

# Correlation between visual function, neurodevelopmental outcome, and magnetic resonance imaging findings in infants with periventricular leucomalacia

Giovanni Cioni, Barbara Bertuccelli, Antonio Boldrini, Raffaello Canapicchi, Barbara Fazzi, Andrea Guzzetta, Eugenio Mercuri

## Abstract

**Aim**—To evaluate the correlation between visual function and neurodevelopmental outcome in children with periventricular leucomalacia at 1 and 3 years.

**Method**—Visual acuity, visual field, ocular motility, and optokinetic nystagmus were tested in 29 infants with periventricular leucomalacia by brain magnetic resonance imaging. All infants also had a structured neurological examination and a Griffiths developmental assessment.

**Results**—21 of the infants showed at least one abnormality of visual function. The degree of visual impairment—that is, the number of visual tests showing abnormal results—correlated well with the results on developmental assessment at both ages.

**Conclusion**—Multivariate analysis showed that visual impairment was the most important variable in determining the neurodevelopmental scores of these infants, more than their motor disability and the extent of their lesions on magnetic resonance imaging.

(Arch Dis Child Fetal Neonatal Ed 2000;82:F134-F140)

Keywords: vision; developmental score; magnetic resonance imaging; periventricular leucomalacia

In the last decade there has been increasing evidence that infants with periventricular leucomalacia (PVL) show a high incidence of abnormalities on tests assessing various aspects of visual function, such as eye movements, visual acuity, visual fields, and visual evoked potentials.<sup>1-6</sup> Visual abnormalities are significantly associated with the postchiasmatic visual pathway and, in particular, optic radiations and visual cortex on magnetic resonance imaging (MRI).<sup>4-6</sup> Abnormal visual function can already be observed in the first months of life and seems to persist at preschool and school age.<sup>3,7</sup> It is also known that visual abnormalities are often associated with motor, perceptual, and global neurodevelopmental abnormalities.<sup>7-10</sup>

The relation between visual function and neurodevelopment in children with brain lesions is not fully understood. The concomitant involvement of visual and neurodevelopmental abilities found in previous studies is not surprising, as children with visual impairment often showed extensive lesions which involved the underlying structures relevant for motor, cognitive, and visual functions.<sup>9,11,12</sup> However, a

causal and direct effect of visual impairment on development may also be hypothesised. Vision plays a crucial role in early motor and cognitive learning,<sup>13</sup> and developmental retardation is often observed in congenitally blind infants, even in the absence of brain lesions.<sup>14</sup>

The aim of this study was to evaluate the correlation between visual function and neurodevelopmental outcome in the first year of life in infants with PVL. More specifically, we aimed not only to evaluate whether developmental scores correlated with the extent of visual impairment but also, by multivariate analysis, whether such a correlation, if confirmed, could be due to other variables, such as the severity of brain lesions, rather than directly to the visual impairment.

## Subjects and methods

The patients included in this research are part of a continuing follow up study of newborns with brain lesions born at the Neonatal Unit of the University Hospital of Pisa between January 1989 and December 1994. As part of this study, all the newborns with brain lesions on sequential neonatal ultrasound, performed with 5 and 7.5 MHz probes, who present clinical neurological abnormalities at term, such as abnormal muscle tone or abnormal quality of spontaneous movements,<sup>15</sup> are referred to the Division of Child Neurology and Psychiatry and are enrolled in a prospective clinical and MRI follow up study.

For the present research we selected all cases fulfilling the following criteria:

- clear signs of PVL on MRI, according to the criteria indicated in the literature<sup>16,17</sup>;
- comprehensive visual assessment performed at the mean (SD) age, corrected for prematurity, of 12 (4) months;
- neurological and neurodevelopmental assessments performed at the same age as the visual assessment.

As the aim of this study was to evaluate cerebral visual impairment, infants who showed severe ophthalmological abnormalities (such as ROP stage III or upwards, major refraction problems, optic nerve atrophy) were excluded. Similarly, we also excluded infants with congenital diseases.

## NEUROLOGICAL EXAMINATION

This was performed by using an examination based on Touwen criteria.<sup>18</sup> The infants were classified into three groups: (1) normal; (2) mildly abnormal (mild retardation and/or

**Stella Maris Scientific Institute, Division of Child Neurology and Psychiatry, Via dei Giacinti 2, I-56018 Calambrone, Pisa, Italy**

G Cioni  
B Bertuccelli  
R Canapicchi  
B Fazzi  
A Guzzetta

**Neonatal Intensive Care Unit, University of Pisa**  
A Boldrini

**Department of Neuroradiology, S Chiara Hospital, Pisa, Italy**  
R Canapicchi

**Department of Paediatrics and Neonatal Medicine, Imperial College, Hammersmith Hospital, London, UK**  
E Mercuri

Correspondence to:  
Dr Cioni  
email: [ciono@inpe.unipi.it](mailto:ciono@inpe.unipi.it)

