# Clinical and Ocular Motor Analysis of Congenital Nystagmus in Infancy

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***Purpose:*** The purpose of this study was to identify the clinical and ocular motility characteristics of congenital nystagmus and to establish the range of waveforms present in infancy. ***Background:*** The clinical condition of congenital nystagmus usually begins in infancy and may or may not be associated with visual sensory system abnormalities. Little is known about its specific waveforms in infancy or their relationship to the developing visual system. ***Methods:*** Forty-three infants with involuntary ocular oscillations typical of congenital nystagmus were included in this analysis. They were evaluated both clinically and with motility recordings. Eye movement analysis was performed off line from both chart recordings and computer analysis of digitized data. Variables analyzed included age, sex, vision, ocular abnormalities, head position, null-zone or neutral-zone characteristics, symmetry, conjugacy, waveforms, frequencies, foveation times, and responses to convergence and to monocular cover. ***Results:*** Patient ages ranged from 3 to 18 months (average, 9.2 months). Seventeen patients (40%) had abnormal vision, 3 had a positive family history of nystagmus, 11 had strabismus, 16 (37%) had a head posture, 26 (60%) had null and neutral positions, 14 (33%) had binocular asymmetry, and all were horizontally conjugate. Average binocular frequency was 2.8 Hz, and average monocular frequency was 4.6 Hz. The waveforms were both jerk and pendular; average foveation periods in patients with normal vision were more than twice as long as those in patients with abnormal vision. ***Conclusions:*** Common clinical characteristics and eye-movement waveforms of congenital nystagmus begin in infancy, and waveform analysis at this time helps with both diagnosis and visual status. (J AAPOS 1999;3:70-9)

Nystagmus in infancy may be caused by structural disease of the brainstem and cerebellum much the same as nystagmus in adulthood.[1,2] The most common types of infantile nystagmus include the following "benign" forms: congenital nystagmus (CN), latent/manifest latent nystagmus (LMLN), and spasmus nutans. This study examines infant (birth to 18 months of age) patients with CN. The etiologic mechanism of this oscillation remains elusive. In many patients with CN, a sensory-system abnormality may be present.[3-6] Gelbart and Hoyt[7] studied 152 patients with CN and found 119 patients to have a diagnosable sensory system defect. Spierer[6] studied 14 patients with CN and decreased vision as a result of amblyopia. Cibis and Fitzgerald[4] studied 105 patients with clinical CN and found electroretinographic abnormalities in 56% of patients. Numerous reports on the ocular motor behavior in human albinos, patients with retinal disease, and visual deprivation amblyopia have shown CN to be the predominant ocular oscillation.[3-5,8-10] There are also groups of patients, or those with familial CN, whose visual systems show no clinically detectable sensory abnormalities.[11-13]

In addition to the above benign forms of infantile nystagmus are "symptomatic" forms associated with gliomas or brainstem disease. Ocular motor recordings allow differentiation between symptomatic nystagmus and CN or LMLN. Gliomas do *not* cause CN; they result in a dissociated pendular nystagmus that mimics spasmus nutans.

Involuntary ocular oscillations have been classified in many ways, which has resulted in some confusion and disagreement among clinicians, physiologists, psychologists, and bioengineers.[7,14-17] Because the *same nystagmus* may coexist with many clinical conditions, discrepancies exist when their differentiation is based solely on clinical evaluations. Classification of nystagmus based on accurate ocular motility investigations more closely reflects the ocular motor pathophysiologic mechanism of these conditions. The primary differentiation in a reasonable and useful classification of involuntary ocular oscillations should involve the genesis of the deficit (eg, slow phases [nystagmus] or fast phases [saccadic intrusions and oscillations]).[1,18,19] This

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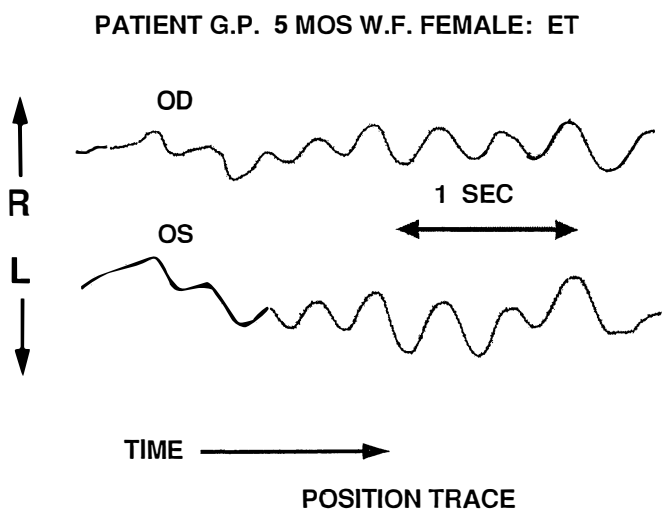


**FIG 1.** Eye movement recording of horizontal eye position in a 5-month-old girl with esotropia (patient #39) shows a 2 to 3 Hz asymmetric pendular waveform that is phase-conjugate (In this and subsequent Figures, *OD,* right eye; *OS,* left eye; upward deflections of tracing are rightward eye movements and downward deflections are leftward).

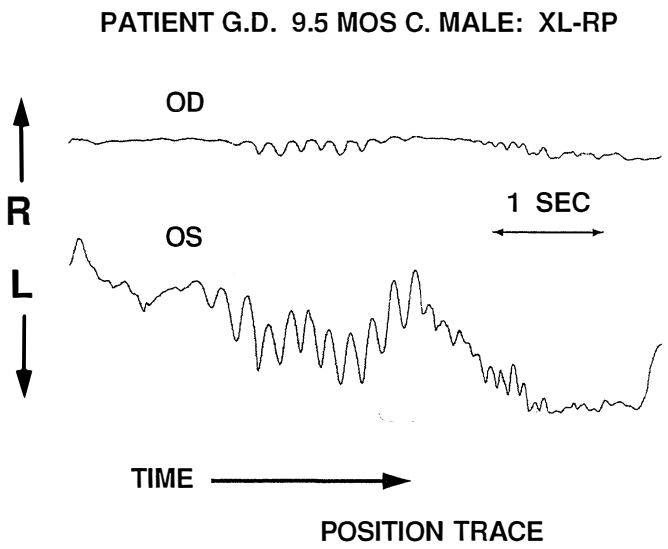


**FIG 2.** Eye movement recording of horizontal eye position in a 9.5-month-old boy (patient#12) with X-linked retinitis pigmentosa shows a 1 to 6 Hz phase-conjugate, pendular waveform with extended foveation in right eye that decreases in intensity with convergence.

classification system has resulted from ocular motor analysis during the past 30 years. Identification of the nystagmus waveform can definitively rule out certain causes and suggest others. However, there is not a one-to-one relationship between *general* waveform characteristics and *specific* clinical conditions; different clinical conditions may affect the ocular motor system in similar ways.

