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Visual outcomes and predictors in optic pathway glioma: a single centre study

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Precis

The majority of children treated for OPG had good vision at follow up. OCT peripapillary retinal nerve fibre layer thickness and pattern VEP responses at presentation conveyed useful prognostic information for visual outcome.

Abstract

Background/Aims

Optic pathway gliomas (OPGs) may cause progressive visual loss despite chemotherapy. Newer, less toxic treatments might be given earlier, depending on visual prognosis. We aimed to investigate the prognostic value of visual evoked potentials (VEP) and optical coherence tomography (OCT).

Methods

A retrospective study of OPG patients (treated 2003-2017) was conducted. Primary outcome was PEDIG category visual acuity in better and worse eyes (good <= 0.2, moderate 0.3-0.6 and poor >=0.7 logMAR). Binary logistic regression analysis was used to identify predictors of these outcomes.

Results

60 patients (32 Neurofibromatosis type 1 [NF1] and 28 sporadic) had median presentation age 49 months (range 17-183) (NF1) and 27 months (range 4-92) (sporadic). Median follow up was 82 months (range 12-189 months). At follow up 24/32 (75%) of NF1 children and 14/28 (50%) of sporadic children had good better eye visual acuity and 11/32 (34%) of NF1 children and 15/28 (54%) of sporadics had poor worse eye acuity. Mean peripapillary retinal nerve fibre layer (RNFL) thickness predicted good *better eye* final acuity (OR 0.799, 95%CI 0.646-0.987, p=0.038). Presenting with visual symptoms (OR 0.22 95% CI 0.001-0.508, p=0.017) and poorer VEP scores (OR 2.35 95% CI 1.1-5.03, p=0.027) predicted poor *worse eye* final acuity. 16 children had homonymous hemianopias at follow up, predicted by poor presenting binocular VEP score (OR 1.449 95%CI 1.052-1.995, p=0.02).

Conclusions

We found that both RNFL thickness on OCT and VEP were useful in predicting future visual acuity and visual field and potentially in planning treatment. We had a high prevalence of homonymous hemianopia.

Introduction

Optic pathway gliomas (OPG) are typically low grade pilocytic astrocytomas involving the visual pathway (optic nerve, chiasm, tracts and radiations) and may involve the hypothalamus. They are a type of low grade astrocytoma which is the most common type of primary central nervous system (CNS) tumour in children[1], making up approximately 50% of all paediatric brain and CNS tumours [2,3] with an overall population incidence rate of 3-4 per 100,000.[4,5] Gliomas that specifically arise from the optic pathway represent approximately 5% of intracranial tumours in children. [6,7,8,9] These tumours principally occur in the first decade of life and the incidence decreases with increasing age.

The most important risk factor for the development of an OPG is the presence of neurofibromatosis type 1 (NF1). NF1 is an autosomal dominant disorder with a high penetrance rate and birth prevalence of approximately 1 in 3,000.[10,11] It has been estimated that 15%-20% of patients with NF1 will develop an OPG, but the incidence is difficult to determine precisely because a significant proportion of NF1-related OPGs never become symptomatic.[8,9,12-17]

Although usually associated with a high survival rate[9], patients with OPG experience multiple sequelae, especially neurological, visual and endocrine, which are likely to affect the quality of life in childhood and into adulthood [18].

OPGs pose a high risk of significant visual loss over time. [17] Previous studies have shown that in both NF1 and sporadic OPG, vision loss occurs between the ages of 1 and 10 years (median 3-5 years). [4,19]. There is a wide spectrum of visual loss in patients with OPG, with some children only experiencing a mild reduction in one eye and others having profound loss of acuity in both eyes. In addition, there may be significant reduction in the visual field, even if the central acuity is preserved [20].

The mainstay of treatment is chemotherapy, though newer treatments such as bevacizumab[21-23] and MAPK inhibitors are the subject of various ongoing studies. [24-25] Visual loss is an important guide to treating these children and any investigations which may help predict the risk of future visual loss would potentially be a valuable guide to treatment. Optical coherence tomography (OCT) with measurement of retinal nerve fibre layer (RNFL) thickness and visual evoked potential (VEP) are potentially useful objective tests to detect and monitor OPG but their role in predicting risk of future visual loss is currently uncertain. [26-29]

Unfortunately, traditional chemotherapy has not been able to improve vision in the majority of cases or even prevent progressive visual loss in many. [30,31] The visual results from the LGG2004 trial were published recently.[32] In addition, clinical factors predicting likely visual deterioration in children with NF1 related OPG have been reported recently.[31] We report visual outcomes from a retrospective single centre study, comparing baseline and follow up visual acuities and fields, aiming specifically to investigate whether the investigations commonly performed in our eye department (pattern VEPs and optic nerve head OCT) contribute to prediction of further visual loss over and above clinical findings.