Accepted 13 August 1999

Table 1 Grading of magnetic resonance imaging findings

Size of lateral ventricles	Grade 1	Normal size of both ventricles	
	Grade 2	Unilateral enlargement or bilateral mild enlargement	
	Grade 3	Bilateral severe enlargement	
WM abnormal signal intensity	Grade 1	Normal WM or only focal involvement of PV-WM	
	Grade 2	Diffuse involvement of PV-WM in both hemispheres or involvement of SC-WM in one hemisphere	
	Grade 3	Involvement of SC-WM in both hemispheres	
WM reduction	Grade 1	Not reduced	
	Grade 2	Reduction of PV-WM in both hemispheres or of deep WM diffusely in one hemisphere	
	Grade 3	Reduction of deep WM diffusely in both hemispheres	
Cysts	Grade 1	No cysts	
	Grade 2	Small cysts (n<3) bilateral in PV regions or unilateral cystic lesion (small or large)	
	Grade 3	Bilateral multiple cysts (small or large) involving PV regions and/or deep WM	
Size of subarachnoid space	Grade 1	No enlargement	
	Grade 2	Bilateral diffuse mild enlargement or severe enlargement only in one hemisphere	
	Grade 3	Diffuse severe enlargement in both hemispheres	
Corpus callosum	Grade 1	Normal or thinning involving the posterior body	
	Grade 2	Thinning involving the total body	
	Grade 3	Diffuse thinning	
Cortical grey matter (ulegyria and cortical dysplasia)	Grade 1	No cortical abnormalities	
	Grade 2	Unilateral cortical abnormalities	
	Grade 3	Bilateral cortical abnormalities	
Total score	Grade 1	Sum of previous scores	7-11
	Grade 2		12-16
	Grade 3		17-21
Visual cortex	Grade 1	No impairment	
	Grade 2	Moderate impairment	
	Grade 3	Severe impairment	
Optic radiations	Grade 1	No impairment	
	Grade 2	Moderate impairment	
	Grade 3	Severe impairment	

WM, white matter; PV, periventricular; SC, subcortical (from Cioni *et al*<sup>11</sup>).

neurological signs, but not cerebral palsy); (3) cerebral palsy with relatively normal head and trunk control; (4) cerebral palsy without head and trunk control.

#### VISUAL ASSESSMENT

This included the assessment of various aspects of visual function as follows.

*Grating acuity*—this was assessed binocularly by the Teller acuity card procedure.<sup>19 20</sup> This method is based on an inborn preference for a pattern (black and white gratings of different

stripe widths) over a uniform field, depicted on cards with decreasing stripe widths. The location of the left/right position of the test stimulus varies randomly. An observer judges the infant's reaction as to the location of the test stimulus on the basis of eye and head movement. The threshold of acuity is taken as the finest stripe width for which the subject consistently responds correctly. Acuity values were expressed in minutes of arc (or cycles per degree) and compared with normative data reported in the literature.<sup>20 21</sup>

Table 2 Clinical and neuroradiological findings

Case	Neurological outcome	US	Magnetic resonance imaging								Total score	VC	OR
			LV	WMS	WMR	GM	Cysts	SS	CC				
1	Hemi	PVL-2	1	1	1	1	1	1	1	1	7	1	1
2	Norm	PVL-1	1	2	2	1	2	2	1	1	11	1	1
3	Dip	PVL-1	1	2	2	1	1	1	3	11	1	1	
4	Reta	PVL-1	1	1	1	1	1	2	1	8	1	1	
5	Dip	PVL-2	1	2	1	1	1	1	3	10	1	3	
6	Reta	PVL-1	1	1	1	1	1	1	1	7	1	1	
7	Hemi	PVL-1/IPE	2	2	2	1	2	2	1	12	1	1	
8	Dip	PVL-3	2	2	2	1	1	1	2	11	1	1	
9	Dip	PVL-1	1	2	2	1	1	1	2	10	1	2	
10	Reta	PVL-2	1	2	2	1	2	2	1	11	1	2	
11	Reta	PVL-1	3	2	2	1	1	1	3	13	1	1	
12	Dip	PVL-1	1	1	1	1	1	2	1	8	1	1	
13	Dip	PVL-2	1	2	2	1	2	1	2	11	1	3	
14	Dip	PVL-3	1	2	2	1	1	1	1	9	1	1	
15	Dip	PVL-2	1	2	1	1	1	1	1	8	1	1	
16	Dip	PVL-1	2	2	2	1	2	1	1	11	1	2	
17	Dip	PVL-1	2	2	1	1	1	2	1	10	1	2	
18	Dip	NA	3	2	2	1	2	2	2	14	1	2	
19	Reta	PVL-1	2	2	2	1	2	1	1	11	1	3	
20	Reta	PVL-2	1	1	1	1	1	1	1	7	1	1	
21	Dip	PVL-2	2	3	3	1	1	2	2	14	1	2	
22	Tetra	PVL-3	3	2	2	1	1	2	2	13	1	3	
23	Dip	PVL-3	2	2	2	1	1	2	2	12	1	2	
24	Dip	PVL-1	3	3	3	1	2	2	3	17	1	1	
25	Dip	PVL-1/IPE	3	2	2	2	2	2	3	16	2	3	
26	Tetra	PVL-3	3	2	2	1	3	1	3	15	1	3	
27	Tetra	PVL-3	3	2	3	1	2	1	3	15	1	3	
28	Tetra	PVL-2	3	2	3	1	1	2	3	15	1	3	
29	Tetra	PVL-3	2	2	2	1	2	1	2	12	1	3	

Hemi, hemiplegia; Dip, diplegia; Tetra, tetraplegia; Reta, retardation; Norm, normal; PVL, periventricular leucomalacia graded as described by deVries *et al*<sup>23</sup>; IPE, intraparenchymatous echodensity; NA, not available; LV, lateral ventricles; WMS, white matter abnormal signal intensity; WMR, white matter reduction; GM, grey matter; SS, subarachnoid space; CC, corpus callosum; VC, visual cortex; OR, optic radiations.

