Extended Slow Phase in Latent/Manifest Latent Nystagmus

Libe Gradstein,^{1,2} Herschel P. Goldstein,³ Sheryl S. Wizov,⁴ and Robert D. Reinecke^{3,5}

PURPOSE. To investigate the slow phase in latent/manifest latent nystagmus (LMLN) by producing long eye-drift intervals devoid of fast phases (extended slow phases [ESPs]) and to relate ESP metrics to clinical findings.

METHODS. Ten patients with LMLN had eye movements recorded while attending to paired visual and auditory cues presented to their left or right. Patients compared location of the visual target with that of the subsequently heard tone. The auditory cue and the comparison task directed attention away from vision and delayed the fast-phase onset to obtain ESPs. ESP metrics were analyzed with regard to patients' clinical characteristics. Five patients' data were further explored by isolating slow-phase components.

RESULTS. All patients exhibited ESPs that resembled the usual slow phase but lasted two to three times longer. Five patients maintained alignment, whereas the other five made vergence movements. Greater eye velocity, excursion, and convergence during an ESP were associated with poor vision and large uncorrected esotropia. These metrics decreased when the viewing eye was in adduction, compared with primary position or abduction. Slow-phase components found in five patients consisted of a dominant decreasing-velocity or linear drift and a low-amplitude periodic oscillation.

Conclusions. Shifting attention away from vision reliably delays the fast phase, revealing long intervals of slow phase, which can facilitate nystagmus investigation. ESP analysis in five patients with LMLN demonstrated two slow-phase components. ESP characteristics suggest that better ocular alignment is associated with improved stability in LMLN and provide metrics of eye drift that correlate with vision. (*Invest Ophthalmol Vis Sci.* 2004;45:1139-1148) DOI:10.1167/iovs.03-0324

L atent nystagmus (LN) is a horizontal jerk nystagmus that occurs with monocular viewing.¹ Its fast phase is directed toward the viewing eye, and the slow phase has a decreasing-

velocity or linear profile.^{1,2} Manifest latent nystagmus (MLN) is identical with LN, but is present when both eyes are open and only one eye is used for vision.¹ Studies have shown that most patients with clinically diagnosed LN have, in fact, small-amplitude MLN evidenced by eye movement recordings.^{1,3} It was suggested therefore that these two nystagmus types be combined into one entity, latent/manifest latent nystagmus (LMLN).⁴

The nystagmus cycle is characterized by slow and fast phases. In congenital nystagmus (CN), the slow phase drags the visual axis off the target, whereas the fast phase brings the fovea back toward the target.⁵ In LMLN, the features of the fast phase depend on the slow-phase velocity.⁶ Therefore, characterization of the slow phase is essential for understanding the ocular motor instability in nystagmus.

Slow-phase duration is usually short because of its interruption by the fast phase. We searched for a way to modify nystagmus to obtain longer intervals of slow phase that could facilitate its investigation. It has been noticed that after the abolishment of the visual target in the dark the nystagmus cycle becomes less regular, and if a distracting mental task (such as performing mental arithmetic) is added to that, the onset of the fast phase can be delayed (Goldstein HP, et al. IOVS 1992;33: ARVO Abstract 2298-84; Gradstein L, et al. IOVS 1996;37:ARVO Abstract 1030).^{7,8} We have used this phenomenon to delay the occurrence of the fast phase in patients with CN, by shifting their attention from a visual target to audition and a mental task (Goldstein HP, et al. IOVS 1995;36:ARVO Abstract 835). The obtained extended period of smooth eye movement devoid of fast phases was called an extended slow phase (ESP). In the present study, we applied the same methodology to patients with LMLN. The purpose of this study was to explore the occurrence of ESPs in LMLN and to determine their possible application in investigations of ocular instability and its clinical correlates. This report represents a first in-depth description of ESPs and a pilot study of ESP analysis for nystagmus investigation.

METHODS

Ten patients with LMLN aged 14 to 65 years were included (Table 1). Monocular, distant visual acuity (VA) was tested by a Snellen chart with +4.00 lens over the fellow eye. Six patients (1–4, 7, 9) had amblyopia (at least two lines difference in VA between the two eyes). All patients had a history of esotropia, and five had undergone strabismus surgery. At the time of testing, eight patients had esotropia of variable degree, and two had small consecutive exotropia. Six patients had dissociated vertical deviations (DVDs).

