Probabilistic diffusion tractography of the optic radiations and visual function in preterm infants at term equivalent age

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Children born prematurely have a high incidence of visual disorders which cannot always be explained by focal retinal or brain lesions. The aim of this study was to test the hypothesis that visual function in preterm infants is related to the microstructural development of white matter in the optic radiations. We used diffusion tensor imaging (DTI) with probabilistic diffusion tractography to delineate the optic radiations at term equivalent age and compared the fractional anisotropy (FA) to a contemporaneous evaluation of visual function. Thirty-seven preterm infants (19 male) born at median (range) 28+4 (24+1–32+3) weeks gestational age, were examined at a post-menstrual age of 42 (39+6–43) weeks. MRI and DTI were acquired on a 3 Tesla MR system with DTI obtained in 15 non-collinear directions with a \( b \) value of 750 s/mm


Introduction
The incidence of preterm birth is increasing and accounts for 13% of all births in the UK. Extremely preterm infants are at high risk for neurodevelopmental impairment compared to infants born at term (Bhutta et al., 2002; Marlow et al., 2005), and show a higher incidence of visual
Impairment that is only partly explained by retinopathy of prematurity (ROP) or brain lesions in the relevant pathways (O’Connor and Fielder, 2007). Most studies of visual function following preterm birth report visual findings after the neonatal period; at the time when more mature cortically mediated aspects of visual function (Atkinson et al., 2002) can be assessed. The only studies that have systematically evaluated early visual findings in preterm infants and their correlation with brain MRI have been performed in preterm infants with periventricular leukomalacia (PVL) showing that the severity of visual impairment is associated with the extent of optic radiation injury (Eken et al., 1996; Cioni et al., 1997, 2000; Fazzi et al., 2004; van den Hout et al., 2004) and of lateral geniculate nuclei or basal ganglia involvement (Uggetti et al., 1996; Ricci et al., 2006). In these studies, however, visual function was assessed after the neonatal period. Less is known about the early phases of development of visual function in preterm infants.

Until recently, clinical assessments of visual function in newborns mainly consisted in evaluation of the ability to fix and follow a target, activities that are thought to be mediated by sub-cortical systems. This is based on data showing that preterm newborns even with severe occipital white matter damage can fix and follow in the first postnatal weeks. It has thus been suggested that cortical systems are not involved in these visual functions (Dubowitz et al., 1986).

A recently published battery of tests for the newborn assesses additionally other aspects of visual function, including attention at distance and colour and stripe discrimination (Ricci et al., 2007). This allows us to explore more complex visual responses in the period around term equivalent age and to assess whether such functions may also involve the cortical visual pathway at a time when the major influences on development will have been antenatal factors and the effects of preterm delivery.

Using Diffusion Tensor Imaging (DTI) with probabilistic tractography it is possible to delineate the white matter tracts in the different regions of the brain by determining the dominant direction of water diffusion at the microstructural level. DTI assesses the Brownian motion of water in tissue (Le Bihan et al., 1986; for review Le Bihan, 2003). Water diffuses more freely parallel to white matter fibres than perpendicular to them, due to a number of factors including fibre coherence, axonal density, cell membranes and myelination (Moseley et al., 1990; Beaulieu and Allen, 1994; Gulani et al., 2001; Beaulieu, 2002). This directional dependence of diffusion in tissue is termed diffusion anisotropy and, by studying the preferred direction of diffusion, it is possible to infer the orientation of major white matter fibre bundles. DTI also allows for the measurement of Fractional Anisotropy (FA) (Baser et al., 1994), a robust measure of microstructure that detects differences in white matter due both to maturation and damage. DTI has identified white matter microstructural abnormalities, which are not always apparent on conventional MRI, in the white matter of the preterm brain (Huppi et al., 1998, 2001; Neil et al., 1998; Miller et al., 2002; Counsell et al., 2006). In addition, probabilistic DTI tractography has proved a successful tool to assess connectivity quantitatively in preterm infants (Counsell et al., 2007), delineating relevant white matter pathways on functional grounds rather than using imaging appearances. DTI thus allows a precise assessment of the optic radiations.