Table 3 Results of visual and neurodevelopmental assessment

Case	Visual findings						Griffith DQs at 1 year						Griffith DQ at 3 years			
	Age at testing	Visual acuity	Visual field	Fix/following	Strabismus	OKN	Total score	Age at testing	Locomotor	Personal-social	Hearing-speech	Hand-eye coordination	Performance	General	Age at testing	General
1	11	N	N	N	-	N	0	14	84	107	93	96	104	97	36	102
2	11	N	N	N	-	N	0	12	109	95	91	87	87	94	36	94
3	8	N	N	N	-	N	0	12	81	96	100	92	100	94		
4	13	N	N	N	-	N	0	13	77	96	104	92	92	92	45	93
5	14	N	N	N	-	N	0	15	80	90	93	90	87	88	39	78
6	14	N	N	N	-	N	0	14	75	93	93	89	85	87	31	102
7	14	N	N	N	-	A	1	14	93	96	107	110	100	101	34	84
8	10	N	N	N	-	A	1	10	85	100	90	90	100	93	31	101
9	14	N	N	N	-	A	1	14	89	89	82	85	89	87	31	95
10	14	N	N	N	-	A	1	13	69	89	100	89	80	85		
11	12	N	N	N	+	N	1	12	88	93	117	87	92	95	37	93
12	9	N	N	N	+	N	1	11	71	81	77	73	73	75	34	65
13	15	N	N	N	+	N	1	16	84	62	69	66	56	67		
14	12	N	N	N	+	A	2	12	69	100	100	96	96	92	36	85
15	16	N	N	N	+	A	2	12	33	100	112	83	83	82	36	95
16	14	N	N	N	+	A	2	14	58	79	75	75	60	69	31	91
17	15	A	N	N	+	N	2	13	77	92	92	89	89	88		
18	15	A	N	N	+	N	2	15	47	70	77	50	53	59	39	75
19	11	A	N	N	+	A	3	10	90	110	85	85	115	97	30	100
20	10	A	N	N	+	A	3	10	80	80	75	75	75	77	36	95
21	15	A	BN	A	+	N	4	15	50	76	76	66	71	68		
22	8	A	BN	N	+	A	4	11	<20	77	77	55	45	54		
23	10	A	BN	A	+	A	5	11	64	91	91	86	73	81		
24	12	A	BN	A	+	A	5	13	46	77	81	69	62	67	34	59
25	12	A	RL	A	+	A	5	8	65	50	42	38	38	47	47	66
26	13	A	BN	A	+	A	5	8	25	57	71	43	<20	42	30	32
27	12	A	BN	A	+	A	5	14	23	28	43	39	39	34	40	41
28	16	A	BN	A	+	A	5	16	<20	37	47	37	<20	28		
29	12	A	BN	A	+	A	5	12	<20	33	54	25	<20	26		

DQ, developmental quotient; BN, bilateral narrow; RL, right loss; N, normal; A, abnormal; +, present; -, absent.

**Visual field**—its size was assessed using kinetic perimetry by the technique described in detail elsewhere.<sup>18,19</sup> The apparatus consists of two 4 cm wide black metal strips, mounted perpendicularly to each other and bent to form two arcs, each with a radius of 40 cm. The perimeter is placed in front of a black curtain, concealing the observer, who can watch the infant's eye and head movements through a peep hole. The infant is held in the centre of the arc perimeter, with the chin supported. During central fixation of a 6° diameter white ball, an identical target is moved from the periphery towards the fixation point along one of the arcs of the perimeter at a velocity of around 3°/s. Eye and head movements towards the peripheral ball are used to estimate the outline of the visual fields. Normative data for full term and preterm infants are available.<sup>21,22</sup>

**Horizontal optokinetic nystagmus (OKN)**—this was elicited by moving a large piece of paper at a distance of 40 cm in front of the infant's face, at a velocity of about 15°/s. The paper is covered with black and white dots of 1 cm<sup>2</sup>. The number of saccades in response to left side stimulation is judged and compared with that of right side stimulation. Normally, binocular OKN is symmetrical from birth onwards, whereas monocular OKN (not systematically tested in this study) shows a better response to stimulation in a temporonasal direction up to about 3 to 6 months of corrected age.

**Oculomotor behaviour (following and fixation) and strabismus**—any abnormality of eye contact, spontaneous nystagmus, fixation and following in all directions, and convergence movements is also noted. Eye alignment was tested by commonly used orthoptic techniques, such as the cover test.

Each test of visual function was scored on a two point scale (0 = normal, 1 = abnormal). A visual function score was given to each infant on the basis of the number of impaired items. Scores ranged from 0 (no item impaired) to 5 (all items impaired).

