CONGENITAL, LATENT AND MANIFEST LATENT NYSTAGMUS—SIMILARITIES, DIFFERENCES AND RELATION TO STRABISMUS

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Summary: Patients with congenital types of nystagmus, including congenital nystagmus (CN), latent/manifest latent nystagmus (LMLN) and combinations of the two, can be identified by waveform analysis and classified into three unambiguous groups. This categorization by waveform is supported by different clinical signs, including the relationship to strabismus. Strabismus is essential for LMLN but incidental to CN; most CN patients do not have strabismus. Seventy-seven percent of CN patients have a convergence null, 57% a gaze angle null and nearly half have both; only 14% have neither. Also supporting this patient grouping by waveform is the high incidence of patients in each of the two major groups (ie, they had either only CN waveforms or only the LMLN waveform). Comparing the incidence of each CN waveform, or combinations of waveforms, in families with that in the general CN population, reveals that heredity plays a role in determining waveform; heredity also affects other characteristics, such as gaze angle or convergence nulls.

The nystagmus blockage syndrome has at least two mechanisms and the patients, therefore, can belong to either of two groups. Spasmus nutans is hypothesized to be an oscillation of the vergence system and therefore, unrelated to CN or LMLN.

Key Words: Congenital nystagmus, latent nystagmus, manifest latent nystagmus, strabismus, waveforms

Introduction

In this report I will attempt to provide the answers to commonly asked questions about congenital nystagmus (CN) and latent/manifest latent nystagmus (LMLN): the clinical and ocular motor characteristics that define and separate CN and LMLN; the relation of CN and LMLN to strabismus; the incidence of each CN waveform or combinations of waveforms; the role of heredity in determining CN waveforms and nulls; the probabilities of a patient with strabismus having CN or LMLN; and the probabilities of a patient with either CN or LMLN having strabismus.

The data included in this report have been derived from a retrospective study of ocular motility records made over the past 20 years in the Ocular Motor Neurophysiology Laboratory. As of the time of this writing, over 350 patients with congenital types of nystagmus have been

studied using the methods of quantitative oculography described below. Depending on the particular variables reported, specific subpopulations of these patients were used and are identified for each Table. Two different types of nystagmus have been identified that, although present at birth (ie, congenital), are not caused by the same defect, do not have the same waveforms, and do not present with the same clinical picture. The two are congenital nystagmus (CN) and latent/manifest latent nystagmus (LMLN). In addition, spasmus nutans appears to be emerging as an oscillation of a totally different ocular motor subsystem. The similarities and differences between CN and LMLN will be discussed as will their very different relation to strabismus.

Another result of this retrospective study has been the refinement of the criteria I use to differentiate distinct patient groups based upon their nystagmus waveforms and the constellation of specific characteristics exhibited by their nystagmus. The advantages of attempting to identify patient types and the choice of the corresponding therapeutic approaches likely to be successful in increasing visual function are obvious. The coincidence that several types of nystagmus can appear at, or shortly after, birth has for too long clouded their individuality and interfered with systematic evaluations of various possible therapies. Unfortunately, the latter have been indiscriminately applied to all nystagmus that, although labeled "congenital", was not always CN. The results of such an ad hoc approach are evident in the myriad of conflicting reports that crowd the nystagmus literature. Due to the absence of objective, accurate ocular motility recordings in such reports, the reader cannot identify the specific type or types of nystagmus present in the patients mentioned. Because, without good recordings, there is a high probability of both misdiagnosis and indiscriminate combining of different nystagmus types under the "congenital" label, one can neither evaluate properly such a report nor compare it with others of a similar nature.

Methods

The method employed to record the eye movements of all patients used in this study was light reflection off the cornea sensed by phototransistors connected for differential amplification. Initially, in an electrical engineering laboratory at the University of Wyoming (1963), dc white light was used[6]. Subsequently, in 1968 in the laboratory of Dr. Lawrence Stark[13] and in the Ocular Motor Neurophysiology Laboratory in Miami between 1970–80, and more recently in Cleveland, infrared light was used. This allowed for quantitative oculography that was much more accurate than the electrooculographic (EOG) methodology in use prior to my studies of CN. The recordings made using dc white light were the first accurate eye movement recordings of CN. Our system is dc coupled and has a full system bandwidth (both eye position and velocity) of dc-100 Hz. This, plus the inherently low noise and drift, allowed for accurate eye position signals of both eyes simultaneously and, coupled with on-line differentiation of each eye signal, enabled us to analyze details of CN waveforms that are undetected by EOG or other low bandwidth systems.

Subjects were seated at the center of a 5-foot radius arc that contained the red light-emitting diode (LED) target lights. Each eye was calibrated monocularly while the other was occluded; this allowed us to record any strabismus whether large or small, latent or manifest, constant or variable. The ability to assess each eye's position and the variation of that position with time was critical in identifying both the fixating eye and relationship of strabismus to CN, LMLN and the nystagmus blockage syndrome (NBS). The ability to judge accurately the part of

the CN oscillation corresponding to target foveation, and therefore calibrate each eye correctly, resulted from cinematographic studies of the foveas of several CN and LMLN patients[7]. This technique has also been realized using an infrared television fundus camera[31]. Note that all of this essential information is lost with EOG, especially bitemporal EOG which does not provide information about the position of either eye.

Each subject's head was fixed in primary position by a head restraint and chin cup and all were instructed to look at the target light with their eyes without moving their heads; the heads of small children were further restrained by one of the experimenters. Target lights were red LEDs easily visible, even without refractive correction. This allowed assessment of the effects of gaze angle and convergence angle uncontaminated by effort-to-see; the use of acuity targets would have introduced this unwanted variable.

Finally, eye movements were recorded on a rectilinear pen strip chart recorder to allow for undistorted registration of all waveforms and a vertical EOG electrode was used to differentiate blinks from eye movements.

Patient Groups

Analysis of the waveforms exhibited by all of the patients studied resulted, in the early 1970's, in identification of the 12 waveforms of CN[9] and the solitary LMLN waveform[14]. In addition, a waveform consisting of a pendular oscillation (CN) superimposed on a decreasing-velocity slow phase jerk nystagmus (LMLN) was also identified. Three distinct patient groups emerged: I) pure CN, II) pure LMLN and III) various mixtures of CN and LMLN. Thus, both CN and LMLN were found to coexist in some patients with either being dominant or equally prevalent. This resulted in some rather complex waveforms that varied with both time and gaze angle.

Before proceeding to further characterize these patient groups, definitions of both CN and LMLN should be presented.

