Cerebral synskada (Cerebral Visual Impairment) – är inte enbart cerebral, utan även retinal

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Sektionen för ögon & syn
Karolinska Institutet
Stockholm

Olika typer av diagnoser

- Etiologisk diagnos

  ex genetisk, infektion

- Morfologisk diagnos

  ex schizencefali, periventrikulär vit substansskada, optikusgliom

- Funktionell eller symptombaserad diagnos

  ex cerebral pares, cerebral visual impairment, ADHD, skelning

Funktionell diagnos

Definition av **cerebral pares**

CP is a group of disorders

- it is permanent but not unchanging;
- it involves a disorder of movement and/or posture and of motor function;
- it is due to a non-progressive interference/lesion/abnormality;
- this interference/lesion/abnormality is in the developing brain

Surveillance of Cerebral Palsy in Europé (SCPE) 2000
ICD G80-83

Funktionell diagnos

Förslag på kriterier för att uppfylla diagnosen **cerebral visual impairment** (CVI):
Synstörning till följd av en primär avvikelse eller skada i det retrogenikulära synsystemet som karaktäriseras av

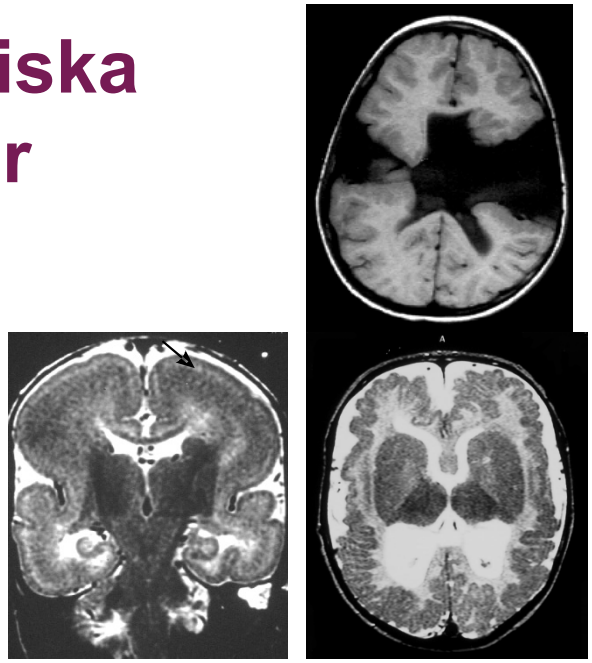
- **subnormal synskärpa** för åldern, mätt med randmönster eller symboler med bästa korrektion och/eller **synfältspåverkan**

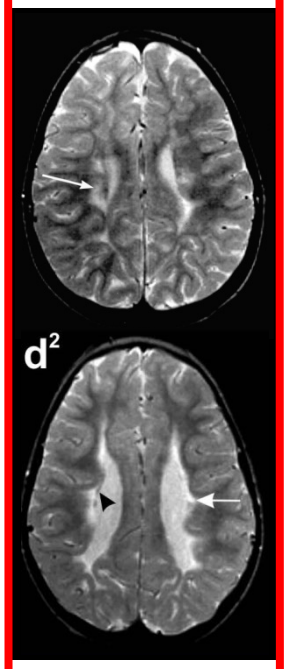
- **visuell perceptuell-kognitiv störning** skattad med neuropsykologisk test och/eller en strukturerad anamnes

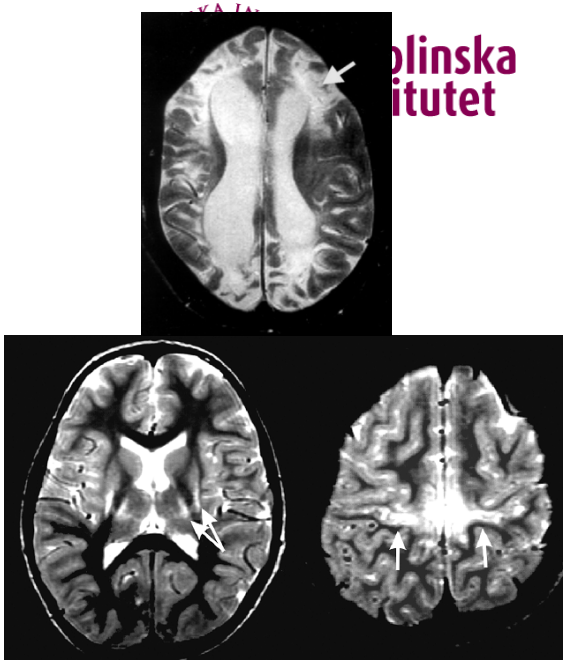
CVI kan kompliceras av ögonmotoriska problem såsom fixationssvårigheter, skelning, nystagmus och svårigheter att utföra visuellt styrda ögonrörelser

Morfologiska diagnoser

bilateral

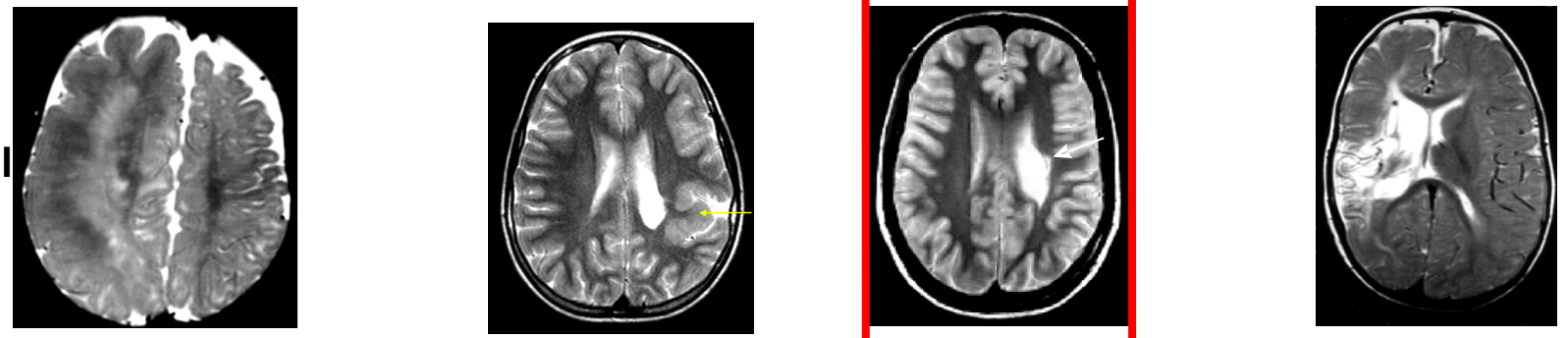






Conception **6 we** **20 we** **30 we** **40 we birth**

unilateral



Krägeloh-Mann I. Experimental Neurology, 190 (2004) S84-90

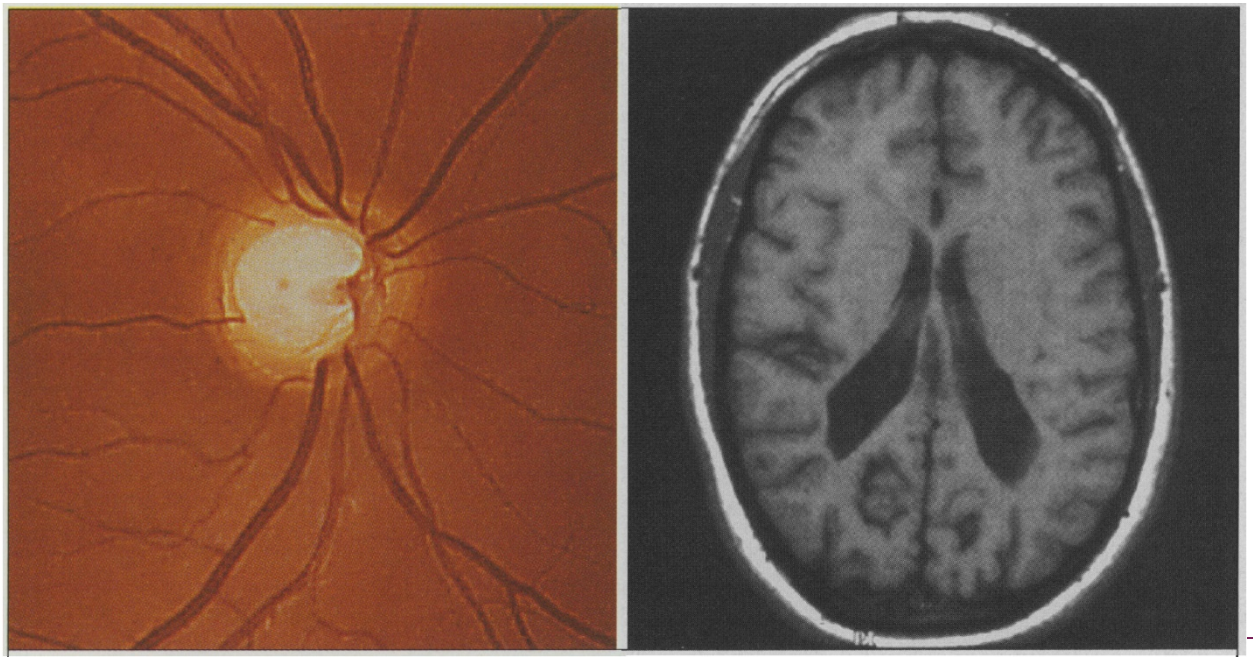
CLINICAL SCIENCES

Large Cups in Normal-Sized Optic Discs

A Variant of Optic Nerve Hypoplasia in Children With Periventricular Leukomalacia