The aim of this study was to test the hypothesis that in preterm infants around term corrected age visual function is related to the microstructural development of white matter in the optic radiations. We measured visual abilities evaluated using a scorable clinical assessment and related this to FA in the optic radiations defined by probabilistic tractography. We took into account possible confounding by gestational age (GA) at birth, post-menstrual age (PMA) at study and the presence of MR-detectable cerebral lesions. In a secondary analysis of the DTI data, we assessed white matter microstructure throughout the brain using tract-based spatial statistics (TBSS) (Smith et al., 2006) to determine whether any correlation between visual function and FA reflected local factors in the optic radiations or global white matter development.

Methods

This study was approved by the Hammersmith Hospitals Research Ethics Committee and written parental consent was obtained prior to scanning.

Subjects

We studied 37 preterm infants (19 male) who were recruited from the neonatal intensive care unit at Queen Charlotte’s and Hammersmith Hospital in the early neonatal period. Infants were eligible for inclusion in this study if they were born at ≤34 weeks GA and had no evidence of congenital anomalies, chromosomal disorders or metabolic disorders. The median [range] GA of the infants at birth was 28+4 [24+1–32+3] weeks and the median birth weight was 1.059 [0.655–1.528] kg. The infants were imaged at a median PMA of 42 [39–43] weeks. Clinical details of the infants are given in Table 1 for the whole group and are compared between those with and without lesions on their conventional MRI scan. All infants were screened for ROP; eight were positive but none more than stage 2. All infants had a standardized visual assessment (Ricci et al., 2007) on the same day as their MRI scan.

Imaging

MRI was performed on a Philips 3 Tesla system with maximum gradient strength of 62 mT/m on each independent axis and slew rate of 100 mT/m/ms on each axis using an eight-channel phased array head coil. The infants were sedated for imaging using oral chloral hydrate (30–50 mg/kg). Ear protection was used for each infant. The infant’s head was immobilized using a pillow filled with polystyrene beads, from which the air was evacuated. Pulse oximetry and electrocardiograph were monitored, and a paediatrician trained in MRI procedures was in attendance throughout the examination.
3D MPRAGE and 3D dual echo weighted imaging was obtained prior to DTI. Single shot echo planar DTI was acquired in 15 non-collinear directions using the following parameters; TR 10000 ms, TE 49 ms, slice thickness 2 mm, field of view 224 mm, matrix 128 x 128 (voxel size = 1.75 x 1.75 x 2 mm$^3$), $b$ value = 750 s/mm$^2$. The data were acquired with a SENSE factor of 2.

Conventional MR images were assessed for the presence of lesions by an experienced perinatal neuroradiologist (M.A.R.).

**Data analysis**

**Probabilistic tractography**

Data analysis was performed using FSL (Smith et al., 2004). Image artefacts due to eddy current distortions were minimized by registering the DT images to the b0 images using affine registration. Images were brain-extracted to remove all non-brain tissue using BET and FA maps were generated using FDT. All tractography analysis was performed by a single investigator (L.B.) while unaware of the results of visual examinations. Seed masks were positioned in the white matter lateral to the lateral geniculate nucleus, on the axial slice at the level of the transition from the posterior limb of the internal capsule to the cerebral peduncle (Ciccarelli et al., 2003), on colour-coded FA maps (Fig. 1). The volumes of seed masks were standardized for all infants (9 voxels). Exclusion masks were generated to restrict the pathway to the region ipsilateral to the seed mask and posterior to the third ventricle as described by Ciccarelli et al. (2003). Connectivity distributions were generated from every voxel in the seed mask and were thresholded to include only those pathways with a probability of $\geq 10\%$; mean FA values of the connectivity distributions were determined and FA distributions were examined for normality. The analysis was repeated in 10 infants in order to determine the intra-observer variation for FA values of the optic radiations. The intraobserver variability was $<2\%$.

**TBSS**

Voxel-wise statistical analysis of the FA data was carried out using TBSS implemented in FSL (Smith et al., 2006). First, FA data were aligned into a common space using a non-linear registration algorithm (www.doc.ic.ac.uk/~dr/software). Then the mean FA image was created and thinned to generate a mean FA skeleton, which represented the centres of all tracts common to the group. This was thresholded to FA $\geq 0.15$ to include the major white matter pathways but exclude peripheral tracts where there was significant inter-subject variability and/or partial volume effects with grey matter. Each subject’s aligned FA data was then projected onto this skeleton. FA data from two infants with focal lesions (one infant with middle cerebral artery infarction and one infant with periventricular haemorrhagic infarction) were excluded from this analysis due to registration errors.