CN is a biphasic ocular oscillation, present at or shortly after birth, that has one or more of the 12 CN waveforms. It is conjugate in direction, frequency and usually amplitude. CN is predominantly horizontal but may have vertical components[5].

LMLN is a nystagmus, also present at or shortly after birth, that has a jerk waveform with a decreasing-velocity slow phase and is manifest only with monocular fixation; the non-fixating eye may be either occluded (LN) or suppressed when both eyes are open (MLN)[14].

For both CN and LMLN, the slow phases initiate the oscillation by bringing the eyes off target and the fast phases are corrective in direction. The direction of all jerk nystagmus is defined as that of the fast phase, regardless of amplitude. The original definition of LN[16], and subsequent studies[18,30], did not restrict the nystagmus to appear only upon occlusion of one eye as is commonly, and mistakenly, thought today. Furthermore, Kestenbaum[23] recognized MLN as an entity present with both eyes open but with only one fixating (the other being suppressed). Additionally, cases of CN may exhibit reversal of their CN waveform upon occlusion of an eye. This was designated as CN with a superimposed latent component[23] and should not be confused with LN, since the CN waveforms remain during occlusion; the reversal is due to a shift in the null position toward the covered eye[4]. The mechanism responsible for LMLN has been hypothesized to be due to inability to shift from binocular to monocular egocentric direction determination[14],

Table 1.   Patient groups from waveform analysis

Analysis	Waveform			Patient Group
	DJ_L	J_L	CN*	
CN	0	0	1	I
LMLN	0	1	0	II
CN & LMLN	0	1	1	IIIa
C-LMLN	1	0	0	IIIb
CN/LMLN	1	0	1	IIIc
LMLN/CN	1	1	0	IIId
CN, LMLN & C-LMLN	1	1	1	IIIe

*Any combination of the 12 CN waveforms
CN   — congenital nystagmus
LMLN   — latent/manifest latent nystagmus
C-LMLN — congenital-latent/manifest latent nystagmus
J_L — jerk latent (decreasing-velocity slow phases)
DJ_L — dual jerk latent (pendular superimposed on decreasing-velocity slow phases)

a proprioceptive imbalance[22], or an optokinetic defect[25]. The incidence of pure LN (ie, no recordable nystagmus with both eyes open at all gaze angles) is extremely rare. More common is LN at primary position and MLN in lateral gaze. Most common is MLN at all gaze angles. Using these definitions we can distinguish between CN and LMLN based on both waveform and clinical signs and avoid the ambiguity resulting from clinical impressions alone.

Returning to the above-mentioned patient groups, what distinct patient groups are identifiable by waveform analysis? As can be seen in Table 1, there are three main groups with group III subdivided into five parts (a–e) based on the particular combination of CN, LMLN or C-LMLN waveforms. C-LMLN is the combination congenital-latent waveform, dual jerk latent (DJ_L). Patients in group I are CN patients and can have any combination of the 12 CN waveforms. Patients in group II are LMLN patients and exhibit only the jerk latent waveform (J_L). Patients in groups IIIa–e have various mixtures of CN, J_L and DJ_L waveforms.

Waveforms

The 12 CN waveforms consist of three pendular (P=pendular, AP=asymmetric pendular and P_{fs}=pendular with foveating saccades), four unidirectional jerk (J=jerk, J_{ef}=jerk with extended foveation, PC=pseudo-cycloid and PJ=pseudo-jerk), four bidirectional jerk (PP=pseudopendular, PP_{fs}=pseudopendular with foveating saccades, T=triangular and BDJ=bidirectional jerk) and one dual jerk (DJ) waveform. The one LMLN waveform is jerk latent (J_L), where the subscript "L" indicates the decreasing-velocity slow phases characteristic of LMLN. The one C-LMLN waveform is dual jerk latent (DJ_L), where the subscript "L" indicates that the pendular oscillation rides on the same decreasing-velocity slow phases. Figure 1 illustrates the difference between the DJ waveform of CN and the DJ_L waveform of LMLN and indicates the patient groups in which these waveforms are found. The distinction between the increasing-velocity slow phases of CN and the decreasing-velocity slow phases of LMLN is not an arbitrary one. It was made because they imply different mechanisms of generation; the former implies a positive-feedback runaway and the latter implies a passive drift to an incorrect eye position[10].

I. CN   IIIʙ   C-LMLN

IIIᴄ   CN/LMLN

IIIᴅ   LMLN/CN

IIIᴇ   CN, LMLN & C-LMLN
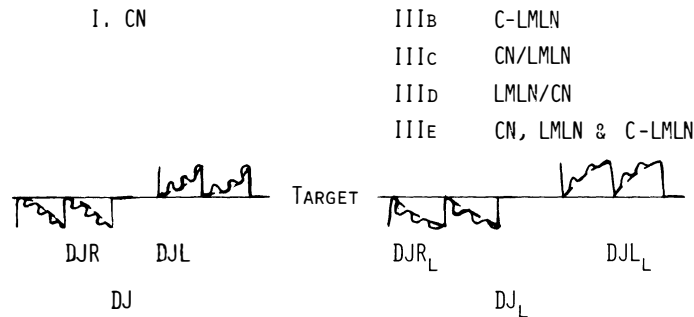

DJR   DJL   Tᴀʀɢᴇᴛ   DJR_L   DJL_L

DJ   DJ_L

Figure 1. Illustrations of slow phases of congenital dual jerk nystagmus (DJ) and latent dual jerk nystagmus (DJ_L) for both right- (R) and left- (L) beating nystagmus. Note that slow phases upon which the pendular oscillation is superimposed are accelerating for congenital and decelerating for latent waveforms. Roman numerals indicate patient groups in which these waveforms are found.

In all unidirectional jerk waveforms (in both CN and LMLN), the slow phases take the eyes away from the target and the fast phases are in the direction of target foveation; foveation occurs after the fast phases of the oscilllation[7,14]. In pendular forms of CN, target foveation occurs at one extreme of the oscillation and can usually be identified by the flattened appearance of those peaks (indicating zero eye velocity). The bidirectional forms of CN are usually transient and appear in the vicinity of the neutral region (ie, the gaze angles where the direction of jerk nystagmus reverses). Since pseudopendular and triangular straddle the target, poor foveation results. Pseudopendular with foveating saccades and bidirectional jerk do allow good foveation and may not be transient in a given patient. Foveation in dual jerk CN or dual jerk latent LMLN occurs after the fast phases.

