Intermittent horizontal saccade failure ('ocular motor apraxia') in children

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Abstract

Background—Ocular motor apraxia (OMA) in childhood is a poorly understood condition involving a failure of horizontal saccades. OMA is thought to be rare but the literature indicates wide clinical associations. OMA is often identified by abnormal head movements, but failure of reflexive quick phases has been reported in all but a few patients. The extent of this oculomotor disorder was examined in a large group of children with diverse clinical backgrounds.

Methods—The degree of quick phase failure during horizontal vestibular and optokinetic nystagmus was measured using DC electro-oculography and video in 74 affected children, aged 17 days to 14 years.

Results—All children showed an intermittent failure of nystagmic quick phases, except for total failure in one case. Other visuomotor abnormalities were common including saccadic hypometria (85%), low gain smooth pursuit (70%), neurological nystagmus (28%), strabismus (22%), and vertical abnormalities (11%). Non-ocular abnormalities were common including infantile hypotonia (61%), motor delay (77%), and speech delay (87%). There was a wide range of clinical associations including agenesis of the corpus callosum, Joubert syndrome, Dandy-Walker malformation, microcephaly, hydrocephalus, vermis hypoplasia, porencephalic cyst, megaloccephaly, Krabbe leucodystrophy, Pelizaeus Merzbacher disease, infantile Gaucher disease, GM1 gangliosidosis, infantile Refsum's disease, propionic acidemia, ataxia telangiectasia, Bardet-Biedl syndrome, vermis astrocytoma, vermis cyst, carotid fibromuscular hypoplasia, Cornelia de Lange syndrome, and microphthalmos. Perinatal and postnatal problems were found in 15% including perinatal hypoxia, meningitis, periventricular leucomalacia, athetoid cerebral palsy, perinatal septicaemia and anaemia, herpes encephalitis, and epilepsy. Only 27% were idiopathic.

Conclusion—Quick phase failure is a constant feature of OMA, whereas abnormal head movements were detected in only about half, depending on the underlying diagnosis. This oculomotor sign is better described as an intermittent saccade failure rather than as a true apraxia. It indicates central nervous system

involvement, has wide clinical associations, but it is not a diagnosis.

(*Br J Ophthalmol* 1996; 80: 151–158)

In 1952 Cogan¹ reported four children who had difficulty generating horizontal saccades, although vertical saccades were normal. He called this disorder 'congenital ocular motor apraxia' (c-OMA), and there have been many reports of this condition since. Infants with c-OMA are often hypotonic^{2–7} and developmentally delayed^{3 6–11} with late sitting and walking.^{1 3 7 12–16} Many develop a wide based gait or are described as ataxic,^{2 3 5 6 10 11 13 17–24} and clumsiness is common.^{2 3 5 8–11 14 17 21} Other cerebellar signs, such as intention tremor, are relatively rare.^{20 23} Reading difficulties appear,^{3 9 19 24} and poor development of speech is often reported.^{5–7 10 11 13 16 20 22} Intellect is usually normal, but mild mental retardation has been reported.^{3 5 6 14 16 21} The strong association with developmental problems has prompted some to consider OMA as part of a wider syndrome.¹⁰

Extensive investigations often reveal no underlying cause or associated clinical entity. However, gestational or perinatal problems are not uncommon.^{1 3 4 7 16 17 25–28} In other cases, neuroimaging reveals CNS structural abnormalities involving the corpus callosum, fourth ventricle, and/or cerebellum.^{6 10 11 14–16 26 29–32} Other reported structural abnormalities include immature development of the putamen, heterotopia of grey matter,³⁰ porencephalic cyst, hamartoma near the foramen of Monro with dilated lateral ventricle,³³ macrocephaly,^{6 33} cystic lesions of the posterior fossa with hydrocephalus,¹⁶ chondrodystrophic dwarfism and hydrocephalus,³ and encephalocele.¹⁶

OMA has also been reported in children with neurodegenerative conditions such as infantile Gaucher's disease type 2^{26 34–36} (in which it can be a presenting sign) and type 3.³⁷ OMA has been reported in Cockayne syndrome.³⁸ Early development may be normal in these children and so the OMA has been considered to be acquired (a-OMA). A-OMA is probably a constant feature of ataxia telangiectasia,^{34 39 40} and is strongly associated with the spinocerebellar degenerations.^{21 34 41–47} Rarely, OMA has been secondary to posterior fossa masses.^{22 48–50} OMA has also been reported with other conditions, including neurofibromatosis type 1,⁵¹ Alagille's syndrome,⁵² Lowe's syndrome,⁵³ juvenile nephronophthisis,⁵⁴ Wilson's disease,⁵⁵ oral-facial digital syndrome,²⁵ X linked muscle atrophy and congenital contractures,⁵⁶ and

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Accepted for publication
9 November 1995

possibly a post immunisation encephalopathy.⁵⁷ A-OMA has also been reported in Huntington's disease.^{58 59} Thus, over the past 40 years this 'rare' oculomotor disorder has had ever wider clinical associations.

