Transient, idiopathic nystagmus in infants

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The aim of this study was to characterize children with transient nystagmus. Eleven children (six males, five females) developed nystagmus in infancy and then experienced regression of the problem, usually within a few months. Mean age at onset was 2.7 months, and mean age at regression was 8.5 months. No etiology could be ascertained in any of the patients, although four children had other eye or vision abnormalities (regressed retinopathy of prematurity, *n*=1; asymmetric fundus colobomata, *n*=1; delayed visual maturation, *n*=2). Results of this study suggest that mechanisms which allow ocular motor stability undergo a period of postnatal maturation, during which nystagmus can occur, but also during which nystagmus may disappear. Not every case of transient nystagmus should be categorized as spasmus nutans. There is a subset of infants and young children who develop transient nystagmus with no other findings and in whom the nystagmus disappears.

In clinical practice, nystagmus in infants is usually classified along etiological lines with ophthalmological and neurological causes being the most common. Bilateral anterior afferent visual pathway disease will cause nystagmus, but unilateral conditions affecting just one anterior visual pathway occasionally lead to bilateral nystagmus (Good et al. 1997). Ophthalmic conditions that cause nystagmus include Leber's congenital amaurosis and optic nerve hypoplasia. Diagnosis of these conditions allows planning and screening for associated neurological, developmental, and endocrinological abnormalities.

Occasionally, infants with nystagmus have an underlying neurological problem. Nystagmus may be a prominent physical finding in optic chiasmal glioma (Schulman et al. 1979, Lavery et al. 1984) periventricular leukomalacia, (Cioni et al. 1997, Phillips et al. 1997, Jacobson and Dutton 2000) and brainstem diseases. When the eye examination is normal, the search for an explanation for nystagmus may lead to neuroimaging studies and an EEG, particularly in infants where an obvious anterior visual pathway problem is not identified. A neurological explanation for nystagmus will occasionally lead to treatment, as may occur in craniopharyngiomas affecting the chiasm, or in certain chiasmal gliomas.

Some infants have no physical findings of anterior visual pathway disease and no discernible neurological abnormalities. An electroretinogram may be abnormal, indicating retinal disease with normal retinal appearance. This is known to occur in Leber's congenital amaurosis, congenital stationary night blindness, and achromatopsia. The refractive error may be abnormal in these children, which is a helpful accompanying physical finding. (Ferrone and Trese 1997, Marr et al. 2001).

Sometimes no explanation can be offered to a family regarding their child's sustained nystagmus. Clinicians may then make the diagnosis of 'motor nystagmus', even though there is no clear evidence that unexplained, sustained nystagmus is caused by any particular defect of ocular motor control per se. Some cases of 'motor' nystagmus can now be classified according to specific genetic mutations, offering families some explanation for their child's nystagmus (Kerrison et al. 1996, 1999). Nevertheless, it has not so far been explained how gene and protein structure abnormalities could lead to the phenotypic expression of nystagmus.

Most cases of constant nystagmus in infants can be explained etiologically and almost all cases can be categorized diagnostically. Another axis for diagnosis of the disorder is a temporal axis. There are children in whom nystagmus is recognized initially by a parent, pediatrician, or ophthalmologist but who later show regression of the problem, usually as a work-up to find the cause of the problem is unfolding. It has been recognized that congenital nystagmus waveforms develop over the first year of life (Reineke et al. 1988, Gottlob 1997) and that the waveforms and clinical manifestations of nystagmus also decrease during childhood in many cases of congenital nystagmus (Jan et al. 1986). However, in these patients the nystagmus remains clinically discernible. Our patients currently show no sign of nystagmus. Although a wide range of potential etiologies for transient nystagmus in infants is known, we have seen children in whom we could find no explanation for the nystagmus. The purpose of this study, therefore, is to describe these children and their condition, which we have termed transient, idiopathic nystagmus in infants.

Method

All patients (n=11; six males, five females) included in this study were examined by one of the authors (WVG) between 1997 and 2001. Examination consisted of a careful review of the patients' history and pertinent laboratory tests. An evaluation of visual functioning, strabismus, refraction, and fundus was also performed. Nystagmus was examined and described. We were not able to perform nystagmus eye movement recordings due either to the young age of the patients or the transient nature of the nystagmus. In one patient, nystagmus was never seen directly by the examiner, but was recorded on video by the infant's parents. Nine children had neuroimaging studies, and these were normal. The children were evaluated for other neurological problems, either by a pediatrician or a neurologist.

