Annotation

# Monocular vision loss can cause bilateral nystagmus in young children

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Nystagmus is a clinical sign of an underlying neurological or ocular disorder. There are many different types of eye oscillations with distinct behavioural characteristics on examination and eye-movement recording. For an accurate diagnosis, extensive investigations may need to be done, but when very young children present with nystagmus, which is influenced by attempts at fixation, the clinician usually faces a straightforward diagnostic task. The majority of babies have their nystagmus on the basis of bilateral loss of vision, i.e. with a sensory defect, with the lesion or disease localized to the anterior visual pathways[1–4]. In some babies no sensory etiology can be found on physical examination. A diagnostic electroretinogram may show that the child has Leber's congenital amaurosis[4]. Even then, a few children are found to be normal, and in these babies the term motor nystagmus is applied, although the possibility that anterior-pathway disease exists as an etiology for so-called motor nystagmus is hotly debated[4].

Monocular loss of vision is arguably far more common than bilateral loss in young children, although exact epidemiological data are not available. Nevertheless, the effects of monocular loss of vision on the developing visual system of the child are not well known. Loss of an eye, or loss of vision in an eye, may have any of several effects on the visual system.

First, after unilateral enucleation in young children, esotropia and abducting nystagmus may occur in the remaining eye[5–8]. The esotropia that develops in some young children after enucleation is amenable to surgical correction[7]. Kushner[5] and Ciancia[8] describe a group of children who developed monocular nystagmus after loss of vision in one eye, and who assumed an anomalous head position to dampen their nystagmus. A few of the children reported below also assumed an anomalous head position to dampen nystagmus, as occurs in many children with bilateral nystagmus and vision loss.

Second, optokinetic nystagmus (OKN) testing is abnormal in children who undergo unilateral enucleation[9] or suffer early onset vision loss[10]. OKN is measured by moving a repetitive pattern across the visual field. Symmetry of the OKN response is observed when the response is the same with either a left- or right-moving stimulus. Asymmetric responses are noted when a temporally moving stimulus cannot elicit as good a response as one moving in a nasal direction (testing is under monocular conditions). Asymmetric responses can also occur in infantile esotropia[11] and in normal children[12, 13], indicating that asymmetric OKN is not specific to monocular enucleation patients.

Third, monocular visual deprivation will cause monocular nystagmus in cynomolgus monkeys, but will cause conjugate nystagmus in rhesus monkeys[14]. The finding of bilateral nystagmus in response to unilateral patching in rhesus monkeys may represent an animal model that mimics our own observations. Variations in sensitive periods for amblyopia development probably account for the fact that one type of monkey develops monocular nystagmus and the other binocular nystagmus in response to prolonged monocular patching.

Monocular vision loss will occasionally cause monocular nystagmus in very young children[15]. This nystagmus is fast frequency and small amplitude and may be related to a monocular gaze-holding mechanism, perhaps mediated through the nucleus of the optic tract or accessory optic system[16, 17]. Very slow monocular oscillations of the involved eye develop in adults who have dense amblyopia – the so-called Heimann-Bielschowsky nystagmus[18]. The exact mechanism of this type of nystagmus is unknown, but it is reversible upon reversal of vision loss.

Fourth, loss of a normal eye, particularly by enucleation, will occasionally have a salutary effect on the fellow, amblyopic, eye. There are several reports of documented improvement of vision in the amblyopic eye of humans after severe

visual loss or enucleation in the fixing eye[19–21]. In a retrospective, multicenter report of 144 patients, Vereecken and Brabant[19] reported an improvement in vision of at least three lines in the amblyopic eye in 28.5% patients following vision loss in the good eye. Typically, the improvement occurred within the first weeks after visual loss. Animal studies have resulted in similar observations. In cats, the removal of a non-deprived eye results in an immediate and permanent six-fold increase in cells responding to the deprived eye in the striate cortex[22,23]. Behaviorally, enucleation of the non-deprived eye in cats results in greater final visual acuity than does mere occlusion.

Fifth, in studies of children with treated congenital, monocular cataracts, the fellow eye may have measurable sensory defects[24,25]. Subtle defects in linear acuity and contrast sensitivity at high spacial frequencies have been noted even in eyes that have received minimal patching. In addition, the severity of the deficit is not related systematically to the duration of patching.

Early-onset, monocular vision loss appears to cause another abnormality, that of bilateral, conjugate nystagmus. The nystagmus mimics so-called sensory nystagmus in that it is horizontal and conjugate. It differs from previous reports of nystagmus[5–8] in that it is not abducting or jerk and not a part of a strabismus-like defect. We have detected this problem in a number of settings and wish to comment on our finding.

We examined ten children with bilateral nystagmus but with unilateral loss of vision. The results are shown in Table I. Persistent hyperplastic primary vitreous (PHPV) was the most common diagnosis (five children), followed, in order of frequency, by retinopathy of prematurity (ROP) (two children), monocular cataract (two children), and Peters' anomaly (one child). In all of these cases, the vision loss occurred at or shortly after birth. The children were usually referred for evaluation of bilateral nystagmus, and therefore were examined in the first year of life. The exceptions were patient 1, examined at age 5 years, and patients 2 and 8, examined shortly after birth for management of ROP.

The affected eye in all children showed signs of dense vision loss. For example, the child with Peters' anomaly had a corneal opacity filling the entire pupil, except under dim lighting. None of the children showed complete unilateral blindness; even in the children with ROP, some aspects of the retina (but not the macula) remained attached.