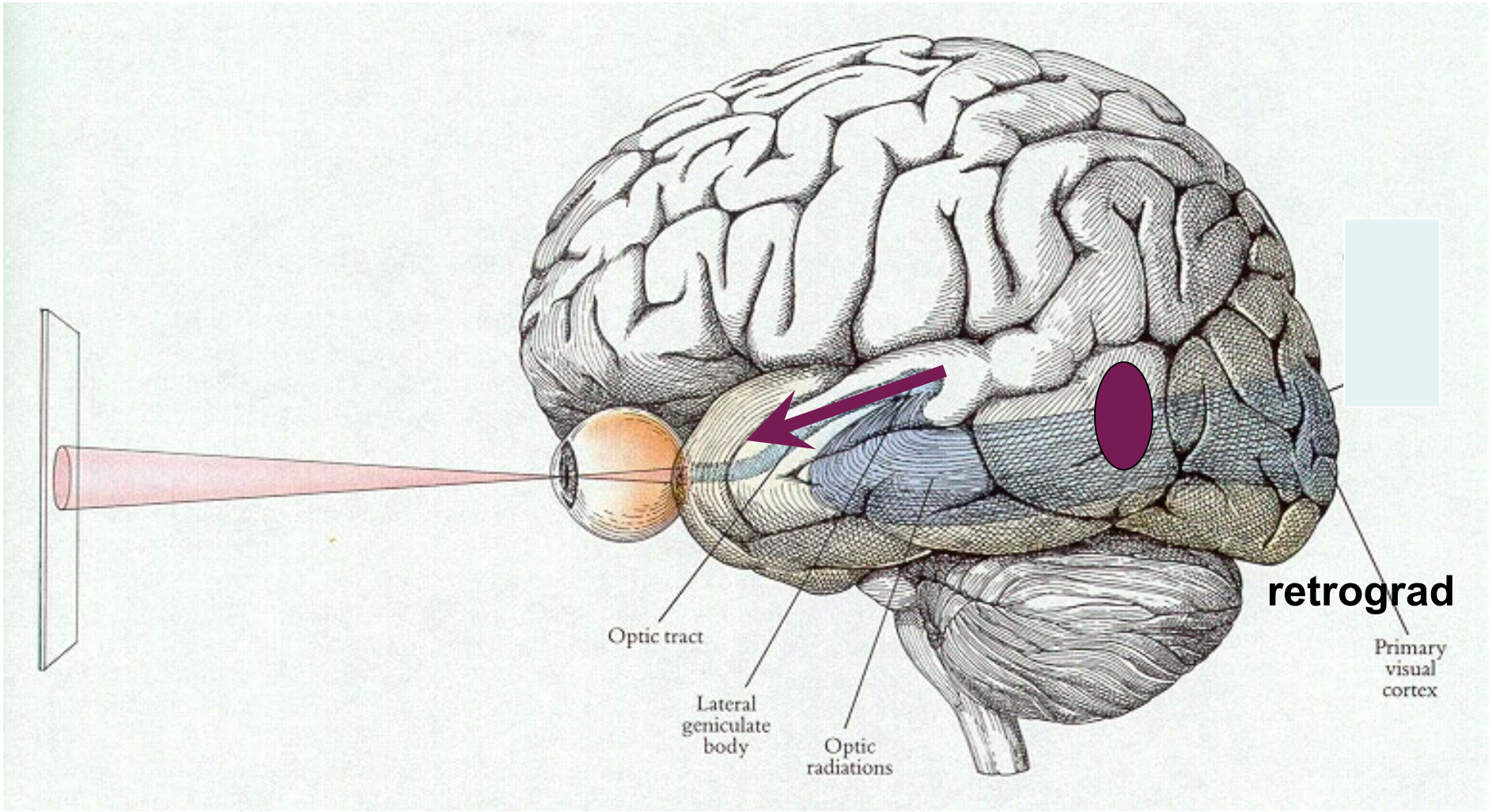
Lena Jacobson, MD; Ann Hellström, MD; Olof Flodmark, MD, PhD

