Visual function in low birthweight children

A R O’Connor, T J Stephenson, A Johnson, M J Tobin, S Ratib, M Moseley, A R Fielder

Aim: To determine the visual functions, at age 10–12 years, of a geographically based cohort of children of birth weight less than 1701 g. The results were compared to a group of children born at full term.

Methods: 572 low birthweight (LBW) “low birthweight cohort” children who had been examined in the neonatal period were invited for review at 10–12 years of age. 169 11 year old schoolchildren born at full term were also recruited, “school cohort.” Visual acuity (at distance and near), contrast sensitivity, colour vision, and visual fields were measured.

Results: 293 of the original 572 participants consented to a further examination. Compared to the school cohort, children born at term the low birthweight cohort showed significantly lower near and distance acuities and contrast sensitivity (p<0.001 for all uniolocular and binocular measures). Retinopathy of prematurity (ROP) was a very poor predictor of outcome and multivariate analysis did not identify any key neonatal factors as predictors of long term visual outcome.

Conclusions: Low birthweight children have a small but statistically significant deficit in both visual acuity and contrast sensitivity. Low birth weight and ROP both impact on long term visual functions.

METHODS

The aims of this component of the study were to compare the visual acuity, contrast sensitivity, colour, and visual field data of a cohort of low birthweight children with a control group of children born at term. In addition, to analyse the relation between neonatal factors (including ROP) and later visual function.

Preterm birth and retinopathy of prematurity (ROP) have both been reported to impact the developing visual system resulting in reduced visual acuity, diminished contrast sensitivity, and an increase in colour deficits. It has also been shown that these effects are not temporary—that is, a delay in development consequent upon premature birth, but permanent, as they have been shown to persist into later childhood and even adult life. It is encouraging that many of these deficits are minor, so that individual values, although they differ significantly from the visual functions of children born at full term, usually fall within the normal range. Nevertheless, performance among preterm children considered as a group (mean value) is consistently and significantly lower than that of their peers born at full term.

Severe ROP is well known to affect visual functions with the loss ranging from mild to total, whereas the impact of mild ROP (stages 1 and 2) on visual function is less well defined. Studies have demonstrated a reduction in acuity associated with mild ROP; however, the multifactorial nature of the deficits in low birthweight children suggests that no single factor is the cause of this reduction.

In 1988, Ng et al reported the ophthalmic findings of a cohort of babies born in the East Midlands, UK. A comprehensive and intensive ophthalmic examination protocol permitted a detailed analysis of the impact of ROP on visual function even in cases of mild disease. This present study is a follow up of these low birthweight children at 10–12 years old. Follow up at this age allows for a comprehensive assessment of visual function with the aim of differentiating the effects of ROP from preterm birth alone. An overview of the ophthalmic outcome of this cohort has been reported previously but here we present greater detail focusing on the visual functions including amblyopia. As this cohort is biased towards mild ROP these data will complement the existing knowledge on the outcome of children with threshold disease. The data will be helpful in deciding what provisions for long term ophthalmic care are required.

The methods of this component of the study were to compare the visual acuity, contrast sensitivity, colour, and visual field data of a cohort of low birthweight children with a control group of children born at term. In addition, to analyse the relation between neonatal factors (including ROP) and later visual function.

Abbreviations: LBW, low birth weight; ROP, retinopathy of prematurity
was not able to read or match the letters on the chart then visual acuity was assessed using the Keeler acuity cards (Keeler, UK).

Near visual acuity was recorded using either the Bailey-Lovie word reading chart (Haag-Streit, UK) at a test distance of 25 cm or, where the child was incapable of word reading, the logarithmic, single letter near visual acuity chart “2000” (Precision Vision, La Salle, IL, USA). If the child was unable to perform either of these tests near acuity was not measured.

**Contrast sensitivity**
This was recorded using the Pelli-Robson chart which measures the (log) threshold contrast required to identify letters of constant size (fundamental spatial frequency = 1–2 cycles/degree). The original test protocol gave credit if two letters out of each three letter triplet was correctly identified.