The fellow eye in these children was carefully examined. In the children with ROP, it was ophthalmoscopically normal with no discernible maculopathy. Likewise, in all the others, there was no ophthalmoscopically discernible abnormality. In one child (patient 6), we performed an electroretinogram with normal results. Assessment of vision in the fellow eye was performed using standardized forced preferential look cards (Teller cards). A visual acuity measurement expressed as a ratio is listed in Table I. In patients 1 to 4, we could not determine an actual acuity either due to the child's age or lack of cooperation. These four children appeared to have no functional vision deficit.

The children were too young to impose eye movement recordings on them. Clinically, their nystagmus was symmetrical, bilateral, and moderate in amplitude and velocity. The nystagmus was horizontal and persisted in upgaze in each child.

Four children had other health problems: patient 1 has Kabuki syndrome and patient 5 has a dysplastic left hip; patient 6 has scoliosis and patient 7 has mild right hemiparesis.

In summary, ten children developed bilateral nystagmus in the setting of unilateral vision loss. In those in whom vision could be tested in the fellow eye, it was slightly reduced. Minimal vision loss in the unaffected eye could have been secondary to

**Table I: Patient characteristics**

| *Patient* | *Ocular diagnosis* | *Clinical findings of diseased eye* | *Clinical findings of fellow eye* | *Nystagmus type* | *Systemic abnormalities* |
|---|---|---|---|---|---|
| 1 | Left Peters' anomaly | ERG WNL | WNL | Bilateral | Kabuki syndrome |
| 2 | Left retinal detachment secondary to ROP | Left macula detached | Regressed ROP<br>No maculopathy<br>Myopia -12.00 D | Bilateral | Normal |
| 3 | Right PHPV | Cataract, small eye | WNL | Bilateral | Normal |
| 4 | Right PHPV | Cataract, small eye | WNL | Bilateral | Normal |
| 5 | Right PHPV with retinal folds | Cataract, small eye | Myopia -9.5 D<br>20/45 | Bilateral | Dysplastic left hip |
| 6 | Right PHPV | Cataract, small eye | ERG/VEP WNL 20/30 | Bilateral | Scoliosis |
| 7 | Left PHPV | Cataract, small eye | WNL<br>20/130 | Bilateral | Mild right hemiparesis |
| 8 | Left ROP | Retinal detachment | WNL<br>20/90 | Bilateral | Normal |
| 9 | Right congenital cataract, no treatment | Cataract, small eye? | WNL<br>20/130 | Bilateral | Normal |
| 10 | Right congenital cataract | Cataract, small eye? | WNL<br>20/50 | Bilateral | Normal |

WNL = within normal limits; PHPV = persistent hyperplastic primary vitreous; ROP = retinopathy of prematurity; ERG = electroretinogram; VEP = visual-evoked potential.

diminished foveation time, caused by nystagmus. As careful as we were in our evaluations, we could not find any other cause for the bilateral nystagmus and so have concluded that it occurred on the basis of unilateral vision loss.

We considered carefully the possibility that the children had motor nystagmus. To our knowledge, none had any condition with known associations to this or any other type of nystagmus. Two of the children had unilateral severe ROP. Patients with regressed ROP, as occurred in the fellow eyes of these children, may suffer certain defects, including refractive error and strabismus[26,27], but bilateral loss of central vision (i.e. acuity) is considered a prerequisite to bilateral nystagmus, and refractive error will not cause nystagmus. In eyes with no, or only mild retinal residua, mean visual-acuity scores are only 0.2- to 0.3-octave below that of normal eyes that never develop ROP[28]. Macular abnormalities may also occur with regressed ROP, and a condition of progressive decline of vision has been reported as a late consequence of regressed ROP[29]. Both these possibilities are unlikely in our patients, because they were young and had completely normal ophthalmoscopic examinations.

It is easier to identify risk factors for the development of bilateral nystagmus after monocular vision loss than it is an etiology. All of the children in this series were young, and all suffered congenital vision loss. Vision loss was profound, in most cases to the level of perception of hand motions or even worse, but no child was completely blind. Still, the mechanism for bilateral nystagmus is elusive. Kushner[30] has suggested that the nystagmus is a sort of manifest, latent nystagmus, mimicking latent nystagmus that may be seen in congenital strabismus. In latent nystagmus, occlusion of one eye results in a jerk nystagmus of the fellow eye. The fast phase in jerk nystagmus is toward the viewing eye. Although we were unable to obtain eye-movement recordings, our patients had pendular, not jerk, nystagmus on clinical examination. We, therefore, suspect a different etiology, at least for children evaluated in this series. Children in our series were monocularly visually deprived at birth. Gaze-holding mechanisms may be susceptible to monocular visual input at such an early age. Perhaps some individuals have a vulnerability to monocular deprivation, or a variable sensitive period that makes them vulnerable to the effects of monocular deprivation. The eye that sees poorly interacts with the normal fellow eye and results in loss of motor control for both eyes, in support of this theory.

On the basis of this study we conclude that monocular vision loss at a very early age may have one of at least three clinically important consequences. First, the fellow eye may be unaffected and may develop normally. Or, the affected eye may develop a fast frequency, small amplitude nystagmus. Lastly, bilateral nystagmus can occur, as we have shown in this study. The importance of this latter observation is in recognizing that it can occur. Children may be spared unnecessary evaluation if examination of the fellow eye is normal.

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