ARCH OPHTHALMOL/VOL 115, OCT 1997

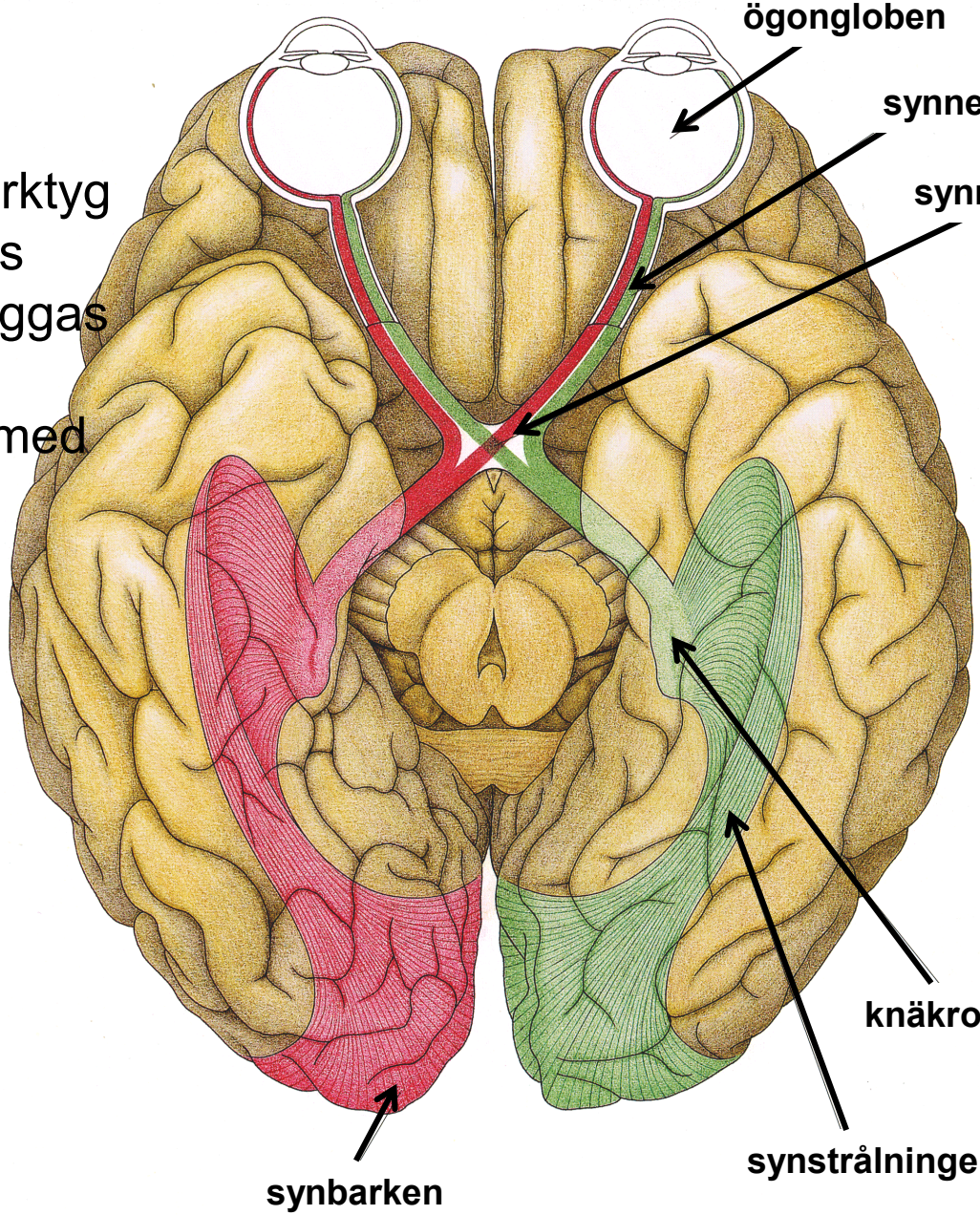


Fledelius, Acta Ophthalmol 1990, Brodsky, Arch Ophthalmol 2001

Transsynaptic degeneration över knäkroppen

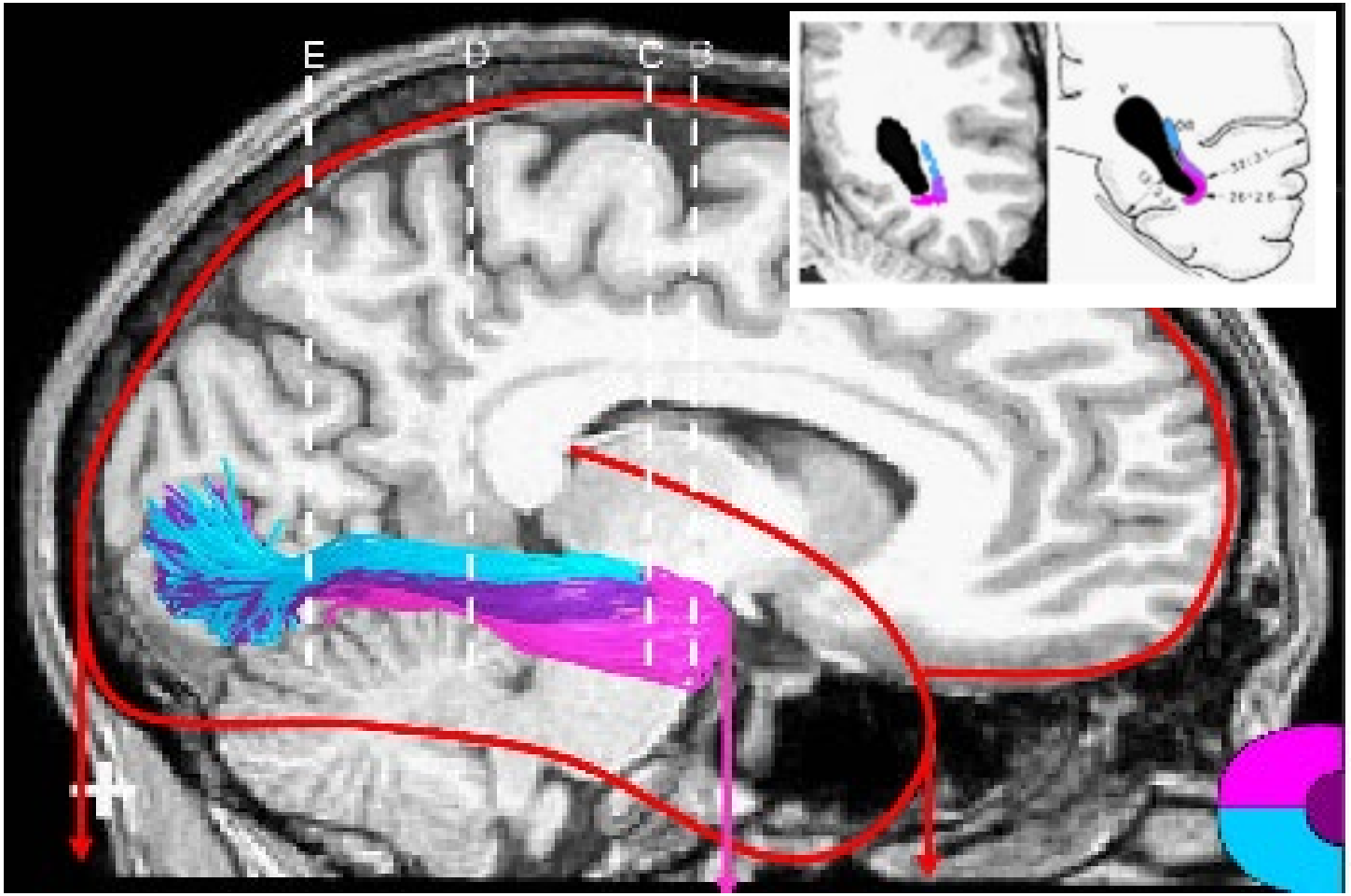


Med nya diagnostiska verktyg kan synorganets morfologi kartläggas ännu bättre – vi närmar oss att med imaging kunna avbilda även funktion



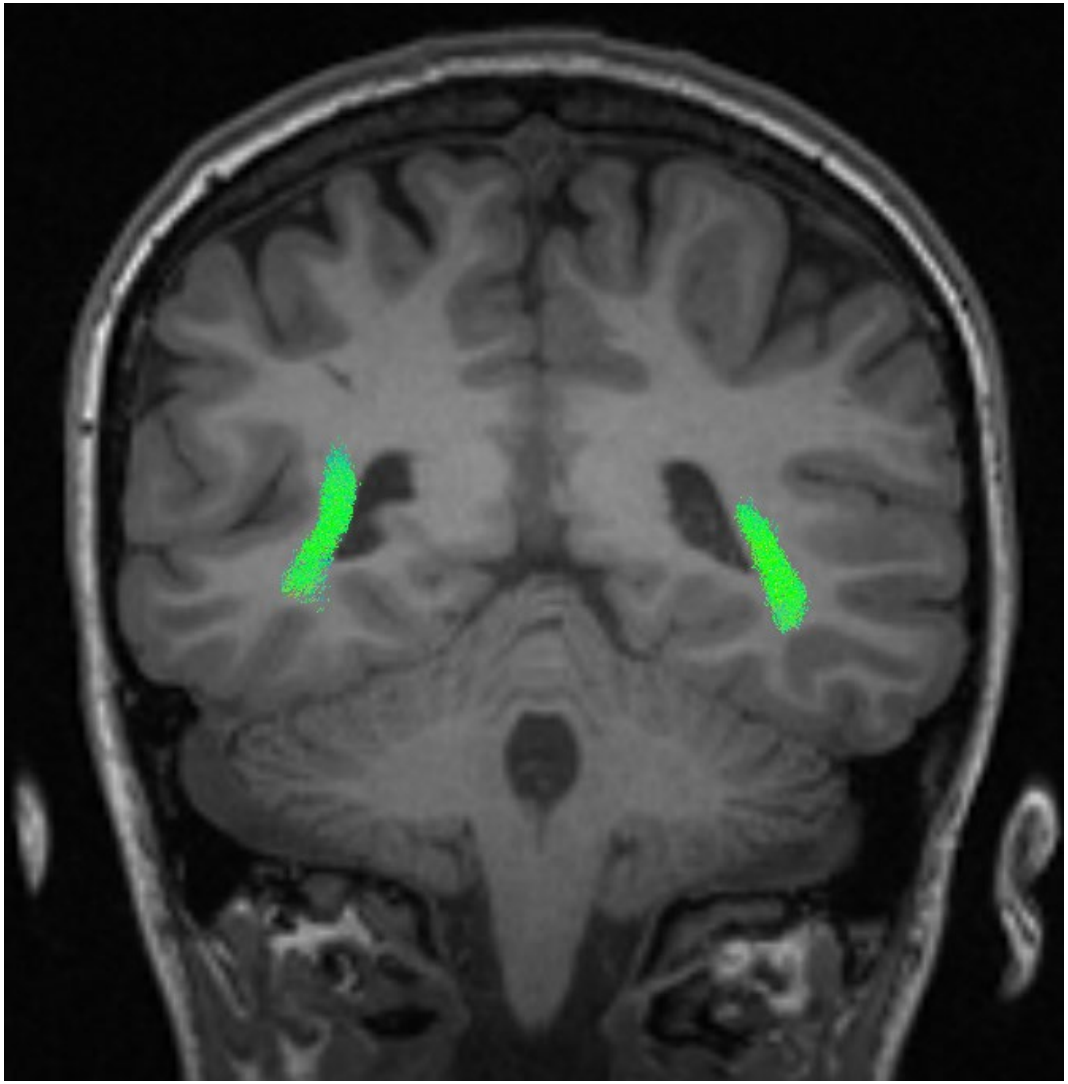
Diffusion-weighted MRI (DWI), fibre tractography of the OR

Topographical representation of the VF in the visual pathways



Sherbondy et al, J Vision 2008

Fibertraktografi av synstrålningen



Available online at www.sciencedirect.com

ScienceDirect

Journal homepage: www.elsevier.com/locate/cortex

Special issue: Research report

Changes in brain morphology in albinism reflect reduced visual acuity

Holly Bridge [a,b,*], Elisabeth A.H. von dem Hagen [c], George Davies [a], Claire Chambers [a], Andre Gouws [d], Michael H
Antony B. Morland [d,f]

OPEN ACCESS Freely available online

PLoS one

Altered Anatomical Network in Early Blindness Revealed by Diffusion Tensor Tractography

Ni Shu[1], Yong Liu[1], Jun Li[1,3], Yonghui Li[1], Chunshui Yu[2]*, Tianzi Jiang[1]*