#### DEVELOPMENTAL ASSESSMENT

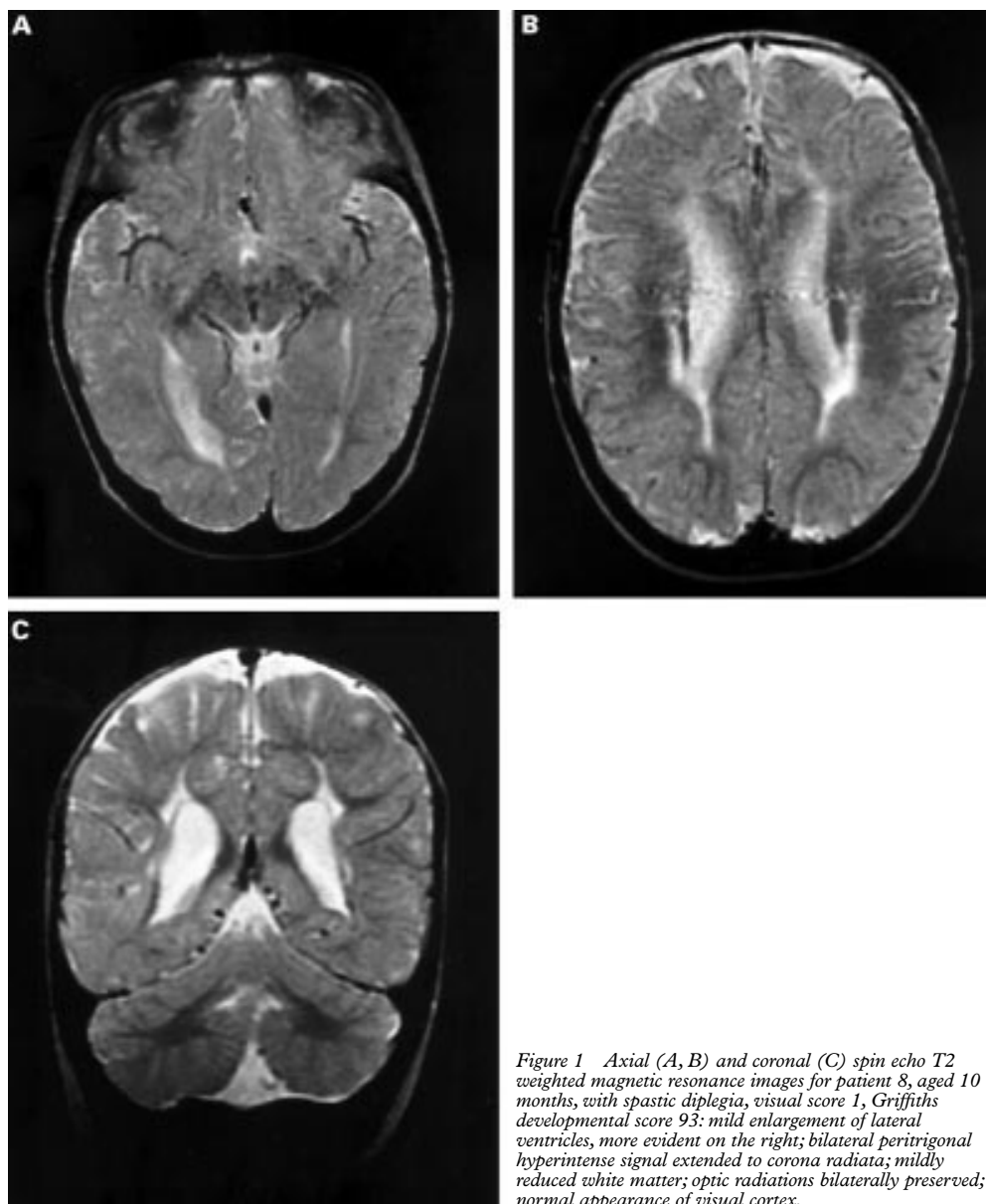
This was assessed using the Griffiths developmental scales.<sup>23</sup> General developmental quotients (DQs) and, separately, the DQ of each subscale (locomotor, personal-social, hearing-speech, hand-eye co-ordination, and performance) were obtained. Scores were classified as normal (85 or above), borderline (84–71), or abnormal (70 or below). The test was performed at about 1 year of age (range 8–16 months), and a follow up assessment was also performed at around 3 years of age (range 30–47 months).

#### MAGNETIC RESONANCE IMAGING

Brain MRI studies were performed under sedation using a 0.5 T system in sequence spin-echo. T1, proton density, and T2 weighted images were obtained in the axial, coronal, and sagittal planes with sections of 5 mm. The images were assessed retrospectively by a neuroradiologist (RC) and separately by a child neurologist (GC), unaware of the prenatal and perinatal histories or of the clinical evaluations. MRI findings were scored according to two different classifications used in our previous studies on PVL<sup>11,24</sup> (table 1).

#### Extent of the lesion

The following items were scored: size of lateral ventricles, evidence and extension of white matter damage (as shown by areas of prolonged T1 and/or T2 relaxation) and of white matter



*Figure 1 Axial (A, B) and coronal (C) spin echo T2 weighted magnetic resonance images for patient 8, aged 10 months, with spastic diplegia, visual score 1, Griffiths developmental score 93: mild enlargement of lateral ventricles, more evident on the right; bilateral peritrigonal hyperintense signal extended to corona radiata; mildly reduced white matter; optic radiations bilaterally preserved; normal appearance of visual cortex.*

loss (as shown by abnormal infolding of cerebral gyri and sulci), thinning of corpus callosum, evidence and size of cystic areas (as shown by areas of hypointensity on T1 and proton density weighted images and hyperintensity on T2 weighted images), size of the subarachnoid space, and abnormalities of cortical grey matter. Each item was scored on a three grade scale, with score 3 indicating the most severe MRI abnormalities. The scores of the seven items were summed to obtain a total score for each infant. The total scores were also classified on a three grade scale.