There are many types of ocular oscillations that result from disturbances in the slow eye movement system that are distinguishable by eye movement recording. These are termed *nystagmus* by most in the ocular motor community, reflecting the identification of the slow phases as the primary eye movement that disrupts fixation. Nystagmus oscillations may also contain fast phases that are corrective in nature (ie, they tend to move the eyes back to the target).[1,2,19] There are also a number of distinguishable types of ocular oscillations that result from disturbances in the fast eye movement system that are termed *saccadic* instabilities.[18] These oscillations may also contain slow phases that are corrective in nature.

The ocular motor systems of patients who have CN but not strabismus (with or without associated sensory deficits) are otherwise normal; they show normal smooth pursuit, saccadic, and vestibulo-ocular systems.[20-22] Because this oscillation usually begins in infancy, a better understanding of its clinical and ocular motor system characteristics at that time may help in explaining the common origin of the oscillation in patients with visual sensory system abnormalities and in those without. That is, because the infantile CN waveform evolves, an infant with a simple CN waveform has the same condition as an infant with a more complex waveform.

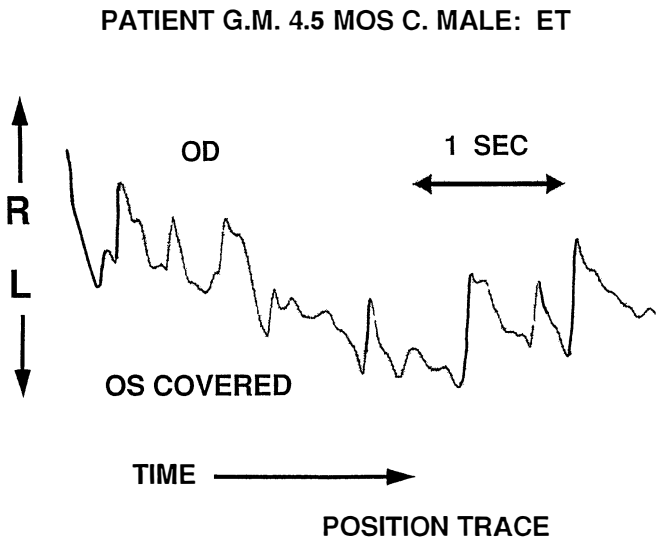


**FIG 3.** Eye movement recording of horizontal eye position in a 4.5-month-old boy (patient #21) with esotropia and left eye covered shows a 1 to 3 Hz jerk right with extended foveation waveforms.

## METHODS

### Clinical Data

Between August 12, 1992, and December 1, 1995, 243 patients underwent eye movement recordings at the ocular motor neurophysiology laboratory of The Children's Hospital of Philadelphia. All patients younger than 19 months of age with eye movement recording evidence of CN were included in this study. The motility-based diag-

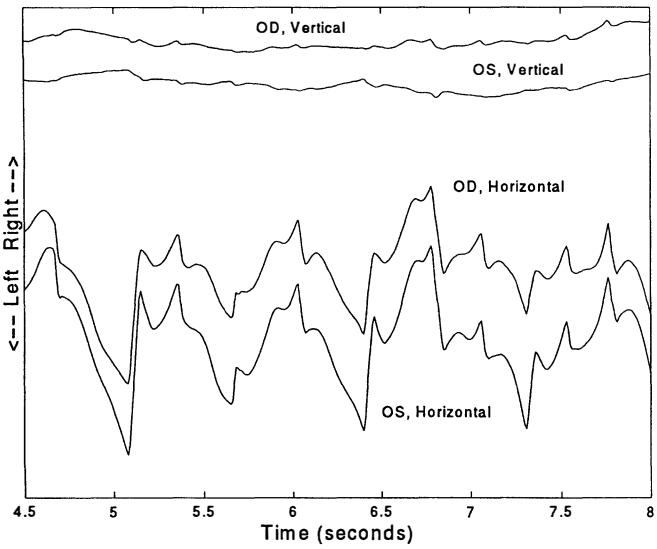


**FIG 4.** Eye movement recording of horizontal and vertical eye positions in a 17-month-old patient (patient #34) shows phase-conjugate horizontal 1.5 to 2.5 Hz bidirectional jerk with foveation waveforms.

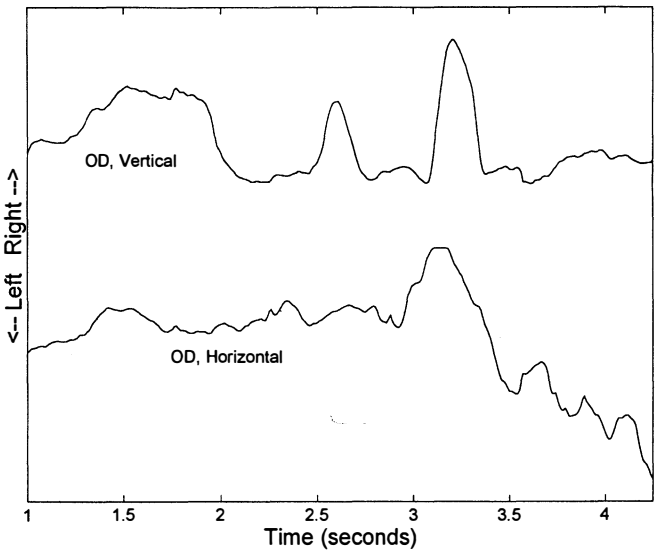


**FIG 5.** Three seconds of an eye movement recording displaying horizontal eye position in an 8-month-old patient with oculocutaneous albinism and optic nerve hypoplasia (patient #28) shows waveform variability

nosis of CN included oscillations that displayed waveforms consistent with CN, specifically increasing exponential slow phases with jerk fast phases or asymmetric pendular (AP) and pendular (P) oscillations with periods of foveation.[23] We included all patients with oculographically diagnosed CN regardless of their other associated ocular or systemic conditions to more fully establish early waveform characteristics. The mature CN waveforms of all patients are some combination of the same 12 waveforms, independent of the presence or type of visual-sensory-system abnormalities. We were primarily interested in each patient's oculographic characteristics as close to clinical presentation as possible. Our purpose was to demonstrate the rich variability of waveforms and foveation abilities present at an early age rather than recording changing waveforms and foveation patterns throughout infancy. Complete ophthalmic examination was performed on all patients by a pediatric ophthalmologist. In patients with clinical visual loss, additional testing included Teller acuity cards, electroretinogram, visual evoked responses, and magnetic resonance imaging (as indicated by clinical diagnosis, for example, optic nerve hypoplasia).