**Assessment of visual function**

The assessment of visual function was performed by experienced neurodevelopmental paediatricians (D.R. and A.V.) who were
unaware of the infants clinical history, using a battery of tests specifically designed for the early neonatal assessment of various aspects of visual function (Ricci et al., 2007).

This assessment includes nine test items assessing: spontaneous ocular motility; ocular movements to a target; the ability to fix and track on a black/white target (horizontally, vertically and in an arc); the ability to track on a coloured target; to discriminate black and white stripes with increasing spatial frequency and the attention at distance evaluated as the ability to keep attention on a target moved slowly away from the infant.

The results of the assessment were scored by comparing the findings to reference data obtained in term-born infants examined 72 h after birth (Ricci et al., 2007, 2007). These data were obtained using the test battery in 110 term-born infants calculating the range and the distribution of frequency and the 90th centile for each item. In the present study, for each of the nine items, the findings falling within the 90th centile for term-born infants were scored as 0 while those falling outside the 90th centile were scored as 1. A total score was obtained by adding the scores of the individual items, ranging from 0 (all the items within the 90th centile) to 9 (all the items outside the 90th centile). As the items reflect nine different aspects of visual function, the total score provides an estimate of the level of visual impairment. The scoring system is shown in Table 2.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Reference data for visual assessment scores</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Spontaneous ocular motility</strong></td>
<td>Mainly conjugated</td>
</tr>
<tr>
<td><strong>Ocular movements with a target</strong></td>
<td>Mainly conjugated</td>
</tr>
<tr>
<td><strong>Fixation</strong></td>
<td>Stable (&gt;3 s)</td>
</tr>
<tr>
<td><strong>Tracking – black/white target</strong></td>
<td>Complete</td>
</tr>
<tr>
<td>Horizontal</td>
<td>Complete</td>
</tr>
<tr>
<td>Vertical</td>
<td>Complete</td>
</tr>
<tr>
<td>Arc</td>
<td>Complete</td>
</tr>
<tr>
<td><strong>Colour/discrimination/attention</strong></td>
<td>Present</td>
</tr>
<tr>
<td>Tracking coloured stimulus</td>
<td>Last card identified ≤ 3</td>
</tr>
<tr>
<td>Stripe discrimination</td>
<td>30–50 cm</td>
</tr>
<tr>
<td>Attention at distance</td>
<td>&lt;30 cm</td>
</tr>
</tbody>
</table>

Shadowed boxes indicate the results found in 90% of full term infants at 72 h from birth.

As ROP is known to be associated with poor visual function, FA values in the optic radiations and visual assessment scores were compared between infants who had ROP and those infants who had no evidence of ROP using a t-test (for visual assessment scores) or a Mann–Whitney test (for FA values) as ROP is known to be associated with poor visual function, FA values in the optic radiations and visual assessment scores were compared between infants who had ROP and those infants who had no evidence of ROP using a t-test (for visual assessment scores) or a Mann–Whitney test (for FA values).

**Results**

**MRI**

Ten infants had evidence of focal abnormalities on conventional MRI. These are described in Table 3. All 10 infants were considered to have mild or moderate ventricular dilation on qualitative visual analysis. In two infants, there were very small lesions along the optic radiations. In two others, there was mild dilation of the ventricle alongside the optic radiation. Five infants showed a degree of thalamic atrophy. Only three infants with focal lesions showed symmetrical myelination within the posterior limb of the internal capsule appropriate for preterm infants at term corrected age. For the other 27 infants, no focal abnormality was seen and the internal capsules appeared appropriately mature.

