CONGENITAL AND LATENT/MANIFEST LATENT NYSTAGMUS: DIAGNOSIS, TREATMENT, FOVEATION, OSCILLOPSIA, AND ACUITY

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Summary: Congenital (CN) and latent/manifest latent nystagmus (LMLN) are the two most common types of benign infantile nystagmus. They can be distinguished definitively by eye-movement recordings; their clinical characteristics are too similar to allow reliable differential diagnosis. Most treatments for CN, surgical or optical, depend on exploitation of either a gaze-angle or convergence null. Other treatments are emerging that may prove beneficial for those individuals lacking either of these nulls. Early surgical treatment for the strabismus accompanying LMLN may convert the nystagmus into LN only, thereby improving visual acuity (OU). Target foveation is preserved in both CN and LMLN and repetitive (cycle-to-cycle) foveation periods appear to be responsible for the absence of oscillopsia in these individuals. The ability to foveate a target for substantial periods of time each cycle, with little variation in eye position or velocity, may result in normal visual acuities despite the nystagmus.

Key Words: Acuity, congenital nystagmus, latent nystagmus, oscillopsia

Introduction

There are several benign types of nystagmus that are commonly associated with infancy. As a group they can be included under the umbrella term, “infantile nystagmus.” However, each is a distinct type of nystagmus with specific waveforms, underlying mechanisms and, to a lesser extent, clinical characteristics. They include: congenital nystagmus (CN), latent/manifest latent nystagmus (LMLN), and spasmus nutans. In addition, some individuals with CN can damp their nystagmus while fixating a distant target by employing a purposive esotropia. This “nystagmus blockage syndrome” results in either a low-amplitude CN or MLN. Finally, some individuals may exhibit both CN and LMLN waveforms, separately or in combination.

Infants may also present with symptomatic nystagmus. This includes: downbeat nystagmus, indicating structural lower brain stem abnormalities; epileptic nystagmus; uniocular nystagmus, indicating a possible optic nerve glioma; vestibular nystagmus, indicating vestibular asymmetry; and the so called, “nystagmus” of the blind. Clearly, symptomatic nystagmus must be differentiated from the benign forms because neurological workup and possible treatment are indicated for the former. Figure 1 lists the types of infantile nystagmus in both broad categories.

The remainder of this review will be focussed on the two most common types of benign infantile nystagmus, CN and LMLN. Specifically, differential diagnosis, treatment,
Figure 1. Tree showing various types of both benign and symptomatic infantile nystagmus.

- CN: congenital nystagmus
- LMLN: latent/manifest latent nystagmus
- SN: spasmus nutans
- LC: latent component
- NBS: nystagmus blockage syndrome (types 1 and 2)
- DBTN: downbeat nystagmus
- EPIN: epileptic nystagmus
- UNIN: uniocular nystagmus
- VN: vestibular nystagmus

Differential Diagnosis

The differential diagnosis of CN or LMLN can be made definitively only by eye movement recordings. Each has one or more specific types of waveform. Because both CN and LMLN can present with similar clinical characteristics, attempts to rely on clinical observation alone will inevitably result in erroneous diagnoses possibly leading to ineffective therapeutic intervention. For instance, individuals with either type of nystagmus may exhibit a head turn, strabismus, or a positive cover test. Reliance on clinical characteristics alone becomes even more risky when one also includes spasmus nutans, the nystagmus blockage syndrome or combinations of CN and LMLN in the mix of possible diagnoses. Table 1 summarizes the clinical characteristics of CN and LMLN.