Children with OMA often adopt a strategy of head thrusting to shift gaze horizontally. Head thrusts are distinctive, and have become virtually the sine qua non of OMA. However, head thrusting is not universal⁶⁰ and, depending on the level of head control, it may not always be discernible in the very young⁶¹ or the child with developmental delay.

It has been reported frequently that there is a failure of quick phases during nystagmus, which can be examined clinically by manual spinning.* Without a quick phase to reset eye position, the unchecked nystagmic slow phase drives the eyes to the mechanical limit of gaze, where they stay 'locked up' (LU) in extreme deviation. Cogan⁵ claimed that quick phase failure is obligatory in c-OMA. One problem is that quick phases have not been examined in all children reported with OMA. Surprisingly, there have been very few objective eye movement studies of children with OMA. In one study, Zee *et al*⁶⁰ reported an *intermittent* failure of quick phases in two cases but no quick phase failure in another. Thus, it is not clear whether LU really is a constant feature of OMA in childhood.

We examined the oculomotor behaviour of 74 children with OMA in an attempt to clarify the nature of this oculomotor disorder and its associations. Emphasis was on the incidence of LU during optokinetic nystagmus (OKN) and during vestibular nystagmus (VN) in the dark. In 47 of these children, OMA had already been identified clinically on the basis of head thrusts or LU during manual rotation. Similar abnormal eye movements were found in a further 27 patients who were under investigation for other reasons, but in whom OMA had not been suspected clinically.

Methods

PATIENTS

Patients were 74 children aged 17 days to 14 years (median age 3.2 years) at the time of eye movement recording. They were referred to the eye movement unit at Great Ormond Street Children's Hospital, either as outpatients visiting the ophthalmology department or as inpatients under the care of the neurology department.

All patients underwent ophthalmic examination, and many also underwent neurological

examination including neuroimaging and metabolic investigations. Overall, the pathology ranged from the idiopathic to severe neurodegenerative conditions. Here, we do not describe individual cases or their investigations, but divide them by diagnoses. The presence or absence of head thrusting, head shaking, abnormal muscle tone, developmental delay, abnormal gait, strabismus, poor vision, and nystagmus were not considered as factors in this grouping, which was as follows.

Group 1

This group consisted of 19 idiopathic children. Apart from developmental delay, these children were well. It should be noted that six children in this group did not have neuroimaging, and so they were not included in statistical tests pertaining to diagnostic grouping. The most common presentation sign in this group was visual unresponsiveness and/or head thrusting.

One patient was referred with developmental delay and oesophageal reflux. Although he had attenuated pattern visual evoked potentials, no underlying explanation could be found. He was included in this idiopathic category, but he is currently being monitored because his development continues to be exceptionally delayed.

Group 2

This group consisted of 20 children with CNS structural abnormalities. These were: agenesis of the corpus callosum (six), which was associated with Lyon's disease in one case; Joubert syndrome (seven), which was associated with hydrocephalus in one case; Dandy-Walker malformation (one); microcephaly (two); hydrocephalus (one); vermis hypoplasia (one); porencephalic cyst (one); and right megaloccephaly (one). The most common presentation sign was visual unresponsiveness.

Group 3

This group consisted of 15 children with neurodegenerative conditions, mostly involving white matter. The diagnoses were: Krabbe's leucodystrophy (three); Pelizaeus Merzbacher disease (two); infantile Gaucher's disease (one); GM1 gangliosidosis (one); infantile Refsum's disease (one); propionic acidemia (one); ataxia telangiectasia (two); unknown progressive neurometabolic disorders (four). The most common presentation signs were developmental delay, nystagmus, seizures, and failure to thrive.

