Nystagmus in infancy

Spontaneous nystagmus in infants may be present at birth but more frequently appears in the first 6 months. We present a classification in which nystagmus with an onset before 6 months is called early onset nystagmus (EON) and is divided into three categories: sensory defect nystagmus (SDN) in which there is a proven sensory impairment, congenital idiopathic nystagmus (CIN) (sometimes called ‘motor nystagmus’ in which no visual or neurological impairment can be found, and neurological nystagmus (NN) which is associated with neurological disease. Though the distinction between SDN and CIN is made by many authors, they are sometimes collectively called congenital nystagmus. The presentation of all types of nystagmus can be similar, but in infants it is important to differentiate between SDN and CIN because of the different underlying defects, investigation, management, and genetic counselling (Fig 1).

Congenital idiopathic nystagmus
CIN is diagnosed after exclusion of any underlying defect. It normally affects acuity moderately, and estimates of its incidence vary from 1 per 350 to 1 per 20,000, reflecting the different definitions of ‘congenital nystagmus’ and ways of data collection.

TYPICAL CIN
Typically, CIN is conjugate and purely horizontal even in depression and elevation. The nystagmus intensity may decrease on convergence or with voluntary eyelid closure, and it may increase or decrease with fixation effort. There is a region of gaze direction where the nystagmus is minimal or absent; this null region may be eccentric, in which case a head turn may be adopted, or it may be in the primary position in which case the nystagmus may go unnoticed for years. The waveform may be pure jerk, pure pendular, a mixture, or both jerk and pendular in different gaze directions. The nystagmus is highly variable between patients, and it often subsides with age. CIN may have a hereditary component – as an X-linked trait with variable expressivity and incomplete penetrance, as an autosomal dominant characteristic, or as a sporadic occurrence. In infants with CIN normal optokinetic nystagmus is not usually recognisable. It has been reported that the quick phases of optokinetic nystagmus are sometimes in the reverse direction; however, we have found this to be uncommon in infants and young children and clinically impossible to analyse. The vestibulo-ocular reflex is also often completely disrupted. Infants can track moving objects with a varying nystagmus waveform superimposed provided the amplitude of the nystagmus is not too large. A completely normal child presenting with a typical CIN, an acuity of 6/18 or better, and no other neurological or eye defects can be diagnosed as having CIN without other investigations.

ATYPICAL CIN
The absence of the typical features by no means rules out the possibility of CIN. The diagnosis of atypical CIN is made by exclusion of an underlying defect and electrophysiological oculomotor, and neurological investigations should be performed. Neuroradiology, of which magnetic resonance imaging is usually the preferred technique in infants, is indicated in patients with a normal electoretinogram and an abnormal visually evoked response or as a part of a neurological work-up. When the nystagmus is monocular or very asymmetrical, and there is a head tilt or turn and a head shake, the diagnosis of spasms of nystagmus nutans may be made: this is a rather unhelpful diagnosis because it is retrospective. There must eventually be improvement and it is without predictive factors. Since monocular nystagmus can be associated with serious intracranial pathology, investigations are essential as in other cases of atypical CIN.

Sensory defect nystagmus
SDN is the most common form of EON and is secondary to a variety of obvious or subtle disorders. Cataracts, corneal opacities, optic disc atrophy, and developmental disorders of the optic disc and retina are among the commoner causes that are associated with visible abnormalities. Others have grossly normal eyes, such as Leber’s amaurosis, achromatopsia, and congenital stationary night blindness. Albinism is a common cause that may be included in this group. These congenital disorders require differentiation by clinical findings, family history, laboratory tests, radiology, and detailed electrophysiological findings under photopic and scotopic conditions. Visual evoked potentials reflect macular function and provide a means of objectively assessing visual acuity in infants, and have specific features in albinism.