*Severity of the lesions in optic radiation and visual cortex (striate, parastriate, and peristriate areas)*

Three degrees of impairment were scored: 1, no impairment; 2, moderate impairment; 3, severe impairment. The left and right sides were graded separately. In the few cases in which side differences were found, the most severe scores were taken.

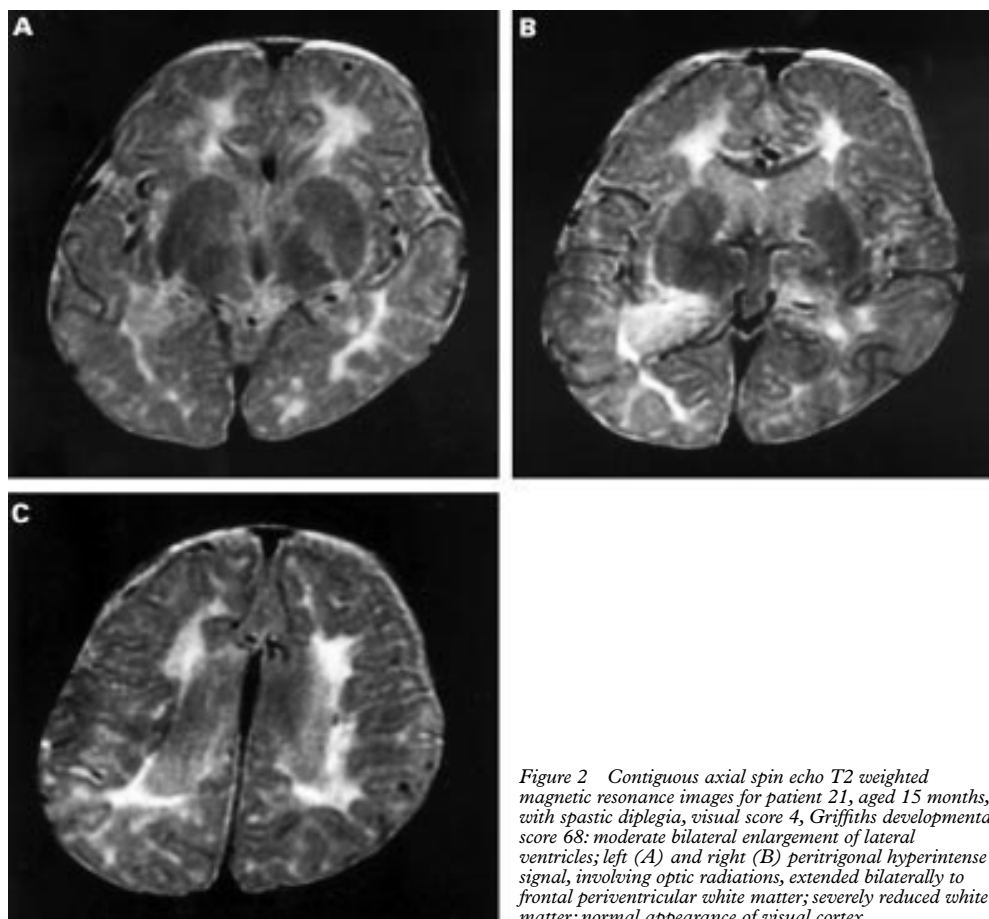
#### STATISTICAL ANALYSIS

Correlation analysis was performed by the Kendall correlation test (tau-b coefficient). A multiple regression analysis was conducted to assess effect of visual impairment, motor outcome, and MRI findings on cognitive development at 1 year. The correlation between DQs at 1 and 3 years was tested by the Spearman test.

Although the aim of this study was to correlate visual and developmental findings at the same age (1 year), we also correlated both visual and cognitive findings at 1 year with developmental scores obtained after 30 months.

#### Results

Twenty nine infants fulfilled the inclusion criteria. Their gestational age at birth ranged from 27 to 36 weeks (mean (SD) 31 (2.8) weeks). Mean (SD) age at testing (corrected for prematurity) was 13 (2.1) months (range



**Figure 2** Contiguous axial spin echo T2 weighted magnetic resonance images for patient 21, aged 15 months, with spastic diplegia, visual score 4, Griffiths developmental score 68: moderate bilateral enlargement of lateral ventricles; left (A) and right (B) peritrigonal hyperintense signal, involving optic radiations, extended bilaterally to frontal periventricular white matter; severely reduced white matter; normal appearance of visual cortex.

8–16). Table 2 summarises the results of all infants tested. Cranial ultrasound results were available in 28 of the 29 infants studied. According to the classification suggested by de Vries *et al*,<sup>25</sup> 13 infants had grade 1 PVL, eight had grade 2, and seven grade 3. Table 2 gives the details of ultrasound findings.

#### NEUROLOGICAL EXAMINATION

One case showed normal and six mildly delayed motor development while the remaining 22 subjects had cerebral palsy. Seventeen infants showed relatively normal head and trunk control (15 diplegic and two hemiplegic cases), which was lacking in the other five infants (all tetraplegic cases).

#### VISUAL ASSESSMENT

Severe fixation and following disorders were present in eight of the 29 infants and strabismus in 19. Abnormal grating acuity was

found in 13, reduced visual field in nine, and OKN abnormalities in 17.

Six infants had a visual function score of 0 (all the items were normal), seven had a score of 1, and five had a score of 2; two had a score of 3, and the other two a score of 4. The remaining seven infants had a score of 5 (all the items abnormal). Table 3 details the visual assessment.