Characteristics

I have defined patient groups I, II and IIIa–e solely by the appearance of either CN waveforms, the LMLN waveform or some combination of them with the C-LMLN waveform. Does this differentiation, based only on waveform, result in two distinct clinical entities? If so, what are the clinical characteristics of CN, LMLN and mixtures of the two? Table 2 contains the salient characteristics of patients in each of the groups. Most CN patients have a null angle, with the nystagmus intensity growing as gaze is directed away from the null angle and the direction of jerk nystagmus determined by the gaze direction from the null (eg, jerk right when looking to the right of the null). The variation of LMLN with gaze angle is monotonic, usually described by Alexander's law[3] and the direction determined solely by the fixating eye (eg, jerk right when fixating with the right eye)[14]. Note that CN exhibits both a stationary null angle (when fixating stationary targets) and a dynamic null angle (when fixating, that is, pursuing, moving targets)[8]. This shift in the static null angle is usually in the direction opposite to the smooth pursuit and is related to pursuit velocity.

Comparing CN patients in groups I and Ia, we see that they differ only slightly. Both have increasing-velocity slow phases, and may have pendular waveforms or convergence nulls. Pa-

Table 2. Nystagmus characteristics of each patient group

Patient Group	Parameters						
	Slow Phase Jerk Nyst.	Direction of Jerk Nyst.	Pendular Nyst.	Static[2] Null Angle	Dynamic[4] Null Angle	Convergence Null	Strabismus
I CN	$\uparrow\dot\theta_E$	$f(\theta_E)$	+ or −	$f(\theta_E)$	$f(\theta_E \& \dot\theta)$	+ > −	− > +
Ia* CN & LC	$\uparrow\dot\theta_E$	$f(\theta_E \& FE)$	+ or −	$f(\theta_E \& FE)$	$f(\theta_E, \dot\theta \& FE)$	+ > − (?)	+ > − (?)
II LMLN	$\downarrow\dot\theta_E$	Toward FE	−	na[3]	na	na	+
IIIa CN & LMLN	$\uparrow\dot\theta_E \& \downarrow\dot\theta_E^{1}$	$f(\theta_E)$ & Toward FE	+ or −	$f(\theta_E)$ & na[3]	$f(\theta_E \& \dot\theta)$ & na	+ > − & na	+
IIIb C-LMLN	DJ_L	Toward FE	+	na[3]	na	na	+
IIIc CN/LMLN	$\uparrow\dot\theta_E \& DJ_L^{1}$	$f(\theta_E)$ & Toward FE	+	$f(\theta_E)$ & na[3]	$f(\theta_E \& \dot\theta)$ & na	+ > −	+
IIId LMLN/CN	$\downarrow\dot\theta_E \& DJ_L^{1}$	Toward FE	+	na[3]	na	na	+
IIIe CN, LMLN & C-LMLN	$\uparrow\dot\theta_E, \downarrow\dot\theta_E$ & DJ_L^{1}	$f(\theta_E)$ & Toward FE	+	$f(\theta_E)$ & na[3]	$f(\theta_E \& \dot\theta)$ & na	+ > − & na	+

*CN with a latent component: all waveforms are CN but eye cover induces a null shift that may mimic the direction reversal of LMLN.
1. CN, LMLN or C-LMLN waveforms occur at different times.
2. The null angle when viewing a stationary target.
3. Nystagmus may vary monotonically with gaze angle (Alexander's Law) but no true null exists.
4. The null angle when pursuing a moving target or during OKN stimulation.
f ( ) — function of argument(s) within ( )
θ_E — eye position (gaze angle)
$\dot\theta_E$ — eye velocity, ↑ increasing, ↓ decreasing
$\dot\theta$ — direction and magnitude of pursuit or OKN velocity
FE — fixating eye
DJ_L — dual jerk latent waveform
na — not applicable

tients in Ia, however, exhibit an influence of the fixating eye on null angle (static and dynamic) and direction of jerk nystagmus. Thus, CN with a latent component is basically CN and not LMLN. If we compare patients in groups I and II we find many distinguishing characteristics. They are, in group I (and group II) respectively: the slow phase is accelerating (decelerating); the direction of jerk nystagmus is a function of gaze angle (toward the fixating eye); pendular nystagmus may be (is not) present; the static null angle is a function of gaze angle (none); the dynamic null angle is a function of both gaze angle and velocity (none); there is usually a convergence null (none); and strabismus is usually not (is always) present.

Another interesting comparison is that between CN/LMLN (IIIc) and LMLN/CN (IIId); patients in both groups have mixtures of CN and LMLN. The characteristics shown in Table 2 reveal that the patient in group IIIc is basically a CN patient and the one in IIId an LMLN pa-

tient; hence, the choice of names. Using Table 2, similar comparisons can be made between any of the other patient groups to identify both common and distinguishing features of the patients' nystagmus.

Strabismus

One of the important characteristics of patients with nystagmus is their ocular alignment. Specifically, what is the relation of strabismus to CN? To LMLN? What are the chances that a patient with CN will have strabismus? A patient with LMLN? Alternatively, if a patient has strabismus and nystagmus, can we predict whether it will be CN or LMLN? Strabismus is defined as a squint or lack of parallelism of the visual axes of the two eyes. This includes both tropias (manifest strabismus) and phorias (latent strabismus) and does not differentiate between subgroups of strabismus patients with differing sensory abnormalities. The ocular motor abnormalities presented herein relate ocular alignment to the presence or absence of nystagmus independent of specific, coincidental sensory defects.

In attempting to answer the above questions the following observations are pertinent: a patient with strabismus may have no nystagmus, CN with (Ia) or without (I) a latent component, or LMLN. Also, CN patients (I) may or may not have strabismus. All CN waveforms have been recorded in CN patients (I) who were binocularly aligned (ie, no manifest strabismus). MLN has never been recorded in patients with binocular alignment (ie, all had manifest strabismus). LN has never been recorded in patients with orthophoria (ie, all had latent strabismus). The terms "latent" in LN and "manifest" in MLN should refer to the strabismus, not the nystagmus. Thus, all patients with LMLN have strabismus (ie, strabismus is a necessary condition for LMLN)[15].

