Visual Function and Ocular Morphology in Children with Surgically treated Hydrocephalus

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To all children with hydrocephalus
and their families

Abstract

Aims

To investigate the frequency of ophthalmological abnormalities, the need and timing of eye-care interventions as well as incidence, aetiology and neurological/ neuropsychological outcomes in children with hydrocephalus needing surgical treatment during the first year of life.

Patients and Methods

Papers I & II: Seventy-five school-aged children (34 girls and 41 boys) with surgically treated hydrocephalus and 140 age and sex matched control participants underwent a comprehensive ophthalmologic examination including structured history taking regarding visual perceptual problems and ocular fundus photography. In paper II, 55 of the children with hydrocephalus (27 girls and 28 boys) had fundus photographs of sufficient quality (correctly focused photographs with the optic disc centered) taken. These children's photographs were analyzed using digital image analysis.

Paper III & IV: These papers comprised a population-based ophthalmologic study of all the children with hydrocephalus born in western Sweden in 1999-2002 (n=54). Aetiological, neurological and neuroimaging information was collected from the case records. Forty of the 48 children available for the study underwent an ophthalmologic examination (paper IV).

Results

Papers I, III, IV: Visual function deficits were identified in more than 80% of the children with hydrocephalus. Common deficits were low visual acuity, refractive errors, strabismus and difficulties with visual processing. A majority of the children had one or more neurological impairments. Children born at term and those with associated myelomeningocele were least likely to be affected. Both aetiology to hydrocephalus and gestational age at birth were important factors for neurological outcome. No child with normal neuroimaging, after surgery, had any visual or neurological impairments. 74% of the children (paper IV) underwent at least one intervention from the ophthalmologic team, such as correction of refractive errors with glasses and/or patching and/ or squint surgery and/or referral to the visual habilitation clinic. A decrease in the prevalence of hydrocephalus was noted but did not continue in 1999-2002, mainly due to increased survival of children born extremely preterm with post-haemorrhagic hydrocephalus.

Paper II: The median optic disc area was significantly smaller in children with hydrocephalus compared with the reference group. There was no difference in cup area and, consequently the rim area was significantly smaller in the hydrocephalic children. Children with hydrocephalus had an abnormal retinal vascular pattern with significantly straighter retinal arteries and fewer central vessel branching points than the controls.

Conclusions

A majority of children with surgically treated hydrocephalus, during the first year of life, regardless of aetiology, had abnormal ocular morphology and visual functions including a history of visual perceptual problems. Children with hydrocephalus born preterm were most commonly affected. The majority of the children with hydrocephalus had other associated neuroimpairments such as epilepsy, cerebral palsy and/or learning disabilities. A large proportion of children with hydrocephalus need some ophthalmological intervention. Using the current knowledge of the visual functions in children with hydrocephalus we present an "ophthalmological safety net" for these children. We suggest an ophthalmological examination soon after shunt surgery and every 4-6 months during the first two years of life, followed by at least a yearly examination to six years of age, in order to optimize vision and thereby enhance general development.

Contents

List of publications

This thesis is based on the following articles :

I **Andersson S, Persson EK, Aring E, Lindquist B, Dutton GN, Hellström A**
Vision in children with hydrocephalus
Dev Med Child Neurol 2006;48:836-841

II **Andersson S, Hellström A**
Abnormal optic disc and retinal vessels in children with surgically treated hydrocephalus
British J Ophthalmol 2009 Apr;93(4):526-30. Epub 2008 Dec 23

III **Persson EK, Andersson S, Wiklund LM, Uvebrant P**
Hydrocephalus in children born in 1999-2002. Epidemiology, outcome and ophthalmological findings
Childs Nerv Syst 2007 Oct;23(10):1111-8

IV **Andersson S, Hård AL, Dutton GN, Aring E, Persson EK, Hellström A**
Timing of interventions and for ophthalmological abnormalities in children with hydrocephalus
In manuscript

Abbreviations

CP	cerebral palsy
CSF	cerebrospinal fluid
CVI	cerebral visual impairment
D	diopter
EP	epilepsy
GA	gestational age
HC	hydrocephalus
IQ	intelligence quotient
IVH	intraventricular haemorrhage
MMC	myelomeningocele
MRI	magnetic resonance imaging
OA	optic atrophy
PVL	periventricular leukomalacia
ROP	retinopathy of prematurity
SD	standard deviation
VA	visual acuity
VP-shunt	ventriculoperitoneal shunt
WHO	World Health Organization
WISC-III	Wechsler Intelligence Scale for Children III
WPPSI-R	Wechsler Preschool and Primary Scale of Intelligense-Revised

Definitions

The definitions used in these studies are taken from the International Classification of Diseases 1987 (ICD 9) and 1997 (ICD 10).

Epilepsy is defined as two or more unprovoked epileptic seizures.

Cerebral palsy is defined according to the criteria proposed by Mutch et al. 1992.

Children born preterm are those born before 36 weeks of gestation, moderately preterm are those born between 32 and 36 weeks of gestation, very preterm are those born between 28 and 32 weeks and extremely preterm are those born before 28 completed weeks of gestation.

Prenatal refers to the period before the onset of labour, perinatal to that from the onset of labour resulting in delivery until the 28th day of life, and postnatal to that from day 29 to the age of one year.

Learning disability in paper III and IV is defined as a score of the full scale intelligence quotient (FSIQ)<70

Visual impairment: In paper I-III it is defined as best corrected visual acuity of 0.3 or less and/or restriction of the visual field to 20 degrees or less.

Introduction

The word hydrocephalus comes from Greek: hydro- water and kefale-head. This condition has scientifically been described since Hippocrates (476-377 BC) and Galen (130-200 AD). They believed that this disease was caused by extracerebral accumulation of water. Many followed and tried to describe the CSF circulation. A breakthrough in modern physiological theory on CSF circulation came 1875 when Kay and Retzius presented their classical study, which is largely valid even today.

Surgical treatment attempts were made during the tenth century with evacuation of intraventricular fluid. But it was not until late nineteenth century/beginning of the twentieth that patophysiological knowledge and surgery techniques made the use of various shunts and endoscopic third ventriculostomy possible (Aschoff et al. 1999).

Treatment of hydrocephalus by ventriculo-atrial shunting was introduced in the 1960s and was followed by ventriculo-peritoneal shunting during the following decade (Forrest 1968, Cinalli 1999). Before the shunting era, there was a very high mortality among children with hydrocephalus, and other conditions than vision was the focus of interest (Hadenius et al. 1962). Nowadays more than 90% of affected children survive.

A large proportion of the brain function is devoted to visual tasks, and since hydrocephalus causes multiple impairments of brain function, the visual system is commonly affected. During the pre-shunting era and from the beginning of the shunting era, in the 1960s, the most commonly reported ophthalmologic findings were the setting sun sign, optic nerve atrophy and strabismus in children with hydrocephalus (Duke-Elder 1964, Walsh & Hoyt 1969). This situation has changed over the years, now involving an understanding of the visual input processing as well as other visual functions (Rabinowicz 1974, Biglan 1990, Gaston 1991, Conolly et al. 1991, Houliston et al. 1999, Heinsbergen et al. 2002). The greatly increased risk of neurological and cognitive impairments in these children has been well described (Fernell et al. 1986, 1994, 1998; Lindquist et al. 2005; Persson et al. 2005, 2006). A clinical strategy is required to evaluate each individual, and assess the nature and degree of cerebral dysfunction and to determine the optimum strategies to circumvent the problems elicited, in order to minimise educational and social disadvantage.

This strategy has to be based on a deeper understanding of the relationship between neurological, cognitive and visual functional deficits in parallel with neuro-radiological findings.

Anatomy
The anterior visual pathways

The anterior visual pathways consist of the eyes, the optic nerves, the chiasm and the optic tracts as shown in Figure 1.

optic nerve
optic chiasm
optic trac
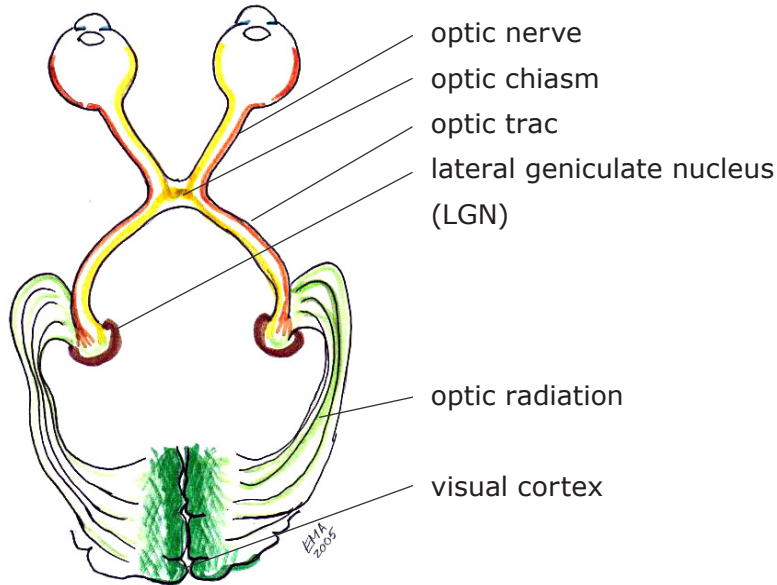lateral geniculate nucleus
(LGN)

optic radiation

visual cortex

Figure 1. The visual pathways.

The transparent retina, which is an extension of the central nervous system consists of several layers including the photoreceptor layer, where the photosensitive rods and cones are located. The foveola, the central part of the retina is used for fixation. Through the bipolar and amacrine cells the photoreceptors are connected to the ganglion cells, the axons of which form the optic nerve. At the chiasm, axons from ganglion cells of the nasal part of one eye cross and join the axons from the temporal part of the other eye, forming the optic tract.

The blood supply of the outer retina including the photoreceptors is provided by the choriocapillaris, while the retinal circulation supplies the inner retina including the ganglion cells.

The posterior visual pathway

Axons from the ganglion cells synapse at the lateral geniculate nucleus, and connect to the axons of the optic radiation continuing further along the lateral ventricles to the visual cortex (Figure 1). The primary visual cortex connects to several other areas of the cerebral cortex, which are involved in processing the

visual information.

In addition to the visual pathway mentioned above, there is another, subconscious, visual system, the collicular visual system. This system is thought to be involved in so-called "blind-sight" i.e. the ability to respond appropriately to visual inputs without a feeling of having seen them.

Associative areas

Beyond the primary visual cortex, visual information is led to a number of extrastriate areas. Despite the complexity, two principal streams have been identified: the ventral and the dorsal stream. These two streams seem to be interconnected (Milner & Goodale 2000, Macintosh 2000, Dutton 2003). The ventral stream projects from the primary visual cortex to the inferior temporal region and serves a conscious appreciation, recognition and understanding of what is seen ("*what*" and "*who*"). The dorsal stream projects to the posterior parietal cortex, accords visual attention and subconsciously assimilates incoming visual information in order to bring about moment-to-moment, immediate visual guidance of skilled action and movement through the visual world ("where") (Figure 2).
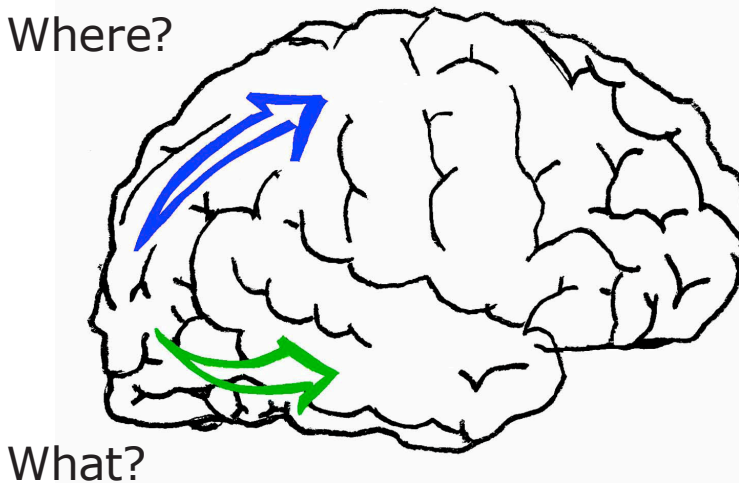

Figure 2. Schematic picture of the two streams of visual processing in the human cerebral cortex.