Methods

Patients with optic pathway glioma were identified from the joint ophthalmology/ oncology optic pathway glioma clinic at Great Ormond Street Hospital, a tertiary paediatric centre in the UK. A retrospective study of patients seen over a 14-year period, presenting 2003-2017, undergoing treatment for OPG was conducted.

Tumours were classified by MRI scan at presentation into Dodge category 1 (optic nerve only), 2 (chiasm) and 3 (post-chiasmal involvement)[33].

Visual acuities (VAs) were measured by a variety of age-appropriate techniques and converted into logMAR values where possible. In order to compare with the LGG2004 study, outcomes are reported by PEDIG category and analysis was done by eyes, counting right and left eyes independently and by child. When the vision of the child was analysed, better eye acuity was used. For analysis of predictors of visual outcome, this was by better and worse eye (classified at follow up). Similar to previous OPG studies, we defined a significant VA response per eye (improvement or worsening) as a ≥0.2 change in logMAR from baseline. For VA response per subject, if one eye improved and the other eye remained stable, the response was defined as improvement. If one eye worsened, irrespective of the response of the other eye (improvement or stable), the response was defined as worsening[32]. For analysis of predictors of visual outcome, it was treated as a categorical variable to allow comparison with other studies and because it was non normally distributed.

Visual fields were assessed by an orthoptist with confrontation or kinetic perimetry where possible. SPECTRALIS® (Heidelberg Engineering Ltd, Hertfordshire, UK) OCT of the RNFL thicknesses were analysed in the inferior, superior, nasal and temporal quadrants and central global score. Since the large majority of values were below published age matched reference limits for age in either eye[34], we treated RNFL as a continuous variable in the analysis. One case was omitted because the discs were believed to be swollen.

Transient VEP recordings were carried out adhering to the International Society for Clinical Electrophysiology of Vision VEP standard.[35] Pattern reversal and onset VEPs (pVEPs) were recorded to high contrast (97%) black and white checkerboards with the test check width subtending 400, 200, 100, 50, 25, 12.5 and 6.25 min of arc. The stimulus field was a 30° display, presented 1m from the subject. Flash VEPs were produced to flashes from a hand-held strobe (Grass model PS22), at a stimulation rate of 3 Hz, and intensity setting 4.0). VEPs were recorded from mid- (Oz), left- (O1) and right-occiput (O2) referred to a mid-frontal electrode (Fz) according to the international 10-20 system. To ensure repeatability of the VEPs, a minimum of two averages, were recorded.

VEP waveforms were graded 1-10 based on the smallest check width to produce a prVEP in each patient, as show in table 1.

Table 1. Pattern visual evoked potential (VEP) grading

Qualitative vision grade	Ranked VEPs	REVERSAL	ONSET	FLASH
no vision	1			absent
rudimentary	2			present
coarse	3		400’	
poor	4	400’	200	
poor	5	200	100’	
moderate	6	100’	50’	
good	7	50’	25’	
good	8	25’	12.5’	
good	9	12.5’	6.25’	
good	10	6.25’		

Results

60 patients with OPG were identified as having full clinical data sets including electro-diagnostic testing, 32 associated with NF1 and 28 sporadic. Median follow up between first VA testing and final VA testing was 82 months (range 12-189 months).

Table 2 shows the baseline characteristics of our patients. Fifty percent of children with NF1 presented with visual symptoms and 61% of those with sporadic disease. Tables 3 and 4 show presenting and follow up VAs by eye and child respectively. 37/60 (62%) children had uniocular quantitative acuities at baseline (24 with NF1 and 13 sporadic), and another 17 had quantitative acuities measured with both eyes open only, 6 did not have quantitative VA. Of the 9 who had poor vision in their better eye at follow up, 7 of these were worse than 1.0 logMAR.

