagmus and vestibular nystagmus. Congenital nystagmus usually has a null (shown in Fig 9 in the primary position), whereas MLN, and presumably LN, diminish with gaze in the direction placing the viewing eye in adduction (in accordance with Alexander's law). Gaze-paretic nystagmus has the same decreasing velocity slow phase waveform as LN and MLN,[2,17,18] but shares with CN its variation over gaze angle with the null of gaze-paretic nystagmus always including primary position as distinct from CN; vestibular nystagmus varies with gaze angle as MLN but has a linear slow phase as does pursuit-defect nystagmus,[19] not shown in the figures. (Also omitted from the figures is gaze-evoked nystagmus with linear slow phases as distinct from the gaze-paretic variety of gaze-evoked nystagmus. The variations of the different forms of nystagmus are diagramed in a less schematic way in Fig 10, where runs of three beats at each gaze angle are depicted and thus simulate more closely the appearance of actual eye movement recordings. These figures also demonstrate the value of quantitative oculography in nystagmus diagnosis.

The invariable coexistence of MLN and strabismus prompted us to consid-

er a correlation between the nystagmus and eye dominance or amblyopia, which should be most obvious in those patients with unidirectional MLN (Table 5). The fact that four of the five patients with left eye amblyopia had only jerk-right MLN (meaning they were viewing with their right eye) supported the postulated correlation, but the remaining ten patients with unidirectional MLN, five in each direction, did not have amblyopia. There was also a lack of consistent correlation with the dominance. Eight of the ten right eye dominant patients had jerk-right MLN; two had jerk-left (Table 5). The remaining five patients who had no visually dominant eye also had unidirectional MLN (one jerk-right and four jerk-left). While there was a strong tendency for the nonamblyopic or the dominant eye to be preferred for vision, the very existence of unidirectional MLN in the opposite direction in a small percentage of the cases precludes any unifying hypothesis. Also difficult to explain was the existence of unidirectional MLN in those subjects without amblyopia or visual dominance.

Alexander's law dictates that nystagmus would be minimal with gaze in the direction of the slow phase (ie, a jerk-right nystagmus should become minimal in left gaze). Nine of the 15 patients with unidirectional MLN had a head turn but three of the four with a right head turn and all five with a left head turn placed the viewing eye in abduction—a situation violating Alexander's law. Approaching the data somewhat differently (Tables 6 and 7), we separated from the total sample those 15 patients with a head turn irrespective as to whether their MLN was unidirectional or bidirectional and there was again no clear relationship between the head turn and the dominant or amblyopic eye. The two patients with both right and left head turns had neither a dominant nor amblyopic eye. To investigate further the purpose of the head turn, we correlated the gaze-evoked magnitude of the nystagmus with the direction that the head turn placed the eyes. As is apparent from Table 7, Alexander's law was followed in eight of the 15 (53.3%) patients (ie, the viewing eye was in adduction when the nystagmus was minimal), but the nystagmus was minimal when the viewing eye was in abduction in six of the patients (40%). In these 14 patients, the nystagmus magnitude was minimized by the head turn regardless of whether Alexander's law was obeyed. The last case shown in Table 7 presented a strange paradox; the viewing eye assumed an abducting gaze angle and the magnitude of the nystagmus was maximal in this preferred position. This particular patient was blind in his left eye from retrolental fibroplasia and had a huge kappa angle in his right eye. Thus, although his jerk-right MLN was minimal in left gaze (in accordance with Alexander's law), he was forced to direct his viewing right eye far to the right presumably because of his large kappa angle.

Ishikawa[20] recently advanced the thesis that LN was secondary to a proprioceptive rather than a visual disturbance. Such an explanation might be supported by our data showing a high correlation with strabismus. In all of Ishikawa's cases, both eyes deviated inward on covering either eye. Further, on performing a forced duction of one eye outward, the other unrestricted eye also moved outward. He attributed this phenomenon to a stretch reflex between the stretched medial rectus of the eye forcibly moved outward and its yoked lateral rectus in the free eye. He did not find these "inversed eye movements" in subjects without LN. Ishikawa states that LN is produced by a stretch reflex activated by the inward-drifting covered eye inducing an inward drift in the viewing eye (thus fast phases always beat toward the viewing eye). This would only be tenable for cases with an esophoria or esotropia (his subjects were either esophoric, esotropic, or "orthophoric") but does not explain the LN direction in patients with exotropia such as in seven of our cases. Another problem with Ishikawa's hypothesis relates to van Vliet's[21] observations. Using an optical device called a "pseudoscope," van Vliet found the direction of the LN to be independent of the eye actually being used for vision but rather beat in the direction of the eye that the patient *thought* was being used. These observations obviously require confirmation by others.