Damage to the dorsal stream leads to inaccurate visual guidance of movement although the visuospatial awareness, being afforded by the ventral stream, remains intact. Damage to the ventral stream, on the other hand, leads to impaired visual recognition, but visual guidance of movement remains intact enabling the person to move accurately through visual space despite having very poor conscious

vision.

The incoming visual signals, processed by the ventral stream, require a quick comparison to the long-term visual memories to facilitate understanding of what is being seen, while visual signals when being processed by the dorsal stream reflect the real geometry of the outside world. Even though these two systems work in parallel, they must interact in order to culminate in normal everyday visual behaviour (Goodale 2010).

Cerebrospinal fluid circulation

Cerebrospinal fluid (CSF) is a clear fluid containing a small amount of protein. The major role of CSF is to protect the brain and spine and to remove waste products. About 80% of the CSF is derived by active secretion from the cerebral arterial blood, in the choroid plexus of the ventricular system (Davson et al. 1987). The CSF leaves the lateral ventricles by passing through the foramen of Monro to the third ventricle, then through the Sylvian aqueduct to the fourth ventricle. The fourth ventricle is connected with the subarachnoid basal cisterns through two lateral openings; the foramina of Luschka and the spinal subarachnoid space through the basal foramen of Magendie. The major part of the CSF passes through the spinal subarachnoidal space, over the cerebral convexities to be absorbed by the arachnoidal villi into the superior sagittal sinus and venous bloodstream (Figure 3).
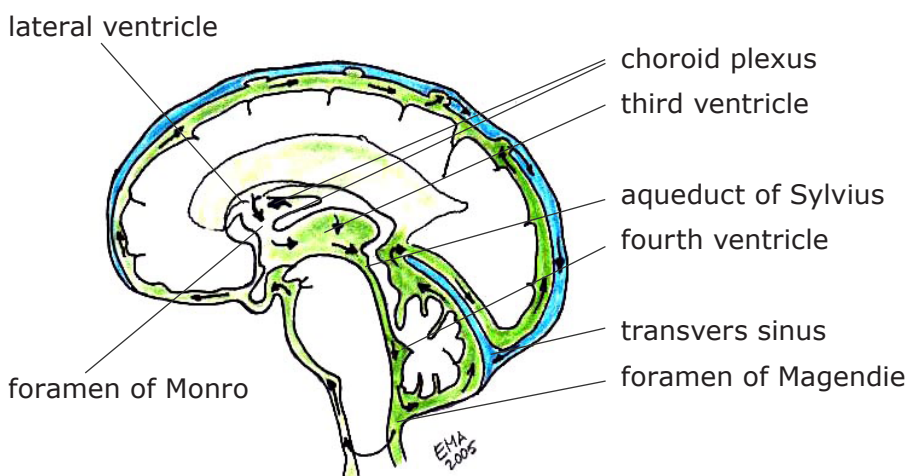

Figure 3. The flow of cerebrospinal fluid (CSF).

Pre and postnatal development of the brain including the visual system

Prenatal development of the eye and brain starts relatively early in comparison to other systems. By the 6th week, after fertilisation, the ocular structures and the differentiation of the brain are fairly well developed (Day 1997).

Refraction and anterior segment of the eye

The refraction of an eye depends on the refractive power of the cornea and the lens, the depth of the anterior chamber, and the axial length. Refractive errors, especially hyperopia and astigmatism, are common in new-borns. These refractive errors reduce during the ensuing few years, particularly during the first year of life, due to ocular growth, in a process called emmetropisation (Saunders et al. 1995, Cook et al. 2003).

Posterior segment of the eye and the optic nerve

The retina is sequestered from the brain of the embryo. The photoreceptors start to differentiate during the fifth month of gestation. Differentiation of the fovea occurs relatively late in comparison to other regions of the retina. The fovea is almost fully developed at about 11-15 months, but continues to develop until 5 years of age (Hendrickson 1994).

The ganglion cells start to develop at the optic nerve head during the 5th week of gestation. The maximum number of ganglion cells is seen at the 16th weeks of gestation, rapidly reducing by apoptosis until the 30th gestational week. About two thirds of the axons are lost (Provis et al. 1985). The optic nerve head itself is relatively full-sized (75%) at birth but continues to grow until one year of age (Rimmer et al. 1993). There are around 1.2 million axons in each adult optic nerve (Jonas et al. 1990). The supporting tissue starts developing during the first trimester, and continues developing until the 9th month of gestation.

Retinal vascularisation

Vascularisation of the retina starts, at the optic nerve head, in the 15th gestational week and is completed at term. It has been suggested that the formation of the retinal vessels is promoted by the increased metabolic demand of neurones (Chang Ling et al. 1995). The ganglion cells begin to develop in the posterior pole before proceeding to the periphery and the vessel growth seems to mimic the pattern of arcuate fibres created by ganglion cell axons that pass around rather than through the future foveal region (Provis et al. 2000).

Chiasm, lateral geniculate nucleus and optic tract and retrogeniculate pathways

The myelination of the anterior visual pathways starts in the lateral geniculate

bodies (20th gestational week), then continues anteriorly via the tract, and the chiasm, reaching the optic nerves at 32 gestational weeks. Synapse formation in the visual cortex starts at 23 weeks of gestation, and the number of synapses in this area continues to change until 8 months postnatally (Huttenlocher et al. 1987). The primary visual cortex is not completely myelinated until three years of age.

Formation of the brain

The neural tube is formed by 3-4 weeks of gestation. Its upper part closes at 24 days and the lower part at 26 days of gestation. Failure of closure of the upper or lower parts of the neural tube results in encephalocele, or myelomeningocele, respectively (Lagercrantz 1999). During the 5-10th week a separation occurs of the telencephalon, which gives rise to the cerebral hemispheres, from the diencephalon, from which the eyes, pituitary gland and thalamus originate. During this period there is also a sagittal cleavage to develop the paired cerebral hemispheres and ventricles. During 10-20 weeks of gestation, neural migration takes place, where the neural cells migrate from their original site to their permanent locations. Synapse formation and programmed cell-death takes place after the 20th week of gestation and onwards.

Neuronal- and vascular tissues

The central retinal artery, derived from the ophthalmic artery, divides into four main branches that supply the retina. The development of the retinal circulation seems to coincide with the establishment of mature retinal ganglion cells (Provis et al. 1983). Temporary hypoxia (caused by increased activity in the retinal neurons) is a stimulus for normal angiogenesis (Chang Ling et al. 1995, Zhang et al. 1996, Provis 2001). It has also been demonstrated that the astrocytes from the optic nerve, guide the development of the blood vessels; that is, the neuroectoderm controls their development.

Development of visual functions

Normal development

Visual acuity and binocular vision: The development of normal vision is dependent on clear visual images in both eyes during a period when the visual system is plastic, i.e. from birth to about 7-8 years of age, a period during which visual function may be modified by visual experience. The classical studies (with kitten lid suture) by Hubel & Wiesel showed that monocular visual deprivation resulted in reduction of cortical neurons to a greater degree than the experiments

for bilateral deprivation show. They concluded that this cortical influence is not only caused by the disuse of one eye but may instead be dependent on interaction of the two visual pathways. Their experiments also showed that the reduction of neurons as a result of monocular deprivation could be driven by a stimulus presented to the deprivated eye (Wiesel & Hubel 1963, 1965). These remarkable findings led to a new understanding in amblyopia. Later studies have showed that the chances of developing amblyopia reduce with the age of the child (Keech & Kutschke 1995).

Visual acuity (VA) is low in healthy infants during the neonatal period but increases gradually to reach adult values at approximately 4-6 years of age (Simons 1983, Mayer & Dobson 1982). The VA appears to improve until it reaches a monocular mean value of 1.4 (90% threshold level) measured at the ages of 20-29 years and thereafter declines gradually (Frisén & Frisén 1981).

In children methods used in VA measurements depend on the children's developmental ages and cooperation. Visual acuity testing in school-aged children is based on recognition of optotypes of letters or symbols of decreasing size. For children below the age of three years and children with mental disabilities these methods can rarely be used and available methods such Cardiff cards and Acuity cards do not provide VA values that are directly comparable to those of optotype tests.

Development of stereopsis occurs between 1 and 6 months of age (Day 1990).

Abnormal development

Strabismus and amblyopia: Amblyopia is usually described as a unilateral or bilateral decrease of visual acuity, for which no organic cause can be found. The condition is a consequence of visual deprivation during a period when the visual system is plastic, i.e. from birth to about 7-8 years of age. The prevalence ranges between 1-4% in populations, with the lower numbers in countries screening for amblyopia (Sjöstrand & Abrahamsson 1990, Kvarnström et al. 1998, Simons 2005). Amblyoipa has traditionally been classified according to the cause of the condition: strabismus, anisometropia and visual deprivation (including ptosis, media opacities, uncorrected bilateral hyperopia, astigmatism and nystagmus) (von Noorden 2002, Campos 1989).

In strabismus only one eye is fixating the object viewed while the other eye deviates. The deviation may be manifest (heterotropia) or latent (heterophoria). The visual axes may converge (esotropia/esophoria) or diverge (exotropia/exophoria). Most cases of strabismus are probably due to sensory and motor functional deficits; however, other risk factors have been reported such as retinopathy of prema-

turity, family history of strabismus and chromosomal defects (Harcourt 1968, Pennefather et al. 1999, Abrahamsson et al. 1999).

If amblyopia is undetected or not treated properly there is a risk of permanent visual loss. Studies have shown improvement in VA, when treating children until the age of 8-10 years or even older (Campos 1995, Holmes et al. 2006). However there appear to be a decrease in treatment response with increasing age, especially in children with a more severe amblyopia (Holmes JM et al. 2011). There are several treatments for amblyopia, which may be used alone or in combination. The treatments used depend of the cause of amblyopia. The most common treatment strategies are correction of refractive errors, occlusion therapy and surgery due to obstruction of the visual axis. Large multi-center studies have evaluated the timing and recommended duration of amblyopia treatment (Pediatric Eye Disease Investigator Group)

Although choosing the correct treatment the result still is dependent of good compliance. However difficulty with compliance is a well-known problem and compliance with treatment is shown to be the most critical factor for a successful outcome (Lithander et al. 1991).

Amblyopia may be superimposed on an organic disease. Good results from amblyopia treatment has been shown in children with unilateral structural anomalies, with best outcome in children with partial media opacities and not as good outcome in those with optic nerve anomalies. (Bradford et al. 1992).

Cerebral visual impairment and visual perception
The terminology for visual dysfunction caused by brain pathology has been a little confusing over the last two decades, some authors using the term "cortical visual impairment" while others used the expression "cerebral visual impairment" when discussing visual impairment due to brain related causes (Soul et al. 2010). The term "cortical visual impairment" has mainly been used when describing disturbance in the occipital lobe while "cerebral visual impairment" has been defined as also including cognitive and perceptual visual disorders due to damage to the brain and visual dysfunction due to cerebral disturbances of eye movement (Fazzi et al. 1997). In this thesis we use the term cerebral visual impairment (CVI).