Although the patient groups defined above are necessary for specificity in research, it is desirable to fall back to more general, less specific, categories for clinical use. Basically, the clinician would like to place a patient into either the CN category or the LMLN category. For this purpose one can consider as CN patients those in groups I, IIIa, c and e, and as LMLN patients those in groups II, IIIa, d and e. The C-LMLN category (IIIb), which exhibits the mixed CN and LMLN waveform (DJ_L) exclusively, is included for completeness, although no such patients have yet been recorded. Figure 2 illustrates the relationships between general patient categories,
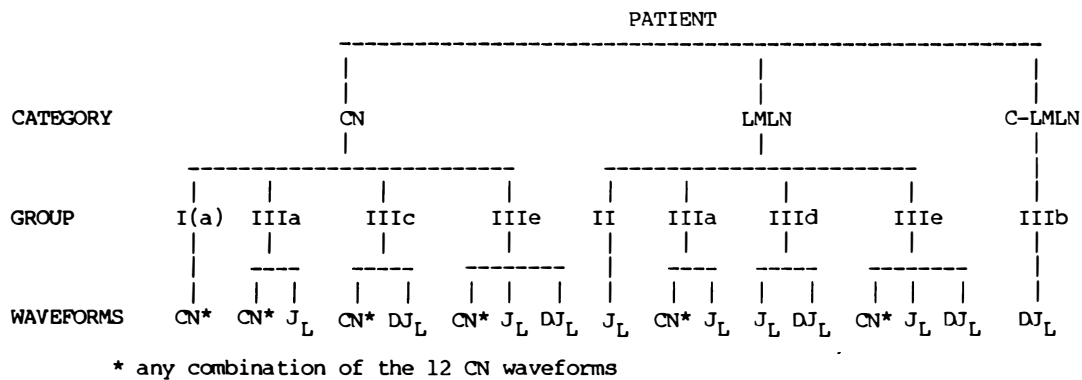

* any combination of the 12 CN waveforms

Figure 2. Tree structure illustrating the relationship between general patient categories, patient groups and the waveforms contained in each.

patient groups and nystagmus waveforms. The ambiguity of including patients in groups IIIa and IIIe in both the CN and LMLN general categories is reduced by considering the predominant waveforms of a given patient as the main criterion for placement into either the CN or LMLN category. This clinical categorization is helpful in answering questions relating strabismus and nystagmus types.

Incidence

Patient groups

To assess the incidence of strabismus in each type of nystagmus we must first determine the relative incidences of CN, LMLN and the various mixtures of the two. Based on the first 100 nystagmus patients we studied, the incidence of CN (I) was 80%, LMLN (II) was 15% and group III had 5% (IIIa and IIIe both had 2% and IIIc had 1%). Thus, as shown in Figure 3a, the great majority of patients were purely CN and the second most prevalent were LMLN; those with mixtures of CN and LMLN were clearly in the minority. If one looks at the first 100 patients in the general CN category (Figure 3b), the results are even more striking with 94% CN (I) patients and only 6% group III (2% in each of groups IIIa, IIIc and IIIe) patients. Similarly, looking at only the first 50 patients in the general LMLN category (Figure 3c), 74% were LMLN (II) patients and 26% group III (4% in both IIIa and IIId and 18% in IIIe) patients. Here again, the large majority of patients had a pure form of nystagmus.

Strabismus

According to Lang, approximately 50% of all patients with strabismus have nystagmus[26]. Since we study only those with nystagmus, I must rely on that estimate. Without accurate recordings, one cannot be sure of the type of nystagmus the patients had, although it was felt that most had LN. As shown in Figure 4a, the incidence of strabismus in the first 100 nystagmus patients we studied was 43% from groups I, II, IIIa, c, e; 57% had no strabismus (all from