Group 4

This group consisted of 11 children who had non-progressive conditions secondary to probable insult occurring either perinatally or during the first 6 months of life: perinatal hypoxia (three); meningitis at 3 weeks (one); periventricular leucomalacia (one); athetoid cerebral palsy (one); septicaemia and anaemia

*Manual spinning

Typically the infant is held at arm's length facing the examiner. The examiner rotates him/herself and the infant en bloc for a few rotations then abruptly stops, repeating the procedure in the opposite direction. In the healthy infant, older than 1 month, typical vestibular nystagmus is observed. In the infant with saccade failure, there is a reduction or absence of quick phases so that the eyes 'lock up' in full deviation in the same direction as rotation (that is, to the examiner's right (infant's left) when the examiner is rotating clockwise), but in the opposite direction after abrupt cessation of rotation. Similar effects can be elicited when the infant, or older child, is rotated on a swivel chair facing outward from the centre of rotation.

at 48 hours following difficult breech delivery (one); herpes encephalitis at 4 months (one); epilepsy (one); epilepsy at 4 months possibly secondary to immunisation (one); unknown encephalopathy (one). The most common presentation sign was seizures.

Group 5

This was a miscellaneous group of nine children who did not fit readily into the other groups. It consisted of Bardet-Biedl syndrome (two); vermis astrocytoma (one); vermis cyst presenting at 3 years (one); carotid fibromuscular hypoplasia (one); Cornelia de Lange syndrome (one); microphthalmos (one); cochlear deafness and optic atrophy (one); unexplained ataxia and nystagmus occurring at 4 months (one). Owing to the nature of this group there was a wide range of presentation signs.

Except for some patients in group 4, there were no discernible factors during pregnancy. Two patients were brother and sister, but there were no other known familial cases. Overall, average birth weight was 3.1 kg, and there were no significant differences in birth weight among the diagnostic groups.

Forty seven patients (64% of the total) had already been identified as having OMA on the basis of either abnormal head movements or LU during manual spinning. We call this the *clinical* group. In this group, head thrusts were reported in 38 patients but not in nine. Manual spinning had been carried out in 39 patients during infancy; of these, 36 showed LU and three showed no LU. Two patients exhibited head thrusts without LU during manual spinning. A further 26 patients were found to have similar eye movement abnormalities as those in the clinical group which, together with the one patient who had no head thrusts and negative manual spinning, formed the *subclinical* group. The breakdowns of various clinical and oculomotor signs among the diagnostic groups are summarised in Table 1.

EYE MOVEMENT RECORDING

Horizontal eye movements were recorded using bitemporal DC coupled electro-oculography. Young patients sat on a parent's lap in a Barany chair. The parent held the child's head as still as possible without upsetting the child. Older children sat alone with a head rest.

Horizontal OKN was elicited by a full field brightly coloured high contrast curtain rotated at 25 and 50 degrees per second (deg/s) in both directions. Per- and post-rotatory horizontal vestibular nystagmus was induced by sustained rotation in complete darkness at 80 deg/s for 40 seconds in both directions with an acceleration/deceleration of 18 deg/s per second. Horizontal smooth pursuit was elicited by ramping a large target horizontally at a constant speed 10, 20, 30, or 40 deg/s through a total angle of 40 degrees symmetrically about the midline, with a 1.5 second pause at the end of each excursion. When possible saccades were elicited by small light emitting diodes or large noisy toys depending on the age and cooperation of the patient. Saccadic latencies were not measured (see Jacobs *et al*⁶²).

Visible and infrared video images of the patient's eyes were monitored simultaneously in the light and dark to aid identifying LU. Locking up was identified by a roughly flat EOG trace in conjunction with the eyes being in extreme deviation as seen on the video monitor (see Harris *et al*⁶³). The degree of LU was measured by the percentage of time when the eyes were in full deviation. For statistical analyses percentage scores were converted by the arcsine transformation to yield more normally distributed scores.

Because of the difficulties in eliciting saccades from these children, calibration was usually unreliable or impossible. Abnormally low gain smooth pursuit was identified by catch up saccades, and the degree of smooth pursuit abnormality was ordinally scaled from 0–3, with 0=normal, 1=catch up saccades only at high speeds (30 and 40 deg/s), 2=catch up saccades at all speeds, 3=no smooth pursuit. The absence of smooth pursuit in some patients could have reflected the conjunction of low gain smooth pursuit and difficulties in making catch up saccades. Abnormal saccadic hypometria was identified by the consistent presence of one or more secondary saccades, where the primary saccade had an amplitude of less than 90% of the target eccentricity.