Common causes of CVI are: Hypoxic-ischemic brain injury in children born preterm/ term (Dutton & Jacobson 2001, Flodmark et al. 1990, Matsuba et al. 2006), infections of the central nervous system (Newton et al. 1985), metabolic disorders (Matsuba et al. 2006), brain malformations (Flodmark 1990) brain injury (De Veber et al. 2000, Morris et al. 2006) and chromosomal disorders (Little et al. 2009)

Cerebral visual impairment is now the leading cause of visual impairment among children in developed countries (Rogers 1996, UK), (Blomé & Tornquist 1997, Sweden), (Matsuba & Jan 2006, Canada). This finding probably results from increasing recognition and identification of CVI and from increased incidence of CVI related to advances in neonatal and paediatric care, with enhanced survival of children born preterm with neurological disease. The timing, location and extent of the pathology determine the severity. (Jan & Groenveld 1993).

It is caused by malformations, lesions or diseases of the posterior and associative visual pathways. This type of impairment is often associated with a reduction of the visual acuity and contrast sensitivity, visual field defects and an impaired ability to process visual information, causing visual perceptual problems. These different dysfunctions may be seen separately or together. All of the defects above have been reported in children with PVL (Jacobson et al. 1996 and 2002, Ricci et al. 2006), congenital hemiplegia (Carlsson et al. 1994) and hydrocephalus (Houliston et al. 1999).

Cerebral visual impairment ranges in severity from delayed visual development but with good improvement to profound permanent visual impairment. A child with severe CVI may tend to gaze at light, later on starting to respond to near objects before responding to more distant ones. Damage to the associative areas results in disturbances of processing visual input. A variety of combinations of impaired recognition, orientation, depth perception, motion perception, and simultaneous perception have been described in children with CVI/hydrocephalus (Dutton et al. 1996, Houliston et al. 1999, Dutton 2003).

Dysfunction of visual perception may also vary in severity on different occasions and time of the day. The dysfunction may be more pronounced if the child is tired or stressed. This variability may be misunderstood by parents and teachers and easily misjudged as bad behaviour.

Children with dysfunction of visual perception from early childhood are often unaware of the visual difficulties, but these can be observed by parents and carers, providing information that can lead to a diagnosis. Characterization of each part of the visual function then allows matched habilitative strategies to be designed and implemented to ensure that an affected child develops at the best of his/her ability.

Neuronal- and vascular tissues
Abnormal development
Hellström et al. (2000) found an increased tortuosity of retinal arterioles and a reduced number of vascular branching-points in the central part of the retina in

children born preterm. Bracher (1982) suggested that hypoxia causes relaxation of the arteriolar muscles, resulting in elongation and abnormal tortuosity of the retinal arterioles. Other conditions reported in association with abnormal tortuosity of the retinal arteries, are for example fetal alcohol syndrome (Hellström et al. 1997), and Fabry´s disease (Sodi et al. 2007).

Impact of abnormal vision on children's general development

Vision is an important sense for general development and education. Babies learn by imitating their environment. Eye contact with parents gives them feedback on their performance. The partially sighted or blind child is deprivated of these parts of normal development (Jan et all 1997). Low vision/blindness may also have an effect on behaviour. Learning disorders and impaired intellectual potential has been found in children with Leber´s amauroses. The impact of vision on development is most severe in children who are blind as opposed to those who have some but reduced sight (Sonksen et al. 1991).

Blindness has also a profound effect on motor development. Blind children have a developmental delay of trunk and head stability as grasping objects and crawling. The start of walking seems on the other hand not to be delayed among these children (Jan et al. 1997). As the child grows older educational needs and mobility gets more important. Mobility is greatly heightened if the child has the slightest remaining vision. This plays an important role not only for the child to get around but also for the awareness of body.

Hydrocephalus in children

Hydrocephalus is a result of CNS abnormalities of different aetiologies, causing neurological, neuropsychological and ophthalmological disturbances of varying kinds and severity, from no impairments at all, to profound neurological/neuropsychological and visual impairments.

Epidemiology

In Sweden, epidemiological studies on children with hydrocephalus have been conducted since the 1960s. The prevalence of live birth hydrocephalus increased between 1967 and 1986 due to increased survival of preterm children, who developed intraventricular haemorrhage and hydrocephalus (Fernell et al. 1986, Fernell et al. 1994). Thereafter the prevalence of hydrocephalus, needing surgical treatment during the first year of life, in the western parts of Sweden, decreased to 0.82 per 1000 live births (Persson et al. 2005) 1989-1998 (Fig 4).
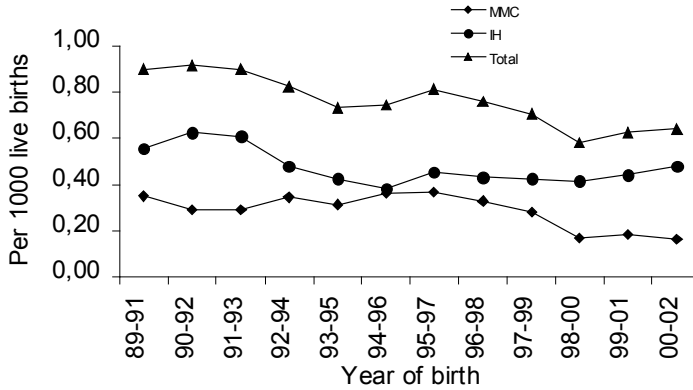
Figure 4. The prevalence of hydrocephalus per 1000 live births in western Sweden in children with infantile hydrocephalus (IH) and hydrocephalus associated with myelo-meningocele (MMC) (birth years 1989-2002; three year moving average). Children born 1999-2002 (paper III).
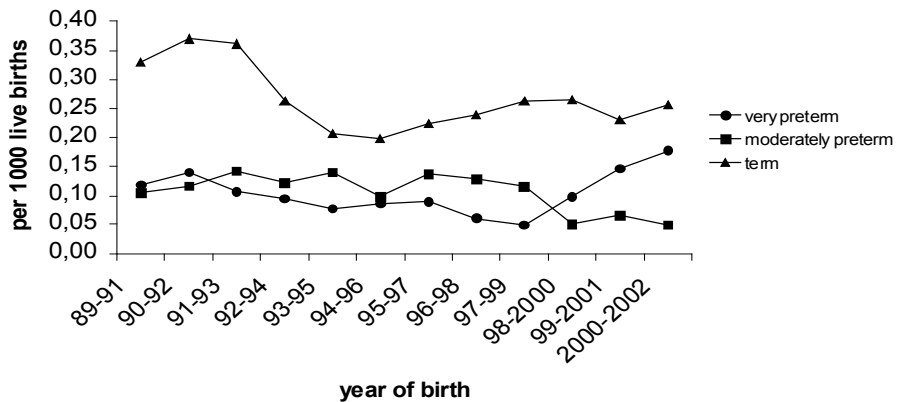

Figure 5. The prevalence of infantile hydrocephalus per 1000 live births in different gestational age groups (three year moving average). (With courtesy of Eva-Karin Persson). Children born 1999-2002 (paper III).

This decrease was probably attributable to improved medical care and maternal nutrition, with supplements of folic acid in food as well as increased use of ultrasonography in early pregnancy, resulting in abortion of foetuses with MMC (Bygdeman et al. 2005, Frey et al. 2003). However, due to increasing survival of extremely preterm infants the incidence is no longer declining (Fig 5).

Pathophysiology and Aetiology

Hydrocephalus leads to changes of the brain, not only of the morphology but also on the circulation, biochemistry, metabolism and maturation. The white matter, especially the periventricular region is the brain region that is most affected in hydrocephalus. The degree of damage seems to be age-related with more pronounced involvement in children compared to adults. Also the cerebral cortex undergoes gross changes with the onset of hydrocephalus, a great thinning of the cortex and extension. Histological and biochemical changes have been noted in the neurons affected by hydrocephalus. Retrograde neural degeneration has been seen in retinal ganglion neurons and cortex (Kriebel et al. 1993). The timing of therapy is crucial in determining the reversibility and outcome.

Hydrocephalus may be of prenatal, perinatal or postnatal origin. The most common prenatal aetiologies are malformations of the CNS and genetic factors. Intraventricular haemorrhage and infections are the most frequent causes in the perinatal period as are tumours, trauma and infections during the postnatal period.

Intraventricular haemorrhage is the most common aetiology among children born preterm. The breakdown of the haemorrhage results in blood product causing an arachnoiditis and may cause obstruction of the aqueduct of Sylvi and posterior fossa.

Malformations of the CNS may be arachnoidal cysts, Dandy-Walker and aqueductal stenosis.

Myelomeningocele (MMC) is a consequence of a very early defective neural tube closure which leads to a negative impact on the medulla, causing problems with bladder control and paralysis of the lower limbs. In addition a majority of the children with MMC have Arnold Chiari malformations, aqueduct stenosis and other CNS malformations contributing to the development of hydrocephalus.

Infections in the CNS may cause development of hydrocephalus due to obstruction to different parts of the CSF pathways. The most common causative infections are: toxoplasmosis, cytomegalovirus infection and bacterial infections.

Different aetiologies have a leading role in causing hydrocephalus, in different countries/parts of the world. While children with post-haemorrhagic hydrocephalus increases in the western world, infections are still a major cause to hydrocephalus in East Africa and south Asia (Persson et al. 2005, Warf et al. 2010, Rashid et al. 2011)

Treatment strategies

Drainage of the CSF into various intracranial and extracranial spaces has been used as a treatment for hydrocephalus since the beginning of the twentieth cen-

tury. The "modern" treatment with ventriculo-atrial shunting and ventriculo-peritoneal shunting has been in use since the 1970s (Forrest 1968, Cinalli 1999). (Figure 6).
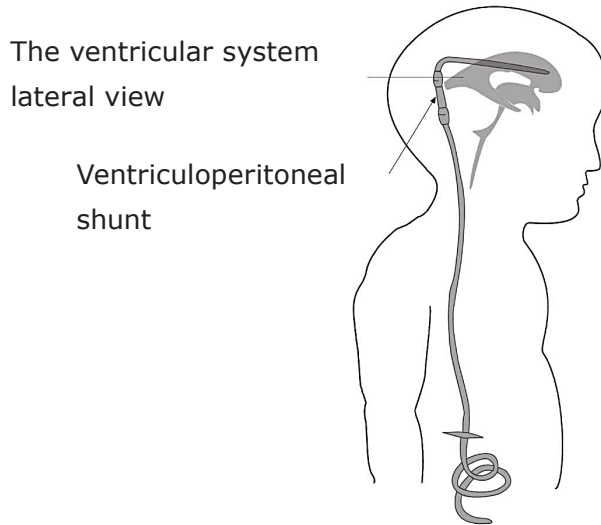
The ventricular system
lateral view

Ventriculoperitoneal
shunt

Figure 6. Diagrammatic drawing of a child with hydrocephalus and ventriculoperitoneal shunt.

Another treatment is endoscopic third ventriculostomy (ETV) in which a perforation is made through the floor of the third ventricle, producing a fistula for the cerebrospinal fluid to drain into the subarachnoid spaces from where it is re-absorbed (Dalrymple et al. 1992). Children born pretem with intraventricular haemorrhage sometimes do not receive a shunt at once but the CSF is temporary drained by repeated lumbar punctures or a subcutaneous reservoir is used. This decreases the risk of mechanical obstruction and infection. In addition, some of the children do not have to have a permanent shunt as some of the haemorrhage resolves without complication spontaneously (Volpe 1981).

The most common treatment of today is ventricular peritoneal shunting although the ETV is increasing. The use of ETV plays an important role in hydrocephalus treatment especially in the developing countries, as shunt complications may be difficult to handle in those countries. The most common causes to shunt complications are infections, shunt obstructions and mechanical failures. The frequency of shunt failure has been reported to be about 40% within the first year after surgery and 50 % by the second (Kestle et al. 2000). Changes in surgical technique and development of new shunt materials are currently the subject of focus in clinical research (Murshid 2000).

Neurology and cognition

Motor impairments are common in children with hydrocephalus. Heinsbergen reported of 61% children with hydrocephalus of having musculoskeletal dysfunction (Heinsbergen et al. 2002).