Our study suggests the following mechanistic considerations: LN and MLN represent disorders of tonic innervation released by an inability to adjust properly to the differences between monocular and binocular perception domains. The relative egocentric direction differs from absolute egocentric direction under these two viewing (monocular and binocular) conditions.[22] A *version* tone imbalance obviously exists or no ocular drift (slow phase) would occur. This imbalance is kept in check if binocular vision is possible and is distinct from the *vergence* tone imbalance causing a phoria or tropia. Disturbance of this binocular vision results in a cortical confusion of ego direction allowing the version tone imbalance to create a conjugate eye drift (see Fig 2). An alternative explanation is that the confusion in ego direction itself causes the conjugate drift toward the new (improper) ego direction. It is irrelevant whether we are discussing true LN or MLN, since only one eye is being used for vision in either condition. The conjugate drift takes the eyes off target, and this is sensed by the viewing eye and a saccadic correction (fast phase) is initiated.

We will now consider a possible explanation for the drift direction. Consider an object directly in front of you (ie, your cyclopean eye) such that the absolute egocentric direction is 0°. Binocularly, you perceive it as being straight ahead ($\theta_P = 0°$). Mathematically, this perception angle (relative egocentric direction) is arrived at by summing the angles of convergence of each eye and dividing the two ($\theta_P = [\theta_L + \theta_R]/2$), where θ_L and θ_R are the angles of the left and right eyes as measured from the straight ahead position of each eye; $\theta_L - \theta_R$ is the total convergence angle. What happens, under normal circumstances, to θ_P when one eye is occluded? θ_P then becomes equal to the angle of the viewing eye and what was once correctly perceived as being 0° (ie, in front of the nose) is now perceived at some nonzero angle, θ_L or θ_R (ie, *not* in front of the right or left eye). This phenomenon is observed easily by binocularly viewing a finger held up directly in front of the bridge of the nose at arm's length. The finger is perceived as being straight ahead (ie, relative and absolute egocentric directions are equal). With the left eye covered, the finger is perceived as being to the left of center, and with the right eye covered, to the right of center (ie, relative egocentric direction does not equal absolute egocentric direction). Somewhere, in normal subjects, the function for determining θ_P changes from $(\theta_L + \theta_R)/2$ to θ_L or θ_R, but this perceptual change does not cause any alteration in the neural command to the eyes (ie, the eyes do not shift). Suppose this mathematical transformation was not properly performed or the apparent shift in perception resulted in a change in neural command causing the eyes to drift toward the new angle (ie, toward the occluded eye). We would then have the initiation of LN with a drift of

both eyes toward the occluded eye followed by a corrective saccade toward the viewing eye. It is important to distinguish the conjugate drift, which initiates and determines LN direction, from the phoria-induced drift of one eye (see below). The conjugate drift is always toward the covered (or unused) eye while the phoria-induced drift may be in either direction (esotropic or exotropic) and thus could not be the cause of the LN. The above explanation for LN, briefly mentioned elsewhere,[1] is the only one we find tenable and consistent with our own observations and the data of others.

Ishikawa's[20] postulation that LN is the result of a proprioceptive stretch reflex disturbance, and the high (95% to 100%) incidence of tropia in patients with LN and MLN, make it essential to record carefully and clearly separate the initial version and vergence movements in such patients when each eye is covered alternately. Only in this way can differences or similarities in the generation of LN and MLN be related to the type of strabismus (esotropic or exotropic). To the extent that the phoria angles of each eye are equal, the eye movements required to move both the newly covered eye to the phoria angle and the newly uncovered eye to the visual target will be conjugate. If the phorias are unequal, an additional vergence component will be added to the movement of one eye. The stimulus for the viewing eye will be vision and we should, therefore, expect refixation saccades to be the main vehicle to accomplish the shift in gaze directions; they will, of course, be accompanied by the ongoing LN.

Figures 11 to 13 show the transient eye movements involved in the shift from one viewing eye to the other and the accompanying reversal of LN direction. For the patient with an esotropia (Fig 11), the gaze direction change is accomplished by what appear to be hypometric saccades[23] since the slow phases of the LN are in a direction opposite to the required shift in gaze direction. Initially, with the left eye viewing, there is a jerk-left nystagmus and the right eye is esotropic. After the switch to right eye viewing, the left eye becomes esotropic by enhanced rightward fast phases and diminished leftward slow phases. In the right eye, which was also amblyopic in this patient, the leftward slow phases were totally inhibited during the gaze shift to the target from the initial esotropia. For the patient with an exotropia (Fig 12 and 13), the gaze direction change was accomplished by enhanced slow phases with the possible addition of saccades. Initially, as in Fig 12, there was a jerk-right nystagmus with the right eye viewing and the left eye was exotropic. After the switch to left eye viewing, rightward saccades and enhanced rightward slow phases allowed the left eye to move to the target and the right eye to become exotropic. In Fig 13 we see variations of the transient eye movements involved in the gaze shift and LN reversal produced by shifting the cover on the eyes. In A, the shift was accomplished by a rightward saccade and enhanced rightward slow phases with diminished leftward fast phases; in B and C, enhanced rightward slow phase with diminished leftward fast phases were used without a rightward saccade. The dynamics of the LN direction changes are summarized in Table 8.