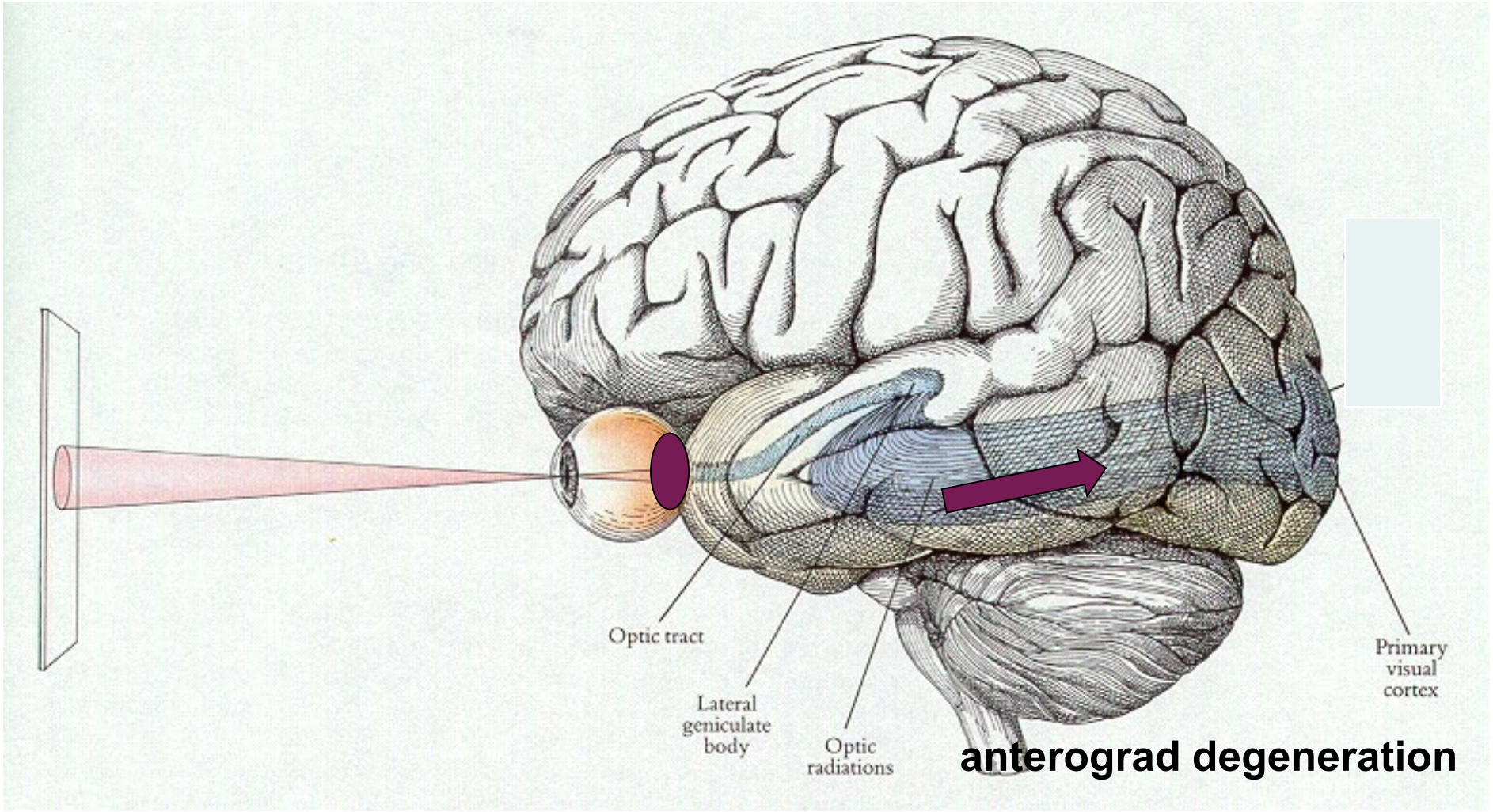
doi:10.1093/brain/awp279 Brain 2009: 132; 3467–3480 | 3467

BRAIN
A JOURNAL OF NEUROLOGY

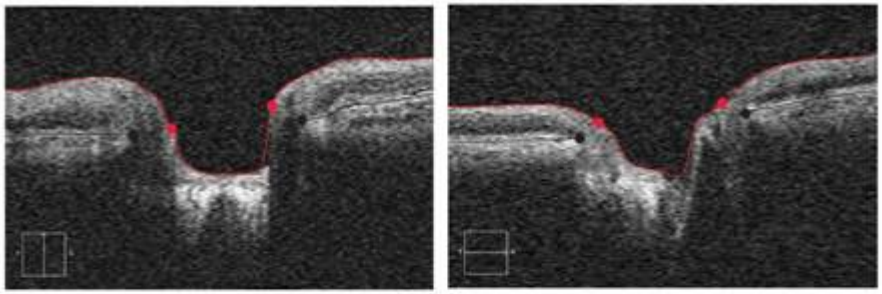
Imaging studies in congenital anophthalmia reveal preservation of brain architecture in 'visual' cortex

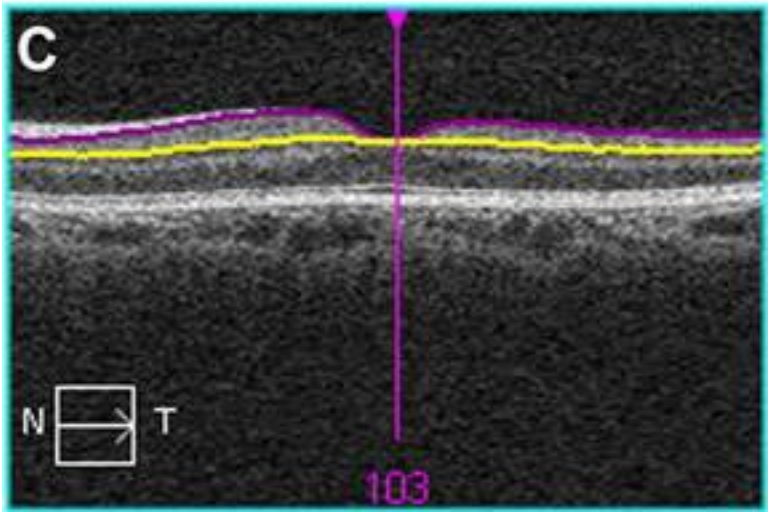
Holly Bridge,[1] Alan Cowey,[2] Nicola Ragge[3] and Kate Watkins[2]

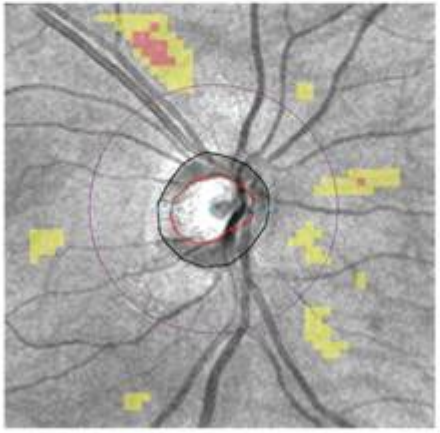
Transsynaptic degeneration över knäkroppen..

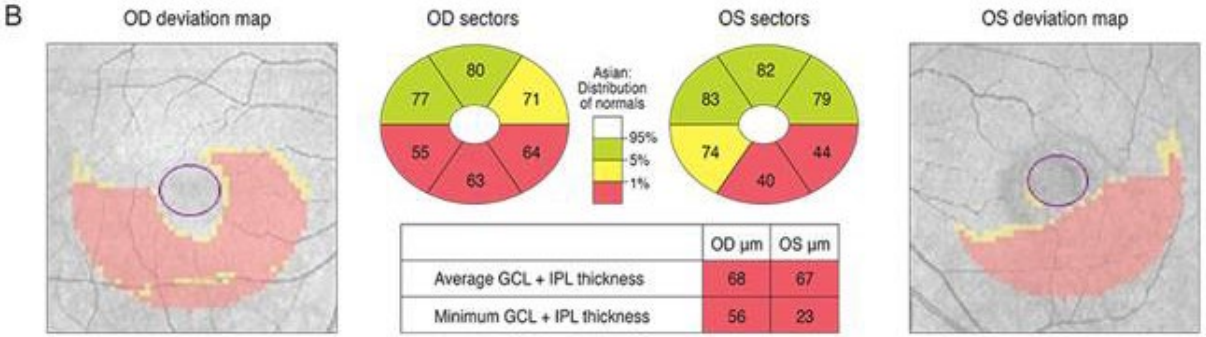


Imaging av näthinnan med Optical Coherence Tomography OCT





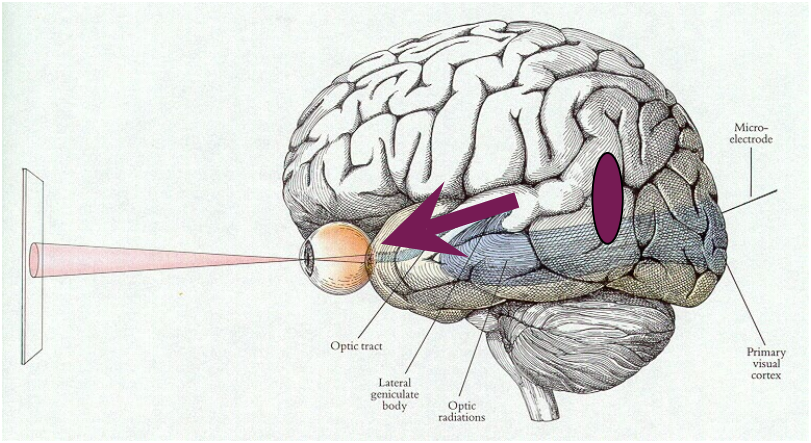




Peripapillära NFL…

..och tjockleken av gangliecells- och inre plexiforma komplexet (GCL_IPL) i macula

…vid primär skada/missbildning av den bakre synbanan/syncortex ses sekundär förlust av retinala ganglieceller…



retrograd transsynaptisk degeneration

Damage to the Immature Optic Radiation Causes Severe Reduction of the Retinal Nerve Fiber Layer, Resulting in Predictable Visual Field Defects

Finn Lennartsson,[1,2] Maria Nilsson,[3] Olof Flodmark,[1,2] and Lena Jacobson[4]

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[2]Department of Clinical Neurosciences, Karolinska Institutet, Stockholm, Sweden
[3]Department of Clinical Neurosciences, Unit of Optometry, Karolinska Institutet, Stockholm, Sweden
[4]Department of Clinical Neurosciences, Ophthalmology and Vision, Karolinska Institutet, Stockholm, Sweden

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Submitted: May 30, 2014
Accepted: October 13, 2014

Citation: Lennartsson F, Nilsson M, Flodmark O, Jacobson L. Damage to the immature optic radiation causes severe reduction of the retinal nerve fiber layer, resulting in predictable visual field defects. *Invest Ophthalmol Vis Sci*. 2014;55:8278–8288. DOI:10.1167/iovs.14-14913

Purpose. The aim of the present study was to seek evidence of a relationship between damage to the optic radiation (OR) in the immature brain and subsequent development of the retinal nerve fiber layer (RNFL) and associated visual manifestations.