## Ocular Motor Recording

An Applied Science Laboratory (ASL) Model 210 Eye Movement Monitor was used in 27 of 43 infants in this study. This is a photoelectric technique that is capable of measuring horizontal eye movements over a range of ±30 degrees (linear within ±20 degrees) with an accuracy of 1 degree and a precision of less than 0.25 degree. With the head stabilized, each eye is independently calibrated while viewing horizontal fixation targets at known visual angles. Analog data from the ASL recording system were filtered with a bandwidth from 38 to 110 Hz and were sent to an R611 8-Channel Beckman Dynograph chart recorder for permanent strip chart recording. Four channels were used to record right and left eye position and velocity. The data in Figures 1, 2, and 3 were obtained using the ASL system.

Eye movement data were obtained on the remaining 16 of 43 infants using an Ober 2 system (Permobil Meditech, Inc; Woburn, Mass). This system uses goggles with an array of pulsed light–emitting infrared diodes, along with an array of photodetectors for each eye. Accurate measurements of eye movements of both eyes are obtained in a horizontal direction to within ±1 degree and vertical movements within ±2 degrees. The digitized data were stored on disk for further analysis. The data in Figs 4, 5, 6, and 7 were obtained using the Ober 2 system.

## Protocol

The infant was seated in a comfortable position in a parent's or caretaker's lap. When using the ASL, the glasses were held over the infant's eyes by the examiner using the forehead and brow to stabilize the goggles in front of the visual axis. After binocular recording, a patch was placed over each eye to record the patient's ocular response to monocular cover. This method, in use for more than 2 decades, produces clear, artifact-free records of CN waveforms in infants and young children. Although the amplitudes of the CN in either eye cannot be determined (ie, the data are not calibrated), all phase and timing information (eg, interocular foveation time, asymmetry) can be accurately measured. When using the Ober 2 system, the goggles are comfortably placed on the child's face, and the head is held steady by the examiner. The left and right eye were occluded with an opaque trial lens placed in a holder

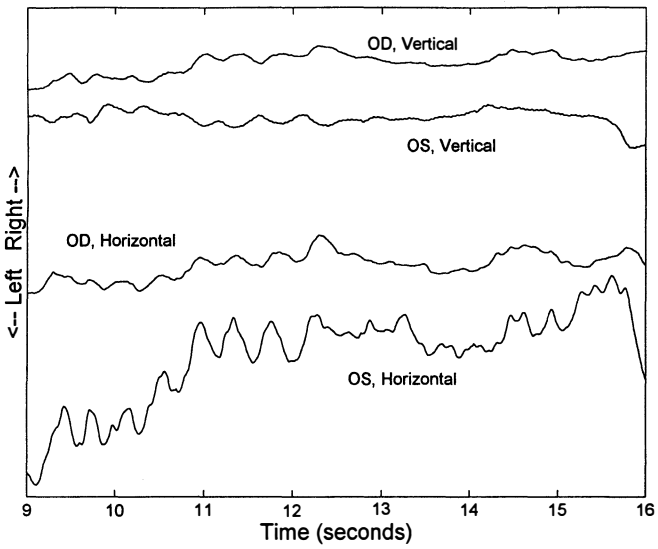


**FIG 6.** Eye movement recording of horizontal and vertical eye positions in a 10-month-old patient (patient# 26) shows 1.5 to 3.0 Hz jerk and asymmetric pendular waveforms.

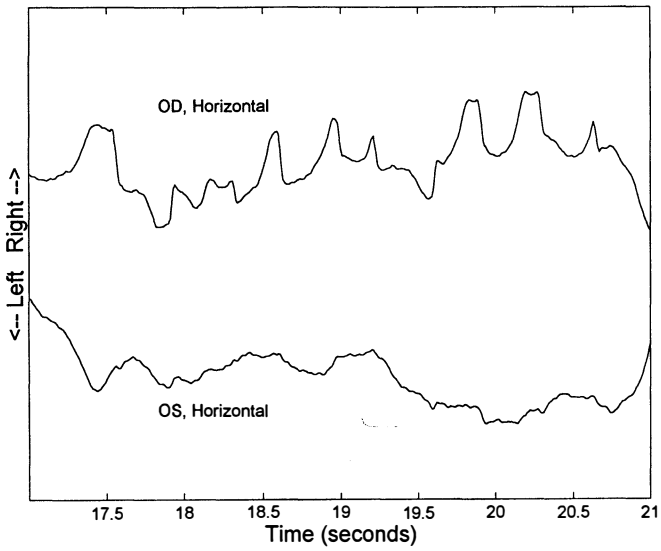


**FIG 7.** Eye movement recording of horizontal eye position in a 13-month-old boy (patient #35) with esotropia and amblyopia of the right eye.

attached to the front of the goggles. At all times during recording, attempts were made to pacify the child and obtain their attention to as distant an object as possible. When possible, attempts were made to have the child look to the right and left as well as near while recording the oscillation's response to gaze and vergence changes.

### Data Analysis

Eye movement data analyzed for this study included the average binocular and monocular frequencies that were computed from at least 60 seconds of data. Interocular conjugacy and amplitude-symmetry were analyzed directly from the recordings by comparing the right-eye and left-eye positions throughout the same periods used for frequency and foveation analysis. If the 2 eyes were moving in the same direction during this time, the movement was considered conjugate. The type of waveforms present were classified according to the previously described 12 waveforms associated with horizontal CN.[23] Because of the sensitivity of these recording techniques, foveation periods and fast and slow phases could be identified during almost all cycles. In the absence of accurate calibration, a foveation period was defined as a relatively constant eye position that occurred during an oscillatory cycle, usually followed a fast phase, and lasted for at least 40 ms. This approximation to foveation-period durations yielded values that were higher than those determined by accurate position and velocity criteria. However, interpatient comparisons could still be made. For foveation periods to be included in data analysis, a minimum of 40 cycles that contained foveation periods were required. All eye movement data were analyzed off line. Waveform percentages were calculated using the following formula: waveform % = (# cycles waveform present / # total cycles) × 100.

## RESULTS

### Clinical Characteristics

All patients in this study met 2 inclusion criteria: (1) they were all younger than 19 months of age; and (2) they had motility-recording evidence of involuntary ocular oscillations with typical waveforms characteristics of CN. Sixty percent were male, with ages ranging from 3 to 18 months (average, 9.2 months). Vision was abnormal in at least 1 eye in 17 patients (40%); this was unilateral in 7 patients. Ophthalmic pathologic findings are reported in Table 1.

### Ocular Motility Characteristics

The average binocular frequency was 2.86 Hz, and the average monocular frequency was 4.57 Hz. Although precise calibration was inconsistent, there was evidence of interocular asymmetry manifested by amplitude differences in 33% of patients. There were occasional episodes of dysconjugate oscillations in many patients that were inconsistent and probably reflected voluntary vergence movements (stimulus parameters were difficult to control). Average foveation time was 139.7 ms for all patients (Table 2). There was a significant difference ($P < .05$) in binocular foveation periods between those patients who had normal vision (180 ms) and those with abnormal vision (77 ms) (Table 2).