Figure 3a
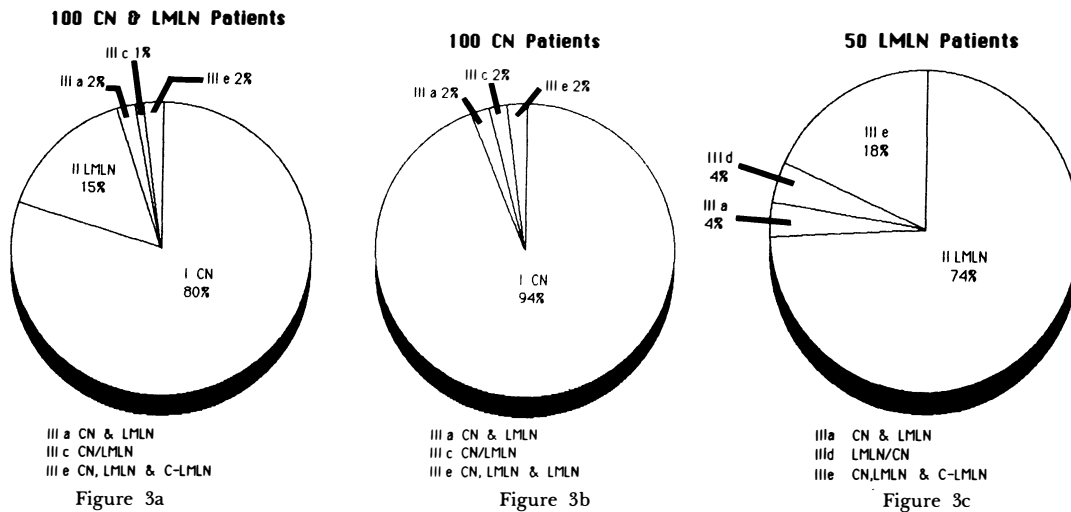
Figure 3b

Figure 3c

Figure 3.   Pie charts illustrating incidence of patients in each group in a) first 100 CN and LMLN patients, b) first 100 CN patients and c) first 50 LMLN patients.
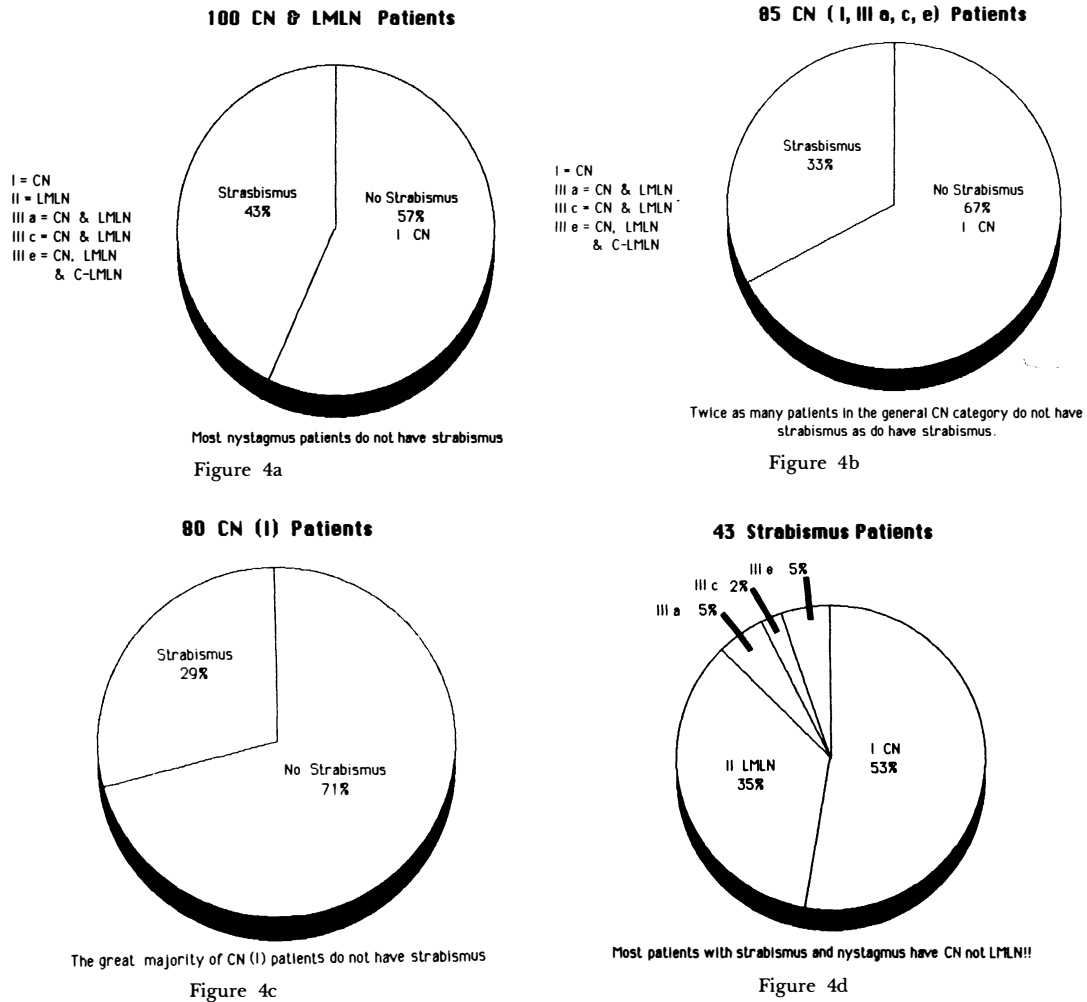
Figure 4. Pie charts illustrating incidence of strabismus in a) first 100 CN and LMLN patients, b) first 85 CN patients and c) first 80 group I CN patients. Incidence of patients in each group in 43 strabismus patients is shown in d).

group I). Published figures for strabismus incidence range from 40-51%[19,20,27]. From this, one can infer that most nystagmus patients do not have strabismus. The incidence of strabismus in the first 85 CN (I, IIIa, c, e) patients (Figure 4b) is only 33% from groups I, IIIa, c, e; 67% had no strabismus (all from group I). Twice as many patients in the general CN category do not have strabismus as do have strabismus. The incidence of strabismus in the first 80 CN (I) patients (Figure 4c) was only 29% with 71% having no strabismus. Clearly, the great majority of CN (I) patients do not have strabismus (see Table 4). Finally, of the 43 patients with strabismus from the first 100 nystagmus patients (Figure 4d), 53% were CN (I), 35% were LMLN (II), and 12% were group III (5% in both IIIa and IIIe and 2% in IIIc). Thus, most patients with strabismus and nystagmus have CN, not LMLN!

Table 3.　Waveform incidences of the first 100 CN patients

%		40	13	10	55	64	61	14	21	6	6	6	20	%
%	WF	P	AP	P_{fs}	J	J_{ef}	PC	PJ	PP	PP_{fs}	T	BDJ	DJ	WF
40	P	(5)	7	4	14	17	19	6	5	1	0	1	14	P
		12.5												
13	AP	17.5	(0)	4	6	4	7	3	2	0	1	0	2	AP
		53.8	0											
10	P_{fs}	10	30.8	(0)	5	7	7	3	5	1	0	2	0	P_{fs}
		40	40	0										
55	J	35	46.2	50	(5)	41	32	1	6	2	3	4	8	J
		25.5	10.9	9.1	9.1									
64	J_{ef}	42.5	30.8	70	74.5	(1)	48	11	17	6	6	6	8	J_{ef}
		26.6	6.3	10.9	64.1	1.6								
61	PC	47.5	53.8	70	58.2	75	(2)	13	19	6	6	6	9	PC
		31.1	11.5	11.5	52.5	78.7	3.3							
14	PJ	15	23.1	30	1.8	17.2	21.3	(0)	8	2	2	2	2	PJ
		42.9	21.4	21.4	7.1	78.6	92.9	0						
21	PP	12.5	15.4	50	10.9	26.6	31.1	57.1	(0)	6	4	5	1	
		23.8	9.5	23.8	28.6	81	90.5	38.1	0					
6	PP_{fs}	2.5	0	10	3.6	9.4	9.8	14.3	28.6	(0)	2	3	0	PP_{fs}
		16.7	0	16.7	33.3	100	100	33.3	100	0				
6	T	0	7.7	0	5.5	9.4	9.8	14.3	19	33.3	(0)	3	0	T
		0	16.7	0	50	100	100	33.3	66.7	33.3	0			
6	BDJ	2.5	0	20	7.3	9.4	9.8	14.3	23.8	50	50	(0)	0	BDJ
		16.7	0	33.3	66.7	100	100	33.3	83.3	50	50	0		
20	DJ	35	15.4	0	14.5	12.5	14.8	14.3	4.8	0	0	0	(0)	DJ
		70	10	0	40	40	45	10	5	0	0	0	0	
%	WF	P	AP	P_{fs}	J	J_{ef}	PC	PJ	PP	PP_{fs}	T	BDJ	DJ	(13)*

*Only 13% were exclusive (5P, 5J, 1J_{ef} and 2PC)

None of the bidirectional jerk forms were exclusive

Most bidirectional jerk forms accompanied unidirectional jerk forms

M/F=62/38　　　　　　　　　　　　　　　　　KEY

PAN=11　SWJ=11　SP=1　　　　　　　　(%)

Convergence:　77-22=1+　　　　　　　　(E)　　　　%

CN=94　　　　　　　　　(I)　　　　　　(X)　　　of

CN & LMLN=2　　　　　(IIIa)　　　　　　　(C)　　Total

CN/LMLN=2　　　　　　(IIIc)　　　　　　　　(L)