Methods. Seven cases (2 males and 5 females ranging in age from 18 to 35 years old) were selected from a large cohort of individuals with known white matter damage of immaturity (WMDI), who had presented with visual dysfunction. They underwent magnetic resonance imaging (MRI), including diffusion-weighted MRI. Visual function was evaluated by best-corrected visual acuity and visual field (VF) testing using Goldmann perimetry and Humphrey field analyzer (HFA). RNFL thickness was measured by optical coherence tomography.

Results. A homogeneous lesion pattern with bilateral WMDI predominantly in the superior posterior periventricular white matter was seen in all subjects. However, as shown by white matter fiber tractography, only cases with injuries to the superior portion of the OR had corresponding inferior VF defects. In the individuals showing structural abnormalities in the OR, a commensurate reduction in the peripapillary RNFL was seen. The RNFL loss was most pronounced in the subjects suffering from the more extensive lesions, and it followed the pattern of OR damage in the sense that damage in the superior portion of the OR gave a reduced RNFL thickness in the superior part of the peripapillary RNFL.

Conclusions. Primary injuries in the immature OR are associated with reduced RNFL thickness, and examination of the RNFL may be a helpful predictor of VF defects.

Keywords: early brain injuries, optic radiation, retinal nerve fiber layer, visual field, visual pathways

Periventricular white matter damage, occurring in the immature brain before 34 gestational weeks, may cause visual impairment in children. This occurs due to adverse events in the neonatal period of prematurely born infants or during the last trimester in utero. Survivors with pre- and perinatal brain damage will present to ophthalmologists who may not be familiar with these clinical features. Patients may exhibit a wide spectrum of visual symptoms, ranging from subnormal visual acuity (VA) or early onset esotropia to severe cerebral visual impairment.[1] Abnormal appearance of the optic discs, which may be small or normal in size with extensive cupping, have been described; the proposed mechanism being retrograde trans-synaptic degeneration.[2]

The primary white matter lesions, often referred to as white matter damage of immaturity (WMDI),[3] occur between 24 and 34 gestational weeks (early third trimester) and are commonly detected with magnetic resonance imaging (MRI). In WMDI, the posterior periventricular white matter is often affected and damage may involve the optic radiation (OR).[4] Injuries to the OR in the immature brain can be detected by conventional structural MRI; however, the exact location and structure of the fiber tract affected cannot be judged. Diffusion-weighted MRI (DWI) is a novel MRI technique which can infer on the structural composition of cerebral white matter,[5] whereas fiber tractography can be used to trace white matter fiber tracts in vivo.[6] The optic radiation's well-known retinotopic organization[7] can be studied by means of fiber tractography.[8] Studies in premature neonates using DWI and fiber tractography show changes in diffusion parameters in the OR indicating altered white matter microstructure.[9–11] These changes show correlation with assessment of visual ability[9,10] and visual evoked potentials[11] but are independent of whether focal brain lesions are detected. This implies the generalized vulnerability of the developing visual system during the third trimester.[12] However, the actual effects of focal lesions to the immature OR on the visual function have yet to be investigated in any detail.

The pathogenesis of WMDI is multifactorial with primary destructive injuries and secondary effects from impaired maturational mechanisms or from trophic disturbances.[13] An interruption in the thalamic neurons that travel from the lateral geniculate nucleus (LGN) to the striate cortex and/or their supporting glial cells can impair both thalamic and cortical development and cause hypomyelination. However, in the early third trimester, thalamostriate afferent nerves are still entering

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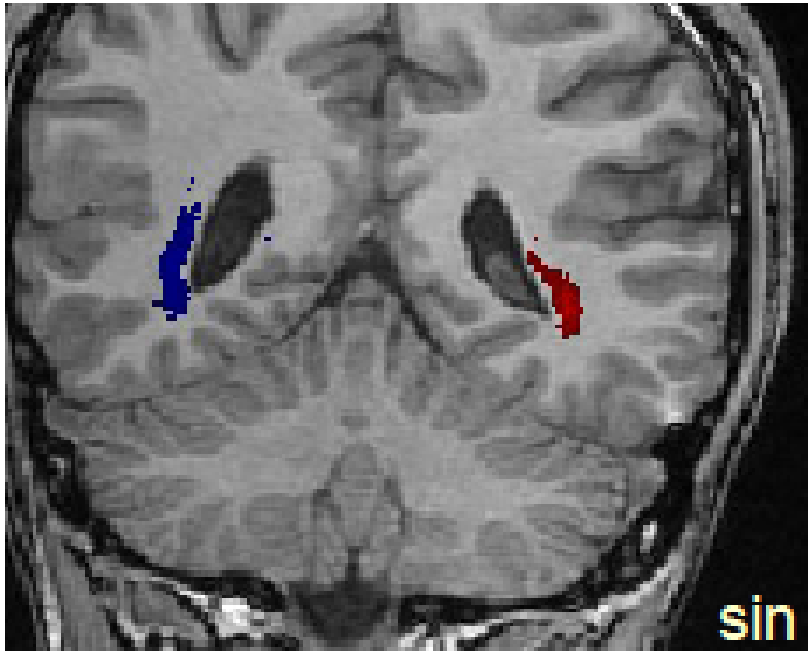
Karolinska Institutet

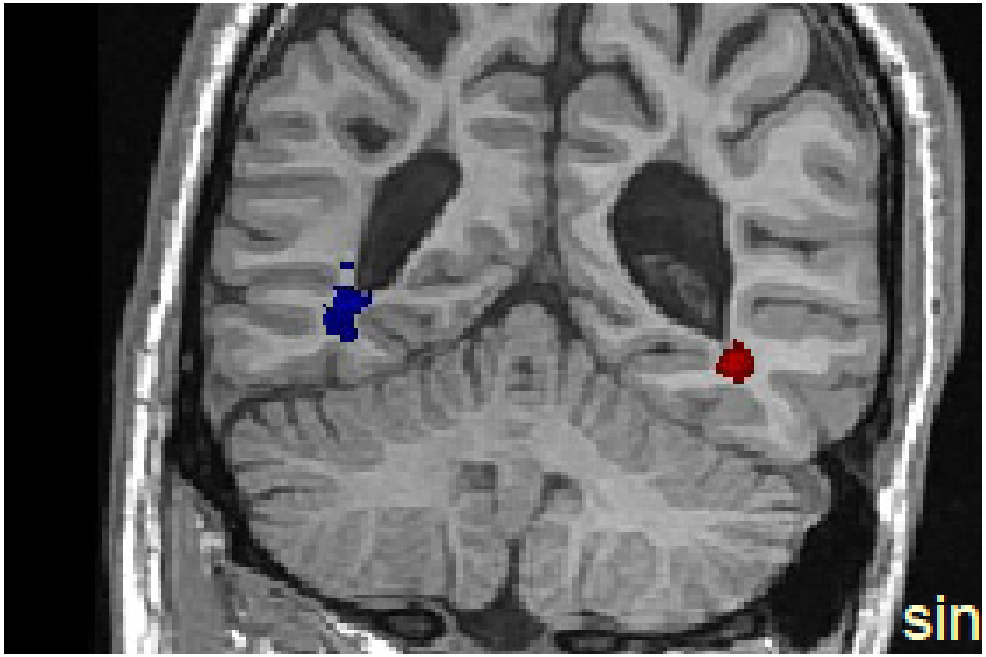
7 individuals aged 18 - 35 years with known white matter damage of immaturity (WMDI) on conventional MRI may affect the OR were examined with fibre tractography of the OR and OCT and perimetry (HFA)