All patients had MLN on eye movement recordings, although patients 8 and 10 had a clinical diagnosis of LN (Table 1). Patient 7 had a mixture of MLN and horizontal CN (increasing velocity slow phases). Patients 3, 4, and 5 had oculocutaneous albinism. Patients 4 and 5 had pendular torsional nystagmus, with amplitude of approximately 1° and frequency of 5 to 7 Hz, coexisting with horizontal MLN, with each eye viewing (documented by torsional-coil recordings before enrollment into the study). Patient 3 had a low-amplitude MLN and square-wave jerks (SWJs).

The research followed the tenets of the Declaration of Helsinki, and each patient (or parent or guardian) signed a consent form approved

From the ¹Laboratory of Sensorimotor Research, National Eye Institute, National Institutes of Health, Bethesda, Maryland; ²Department of Ophthalmology, Soroka Medical Center, Ben Gurion University, Beer Sheva, Israel; the ³Jefferson Medical College of Thomas Jefferson University, Philadelphia, Pennsylvania; the ⁴Glaucoma Research Center, and the ⁵Foerderer Eye Movement Center for Children, Wills Eye Hospital, Philadelphia, Pennsylvania.

This study was conducted at the Foerderer Eye Movement Center for Children at Wills Eye Hospital, Philadelphia, Pennsylvania.

Supported by the Research Award from the Knight's Templar Eye Foundation (LG).

Submitted for publication March 28, 2003; revised October 24, 2003; accepted November 19, 2003.

Disclosure: L. Gradstein, None; H.P. Goldstein, None; S.S. Wizov, None; R.D. Reinecke, None

The publication costs of this article were defrayed in part by page charge payment. This article must therefore be marked "*advertise-ment*" in accordance with 18 U.S.C. §1734 solely to indicate this fact.

Corresponding author: Libe Gradstein, Laboratory of Sensorimotor Research, National Eye Institute, NIH, Building 10, Room 10S229, Bethesda, MD 20892-1863; libe@nei.nih.gov.

Investigative Ophthalmology & Visual Science, April 2004, Vol. 45, No. 4 Copyright © Association for Research in Vision and Ophthalmology

						Best	Correcte	d VA			Vergence	
Pt	Gender	Age (yr)	Nystagmus Type	Strabismus* (PD)	Strabismus Surgery	RE	LE	BE	Refraction	Recording Technique	with ESP † (deg)	Remarks
-	W	14	MLN	Right ET 40	None	20/200	20/80	20/40	$RE - 24.50 + 2.50 \times 160$	IR	Convergence 2-23	
0	н	65	MLN	Right ET 25	None	20/80	20/40	20/30	$\begin{array}{c} \text{LE} - 21.00 + 1.25 \times 55 \\ \text{RE} - 2.50 + 1.00 \times 150 \\ \text{re} & 1.75 \\ \text{re} & 1.75 \end{array}$	Coil	Convergence 3-12	
$\tilde{\mathbf{w}}$	Ц	55	Fine MLN	Left ET 25	None	20/40	20/60	20/40	$\begin{array}{c} \text{LE} = 1.75 \\ \text{RE} + 7.00 + 2.50 \times 105 \\ \text{TE} \pm 7.25 \pm 2.50 \times 75 \end{array}$	Coil	Convergence 2-3	OCA
4	ы	38	MLN and torsional	Left ET 20	None	20/25	20/40	20/25	$\frac{112}{RE} + 7.25 + 2.50 \times 72$ $\frac{112}{RE} - 7.00 + 1.25 \times 105$ $\frac{112}{RE} - 3.50$	Coil	RE viewing: convergence 1-2	OCA
											or divergence 2-3; LE viewing: convergence 2-7	
Ś	Ч	41	MLN and fine torsional	Alternating ET 20 DVD left > right	For ET ages 5 and 22 v	20/40	20/30	20/30	$RE + 1.75 + 2.50 \times 75$ $LE + 2.00 + 1.00 \times 105$	Coil	None	OCA
9	ц	24	MIN	Left ET 14 Right HT and DVD	For ET ages 1 and 20 y	20/25	20/25	20/20	$RE = 5.00 + 1.25 \times 80$ $LE = 3.50 + 1.00 \times 120$	Coil	None	
\sim	Ч	21	MLN and CN	Alternating ET 10 DVD each eve	None	20/20 -	20/30	20/20-	NA	Coil	Convergence 1-4	
8	Μ	23	Fine MLN [‡]	Alternating ET 6 DVD each eve	For ET age 1 y, For DVD age 14 vr	20/20 - 2	20/20	20/20	$RE - 1.00 + 0.75 \times 90$ $IE - 1.25 + 0.75 \times 90$	IR	None	
6	Ч	26	MIN	Alternating XT 4 DVD right > left	For ET age 18 mo, For consecutive XT	20/60	20/200	20/50 + 2	$RE - 4.25 + 2.50 \times 20$ $LE - 2.25 + 1.25 \times 145$	Coil	None	
10	Ľ	27	Fine MLN‡	RXT 4 DVD each eye	age 6 y For ET age 18 y For consecutive XT and diplopia age 19, 26, 27 y	20/20 – 2	20/25	20/20 - 2	$\begin{array}{l} \mathrm{RE-8.50} + 1.75 \times 100 \\ \mathrm{LE-8.25} + 2.00 \times 85 \end{array}$	IR	None	
	BE, both ε * Deviation † Change ‡ These pa	yes; ET 1 for dis of aligni ttients h	, esotropia; HT, I stant fixation (pau ment during the ad latent nystagr	nypertropia: IR, infra tients are ordered acc test: convergence, di mus on clinical exam	ed; OCA, oculocutanec cording to deviation any vergence, or no change ination and fine MLN o	ous albinism; F gle: greater ese e (vergence < n eye moveme	D, prism- otropia in 1°).	diopters; Pt, the top, less ling.	patient; XT, exotropia. er esotropia or exotropia i	n the bottom		