CN, LMLN & C-LMLN=2　(IIIe)　　　　% ↑　　　(U)

J_L=4　DJ_L=4　　　　　　　　　　　　　　　　(S)

Torsional component=2　　　　　　　% ←　　　　　(I)

Diagonal component=6　　　　　　　　　　　　　　(V)

Circular component=3　　　　　　　　　　　　　　　　(E)

　Torsional + Diagonal=1; Diagonal + Circular=2

Vertical component=0

In summary, as shown in Figure 5, 50% of patients with strabismus will not have nystagmus and, of the other 50%, 26.5% will have CN (I), 17.5% will have LMLN (II) and 6% will have mixed nystagmus (III).
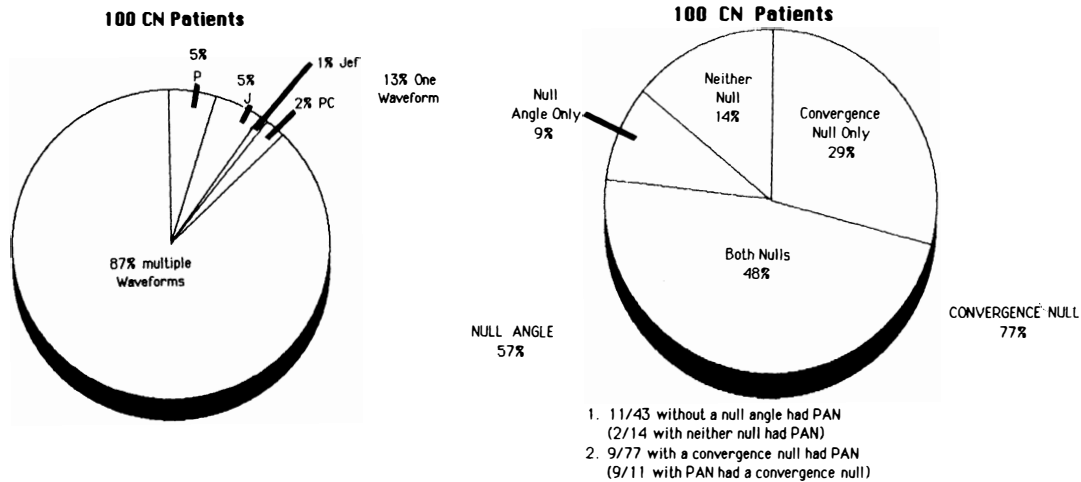
Table 4.   Waveform group incidences of the first 100 CN patients

%	Waveforms	50 / 3P	87 / 4UDJ	24 / 4BDJ	20 / DJ
50	3P	(7) 14	35	9	14
87	4UDJ	70 40.2	(32) 36.8	24	14
24	4BDJ	18 37.5	27.6 100	(0) 0	1
20	DJ	28 70	16.1 70	4.2 5	(0) 0
					(39)

Only all 3P=1; All 3P=1
Only all 4UDJ=1; All 4UDJ=1
Only all 4BDJ=0; All 4BDJ=2
Only all 8J=0; All 8J=0
    2 had 7/8 J wf's
    2 had 6/8 J wf's
    3 had 5/8 J wf's
Only wf's in the 8J=46

KEY
(%)
(E)   %
  (X)   of
   (C) Total
    (L)
% ↑   (U)
     (S)
% ←   (I)
      (V)
       (E)

```
                 STRABISMUS
         _____
        |                   |
   No Nystagmus        Nystagmus
        |                   |
      ~50%               ~50%
                           |
                  _____
                 |         |       |
              I CN     II LMLN  III Mixed
                 |         |       |
              26.5%    17.5%     6%
```

Figure 5.   Relationship of strabismus to presence or absence of nystagmus and to patient groups exhibiting nystagmus.

Waveforms and nulls

It is interesting to speculate on the relative incidences of each of the CN waveforms. What is the most common waveform? The least common? The most likely to be an exclusive waveform in a given patient? If a patient has one of the 12 CN waveforms, what are the chances that he has any of the remaining 11? What are the incidences of certain combinations of the 12 CN waveforms? These questions are aimed at ascertaining the role of heredity in determining CN waveforms.

In the first 100 CN (I, IIIa, c, e) patients, most (87%) had multiple waveforms, leaving only 13% with an exclusive waveform (see Figure 6a). Of these, 5% had P, 5% had J, 2% had PC and 1% had J_{ef}. This group consisted of 62 males and 38 females; 11% had periodic alternating nystagmus (PAN), 11% had square wave jerks and 1% had saccadic pulses. Convergence nulled the CN of 77% of these patients, gaze angle nulls were found in 57% and both types of null were

100 CN Patients

5%
P
5%
J
1% Jef
2% PC

13% One
Waveform

87% multiple
Waveforms

100 CN Patients

Neither
Null
14%

Null
Angle Only
9%

Convergence
Null Only
29%

Both Nulls
48%

NULL ANGLE
57%

CONVERGENCE NULL
77%

1. 11/43 without a null angle had PAN
    (2/14 with neither null had PAN)
2. 9/77 with a convergence null had PAN
    (9/11 with PAN had a convergence null)

Figure 6a   Figure 6b

Figure 6.   Pie charts illustrating a) incidence of multiple and exclusive waveforms in first 100 CN patients and b)
incidence of convergence and gaze angle nulls in this same population.

pos

RE

vel

R ↑
¦
¦
L ↓

pos

LE

vel

Figure 7.   Example of the disconjugate pendular nystagmus recorded in
very young patients and not seen in patients over five years of
age. Note difference in amplitudes of oscillation in two eyes.
RE—right eye, LE—left eye, R—right, L—left, pos—position
and vel—velocity.

present in 48%; only 14% had neither type of null (13 were in group I and one in IIIe). One of
these was a three-year-old in whom we could not determine a null but who did show a head turn
and, thus, presumably had a null angle. Patients with only a convergence null were 29% (26 in

group I and one in each of groups IIIa, e, e) and those with only a gaze angle null were 9% (all in group I) of this population. Interestingly, 11 of the 43 without a gaze angle null (and 2 of the 14 with neither null) had PAN. The presence of PAN in these patients (all of whom were in group I) precludes a stationary null. Of the 77 CN patients with a convergence null, 9 had PAN; thus, 9 of the 11 with PAN had a convergence null. Figure 6b illustrates these findings.