The diagnosis of SDN is difficult when the sensory defect is subtle – for example, in a group of 64 children with EON,
29% had achromatopsia but 40% of this group were first diagnosed as having CIN. Surveys of EON show the presence of sensory defects to be high (82%, 88%, and 91%). SDN is sufficiently common for an electrophysiological test to be the initial test. Even if there is no direct family history other members of the family should be examined to help establish the diagnosis and prognosis and for genetic advice to be given. The presence of a family history of a similar form of nystagmus does not preclude that nystagmus being SDN.

**Neurological nystagmus**

When the nystagmus is asymmetrical or unilateral, neurological disease should be suspected and a neurological consultation may be indicated. Visual pathway disease giving rise to nystagmus includes chiasmal and optic nerve glioma, craniopharyngioma, and optic nerve compression by other tumours or bone anomalies. Many patients with NN also have associated neurological symptoms or present as very sick children with vomiting and headaches due to elevated intracranial hypertension.

Systemic disorders associated with nystagmus include Down's syndrome, hypothyroidism, maple syrup urine disease, and Pelizaeus-Merzbacher disease. Monocular nystagmus is sometimes associated with epileptic seizures. Seesaw nystagmus is readily identifiable and is usually secondary to a suprasellar defect (although an idiopathic seesaw nystagmus has been reported in an older child). Early onset vertical nystagmus is often associated with toxic causes or intracranial space-occupying lesions and demyelinating disorders, though it can sometimes be idiopathic.

**Latent nystagmus**

LN is a binocular jerk nystagmus which is absent with both eyes open. It may be detected in infancy and it usually becomes manifest on occlusion or blurring of the eye. The fast phase beats in the direction of the viewing eye. It is often associated with amблиopía and it is also found in conjunction with SDN in which case a complex nystagmus wave form is seen to change on occlusion. LN may be manifest in patients with alternating strabismus in which case the nystagmus fast phases always beat in the direction of the fixing eye. LN may be always manifest but this can be detected only by detailed studies.

**Waveforms analysis in early onset nystagmus (Fig 2)**

Nystagmus has been categorised clinically into jerk and pendular waveforms thought to correspond to CIN and SDN. It is difficult to distinguish between waveforms clinically. Eye movement recordings have revealed 12 waveforms associated with SDN and CIN consisting of variants of pendular, jerk, and mixed jerk-pendular types, with no correlation between waveform and aetiology. In hereditary CIN affected individuals within the same family may have different waveforms, and even affected monozygotic twins can have different waveforms. Thus, it is not possible to differentiate between CIN and SDN on the basis of the nystagmus alone. Eye movement recordings have shown some clinically useful findings: in patients with rod monochromacy the horizontal nystagmus in centre gaze often has pendular and jerk waveforms with much lower amplitude than that in patients with other forms of SDN; in infants, typical CIN is purely horizontal but SDN is often complex and multidirectional (often with a torsional component). The finding of jerk nystagmus with an accelerating slow phase does not distinguish between SDN and CIN but it does exclude NN. Acquired accelerating slow phase jerk nystagmus, caused by a cerebellar lesion, has been described in adulthood but is extremely rare. Jerk nystagmus with decelerating slow phases is usually associated with latent nystagmus or gaze paretic nystagmus.

**Management**

All patients require refraction and spectacles if appropriate. At school age, educational needs should be taken into account, including sitting at an appropriate place in the classroom, informing the teachers that an abnormal head posture and head shaking may be useful adaptive behaviours which help the child to see better. Since many of these children are also strabismic, occlusion and other strabismus management are important.

In older children and adults improvement in visual acuity resulting from a decrease in nystagmus has been reported with baclofen, 5-hydroxytryptophan therapy, biofeedback, contact lenses, prisms, and surgical procedures. Most of these treatments have not stood the test of time.

Treatment directed at the nystagmus to improve visual acuity was first described by Bietti and Bagolini. They performed a large recession of the four horizontal muscles. This technique has enjoyed a recent revival but is not yet fully evaluated.