Cerebral palsy (CP) is often reported in children born preterm with hydrocephalus secondary to intraventricular haemorrhage. Fernell found cerebral palsy in 47% of children born preterm compared to 26% of those born at term, with hydrocephalus (Fernell et al. 1987, Fernell et al. 1988), which is in accordance with the results of Persson who reported 51% cerebral palsy among children born preterm and 14% of those born at term. Those children born very preterm (‹32 gestational weeks) had the highest frequencies of 88% cerebral palsy.

Epilepsy is often associated with hydrocephalus, especially in children born preterm. Persson found 30% of the children with hydrocephalus to have epilepsy with higher frequency in children born preterm (45%) especially those born very preterm, ‹32 gestational weeks (58%) (Persson et al. 2005).

The overall IQ in children with hydrocephalus has been reported by many to be in the low average or below. Children with MMC have been reported to have a higher IQ than those with other aetiologies to hydrocephalus (Dennis et al. 1981, Kao et al. 2001). Lindquist and co-workers found 33% of a population of children with hydrocephalus having normal IQ(›85), 30 % having IQ of 70-84 and 37% had learning disabilities and an IQ of less than 70 (Lindquist et al. 2005). Children with hydrocephalus often have a characteristic test profile with higher scores in verbal intelligence compared to non-verbal (Dennis 1981, Lindquist et al. 2005).

Vision and the visual system

Visual acuity: Visual acuity is often reduced in children with hydrocephalus (Rabinowicz 1974, Ghose 1983, Mankinen-Heikkinen et al. 1987, Biglan 1990) due to lesions at various levels of the visual system. The anterior visual pathway may be affected as in optic atrophy or optic nerve hypoplasia or the posterior visual pathway as in periventricular leucomalacia. However, it is difficult to distinguish the results of anterior and posterior visual pathway lesions from each other and most likely there is a combination of both in many children with brain lesions. Some authors have reported reduced visual acuity with repeated shunt dysfunctions (Arroy et al. 1985, Gaston 1991). In addition, several children with hydrocephalus have refractive errors and strabismus which can result in amblyopia.

Strabismus and nystagmus: Strabismus is a common complication in children with hydrocephalus. A majority of these children have horizontal deviations, where esotropia is more common than exotropia (Rabinowitz 1976, Aring et al. 2007).

Nystagmus is also common and may have various causes and appearances. It could easily be missed if not sought specifically (Rabinowitz 1976, Gaston 1991, Aring et al. 2007).

Refraction: In comparison with healthy children, children with hydrocephalus are more often hypermetropic, a result which has also been reported for other children with cerebral damage (Saunders 2002). Impaired emmetropisation related to abnormal visual input and processing is a potential contributory factor. Astigmatism is also common in children with hydrocephalus while myopia has been reported to occur with the same frequency as observed in healthy children (Mankinen-Heikkinen et al. 1987)

Visual perception

In order, for the child, to understand the visual input, signals running through the visual pathways have to be interpreted. Few reports describe visual problems due to cognitive dysfunction in children with hydrocephalus. The relationship between brain function and behaviour is traditionally tested by neuropsychologists, using different tests such as the WISC-III (Wechsler Intelligence Scale for Children, constructed for ages 6 to 16) and the WPPSI-R (Wechsler Preschool and Primary Scale of Intelligence, for ages 3 to 7 years).

These IQ tests are divided into different parts, and measure many different cognitive abilities. A structured history-taking strategy, addressing difficulties in daily life which may be attributed to impaired visual perception, was used by Houliston et al. 1999, who found that approximately 50% of the children with hydrocephalus had difficulties interpreting their visual input.

Prematurity and visual outcome

Prematurity is associated with an increased risk of visual function abnormalities. The visual system undergoes an extensive development during the last part of pregnancy and is therefore susceptible for consequence of preterm birth.

A large portion of children born preterm have been reported to have ocular morphological abnormalities (Hellström et al. 2000) as well as periventricular leukomalacia (Volpe 2003, Jacobson & Dutton 2000, Fazzi et al. 2004). Hellström (2000) found significantly smaller optic disc areas, increased tortuosity of retinal arteries and veins as well as reduced number of vascular branching points in

children born before 29 gestational weeks. Significant refractive errors are common among the children. 38% refractive errors was found among premature infants(‹29 weeks of gestation) in a study by Hård et al. 2000, which is well in accordance with Holmström et al. 1998. Also low visual acuities, decreased contrast sensitivity and visual field defects are common in this group (Larsson et al. 2004, 2006). Further, children born preterm have been found to have poor performance in visual processing.

Intraventricular haemorrhage is common in children born preterm and often occurs during the first postnatal weeks. The bleeding originates from the germinal matrix, a structure of the ventricular wall, which has many fragile capillaries. The large portions of blood clots induce secondary arachnoiditis, which obstructs the CSF pathway leading to a ventricular dilatation. About 10% of the children affected need shunt insertion (Resch et al. 1996).

Reflection

Children with hydrocephalus constitute a heterogeneous group with high frequencies of ophthalmological, neurological and cognitive impairments. It is a challenge to understand the different aspects of impairments in each child. This requires a multi-disciplinary approach and close cooperation between doctors, nurses, orthoptists, occupational therapists and parents in order to optimize habilitation and secure a good development for each child.

Aims and hypotheses

General aims

The general aims of this thesis were to investigate the frequency of ophthalmological abnormalities in children with hydrocephalus, which was surgically treated during the first year of life, and to evaluate the need and timing of eye-care interventions in these children. In addition, the incidence and aetiology of hydrocephalus treated surgically during the first year of life as well as neurological and neuropsychological outcomes in these children, were investigated.

Specific aims

Paper I

To detect and quantify visual and visuoperceptual dysfunction in children treated surgically for hydrocephalus with/without myelomeningocele, and to relate the results to the associated diagnoses, neuroradiological findings and the results obtained from a comparison group.

Reflection: Many studies have reported on ophthalmological abnormalities among children with hydrocephalus. Most were conducted decades ago. The neonatal and paediatric care has improved remarkably during the last decade.

Our hypothesis was that the visual outcome will have improved, compared to earlier studies, due to improved neonatal/paediatric care.

Paper II

To investigate the morphology of the optic disc and retinal vessels in children with surgically treated hydrocephalus and to compare these findings with the results of a normal comparison group.

Reflection: Earlier studies have reported on optic atrophy and disc oedema in children with hydrocephalus, no other reports have to our knowledge described other changes in the ocular fundus. In preterm children ocular fundus abnormalities such as small optic discs and tortuous retinal arterioles have been described.

Our hypothesis: Hydrocephalus is of prenatal origin in many children, which may have influenced the neural and vascular tissue development. We therefore suspect that children with hydrocephalus may have abnormal ocular fundus appearance.

Paper III

To determine the incidence of children treated surgically for hydrocephalus with/ without myelomeningocele during the birth-year period 1999-2002 and to relate this to previous epidemiological studies from the same region. In addition, to discover whether modern neurosurgery has a lower morbidity and mortality than hitherto, and whether aetiology, treatment, complications and neuroradiological findings correlate with outcome. Finally, we sought to investigate the ophthalmological consequences of hydrocephalus and their relationship to aetiology and the structural patterns of brain pathology.

Our hypothesis was that modern neonatal care and surgical technique had reduced the mortality, morbidity and complications in children with hydrocephalus.

Paper IV

To investigate the onset of ophthalmological dysfunctions, and the need and timing of eye-care interventions in children with hydrocephalus.

Reflection: A large proportion of children with hydrocephalus have abnormal visual functions, but this is difficult to reveal in very young children. It is of outmost importance for the development of these infants to intervene both ophthalmologically and developmentally as early as possible.

Patients and Methods

Patients

The study area was a western part of Sweden with a population of 2.03 million inhabitants comprising 23% of the total Swedish population.

The identification of children with the diagnosis of hydrocephalus (ICD 9, ICD 10), was based on their referrals to and registration at the paediatric and/or neurosurgical units at the Queen Silvia Children's Hospital/Sahlgrenska University Hospital, Gothenburg, Sweden. All children born within this area and registered at these units fulfilling the criterion of hydrocephalus, with a need of surgical treatment, during their first year of life, were involved in the studies.

Papers I and II

All 103 children born between April 1989 and April 1993, in Sweden, in the counties of Västra Götaland, Halland and Värmland, with hydrocephalus which was surgically treated, at the Queen Silvia Children's Hospital, were invited to participate in the present study (Figure 7).
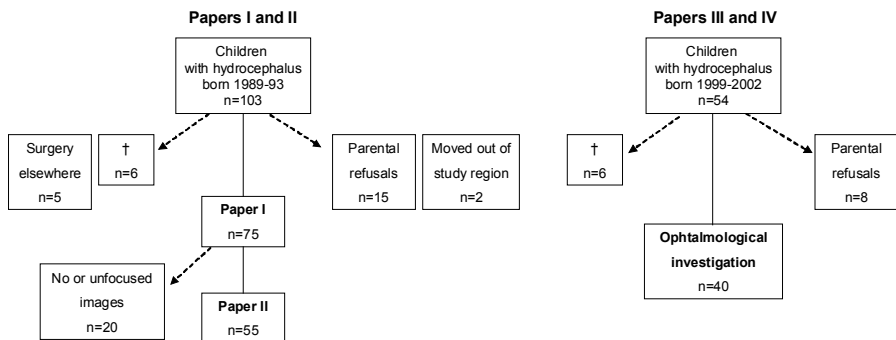

Figure 7. Children born in the counties of Västra Götaland, Halland and Värmland with hydrocephalus, surgically treated at the Queen Silvia Children's Hospital.

Six children died shortly after surgery. A further five underwent surgery elsewhere and were thus excluded from the study. Of the remaining 92 children, 15 declined and two had moved out of the region. Hence, 75 children (34 girls and 41 boys) with a median age of 9 years and 4 months (range 7 years and 4 months to 12 years and 10 months) were included. Of the 75 children 47 had hydrocephalus not associated with MMC while 28 children had MMC.

Nineteen of the 75 children were born preterm.

In paper II, only correctly focused photographs with the optic disc centered were accepted for analysis and 55 of the children (27 girls and 28 boys) fulfilled these criteria.

Papers III and IV

All 54 children with hydrocephalus which was surgically treated during the first year of life, at the Queen Silvia children's Hospital, born between 1999 and 2002, in the same region of Sweden as in papers I and II, were invited to participate in the present study. (Figure 7)

Six children died during follow up and were not included in the study. Of the remaining 48 surviving children, 8 declined ophthalmological examination. Twenty-seven of the children examined had infantile hydrocephalus not associated with a spinal lesion (Fernell et al. 1986) and thirteen had hydrocephalus associated with myelomeningocele (MMC). Fifteen children were born preterm, six of whom were born extremely preterm, before 28 weeks of gestation.

Median ophthalmological follow-up period was 7.4 years (3.3 – 10.1 years). Five children were only examined on 1-3 occasions. Two of these children had severe neurological impairments and declined further ophthalmological examination; three children moved out of the area/country and could therefore not be followed.

Children with hydrocephalus associated with malignant tumours were not included in these studies.

Comparison group
Paper I

One hundred and forty healthy children (76 boys and 64 girls), recruited from four different pre-schools and schools in the Göteborg area, aged 4–15 years, (mean 9.8 years) comprised the age and sex matched comparison group for ophthalmic assessment (Andersson Grönlund et al. 2006). The comparison group was tested by the same ophthalmological team and under the same conditions as the children with hydrocephalus. Two of the schools were from the suburban areas, one school from the down town area and the last school from a more rural area, in order to reflect the socioeconomic mix of the area. The living conditions in our population did not differ from those in other communities in Sweden. Nineteen of the 75 children were born preterm, six of whom were born before 32 weeks of gestation.

Paper II

99 healthy Swedish children and adolescents (56 boys and 43 girls) aged 3-19 (mean 10.1 years) constituted the comparison group for the ocular fundus photographic evaluation, by the digital analysing system (Hellström & Svensson 1998). No association could be found between the variables studied and age and sex, in this group of participants.