Table 2. Patient Baseline Characteristics, Survival Outcome and Treatment by NF1 status

		NF1 (N=32)	Sporadic (N=28)
Baseline characteristics			
Gender	Male	17 (53%)	15 (54%)
	Female	15 (47%)	13 (46%)
Age at presentation	Age - median	49 months	27 months
	Age range	17-183 months	4-92 months
	<2yrs	6 (19%)	13 (46%)
	2-5yrs	16 (50%)	10 (36%)
	>5yrs	10 (31%)	5 (18%)
Dodge classification	1	10	2
	2	9	15
	3	13	11
Presenting symptom	Visual	16 (50%)	17 (61%)
	Neurological	16 (50%)	11 (39%)
Histology	Pilocytic Astrocytoma	5 (16%)	14 (50%)
	Astrocytoma NOS	0	3 (11%)
	Ganglioglioma	0	2 (7%)
	Pilomyxoid Astrocytoma	0	2 (7%)
	Unbiopsied	27 (84%)	7 (25%)
WHO Grade	WHO Grade 1	5 (16%)	18 (64%)
	WHO Grade 2	0	3 (11%)
	Unbiopsied	27 (84%)	7 (25%)
BRAF Status	BRAF Wildtype	1 (3%)	3 (11%)
	BRAF V600E Mutation	0	6 (21%)
	BRAF: KIAA1549 Fusion	0	9 (32%)
	BRAF Status unknown	31 (97%)	10 (36%)
Survival Outcome Data			
Survival	Alive	31 (97%	28 (100%)
	Died	1 (3%)	0
Treatment Data			
Upfront Surgical Resection	Upfront Surgical Resection	1 (3%)	4 (14%)
	No Upfront Surgical Resection	31 (97%)	24 (86%)

Overall Surgical Interventions	Patients Having Any Form of Surgical Intervention	8 (25%)	22 (79%)
	Gross Total Surgical Resections	2 (6%)	3 (11%)
	Partial Surgical Resections	2 (6%)	10 (36%)
	No Surgical Resection	28 (88%)	15 (54%)
	Surgical Biopsy	1 (3%)	11 (39%)
	CSF Diversion (of any kind)	4 (13%)	13 (46%)
	Average Number of All Surgical Interventions (Range)	2 (1-5)	2 (1-7)
Chemotherapy Treatment	Number Patients Receiving Chemotherapy (At least one course)	12 (38%)	24 (86%)
	Average Number of Chemotherapy Regimes	1.9	3
	Median Number of Chemotherapy Regimes	2	3
	Range of Number of Chemotherapy Regimes	1-3	1-7
Radiotherapy Treatment	Number Receiving Radiotherapy Treatment	0	12 (43%
	Craniospinal (CSI) Photon Radiotherapy (35 CSI Gy* with 19 Gy focal boost)	0	1 (4%)
	Focal Photon Radiotherapy (50.4-54 Gy)	0	5 (18%)
	Focal Proton-Beam Radiotherapy (54 Gy)	0	6 (21%)
Total		**32**	**28**

*Gy= Gray

Table 3. Visual acuities (PEDIG categories) at presentation and follow up by eye for NF1 and sporadic OPG (figures from LGG2004[26] for comparison in bold)

	NF1		Sporadic	
	Baseline	Follow up	Baseline	Follow up
Good (<=0.2)	16 (33%)	36 (50%) **(49%)**	8 (31%)	21 (40%) **(32%)**
Moderate (0.3-0.6)	20 (42%)	12 (26%) **(23%)**	4 (19%)	11 (21%) **(11%)**
Poor (>=0.7)	12 (25%) **(26%)**	15 (24%) **(28%)**	13 (50%) **(49%)**	21 (39%) **(57%)**
Total	48	63	26	53

Table 4. Visual acuities (PEDIG categories) at presentation and follow up by child for NF1 and sporadic OPG

		NF1		Sporadic	
		Baseline	Follow up	Baseline	Follow up
Better eye	Good (<=0.2)	13 (45%)	24 (75%)	8 (31%)	14 (50%)
	Moderate (0.3-0.6)	13 (45%)	5 (16%)	7 (27%)	8 (29%)