Table 3 contains information about waveform incidences in the first 100 CN (I, IIIa, c, e) patients. The numbers across the first row (or down the first column) of the matrix are the incidences of each of the CN waveforms; the waveforms are indicated around the periphery of the matrix. As shown in the key below the matrix, it is divided along the major diagonal so that the numbers above the diagonal represent percentages of the whole population and those below, represent percentages of their respective column and row. The diagonal terms (in parentheses) are the percentages of the population where the particular waveform was exclusive for a patient. The terms just below each diagonal term represent the percentage of those patients with that waveform for which it was the exclusive waveform. From the first row (or column) we see that the most common waveform was J_{ef} at 64%, followed by PC (61%), J (55%) and P (40%). Bidirectional jerk waveforms are not common except for PP which has a 21% incidence. Dual jerk, while common, was never exclusive; no bidirectional jerk waveform was exclusive in any patient.

To use Table 3 to determine the percentage of patients with two particular waveforms, one must look above the diagonal for the number at the intersection of the row and column of interest. For instance, to find the percent of patients with both J and J_{ef}, locate the intersection of these waveforms above the diagonal and read 41%. That is, 41% of CN patients will have both J and J_{ef} waveforms. To use Table 3 to determine the probability of a patient who has one waveform having another, the pairs of numbers below the diagonal are used. For instance, the probability of a patient with P having P_{fs} is found below the diagonal as the upper number at the intersection of these waveforms; it is 10%. That is, 10% of patients with the P waveform will have the P_{fs} waveform; the lower number in the pair indicates that 40% of patients with the P_{fs} waveform have the P waveform. Using this example it is easy to see how the numbers in the matrix were generated. Patients with P amounted to 40%, 10% had P_{fs} and 4% had both. Thus, the four with both represented 10% (4/40) of those with P and 40% (4/10) of those with P_{fs}.

Table 3 indicates a high degree of mixtures of unidirectional jerk waveforms; patients with one are likely to have another. All patients (100%) with PP_{fs} also had PP nystagmus. Note also that all patients (100%) with the bidirectional waveforms PP_{fs}, T and BDJ had the unidirectional jerk waveforms J_{ef} and PC. These figures support the contention that the bidirectional waveforms cannot be sustained under a wide variety of conditions whereas the unidirectional waveforms are more impervious to changes related to gaze angle or emotional state.

If the matrix in Table 3 is consolidated so that it is arranged in major waveform groups (pendular, unidirectional jerk, bidirectional jerk and dual jerk) the result is Table 4. This format yields information about incidences of these major waveform groups. As the key illustrates, the construction of Table 4 is identical to Table 3. The diagonal terms indicate that 39% of patients had waveforms that were exclusively of one major group (7% were pendular waveforms and 32% unidirectional jerk waveforms). No patients had exclusively bidirectional jerk waveforms or dual jerk nystagmus. The great majority (87%) of patients had waveforms in the unidirectional jerk group and half (50%) had pendular waveforms. Again, all (100%) patients

with waveforms in the bidirectional group had unidirectional jerk waveforms. Only one patient had exclusively all three pendular waveforms and the same was true for all four unidirectional jerk waveforms. No patient had all 8 jerk waveforms but two had 7 of 8, two had 6 of 8 and three had 5 of 8. Forty-six percent of patients had waveforms restricted to the 8 jerk waveforms. These figures form the fundation for ascertaining the role of heredity in waveform incidence.

Heredity

It is well known that heredity plays a role in the incidence of CN[12,17]. Does heredity help determine the particular combination of waveforms that a CN patient has? Or whether there is a gaze angle or convergence null? In a study of four male cousins, two of whom were brothers, and the female child of one of the nonsibling males, it was determined that many of the 12 CN waveforms were exhibited in various combinations by these patients[12]. As shown in Table 3, the probability of a patient having the P_{fs} waveform is 10% or .1. In this family, three of the five had this waveform. Thus, the probability of three members of this family having P_{fs} was .216 (.6 ×.6 × .6) as opposed to .001 (.1 × .1 × .1) in the CN population. The probability of P_{fs}, J, J_{ef} and PC was .02 in the CN population and both of these individuals were members of this family. Thus, their probability of .16 (.4 × .4) was much larger than the .0004 (.02 × .02) in the CN group as a whole. The probability of J, J_{ef} and PC in the CN population was .27; three of them were cousins from this family. Thus, their probability of .216 (.6 × .6 × .6) was much greater than the general probability of .02 (.27 × .27 × .27). As shown in Table 3, the probability of having J_{ef} and PC is .48; four of these were cousins in this same family. Thus, their probability of .410 (.8 × .8 × .8 × .8) far exceeded the expected .05 (.48 × .48 × .48 × .48). Finally, the probability, from Table 3, of PP was .21; two of these were the brothers in this family. Thus, their probabilities of .16 (.4 × .4), relative to all five in the family, or 1.00, relative to only the two brothers, are much greater than the .04 (.21 × .21) one would expect.

In addition to the family studied above, other related patients were studied. From Table 3, the probability of P and DJ_L was .02; the probability of these being the only waveforms was .01. After the initial 100 patients, we tested another patient who had only these two waveforms; this patient was the identical twin to the one patient who had them in the original 100 patients. Thus, their probability of 1.00 far exceeded the .0001 (.01 × .01) that one would expect in the CN population. From Table 3, the probability of P_{fs} and J_{ef} was .07; two of them were brothers. Their probability of 1.00 was greater than the .0049 (.07 × .07) in the CN population. Finally, the probability of P, J, J_{ef} and PC was .04. The probability of having these waveforms exclusively was .03 and of only these plus PAN was .02; both of these patients were related (mother and son). Their probability of 1.00 was much greater than the .0004 (.02 × .02) in the CN population.

Heredity also plays a role in other characteristics. The probability of having only a convergence null was .29 (Figure 6b). We studied a mother and son and the identical twins mentioned above who exhibited this trait. Their probability of 1.00 far exceeds the expected value of .08 (.29 × .29) in the general CN population. Also, we studied another mother and son where neither had a convergence null. Their probability of 1.00 is much greater than the expected value .05 (.23 × .23) in the general CN population. The waveforms of both mother and son pairs were limited to unidirectional jerk waveforms. From Table 4, the probability of having only

unidirectional jerk waveforms is .32. Thus, their probabilities of 1.00 (in each family) also exceed the expected value of .10 (.32 × .32) in the general CN population.