Methods

Papers I and II

Visual acuity

Visual acuity was tested with best possible refractive correction using the KM-letter chart, a letter matching chart with 7 different characters. Distance VA was tested monocularly and binocularly at 3 metres with a linear chart and binocularly with single symbols to investigate for crowding. Near VA was tested binocularly with a linear KM-Boks chart at 0.33 metres. The crowding ratio was determined by dividing the binocular single optotype VA by the binocular linear optotype VA. A crowding ratio of ≥2 was taken to indicate pathological crowding.

Reflections: Visual acuity testing may be a challenge in children and is often even more challenging in children with associated neurological and neuropsychological impairments. The methods used in this study are the ones used in every day practice at our department. The results are dependent on the child's ability to cooperate and to concentrate, which may vary in time. However the testing was done by skilled paediatric ophthalmologic personnel. Moutakis et al. 2004 found the KM chart more effective (twice as effective) than the HOTV chart to discover evidence of mild to moderate amblyopia. This study also confirmed the clinical impression that the VA obtained by the HOTV chart is somewhat higher than that obtained with the KM chart.

Orthoptic examination

An orthoptic examination was performed, including cover testing at near and distant fixation, stereoacuity testing with the TNO test (if the child was unable to identify the TNO figures the Titmus test was used) and evaluation of ocular motility and convergence, was performed. Heterotropia was defined as any kind of re-fixation movement of one eye when the other eye was covered while fixating targets at 3 and/ or 0.33 m distance. If the child was unable to cooperate with cover testing, a deviation of >10 degrees on Hirschberg light reflex testing was considered to constitute heterotropia.

Reflections: It may be difficult to examine whether a child has strabismus or not on a single occasion. However all the children were examined by the same orthoptist, who has considerable experience in paediatric ophthalmology. We found that, among children examined with both the cover test and the Hirschberg test, the last test underestimated the presence of heterotropia by approximately 30%. It is important to have this in mind especially when examining children who only can cooperate for Hirschberg testing (Aring et al. 2007).

Visual fields

The visual fields were tested using Goldmann perimetry. The V4e target was used to delineate the outer limits of the visual fields. Since visual-field testing in young children is difficult to evaluate, only larger defects like hemianopias or quadrantanopias were ascertainable.

Reflections: A majority of the different methods used for visual field testing are constructed for adults and therefore difficult to manage for small children or children with learning disabilities. In our everyday practise we often use Goldmann perimetry. Although it demands a skilled examiner it is easy to adjust to the child's ability ie the light may be moved really slowly so it can be noticed by the child and reflect the "true" visual field rather than requiring the ability of a quick response.

Refraction in cycloplegia

For cycloplegia, one drop of cyclopentolate (0.85%) and phenylephrine (1.5%) combined was employed 45 minutes before auto-refraction (Topcon RM). Significant refractive errors were defined as a spherical equivalent of myopia ≥0.5 dioptres (D), hyperopia ≥2.0 D, astigmatism ≥0.75 D and anisometropia of ≥1.0 D. (Negrel et al. 2004)

Reflections: There may be variability in results between different auto-refractors and also from retinoscopy. We used the same auto-refractor for all children who could cooperate for the measurement. The children who could not cooperate underwent retinoscopy, as did the children whose results varied significantly.

Anterior segment and ocular fundus

Slit lamp examination of the anterior segment was performed. The ocular fundus was examined by indirect ophthalmoscopy, and fundus photographs were taken. The presence of nystagmus was noted.

Reflections: Sometimes ocular fundus examination could be a challenge, with very little time to detect the presence of pathology. This is often the reality when examining children with learning disabilities. We noted that, in a few cases, a pale optic disc was diagnosed as optic atrophy, but later with repeated examinations or ocular fundus photograph, the optic disc had a large symmetrical excavation. In some cases we found it easier to diagnose nystagmus during slit lamp examination or by ophthalmoscopy than macroscopically.

Visual perception

Visuo-perceptual problems were identified by structured history-taking concerning five different functions namely: recognition (questions 1-4), orientation (questions 5-7), perception and movement through depth (question 8), perception of motion (questions 9-10), and simultaneous perception (questions 11-12). (Dutton et al. 1996, Houliston et al. 1999). The questions employed are provided in the Appendix.

Problems reported to occur frequently or always were considered as indications of visual perceptual problems.

Reflections: There was a huge difference in answers between the group of children with hydrocephalus and the comparison group (some of the children in the comparison group asked why I was asking such silly questions, because "of course they recognise family members" or "are able to find their way around"). Among the group of children with hydrocephalus the questions initiated a discussion and often gave an explanation for the parents' worries about their child's unusual behaviour. We found the structured history taking a good complement in revealing visual perceptual problems to the classical neuropsychological tests; the Griffith´s Developmental Scales, WISC-III and WPPSI-R tests.

Quantitative digital image analysis

The ocular fundus photographs were quantitatively analysed, using a specifically designed computer-assisted digital mapping system (Hellström et al. 1998).

The optic disc area was measured by marking the outlines with a cursor. The inner border surrounding the nerve tissue defined the optic disc; care was taken not to include the white peripapillary scleral ring. The cup was defined by contour, and its definition was facilitated by its pallor and the course of the vessels. The neuroretinal rim area was obtained by subtraction of the cup area from the disc area. The indices of tortuosity for arteries and veins were defined as the path length of the vessel divided by the linear distance from the vessel origin to a reference circle 3mm from the centre of the optic disc.
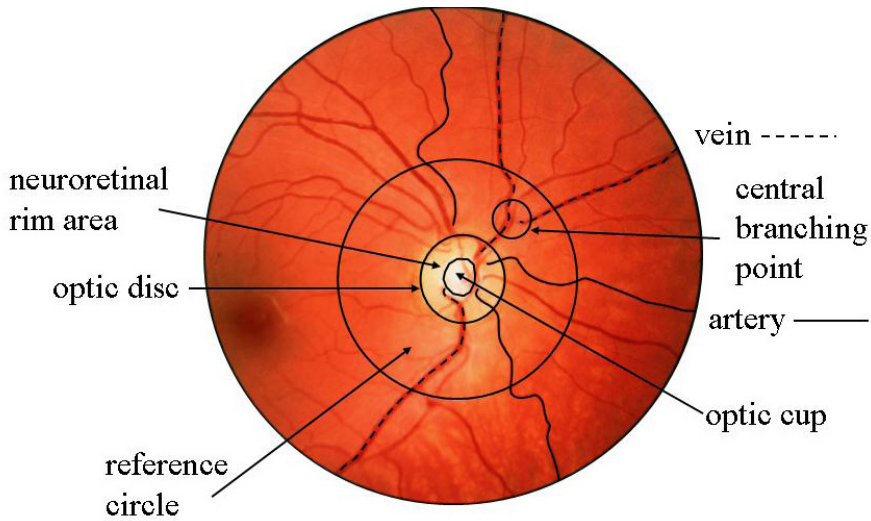
Figure 8. Digital mapping of ocular fundus photograph. (With courtesy of Andersson-Grönlund and Acta Ophthalmol Scand)

Vessels were also marked between their branching points and the reference circle, and the total number of branching points (arteries and veins), i.e. retinal vessels, within this area was calculated. (Figure 8) The same digital analysis method was used for both the hydrocephalic children and the comparison group, and all measurements were performed by the same person.

Reflection: A skilled person was required to do the measurements in order to minimize inter- and intra- measurement variability.

Paediatric and Psychological examinations

The neuropsychological assessment in paper I, was performed using the WISC-III (Wechsler Intelligence Scale for Children 1992) and the WPPSI-R (Wechsler Preschool and Primary Scale of Intelligence 1991), which are constructed for school and pre-school children. Griffith´s Developmental Scales (1980) was used for children with a developmental age below three years. Mental disability was defined as an FSIQ < 70. Fifteen or more IQ points of difference between verbal IQ (VIQ) and performance IQ (PIQ) was considered to signify an uneven cognitive profile. A paediatric neurologist examined 71 of the 75 children.

Papers III and IV

Information concerning aetiology, treatment, complications and outcome was gathered consecutively from clinical records from paediatric, neurosurgical, and

habilitation departments.

Due to the younger age of the children participating in this study, the ophthalmological methods were slightly different from those used in paper I (see below). For reflections see under methods paper I and II:

Visual acuity

The best corrected binocular (monocular if possible) visual acuities (VA) were tested with the KM test or HOTV or Kay's charts at a distance of three metres and, in the youngest children, with the Cardiff cards at a distance of one metre.

Reflections: See under visual acuity paper I and II.

It is difficult to compare visual acuity results obtained by the different visual acuity charts. Therefore we have sub-analyzed the results from those children who managed to cooperate on VA testing using a letter chart and those who did not. Kay´s picture has showed a good correlation between the VA results when using Kay´s picture and Snellen charts (Kay 1983).

Refraction in cycloplegia

In paper III refractive errors were defined as a spherical equivalent of myopia ≥ 0.5 dioptres (D), hyperopia ≥ 2.0 D, astigmatism ≥ 0.75 D and anisometropia of ≥ 1.0 D for children of four years of age and above (Negrel et al. 2004). For children less than four years of age, significant refractive errors were defined as a spherical equivalent of myopia ≥ 5.0 dioptres (D), hyperopia ≥ 4.5 D, astigmatism > 3.0 D and anisometropia of ≥ 1.5 D (Am Academy of Ophthalmol 1993).

Correction of refractive errors

Paper IV: There is no evidence based recommendation for correction of refraction at different ages. However the American Academy of Ophthalmology has given guidelines for "preferred practice patterns". We used these guidelines in order to decide when to prescribe glasses for the youngest children. See table 1.

Table 1. The American Academy of Ophthalmology guidelines for prescription of glasses to young children.

	Diopters		
	Age 0-1 year	Age 1-2 year	Age 2-3 year
Isometropia			
(similar refractive error in both eyes)			
Myopia	≥ -5.00	≥ -4.00	≥ -3.00
Hyperopia (no manifest devation)	≥ +6.00	≥ +5.00	≥ +4.50
Hyperopia with esotropia	≥ +3.00	≥ +2.50	≥ +2.00
Astigmatism	≥ 3.00	≥ 2.50	≥ 2.00
Anisometropia			
Myopia	≥ -2.50	≥ -2.50	≥ -2.00
Hyperopia	≥ +2.50	≥ +2.00	≥ +1.50
Astigmatism	≥ 2.50	≥ 2.00	≥ 2.00

Referral to the vision habilitation clinic

Children were referred to the vision habilitation clinic when there was a suspicion of visual impairment in the young children who were not able to cooperate on ophthalmological examination, if visual acuity was below 0.3 (LogMar0.5), if there was visual field defects and/or suspicion of the presence of visual perceptual problems.

Orthoptic examination

Strabismus was diagnosed using cover and uncover tests for near and, if possible, distance fixation. Strabismus was defined as heterotropia, manifested intermittently or constantly. Patching or atropine were used as applicable in children with amblyopia or the risk of developing amblyopia.

Reflections: See reflections under "Orthoptic examination" in Paper I and II

Anterior segment and ocular fundus

The anterior segments were examined with a slit lamp. Indirect ophthalmoscopy was performed after pupil dilatation for fundus evaluation.

Reflections: See reflections under "Anterior segment and ocular fundus "in Paper I and II

Neuroradiology

All the children underwent a neuroradiological examination before the first sur-

gical intervention and after the latest shuntrevision (until 2006). All examinations were evaluated by an experienced neuroradiologist. The findings were categorised as follows; 0: no parenchymal lesion, I: small/moderate periventricular leukomalacia, II: extensive white matter loss, III: focal white matter loss with grey matter lesion, and IV: generalised severe white and grey matter pathology.

Statistical methods

Paper I: For descriptive purposes, means, standard deviations (SD), medians and ranges were determined. For comparisons between two groups, the Mann-Whitney U-test was used for ordered and continuous variables. Fisher's exact test was used for dichotomous variables. All tests were two-tailed and conducted at the 5% significance level. Also Relative Risks with 95% confidence limits were calculated for descriptive purposes.