Moving a null point nearer to primary position obviates the need for the head turn: this can be accomplished with prisms for small head turns. Surgery for an unacceptable head position has been performed in very young children. Factors other than the null zone influence the final head posture and were studied by Abad. Kestenbaum performed equal recessions and resections with shifting of the eyes in the direction of the rapid phase of the nystagmus, away from the null point. Anderson recessed the muscles responsible for the slow component of the nystagmus, and Goto resected the appropriate muscles without a corresponding recession. Pratt-Johnson recommended symmetrical surgery on all four horizontal recti when there was no other associated strabismus present. Parks suggested recession of one medial rectus 5 mm and a resection of the lateral rectus 8 mm with the opposite eye receiving a recession of the lateral rectus 7 mm and resection of the medial rectus muscle 6 mm. Because of the high rate of recurrence Calhoun and Harley recommended no surgery in a 15 degree head turn and increased the amount of the ‘classic Parks’ surgery by 40%.

**Figure 2** Illustration of the three basic slow phase profiles seen in early onset nystagmus. (a) Accelerating slow phase is almost always associated with SDN or CIN. (b) Decelerating slow phases are usually associated with latent nystagmus or gaze paretic nystagmus, and sometimes SDN or CIN. (c) Pendular nystagmus with no quick phases can be associated with CIN, SDN, or NN.
resulting in surgery of 7, 8, 4, 9, 8 and 11.2 mm for a 30 degree head turn and a classic plus 60% for a 45 degree head turn. Taylor recommended an 8 to 9 mm resection of the lateral rectus muscle on the side of the slow phase of the nystagmus and a 6 mm resection of the medial rectus muscle of the opposite eye in conjuction with 6 mm resection of the antagonists. The recommended dosages of surgery reported by Scott and Krafft are: (1) classic maximum for 20 degree turn; (2) classic plus 10% to 40% for 25-45 degrees turn; (3) classic plus 40% for 45 degrees or more. Turns over 50 degrees require augmentation of 50% to 60% to obtain an excellent result. Mitchell et al. reviewed the records of 48 patients with nystagmus and head turn. They were sub-divided in six groups receiving different types of surgery. The results of this series is comparable to the series reported by Scott and Krafft, and by Nelson.

It does not require excessive cynicism to wonder why, when each report claims success, that successive publications recommend ever more surgery, even to the point of creating a gaze palsy. Null point surgery should be reserved for those with genuine and significant symptoms.

Pathophysiology

The mechanisms underlying SDN and CIN are not known. Defects involving the saccadic system, the optokinetic system, the fixations system, and the neural integrator for conjugate horizontal eye movements have been proposed. Optican and Zee have succeeded in modelling most of the waveforms of CIN/SDN with a defect in the integrator. They suggest that the variable onset results from a congenital miswiring of proprioceptive signals which may only manifest as gaze instability when the infant learns to fixate. However, the association of SDN with such a wide range of apparently unrelated anterior visual defects points to a maladaptation to deprived macular vision during a critical period of visual development, rather than to an inborn structural anomaly. This is supported by reports of SDN occurring secondary to corneal opacities known to be acquired neonatally. On the other hand, a maldevelopment during a critical period does not account for CIN that appears at birth or occasionally much later in life.

Conclusion

It is important to classify EON correctly. SDN and NN, with subtle abnormalities, are often mistaken for CIN. Good clinical examination, family history, electrophysiology, eye movement recordings, and if necessary, neuroradiological and neurological examination should be considered in every infant presenting with nystagmus. The more rigorous investigations can be spared in cases of SDN with obvious defects or in typical CIN. By using a clear clinically relevant terminology, the confusion and labeling can be minimised. The term 'congenital nystagmus' should be avoided in describing EON since it has variable use.

References:

45. Ye YD, Baloh RW, Honrubia V. Effects of baclofen on congenital nystagmus.
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