Downloaded from iovs.arvoiournals.org on 06/28/2019

TABLE 1. Clinical and Eye Movement Data

by the Wills Eye Hospital Institutional Review Board. Eye movements of seven patients were recorded with a magnetic search coil⁹ (Table 1). Horizontal eye movements of an additional three patients who could not tolerate wearing the contact annulus (patients 1, 8, and 10) were recorded by an infrared system (model B210; ASL, Waltham, MA) using adjustable glasses with limbal reflection hardware mounted on either side of each eye.

Patients viewed a green (543 nm) laser spot target, rear projected onto a tangent screen at 1 m, while both eyes were recorded simultaneously. The head was stabilized with adjustable restraints placed around the skull and under the chin. A computer controlled the position and brightness of the target and the presentation of an auditory tone heard through a stereo headset. Digitized data (12 bits per 80°) were sampled at 500 Hz. Equipment calibration was established monocularly by aligning the horizontal position of each eye to the target over the central 25°. In the same manner, a vertical calibration was established for the magnetic search coil technique. Liquid crystal shutters mounted on goggles controlled the occlusion of the nonviewing eye with the search coil technique, and manual occlusion was used with the infrared technique.

The experimental paradigm consisted of visual and auditory reference and flash tests. Each trial began with the visual reference target (laser spot seen for 1 to 3 seconds, 1 to 2 log units above background illumination) which was followed by a visual test target (2 ms duration and 3 log units above the background) flashed randomly 10° to the right or to the left of the fixation spot. Patients were asked to note, but not look at, the location of the flashed target relative to the previously visible reference. The auditory test followed immediately: A centrally heard reference tone (binaural, ~1000 Hz, 1-3 seconds' duration) was followed by a monaural test tone (same tone but 200-ms duration), presented to the right or left ear. Patients used a joystick to signal whether the directions of the visual and auditory test stimuli agreed. The auditory cue and the mental task of comparison of visual and auditory target directions shifted the patients' attention away from vision (no visual target was present during this stage), while maintaining general alertness. All patients performed the test with each eye viewing and with the visual reference positioned at left 20°, straight ahead, and right 20° (10 presentations at each reference position).

The obtained data were analyzed off-line using programable data review software written by Paul Sealaus (Department of Cardiology, University of Pennsylvania Medical Center, Philadelphia, PA) and one of the authors (HPG). The ESPs generated during the test were analyzed with regard to their direction, duration, and waveform, as well as eye excursion, velocity and vergence during the ESP. A relationship was sought between the ESP metrics and eye position, as well as the patients' clinical characteristics (VA, amblyopia, and ocular alignment). ANOVA and Student's *t*-test were used to check the statistical significance of these associations.