As is apparent from Fig 11 to 13, we did not observe any inward drifting of both eyes consequent to covering either eye as reported by Ishikawa,[20] and our data do not support his thesis that a stretch reflex is responsible for LN. On the contrary, immediately on cover reversal, the eyes both reversed their existing conjugate slow phase directions before the adjustment was made in gaze direction that was required for the viewing eye to be on target; this was especially evident in Fig 5, which shows the transition from MLN (jerk right) to LN (jerk left). These observations support our thesis that a basic central abnormality is the underlying mechanism for LN and MLN.

We would like to reemphasize the absolute necessity of quantitative eye movement recording for the identification and classification of nystagmus. Only accurate eye movement recordings can identify clearly those patients with CN, MLN, LN, or combinations of these functionally different disorders. Similarly, recordings can document MLN in patients where the nystagmus during binocular viewing is of very low amplitude (these patients would be diagnosed as pure LN) and, for those patients with a large amplitude MLN, recordings of the waveforms will prevent misdiagnosis of CN.

The literature abounds with misconceptions and erroneous conceptualizations based on purely clinical observations of nystagmus. Although the clinical examination of nystagmus and ocular oscillations will remain the mainstay of office and bedside diagnoses, "scientific" articles should no longer be published without quantitative oculographic documentation as these articles only compound the already confused literature on nystagmus.

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References

1. Daroff RB, Troost BT, Dell'Osso LF: Nystagmus and related ocular oscillations, in Glaser JS (ed): *Neuro-ophthalmology*. Hagerstown, Md; Harper & Row Publishers, 1978, pp 219-243.

2. Daroff RB, Dell'Osso LF: Nystagmus, a contemporary approach, in Thompson HS, Daroff RB, Glaser JS, et al (eds): *Topics in Neuro-ophthalmology*, Baltimore, Williams & Wilkins Co, to be published.

3. Shults WT, Stark L, Hoyt WF, et al: Normal saccadic structure of voluntary nystagmus. *Arch Ophthalmol* 95:1399-1404, 1977.

4. Dell'Osso LF, Flynn JT, Daroff RB: Hereditary congenital nystagmus: An intrafamilial study. *Arch Ophthalmol* 92:366-374, 1974.

5. Dell'Osso LF, Daroff RB: Congenital nystagmus waveforms and foveation strategy. *Doc Ophthalmol* 19:155-182, 1975.

6. Sorsby A: Latent nystagmus. *Br J Ophthalmol* 15:1-18, 1931.

7. Cogan DG: *Neurology of the Ocular Muscles*, ed 2. Springfield, Ill, Charles C Thomas Publisher, 1956.

8. Kestenbaum A: *Clinical Methods of Neuro-ophthalmologic Examination*, ed 2. New York, Grune & Stratton, 1961.

9. Walsh FB, Hoyt WF: *Clinical Neuro-ophthalmology*, ed 3. Baltimore, Williams & Wilkins Co, 1969, vol 1.

10. Daroff RB, Dell'Osso LF: Periodic alternating nystagmus and the shifting null. *Can J Otolaryngol* 3:367-371, 1974.

11. Jung R, Kornhuber HH: Results of electronystagmography in man: The value of optokinetic, vestibular and spontaneous nystagmus for neurologic diagnosis and research, in Bender MB (ed): *The Oculomotor System*. New York, Harper & Row Publishers, 1964.

12. Fredrickson JM, Kornhuber HH, Goode RL: Diagnostic significance of recent observations. *Arch Otolaryngol* 89:88-95, 1969.

13. Forssman B: A study of congenital nystagmus. *Acta Otolaryngol* 57:427-449, 1964.

14. Kornhuber HH: Über Begleitschielen und latenten Nystagmus aus neurologischer Sicht. *Sitzungsbericht* 102:45-48, 1960.

15. Anderson JR: Latent nystagmus and alternating hyperphoria. *Br J Ophthalmol* 38:217-231, 1954.

16. Bahill AT, Clark MR, Stark L: Dynamic overshoot in saccadic eye movements is caused by neurological control signal reversals. *Exp Neurol* 48:107-122, 1975.

17. Abel LA, Dell'Osso LF, Daroff RB: Analog model for gaze-evoked nystagmus. *Instit Elect Electron Engin Trans Biomed Eng* 25:71-75, 1978.

18. Daroff RB: Nystagmus. *Neurol Neurosurg Weekly Update* 1:1-8, 1978.

19. Abel LA, Daroff RB, Dell'Osso LF: Horizontal pursuit-defect nystagmus. *Ann Neurol* 5:449-452, 1979.

20. Ishikawa S: Latent nystagmus and its etiology. Read before the third meeting of the International Strabismological Association, Kyoto, Japan, May 12, 1978.

21. Van Vliet AGM: On the central mechanism of latent nystagmus. *Acta Ophthalmologica* 51:722-781, 1973.

22. Burian HM, von Noorden GK: *Binocular Vision and Ocular Motility*. St Louis, CV Mosby Co, 1974.

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