Accurate recordings alone allow one to reliably differentiate each of these types of nystagmus. Eye motion, as reflected in CN waveforms (there are 12 of them), characteristically accelerates away from the target. LMLN slow phases are either linear (low-amplitude nystagmus) or of decreasing velocity (high-amplitude nystagmus). The nystagmus of spasmus nutans is a pendular oscillation of variable conjugacy; both CN and LMLN are conjugate oscillations. Jerk waveforms of CN beat away from the null position; that is, if gaze is directed to the right of the null, the CN will be jerk right and vice-versa. Unless accompanied by a latent component, eye cover will not change the direction of CN. The direction of LMLN is always that of the fixating eye, whether the other is
occluded or not. LMLN is always accompanied by strabismus; that is, strabismus is a necessary condition for LMLN. The presence of strabismus in CN is idiosyncratic. However, because of the greater incidence of CN in the population, more patients who present with both strabismus and nystagmus will have CN rather than LMLN.

**Treatment**

There are several therapeutic approaches available for treating CN. Most depend on whether the CN damps with either gaze angle or convergence. A gaze-angle null can be exploited by either surgery (a resect and recess procedure) or, if the null angle is small, by the use of version prisms (both bases left if the null is to the right and vice versa). The Anderson-Kestenbaum procedure can be used to rotate the CN null to primary position. Under this procedure, the attachments of the extraocular muscles are moved to positions that would tend to rotate the eye away from the null position. This operation is best planned after eye-movement data are obtained to determine the null angle and with knowledge of the particular surgeon’s “calibration factor” that relates mm of surgery to resulting null-angle shift. This procedure not only shifts the null but also broadens it and reduces the off-null nystagmus.

A convergence null can also be treated by both surgical and optical methods. The surgical approach is a bimedial recession after Cüppers which produces an artificial divergence. The patient should have stereopsis if this procedure is to be attempted. The optical treatment when a convergence null is present consists of base-out vergence prisms in combination with −1.00 S added OU to the patient’s refraction. If presbyopia exists (or develops subsequently), the −1.00 S addition is not necessary (or must be removed). For patients with both types of nulls, exploitation of the convergence null will, in our experience, be more beneficial; it damps the CN to a greater extent than gaze shifts and increases acuity more. Studies comparing the Anderson-Kestenbaum procedure with bimedial recession and combining both procedures concluded that acuity increased more from the latter. The main factor responsible for these increases in acuity is increased foveation time per CN cycle due to both waveform changes and damping.

Each of these therapies results in damping the CN to a greater extent than the patient’s head turn. This is thought to be due to the overall lowering of the patient’s “fixation attempt” and tends to lower the CN at all gaze angles. If the patient’s visual acuity is primarily limited by the CN and not an afferent defect, these methods should result in a higher visual acuity.

Another surgical procedure has been proposed, large recession of all horizontal recti. This procedure would be used on those without gaze-angle or convergence nulls. However, careful studies are needed to determine if ocular motor plasticity limits the long-term effects of this procedure and if, in binocular patients, diplopia does not result at lateral gaze angles; the latter may occur due to the reduced mechanical advantage of the muscles.

The injection of botulinum toxin into either specific extraocular muscles or into the retrobulbar space has been tried in acquired nystagmus. Our experience in two patients...
with multiplanar acquired pendular nystagmus suggested that this approach was only temporarily effective. Also, ocular motor plasticity appeared to limit the effectiveness of this approach. For the same reasons, it is not recommended for the treatment of CN.

There are other therapeutic approaches that have proved useful in CN, especially if the patient has neither a gaze-angle nor a convergence null. The use of soft contact lenses may damp the CN. This is due to stimulation of the ophthalmic division of the trigeminal nerve. That observation has led us to explore other types of stimulation of both the forehead and neck. Both electrical and vibratory stimulation of these sites has been demonstrated to damp CN. Acupuncture, applied to the neck muscles, may work by a similar mechanism. Finally, biofeedback has been shown to damp CN in a controlled laboratory environment but its usefulness in real-world situations is yet to be demonstrated.

For patients with LMLN, surgical correction of their strabismus is indicated. Early surgical correction of the underlying strabismus in infants with LMLN has been shown to convert MLN to LN. This should result in higher visual acuities with both eyes open. Strabismus surgery done at a later time may still reduce the MLN, although it may not eliminate it.