Further analysis of ESPs of patients 2, 4, 5, 6, and 9 was performed using techniques designed to fit the data. This revealed two additive slow-phase components. Decomposition of ESPs of the other patients was not possible for two reasons: Patients 1, 8, 10 were recorded by an infrared technique with insufficient resolution for component analysis, whereas patients 3 and 7 had confounding factors in their nystagmus that made the interpretation of the results difficult (combined MLN-CN waveforms in patient 7 and SWJs in patient 3). The first component was isolated by determination of the best fit to the ESP, either exponential or linear (whichever fits best), using a least-squares method (Marquardt-Levenberg). The residual second component was separated by subtraction of the first component from the original ESP. Component analysis of the slow phase of the nystagmus cycle preceding the ESP was also performed in these patients. The exponential or linear first component isolated for ESP was applied to fit the slow phase (whenever necessary, slight time-shift of the exponential or adjustment of the linear slope were made to compensate for some temporal variability). The second component was isolated by subtraction of the first component from the slow-phase curve.

RESULTS

General ESP Features

All patients exhibited ESPs that occurred after the visual target was extinguished, either during the auditory stimulation or while performing the comparison task. Figure 1 shows a slow eve drift devoid of fast phases (an ESP) in patient 2, with either eye viewing. ESP characteristics varied among patients and depended on viewing eye acuity and position (discussed later), but for a given patient and test condition ESPs were reproducible. In general, ESPs were characterized by a horizontal drift of both eyes away from fixation, toward the occluded eye. The initial ESP segment resembled a preceding slow phase (Figs. 1, 2, 3). ESPs lasted 0.7 to 4.5 seconds (two to three times longer than the usual slow phases), mean eye velocity during the ESP ranged from 0.1 to 7.5 deg/s, and eye excursion ranged from 0.2° to 14°. Except for patient 7, ESPs had a decreasing-velocity or linear profile (Figs. 1, 2, 3). Patient 7 with combined LMLN-CN waveforms had ESPs with a mixed-velocity profile (Fig. 4). No significant vertical deflections were noted during the ESP. In patients with DVD, the vertical deviation was usually established with monocular occlusion in the beginning of the trial and remained stable during the attention task.

After the ESP and before appearance of the visual target for the next trial, the nystagmus was often less regular than usual. This period, which lasted 2 to 3 seconds, was characterized by a high-amplitude and low-frequency nystagmus (Fig. 4), and in patient 2, even by an inversion of the fast phase direction (Fig. 1). With reappearance of the visual target in the beginning of the following trial, the regular nystagmus resumed.

Vergence during the ESP

Two ESP response types were found among our patients: in one type (patients 5, 6, 8, 9, and 10), both eyes drifted approximately equally (vergence $<1^{\circ}$) and in the other type (patients 1, 2, 3, 4, and 7), the eyes drifted asymmetrically, which resulted in a significant (>1°) vergence (Table 1). Figures 2 and 3 illustrate the first response type, and Figure 1 illustrates the other. Patients with the second response type converged between 1° and 23°, except for patient 4 who diverged 2° to 3° with her right eye viewing (Table 1).

Comparison between the two response types revealed that patients in the vergence group were more likely to have large, uncorrected, nonalternating esotropia and amblyopia than were those in the nonvergence group, all of whom had had strabismus surgery in the past (Table 1). Comparison was also made between the ESP metrics of patients 1 to 5 with esotropia of at least 20 prism-diopters and patients 6 to 10 with smaller deviations. The former group had, on average, more convergence (4.1° compared with 0.6°), larger eye excursion (5.2° compared with 3.4°), and higher velocity (2.9 deg/s compared with 1.4 deg/s) during ESPs. The difference in convergence was statistically significant (P = 0.02).

Dependence on Visual Acuity and Eye Position

Eye excursion, mean velocity, and convergence during the ESP were related to the acuity and position of the viewing eye. Figure 5A shows average values of excursion, velocity, and convergence of all patients for all testing positions as a function of the VA of the viewing eye. For the sake of the statistical



FIGURE 1. Coil recording of patient 2. Traces show RE and LE horizontal positions and vergence (V) (LE-RE). Upward deflection indicates rightward movement or increased convergence. Time 0: fixation spot extinguished, target flashed. Top: leftbeating nystagmus with left eye viewing. ESP (bold segment) started 100 ms after target flashed and lasted approximately 1 second. Eyes drifted right with 7° convergence (in addition to initial 13.1° esotropia). Note large-amplitude nystagmus and inversion of fast-phase direction after the ESP, when no visual target was present. Bottom: right-beating nystagmus with right eye viewing and then 1.5-second ESP directed left, with 4° convergence (in addition to initial 8.9° esotropia).