However, we adopted a test protocol based on the findings of Elliott et al., who showed that the reliability of the test can be improved substantially (narrowing the 95% confidence limits from ±0.45 to ±0.2 log contrast sensitivity units) by scoring each letter individually (0.05 log contrast units). In addition, the repeatability of the test was unimpaired if subjects were not penalised for mutually confusing the letters C and O.

**Colour vision**
Colour vision was assessed using the Farnsworth D15 desaturated test (Haag-Streit, UK), which is an adaptation of the Farnsworth-Munsell 100 hue test. This was tested unicocularly and the child was required to place the 15 coloured spots in order.

**Visual field**
The visual field was assessed using the Damato Campimeter (Precision Vision, La Salle, IL, USA), an oculokinetic perimetry chart able to detect major visual field defects. The adoption of this test was governed largely by the constraints imposed by the size of the mobile vision laboratory and the length of time available to administer the test battery (90 minutes). The Damato Campimeter measures the visual field up to 30° in all meridia and is conducted without refractive correction.

**Autorefraction**
Every child in the low birthweight cohort underwent a cycloplegic (cyclopentolate 1%) autorefraction utilising the Retinomax K-plus.

**Statistical methods**
All analysis was performed using the statistical package SPSS version 10 (SPSS, Inc, Chicago, IL, USA). All data were investigated for normality to determine whether parametric or non-parametric methods should be used. Student’s t tests and Mann-Whitney U tests were used to compare continuous data between two groups. For comparisons involving three or more groups, the Kruskal-Wallis test was used. χ² tests were performed for categorical data. Analysis of covariance was used to adjust for birth weight. Univariate linear regression was used to determine whether the stage of ROP could be used to predict visual function outcomes. Backward linear regression was used (at 10% level of significance) to determine whether any other neonatal factors would be significant predictors of the visual outcomes. All tests were two sided.

Permission for this study was obtained from Nottingham University hospital ethics committee.

**RESULTS**
From the original cohort of 572 low birthweight infants 33 died after the original study was completed seven had moved outside the United Kingdom, and it was not possible to trace 23 children. At the general practitioner’s request, the families of two children were not contacted. Among the remaining 507 children, there were 17 parental refusals and 197 non-responders despite repeated reminders, leaving 293 who consented. There was no significant difference between the 293 children tested (group A) and the 279 children not tested but known to be alive (group B) in terms of the birth weight (median A 1395 g, B 1387 g), gestational age (median A 31, B 31), or severity of ROP (group A 51.9% had any ROP (n = 152), was severe in 4.8% (n = 14): group B, 49.8% had ROP (n = 139) and was severe in 4.7% (n = 13)), p = 0.1 in all cases.

There was no statistically significant difference between the low birthweight cohort and the controls in terms of ethnic origin (Pearson χ² = 1.729, p = 0.6); 86.7% of the low birthweight cohort and 86% of the controls being white, 7.2% and 5.3% being Asian, 3.1% and 4.1% being Afro-Caribbean, and 3.1% and 4.7% being of mixed race. The mean age in both groups was 11.3 years (range in LBW cohort 10.4–12.9 years, controls 10.9–12.4 years).

Distance visual acuity was measurable in 289 of the 293 low birthweight cohort. Four children, with multiple disabilities, were unable to carry out the logMAR acuity test. Visual acuity data are presented for 288 right eyes (RVA), as one right eye had no perception of light.

Right, left, and binocular distance logMAR acuities for the study and control cohorts are presented in table 1. Statistically significant differences exist between the study cohort and control group. In all cases the study cohort had a lower median acuity and a greater spread of values. However, the median acuity of the study cohort was equal to or better than 0.0 logMAR (that is, within the normal range). Despite this in the low birthweight cohort there were 55 (18.8%) cases with binocular acuity below 0.0 with no known ocular pathology. However 35 of these cases were less than one line below 0.0 which could reflect the normal acuity variation.

Eighteen cases had acuities in the range 0.1 to 0.3 logMAR but known to be alive (group B) in terms of the birth weight (median A 1395 g, B 1387 g), gestational age (median A 31, B 31), or severity of ROP (group A 51.9% had any ROP (n = 152), was severe in 4.8% (n = 14): group B, 49.8% had ROP (n = 139) and was severe in 4.7% (n = 13)), p = 0.1 in all cases.