Waveform subtypes could be clearly distinguished on tracings from both eye movement recording systems (Figures 1 and 2). All patient recordings displayed mixtures of P, AP, jerk (J), jerk with extended foveation (Jef), and bidirectional jerk/dual jerk (BDJ/DJ) waveforms. Analysis of waveform types and age are illustrated in Figures 8 and 9 and in Table 2.

**TABLE 1.** Clinical characteristics

| Patient | Age (mo) | Sex | Vision | Eye disease | Head posture | Null | Neutral |
|---|---|---|---|---|---|---|---|
| 1 | 12 | F | Abnormal | XT, amblyopia | No | Yes | Yes |
| 2 | 11.5 | M | Normal | | Yes | Yes | Yes |
| 3 | 13 | M | Abnormal | NF, ONA | No | No | No |
| 4 | 6 | M | Normal | | Yes | Yes | Yes |
| 5 | 6 | M | Abnormal | FH, OCA, ET | Yes | Yes | Yes |
| 6 | 5 | M | Normal | | No | Yes | Yes |
| 7 | 4.5 | M | Abnormal | OCA, ONH, FH | No | No | No |
| 8 | 4 | M | Normal | | No | Yes | Yes |
| 9 | 12 | F | Abnormal | CVI, prematurity | No | No | Yes |
| 10 | 6 | F | Normal | | No | No | No |
| 11 | 15 | F | Abnormal | ET, amblyopia | Yes | Yes | Yes |
| 12 | 9.5 | F | Abnormal | X-L-RP | No | Yes | Yes |
| 13 | 4 | M | Normal | | No | No | No |
| 14 | 11 | M | Normal | | Yes | Yes | Yes |
| 15 | 6 | F | Abnormal | OCA, ONH, XT | No | No | No |
| 16 | 12 | M | Normal | | Yes | Yes | Yes |
| 17 | 9 | M | Normal | | No | No | No |
| 18 | 3 | F | Abnormal | CVI | No | Yes | Yes |
| 19 | 14 | F | Normal | | Yes | Yes | Yes |
| 20 | 10 | F | Abnormal | ET, CVI | Yes | Yes | Yes |
| 21 | 4.5 | M | Normal | ET, amblyopia | Yes | Yes | Yes |
| 22 | 11 | F | Normal | | No | No | No |
| 23 | 12 | M | Normal | ET, amblyopia | No | Yes | Yes |
| 24 | 11 | M | Normal | | No | No | Yes |
| 25 | 5.5 | F | Normal | | No | Yes | Yes |
| 26 | 10 | F | Normal | | No | No | No |
| 27 | 11 | M | Abnormal | CVI | No | No | No |
| 28 | 8 | F | Abnormal | OCA | Yes | Yes | No |
| 29 | 7 | M | Abnormal | ONH | No | No | No |
| 30 | 13 | M | Abnormal | ET, amblyopia | Yes | Yes | Yes |
| 31 | 7.5 | F | Normal | ET | Yes | Yes | Yes |
| 32 | 16 | M | Normal | | No | No | No |
| 33 | 4 | M | Normal | | No | Yes | Yes |
| 34 | 17 | M | Normal | | Yes | Yes | Yes |
| 35 | 13 | M | Abnormal | ET, amblyopia | Yes | Yes | Yes |
| 36 | 5 | M | Normal | | No | Yes | Yes |
| 37 | 9 | F | Normal | | Yes | Yes | No |
| 38 | 14 | M | Normal | | No | No | No |
| 39 | 5 | F | Abnormal | ET, amblyopia | No | Yes | Yes |
| 40 | 18 | F | Normal | | No | No | No |
| 41 | 10 | M | Normal | | Yes | Yes | Yes |
| 42 | 5.5 | M | Normal | | No | No | No |
| 43 | 5 | M | Abnormal | ONH, CVI | No | No | No |
| Totals | 9.2* | 60%† | 40%‡ | | 37 | 60 | 60 |

*Average age (mo).

†Percent male.

‡Percent with abnormal VA.

*XT,* Exotropia; *NF,* neurofibromatosis; *ONA,* optic nerve atrophy; *FH,* foveal hypoplasia; *OCA,* oculocutaneous albinism; *ET,* esotropia; *ONH,* optic nerve hypoplasia; *CVI,* cortical visual impairment; *X-L-RP,* x-linked retinitis pigmentosa.

Both patients with normal vision and those with abnormal vision had all types of waveforms documented by eye movement recording. Further analysis showed that a higher percentage of patients with abnormal vision had pendular and asymmetric pendular waveforms than patients with normal vision, whereas a higher percentage of patients with normal vision had jerk waveforms than those with abnormal vision (Figure 10, Table 2). In addition to horizontal oscillations, occasional vertical oscillations were noted. They were characterized by P and occasionally AP waveforms of the same frequency as the horizontal oscillation (Figure 6). Asymmetric recording characteristics