analysis, patients' eyes were divided into three VA groups: 20/200 to 20/80 (4 eyes), 20/60 to 20/40 (6 eyes), and 20/30 to 20/20 (10 eyes). All three ESP metrics decreased as VA increased in a statistically significant manner (P < 0.001 for excursion, P = 0.003 for velocity, P = 0.003 for convergence, ANOVA). For patients with amblyopia, the response depended on the viewing eye, so that faster ESP drift occurred when the amblyopic eye viewed (Figs. 2, 3).

To investigate the effect of eye position, we compared ESP metrics in three testing positions (primary, abduction, and adduction) judged with respect to the viewing eye. Figure 5B shows average values of eye excursion, velocity, and convergence of all patients calculated for each testing position with the same viewing eye (one eye for each patient selected arbitrarily). All metrics were smaller when the viewing eye was in adduction than in primary position or abduction. This difference was statistically significant for excursion (P = 0.006) and velocity (P = 0.002). Figure 6 shows an ESP from patient 9 viewing in adduction, demonstrating that her eyes were more stable compared with the recording in primary position (Fig.

3). The same trend was noted for convergence, but did not reach statistical significance, probably because patients who minimally converged did so in all testing positions. Patients with significant vergence responses, however, converged less in adduction. For instance, patient 4 converged only 2° viewing with her left eye in adduction versus approximately 6° in primary position.

ESP Components

Further analysis showed that the ESPs of patients 2, 4, 5, 6, and 9 could be decomposed into two components: a larger-amplitude component (C1), and a residual, lower-amplitude component (C2; Figs. 7, 8, 9). Component C1 moved the eye toward the occluded eye and appeared to approach a steady state position. Component C2 was periodic. In patients 4, 6, and 9, C1 had entirely an exponential form (Figs. 7, 8), whereas in patients 2 and 5, it was initially linear before decelerating (Fig. 9). For the exponential C1, the amplitude ranged from 1° to 5° ,





and the time constant ranged from 0.4 to 0.6 seconds. For the linear C1, the slope was 1.6 deg/s in patient 5 and 2.8 deg/s in patient 2, with the intercept at -25.7° and -1.5° , respectively. The ESPs of all five patients were dominated by C1, which gave either an overall decreasing-velocity or linear profile to the drift (Figs. 2, 3). The pendular oscillations of the second component had a frequency of 1.5 to 3 Hz and amplitude of 0.1° to 0.3°. Because of its low amplitude, C2 made little contribution to the ESP curve in patients 6 and 9, but was slightly more noticeable in patients 2, 4, and 5 (Figs. 7, 8, 9).

Analysis of the nystagmus cycle preceding the ESP indicated that two components, similar to those of the ESP, were present in the usual slow phase of these patients. Because of the short slow phase duration, it was difficult to isolate these components. Isolation was accomplished using the parameters found from the ESP. Only minor changes in C1 were needed to fit the slow phase (a small time shift of the exponential for patients 4, 6, and 9 and a slight adjustment of the linear slope for patients 2 and 5). Comparison of the component metrics between the usual slow phase and the ESP in each patient showed a similar C1 profile, although its eventual deceleration was better seen in the ESP. Moreover, because the usual slow phase revealed only a fraction of the C2 periodicity, the frequency and amplitude of the second component could not be determined (Figs. 7, 8, 9).







FIGURE 4. Two trials of patient 7 with mixed LMLN-CN waveforms. *Top trace*: left eye horizontal position when left eye is viewed; *bottom trace*: right eye horizontal position when right eye viewed. *Bold segments*: ESPs; *arrow*: fixation spot extinguished, target flashed. Patient exhibited variable-velocity ESPs; increasing velocity prevails in the record shown. An initial ESP segment on both traces resembles the usual slow phase. Note high-amplitude and low-frequency nystagmus after the ESP.

DISCUSSION

Influence of Visual Attention on LMLN

In agreement with other authors,^{3,10,11} our study demonstrates that eye movements in LMLN depend on visual attention. A regular nystagmus cycle is usually present during active target viewing. Auditory and cognitive tasks divert the patient's attention from the visual target, which reliably delays the onset of the fast phase and results in a longer than usual slow phase, the ESP. This extends previous observations made in patients with CN (Goldstein HP, et al. *IOVS* 1995;36:ARVO Abstract 835). Abadi and Scallan^{3,10} also reported ESPs in MLN and in a patient who exhibited MLN and CN waveforms. Thus, ESP occurrence is probably a universal phenomenon revealed when the patient's attention is directed away from vision.