	Poor (>=0.7)	3 (10%)	3 (9%)	11 (42%)	6 (21%)
	Total	29	32	26	28
Worse eye	Good (<=0.2)	4 (16%)	14 (44%)	3 (17%)	7 (25%)
	Moderate (0.3-0.6)	11 (44%)	7 (22%)	2 (11%)	6 (21%)
	Poor (>=0.7)	10 (40%)	11 (34%)	13 (72%)	15 (54%)
	Total	25	32	18	28

All patients had VEPs performed soon after presentation and 50/60 (83%) had each eye tested separately. OCT was performed in 38/60 (63%) at least 10 months before final follow up (median 37 months, range 10-94 months). These 38 were older (t=2.02, p=0.048) and more likely (Chi-square =10.2, p=0.001) to have good visual outcome in the better eye than those for whom we did not get OCT readings. One was excluded from further analysis of OCT because the discs were thought to be swollen (RNFL 276 microns better eye and 309 microns worse eye). At baseline 40/60 (67%) had visual fields, 13 GVF (20%) and 29 (47%) confrontation (see table 5). At follow up 47/60 had visual field testing performed; 30 (49%) GVF and 17 (28%) confrontation.

Table 5. Visual fields at baseline and follow up

	Baseline	Follow up
Normal	18 (30%)	26 (43%)
Homonymous hemianopia	12 (20%)	16 (26%)
Bitemporal hemianopia	0 (0%)	0 (0%)
Homonymous quadrantanopia	1(2%)	1 (2%)
General constriction	7 (12%)	1 (2%)
Enlarged blind spot	1 (2%)	3 (5%)
Binasal deficit	1 (2%)	1 (2%)
Missing	20 (33%)	12 (20%)
Total	60	60

Mean peripapillary retinal nerve fibre layer thickness was 73 microns (range 35-120, SD=39) for better eyes and 71 microns (range 30-110 SD=49) for worse eyes with no significant difference. Mean RNFL thickness was higher (t=1.79, p=0.08) for NF1 cases (82 microns SD=48) than sporadic cases (60 microns, SD=16) for best eyes and there were similar findings for worse eyes.

By child, between baseline and follow up VA improved in 44%, stayed same in 30% and worsened in 26% overall. These percentages were 50%, 31%, and 19%, for NF1 and 35%, 30%, and 35% for sporadic. There was no significant effect of age on these proportions. (Table 6)

Table 6. Changes in visual acuity between baseline and follow up by age and NF1 status.

	NF1				**Sporadic**				total
age	n	**improved**	stable	worse	n	**improved**	stable	worse	
<2yrs	2 (100%)	1 (50%)	1 (50%)	0 (0%)	5 (100%)	3 (60%)	0 (0%)	2 (40%)	7
2-5yrs	14 (100%)	8 (58%)	3 (21%)	3 (21%)	6 (100%)	2 (33%)	2 (33%)	2 (34%)	20

>5yrs	10 (100%)	4 (40%)	4 (40%)	2 (20%)	6 (100%)	1 (17%)	3 (50%)	2 (33%)	16
TOTAL	26 (100%)	**13** (50%)	8 (31%)	5 (19%)	17 (100%)	**6** (35%)	5 (30%)	6 (35%)	43

	NF1				Sporadic				total
age	n	improved	stable	worse	n	improved	stable	worse	
<2yrs	2 (100%)	1 (50%%)	1 (50%)	0 (0%)	5 (100%)	3 (60%)	0 (0%)	2 (40%)	7
2-5yrs	14 (100%)	8 (58%)	3 (21%)	3 (21%)	6 (100%)	2 (33%)	2 (33%)	2 (34%)	20
>5yrs	10 (100%)	4 (40%)	4 (40%)	2 (20%)	6 (100%)	1 (17%)	3 (50%)	2 (33%)	16
	26 (100%)	13 (50%)	8 (31%)	5 (19%)	17 (100%)	6 (35%)	5 (30%)	6 (35%)	43

Regarding visual fields, between baseline and follow up 7 (11%) deteriorated, 21 (34%) stayed stable and 9 (15%) improved their fields. 16 children had homonymous hemianopias at follow up including 9 with good visual acuity in their better eye.