**TABLE 2.** Ocular motor characteristics

| Patient | Asymmetry | Conjugacy | Waveform type | Mean frequency, binocular (ms) | Mean frequency, cover (ms) | Mean binocular foveation (ms) | Foveation VA normal (ms) | Foveation VA abnormal (ms) |
|---|---|---|---|---|---|---|---|---|
| 1 | Yes | Yes | P/AP/JEF | 3.5 | 4.5 | 75 | — | 75 |
| 2 | No | Yes | P/AP/JEF | 2 | 3.5 | 160 | 160 | — |
| 3 | Yes | Yes | P/AP/JEF/DJ | 3 | 5 | 80 | — | 80 |
| 4 | No | Yes | AP/JEF | 2.5 | 3 | 190 | 190 | — |
| 5 | Yes | Yes | P/JEF | 4.5 | 6 | 60 | — | 60 |
| 6 | No | Yes | P/JEF | 3 | 5.5 | 180 | 180 | — |
| 7 | Yes | Yes | P/AP/JEF | 3.5 | 6.5 | 40 | — | 40 |
| 8 | No | No | P/JEF/J | 1.5 | 3 | 210 | 210 | — |
| 9 | Yes | Yes | P/AP | 4 | 5.2 | 80 | — | 80 |
| 10 | No | Yes | AP/JEF | 2.2 | 4 | 130 | 130 | — |
| 11 | Yes | Yes | P/AP/DJ | 3.6 | 4.8 | 120 | — | 120 |
| 12 | Yes | Yes | AP/JEF/BDJ | 4.5 | 5.8 | 40 | — | 40 |
| 13 | No | Yes | P/AP/JEF | 2.3 | 4.8 | 240 | 240 | — |
| 14 | No | Yes | AP/JEF | 1.8 | 3.3 | 200 | 200 | — |
| 15 | Yes | Yes | P/AP | 3 | 4.5 | 100 | — | 100 |
| 16 | No | Yes | JEF/BDJ | 1.8 | 2.9 | 190 | 190 | — |
| 17 | No | Yes | AP/JEF/J | 2 | 4.4 | 260 | 260 | — |
| 18 | No | No | AP/P | 2.7 | 5.6 | 90 | — | 90 |
| 19 | No | Yes | JEF/AP/J | 1 | 3.3 | 110 | 110 | — |
| 20 | Yes | Yes | AP/P | 3 | 5.2 | 40 | — | 40 |
| 21 | No | Yes | AP/J/JEF | 1.7 | 3.2 | 215 | 245 | — |
| 22 | No | Yes | J/JEF | 2.2 | 3.8 | 145 | 145 | — |
| 23 | No | Yes | J/JEF/AP | 2.7 | 4.2 | 180 | 180 | — |
| 24 | No | Yes | AP/J/JEF | 2.2 | 3.6 | 150 | 150 | — |
| 25 | No | Yes | AP/P/J | 2.8 | 4.7 | 200 | 200 | — |
| 26 | No | Yes | AP/JEF | 1.9 | 3.4 | 240 | 240 | — |
| 27 | No | Yes | P/AP | 4.4 | 5.9 | 60 | — | 60 |
| 28 | No | Yes | P/AP/JEF | 3.2 | 4.6 | 80 | — | 80 |
| 29 | No | Yes | P/AP | 5.5 | 6.6 | 70 | — | 70 |
| 30 | Yes | Yes | J/JEF | 3.2 | 4.4 | 140 | — | 140 |
| 31 | No | Yes | J/JEF | 2.2 | 3.6 | 160 | 160 | — |
| 32 | No | Yes | J/JEF/BDJ | 2.8 | 4.5 | 210 | 210 | — |
| 33 | No | Yes | AP/J | 2.9 | 4.1 | 185 | 185 | — |
| 34 | No | Yes | AP/J/JEF | 2 | 3.7 | 200 | 200 | — |
| 35 | Yes | Yes | AP/JEF | 3.3 | 4.5 | 110 | — | 110 |
| 36 | No | Yes | AP/JEF | 3 | 5 | 180 | 180 | — |
| 37 | Yes | Yes | AP/P/J/JEF | 2.5 | 4.8 | 240 | 240 | — |
| 38 | No | Yes | J/JEF | 2.5 | 5 | 215 | 215 | — |
| 39 | Yes | Yes | AP/J/JEF | 3.8 | 4.3 | 60 | — | 60 |
| 40 | No | Yes | J/JEF/DJ | 2 | 4.5 | 190 | 190 | — |
| 41 | No | Yes | J | 2.8 | 5.2 | 160 | 160 | — |
| 42 | No | Yes | J/JEF | 3.3 | 6.2 | 80 | 80 | — |
| 43 | Yes | No | AP/P/J | 4.8 | 5.8 | 70 | — | 70 |
| Totals | 33%* | 93%† | | 2.86 | 4.57 | 142.67 | Ave 185 | Ave 77 |

*Percent with asymmetry.
†Percent with conjugacy.
*VA,* Visual acuity; *P,* pendular; *AP,* asymmetric pendular; *JEF,* jerk with extended foveation; *DJ,* dual jerk; *J,* jerk; *BDJ,* bidirectional jerk.

between the eyes, either under binocular or monocular viewing conditions, often reflected clinical afferent visual system asymmetry (Figure 7). A latent component was present in 47% of patients. Clinically, an erroneous diagnosis of manifest latent nystagmus was made before recordings in 5 of 8 infants in this study who had esotropia and nystagmus.

## DISCUSSION

*Congenital* means, by definition, "present at birth." Strict application of this term to the different types of infantile nystagmus has caused confusion. CN has been documented to be present at birth (especially in cases of hereditary CN, where it was observed by family members and physicians). CN is but 1 of a number of types of nystagmus (eg,

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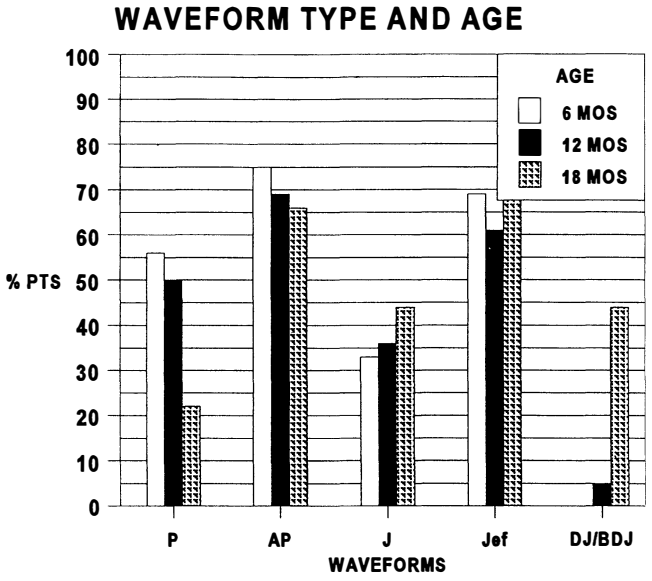


**FIG 8.** Percentages of 16 patients 2 to 6 months of age, 18 patients 7 to 12 months of age, and 9 patients 13 to 18 months of age who exhibit CN waveform subtypes. *P,* Pendular waveform; *AP,* asymmetric pendular waveform; *J,* jerk waveform; *Jef,* jerk waveform with extended foveation; *DJ/BDJ,* dual jerk and bidirectional jerk waveforms.

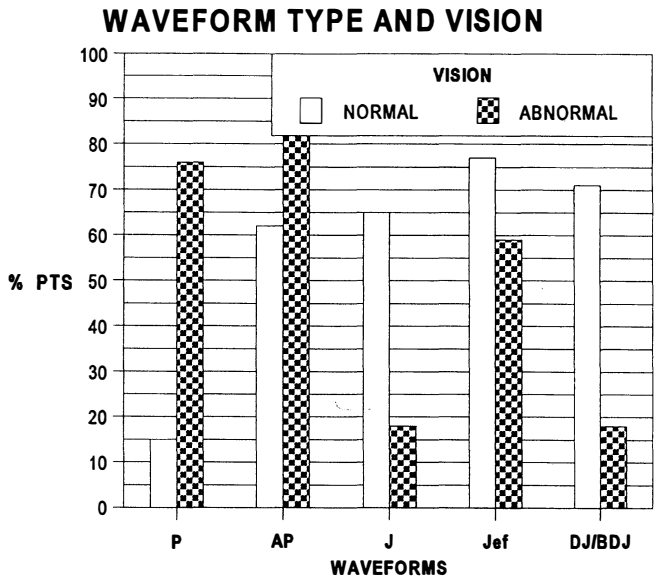


**FIG 10.** Comparison of percentage of 26 patients with normal vision with percentage of 17 patients with abnormal vision who display each CN waveform. *P,* Pendular waveform; *AP,* asymmetric pendular waveform; *J,* jerk waveform; *Jef,* jerk waveform with extended foveation; *DJ/BDJ,* dual jerk and bidirectional jerk waveforms.