MRI tractografi synstrålningen

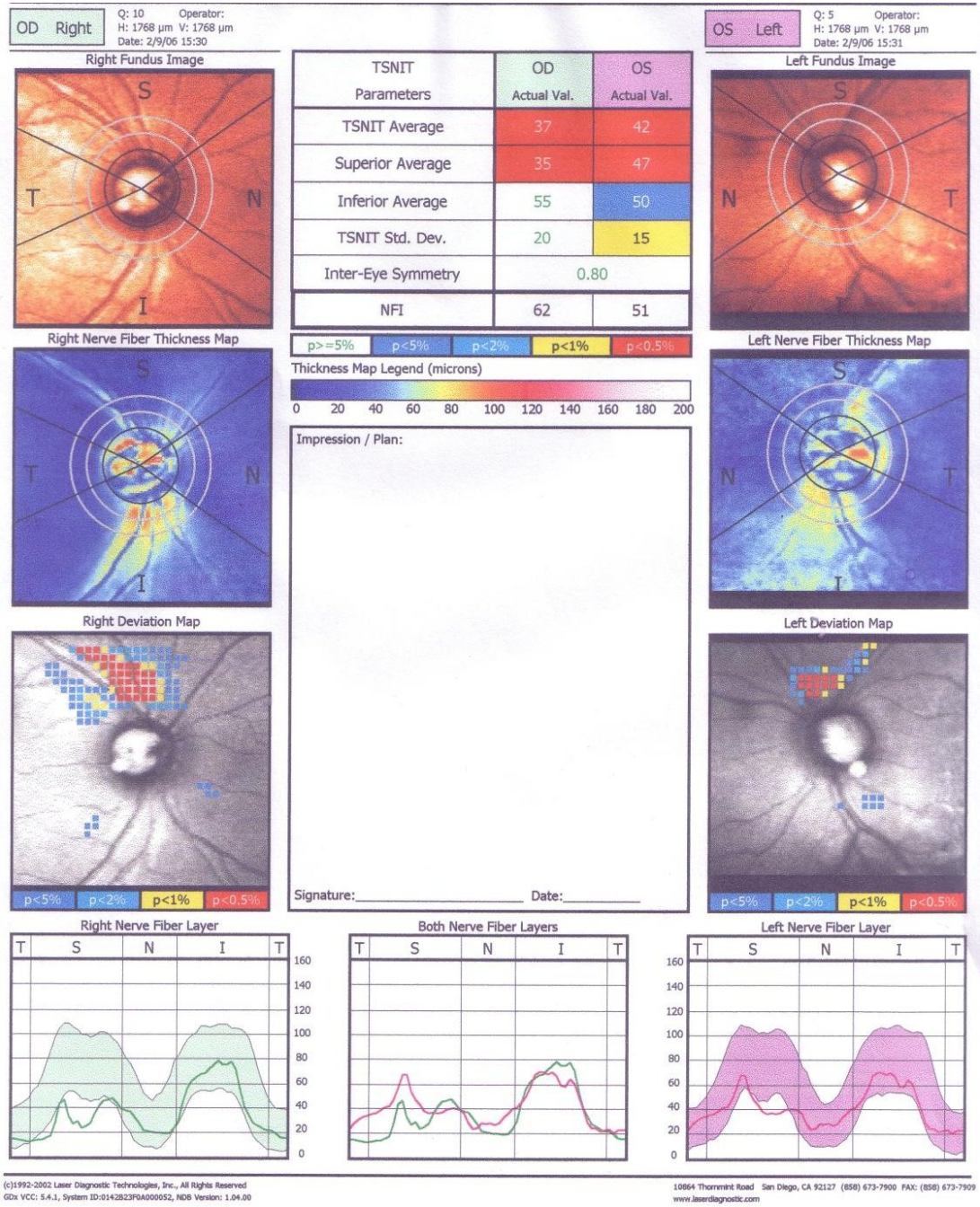
kontroll



M 31 år



bilateral spastisk cp och cvi med stora dorsal och ventral stream problem – ex-preterm


OD Right
Q: 10 Operator:
H: 1768 µm V: 1768 µm
Date: 2/9/06 15:30
OS Left
Q: 5 Operator:
H: 1768 µm V: 1768 µm
Date: 2/9/06 15:31
Right Fundus Image
Left Fundus Image
TSNIT Parameters
OD Actual Val.
OS Actual Val.
TSNIT Average 37 42
Superior Average 35 47
Inferior Average 55 50
TSNIT Std. Dev. 20 15
Inter-Eye Symmetry 0.80
NFI 62 51
p>=5% p<5% p<2% p<1% p<0.5%
Thickness Map Legend (microns)
0 20 40 60 80 100 120 140 160 180 200
Right Nerve Fiber Thickness Map
Left Nerve Fiber Thickness Map
Impression / Plan:
Signature:_____ Date:_____
Right Deviation Map
Left Deviation Map
p<5% p<2% p<1% p<0.5%
Right Nerve Fiber Layer
Both Nerve Fiber Layers
Left Nerve Fiber Layer
T S N I T
160 140 120 100 80 60 40 20 0
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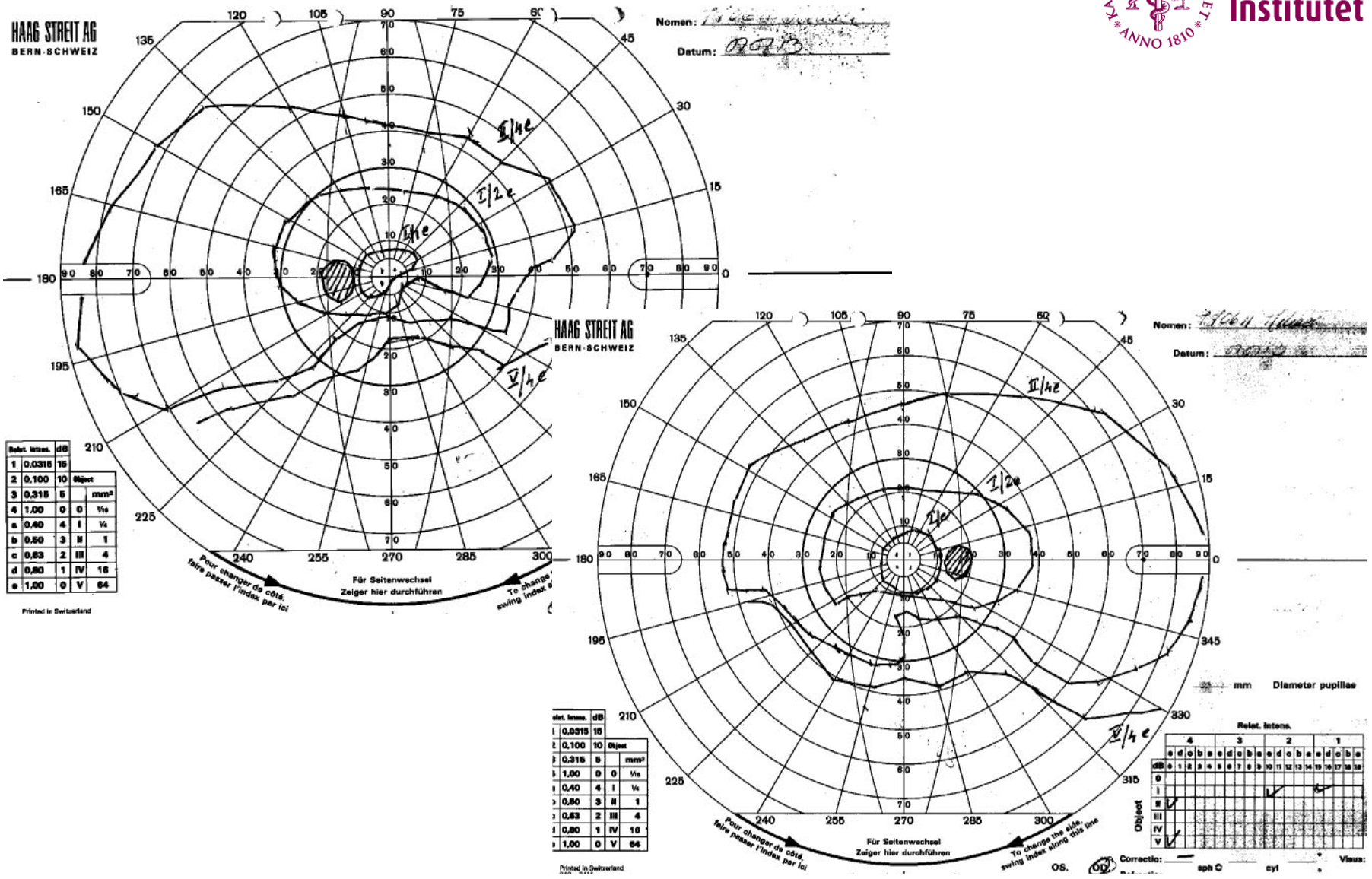
GDx VCC: 5.4.1, System ID:0142B23F0A000052, NDB Version: 1.04.00
10864 Thornmint Road San Diego, CA 92127 (858) 673-7900 FAX: (858) 673-7909
www.laserdiagnostic.com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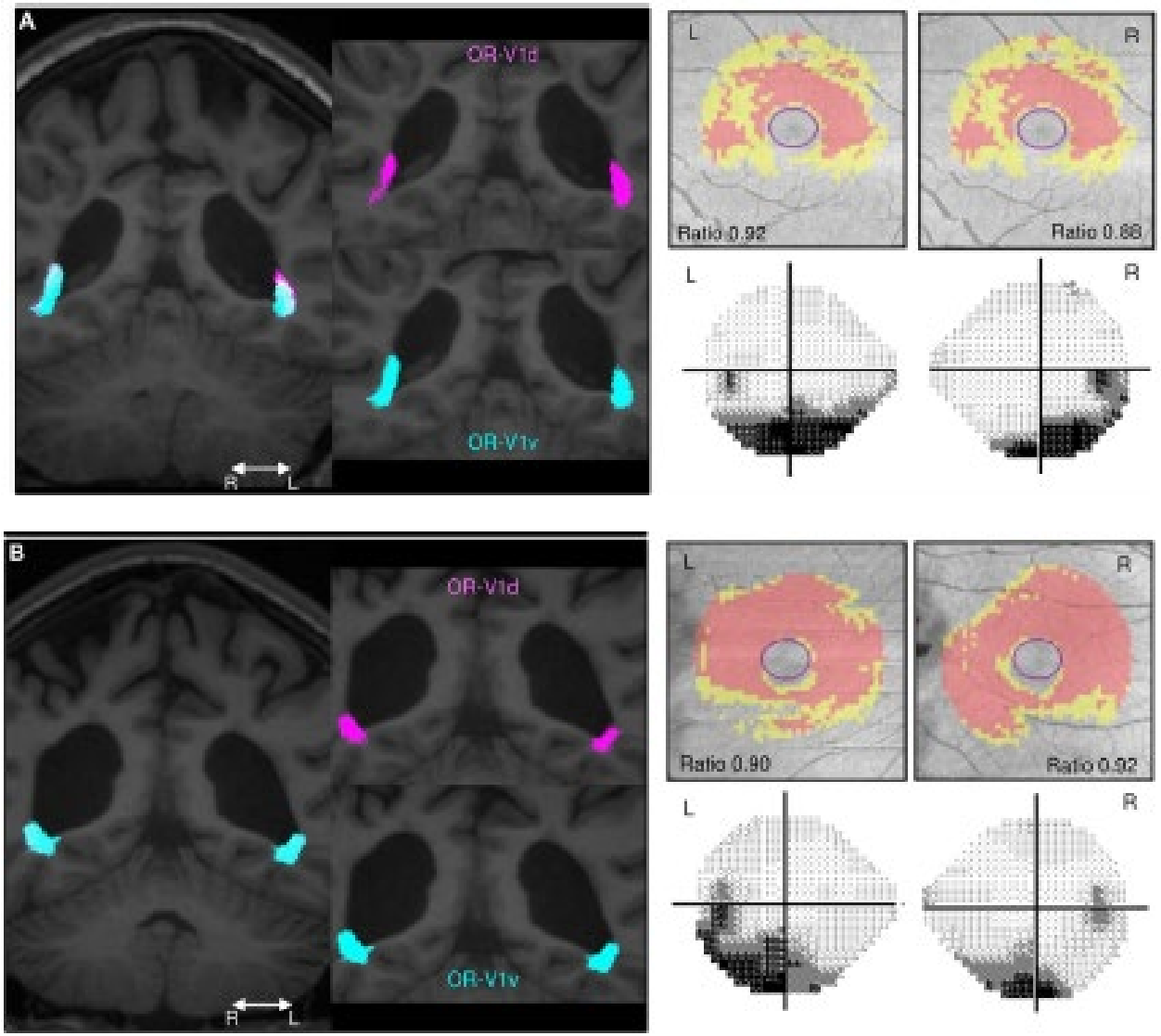
frontiers in Neurology