Significant ($p<0.05$) univariate predictors of having good vision in the better eye at follow up included grade of vision in the better eye at presentation and VEP grade (better eye or both eyes open) at presentation, and mean RNFL thickness at presentation. In a binary logistic regression analysis only the RNFL thickness finding was an independent predictor (OR 0.799, 95%CI 0.646-0.987, p=0.038) (Supp Table 1)
Younger children (than median) and those with sporadic disease were less likely to achieve good vision in the better eye at follow up but these were not statistically significant (p=0.06) nor independent of presenting VA and VEP in a multiple logistic regression model. Sex did not predict visual outcome generally but did for NF1 patients where girls were more likely (p=0.05) to have good visual outcomes in their better eye (OR 1.449, 95% CI 1.052-1.995). Dodge category 3 was associated with poor visual outcome in NF1 patients only (p=0.06)
Significant ($p<0.05$) univariate predictors of poor vision in the worse eye at follow up included having poor vision at presentation, presenting with visual symptoms, having poorer VEP scores (worse eye) at presentation and thinner RNFL measurements on OCT. Binary logistic regression analysis showed that presenting with visual symptoms (OR 0.22 95% CI 0.001-0.508, p=0.017) and poorer VEP scores (OR 2.35 95% CI 1.1-5.03, p=0.027) retained independent significance and presenting acuity retained borderline independent significance (OR 0.130, 95% CI 0.16-1.041, p=0.055) [supplementary table 2]. Neither young age or having sporadic disease were predictive of poor vision in worse eye.
Predictors of having a homonymous hemianopia at follow up included sporadic disease (OR 0.273, 95% CI 0.77-0.960, p=0.04), and poor presenting VEP score both eyes open (OR 1.449 95%CI 1.052-1.995, p=0.02) and in multiple regression model they were not found to be independent of each other and the VEP score was a better predictor. Dodge score did not predict the presence of a hemianopia.

Discussion

Our results show a similar distribution of outcomes with a trend towards a better chance of improvement in vision in sporadic cases than was reported in LGG2004 (table 2). By child, VA improved in 44% stayed

same in 30%, and worsened in 26% overall. These percentages were 50% *(24%),* 31% *(35%)* and 26% *(41%)* for NF1 and 35% (*18%),* 30% *(43%)* and 35% *(39%)* (the figures in italics are from LGG2004 for comparison). Some improvement in visual acuity would be expected through age maturation but our age stratification is similar to that of LGG2004, though we had a larger proportion of children under 2 years in the sporadic group. We set out visual results in a similar way to the paper reporting visual outcomes from the LGG2004 study[32] for comparison. Our data did not demonstrate an age effect on likelihood of visual change between baseline and follow up. In some cases, visual acuity testing methods will have been different between baseline and follow up since age-appropriate methods were used, and we have relied on logMAR conversion of each methodology for comparison. For this reason and because quite a few children did not have quantifiable acuities at baseline, we have used follow up acuity as our primary outcome rather than change in acuity.

However, our series is not directly comparable with the LGG2004 study, since ours is a retrospective single centre series and patients were treated according to clinical protocols rather than a research protocol. The majority of our patients received a standard chemotherapy regimen the same as in the LGG2004 protocol of vincristine and carboplatin. If there was evidence of radiological or clinical deterioration patients would have been treated with a variety of regimens either as per of a clinical trial or accepted standard of care including single agent vinblastine, bevacizumab containing regimen or targeted therapies with MAPK (BRAF or MEK) inhibitors. The design of our study therefore does not allow us to investigate the effect of different treatments on visual outcome. Nevertheless, as discussed, as there is currently no evidence that any treatments make any difference to visual outcome from natural history, despite the variation in treatments received, our series serves as a longitudinal study and shows slightly better visual results than those reported from LGG2004.

Falzon et al reported both eyes of the same patient as independent variables and also analysed visual outcome by child.[32] We have also described outcomes in this way but our analysis of predictors of visual outcome are by child rather than by eye since this is statistically more robust[36]. We have reported outcomes by better and worse eye since we feel this is the most clinically relevant outcome for the child. Best eye vision is the most important in terms of the child's quality of life and education and worst eye outcome reflects the maximal morbidity caused by the disease. An expert group recently proposed a way of combining the acuities between the 2 eyes[31] but we have not chosen to follow this because that scheme seems not to reflect the child's functional vision. For instance, a child with logMAR 1.1 in their worse eye and 0.2 in the better eye is classed as severely visually impaired whereas a child with logMAR 1.0 worse eye and 0.5 better eye is classed as mild/moderately impaired whereas the likelihood is that the first child will have better functional vision, which is strongly related to the better eye. WHO classification of a child's visual status for instance relates to the acuity in the better eye or with both eyes open.[37]

We also report visual field deficits in this paper and our data illustrate the importance of doing so. For instance, 9 of our 60 children would have been certifiable as visually impaired based on their homonymous hemianopia despite having good visual acuity in their better eye. The predominance of homonymous hemianopias over bitemporal hemianopias is suggestive of involvement of the disease posterior to the chiasm even if not radiologically evident.