ESP and Usual Slow Phase in LMLN

ESP Components. Analysis of ESPs in five patients revealed a larger-amplitude component, C1, and a lower-amplitude, periodic component, C2. The longer time course of the ESPs allowed better characterization of the components also seen in the usual slow phase. Although our sample is small and the results may not apply to all patients with LMLN, we believe that the slow phase in LMLN is determined by the interaction of these components. The isolated LMLN components are analogous but not identical with the two components previously described in CN (Goldstein HP, et al. IOVS 1995;36:ARVO Abstract 835). The dominant first component bears the typical slow-phase features in LMLN. For instance, unlike in CN where the first component reverted in neutral zone, in our patients C1 was directed toward the occluded eye, which corresponds to the occlusion dependence in LMLN.¹ Furthermore, whereas in CN, C2 velocity often dominated in the increasing-velocity ESPs, the dominance of C1 in LMLN is in agreement with the decreasing-velocity or linear slow phase typical of LMLN.^{1,12} Finally, the first component might reflect the nasal drift found not only in patients with LMLN, but also in strabismic amblyopes without overt nystagmus.^{1,2,13,14}

The periodic second component is often not evident in usual, jerk LMLN. However, pendular oscillations have been reported in a dual-jerk variant of LMLN.^{1,12} Abadi and Scallan³ also noted the presence of a pendular component in two of the six slow-phase classes they described in MLN. We would explain the various slow-phase classes as an interplay between the two slow-phase components. Whereas in these authors' slow-phase class I or II C1 predominance causes only jerk waveforms, in class III, C2 also expresses itself, causing the presence of pendular elements.³ This superimposition of jerk and pendular waveforms is similar to that reported in CN and nystagmus due to low vision, where the pendular waveform is more obvious than in LMLN.^{7,15}

Dependence on Eye Position and Visual Acuity. Similar to the usual LMLN slow phase, the ESP drift in our patients depended on the viewing eye position and acuity. Whereas in CN, the drift was minimal in some orbital positions (null zones), in LMLN, smaller ESP excursions were measured in adduction, compared with primary position or abduction (Goldstein HP, et al. IOVS 1995;36:ARVO Abstract 835). Although the adducted eye has a limited excursion toward the fellow eye, it is unlikely to be the only reason for smaller excursions. Patients were tested in 20° adduction and ESP excursions were typically only a few degrees, such that the eyes usually did not reach the adduction limit. In addition, ESP velocity and convergence also took on their minimum values in adduction. These findings are in agreement with Alexander's law variation and mirror the clinical phenomenon of the adduction null zone in LMLN.^{1,4,14}

We found an inverse relationship between viewing-eye acuity and ESP metrics (velocity, excursion, and convergence). Accordingly, in patients with amblyopia, higher ESP velocity was measured with the worse eye viewing. This parallels the LMLN behavior observed in amblyopes under usual testing conditions, in which more brisk nystagmus is noted with the amblyopic eye viewing, and the slow-phase velocity decreases after amblyopia treatment.^{7,16}

Convergence with ESP

Although some LMLN patients develop purposive esotropia to lessen their nystagmus,¹⁷ ESP convergence in our patients does not seem to be an active effort to see better, because the convergence occurred when their attention was shifted to the nonvisual task. Instead, ESP convergence may reflect persistent nasalward tonus, a proposed mechanism of strabismus and LMLN in infants with a faulty development of binocular vision.^{2,13,18} In any case, ESP convergence represents yet another parameter of ocular instability added to the conjugate eye drift. The finding that patients converged less when the viewing eye was in adduction null zone supports this notion.