Paper II: The ocular fundus variables for each child were calculated from the mean of the two eye measurements. The median and 95% confidence interval (CI) for the median were calculated for optic disc, cup and rim areas and for tortuosity of arteries and veins as well as for number of vascular branching points. The Wilcoxon Mann-Whitney test was used to compare the medians of the group of hydrocephalic children with those of the reference group.

Paper III: For comparisons between two groups, the Mann-Whitney U-test was used for ordered and continuous variables. Fisher's exact test and the χ^2 test were used.
A p-value of < 0.05 was considered significant

Paper IV: Continuous variables were described with median and range, and categorical variables with number and percentages. For comparison between two groups Fisher's exact test was used for dichotomous variables and Mantel-Haenszel Chi Square test for ordered categorical variables.
All significance tests were two-tailed and conducted at the 0.05 significance level.

Results and discussion

Papers I & III

The aims were to investigate visual function in children surgically treated for hydrocephalus with/without myelomeningocele, and to relate the results to the associated diagnoses, neuroradiological findings and the results obtained from a comparison group. The aims of paper III were to investigate the live birth prevalence of hydrocephalus needing surgical treatment as well as aetiology, treatment and clinical outcome in affected children.

Our hypothesis was that modern neonatal care and surgical technique would have probably reduced the mortality, morbidity and complications, compared to earlier studies in children with hydrocephalus.

To evaluate a comprehensive examination of visual functions, which was performed, including: visual acuity testing, refraction in cycloplegia, orthoptic examination including ocular motility evaluation and cover test as well as stereo acuity testing, visual field testing with Goldmann perimetry, structured history-taking in order to detect the presence of visual perceptual problems and ocular fundus examination with indirect ophthalmoscopy and ocular fundus photographs. Information about aetiology, treatment, complications and neurological/neuropsychological outcome was gathered from clinical records.

We found in children with hydrocephalus born 1989-1993 that 83%, manifested ophthalmologic abnormalities. The results of the ophthalmologic examination did not differ between aetiological groups in children with other causes to hydrocephalus than MMC.
Table 2 shows the salient results from paper I concerning visual acuity, refraction, strabismus, stereopsis, and reported visuo-perceptual problems for the children with hydrocephalus (n=75).
Visual impairment was found in 15% (comparison group 0%) of all children with hydrocephalus but in none with myelomeningocele. Visual perceptual problems were reported in 59% (comparison group 3%). These disorders were more common in those children who had additional diagnoses such as cerebral palsy, epilepsy, and IQ<70, than in children without such diagnoses.
Cerebral palsy and epilepsy were diagnosed in 13 and 19 children respectively.
Children with cerebral palsy and epilepsy manifested higher frequencies of visuo-perceptual problems (p=0.04 and p=0.002 respectively), and children with

Table 2. Visual acuity, refraction, strabismus, stereopsis and visuo-perceptual problems in children with surgically treated hydrocephalus born 1989-1993 (n=75).

Aetiology Variables	Hydrocephalus without MMC n= 47	Hydrocephalus with MMC n=28	Comparison group n=140	Hydrocephalus with MMC vs without MMC	Hydrocephalus vs comparison group
Visual acuity Binoc.3m Md (range)	0.65 (fix-1.25)	0.9 (0.4-1.25)	1.0 (0.5-1.25)	VA<0.3 N/A VA>0.3 ns	VA<0.3 N/A VA 0.3-0.65 p<0.05
Refraction					
Hyperopia	23/43 (53%)	9/27 (33%)	12/140 (9%)	ns	p<0.001
Myopia	5/43 (12%)	2/27 (7%)	7/140 (5%)	ns	ns
Astigmatism	21/43 (49%)	14/27 (52%)	31/140 (22%)	ns	p<0.001
Strabismus					
Esotropia	14/46 (30%)	12/28 (43%)	4/140 (3%)	ns	p<0.001
Exotropia	17/46 (37%)	4/28 (14%)	1/140 (1%)	ns	p<0.001
Dyskinetic	3/46 (7%)	1/28 (4%)	0	ns	p<0.05
Stereopsis>60"	26/38 (68%)	19/28 (68%)	6/140 (4%)	ns	p<0.001
Visual perceptual problems	25/36 (69%)	13/28 (46%)	4/140 (3%)	ns	p<0.001
N/A=not available due to the lack of events, VA=visual acuity, fix=fixating a penlight					

two of these diagnoses had more visuo-perceptual problems than those with only one of them.

Sixty-two of the 75 children were also tested by the neuropsychologist. Among children with FSIQ less than 70 (n=23), a large proportion had low VA (29%), nystagmus (74%) and strabismus (95%) and for 82% visual perceptual problems were reported. Children with an uneven IQ profile (n=22) had as many visual perceptual problems and ocular findings as the children with IQ<70, although only 3 of these 22 children with an uneven profile had a FSIQ<70. The fifty-four percent (21/39) of the children with a full scale IQ above 70 were reported as having frequent visual perceptual difficulties.

We found in children with hydrocephalus born 1999-2002 that 80%, manifested ophthalmologic abnormalities. There were no significant differences in outcome amongst different hydrocephalus aetiologies (MMC, intraventricular haemmorhage, malformation, infection or idiopathic) to the hydrocephalus. Table 3 shows the visual acuity, refraction and strabismus findings. Visual acuity ≤0.3 was found in one third and refractive errors in almost two thirds of the children. Low visual acuity (binocular VA < 0.8) was significantly more common among children with optic atrophy, IQ<70, cerebral palsy, and epilepsy (p < 0.001, p = 0.01, p < 0.05, and p = 0.05 respectively). Strabismus was found in 19

Table 3. The results of visual acuity, refraction and strabismus in children with hydrocephalus born 1999-2002, at a median age of 4 years and 4 months.

Variables	
Visual acuity ≤0.3	13/39 (33%)
Refraction	
hyperopia	14/34 (41%)
astigmatism	13/34 (38%)
myopia	1/34 (3%)
total	21/34 (62%)
Strabismus	
esotropia	14/36 (39%)
exotropia	5/36 (14%)
total	19/36 (53%)

of 36 (53%) children, a majority of whom (14 of the 19 children) had esotropia. Optic atrophy was noted in eight of 37 (22%) children, all of whom had learning disabilities; six had epilepsy and seven had cerebral palsy.

The prevalence of hydrocephalus needing surgical treatment was 0.66 per 1,000 live births, in comparison with 0.82 per 1,000 during 1989-1998 (Fig 4). The incidence of post-haemorrhagic hydrocephalus in children born extremely preterm increased (Fig 5), while the group of children with MMC decreased compared to 1989-1998. Ventriculo-peritoneal shunt treatment was used in 42 of the 54 children, and endoscopic third ventriculostomy in 12. Revisions were performed in 33 (61%) children. The most common causes of revision were obstruction and/or disconnection (n = 45) followed by infection (n=20), of the shunt system. Neurological impairments (CP and/or EP and/or learning disabilities) were present in 63% and were more common in children born preterm than in those born at term. The radiological extent of parenchymal lesions correlated significantly with neurological outcome.

Paper II

The aim was to investigate the morphology of the optic disc and retinal vessels in children with surgically treated hydrocephalus and to compare with the results with those from of a comparison group.

Our hypothesis was that children with hydrocephalus would have an abnormal ocular fundus appearance, as hydrocephalus is frequently of prenatal origin and this may have influenced both neural and vascular tissue development.

To evaluate ocular fundus morphology, fundus photographs were quantitatively

analysed, using a specifically designed computer-assisted digital mapping system (Hellström et al. 1997, 1998).

The optic disc area was measured. The indices of tortuosity for arteries and veins were defined and vessels were also marked from their branching point to a reference circle in order to calculate the total number of branching points within this area. The same digital analysis method was used for both the hydrocephalic children and the comparison group, and all measurements were performed by the same person.

We found that the median optic disc and rim areas were significantly smaller in children with hydrocephalus than in the comparison group. Abnormalities of the central retinal vasculature were common in children with hydrocephalus. Less tortuous retinal arteries as well as reduced numbers of central branching points was found among the eyes of the children with hydrocephalus compared to controls. (Figure 9) There was no correlation found between aetiology of hydrocephalus, nor the presence of hydrocephalus at birth versus its development during the first year of life and the measured ocular fundus variables.
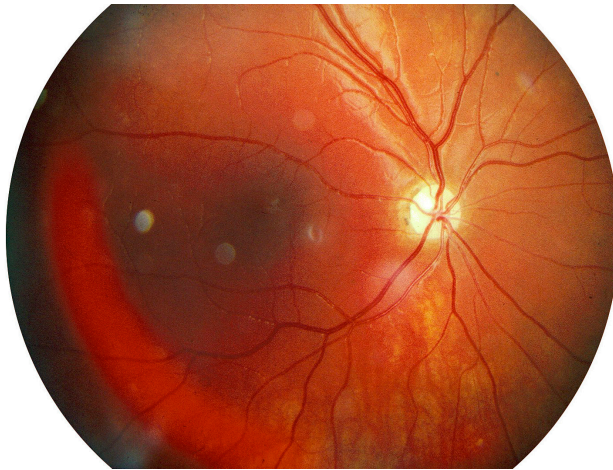

Figure 9. Fundus photography of a girl with hydrocephalus showing an example of a small optic disc area, a small neuroretinal rim area, a decreased tortuosity of retinal arteries and a decreased number of retinal vascular branching points.

Paper IV

This longitudinal follow-up study is based on observation from the same children as described in paper III (born 1999-2002). The 40 children, included in the study, underwent a total amount of 464 ophthalmologic examinations (excluding the visits for retinopathy of prematurity screening) at the paediatric ophthalmological unit. (Figure 10)
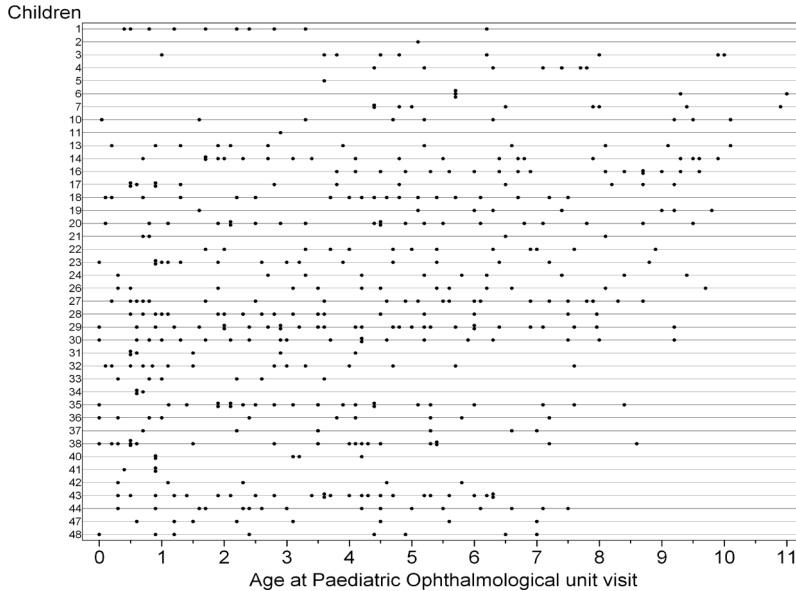

Figure 10. The ages, of the children with hydrocephalus, at each visit to the paediatric ophthalmological unit.

Our hypothesis was to investigate the onset of ophthalmological dysfunctions, the need and timing of eye-care interventions in children with surgically treated hydrocephalus during the first year of life.

To evaluate the need for structured follow-up of these children, a comprehensive examination of visual functions was performed longitudinally, including: visual acuity testing; refraction in cycloplegia; orthoptic examination (including ocular motility evaluation and cover testing and stereo acuity testing); structured history-taking (in order to detect evidence of visual perceptual problems) and ocular fundus examination with indirect ophthalmoscopy. The median ophthalmological follow-up period was 7.4 years (3.3 – 10.1 years).