The four children whom it was not possible to test with the distance logMAR chart were assessed by other methods. One child had vision measured with the acuity cards (binocular acuity = 3.8 cycles/degree) and three had a qualitative assessment of their vision. From these tests all four children were categorised as having moderately reduced vision.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Distance visual acuity (logMAR) of the study cohort and control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohort (n = 289)</td>
<td>Control (n = 169)</td>
</tr>
<tr>
<td></td>
<td>Median (IQR)</td>
</tr>
<tr>
<td>Right eye</td>
<td>−0.02 (−0.08, 0.06)</td>
</tr>
<tr>
<td>Left eye</td>
<td>0.00 (−0.08, 0.1)</td>
</tr>
<tr>
<td>Binocular</td>
<td>−0.08 (−0.16, 0.0)</td>
</tr>
</tbody>
</table>
**Table 2 Classification of residual amblyopia, (n)**

<table>
<thead>
<tr>
<th></th>
<th>Study cohort</th>
<th>Control group</th>
<th>Olhsson$^{16}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=37</td>
<td>n=6</td>
<td>n=29</td>
<td></td>
</tr>
<tr>
<td><strong>Strabismic</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alone</td>
<td>35.1% (13)</td>
<td>16.7% (1)</td>
<td>24.1% (7)</td>
</tr>
<tr>
<td>With anisometropia</td>
<td>27% (10)</td>
<td>0</td>
<td>10.3% (3)</td>
</tr>
<tr>
<td>Anisometropic only</td>
<td>8.1% (3)</td>
<td>33% (2)</td>
<td>4.3% (13)</td>
</tr>
<tr>
<td>Form deprivation</td>
<td>2.7% (1)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Other/unknown</td>
<td>27% (10)</td>
<td>50% (3)</td>
<td>20.7% (6)</td>
</tr>
</tbody>
</table>

**Intercocular acuity differences**

Residual amblyopia has been defined as acuity worse than 0.0 logMAR in at least one eye with an interocular acuity difference greater than 0.2 logMAR.$^{26}$ The number of children with residual amblyopia was significantly higher in the low birth weight cohort (n = 37/288) compared to the control group (n = 6/169) $\chi^2 = 10.80, p = 0.001$.

Type of amblyopia was categorised as follows: strabismic, anisometropic, strabismus and anisometropic combined, form deprivation, and unclassified. Table 2 compares the prevalence and type of residual amblyopia seen in the study cohort and control group with that reported by Olhsson et al.$^{16}$

Previously published data have been added here as the number of children with visual deficits in the control group is very small. This study was chosen for comparison as the cohort was very similar to this study in age at testing, the inclusion criteria were that the children were born in 1985, in Sweden and were recruited from schools in one area, there were no stated exclusion criteria. From a population of 1046 children aged 12–13 years who were previously screened for visual disorders at the age of 4.5 years Olhsson reported residual amblyopia in 29 (2.8%) eyes and reduced binocular acuity in 20 (1.9%) eyes. Table 3 shows the number of eyes with residual amblyopia in Olhsson’s cohort compared to the low birthweight cohort and the control group. There is an increase in the number of eyes with reduced acuity in the low birthweight cohort but this is not statistically significant ($p>0.1$).

To determine whether the reduction in distance acuity is related to the increase in amblyopia the comparison of unisocular distance acuities was repeated after removal of the cases of amblyopia. Analysis by Mann-Whitney shows that the difference between the two groups remains after removal of the cases of amblyopia ($p<0.001$). In addition, the analysis was repeated after removal of all cases of ocular pathology (including ROP) or amblyopia were removed and again the difference between the groups remained ($p<0.001$).

**Visual acuity at near**

Table 4 shows the descriptive statistics for near visual acuity. One right eye had no perception of light and four children were unable to perform the test.