Saccade abnormalities were also ordinally scaled from 0–2, with 0=normal, 1=hypometric, 2=absent. Saccade velocities were not measured. Although it appeared from the EOG and video records that OKN gain was frequently low, there was no objective way of assessing this without calibration, and so OKN gain was not analysed (because of the prevalence of quick phase failure, beat frequency could not be used as a measure of OKN).

Table 1 Summary of clinical and oculomotor findings by patient group, showing median age, percentage males, mean birth weight (B/W), percentage exhibiting head thrusts (HT), and with clinically identified ocular motor apraxia (Clin), percentage with motor delay, speech delay, hypotonia, and hypertonia; percentage of time in lock up during optokinetic nystagmus (OKN) at 25 and 50 deg/s and rotation in dark vestibular nystagmus (VN), and percentage of patients with smooth pursuit and saccade abnormalities

Group	No	Age (years)	Males (%)	B/W (kg)	HT (%)	Clin (%)	Speech (%)	Motor (%)	Hypo (%)	Hyper (%)	OKN25 (%)	OKN50 (%)	VN (%)	Pursuit (%)	Sac (%)
1 Idiopathic	19	3.7	42	3.34	79	90	88	68	53	0	28	31	48	70	79
2 Structural	20	3.8	60	3.01	70	75	100	90	72	6	57	58	59	79	94
3 Degenerative	15	2.6	60	3.01	13	33	63	77	46	31	36	38	62	75	80
4 Perinatal insult	11	1.8	36	3.16	45	64	90	91	80	10	36	40	51	100	100
5 Miscellaneous	9	3.7	33	3.21	22	33	71	50	50	12	24	31	50	88	78
Total	74	3.2	49	3.14	51	64	87	77	61	11	37	40	54	79	85

Figure 1 Typical example of locking up during optokinetic nystagmus (OKN) with full field curtain rotating at 50 deg/s to the right (upper panel) and to the left (lower panel). Note intermittent periods of missed quick phases allowing the eyes to deviate to mechanical limit of gaze (shown by arrows), followed by resumption of normal OKN. Patient was a 17-month-old male with microcephaly and history of neonatal septicaemia, hyperbilirubinaemia, and hypoglycaemia.

Owing to lack of cooperation, OKN could not be examined in 10 children, and VN could not be examined in two children, but no child failed on both OKN and VN.

Results

All 74 children, regardless of aetiology, showed some degree of locking up (LU) during optokinetic and/or vestibular nystagmus. A typical example is shown in Figure 1, where the normal OKN is intermittently interrupted by a failure of quick phase generation (shown by arrows), allowing the eyes to deviate to the slow phases. After some variable time, quick phases resumed and the OKN continued in a normal fashion until the next apparently random quick phase failure. In most patients, quick phases resumed spontaneously, although in some they were sometimes accompanied by a synkinetic blink. Using the same apparatus, we have recorded OKN in 23 normal infants aged 1–7 months, and have never observed this phenomenon.

Except for one infant the LU was always intermittent with the proportion of time spent in LU varying widely among patients. In one case, an infant diagnosed with infantile Gaucher's disease never exhibited any saccades or quick phases during our investigation (see Vivian *et al*³⁶). Despite this variability, the

Figure 2 Comparison of the percentage of time spent with eyes locked up (LU) in full lateral deviation. Each symbol represents one patient. (A) LU during optokinetic nystagmus (OKN) at 50 deg/s versus OKN at 25 deg/s; ($r=0.88$). (B) LU during vestibular nystagmus (VN) versus OKN at 25 deg/s; ($r=0.57$); note LU greater for VN than OKN.

degree of LU was significantly correlated between the two speeds of OKN ($r=0.88$, $p<0.001$) (Fig 2A), and between LU during vestibular nystagmus and OKN LU ($r=0.57$, $p<0.001$ at 25 deg/s, and $r=0.65$, $p<0.001$ at 50 deg/s) (Fig 2B). Thus, a patient who showed strong LU at one speed was likely to show strong LU at the other speed and during VN. For a given patient, the speed of OKN stimulus did not have a significant effect on the degree of LU ($p<0.21$), but LU during VN was significantly greater than for OKN ($p<0.001$). This difference was also reflected in a principal components analysis of the three measures of LU, which showed two significant components: (i) the main component, which explained 81% of the total variance, weighted LU for the two OKN speeds roughly equally (0.92, 0.95), but with a lower weight for LU during VN (0.81), and reflected a general LU factor; (ii) a minor component (16% of the variance) that strongly weighted LU during VN (0.6) against LU during OKN (-0.32 , -0.19), which represented an additional vestibular LU factor.