We found that 28 of 38 (74%) children with hydrocephalus required at least one intervention from the ophthalmology team. (Figure 11.)
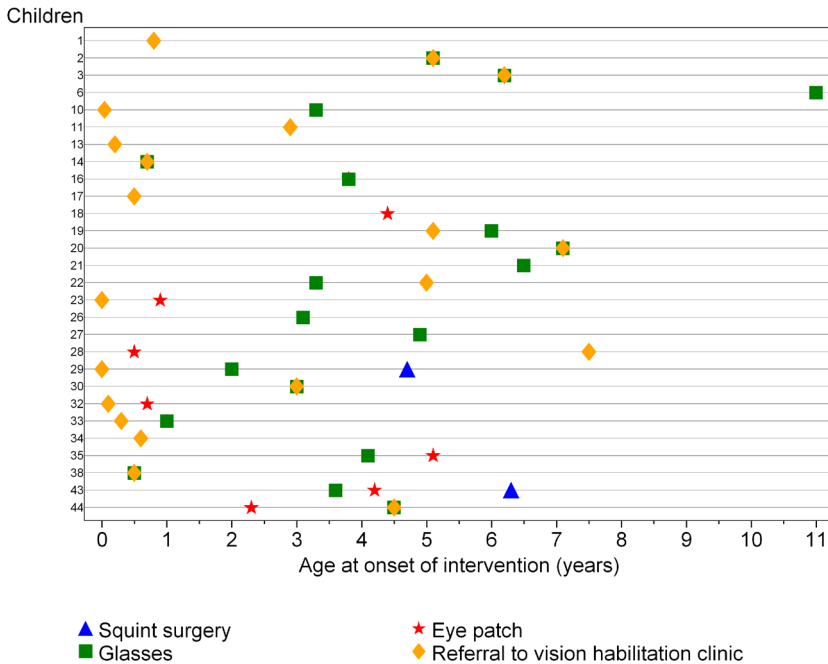
Figure 11. The onset of ophthalmological intevention with prescription of glasses, patching and referral to the visual habilitation clinic in each child.

Seventeen of thirty-five children were prescribed glasses during the study period. Another two children received glasses for reading only, to ameliorate afternoon headache and reading difficulties. Of the 19 children, VA improvement was detected in 15 children. The age range at which glasses were prescribed was spread out during the study period. Thirteen of 19 (68%) children were prescribed glasses before the age of five years, and all but one before the age of eight.

All together, eight children underwent patching; 2 children had exotropia (XT) and 6 had esotropia (ET). Of the children with ET, two also had anisometropia and optic atrophy. The result after treatment was an almost equal (one line or less difference between the eyes) VA in both eyes in five children, while three children could not cooperate for monocular VA testing (VA=0.15 in one child and fixation in two children).

The age at which treatment with patching or atropine was initiated was less than 1 year for 3 children, 1-4 years for 2 children and 4-6 years for 3 children.

During the study period 20/40 (50%) children were referred to a visual habilitation clinic. Median age at referral was 0.8 years, ranging from just a few weeks of age to 7.5 years. A majority of the (12/20, 60%) children were referred before three years of age. Three of the children with normal visual acuities were referred at ages 3.3, 6.2 and 8.4 years respectively due to visual perceptual problems.

Neuropsychological evaluation was done by either the visual habilitation clinic or the neurological habilitation clinic.

The results of visual acuity, refractive errors and strabismus, at the last visit, are shown in table 4. The median age at last visit was 8.7 (3.6-11.3) years. Figure 12 shows the different visual acuity charts that children with hydrocephalus managed at different ages. All children of the healthy comparison group could cooperate on VA testing with the KM chart at four years of age (Andersson-Grönlund et al. 2006).

Table 4. The results of visual acuity, refraction and strabismus in children with hydrocephalus born 1999-2002 at their last visit (Md age 8.7 years) at the Ophthalmological unit.

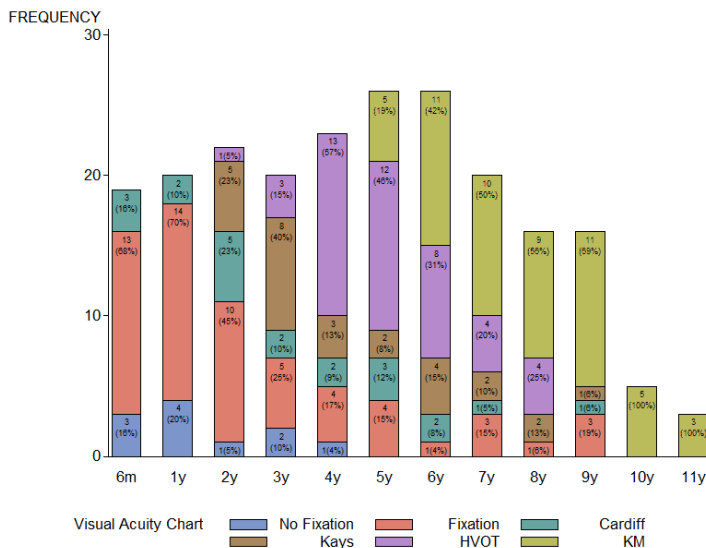| Variables	
Visual acuity ≤0.3	10/35 (29%)
Refraction	
hyperopia	15/35 (43%)
astigmatism	18/35 (51%)
myopia	1/35 (3%)
total	21/35 (60%)
Strabismus	
esotropia	12/38 (32%)
exotropia	8/38 (21%)
total	20/38 (53%)

Figure 12. Distribution of Used Visual Acuity Chart in Relation To Age

Discussion of papers I-IV

Vision plays a central role in early human development (Thevarthen & Aitken 2001). It is therefore crucial to detect signs of all types of visual dysfunction in children, not only impaired visual acuity, strabismus and refractive errors, but also the child's ability to interpret the visual input.

In a study by Jacobson, children with periventricular leukomalacia, showed abnormal visual function including evidence of delayed visual acuity development (Jacobson et al. 2002). This pattern is similar to the one noted in children with hydrocephalus (paper IV). The delayed visual acuity development accords with the delayed development of motor and psychological skills noted in children with hydrocephalus. Persson presented data on learning disabilities and delay in fine- and gross- motor skills ie the start of walking (Persson et al. 2006). We believe that there is a high probability of actual delayed visual acuity development in these children, which is probably an expression of their cerebral visual impairment.

The frequency of visually impaired children amongst those described in paper I, at 15%, is lower than reported by earlier studies (Rabinowitz 1974), but well in accordance with other studies conducted during the same time period as the study (Heisenberg 2002). The lower frequency of visual impairment in these studies may relate to early diagnosis and improved neonatal care of children with hydrocephalus. However, by the later period of papers III & IV, the frequency of visual impairment in children with surgically treated hydrocephalus had increased again. This may be explained by the changing aetiology of hydrocephalus. The number of children with MMC, which is associated with a comparatively favourable prognosis, is decreasing while the survival of preterm children, who often have a history of haemorrhagic-ischaemic brain lesions with a less favourable prognosis, is increasing. The same pattern is also found for other neurological impairments such as epilepsy and cerebral palsy. This correlation between children with hydrocephalus, born very or extremely preterm and a poor neurological outcome was also found by Heinsbergen (Heinsbergen et al. 2002). Casey reported children with hydrocephalus caused by infections or intraventricular haemorrhage to have high frequencies of cognitive dysfunctions being twice as likely to require special schooling as children with other aetiologies to hydrocephalus (Casey et al. 1997). This is well in accordance with our findings where a majority (13/17) of children with infantile hydrocephalus born preterm had learning disabilities.

Refractive errors were common in the two study groups (paper I 67%, and paper III 62%, paper IV 60%). Hyperopia was the most common refractive error which is in accordance with the findings by Mankinen-Heikkinen 1987. Hyperopia is more common in children with brain pathology (Saunders 2002). The cause remains obscure. Impaired emmetropisation related to abnormal visual input and processing may be a contributory factor (Woodhouse 2010). Atkinson and co-workers found that correction of hyperopia may impede the ability for the child to emmetropize (Atkinson et al. 1988). However, in a more recent study by Atkinson and co-workers 2007 showed that spectacle wear by infants, having large degree of hyperopia, produced a better visual outcome (Atkinson et al. 2007).

There are, to our knowledge, no evidence based guidelines for when it is appropriate to prescribe glasses in different ages. Therefore we used the Academy of Ophthalmology guidelines (AAO Preffered practice patterns 2007) for children under the age of four. Nineteen of thirty-five children, in paper IV, were prescribed glasses during the study period, two for reading only. Of the 19 children, VA improvement could be detected in 15.

In accordance with previous studies we found a high frequency of strabismus (paper I 69% and paper III 53%) (Rabinowicz 1976, Mankinen-Heikkinen et al. 1987, Biglan 1990, Gaston 1991) predominantly esotropia. The lower prevalence found in paper III is probably partly due to methodological difficulties: The older children in paper I, were able to co-operate on cover test examination as well as the Hirschberg test, while a larger portion of the younger children in paper III, only co-operated in Hirschberg testing. Aring et al. (2007) found that the frequency of strabismus, in children with hydrocephalus, in the study group of paper I, was underestimated by about one third, when the Hirschberg test was used alone, in comparison to the cover test. Studies have pointed out the benefit of patching or atropine treatment in order to reduce amblyopia in children with strabismus (Holmes et al. 2006). Although 53% of the children in paper IV had a squint only 8 children underwent an intervention with patching. This was due to different reasons as some children having an alternating or intermittent squint, not benefiting from patching, others having a co-existing nystagmus which increased in frequency with patching or severe optic atrophy and some children having too severe neurological conditions to be able to follow a patching treatment regime. Amblyopia may also be superimposed on an organic disease such as optic atrophy. Good results from amblyopia treatment also has been shown in children with unilateral structural anomalies, with best outcomes in children with partial media opacities and not as good outcomes in those with

optic nerve anomalies (Bradford et al. 1992). However one has to be especially careful with amblyopia treatment in such cases with timely interruption of treatment for a poor treatment response, to prevent reverse amblyopia in the other eye, and the adverse developmental consequences of impaired vision in both eyes during the period of patching, which should therefore not be prolonged. It is to be remembered that vision is crucial for the general development of the child (Thevarthen & Aitken 2001).

Independently of aetiology, children with hydrocephalus were found to have abnormal optic nerve head morphologies illustrated by smaller optic disc and rim areas, as well as an abnormal retinal vascular patterns with less tortuous arteries and a reduced number of central vascular branching points when compared with controls. Hellström et al. (2000) found a small optic rim area in children born before 29 gestational weeks. This is well in accordance with our findings that children with hydrocephalus born preterm had smaller rim areas compared to those born at term. The mechanisms that result in the varying optic disc morphology, thought to reflect a reduction in the number of axons or reduced size of axons, have been suggested to be caused by, for example secondary degeneration of ganglion cells and their fibres (either directly or through retrograde transsynaptic degeneration), defective trophic mechanisms or deficient myelination (Hoyt & Good 1992, Taylor 1992 , Philips 1992, Brodsky& Glasier 1993). Experimental and clinical studies have indicated that the size of the optic disc, especially in small discs, is related to the number of axons. One could speculate that the reduced optic disc and rim areas in children with hydrocephalus are therefore of prenatal origin. The straighter arteries and fewer branching points may reflect the reduced nutritional demands of fewer neural elements.