LMLN is usually associated with strabismus, especially infantile esotropia.^{1,2,13,19} All our patients have a history of esotropia, but their current alignment status varies. Our finding that large uncorrected esotropia is associated with greater ESP convergence and drift suggests that ocular motor stability in patients with LMLN may be improved with strabismus surgery.^{19,20}

Clinical Correlates and Applications

We described ESPs, which can be studied for nystagmus characterization. A detailed analysis of ESPs of five patients with LMLN revealed two additive slow-phase components. It was beyond the scope of this article to study LMLN pathogenesis, although investigations of slow-phase structure might contrib-



FIGURE 5. Eye excursion, velocity, and convergence during ESP versus viewing eye acuity (A) or position (B). Left scale: excursion and convergence; right scale: velocity. Error bars, standard deviations. (A) All eyes were divided into three visual acuity levels. The average of each ESP metric was calculated for each acuity level. All metrics decreased significantly as VA increased. (B) Average of each ESP metric across all patients was calculated for each testing position with the same viewing eye. All metrics took on minimal values in adduction compared with primary position or abduction.

ute to an understanding of nystagmus mechanisms. Abadi and Scallan³ described six slow-phase classes in MLN based on waveform, but none of their subjects fell into a single class. As an alternative analysis, we suggest that the ESP represents the

fingerprint of a patient's ocular instability where the particular interaction of components determines the specific slow-phase waveform, although more work is needed to establish this claim. Our analysis of extended and usual slow phase revealed that





FIGURE 6. Patient 9 viewing with her right eye in adduction (fixation target F at 20° left). Traces as in Figure 2. During 2.4-second ESP, eyes were more stable compared with Figure 3 recorded with same eye viewing straight ahead. Each eye's excursion was less than 1°, versus 3° in Figure 3. There was no significant vergence.

proper component characterization, in particular of the periodic second component, is not possible on a short-duration slow phase. Therefore, the ESP method may be particularly useful to uncover and study the pendular components in LMLN.

As we and others have shown, eye movements in LMLN depend on visual attention,^{3,10} similar to CN, where nystagmus intensity, foveation duration, and even VA depend on the visual task and attention level.^{8,21} Therefore, control of attention is

needed for any meaningful clinical and oculographic assessment of patients with nystagmus. The ESP technique, unlike other methods, maintains a high level of general alertness, but reduces the influence of visual attention on nystagmus variables by shifting attention to other modalities.

Several mathematical functions have been proposed to relate the nystagmus parameters to VA.^{4,21-23} Some of these track less accurately acuity in individuals with LMLN and good vision.⁴



FIGURE 7. Components of ESP (top) and of the slow phase of the preceding nystagmus cycle (bottom), of patient 4 viewing with her right eye. Left traces: fast phase followed by ESP, duration 1.3 seconds, or slow phase, duration 0.5 second. ESP and usual slow phase dominated by C1 (dashed line), decaying exponential directed left, time constant 0.46 second (to fit slow phase, exponential was time shifted back by 0.3 second). Right traces: residual C2 (magnified), isolated in both ESP and usual slow phase, but its metrics (frequency approximately 2 Hz, amplitude approximately 0.1°) can be assessed only from ESP (fine oscillations on C2 curve, frequency ~60 Hz, are noise).



FIGURE 8. Component analysis of ESP (top) and of preceding slow phase (bottom) of patient 9 viewing with her right eye. Left traces: ESP, duration 1.1 second, and usual slow phase, duration 0.3 second. In both cases, C1 (dashed line) is exponential directed left, time constant 0.52 second (0.3-second time shift back was done to fit slow phase). Right traces: residual C2 (magnified), amplitude approximately 0.14°, seen in ESP and usual slow phase. Because of short slow-phase duration, the C2 frequency (~3 Hz) was revealed only by the ESP.



FIGURE 9. Components of ESP (top) and of preceding slow phase (bottom) of patient 2 viewing with her left eye. Left traces: ESP, duration 1.6 seconds, and usual slow phase, duration 0.5 second, with their preceding fast phases. During the slow phase and first 1.2 second of ESP, the dominant, directed to right C1 (dashed line) is linear (slopes 2.6 and 2.8, respectively). Eventual eye deceleration can be discovered only on ESP. Right traces: residual C2 (magnified) traced in both ESP and usual slow phase, but its amplitude (approximately 0.3°) and frequency (approximately 1.5 Hz) can be ascertained only from the ESP.

Although our series is small, ESP analysis provides metrics of eye drift correlating with VA in patients with LMLN. Our results also demonstrate that large uncorrected esotropia and amblyopia are associated with greater ocular instability. In the future, by simplifying and shortening the recording paradigm (such as, using a noise distraction without a mental task), it may be possible to apply the ESP method on young children with nystagmus to estimate better their acuity, the presence of amblyopia, and ocular alignment, which may be hard to assess because of the nystagmus.