#### DEVELOPMENTAL ASSESSMENT

The global DQs in the cohort at 1 year ranged from 26 to 101 (mean DQ = 74.7). Fourteen subjects had a normal DQ, four fell in the borderline range (70–84), and 11 had abnormal DQ (< 70). Table 3 shows results obtained in each subscale.

The global DQ at follow up was available in 20 of the 29 infants. This ranged from 32 to 102 (mean DQ = 82).

**Table 4** Correlation between Griffiths developmental quotients (DQs) and visual function score, motor, and magnetic resonance imaging (MRI) scores (all subjects included n = 29)

	Griffiths DQs					
	Locomotor	Personal-social	Hearing-speech	Eye-hand coordination	Performance	Global
Visual function score (0–5)	–0.53 p = 0.000	–0.48 p = 0.001	–0.50 p = 0.000	–0.60 p = 0.000	–0.54 p = 0.000	–0.58 p = 0.000
Motor score (1–3)	–0.55 p = 0.000	–0.46 p = 0.003	–0.44 p = 0.004	–0.43 p = 0.005	–0.47 p = 0.002	–0.53 p = 0.000
MRI score (1–3)	–0.38 p = 0.02	–0.48 p = 0.002	–0.30 p = 0.054	–0.46 p = 0.004	–0.47 p = 0.003	–0.43 p = 0.006

Kendall tau-b.

Table 5 Correlation between Griffiths developmental quotients (DQs) and visual function score, motor, and magnetic resonance imaging (MRI) scores (tetraplegic subjects excluded  $n = 24$ )

	Griffiths DQs					
	Locomotor	Personal-social	Hearing-speech	Eye-hand coordination	Performance	Global
Visual function score (0-5)	-0.38 p = 0.01	NS	-0.35 p = 0.02	-0.47 p = 0.003	-0.36 p = 0.02	-0.43 p = 0.006
Motor score (1-3)	NS	NS	NS	NS	NS	NS
MRI score (1-3)	NS	NS	NS	NS	NS	NS

Kendall tau-b.

#### MAGNETIC RESONANCE IMAGING

Table 2 shows details of the MRI findings. The total score, summing the results of the individual items assessing the extent of the lesions, ranged from 7 to 17. When optic radiation and visual cortex were assessed, 16 infants had involvement of the optic radiation. One of the 16 also showed involvement of the visual cortex.

Figures 1 and 2 show magnetic resonance images for cases 8 and 21 respectively.

#### CORRELATION BETWEEN VISUAL FUNCTION AND MRI FINDINGS

There was a significant correlation between visual function score and size of lateral ventricles ( $\tau\text{-b} = 0.63$ ;  $p < 0.000$ ), white matter damage ( $\tau\text{-b} = 0.40$ ;  $p = 0.01$ ), white matter loss ( $\tau\text{-b} = 0.48$ ;  $p = 0.003$ ), and corpus callosum ( $\tau\text{-b} = 0.35$ ;  $p = 0.03$ ).

A very high correlation coefficient was also found with optic radiation ( $\tau\text{-b} = 0.76$ ;  $p < 0.000$ ). Visual cortex was not included in this kind of analysis because only one infant of our sample showed abnormalities; this infant presented severe visual impairment in all the items evaluated, as well as mental retardation and severe diplegia.

#### CORRELATION BETWEEN VISUAL FUNCTION AND DEVELOPMENTAL SCORES

There was a significant correlation between visual impairment and general DQ ( $\tau\text{-b} = 0.58$ ;  $p = 0.000$ ); the correlation also reached significance for all subscale DQs (table 4).

#### CORRELATION BETWEEN BRAIN LESIONS AND MOTOR ABILITY AND DEVELOPMENTAL SCORES

Both brain lesions and motor impairment also showed a significant correlation with developmental scores ( $\tau\text{-b} = -0.53$ ,  $p = 0.000$  and  $\tau\text{-b} = 0.43$  and  $p = 0.000$ , respectively). Table 4 shows details of the correlation with the subscale DQs.

#### DIRECT COMPARISON OF THE INFLUENCE OF VISUAL, MOTOR, AND MRI FINDINGS ON DEVELOPMENT ASSESSMENT

To examine the influence of visual, motor, and MRI impairment on developmental scores, we also did a multiple regression analysis (stepwise method), which always indicated the visual deficit to be the most important variable in determining cognitive performances of our sample ( $F = 40.9$ ,  $p < 0.000$ ); motor impairment entered as the second variable ( $F = 32.9$ ,  $p < 0.000$ ), while brain lesions, as detected by MRI, did not reach significance.

The results were quite different when tetraplegic infants were not included in the sample. Both the global DQ and the subscale DQ remained correlated with visual impairment (except for personal-social DQ) but not with motor outcome and MRI findings. On multivariate analysis, visual function was the only variable to reach significance ( $F = 12.8$ ,  $p = 0.002$ ) (table 5).

#### CORRELATION BETWEEN EARLY AND LATE ASSESSMENT

There was a significant correlation between visual impairment at 1 year and general DQ at 3 years ( $\tau\text{-b} = 0.40$ ;  $p = 0.02$ ). Moreover the DQs at the two assessments were significantly correlated ( $r = 0.65$ ;  $p = 0.002$ ).