**Foveation**

CN has been described as a “fixation” nystagmus, implying a primary disorder of the fixation mechanism. This description ignored the fact that CN is also present in the dark, where visual fixation is impossible. It is true, however, that “fixation attempt” is responsible for both the genesis and exacerbation of CN. Furthermore, careful study of CN waveforms revealed “foveation periods”, repetitive (cycle-to-cycle) intervals of time during which the target image is both in the foveal area and has minimal retinal slip velocity. Foveation periods usually follow foveating saccades and delay the characteristic acceleration of the eyes away from the target.

Studies of the foveation ability present in CN demonstrated the remarkable accuracy of the fixation mechanism despite the presence of this large oscillation. Standard deviations of 10–20 minarc of cycle-to-cycle foveation periods were found; normal fixation is 5–10 minarc. In addition, fixation in the vertical plane was found to be normal in a subject with horizontal CN; most CN is horizontal with a small torsional component. The use of phase planes (plots of eye position vs eye velocity) have been very helpful in studying CN fixation, smooth pursuit and the vestibuloocular reflex. The functioning of each of these subsystems was found to be within normal limits during the important foveation periods. The ability to repeatedly achieve and hold target foveation during fixation, smooth pursuit and the VOR supports the hypothesis that individuals with CN have strong fixation reflexes and that CN is not due to a primary deficit in the fixation mechanism.

**Oscillopsia**

**Congenital nystagmus**

A question that is probably as old as the recognition of CN is, “Why do individuals with CN not perceive oscillopsia?” Adults who acquire nystagmus experience this illusory movement of the environment. Our studies of four CN subjects eliminated several possible explanations for their ability to suppress oscillopsia. It was not due to: low acuity raising their motion detection threshold; vision being totally suppressed except during foveation periods; or saccadic suppression from the fast phases of the CN waveforms. Two other possibilities, extra-retinal information or the ability to preferentially use foveation-period information were not ruled out by these studies. Oscillopsia suppression remained an unexplained phenomenon until two rare CN subjects were studied. One developed transient horizontal oscillopsia later in life and the other de-
veloped an oscillopsia, the plane of which depended on the fixating eye.

Studying the first subject revealed that when the waveforms contained foveation periods that repeatedly (on a cycle-to-cycle basis) satisfied position and velocity criteria associated with good acuity in normals, he experienced no oscillopsia. Oscillopsia was present only when his CN waveforms lacked such “well-developed” foveation periods. Phase planes with “foveation windows” superimposed on the CN trajectories demonstrated the presence or absence of this stability. Failure of the trajectories to enter the window corresponded with the perception of oscillopsia. Since both the CN and oscillopsia were in the horizontal plane, it could not be determined whether the oscillopsia direction was determined by the CN waveform itself or by the motion of the foveation periods.

The second subject with CN and acquired oscillopsia helped clarify the mechanism involved in oscillopsia suppression and the relation of oscillopsia direction to both the CN and the foveation periods. She had predominantly horizontal oscillopsia while fixating with her right eye and vertical oscillopsia while fixating with her left eye. Her CN was diagonal in the right eye and horizontally elliptical in the left. Fast phases depended on which eye was fixating: they beat downward and nasally in the fixating eye and upward and temporally in the suppressed eye. In the horizontal plane, that represented a reversed latent component. Through the use of phase planes, conjugacy plots (right eye vs left eye), and both position and velocity scan paths (horizontal vs vertical motion), we were able to relate the oscillopsia direction in each plane to the relevant parameter of eye motion. Her perception of horizontal oscillopsia with right-eye fixation was due to horizontal position instability of the foveation periods of her CN waveform. Her perception of vertical oscillopsia with left-eye fixation was due to vertical velocity instability of the foveation periods. The oscillopsia direction reflected the motion of the fixating eye only when there was a lack of repeatable, well-developed foveation periods in both planes. Thus, the ability to repeatedly (cycle-to-cycle) foveate a target within the foveation window criteria allowed suppression of oscillopsia. Failure to do so in either plane resulted in oscillopsia in that plane, independent of the plane(s) of the CN. Failure to do so in both planes resulted in oscillopsia dictated by the CN motion.

