Introduction

Children with visual impairment due to damage to the retro-geniculate visual pathways constitute an increasing group among visually impaired children in the Western world. The developing visual system may be affected by malformations arising early in gestation, by white matter damage of immaturity (WMDI) both in utero and as a sequel to premature birth, and by asphyxia as well as by cortical-subcortical damage due to perinatal cerebral infarcts in children born at term. Infections and trauma in the neonatal period may also affect the visual system. Much of the brain is devoted to vision. Damage causes visual problems ranging from profound impairment to cognitive visual problems only.

Visual and ocular outcome after pre- or perinatal brain damage depends on localisation and extension of the lesion, but also on at what stage the developing system was injured. Plasticity of the brain may modify the functional outcome when the visual system is injured early in gestation. Thus, reorganisation of the visual system by by-passing the lesion in the ipsilateral hemisphere or maybe by inter-hemispheric reorganisation may take place in the immature brain. In addition, retrograde trans-synaptic degeneration may affect the appearance of the optic disc in retro-geniculate lesions occurring during the pregnancy or in the neonatal period in children born preterm.

Brain imaging techniques

Examination of the newborn infant brain with ultrasound (US) may detect lesions engaging the posterior visual pathways, but US is an insensitive method to find minor injuries. Later during infancy and childhood magnetic resonance imaging (MRI) is the most sensitive
imaging modality to detect permanent lesions to the posterior visual system. The paediatric neuroradiologist thus plays an important part in the identification of children with cerebral visual impairment. White matter lesions may be further understood and mapped out with diffusion tensor imaging techniques.

**Visual dysfunctions**

The manifestations of this kind of visual impairment include subnormal visual acuity and crowding, affected visual field function and associated disorders of higher visual processing. The principal cognitive visual pathways comprise the dorsal and the ventral streams. The dorsal stream runs between the occipital lobes, which process incoming visual data, the posterior parietal lobes, which process the whole visual scene and give attention to component parts, the motor cortex, which facilitates movement through the visual scene and the frontal cortex, which directs attention to chosen parts of the visual scene. The ventral stream runs between the occipital lobes and the temporal lobes, which enable recognition of people and objects facilitating route finding and serve visual memory. In addition, impaired control of the eye movements and disordered focusing may further complicate the effective use of vision. These problems can occur in any combination and severity. Visual function may improve over time.

Cerebral palsy, learning disabilities and behaviour and attention problems are other well-known consequences of pre- and perinatal brain damage. Concomitant cerebral visual impairment is common but often remains undetected, and therefore is not taken into account when designing habilitation programs for the individual child. Early brain damage may however cause only visual problems, and often manifests itself as early-onset strabismus. In these cases, the paediatric ophthalmologist is responsible for identification of children with cerebral visual impairment, for assessment of visual function, and for initiating habilitation. The habilitation of these children demands a multi-disciplinary team including paediatric ophthalmologist, orthoptist, neuropsychologist, paediatric neurologist, occupational therapist, physiotherapist, low vision teacher and remedial teacher.

Our research team at Karolinska Institutet has in collaboration with researchers from Gothenburg during the years 1996-2009 contributed to the bank of new knowledge of visual and ocular outcome in children with pre- and perinatal brain damage.
Prematurely born children with WMDI

Crowding and cognitive visual problems in children with WMDI

In a study of prematurely born children with visual impairment due to WMDI, we described subnormal visual acuity and crowding (Jacobson et al 1996). Using standard neuropsychological tests we described visuo-spatial deficiencies in this group with problems judging depth and movement, with simultaneous perception, with face recognition and with orientation. Other groups described similar findings; among them Dutton et al. 1996.