**DTI**

FA values in the connectivity distributions of the optic radiations in each individual infant were normally distributed, and so the mean FA value was determined. The average of all mean (±SD) FA values for the optic radiations was 0.247 ± 0.017. Figure 2 shows connectivity distributions in the optic radiations of an infant who was born at 26 weeks GA and imaged at 40 weeks PMA. There was no significant difference in FA values between the infants with and without ROP (mean FA ROP = 0.245 ± 0.021, mean FA no ROP = 0.244 ± 0.010, P = 0.90).
<table>
<thead>
<tr>
<th>Case</th>
<th>Ventricular dilatation</th>
<th>Optic radiation lesions</th>
<th>Thalamic atrophy</th>
<th>PLIC</th>
<th>Focal lesions</th>
<th>FA</th>
<th>Visual score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Mild posteriorly</td>
<td>Small bilateral</td>
<td>Minimal (Lt &gt; Rt)</td>
<td>Abnormal SI bilaterally</td>
<td>Multiple punctate lesions in PVWM (posterior &gt; anterior)</td>
<td>0.231</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>Mild Lt</td>
<td>No</td>
<td>Normal</td>
<td>Normal</td>
<td>Bilateral cerebellar haemorrhagic lesions</td>
<td>0.252</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>Mild Rt &gt; Lt</td>
<td>No</td>
<td>Normal</td>
<td>Normal</td>
<td>Haemorrhagic punctate lesions in PVWM. Rt GLH</td>
<td>0.252</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>Moderate posterior &gt; anterior</td>
<td>No</td>
<td>No atrophy. Minimal abnormal SI on Lt</td>
<td>Mild asymmetry Rt &lt; Lt</td>
<td>Lt GLH</td>
<td>0.226</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>Mild posteriorly</td>
<td>No</td>
<td>Normal</td>
<td>Normal</td>
<td>Small cyst in Rt posterior PVWM. Small infarct Lt insula</td>
<td>0.239</td>
<td>4</td>
</tr>
<tr>
<td>6</td>
<td>Moderate Lt</td>
<td>No</td>
<td>Marked on Lt</td>
<td>Decreased myelin on Lt. No myelin on Rt</td>
<td>Large Lt MCA</td>
<td>0.226</td>
<td>5</td>
</tr>
<tr>
<td>7</td>
<td>Moderate Rt &gt; Lt</td>
<td>Small lesion on Lt</td>
<td>Minimal on Rt</td>
<td>Decreased myelin</td>
<td>Rt caudate GLH. Lt temporal GLH</td>
<td>0.212</td>
<td>5</td>
</tr>
<tr>
<td>8</td>
<td>Mild posteriorly</td>
<td>No</td>
<td>Normal</td>
<td>Decreased myelin</td>
<td>Severe bilateral cerebellar haemorrhagic lesions. Vermis atrophy. Caudo-thalamic cysts</td>
<td>0.196</td>
<td>6</td>
</tr>
<tr>
<td>9</td>
<td>Mild Rt</td>
<td>No</td>
<td>Moderate on Rt</td>
<td>Abnormal myelin Rt</td>
<td>Rt porencephalic cyst.</td>
<td>0.217</td>
<td>7</td>
</tr>
<tr>
<td>10</td>
<td>Moderate posterior &gt; anterior</td>
<td>No</td>
<td>Moderate bilaterally</td>
<td>Decreased myelin on Rt. No myelin on Lt</td>
<td>Rt lentiform infarct. Posterior PVWM cyst</td>
<td>0.204</td>
<td>7</td>
</tr>
</tbody>
</table>

GLH = germinal layer haemorrhage; Lt = left; MCA = middle cerebral artery; PLIC = posterior limb of the internal capsule; PVWM = periventricular white matter; Rt = right; SI = signal intensity.
Visual assessment scores
The scores ranged between 0 (i.e. all results within the 90th centile range for our normal full term cohort) and 7. Sixteen infants had a score of 0, 7 a score of 1 and 5 a score of 2. The remaining nine had a score of $\geq 3$. All but two of the 27 infants without lesions had scores between 0 and 2 while 7 of the 10 infants with lesions had scores $\geq 3$ (Table 3). There was no significant difference in visual assessment scores between the infants with and without ROP [median (range) visual assessment score ROP = 0.5 (0–5), median (range) no ROP = 1 (0–7), $P = 0.62$].

DTI and visual function assessment
Figure 3 shows the univariate relationship between visual assessment score and FA values. Following multiple regression analysis, visual assessment score remained significantly correlated with FA values ($P<0.001$, adjusted $r^2 = 0.669$), and GA at birth ($P = 0.60$), PMA at scan ($P = 0.85$) and the presence of lesions on conventional MRI ($P = 0.63$) did not independently predict visual performance (Table 4). Partial regression plots showed homoscedacity without significant outliers (Fig. 4), and residuals from the analysis were normally distributed. FA values in the optic radiations and visual assessment scores for the infants who had lesions on their conventional MRI are shown in Table 3.