**Latent/manifest latent nystagmus**

A related question is, “Why do subjects with LMLN not experience oscillopsia?” CN waveforms exhibit post-saccadic foveation periods followed by an acceleration away from the target. The LMLN waveform has no such foveation periods and the initial velocities of the decelerating slow phases may be high. Such waveforms are neither conductive to good acuity nor oscillopsia suppression, yet both are characteristic of subjects with LMLN. We applied the same techniques of analysis that were used in CN to subjects with LMLN. We chose a subject with LMLN who had excellent acuity (20/15), thereby ensuring that the central fovea was being used. We found that during intervals of no strabismus (ie, the target image was within the foveal area of both eyes) there was no MLN. In the presence of strabismus and a low-amplitude MLN, linear slow phases took the image of the target away from the center of the fovea with low retinal slip velocities and saccadic fast phases returned it to the center. This conformed to the analysis of prior laser-target retinal cinematography and ophthalmoscopic examination. The low drift velocities did not prevent good acuity nor induce oscillopsia. However, our records of higher amplitude LN and MLN (both in the presence of strabismus) revealed that the saccadic fast phases took her fixating eye past the target, thereby allowing target foveation during the low-velocity tail ends of the decelerating slow phases. Phase planes confirmed satisfaction of the same foveation-window criteria by subjects with LMLN as was required by subjects with CN. This was a
novel use of the saccadic system to create retinal position errors rather than its normal role, which is to reduce retinal position errors. Thus, individuals with LMLN are able to achieve good acuity and suppress oscillopsia by utilizing the low-velocity, low-position-error portions of their slow phases for target foveation, just as those with CN do. The difference lies only in the location of the foveation periods—at the beginnings of the slow phases in CN and at the ends in LMLN.

Visual Acuity

The questions posed with regard to oscillopsia and both CN and LMLN can also be asked with regard to visual acuity. “How can an individual with either CN or LMLN achieve normal, or near normal, visual acuity?” Again the answer lies in the foveation periods of each nystagmus cycle. The foveation periods of both CN and LMLN are the only intervals of time during which the image of the visual target of interest is near the center of the fovea and when the retinal slip velocity of all visual images (across the whole visual scence) is low\(^1,^{14,23,30}\). They are, by default, the only intervals where high acuity is possible; this is in addition to our findings that successive, well-developed foveation periods also appear to be required for the suppression of oscillopsia. The durations of low-velocity (\(<\mathcal{A}^\circ/s\)) portions of CN waveforms has been correlated to visual acuity\(^5,^{32,43}\).

In the course of our studies of fixation in CN, we developed a nystagmus foveation function (NFF) that provided a more sensitive measure of the CN null angle than did CN intensity\(^23\). The NFF contains the variables of foveation time per cycle and the standard deviations of foveation position and velocity measured during foveation periods. Since these are the variables that could severely impact visual acuity, we were not surprised to note that the NFF also tracked potential visual acuity, at least for below-normal acuities. The NFF was equally useful in predicting acuity, within the same range; for those with LMLN\(^26\). This suggests that the same criteria need to be satisfied for good acuity, independent of the type of nystagmus causing the decrement of vision. For higher acuity, the NFF saturated and was insensitive to small changes in acuity. We are presently developing a nystagmus acuity function (NAF) that uses the same variables as the NFF but varies linearly with visual acuity\(^27\). Such a function could be useful in determining a priori if an increase in visual acuity could be expected from a particular therapeutic approach. The NAF will provide a measure of potential visual acuity only for those individuals in whom it is the nystagmus that limits acuity rather than an afferent deficit.

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