EFFECT OF DIAGNOSTIC GROUP, AGE, AND SEX

Analysis of variance using the main LU factor as a dependent variable with age as a covariate and diagnostic group and sex as factors, was significant ($p<0.005$). LU was significantly dependent on diagnostic group ($p<0.004$) which showed that the patients with structural abnormalities had significantly more LU than the idiopathic group (Bonferroni adjustment, $p<0.001$). The other groups were not significantly different from the idiopaths. There was a significant decrease in LU with age ($p<0.015$), but the effect of sex was not significant. The proportion of affected males and females was not significantly different either overall or for any diagnostic group. Thus, we have no evidence that males are more affected than females, as claimed by Vasella *et al*.²³ There were no significant effects with the minor LU factor (which was dominated by LU during VN).

SACCADIC ACCURACY

Sufficient cooperation was obtained from 61 patients (82%), and 85% of these showed some abnormality. This frequency of incidence was not significantly different among the diagnostic groups. Severity was least in the idiopathic and miscellaneous groups, but this was also not significant (Kruskal-Wallis, $p<0.28$).

The degree of severity in saccadic abnormality was significantly correlated with LU during OKN both at 25 deg/s (Spearman $r=0.28$, $p<0.04$), and at 50 deg/s ($r=0.27$, $p<0.05$), as well as during VN ($r=0.30$, $p<0.02$). Given the nature of the condition, this relation is not surprising.

SMOOTH PURSUIT

Smooth pursuit could be examined in only 52 patients (70%). Of these, 79% showed some

abnormality, but this incidence did not differ significantly among the diagnostic groups. The idiopathic group showed less severity than the other groups (which were more or less equal) but this was not significant (Kruskal-Wallis, $p < 0.16$). Overall, severity of smooth pursuit was only significantly correlated with the degree of LU during vestibular testing (Spearman $r = 0.32$, $p < 0.02$), and not with LU during OKN or severity of saccade abnormality.

STRABISMUS

Strabismus was present in 23 patients, being esotropic in 16 cases (22%), and exotropic in seven (10%).

NYSTAGMUS

Nystagmus was present in 21 patients (28%). Latent nystagmus was manifest in one child with agenesis corpus callosum, esotropia, and an optic disc coloboma. Latent nystagmus was also seen compounded with pendular nystagmus in the one child with Dandy-Walker malformation. Horizontal 'acquired' pendular nystagmus was found in 12 patients: Pelizaeus Merzbacher disease (two), Joubert's syndrome (three), Cornelia de Lange (one), perinatal anoxia (circumrotatory nystagmus) (one), Dandy-Walker malformation (one), athetoid cerebral palsy (one), unknown disorder with ataxia (one), unknown disorder with congenital right ptosis (one), unknown neurometabolic disorder (one). One patient with suspected peroxisomal disorder had a vertical pendular nystagmus. Horizontal gaze-paretic nystagmus, with or without rebound nystagmus or upbeat gaze-paretic nystagmus in upgaze was found in three: ataxia telangiectasia (one), idiopath (two). Upbeat nystagmus was seen in one child with birth trauma, and downbeat nystagmus in one infant with neonatal meningitis.

VERTICAL EYE MOVEMENTS

In 89% of patients, vertical eye movements appeared normal. In the remaining eight cases, a vertical saccade failure was present in three (herpes encephalitis, agenesis of the corpus callosum, infantile Gaucher's disease), a bilateral upgaze palsy was found in one case of perinatal hypoxia and optic atrophy; and a unilateral right upgaze palsy in a case of congenital right ptosis. Vertical nystagmus was present in three cases.

TONE, MOTOR, AND SPEECH

When described ($n = 66$), 61% of patients were described as hypotonic in infancy, 11% as hypertonic, and 28% as having normal tone. Hypotonia was not related significantly to diagnostic group. Hypertonia ($n = 7$) was reported in four cases in the neurodegenerative group, and absent in the idiopathic group. When reported ($n = 70$) there was a similar high incidence of delayed motor development,

with 77% of patients sitting and walking late. This was not related to diagnostic grouping. In a total of 70 reports, delayed development of speech was reported in 87%, which was not related to diagnostic grouping. Many of these required speech therapy.