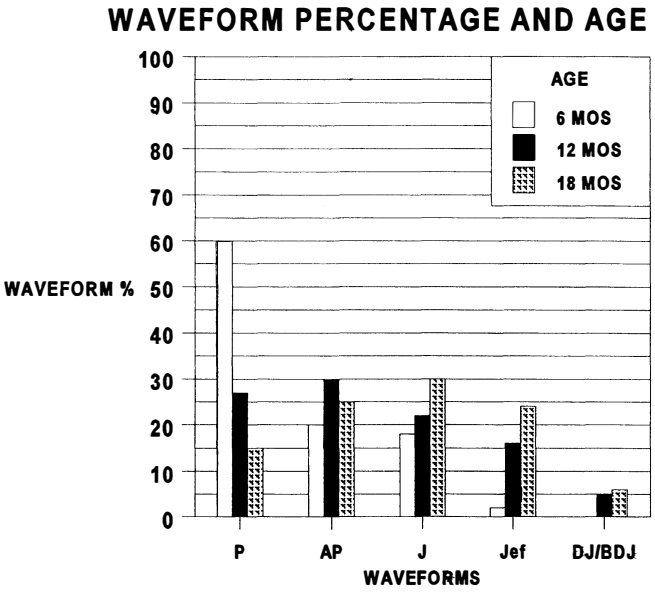


**FIG 9.** Percentage of each waveform present in 16 patients 2 to 6 months of age, 18 patients 7 to 12 months of age, and 9 patients 13 to 18 months of age. *P,* Pendular waveform; *AP,* asymmetric pendular waveform; *J,* jerk waveform; *Jef,* jerk waveform with extended foveation; *DJ/BDJ,* dual jerk and bidirectional jerk waveforms.

LMLN or spasmus nutans) that are usually observed in the first few months of life.[1,2,7,17-19] Estimates of its incidence range from 1 in 350 to 1 in 6550.[15,17,23] Before ocular motility analysis demonstrated that CN was a single entity (ie, the same ocular motor sign regardless of the presence of associated sensory abnormalities), CN was classified as "pathologic" if a central nervous system abnormality was found that "explained" the oscillation (for example, tumor). It was classified as "sensory" nystagmus if the patient also had an ocular abnormality associated with decreased vision (for example, retinal dysplasia). By process of exclusion, it was classified as "motor" nystagmus if no associated central nervous system or vision abnormality was clinically evident. Unfortunately, some clinical literature still contains these antiquated and misleading terms.

CN is an eye sign (quite simply, a motor oscillation); its direct cause appears to be an increase in the normal oscillation of the pursuit system.[24] Attempts to split 1 oscillation into 2 ("sensory" and "motor") miss the point of the past 3 decades of ocular motor research into CN and will continue to mislead all but the few with expertise in this area. A patient with both CN and a sensory disorder has *2* disorders, each deserving of a specific, descriptive diagnosis (eg, CN plus aniridia or CN plus albinism). Neither is the direct cause of the other; such patients share the same CN as those with idiopathic or hereditary CN. If the historical name *CN* is no longer deemed adequate to describe this specific type of infantile nystagmus, we recommend that the name be changed to one that accurately describes the underlying mechanism and *does not* mislead the reader into believing that the nystagmus is dependent on either the time of onset or the presence of associated sensory abnormalities. We suggest *pursuit system nystagmus* or

*smooth pursuit nystagmus*. This nomenclature meets the above criteria; *infantile nystagmus* does not, and it should continue to be used as a general "catch-all" term for the group of nystagmus types that usually become manifest in infancy (eg, CN, LMLN, spasmus nutans).

Recordings have repeatedly demonstrated that the initial clinical impression of the type of nystagmus was incorrect in a percentage of cases.[1,2,15,17,18,23] Because most clinical diagnoses are not checked by objective eye movement recordings, clinicians may not realize how often their diagnosis is incorrect. CN does have well-described, but not diagnostic, clinical characteristics. These include onset in infancy, conjugacy, uniplanar movement (usually horizontal), increased intensity in eccentric gaze and with increased fixation effort (sometimes with monocular cover), disappearance with sleep, decreased intensity with eyelid closure (unless the subject is willfully directing their gaze), and convergence. Well-defined null and neutral positions of gaze and associated head posturing, head oscillations, or both may also be present. These characteristics are based on descriptions of CN in its mature form in older children and adults.[1,7,13-15,23] Formal reports on its appearance limited to infancy are rare.[31]

In this study, strabismus was present in 11 patients (26%). Vision was abnormal in at least 1 eye in 17 patients (40%); this was bilateral in 10 patients. The most common visual abnormalities were caused by congenital optic nerve or retinal anomalies. Other visual abnormalities occurred as a result of mixed-mechanism visual system disease (anterior and posterior visual impairment) and strabismic amblyopia. Associated clinical characteristics included intermittent head or face posturing in 67% and a null and neutral zone other than primary position in 60% of patients (Table 1). The absence of a head turn could indicate either a null position in primary position or no null position at all. The high incidence of associated clinical conditions could reflect a referral bias. Despite the incidence of associated clinical conditions in the CN population, this study shows that the clinical spectrum of CN can be well developed by the end of infancy. The fact that normally sighted as well as visually impaired patients had typical CN waveforms is not a new finding.[4-6,25-30] This finding in infancy reemphasizes the need to recognize CN as a single entity.