Results

Table I summarizes the clinical findings for each patient. For every child, onset of nystagmus had been in infancy and not later than age 10 months. Four children had vertical nystagmus; in one child the nystagmus was dissociated. Nine children underwent neuroimaging which was normal in each case. Nystagmus lasted only a few months in all patients and disappeared by age 12 months at the latest. Four children had associated visual problems, although not the sort commonly associated with nystagmus: one child had colobomata, with one eye's macula affected; two children had delayed visual maturation; and one child had Zone I retinopathy of prematurity (ROP) with a good outcome after laser ablation of the anterior retina. Formal neurodevelopmental assessment was not performed but one child had Trisomy 21 (participant 8) and another showed mild delays in motor milestones (participant 5). One participant had Sweet syndrome shortly after birth (participant 7). This problem resolved without known complications.

Discussion

Transient nystagmus in infants and young children can be caused by many different conditions. In this series of infants and young children we occasionally discovered an associated developmental or medical illness, but nothing that could explain nystagmus. Most children had a normal eye examination, although ROP was present and resolved after treatment in one child, and colobomata affected another child. Two additional children had delayed visual maturation (DVM). When neurological testing or neuroimaging was performed, it was normal. All indications are that these children had normal, or nearly normal, visual acuity and normal eye movements, when the nystagmus had disappeared. Extensive history taking and examination could not explain the cause of the nystagmus in any of these children. Eye movement recordings were unavailable in these patients, mostly due to the transient nature of the nystagmus. Infants show the characteristics of adult congenital nystagmus on recordings, so if these had been performed they might have been helpful in the diagnosis of congenital nystagmus (Hertle and Dell'Osso 1999).

The differential diagnosis for transient nystagmus includes many known conditions, one of which is nystagmus associated with strabismus (latent nystagmus, or manifest latent nystagmus). The possibility arises that some of the participants in this series actually had sustained but variable nystagmus. Nystagmus can vary throughout the day, and at times be difficult to perceive. Anxiety makes nystagmus worse; sleep eliminates it, although it may reappear during the rapid eye movement phase of sleep. Covering one eye of an individual with nystagmus may worsen it in the other eye. We observed the nystagmus in all but one child, and noted that once it regressed, it remained permanently absent and not subject to day-to-day fluctuations. None of the children had an abnormal head posture to suggest a null point (i.e. a position in gaze in which nystagmus is diminished and, therefore, visual acuity improved), although full neck control to allow a sustained head posture was not yet present in some children. Nystagmus was not elicited by covering one eye in the children in this series.

None of these children had spasmus nutans, at least in its

Table I: Clinical findings

Patient	*Sex*	*Onset*	*Type*	*CT/ MRI*	*EEG*	*Age at regression (m)*	*Ophthalmological findings*
1	F	Congenital	Vertical	N	N	11	N mild DVM
2	M	Congenital	Vertical	N	N	8	N
3	F	Early infancy	Unusual pattern (R>L)	N	NT	7	N
4	F	Early infancy 5 mo	Horizontal	N	N	6–8	N
5	F	Early infancy	Monocular	N	NT	8	N
6	M	Early infancy	Vertical	N	NT	9	N
7	M	Early infancy	Upbeat	N	NT	10	N
8	M	1 mo	Horizontal	NT	NT	10	N
9	M	6 mo	Horizontal	NT	NT	12	Zone 1 treated ROP
10	M	6 wk	Horizontal	N	NT	8	DVM/ strabismus now
11	F	10 mo	Horizontal	N	N	11	Colobomata

N, normal; DVM, delayed visual maturation; NT, not tested; ROP, retinopathy of prematurity.

classical presentation. Spasmus nutans was perhaps the first label ever applied to transient nystagmus, but the condition consists of more than nystagmus. A triad of asymmetric nystagmus, head tilt, and head nodding (titubation) should be present. When these criteria are adhered to the diagnosis becomes rare (Shaw et al. 2001). Spasmus nutans has been studied carefully in recent years but its cause remains enigmatic (Arnoldi and Tychsen 1995). Ultimately, spasmus nutans is diagnosed when it goes away, but in the meantime, many children with the condition will have undergone neuroimaging to exclude chiasmal tumors as a cause of the dissociated nystagmus (Kelly 1970, Koenig et al. 1982, Lavery et al. 1984). Nystagmus regression in spasmus nutans occurs between the first 2 to 3 years of life. Our participants would not fit the conventional definition of spasmus nutans because nystagmus disappeared earlier, usually was not dissociated, and was not accompanied by head nodding or tilting.