**Table 3 Reduced unisocular acuity. Comparison between published data and LBW and control cohorts**

<table>
<thead>
<tr>
<th>Acuity</th>
<th>logMAR</th>
<th>Olhsson 1046</th>
<th>LBW 576</th>
<th>Controls 338</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.3</td>
<td>&gt;0.52</td>
<td>0.5% (5)</td>
<td>2.1% (12)</td>
<td>0.3% (1)</td>
</tr>
<tr>
<td>0.3 to 0.7</td>
<td>0.18 to 0.52</td>
<td>2.9% (30)</td>
<td>11.5% (66)</td>
<td>3% (10)</td>
</tr>
<tr>
<td>0.7 to 0.9</td>
<td>0.04 to 0.16</td>
<td>3% (31)</td>
<td>20.1% (116)</td>
<td>10.9% (37)</td>
</tr>
</tbody>
</table>

Right, left, and binocular near acuity of the cohort and control groups differ significantly ($p<0.001$). The median acuity of the study cohort was lower than the control group, although they demonstrated a similar pattern to distance acuities as the median was again above the normal level (0.0 logMAR approximately equivalent to N5).

**Contrast sensitivity**

Contrast sensitivity is lower in the study cohort compared with the control group. Table 5 shows the median values for contrast sensitivity and again, although there was a statistically significant difference between the two groups (Mann Whitney, $p<0.001$ for all measures), this difference is subtle (one to two letters).

**Colour vision**

Two children (0.68%) in the low birthweight cohort had colour defects, one protanopia and one deuteranopia, and four in the control group (2.4%), two protanopia and two deuteranopia, all of which were in boys. With these small numbers statistical analysis is not appropriate.

**Visual field**

One child in the low birthweight study cohort had a right homonymous hemianopia. No other visual field defects were detected in the study cohort or in the control group.

**ROP**

The statistical significance of the impact of ROP on visual acuity or contrast sensitivity was determined for all unisocular and binocular measures by Kruskal-Wallis ANOVA. For unisocular measures, the maximum stage of ROP in that eye was used: (right eye no ROP = 157, stage 1 = 85, stage 2 = 38, stage 3 = 12, stage 4 = 1, left eye no ROP = 149, stage 1 = 96, stage 2 = 34, stage 3 = 14, stage 4 = 0). Of all measures of outcome only left distance acuity is significantly associated with the maximum stage of ROP. The significant difference in acuity was between those with ROP stage 3 and above compared to those with stage 1, 2, or no ROP. Although ROP can be asymmetrical, which may account for the difference in findings between right and left distance acuity, in this cohort the numbers with severe ROP differ only by one between the eyes.

As ROP is known to be associated with both birth weight and gestational age they may be confounding variables in the above analysis. Univariate linear regression shows gestational age is not associated with the measures of visual function ($p>0.05$). Birth weight, however, is associated with right visual acuity and binocular visual acuity ($p<0.05$) but not left distance acuity. Therefore analysis of covariance was used to determine whether birth weight was influencing the results. The results showed that even after adjusting for birth weight there was no association between right visual acuity and the stage of ROP ($p = 0.40$), however binocular acuity remained significantly associated with stage of ROP ($p = 0.002$) and as
birth weight was not associated with left distance acuity this also remains associated with stage of ROP. Analysis by Kruskal-Wallis shows that interocular acuity difference is not significantly associated with stage of ROP (p = 0.15).

Can visual outcome be predicted?
To determine whether the stage of ROP could be used to predict visual functions, Univariate linear regression was performed on the variables that are significantly associated with ROP—that is, left, and binocular, distance acuities. Analysis shows that ROP is a poor predictor of these variables (adjusted R² = 0.053 and 0.066 respectively).

Multivariate analysis
To determine which neonatal variables should be entered into the analysis for predicting outcome linear regression was used to identify any associations. The next stage in the analysis was to perform backward linear regression modelling to determine whether any other neonatal factors would be significant independent predictors of visual outcome. The neonatal factors entered into the analysis, which showed a significant association on univariate analysis, were cerebral palsy (n = 17), strabismus present at 6 months (n = 27), mean spherical equivalent (mean (SD), right eye +0.69 (1.64), left eye +0.63 (1.99)), ROP, cranial ultrasound abnormality (n = 91), milk feed type (breast milk n = 113, preterm formula n = 62, term formula n = 37, unknown n = 81), birth weight (mean (SD), 1339 (256)), gestational age (30.9 (3)), and small for gestational age (n = 61). For uniocular measures of outcome the ROP data used were eye adjusted R² = 0.053 and 0.066 respectively.