Nystagmus, eye motility disorders, strabismus in children with WMDI

Nystagmus was previously reported to be absent in children with cerebral visual impairment. In fact, the presence or absence of nystagmus was thought to reveal whether the cause of visual impairment in a child was of ocular or cerebral origin. In the 1990ies we studied fixation with infrared technique in a group of prematurely born children with cerebral visual impairment due to WMDI and reported latent or manifest nystagmus in a majority of these children (Jacobson et al. 1998). However, children with the most severe WMDI, with cerebral palsy and visual impairment presented an ocular motor apraxia with complete disruption of ocular motor organization, including absence of fixation and they had no nystagmus. Children with less extensive WMDI, representing the other end of the clinical spectrum, all exhibited nystagmus. Thus, nystagmus may be seen in children with cerebral visual impairment and the presence of nystagmus may depend on the extent, and maybe, on the timing of the insult which may affect input to the visual integrating circuits.

Defective smooth pursuit movements and inability to perform visually guided saccadic movements in children with WMDI were found by us and by Cioni et al (1997) and Lanzi et al (1998). Strabismus as a consequence of WMDI was reported by Scher et al (1989) and also by us. The frequent finding of early-onset strabismus associated to WMDI may be the consequence of a deficient afferent pathway caused by axonal interruption in the optic radiation.

Optic disc appearance in children with WMDI

Brodsky and Glasier (1993) found a link between optic nerve hypoplasia and WMDI, but did not confirm their observations by fundus photography. We performed digital analysis of the fundus photographs of children with WMDI and found that the time at which the primary
lesion of the optic radiation occurred was of importance for the appearance of the optic disc (Jacobson et al. 1997, Jacobson et al. 2003). Early WMDI, sometimes of prenatal origin, before gestational week 28 was associated with small discs. Normal-sized optic discs with large cupping and consequently a reduced neuro-retinal rim area was the consequence of later lesions, occurring after 28 weeks of gestation. In this developmental phase, the supportive structures of the optic nerve have become established and probably do not adapt to the smaller number of nerve fibers. The reduced rim area, either expressed as a small disc or as a large cup in a normal-sized disc is probably the result of retrograde trans-synaptic degeneration of optic nerve axons caused by the primary bilateral lesions in the optic radiation. Thus, optic disc appearance together with the pattern of cerebral morphology depicted by MRI may give information about the timing of the lesion.

Visual field defects in children with WMDI

Interruption of axons in the optic radiation may explain restriction of visual field (VF). Variable restriction of the fields may also be attributable to problems with simultaneous attention. Thus the functional VF may vary depending on the amount of visual stimuli present and on the degree of attention paid to the fixation target. We assessed VF function in a group of children with WMDI (Jacobson et al. 2006). All subjects had subnormal VF function, although the depth and extension of the defects differed between subjects. The lower VF was often more affected than the upper, which could be interpreted as a bilateral homonymous lower quadrant dysopia due to the bilateral lesions in the upper part of the optic radiation. The VF abnormalities could be demonstrated by both manual and computerized perimetry.

Case report

This case illustrates visual outcome associated to WMDI (Jacobson & Dutton 2000). A boy was born prematurely at 32 full gestational weeks, with asphyxia at birth and he was early diagnosed with cerebral palsy (spastic diplegia). His verbal development was normal. Visual function is characterized by normal visual acuity (RE=LE 1.0) inferior altitudinal visual field defects (Fig. 1), strabismus, nystagmus, defect saccades and smooth pursuit movements and severe dorsal and ventral stream dysfunction. Thus, he is not able to judge depth by vision, he cannot find his way around and he cannot recognise even family members if he meets them unexpectedly. He is a slow reader, and often gets lost in the text. He has developed a battery of compensating strategies based on hearing, tactile information and memory.
The optic discs are of normal size with large cupping (Fig. 2); the intraocular pressure is normal. GDx of the fundus (Fig. 3) documents loss of ganglion cell axons above the optic disc secondary to the brain lesions. MRI of the brain (Fig. 4 and 5) illustrates bilateral periventricular WMDI. With fiber tractography of the optic radiation (Fig. 6) connecting fibres are only detectable in the lower part of optic radiation on both sides which corresponds well with the finding of an inferior bilateral homonymous quadrant anopia.