TBSS
TBSS demonstrated a significant linear correlation between visual assessment scores and FA in the optic radiations (voxel-wise thresholding uncorrected for multiple comparisons, $t > 3$, $P < 0.05$). Although a few additional voxels throughout the brain demonstrated a correlation between visual score and FA, these voxels were isolated and did not correspond to any well-defined region (Fig. 5).

Discussion
This study has shown that probabilistic diffusion tractography provides quantitative information regarding white matter microstructure in the optic radiations in preterm infants at term equivalent age. FA correlated with visual assessment scores performed on the same day, and this relationship remained significant when taking into account GA at birth, PMA at scan and the presence of lesions on conventional MRI. TBSS revealed that the correlation between visual function and white matter microstructure was specific to the optic radiations and did not reflect a widespread white matter abnormality.

DTI has previously been used to assess maturational changes and to investigate white matter abnormalities in preterm infants (Huppi et al., 1998, 2001; Neil et al., 1998; Miller et al., 2002; Counsell et al., 2006; Anjari et al., 2007). Most of these studies used a region-of-interest (ROI)-based approach to determine FA values at a subjectively defined site. More recently, diffusion tractography has been performed on DTI data of the preterm brain (Partridge et al., 2005, 2006; Berman et al., 2005; Counsell et al., 2007).
and diffusion tractography has previously been used to delineate the optic radiations using streamline techniques (Yoo et al., 2005; Dubois et al., 2006). However, this is the first study to correlate FA values obtained from regions defined by probabilistic tractography with visual function in preterm infants at term equivalent age.

There are a number of limitations with this study. We positioned our seed mask in the white matter adjacent to the lateral geniculate nucleus, similar to the approach by Ciccarelli et al. (2003, 2005), as we were unable consistently to generate tracts from a seed mask positioned entirely in the lateral geniculate nucleus in these infants. Using this approach, our results were highly reproducible; nevertheless we accept our tracts may include contributions from other white matter fibre bundles such as the inferior fronto-occipital fasciculus, arcuate fasciculus and sublenticular thalamic radiation. In addition, at the resolution achievable in vivo, the imaging voxels will inevitably contain fibre populations with different orientations, thus the principle direction of diffusion may not be co-incident with the true orientation of the tract. However, probabilistic tractography approaches are more tolerant to this problem than streamline tractography techniques, as they allow a number of potential pathways to be considered and errant pathways, which disperse quickly, will be classified as low probability (Behrens et al., 2003). Whilst our TBSS findings did not survive correction for multiple comparisons, our aim with this secondary analysis was to determine whether the correlation between visual function and FA in the optic radiations reflected a widespread white matter abnormality. The lack of correlation between other white matter regions and visual function suggests this structure–function relationship is specific to the optic radiations. Further limitations include the relatively small sample size and that we were not able to assess visual function and tractography in a control group of healthy term-born infants. We cannot,

<table>
<thead>
<tr>
<th>Visual score</th>
<th>Coefficient</th>
<th>Standard error</th>
<th>t</th>
<th>P</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>FA</td>
<td>-88.835</td>
<td>19941</td>
<td>-4.45</td>
<td>0.000</td>
<td>-129454 to -48.216</td>
</tr>
<tr>
<td>GA</td>
<td>0.062</td>
<td>0.177</td>
<td>0.53</td>
<td>0.602</td>
<td>-0.176 to 0.299</td>
</tr>
<tr>
<td>PMA at scan</td>
<td>-0.041</td>
<td>0.214</td>
<td>-0.19</td>
<td>0.851</td>
<td>-0.477 to 0.396</td>
</tr>
<tr>
<td>Lesions on conventional imaging</td>
<td>0.334</td>
<td>0.687</td>
<td>0.49</td>
<td>0.630</td>
<td>-1.065 to 1.733</td>
</tr>
</tbody>
</table>

FA = fractional anisotropy; GA = gestational age; PMA post-menstrual age.

Fig. 4 Partial regression plots demonstrating the variance in (i) FA, (ii) MRI-detected brain lesions, (iii) post-menstrual age at scan, (iv) gestational age at birth attributable to the model.
therefore, determine whether our results are due to physiological mechanisms related to maturation or are due to pathological processes specific to the preterm population.