ORIGINAL RESEARCH
published: 07 May 2018
doi: 10.3389/fneur.2018.00321

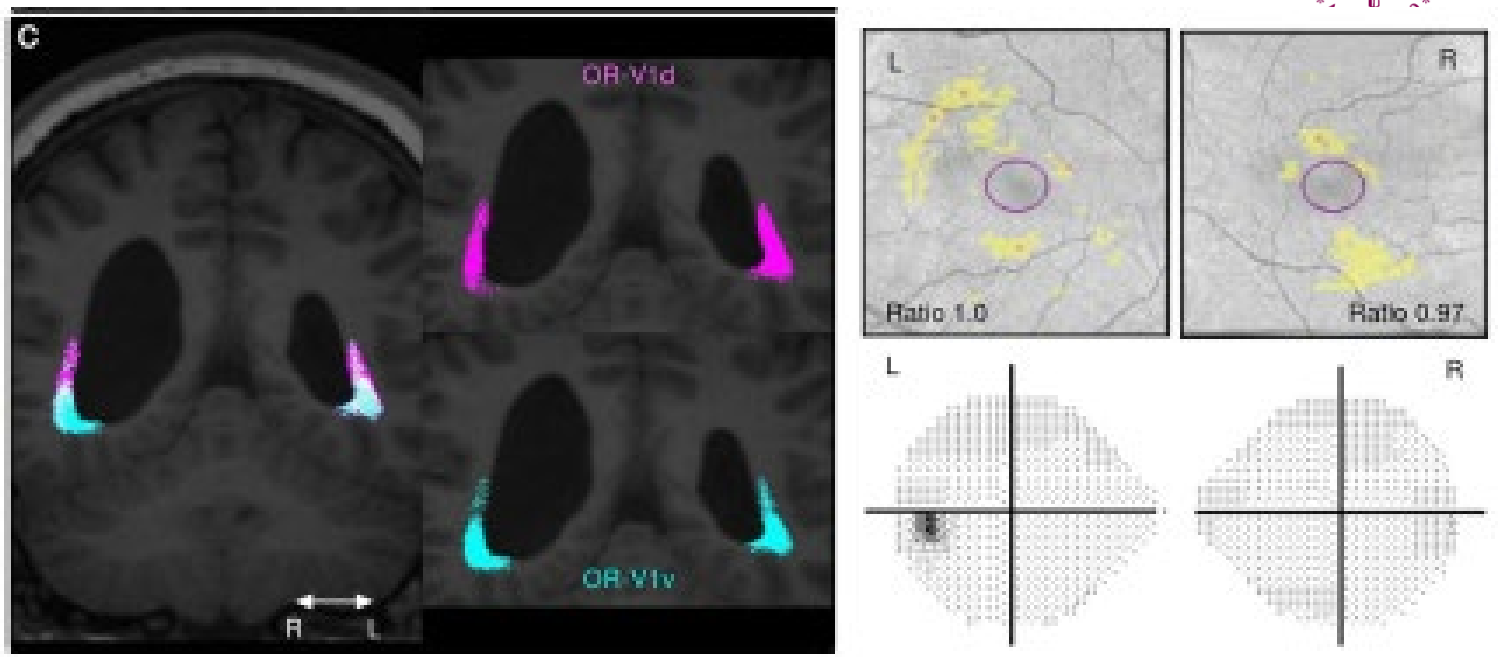
Injuries to the Immature Optic Radiation Show Correlated Thinning of the Macular Ganglion Cell Layer

Finn Lennartsson[1,2], Maria Nilsson[3], Olof Flodmark[1,2], Lena Jacobson[4] and Jonas Larsson[5]*

[1]Department of Neuroradiology, Karolinska University Hospital, Stockholm, Sweden, [2]Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden, [3]Unit of Optometry, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden, [4]Ophthalmology and Vision, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden, [5]Department of Psychology, Royal Holloway, University of London, Egham, United Kingdom



Note the topographical correspondence between the spatial displacement of the OR-V1d tract into the space occupied by the OR-V1v tract



Despite having a large white-matter damage of immaturity [bilateral intra-ventricular hemorrhage (L > R) and right-sided periventricular hemorrhagic infarct, the primary visual system is not affected in this patient.

- I våra första studier var urvalet gjort efter en känd morfologisk diagnos – periventrikulär vit substansskada från GÅ 24-34 veckor
- I vår andra studie valde vi individer med funktionell diagnos – homonyma synfältsdefekter – av olika genes och morfologisk skada uppkommen vid olika mognadsskede

NEURO-OPHTHALMOLOGY
https://doi.org/10.1080/01658107.2019.1583760

Ganglion Cell Topography Indicates Pre- or Postnatal Damage to the Retro-Geniculate Visual System, Predicts Visual Field Function and May Identify Cerebral Visual Impairment in Children – A Multiple Case Study

Lena Jacobson[a], Finn Lennartsson[b], and Maria Nilsson[c]

[a]Department of Clinical Neuroscience, Eye and Vision, Karolinska Institutet, Stockholm, Sweden; [b]Department of Clinical Sciences, Diagnostic Radiology, Lund University, Lund Sweden; [c]Departmentof Clinical Neuroscience, Unit of Optometry, Karolinska Institutet, Stockholm, Sweden

ABSTRACT

In this paper, we quantify the degree of ganglion cell layer thinning due to retrograde trans-synaptic degeneration (RTSD) from retro-geniculate damage in six cases who had homonymous visual field defects known since childhood. Three had prenatal injuries, occurring close to mid-gestation and in the first parts of the early and late third trimester, respectively, and representing injuries at different early developmental stages. Three had later acquired injuries, at age 1.5, 4 and 13 years. The impact of the injury to the optic radiations was revealed by fibre tractography. The ganglion cell thinning corresponded with the visual field defects and the extent and location of the primary brain damage. The most important sign of RTSD was asymmetry of the ganglion cell topography within the macular area.