Most of the specific waveforms identified in CN are diagnostic, being found in no other type of nystagmus.[1,2,18,20,21,23] Increasing velocity exponential slow phases, with no other distinguishing characteristics, strongly suggest CN; they have only been noted in 1 other form of nystagmus acquired after a cerebellar hemorrhage.[31] Different jerk waveforms may be present at any one time or position of gaze in the same patient.[19,23] Individuals and families with CN consistently display the same subset of the 12 possible CN waveforms.[12,13] As seen in Figures 8 and 9, combinations of representative CN waveforms are present in infants with CN. The most common waveforms for infants younger than 7 months of age were pendular, asymmetric pendular (80%), and jerk with and without extended foveation. More complicated jerk waveforms (60%) were observed when patients were older than 6 months of age. In a previous study of 35 infants using contact electro-oculography, "triangular" waveforms were present most commonly (70%) in infants younger than 6 months of age, with 18% pendular and 12% jerk.[32] By 18 months of age, only 7% of waveforms were triangular with pendular and jerk predominating; the triangular waveforms disappeared by 2 years of age. Our study also showed changes in the predominant waveforms with age (Figure 9). The absence of purely triangular waveforms (ie, with linear slow phases) in our patients may be a result of the use of different recording methods. It is possible that such waveforms may have been observed if our recording apparatus was linear at amplitudes greater than ±20 degrees. Contact electro-oculography is less able to depict waveform details than infrared oculography. More subtle changes in waveform with age (eg, breaking and foveating saccades and extended foveation periods) reflect the effect of visual system maturation on the oscillation. Many parallel visual processes (eg, acuity, contrast, color, fusion, and motion perception) may influence the clinical and waveform maturation of CN.[33,34]

Attempts have been made to correlate visual function with clinical characteristics and waveforms in patients with CN[6,19,20-22,25,35-37]; in any 1 patient they may ultimately be determined by the integrity of the afferent visual system. A sensitive measure of the afferent system is represented in motility recordings by "foveation" periods,[13] periods during a CN cycle when the eyes are most stable and the patient sees most clearly. Patients with more normal visual sensory systems exhibit "well-developed" foveation strategies (ie, beat-to-beat accuracy). Foveation time is a better indicator of visual function than the often-used nystagmus "intensity."[12,13,20-23] Recently, a "nystagmus acuity function" was created that is linearly related to visual acuity.[37] This is a motility-based function obtained from well-calibrated oculographic recordings in older children and adults. It is calculated on the basis of the period of time during the nystagmus cycle in which the fovea is within ±0.5 degrees of the target and the eye is traveling at less than 4 degrees per second. The longer these periods of time, the better the visual acuity. In our study, the average foveation time viewing binocularly was considerably greater in patients with clinically normal vision (180 ms) than in those patients with abnormal vision (77 ms) (Table 2).

Our data demonstrate that "mature" CN waveforms are present and continue to develop during infancy and that accurate diagnosis of CN in infancy can be easily accomplished using standard ocular motor recording techniques. An evolution of waveforms during infancy from pendular to jerk was also shown, which is consistent with the theory that jerk waveforms reflect modification of the CN oscillation by growth and development of the visual sensory system. We demonstrated that many forms of sensory

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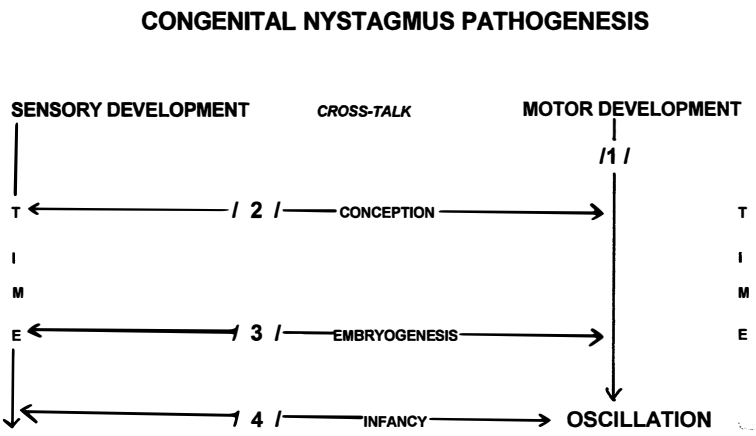


**FIG 11.** Developmental model suggests pathophysiologic interruption of normal sensory-motor system development as a result of a primary abnormality of the motor system (eg, genetic) leading to CN.

abnormalities[4,9,10,16,24] may be associated with typical CN motility. Accurate and repeatable classification and diagnosis of CN is best accomplished by a combination of clinical and motility findings; the latter are sometimes indispensable for diagnosis. Additional benefits of eye movement recordings include differentiating CN from MLN; differentiating CN with a latent component from LMLN; differentiating the nystagmus blockage syndrome from either convergence damping in CN or esotropia damping in LMLN; and differentiating the variable phase waveforms of spasmus nutans from CN. They also identify the exact null position in CN to determine the proper amount of globe rotation required in the Anderson-Kestenbaum procedure; to determine whether convergence will allow greater foveation time per cycle and thus better visual acuity; and to allow the use of the nystagmus acuity function to predict the best possible acuity at any gaze angle and to predict this result after Anderson-Kestenbaum surgery.

Analysis of binocular or monocular differences in waveforms and foveation periods reflect development of the afferent visual system. Pure pendular or jerk waveforms *without foveation periods* are usually associated with poorer vision, whereas waveforms of either type *with extended periods of foveation* may indicate better vision. Significant interocular differences in a patient may reflect similar differences in vision. Ocular motility analysis in infants also accurately determines nystagmus changes with gaze (null and neutral zones). Differentiating CN from other childhood oscillations is important when making decisions regarding surgical treatment. For example, in a child with both nystagmus and strabismus who has a head posture, the latter may be caused by either. There may be a "gaze null" associated with CN or an "adduction null" associated with LMLN. Differentiation is crucial for both the strabismus and nystagmus to be properly treated.

Despite numerous studies of CN pathophysiologic mechanism, its cause remained elusive. Defects involving the saccadic, optokinetic, smooth pursuit, and fixation systems, as well as the neural integrator for conjugate horizontal gaze, have been proposed.[16,17] Control-system models have reproduced this oscillation, and it has been attributed to a "high-gain instability" in the ocular motor system.[1,2,18,19,23] This loosely translates as an error in "calibration" of the eye movement system during attempted fixation. Many clinical conditions, including genetic predisposition, are associated with the CN oscillation. Regardless of the clinical associations, nearly all patients with CN have infantile onset in common; this oscillation is most likely to occur in an immature ocular motor system. The etiologic mechanism can be multifactorial if the final common pathway is interference with ocular-motor calibration during a period of sensitivity. Sensitive periods during development of visual function are well recognized, for example, visual acuity and binocularity.[33,34]

A model for development of CN is illustrated in Figure 11. Motor-system calibration is an active process that may start in utero and continue at least through early infancy. Sensory-system development is a parallel visual process that continues to develop through the first decade of life.[29,30] Previous studies documented connections between parallel visual processes (cross-talk) that modify, instruct, and coordinate these systems, resulting in smooth and coordinated function.[30] CN may result from a primary defect (familial, genetic) (*1*, Figure 11) of ocular-motor calibration. CN may also result from abnormal cross-talk from a defective sensory system to the developing motor system at any time during the motor system's sensitive period. This can occur: from conception as a result of a primary defect (retinal dystrophy) (*2*, Figure 11), during embryogenesis as a result of a developmental abnormality (optic nerve hypoplasia) (*3*, Figure 11), or after birth during infancy (congenital cataracts) (*4*, Figure 11). This hypothetical genesis of CN incorporates a pathophysiologic role for the sensory system. Although the physiologic circumstances may differ, the final common pathway is abnormal calibration of the ocular motor system during its

sensitive period. The primary ocular motor instability that underlies CN remains the same, but its clinical and oculographic expression are modified by both initial and final developmental integrity of all parallel afferent visual system processes. As the bidirectional arrows suggest, abnormal motor development also affects sensory development.