In regard to predicting visual outcome, Azizi et al reported symptoms of visual impairment and clinical optic atrophy predicted poor visual outcome in NF1 patients only.[31] We looked at whether the investigations commonly performed in the eye clinic, OCT and VEP contribute predictive information additional to clinical symptoms or signs. We did not report clinical optic atrophy because we find it hard to quantify this in a retrospective study and OCT is replacing clinical assessments of degrees of disc pallor.

We found that mean peripapillary nerve fibre thickness was reduced compared to age standardized reference limits in both better and worse eyes and that higher (thicker) values predicted good visual outcome in the better eye and was a better predictor of visual acuity at final follow up even than presenting acuity (mean global RNFL 107 micrometres in children aged 5-15 years[34]). This may be because visual acuity can be difficult to reliably quantify in young children and that RNFL is a more objective and discriminating

indicator of the state of the optic nerve of the better eye. Gu et al reported that macular ganglion cell inner plexiform layer thickness had better correlation with concurrent (not future) visual acuity than peripapillary nerve fibre layer thickness and they and we would agree that a prospective longitudinal study to evaluate the prognostic accuracy of both would be helpful.[27] We chose the RNFL for this study because it is easier to obtain in our patient population and because we had a high rate of visual field loss in addition to central visual loss which might be expected to affect the RNFL more than the macular structures.

For predicting severe visual loss in the worse eye, pattern VEP response was helpful and poor responses at presentation predicted severe visual loss at follow up, independent of presenting visual acuity and presenting with visual symptoms. Of note we were able to get VEP recordings in each eye separately in a higher proportion of children at baseline than we were able to obtain quantitative acuities in each eye separately.

The reason why RNFL thickness shows correlation with vision in the better eye and VEP with vision in the worse eye might be that OCT readings were more likely to be obtained in eyes with better acuities so may be more discriminating for such eyes and less so for eyes with poorer vision. Also, the better eye acuities were skewed towards the good end, where VEP measurements are known to be less discriminating.[30] A deficit of fibres as in optic atrophy will 'dilute or washout'vision. If the remaining few functioning axons produce a poor VEP, but just happen to represent the fovea it is possible for a high contrast visual acuity to be recorded and the relationship between pVEP and VA diverge.[38] Low contrast VA is likely a better associate with the pVEP. Another possibility is that at the severe stages of the disease, axonal damage may be occurring mediated by toxic factors produced by the glioma cells or microglial cells and that damage to their function may precede cell death as would be reflected in thinning of the RNFL. Therefore, a functional measurement such as VEP gives a better indication of residual visual function.

The usual limitations of a retrospective study apply to this work. In addition the chronological and developmental age limited the accuracy of the some of the clinical data eg uniocular acuities and formal visual fields were not always obtained. In addition the OCT scans were perfomed a bit later after presentation than the VEPs becaue the latter was the more established rtechnique for younf children. The children for whom we were able to get OCT scans were older and had better vision which may have introduced systematic bias.

Nevertheless, these findings suggest that both these investigations may be helpful in guiding treatment decisions, being more predictive of final visual acuity than presenting visual acuity for both better and worse eyes, and that perhaps OCT is more useful in eyes with better vision and VEP in eyes with worse vision. These findings warrant further prospective evaluation. In the future we may be add macular ganglion cell layer thickness to our protocol more often and as treatments become less toxic and more effective, accurate visual prognostication may become an even more oimprtant part of management of these children.

In summary at final follow up 75% of NF1 patients and 50% of sporadic patients had good visual acuity, as defined by PEDIG, (logMAR <=0.2) in their better eye, and 34% of NF1 and 54% of sporadic cases had poor vision in their worse eye. 9 children with good vison in their better eye had significant field loss worthy of certification as sight impaired. As our treatment options for these children increase with less drug associated morbidity, predicting future visual loss may become more important in guiding treatment and these data suggest that both OCT and VEP testing may be helpful in this regard.

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