DISCUSSION
This study of a cohort of low birthweight children provides detailed information on visual functions at 10–12 years. In this cohort, despite a bias towards mild ROP, we showed a significant reduction in visual acuity and contrast sensitivity compared to children who had been born at full term. In addition, the low birthweight children without ROP had lower acuities than the control group, which shows that both ROP and low birth weight are impacting visual functions in the long term. One weakness of this study is the lack of detailed visual field function; however, this restriction was imposed by using a mobile vision laboratory to visit the children and improve consent rates.

The increase in the prevalence of amblyopia is to be expected with the increased prevalence of strabismus within this low birthweight cohort. However, there are limitations in the comparisons we can make with other studies owing to the lack of data on previous treatment regimens—for instance, age when amblyopia was detected, length of treatment and compliance, and variation in screening programmes between localities all of which might impact on the outcome of amblyopia therapy.

A significant difference between the study cohort and the published data is the large number of cases of amblyopia of unknown aetiology in this study cohort. When the records were analysed only two out of the 10 children with unknown aetiologies had ROP and they were both stage 1. Therefore, ROP cannot account for the reduction in acuity. It is unknown whether low birthweight children respond differently to amblyopia treatment; therefore, the difference in acuity between the two groups may be the result of an increase in amblyopia. In addition, there are cases of reduced binocular acuity with no apparent ocular pathology. This condition, where there is acuity below 6/6 with no known ocular pathology, was called subnormal visual acuity syndrome by Ohlsson et al. Although this is not a currently recognised syndrome it may be a useful way to describe the vision loss in these children but it is recognised that the vision loss may be due to an undiagnosed retinal or neurological defect.

Reduced contrast sensitivity in our cohort confirms previously reported findings. As the Pelli-Robson chart uses letters of a low spatial frequency it is therefore unaffected by mild acuity losses such as those demonstrated in the low birthweight cohort. While this effect is small, and is independent of visual acuity it may signify a subtle underlying adverse effect of preterm birth on neurological development.

The number of children with colour deficits in both the low birthweight and control groups was small and may not be related to prematurity as they are all red-green defects which commonly occur in the male population. This is in contrast

| Table 4 | Near VA (logMAR) of the study cohort and control group |
|------------------------|---------------------------------|------------------------|
| **Cohort (n = 289)** | **Control (n = 169)** | **p Value** |
| **Median (IQR)** | **Median (IQR)** | **Median (IQR)** |
| **Right eye** | -0.1 (-0.2, 0.0) | -0.2 (-0.3, -0.15) | <0.001 |
| **Left eye** | -0.1 (-0.2, 0.0) | -0.2 (-0.3, 0.1) | <0.001 |
| **Binocular** | -0.3 (-0.3, -0.2) | -0.3 (-0.35, -0.3) | <0.001 |

| Table 5 | Descriptive data of contrast sensitivity (log contrast sensitivity units) and comparison between groups |
|------------------------|---------------------------------|------------------------|
| **Cohort (n = 289)** | **Control (n = 169)** | **p Value** |
| **Median (IQR)** | **Median (IQR)** | **Median (IQR)** |
| **Right eye** | 1.60 (1.5, 1.65) | 1.65 (1.575, 1.65) | <0.001 |
| **Left eye** | 1.60 (1.5, 1.65) | 1.65 (1.6, 1.65) | <0.001 |
| **Binocular** | 1.80 (1.75, 1.9) | 1.90 (1.8, 1.95) | <0.001 |
with the findings of the CRYO-ROP Study which reported an increase in blue-yellow defects about 200 times that of the general adult population. This difference in the findings is likely to be accounted for by the lower birthweight criteria in the CRYO-ROP group and the small percentage with severeROP in this cohort. Also the D15 test is designed to be used as a screening tool rather than to permit a full characterisation of a colour anomaly.

In summary, this study confirms that visual functions are reduced in low birthweight children even without ROP. It is encouraging to note that the difference between the low birthweight cohort and control children who had been born at full term is small. However the functional importance of such deficits is unknown. There is a link between educational attainment in this low birthweight cohort and visual functions which is discussed elsewhere. As mild ROP was a very poor predictor of outcome and multivariate analysis did not identify any neonatal factors as predictors of long term visual outcome it highlights the difficulty of creating a targeted screening programme for low birthweight children.

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