The presence of hypotonia, delayed motor development, and delayed speech development were significantly correlated with each other ($p < 0.04$), but the presence of abnormal tone and speech delay were not correlated with degree of LU, while motor delay was only mildly correlated with LU, reaching significance for OKN at 50 deg/s (Spearman $r = 0.26$, $p < 0.04$) but not at 25 deg/s or with LU during VN.

CLINICAL AND SUBCLINICAL GROUPS AND HEAD THRUSTING

OMA had been clinically identified in 47 children (the clinical group), mostly on the basis of head thrusting. However, LU was detected in a further 27 children (the subclinical group), who had been referred for oculomotor assessment but in whom OMA was not suspected; head thrusting was absent and, except for one case, manual rotation had not been performed (see Methods). One possible explanation for this discrepancy was that LU was much more subtle in the subclinical group. However, although the degree of LU was slightly greater in the clinical group, it was not significant ($p < 0.29$) and could not account for the difference.

Another possible reason for the lack of head thrusting in some patients was poor head control owing to developmental delay. However, the opposite seems to have occurred with the incidence of motor delay and speech delay being significantly more likely in the head thrusting group (Spearman $r = +0.25$, $p < 0.036$; $r = +0.38$, $p < 0.001$).

The incidence of clinical OMA was significantly different among the diagnostic groups (χ^2 , $p < 0.015$) (this was also the case when the six patients, who were considered idiopathic without neuroimaging, were included (see Methods)). As can be seen from the proportions in Table 1, there was a clear tendency to not identify OMA clinically in the neurodegenerative group.

Discussion

All patients with clinically identified OMA exhibited a failure of quick phases during induced optokinetic and/or vestibular nystagmus. These data clearly support Cogan's claim⁵ that LU is obligatory in OMA in children. We have not found LU in the normal infant older than 1 month and propose, therefore, that quick phase failure should be a defining feature of this disorder. Although the presence of LU can be tested at any age, missed quick phases during vestibular nystagmus are common in the neonatal period⁶⁴ and we are also aware of vestibular LU occurring transiently in some healthy infants under about 3 weeks of age. Thus, the determination

of pathological LU during vestibular nystagmus, which is induced during manual spinning, cannot be reliable until after 1 month of age. To our knowledge, the possibility of physiological LU during OKN has not been examined under 1 month of age.

In contrast with LU, a reliance on head thrusting to identify OMA is unsatisfactory. Among the clinical group of 47 children, 81% showed head thrusting, which reduced to 51% when the subclinical group was included. As a presenting sign, head thrusting was reported in only eight patients, and head shaking was reported in a further five, out of a total of the 38 in which head thrusting was detected at this tertiary referral hospital. It is unlikely that this large discrepancy was due solely to a failure to recognise head thrusting by the referring physician. Head thrusting may be absent in the young affected infant,⁶¹ and in some cases finding head thrusting at the tertiary referral centre may reflect the interim development of head control. Head thrusting is not exclusive to OMA, but may occur in children with gaze palsies, slow saccades, visual field defects, or even poor eccentric gaze holding.⁶⁵ Therefore, testing for quick phase failure by manual spinning, or more formal eye movement assessment if available, is the preferred method for detecting OMA.

ASSOCIATIONS

The term congenital ocular motor apraxia has come to imply a rare benign idiopathic condition. Yet, from both the literature and our patients it is clear that LU during OKN and/or VN is associated with a very wide range of conditions ranging from the relatively benign to the rapidly progressive neurometabolic degenerations, with the idiopathic group representing a large minority of cases. Although there were differences in the oculomotor abnormalities among the diagnostic groups, they were insufficient to discriminate reliably between the groups. Diagnosis must be made on other signs and investigations, and the label 'idiopathic' can only be justified after exclusion of other conditions and CNS malformations. Among the group with structural abnormalities, both this study and other published reports indicate that posterior fossa malformations are common; thus, magnetic resonance imaging should be the investigation of choice. Perinatal and postnatal problems are common, although it is not usually possible to make a definite causal link. Any indications of progressive disease require full neurometabolic investigations. Seizures, failure to thrive, loss of skills, nystagmus, or vertical abnormalities usually indicate a more severe association. However, mild/moderate delayed development may occur in idiopaths. Clearly, OMA is not a diagnosis in itself and should be considered only as an oculomotor sign indicating CNS involvement. Presumably the structures for timing quick phases are particularly vulnerable to insult and, in idiopaths, may reflect subtle defects beyond the resolution of current neuroimaging techniques.