The use of probabilistic tractography to delineate brain structures derived from specific intracerebral connections with objective definition of ROI based on neural function represents a significant advance on subjective placements of ROI. Probabilistic approaches have the additional benefit of being able to track reproducibly through regions of relatively low FA, such as in the unmyelinated white matter of the optic radiations in these infants. Using this approach, it was possible to sample the entire tract of interest rather than an arbitrary section of that tract. Furthermore, as this study used DTI data acquired at 3 Tesla, which offers higher signal-to-noise ratio (SNR), higher spatial resolution imaging provided better depiction of tracts than could be achieved at lower field strengths (Okada et al., 2006).

The results suggest that the microstructure of the optic radiations is important for visual function even in infants as young as term equivalent age. This is perhaps unexpected as at term equivalent age visual function is thought to be predominantly mediated by a subcortical visual system responsible for the early ability to fix and follow or for preferential looking (Morante et al., 1982; Atkinson, 2000). The subcortical system, not only involving the lateral geniculate nucleus but also connections via thalamus and basal ganglia, appears to be essential in processing early visual information. This is based on data showing that preterm newborns even with severe occipital white matter damage can fix and follow in the first post-natal weeks suggesting that cortical systems are not involved in these visual functions (Dubowitz et al., 1986). Other studies have also reported cases of relatively conserved visual function in infants with severe lesions in the occipital primary visual cortex, supporting the idea of subcortical control of early visual function mediated via extra-geniculate pathways (Aylward et al., 1978; Holtzman, 1984; Snyder et al., 1990). Further evidence for basal ganglia involvement comes from our studies on term-born infants with neonatal encephalopathy (Mercuri et al., 1997, 1999). While infants with severe lesions in the basal ganglia but relatively preserved white matter and cortex had poor visual abilities, those with relatively large lesions involving both occipital lobes and optic radiations, especially if associated with
preserved basal ganglia and thalami had normal results on the assessment of visual function performed at 5 and 12 months and at school age. A subcortical system involving the basal ganglia has recently been suggested by functional MRI (f-MRI) studies in adults (Scholz et al., 2000; Gerardin et al., 2003) showing that the caudate and putamen are active during voluntary saccadic eye movements.

In the present study, not all infants with lesions or atrophy of the basal ganglia and thalami had poor visual function but often the lesions were small, unilateral and relatively anterior. The difference between our findings highlighting the involvement of optic radiations and previous studies of infants at term equivalent age may also be due to the more detailed visual assessment. Previous assessment of visual function at term corrected age have generally been limited to assessment of the ability to fix and follow and preferential looking; the battery used in this study provides other measures of visual function such as attention at distance and discrimination of colours that may reflect more mature aspects of visual processing which would implicate involvement of the cortex. Differences from previous data might also be due to the more precise analysis of the optic radiations. As there were no correlations between visual function and FA in any other white matter tract, our data suggest that low FA in the optic radiation is not a marker for widespread abnormality. Rather it implies that low FA in the optic radiation reflects local neural function and thus connection to the visual cortex. This is supported by a combined DTI and f-MRI study which demonstrated absence of the f-MRI response in the occipital cortex in an infant with extensive optic radiation injury following perinatal stroke (Seghier et al., 2004).

We did not find any difference in FA values or visual assessment score in the infants who hadROP. Whilst ROP is known to be associated with poor visual function (O’Connor et al., 2002), in our study cohort only 8 of the 37 infants had ROP and this was mild (either grade 1 or 2), did not require cryotherapy and had resolved by term equivalent age.

The presence of MR-detectable lesions did not predict visual performance independently of FA, but this does not imply that brain lesions may not affect visual function. Instead, it suggests that lesions influence vision through factors affecting FA in the optic radiation. Low FA values may reflect axonal degeneration, less well-organized tracts and/or delays in maturation, and may be induced by a variety of influences so these data suggest possible mechanisms for visual impairment with and without focal damage. This interpretation is supported by the observation that mean FA is lower in infants with lesions, as shown in Fig. 3.

Our results therefore suggest that even at term equivalent age the maturation and integrity of optic radiations is a major factor for the normal development of visual function in preterm infants.

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