Nystagmus Blockage Syndrome

The nystagmus blockage syndrome (NBS) was originally described by Adelstein and Cüppers in 1966[2]. NBS is found in CN patients who have an accompanying esotropia. When the esotropia increases the nystagmus decreases. Kommerell[24] described an NBS patient whose waveforms were always CN waveforms. In a recent study of NBS we identified two different mechanisms operative in patients with NBS[11]. One subset of these patients maintain their CN waveforms with the onset of the purposive esotropia but at a much reduced amplitude; this appears to be the same mechanism seen in most (77%) CN patients during normal convergence on a near target. These patients are employing the esotropia and suppression during fixation of a distant target; however, such a maneuver would result in diplopia in most CN patients and would not be beneficial. The second subset of NBS patients convert their CN waveform to a very low-amplitude LMLN waveform with the onset of the esotropia. Although the decelerating slow phases of LMLN are not as conducive to good acuity as most CN waveforms, their very low amplitude is apparently sufficient to raise the patient's acuity. Patients in the first subset are CN patients and belong in group I since they always maintain CN waveforms. Those in the second subset are group IIIa patients since they exhibit both CN waveforms (when their eyes are aligned) and the LMLN waveform (with the emergence of esotropia).

Spasmus Nutans

Spasmus nutans, first described by Raudnitz in 1897[29], is a congenital (although it may appear a few months after birth) pendular oscillation of the eyes that ceases by the age of three to four years. It is usually disconjugate (or monocular) and accompanied by a head oscillation. The age of onset and the duration have been reported to be quite variable, ranging from two weeks to three and one half years, and four months to over eight years, respectively[28]; it is not clear that all of these patients had spasmus nutans. The only good published recordings show pendular oscillations 180° out of phase[21]. In that study it was concluded that the head oscillations were purposive and canceled the oscillation of the eyes. Although we have never recorded a disconjugate pendular CN in patients over five or six years of age, we have recorded several under the age of three years with such eye movements (see Figure 7). Based on these observations, I would suggest that these patients had spasmus nutans and, further, that spasmus nutans is a vergence system oscillation rather than a version oscillation like CN. The frequencies (three to five Hz.) overlap but spasmus nutans consists of either uniocular or out-of-phase oscillations of both eyes with equal or unequal amplitudes; CN and LMLN are conjugate oscillations of both eyes. Further study of these, and similar, patients is ongoing in our lab. Particular attention will be paid to the variable phase relationship of the oscillations of the two eyes.

Conclusions and Caveats

I have presented a means to objectively and unambiguously differentiate patients with CN, LMLN and various combinations of the two. Such categorization is necessary for research purposes, given the complexities of the waveforms and the accompanying clinical signs. By far, most

patients have pure CN (80%) or pure LMLN (15%) with various mixtures accounting for only 5%. For clinical purposes, less specific general categories for CN and LMLN were also included. Accurate clinical differentiation is necessary to insure proper therapeutic approaches are taken for each patient. Although based on waveform alone, the patient groups showed specific clinical characteristics. This was not unexpected since different basic mechanisms are suggested by the slow phases of CN and LMLN. While some of the signs by which CN can be differentiated from LMLN are apparent clinically, others require quantitative oculography. It is simply impossible to properly identify some patients without such recordings; it has been our experience that when recordings are available to establish the diagnosis, guesses based on clinical signs alone are often in error, even when made by experienced observers.

Strabismus is uncommon in CN but always present in LMLN. However, because of the higher incidence of CN, patients with both nystagmus and strabismus are most likely to have CN, not LMLN.

Most CN patients have either a convergence null (77%) or a null angle (57%); 48% have both and only 14% have neither. It is, therefore, possible to improve the acuity in many CN patients by either surgery or prisms if there is no primary afferent limitation to good vision. Also, most CN patients (87%) have multiple waveforms; only 13% have one exclusive waveform. The unidirectional jerk waveforms are most common, followed by pendular; the bidirectional jerk waveforms are least common and never exclusive. Combinations of two or more unidirectional jerk waveforms are also common.

Heredity plays an important role in determining the particular waveform or combination of waveforms a patient may have. A recent paper on the subject contains the waveforms of another pair of identical twins[1]. The authors stated that both had PC waveforms. The probability of having only this waveform is .02; the probability of two patients having this is .0004 which is far less than their 1.00. Looking at the records shown in the paper, however, it can be seen that they both had J_{ef} also. The probability of this combination is .48 (from Table 3) and the probability of two patients having this combination is .25 (.48 × .48); again, they exceed this by their probability of 1.00. The authors further state that neither had a convergence null but both had null angles. We found that the probability of a patient having only a null angle was .09; the probability of two patients having only a null angle would be .0081. Here again, the twins, with their probability of 1.00, far exceed the expected incidence. The only real difference found was that the null angles were in opposite gaze directions in each twin causing their nystagmus in primary position to be oppositely directed. This mirror imaging in identical twins is not uncommon. These observations support my hypothesis that heredity plays a large role in determining both waveforms and other characteristics of CN and do not support the contention that environmental influences are the determining factors.

To the extent that the Figures and Tables presented in this paper can be extrapolated to represent the general CN and/or LMLN population, they can be used to predict incidences of waveforms, nulls and nystagmus types, and to assess the influence of factors such as heredity, environment, defects of the afferent visual system, etc. Some of the numbers may contradict generally held opinions but they are internally consistent and understandable when one considers both the factors contributing to them and their implications. To date, no such numbers were available and the questions raised in this paper could only be speculated upon; the numeri-

cal answers to these questions provided herein should help reduce unsubstantiated and anecdotal statements regarding these matters.

Certain caveats require mention. All recordings were made at 100 Hz. bandwidth and there is some evidence that a higher bandwidth (200–300 Hz.) might cause the incidence of PP waveforms to rise slightly. Waveforms were recorded between gaze angles of $+/-$ 25 or 30° (the range of normal gaze); at more lateral gaze angles the incidence of unidirectional jerk waveforms (already the highest) would be even higher. The incidence of each given waveform is not indicative of its predominance in a given patient; this is especially true of the bidirectional jerk waveforms. Most of these appeared only transiently at gaze angles near the neutral region where the direction of jerk nystagmus reverses. Since some of these waveforms cause the eyes to cross the target without slowing, they are not of any utility in good acuity. Finally, the waveforms of CN patients are determined while fixating at various gaze angles to preclude the contaminating effects on slow phase shape of wandering due to inattention. Similarly, the LMLN waveform is determined by the fixating eye since the nonfixating eye (either the phoric eye under cover or the tropic eye in MLN) is not usually fully yoked to the fixating eye and may exhibit vergence fluctuations that contaminate the slow phase waveform.

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Note added in proof: New data from our continuing studies of spasmus nutans suggest that it is not simply an oscillation of the vergence system.