The majority of affected children had other developmental problems, and we concur with Rappaport *et al*¹⁰ and Steinlin *et al*³⁰ that OMA should be viewed in a wider context. Most affected children were slow in attaining early developmental milestones, and later they tended to be clumsy. Difficulties in speech development were very common (87%), and reading difficulties are also well recognised in this condition (although not examined in this study). These delays occur regardless of the underlying diagnosis, occurring in idiopathic children as well. Thus, in the long term, the possibility of mild/moderate educational difficulties should be recognised. The eventual outcome in patients with non-progressive OMA has often been questioned, but there has been no definitive answer, and we have not yet been able to follow our patients over sufficient time. Over the age range of our patients (from infancy to 14 years) we have found a significant decrease in LU with age. Although this may be due to an improvement in the disorder, there are other possible explanations: Firstly, over the first few years, normal children have a lower beat frequency than adults during induced nystagmus, which may reflect a higher threshold for quick phase triggering. Any decrease in LU with age may, therefore, reflect just a normal maturation process rather than an improvement in the disorder itself. Secondly, we observed a tendency for older children to employ synkinetic blinks rather than head thrusts as a compensating strategy. These blinks also occurred during OKN and VN, and prevented LU.

It is difficult to establish the incidence of OMA because of its poor detection and different referral patterns. Originally thought to be rare, there has been an increase in reported cases over the past 40 years, and some authors have suspected that it may be underreported. Clearly, a reliance on head thrusting as sign of OMA will lead to underdetection. On the other hand, finding LU in patients with already established neurodegenerative conditions is usually of little clinical value.

The distinction and clinical significance between congenital and acquired OMA is not always clear. In some cases the saccade failure has a clear late onset, which indicates acquired and usually progressive neurological disease. However, it is not always possible to establish the time of onset, which is compounded by the fact that head thrusting may not develop until after 3 months, and that physiological LU may occur transiently in the first month.

'APRAXIA' OR PAN-SACCADIC FAILURE?

Many regions of the brain are involved in the mediation and regulation of saccades and smooth pursuit, including the frontal eye fields, parietal cortex, basal ganglia, cerebellum, and brainstem,⁶⁶ which prevent localisation of this disorder in the brain. Some have argued for a cortical anomaly^{6 8 9 17 18 20 25} because ocular motor apraxia can be acquired with bilateral frontoparietal lesions acquired in adulthood (Balint's syndrome)⁶⁷ or because of

the association with agenesis corpus callosum (ACC). However, there is little direct evidence to support this. Children with OMA do not show the complex visuospatial disorders typical of Balint's syndrome, such as optic ataxia, visual agnosia, and visual neglect. On the contrary, head thrusts testify to the intactness of visual fields and peripheral attention. Extensive reviews of ACC do not mention OMA,⁶⁸ whereas ACC can be accompanied by other midline malformations including an enlarged fourth ventricle and cisterna magna¹⁵ implying cerebellar vermis hypoplasia.¹⁴ Indeed, in many cases with congenital or acquired OMA, a subtentorial site seems the most likely, which is consistent with post-mortem results showing dorsal cerebellar cortical dysplasia in an idiopathic case,⁷ or brainstem gliosis in a case of juvenile Gaucher's disease with congenital OMA.⁶⁹ Thus, although the site(s) of childhood OMA are unknown, it is clear that most OMA occurring in childhood is distinct from the OMA acquired in adulthood through bilateral cortical lesions.

Although the term 'ocular motor apraxia' has become ingrained, it is inappropriate. According to Johnstone *et al*,⁷⁰ 'ocular motor apraxia consists of a defective initiation of voluntary saccades in the presence of normal reflexive saccades to visual targets and normal nystagmus fast phases'. Since all our patients showed a failure of reflexive quick phases, by this definition, OMA in children is not a true apraxia. We agree with others²³ that the term 'apraxia' should not be used in this context, and recommend that this oculomotor sign be described as an intermittent 'saccadic failure',* reserving the term 'ocular motor apraxia' as Johnstone *et al* describe.⁷⁰

We thank the charities Iris Fund and Help a Child to See for their support.

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*The term 'saccade palsy' would be more appropriate, but this term is already used by some to indicate slow saccades.

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