Transient disorders of ocular motor control in infants have been described and may include a variety of eye movement abnormalities (Hoyt 1977, Hoyt et al. 1980). To our knowledge, only transient opsoclonus, a condition that may mimic nystagmus, has been reported in the newborn period. Transient ocular motor findings regress promptly, almost always before 6 weeks of life, in contrast to our patients, where onset occurred after 2 months of life and cleared months afterwards. Still, it is plausible that ocular motor control development may be delayed in some infants and lead to more persistent, albeit transient, eye movement abnormalities. Note, however, that in our patients, the onset of nystagmus was preceded by a period of apparently normal ocular movements, and absent nystagmus.

DVM will occasionally be associated with transient nystagmus. It is unclear whether nystagmus and DVM are somehow linked. Two of the children in our series had a delay in visual maturation, lending support to the observations of Bianchi and colleagues (1998). However, the rest did not show DVM, demonstrating that it is not always the cause of transient nystagmus.

Various medications are known to cause nystagmus, which will clear when the drug is withdrawn. In some cases, a medication or drug taken during pregnancy is responsible for transient nystagmus seen in infants. This occurs with maternal use of sertraline (Oca and Donn 1999), cocaine (Borruat and Gaillard 2001), and, perhaps, anticonvulsants (Fahnehjelm et al. 1999). In other cases, drug ingestion, particularly an overdose, will cause transient nystagmus in children (Hall et al. 1986). Anticonvulsants such as carbamazepine and diphenylhydantoin may cause transient nystagmus (Herberg 1975, Tiballs 1992).

A number of neurological conditions are known to cause transient nystagmus in children. In Pelizaeus–Merzbacher disease, individuals occasionally show intermittent or transient nystagmus as an initial manifestation (Scheffer et al. 1991). Head trauma can cause an acute, transient cerebellar syndrome in which gaze-evoked nystagmus is a prominent feature (Cantu et al. 1969). Migraine may also cause transient nystagmus, although there are usually other prominent neurological findings, such as transient hemiplegia (Elliot et al. 1996, Szirmai 1997). Diseases of the inner ear are occasionally associated with transient nystagmus (Barber and Morrison 1973), and even infectious diseases, such as parvoviruses (erythema infectiosum) may cause transient nystagmus, probably by transiently affecting cerebellar function (Shimizu et al. 1999). None of these conditions was present in the children in this series.

Epileptic nystagmus rarely presents as isolated, transient nystagmus (Beun et al. 1984, Gire et al. 2001). Nystagmus may be symmetrical and pendular, or even monocular (Jacome and Fitzgerald 1982). Again, none of the children in this series demonstrated signs of epileptic nystagmus, and all cases of nystagmus resolved.

Wernicke's encephalopathy caused by thiamine deficiency may occur in infants. The cause may be an inborn error of metabolism (Ebels et al. 1965, Richter 1968, Dayan et al. 1970) or failure to administer supplemental thiamine to children receiving hyperalimentation. In the latter, prompt diagnosis and treatment may allow reversal of nystagmus.

Some of the children in this series had other medical problems or conditions. One child had Down syndrome and transient nystagmus (Shapiro and France 1985). Down syndrome is strongly associated with permanent, motor-type nystagmus. We do not suspect that this child had the classical type of motornystagmus, because the nystagmus disappeared at age 10 months. Disappearance of nystagmus is not a known feature of motor-type nystagmus. Sweet syndrome, which is an acute febrile neutrophilic dermatosis, may be associated with inflammatory, infectious, or neoplastic diseases (Rappaport et al. 2001). It occurred early in infancy in another child in this series. We are not aware of any association between Sweet syndrome and nystagmus. Another child had Zone I ROP which was treated with laser with a good outcome. Two additional children had DVM.

The etiology for the transient nystagmus seen in these children is unknown. These cases suggest that the ocular motor control mechanism is likely to be potentially unstable and 'plastic' during a short period of time postnatally. Transient disruption of afferent visual input, as occurred in one child with severe ROP, one with colobomata, and perhaps in two with DVM, could have transiently affected the motor control mechanism. Medical illness (Sweet syndrome and Down syndrome) in infancy may also have affected ocular motor stability. But seven of the children in this series had no known medical or developmental problems, indicating that more subtle unknown events could lead to transient nystagmus.

It follows that if neural control for nystagmus undergoes a postnatal developmental phase, then elimination of events or diseases that adversely affect neural control could reduce or eradicate nystagmus. In support of this theory is the fact that removal of congenital cataracts after the onset of nystagmus will occasionally result in the elimination of nystagmus (Good 2001, Yorston et al 2001). In these children, nystagmus had clearly been caused by anterior visual pathway disease. Thus the clinician should carefully evaluate children for all the conditions, which can cause nystagmus, even though the etiology of transient nystagmus in some children will remain unexplained.

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