**Figure 1.** Altitudinal inferior visual field defects (bilateral inferior homonymous quadrant anopias) due to bilateral WMDI affecting the upper parts of the optic radiations.

**Figure 2.** Large cupping of normal-sized optic discs; a consequence of retrograde trans-synaptic degeneration from interruption of axons in the optic radiation occurring after 28 gestational weeks.
Figure 3. GDx fundus images illustrating loss of nerve fibres layer above the optic discs, due to retrograde trans-synaptic degeneration from the lesions in the upper part of both optic radiations, corresponding to the visual field defects
**Figure 4.** This MRI at the level of the posterior horns and trigonum shows the occipital horns to be dilated due to reduced periventricular white matter volume and consequent loss of axons in motor and visual pathways. Note how cortex abuts the ventricular wall giving trigonum of the ventricles a slight irregular shape. Also note increased signal in remaining white matter adjacent to the frontal horns and extending deep into white matter in both frontal lobes. (Courtesy of Olof Flodmark, Dept of Neuroradiology, Karolinska University Hospital)

**Figure 5.** This image is at a level just at the top of the lateral ventricles. Increase signal beyond the borders of the lateral ventricles in the parietal and frontal lobes represent gliosis in damaged white matter. (Courtesy of Olof Flodmark, Dept of Neuroradiology, Karolinska University Hospital)
Figure 6. Fiber tractography of the optic radiation (OR). It is difficult to accurately track the OR with tensor-based tracking. Here, instead tractography between LGN and primary visual cortex is performed with probabilistic tractography in a crossing-fiber model. The results show a normal periventricular extent of OR in a healthy volunteer (Left). In our case (Right) connecting fibers are only detectable in the lower part of OR. The degree of connectivity is also lower (i.e. lower probability that initiated fibers in LGN reach the target area in primary visual cortex), and more so on his left than on his right side. This finding corresponds well with loss of nerve fibres in the upper part of the fundi and with an inferior bilateral homonymous quadrant anopia. (Courtesy of Annika Kits and Finn Lennartsson, Dept of Neuroradiology, Karolinska University Hospital)
Visual field outcome in children with unilateral cerebral palsy

The frequency of VF defects in different groups of children with cerebral palsy has been estimated to 20-25%. However, in most studies only confrontation techniques have been used.

We have recently assessed VF function in a group of children with unilateral cerebral palsy (CP) with confrontation technique and with Goldmann perimetry. The type and extension of brain lesion was documented with cerebral imaging. 62% had subnormal VF function, and the VFs were severely restricted in 21%. The underlying brain lesions were malformation, WMDI and cortico-subcortical lesions. VF function could be correlated to the pattern of brain damage in cortico-subcortical lesions and in extensive lesions due to malformation or WMDI. Total homonymous hemianopia was common in the cortico-subcortical group but rarely found in children with malformation or WMDI. Five children had malformation or WMDI engaging parts of the brain that usually contain the posterior visual system, but they had normal VF function.

Thus, the VF function may be preserved by plasticity of the immature brain in children with malformation and WMDI. Severely restricted VF function was more often associated with brain damage occurring later in the developing brain. All children with severely restricted VFs were identified with confrontation technique. Goldmann perimetry was a suitable method to identify also relative VF defects in this age group of children with unilateral CP (Jacobson et al. 2010).

Conclusions

Visual impairment due to pre-and perinatal brain damage has become the most common cause of visual disturbance among children in the Western world; a consequence of increased survival of very immature and very sick infants. The resulting visual dysfunction depends on localisation and extension of the lesion involving the visual brain, but also on at what stage of maturity the brain was damaged. As there is considerable plasticity of the developing visual system, the outcome may be difficult to predict by routine imaging of the brain. Assessments of acuities, visual field function, fixation, eye motility and of cognitive visual function constitute the basis for implementation of developmental programmes designed for these children.
References


Jacobson L, Rydberg A, Eliasson AC et al. submitted manuscript. Visual field function at school age in children with spastic unilateral cerebral palsy, related to different patterns of brain damage