#### Discussion

Our results show a high incidence of abnormalities in various aspects of visual function, such as grating acuity, ocular motility, visual field, and OKN in infants with PVL. Twenty three out of 29 of our children had at least one abnormality on one of these tests, and more than 50% had multiple abnormalities. These are higher than in previous studies,<sup>1 5 6 9</sup> and the difference may be explained by the different inclusion criteria used. In our study, only infants with PVL on ultrasound examination who had overt clinical signs at term underwent MRI, and those with PVL who had a normal neurological examination at term were not enrolled in the prospective clinical and imaging follow up study. The aim of this study, however, was not to replicate previous studies reporting the incidence of visual abnormalities in a population of infants with PVL,<sup>5 9</sup> but to evaluate whether visual abnormalities at 1 year, if present, were associated with the extent of the lesions on MRI and with neurocognitive abnormalities assessed at the same time.

In agreement with previous studies,<sup>4 6 24</sup> we found a strong association between the degree of visual impairment and the involvement of optic radiation on MRI.

We were also able to show a significant correlation between visual function and neurodevelopmental quotients at 1 year. The infants with normal visual function had normal cognitive performances, while those with the most severe visual impairment also had the lowest DQ. The correlation was significant not only with the developmental assessment performed at 1 year, but also with that performed after 2 years of age. These results confirm our previous findings in full term infants with hypoxic-ischaemic encephalopathy,<sup>12</sup> in whom

we also found a strong correlation between visual function and DQ.

The only study to report an association between early visual and developmental abnormalities in preterm infants with PVL is by Eken *et al.*<sup>9</sup> Their findings, however, cannot be easily compared with ours, as they also included preterm infants with other types of brain lesion, and visual acuity was the only measure of visual function assessed.

Our study has also highlighted the importance of assessing various aspects of visual function, as these may play an important role in global development.

In this study we were also interested to evaluate whether the low developmental scores could be mainly due to the severity of the brain lesions or motor impairment, rather than to a direct effect of the visual impairment. The values of the correlation coefficients, as well as the results of multiple regression analysis in our cohort, suggest that visual function is crucial per se in the early development of these children. This finding is not surprising and is in agreement with previous studies,<sup>13, 14</sup> indicating the important role played by vision in the early phases of infant development.

Although in this study the correlation between visual function and DQ was significant, some exceptions were observed. For example, cases 12 and 13 had low DQs, despite normal visual function and a mild strabismus. In contrast, other infants had a DQ within the normal range for age, but showed a strabismus associated with asymmetrical OKN (case 14) or abnormal visual acuity (cases 17 and 19). These results can be explained by the fact that, although vision plays an important role in cognitive development, the latter is a complex and multifactorial event. Other factors, related partly to biological structure of each individual (including the presence of brain lesions) and partly to environmental conditions, will also influence the outcome.

In conclusion, our findings confirm the importance of a comprehensive assessment of infants with PVL. Further studies are also needed, including other aspects of cortical visual function such as orientation-reversal visual evoked potentials,<sup>26, 27</sup> to evaluate the relation between early abnormalities of visual function and cognitive and perceptual motor abilities at school age. Early detection of impaired visual function may permit these infants to be enrolled in early intervention programmes, which can improve their visual outcome.<sup>28</sup> Longitudinal studies are needed to evaluate the plasticity of the central visual areas after early brain damage and the possible role of the environment in brain reorganisation.

This work was supported by grant RC 1/98 from the Italian Ministry of Health. The authors gratefully acknowledge the contribution of Jackie Van Hof-van Duin, Carlo Romano, and Michele Coluccini to the visual assessments, and Paola B Paolicelli to the neurological examinations.

- 1 Scher MS, Dobson V, Carpenter NA, Guthrie RD. Visual and neurological outcome of infants with periventricular leukomalacia. *Dev Med Child Neurol* 1994;31:353–65.