## References

1. Dell'Osso LF, Schmidt D, Daroff RB. Latent, manifest latent and congenital nystagmus. Arch Ophthalmol 1979;97:1877-85.
2. Dell'Osso LF. Congenital and latent/manifest latent nystagmus; diagnosis, treatment, foveation, oscillopsia, and acuity. Jpn J Ophthalmol 1994;38:329-36.
3. Abadi RV, Pascal E. Ocular motor behavior of monozygotic twins with tyrosinase negative oculocutaneous albinism. Br J Ophthalmol 1994;78:349-52.
4. Cibis GW, Fitzgerald KM. Electroretinography in congenital idiopathic nystagmus. Pediatr Neurol 1993;9:369-71.
5. Stang HJ. Developmental disabilities associated with congenital nystagmus. J Dev Behav Pediatr 1991;12:322-3.
6. Spierer A. Etiology of reduced visual acuity in congenital nystagmus. Ann Ophthalmol 1991;23:393-7.
7. Gelbart SS, Hoyt CS. Congenital nystagmus: a clinical perspective in infancy. Graefes Arch Clin Exp Ophthalmol 1988;226:178-80.
8. Apkarian P, Shallo-Hoffmann J. VEP projection in congenital nystagmus: VEP symmetry in albinism: a comparison study [published correction appears in Invest Ophthalmol Vis Sci 1992;33:691-2]. Invest Ophthalmol Vis Sci 1991;32:2653-61.
9. Abadi RV, Pascal E. Visual resolution limits in human albinism. Vision Research 1991;31:1445-7.
10. Lambert SR, Taylor D, Kriss A. The infant with nystagmus, normal appearing fundi, but an abnormal ERG [review]. Surv Ophthalmol 1989;34:173-86.
11. Fielder AR, Evans NM. Is the geniculostriate system a prerequisite for nystagmus? Eye 1988;2:628-35.
12. Dell'Osso LF, Flynn JR, Daroff RB. Hereditary congenital nystagmus: an intrafamilial study. Arch Ophthalmol 1974;92:366-74.
13. Dell'Osso LF. Fixation characteristics in hereditary congenital nystagmus. Am J Optom Arch Am Acad Optom 1973;50:85-90.
14. Jan JE, Carruthers JD, Tillson G. Neurodevelopmental criteria in the classification of congenital motor nystagmus. Can J Neurol Sci 1992;19:76-9.
15. Casteels I, Harris CM, Shawkat F, Taylor D. Nystagmus in infancy [review]. Br J Ophthalmol 1992;76:434-7.
16. Willshaw HE. Assessment of nystagmus [review]. Arch Dis Child 1993;69:102-3.
17. Scott AB. Nystagmus. Int Ophthalmol Clin 1964;4:755-73.
18. Dell'Osso LF. Nystagmus, saccadic intrusions/oscillations and oscillopsia. In: Lessell S, Van Dalen JTS, editors. Current neuro-ophthalmology. Vol 3. Chicago: Mosby–Year Book; 1991. p. 153-91.
19. Dell'Osso LF, Gauthier G, Liberman G, Stark L. Eye movement recordings as a diagnostic tool in a case of congenital nystagmus. Am J Optom Am Acad Optom 1972;49:3-13.
20. Dell'Osso LF, van der Steen J, Steinman RM, Collewijn H. Foveation dynamics in congenital nystagmus. II: Smooth pursuit. Doc Ophthalmol 1992;79:25-49.
21. Dell'Osso LF, van der Steen J, Steinman RM, Collewijn H. Foveation dynamics in congenital nystagmus. III: Vestibulo-ocular reflex. Doc Ophthalmol 1992;79:51-70.
22. Dell'Osso LF, van der Steen J, Steinman RM, Collewijn H. Foveation dynamics in congenital nystagmus. I: Fixation. Doc Ophthalmol 1992;79:1-23.
23. Dell'Osso LF, Daroff RB. Congenital nystagmus waveforms and foveation strategy. Doc Ophthalmol 1975;39:155-82.
24. Dell'Osso LF, Averbuch-Heller L, Leigh RJ. Oscillopsia suppression and foveation-period variation in congenital, latent, and acquired nystagmus. Neuroophthalmology 1997;18:163-83.
25. Abadi RV, Rascal E. Periodic alternating nystagmus in humans with albinism. Invest Ophthalmol Vis Sci 1994;35:4080-6.
26. Bedell HE, Loshin DS. Interrelations between measures of visual acuity and parameters of eye movement in congenital nystagmus. Invest Ophthalmol Vis Sci 1991;32:416-21.
27. Tusa RH, Repka MX, Smith CB, Herdman SJ. Early visual deprivation results in persistent strabismus and nystagmus in monkeys. Invest Ophthalmol Vis Sci 1991;32:134-41.
28. Gottlob I. Eye movement abnormalities in carriers of blue-cone monochromatism. Invest Ophthalmol Vis Sci 1994;35:3556-60.
29. Keith CG. Incomplete achromatopsia; diagnosis in infancy. Birth Defects: Original Article Series 1982;18:269-80.
30. Wybar K. Significance of nystagmus in suspected blindness in infancy. Isr J Med Sci 1972;8:1492-5.
31. Barton JJS, Sharpe JA. Oscillopsia and horizontal nystagmus with accelerating slow phases following lumbar puncture in the Arnold-Chiari malformation. Ann Neurol 1993;33:418-21.
32. Reinecke RD, Guo S, Goldstein HP. Waveform evolution in infantile nystagmus: an electro-oculographic study of 35 cases. Binocular Vision 1988;4:191-202.
33. Braddick O, Atkinson J. The development of binocular function in infancy. Acta Ophthalmol Scand Suppl 1983;157:27-35.
34. Braddick O, Atkinson J. Some recent findings on the development of human binocularity: a review. Behav Brain Res 1983;10:141-50.
35. Dell'Osso LF. Eye movements, visual acuity and spatial constancy. Acta Neurol Belg 1991;91:105-13.
36. Funahashi K, Yabumato M, Nakai M, Miyamoto T, Fujii T, Komai N. Relations between visual acuity and waveform on electronystagmograms (ENG) of congenital nystagmus. Neuroophthalmology Jpn 1984;1:414-9.
37. Sheth NV, Dell'Osso LF, Leigh RJ, Van Doren CL, Peckam HP. The effects of afferent stimulation on congenital nystagmus foveation periods. Vision Res 1995;35:2371-82.