Learning disabilities are common in children with hydrocephalus. Lindquist and co-workers found 33% of a population of children with hydrocephalus having normal IQ (›85), 30 % having IQs of 70-84 and 37% had learning disabilities and an IQ of less than 70 (Lindquist et al. 2005). Children with hydrocephalus often have a characteristic test profile with higher scores in verbal intelligence compared to non-verbal (Dennis 1981, Lindquist et al. 2005). Earlier studies have shown that early onset of hydrocephalus and measurable reduction of white matter structures, have a positive correlation with impaired non-verbal functions. It appears that like hydrocephalus, independent of its aetiology, is associated with greater impairment of non-verbal cognitive skills than verbal skills (Dennis et al. 1981). We found a structured history taking strategy to be useful in detecting visuo-perceptual problems at the ophthalmological unit. In paper I, visuo-

perceptual problems were reported in 59% of the children with hydrocephalus, resembling the results of Houliston (Houliston et al. 1999). The visual difficulties described, in paper I, include those relating to dorsal stream dysfunction (crowding, impaired visual guidance of movement) and to ventral stream dysfunction (problems with orientation and recognition). In the most recent study (paper IV) we became aware of the difficulties in detecting these problems in the younger children, primarily because the question inventory seeks disturbance of visual behaviours yet to be acquired. Also the parents were often unaware of the visuo-perceptual difficulties. As a large proportion of children with hydrocephalus have neurological deficits affecting several parts of the brain, it might be difficult to detect the visuo-perceptual difficulties specifically. As the children grew older the difficulties became more apparent. Even when the difficulties were more obvious they were not always understood, but interpreted as clumsiness or behavioural problems. We found a huge relief among children, parents and caretakers when being able to explain their visual perceptual difficulties. During the study period 12/35 (34%) children were referred to a visual habilitation clinic because or partly because of having visual perceptual problems (paperIV). We found that normal VA and even normal stereopsis do not preclude severe visual perceptual problems which affected 13 of the children with normal VA (≥0.8) (paper I). Additional diagnoses such as cerebral palsy and epilepsy conferred higher frequencies of visuo-perceptual problems, as did low VA, nystagmus and strabismus. In order to be able to interpret visual input, the visual acuity must not be too low, therefore we excluded the results of structured history-taking in children with visual acuities of 0.1 or less (LogMar≥1.0).

In total 28 of 38(74%) children with hydrocephalus described in paper IV underwent at least one intervention from the ophthalmologic team, such as correction of refractive errors with glasses and/or patching and/or squint surgery and/or referral to the visual habilitation clinic. Half of the interventions were initiated before two years of age, while some were initiated during pre-school years or after school start. No relationships were identified with respect to whether children required ophthalmic intervention or not, and the aetiology of the hydrocephalus or the frequency of epilepsy, cerebral palsy or learning disabilities. However the greater the severity of abnormal brain findings on neuroimaging the greater the probability of ophthalmic intervention being required (p=0.006).
The radiological extent of parenchymal lesions was also correlated significantly with neurological outcome (paper III). Almost all (11 of 12) children with generalised parenchymal lesions on neuroimaging had some associated impairments, while none of the children with normal imaging had any associated neurological

impairment. There was also a tendency towards a correlation between the severity of visual impairment and both the neuroimaging findings and decreasing gestational age, although this was not statistically significant, possibly due to the limited number of children in this study.

Neurological impairments are common in children with hydrocephalus. The frequencies of cerebral palsy (31%) and epilepsy (30%) described in paper III resembles the results of earlier studies (Fernell et al. 1987, Fernell et al. 1988). Neurological impairments such as FSIQ<70, cerebral palsy, and epilepsy were found to be more common among children with hydrocephalus, due to causes other than MMC, and in children born preterm, than in children with MMC or born at term. FSIQ<70, for example, was more than twice as common in children born preterm, than in those born at term, and, in the total group of children with hydrocephalus not associated with MMC, more than two-thirds had some impairment, compared with 50% of the children with MMC; a finding also in accordance with Heinsbergen et al. (2002).

There was a need for shunt revision in 60% of the children (paperIII). The most common causes were obstruction of the shunt and infections. Although Lumenta and Riva did not find any correlation between the number of shunt revisions and outcome (Lumenta et al. 1995, Riva et al. 1994), it was found in our study that there was a trend towards neurological impairments being more common after two or more revisions (paper III). Our result was not statistically significant, maybe due to a small number of children, but it was well in accordance with earlier studies by Persson (Persson et al. 2005). We found no correlation between the number of shunt revisions and the results of visual acuity (paper I).

Conclusions and responses to given aims

I. In total 83% of the children with surgically treated hydrocephalus manifested ophthalmologic abnormalities such as visual impairment (15%), refractive errors (67%), strabismus (69%), visual field defects (17%), optic atrophy (14%) and visual perceptual problems (59%). There was no significant correlation between the size of the lateral ventricles after surgery, on neuroimaging, and visual acuity. Visual disorders were most frequently found in children with associated diagnoses such as epilepsy, cerebral palsy and or learning disabilities. Children with hydrocephalus associated with myelomeningocele were least commonly affected. **II.** Our results showed a relatively low frequency of optic atrophy compared to earlier studies, which may reflect the improved medical care now given to

children with hydrocephalus. We found a small optic disc and optic rim area, and also an abnormal vascular pattern, with a decreased tortuosity of the retinal arteries and fewer vascular branching points. These abnormal findings indicate a pre/perinatal influence on development of neural and vascular tissues in children with hydrocephalus.

III. The decreasing incidence of hydrocephalus found in earlier studies (Persson et al. 2005) continued in 1999-2002, but no further decrease was noted during this period, mainly because of an increase in the survival of children with post-haemorrhagic hydrocephalus born extremely preterm. Neurological impairments were present in almost two-thirds of the children and were most frequent in those born preterm. Neuroimaging was useful for aetiological, prognostic and treatment considerations. A majority (80%) of the children had ophthalmological abnormalities such as visual impairment (39%), refractive errors (62%), strabismus (53%) and optic atrophy (22%). This study showed on one hand a decrease of the incidence of hydrocephalus but on the other hand a tendency of more severely affected children, probably due to the increasing number of children born very/extremely preterm.

IV. A majority of children with hydrocephalus need some ophthalmological intervention, making ophthalmological surveillance warranted. Using the current knowledge of the visual functions in children with hydrocephalus we present an "ophthalmological safety net" for these children. We suggest an ophthalmological examination soon after shunt surgery and every 4-6 months during the first two years of life, followed by at least a yearly examination to six years of age, in order to optimize the visual and ameliorate general development.

Future perspectives

The high rates of neurological impairments (ophthalmological, neurological and neuropsychological), in children with surgically treated hydrocephalus, require multidisciplinary care to ensure optimal treatment and habilitation, in order to optimize these children's quality of life. Further developments to optimize appropriate prevention and treatment strategies for hydrocephalus is crucial (Persson et al. 2005, Lidquist et al. 2008).

Sammanfattning på svenska

Introduktion:
I hjärnan finns hålrum (ventriklar) som innehåller en speciell vätska, cerebrospinalvätskan. Vätskans främsta uppgift är att transportera näringsämnen, forsla bort avfallsprodukter samt att vara ett skydd för hjärnan och ryggmärgen. Cerebrospinalvätskan cirkulerar genom de olika hålrummen och absorberas till sist av blodet. Störningar i denna cirkulation leder till ansamling av vätska, vilket kan ge ett förhöjt tryck med vidgade ventriklar som följd (utveckling av hydrocefalus = vattenskalle). Hydrocefalus drabbar ca 0.66 av 1000 levande födda barn i Sverige. Förekomsten varierar dock mellan olika länder/världsdelar.
De vanligaste orsakerna till hydrocefalus är blödningar in i hjärnans ventrikelsystem (vanligast hos de för tidigt födda barnen), missbildningar, infektioner, tumörer, genetiska faktorer och trauma. Behandlingen innebär oftast att vätskan leds förbi hindret som orsakat stoppet. Detta sker vanligtvis med en slang som löper mellan hjärnans hålrum och bukhålan eller med ett hål från en ventrikel till hjärnans utsida.

Syfte med studierna var att kartlägga synfunktion, ögonrörelser och ögonbottenutseende hos barn som opererats för hydrocefalus under första levnadsåret, notera tidpunkten för upptäckt av eventuella avvikelser samt att relatera dessa till andra funktionshinder och neuroradiologiska fynd. Vi ville även ta reda på vilka interventioner barnen är i behov av från ögonsjukvården och när. Dessutom ville vi analysera trender i förekomsten av hydrocefalus över tid där vi studerade barn födda under två tidsperioder, 1989-1993 och 1999-2002.

Metodik: Alla barn som var med i studierna fick genomgå noggranna undersökningar av: synskärpa, ögonrörlighet, skelning, synfält och brytningsfel samt frågor angående tolkning av synintryck. Dessutom kontrollerades ögonbottenutseendet och ögonbottenfotografier togs.

Resultat: Vi fann att totalt ca 80% av barnen med hydrocefalus hade någon form av påverkan på öga och/eller synfunktion såsom synskada (barn födda 1989-93 15%, barn födda 1999-02 29%), brytningsfel (barn födda 1999-02 62%, barn födda 1989-93 67%), skelning (barn födda 1999-02 53%, barn födda 1989-93 69%), synfältsdefekter (barn födda 1989-93 17%), svårigheter med tolkning av synintryck (barn födda 1989-93 59%), atrofi av synnerven (barn födda 1989-93 14%, barn födda 1999-02 22%).

I en jämförelse med en grupp friska barn, fann vi att barn med hydrocefalus i större utsträckning har mindre synnervshuvud, rakare artärer i ögonbotten samt färre förgreningar av artärerna.

Ca 70% av barnen (i studie IV) var i behov av intervention via barnögonsjukvården, såsom förskrivning av glasögon, lappbehandling mot amblyopi, skeloperation eller remiss till syncentralen. Hälften av interventionerna initierades under barnens två första levnadsår.

De barn som var födda i fullgången tid och vars orsak till hydrocefalus var ryggmärgsbråck hade minst påverkan på synen medan barnen som var för tidigt födda med blödning in i ventriklarna som orsak till hydrocefalus var de som var mest drabbade. Hög förekomst av synpåverkan kunde även ses hos de barn som hade andra funktionshinder såsom epilepsi, cerebral pares och mental retardation. Andelen barn med funktionshinder ökade vid kortare graviditetslängd.

Antalet barn som behövde opereras för hydrocefalus under sitt första levnadsår minskade mellan perioderna 1989-99 och 1999-2002, men ingen kvarvarande minskning kunde noteras i slutet av perioden då antalet mycket för tidigt födda barn ökade inom gruppen.

Inget barn med normal neuroradiologisk bild hade neurologiska funktionshinder, inte heller synskada.

Slutsats:

En majoritet av barnen med hydrocefalus har påverkan på ögon och syn samt är i behov av interventioner från barnögonsjukvården för att ges möjlighet att använda synen på bästa sätt, vilket är av betydelse för deras utveckling generellt.

Mot bakgrund av nuvarande kunskap föreslår vi en ögonundersökning strax efter shuntkirurgi och var 4-6 månad de två första levnadsåren, därefter minst årligen fram till sex års ålder.

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Appendix 1

1. Do you experience difficulties recognising people?

2. Do you experience difficulties recognising people in photos?

3. Do you experience difficulties recognising shapes?

4. Do you experience difficulties recognising colours?

5. Do you have trouble finding your way around at home?

6. Do you have trouble finding your way around at school?

7. Do you have trouble finding your way around in new surroundings?

8. Do you have problems distinguishing a line from a step?

9. Do you have problems seeing a moving object?

10. Do you have problems seeing/finding an object while moving?

11. Do you have problems finding an object on a patterned carpet?

12. Do you have problems finding objects in complex pictures?

Appendix 2

Relationship between the logarithmic minimal angle of resolution (logMAR) and the decimal notation.

LogMAR	Decimal notation of MAR
1.0	0.1
0.9	0.13
0.8	0.16
0.7	0.2
0.6	0.25
0.5	0.32
0.4	0.4
0.3	0.5
0.2	0.63
0.1	0.8
0.0	1.0
-0.1	1.25
-0.2	1.58
-0.3	2.0