Acknowledgments

The authors thank Edmond J. FitzGibbon, MD, for help with the revision of the manuscript.

References

- Dell'Osso LF, Schmidt D, Daroff RB. Latent, manifest latent and congenital nystagmus. Arch Ophthalmol. 1979;97:1877-1885.
- Gresty MA, Metcalfe T, Timms C, Elston J, Lee J, Liu C. Neurology of latent nystagmus. *Brain*. 1992;115:1303–1321.
- 3. Abadi RV, Scallan CJ. Waveform characteristics of manifest latent nystagmus. *Invest Ophtbalmol Vis Sci.* 2000;41:3805-3817.
- 4. Dell'Osso LF, Leigh RJ, Sheth NV, Daroff RB. Two types of foveation strategy in "latent" nystagmus: fixation, visual acuity and stability. *Neuroophthalmology*. 1995;15:167–186.
- 5. Dell'Osso LF, Daroff RB. Congenital nystagmus waveforms and foveation strategy. *Doc Ophthalmol.* 1975;39:155–182.
- Erchul DM, Dell'Osso LF, Jacobs JB. Characteristics of foveating and defoveating fast phases in latent nystagmus. *Invest Ophthalmol Vis Sci.* 1998;39:1751–1759.
- 7. Reinecke RD. Costenbader Lecture. Idiopathic infantile nystagmus: diagnosis and treatment. J AAPOS. 1997;1:67-82.
- Abadi RV, Dickinson CM. Waveform characteristics in congenital nystagmus. Doc Ophthalmol. 1986;64:153-167.
- 9. Robinson DA. A method for measuring eye movement using a scleral search coil in a magnetic field. *IEEE Transactions on Bio-Medical Electronics*. 1963;10:137-145.

- 10. Abadi RV, Scallan C. Manifest latent and congenital nystagmus in the same subject: a need to reconsider the underlying mechanisms of nystagmus. *Neuroophthalmology*. 1999;21:211–221.
- Shawkat FS, Harris CM, Taylor DS. Spontaneous reversal of nystagmus in the dark. *Br J Ophthalmol.* 2001;85:428-431.
- Dell'Osso LF. Congenital, latent and manifest latent nystagmussimilarities, differences and relation to strabismus. *Jpn J Ophthalmol.* 1985;29:351–368.
- Bedell HE, Flom MC. Bilateral oculomotor abnormalities in strabismic amblyopes: evidence for a common central mechanism. *Doc Ophthalmol.* 1985;59:309–321.
- 14. Kommerell G. The relationship between infantile strabismus and latent nystagmus. *Eye*. 1996;10:274–281.
- Gottlob I, Wizov SS, Reinecke RD. Head and eye movements in children with low vision. *Graefes Arch Clin Exp Ophthalmol*. 1996;234:369-377.
- Simonsz HJ. The effect of prolonged monocular occlusion on latent nystagmus in the treatment of amblyopia. *Doc Ophthalmol.* 1989;72:375-384.
- Gradstein L, Goldstein HP, Wizov SS, Hayashi T, Reinecke RD. Relationships among visual acuity demands, convergence, and nystagmus in patients with manifest/latent nystagmus. J AAPOS. 1998;2:218-229.
- Tychsen L, Lisberger SG. Maldevelopment of visual motion processing in humans who had strabismus with onset in infancy. *J Neurosci.* 1986;6:2495-2508.
- Dell'Osso LF, Traccis S, Abel LA. Strabismus. A necessary condition for latent and manifest latent nystagmus. *Neuroophthalmology*. 1983;3:247–257.
- Zubcov AA, Reinecke RD, Gottlob I, Manley DR, Calhoun JH. Treatment of manifest latent nystagmus. *Am J Ophthalmol.* 1990; 110:160-167.
- 21. Sheth NV, Dell'Osso LF, Leigh RJ, Van Doren CL, Peckham HP. The effects of afferent stimulation on congenital nystagmus foveation periods. *Vision Res.* 1995;35:2371-2382.
- Dell'Osso LF, Van der Steen J, Steinman RM, Collewijn H. Foveation dynamics in congenital nystagmus I: fixation. *Doc Ophthalmol.* 1992;79:1–23.
- Dell'Osso LF, Jacobs JB. An expanded nystagmus acuity function: intra- and intersubject prediction of best-corrected visual acuity. *Doc Ophtbalmol.* 2002;104:249–276.