- 2 Eken P, de Vries LS, van Nieuwenhuizen O, Schalijs-Delfos N, Reits D, Spekreijse H. Early predictors of cerebral visual impairment in infants with cystic leukomalacia. *Neuropediatrics* 1996;27:16–25.
- 3 Jacobson L, Ek U, Fernell E, Flodmark O, Broberger U. Visual impairment in preterm children with periventricular leukomalacia: visual, cognitive and neuropsychiatric characteristics related to cerebral imaging. *Dev Med Child Neurol* 1996;38:724–35.
- 4 Uggetti C, Egitto MG, Fazzi E, *et al.* Cerebral visual impairment in periventricular leukomalacia: MR correlation. *AJNR Am J Neuroradiol* 1996;17:979–85.
- 5 Cioni G, Fazzi B, Coluccini M, *et al.* Cerebral visual impairment in preterm infants with periventricular leukomalacia. *Pediatr Neurol* 1997;17:331–8.
- 6 Lanzi G, Fazzi E, Uggetti C, *et al.* Cerebral visual impairment in periventricular leukomalacia. *Neuropediatrics* 1998;29:145–50.
- 7 van Hof-van Duin J, Cioni G, Bertuccelli B, *et al.* Visual outcome at 5 years of newborn infants at risk of cerebral visual impairment. *Dev Med Child Neurol* 1998;40:302–9.
- 8 Koeda T, Takeshita K. Visuo-perceptual impairment and cerebral lesions in spastic diplegia with preterm birth. *Brain Dev* 1992;14:239–44.
- 9 Eken P, de Vries LS, van der Graaf Y, Meiners LC, van Nieuwenhuizen O. Haemorrhagic-ischaemic lesions of the neonatal brain: correlation between cerebral visual impairment, neurodevelopmental outcome and MRI in infancy. *Dev Med Child Neurol* 1995;37:41–55.
- 10 Jongmans M, Mercuri E, Henderson S, de Vries L, Sonksen P, Dubowitz L. Visual functions of prematurely born children with and without perceptual-motor difficulties. *Early Hum Dev* 1996;45:73–82.
- 11 Cioni G, Di Paco C, Bertuccelli C, Paolicelli PB, Canapicchi R. MRI findings and sensorimotor development in infants with bilateral spastic cerebral palsy. *Brain Dev* 1997;19:245–53.
- 12 Mercuri E, Haataja L, Guzzetta A, *et al.* Visual function in term infants with hypoxic-ischaemic insults: correlation with neurodevelopment at 2 years of age. *Arch Dis Child Fetal Neonatal Ed* 1999;80:F99–104.
- 13 Shumway-Cook S, Woollacott M. *Motor control: theory and practical applications*. New York: Williams and Wilkins, 1995:143–68.
- 14 Tröster H, Hecker W, Brambring M. Longitudinal study of gross-motor development in blind infants and preschoolers. *Early Child Development and Care* 1994;104:61–78.
- 15 Cioni G, Ferrari F, Einspieler C, *et al.* Comparison between observation of spontaneous movements and neurologic examination in preterm infants. *J Pediatr* 1997;130:704–11.
- 16 Cioni G, Bartalena L, Biagioni E, *et al.* Neuroimaging and functional outcome of neonatal leukomalacia. *Behav Brain Res* 1992;49:7–19.
- 17 de Vries LS, Eken P, Groenendaal F, *et al.* Correlation between the degree of periventricular leukomalacia diagnosed using cranial ultrasound and MRI later in infancy in children with cerebral palsy. *Neuropediatrics* 1993;24:263–8.
- 18 Touwen BCL. *Neurological development in infancy. Clinics in developmental medicine*. Vol 58. London: Heinemann, 1976.
- 19 McDonald MA, Dobson V, Sebris SL, Baitch L, Varner D, Teller DY. The acuity card procedure: a rapid test of infant acuity. *Invest Ophthalmol Vis Sci* 1985;26:1158–62.
- 20 Mohn G, Van Hof-van Duin J, Fetter WPF, Groot de L, Hage M. Acuity assessment of non-verbal infants and children: clinical experience with the acuity card procedure. *Dev Med Child Neurol* 1988;30:232–44.
- 21 van Hof-van Duin J, Heersema DJ, Groenendaal F, Baerts W, Fetter WPF. Visual field and grating acuity development in low-risk preterm infants during the first 2½ years after terms. *Behav Brain Res* 1992;49:115–22.
- 22 Mohn G, van Hof-van Duin J. Development of the binocular and monocular visual field during the first year of life. *Clinical Visual Sciences* 1986;1:51–64.
- 23 Griffiths, R. *The abilities of babies: a study in mental measurement*. London: University of London Press, 1954.
- 24 Cioni G, Fazzi B, Ipata AE, Canapicchi R, Van Hof-Van Duin J. Correlation between cerebral visual impairment and MR imaging in children with neonatal encephalopathy. *Dev Med Child Neurol* 1996;38:120–32.
- 25 de Vries LS, Eken P, Dubowitz LMS. The spectrum of leukomalacia using cranial ultrasound. *Behav Brain Res* 1992;49:1–6.
- 26 Braddick OJ, Wattam-Bell J, Atkinson J. Orientation-specific cortical responses develop early in infancy. *Nature* 1986;320:617–19.
- 27 Mercuri E, Braddick O, Atkinson J, *et al.* Orientation-reversal and phase-reversal visual evoked potentials in full-term infants with brain lesions: a longitudinal study. *Neuropediatrics* 1998;29:169–14.
- 28 Sonksen PM, Petrie A, Drew KJ. Promotion of visual development of severely visually impaired babies: evaluation of a developmentally based program. *Dev Med Child Neurol* 1991;22:320–35.



## Correlation between visual function, neurodevelopmental outcome, and magnetic resonance imaging findings in infants with periventricular leucomalacia

Giovanni Cioni, Barbara Bertuccelli, Antonio Boldrini, et al.

*Arch Dis Child Fetal Neonatal Ed* 2000 82: F134-F140

doi: 10.1136/fn.82.2.F134

---

Updated information and services can be found at:

<http://fn.bmj.com/content/82/2/F134.full.html>

---

### References

*These include:*

This article cites 25 articles, 2 of which can be accessed free at:

<http://fn.bmj.com/content/82/2/F134.full.html#ref-list-1>

Article cited in:

<http://fn.bmj.com/content/82/2/F134.full.html#related-urls>

### Email alerting service

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

---

### Topic Collections

Articles on similar topics can be found in the following collections

[Clinical diagnostic tests](#) (437 articles)

[Radiology](#) (420 articles)

[Radiology \(diagnostics\)](#) (389 articles)

[Disability](#) (44 articles)

[Ophthalmology](#) (83 articles)

---

### Notes

---

To request permissions go to:

<http://group.bmj.com/group/rights-licensing/permissions>

To order reprints go to:

<http://journals.bmj.com/cgi/reprintform>

To subscribe to BMJ go to:

<http://group.bmj.com/subscribe/>