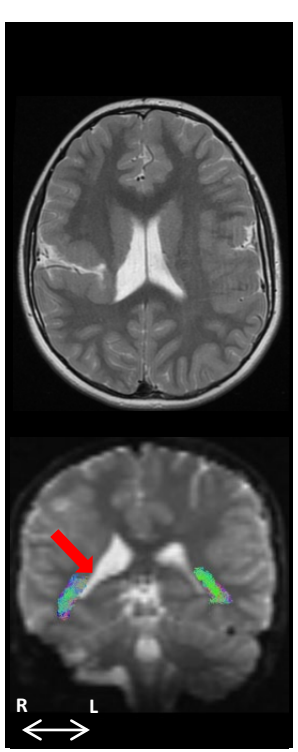
ARTICLE HISTORY
Received 2 May 2018
Accepted 10 February 2019

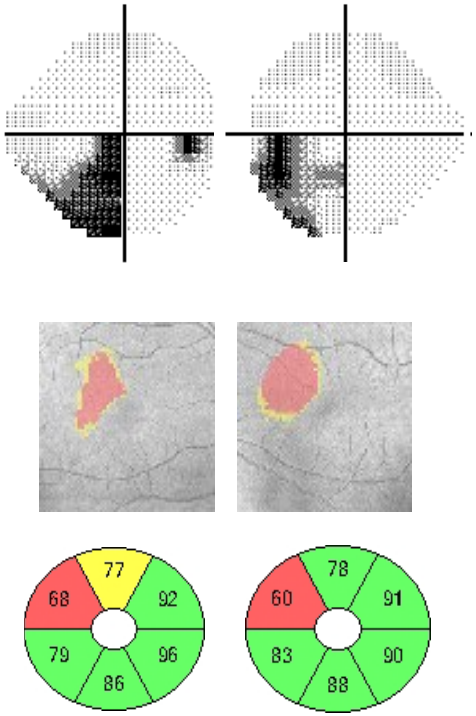
KEYWORDS
Retro-geniculate brain damage; retrograde trans-synaptic degeneration; retinal ganglion cells; homonymous visual field defects; cerebral visual impairment

Ungdomar med känd homonym synfältsdefekt valda för att representera skada av retro-genikulära synsystemet vid olika mognadsgrad –pre-och postnatal

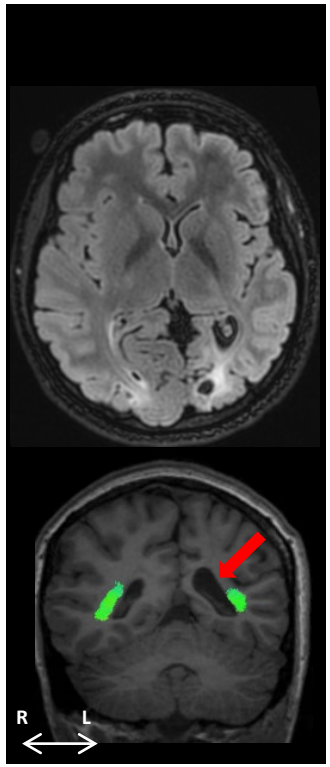
Prenatal missbildning/skada

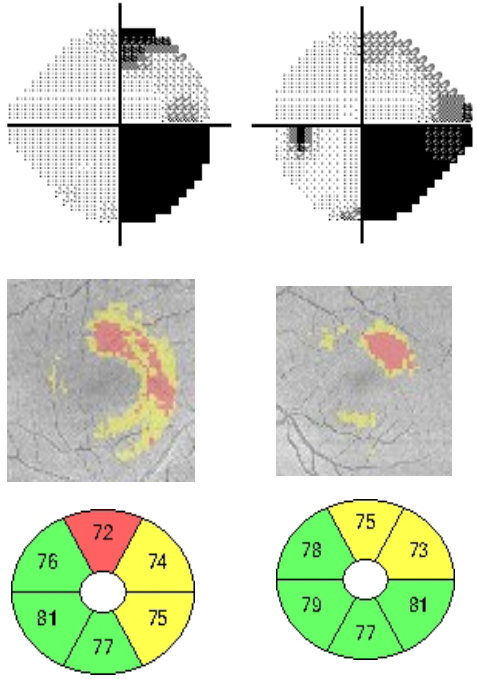
GA (weeks) **<20** **37**





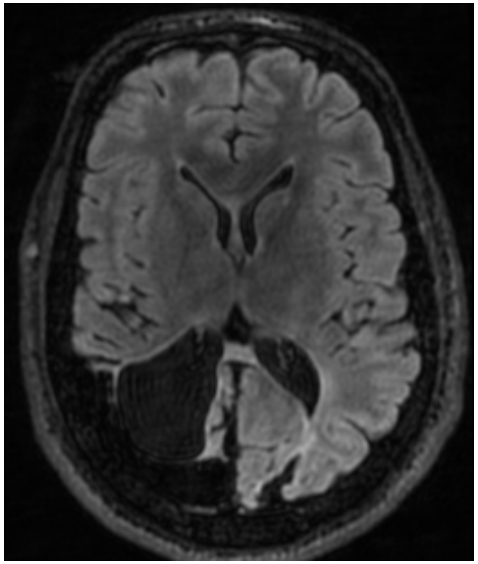
malformation

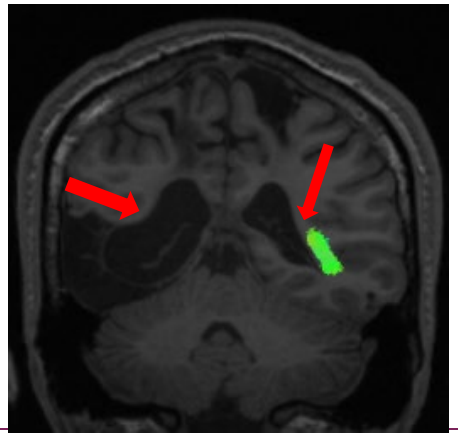


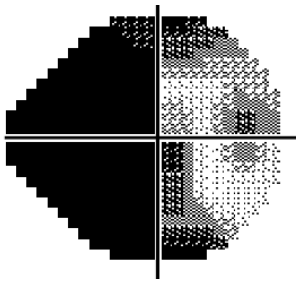


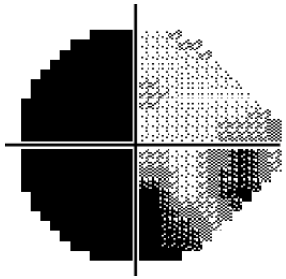
watershed-infarkt

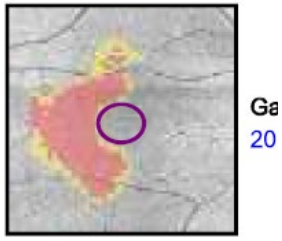
Postnatalt förvärvad skada

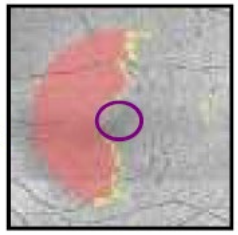


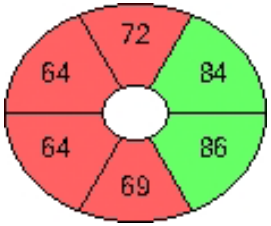


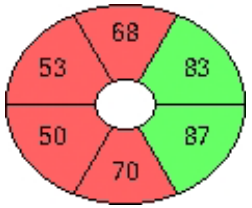












Cystisk skada efter bilaterala asymmetriska PCA-infarkter vid **18 månaders ålder**

DEVELOPMENTAL MEDICINE & CHILD NEUROLOGY ORIGINAL ARTICLE

Visual field function in school-aged children with spastic unilateral cerebral palsy related to different patterns of brain damage

2010

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29 av 34 barn 7-17 år med unilateral CP kunde undersökas med konfrontation, Goldmann och Rarebit datoperimetri

MRI: missbildning (n=7), WMDI (n=13), kortikal-subkortikal skador (n=9)

18 (62%) hade någon synfältspåverkan

6 (20%) hade total homonym hemianopsi

Studiedeltagarna var utvalda för sin förmåga att medverka i de krävande undersökningarna. Individer med större hjärnskador har svårare funktionella begränsningar såsom svår cerebral pares, intellektuella och uppmärksamhetsproblem, svår synskada utan förmåga att hålla fixation vilket omäöjliggör medverkan i studierna, Det finns, emellertid, ingen anledning att tro att vare sig GCL-IPL eller synfältsfunktionen skulle sparas vid mer utbredda skador. Barn med mycket svår bilateral spastisk cerebral pares har ofta samtidig blindhet eller grav synskada, och kan inte förväntas bygga sin kommunikation med hjälp av synfunktionen.

Varför är det viktigt att med OCT påvisa förlusten av retinala GC hos barn/ungdomar/vuxna med retro-genikulär synbaneskada?

- Förutsäger synfältsfunktionen
- Hjälp att identifiera individer med CVI
- Hjälp att få förståelse inom ögonsjukvården, som har ett diagnostiskt ansvar, barnneurologi och habilitering, för konsekvenserna av en lesion i de bakre synbanorna
- Utgöra underlag för att belysa behovet av habiliteringsinsatser, och för att utforma dessa insatser

Childhood visual impairment in England: a rising trend

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ABSTRACT

Aim To explore temporal trends in the incidence of childhood blindness and partial-sight registration in England between 1982 and 2011.

Methods We obtained blind and partial-sight registration data for all new individuals registered annually in England. We calculated the age-specific incidence of new registrations for childhood blind and partial sight.

Results The incidence of new registration for blindness of all ages has decreased from 2.6 per 10 000 in 1982 to 1.7 per 10 000 in 2011, however the annual incidence of new paediatric blind registration has increased, with an incidence of 0.17 per 10 000 in 1982, doubling to 0.41 per 10 000 in 2011. The annual incidence of new paediatric partial-sight registration showed a comparable trend.

Conclusions Over 30 years, there has been a greater than twofold increase in blind and partial-sight registration in children in England. Better awareness of this is needed to ensure adequate resources are available to help these children.

What is already known on this topic

- There are very few large longitudinal studies on the incidence of childhood blind and partial sight in the UK.
- Previous studies have suggested that this number may be rising.

What this study adds

- Examining national data over 30 years has demonstrated a greater than twofold increase in blind and partial-sight registration in children in England.
- Better awareness of this important trend is needed to ensure adequate resources can be made available.

- 1982 jmf 2011
- Incidens av blindhet hos barn **ökade** från 0.17 till 0.41 per 10000 medan incidensen hos vuxna minskade
- Incidensen av synsvaghet hos barn **ökade** från 0.21 till 0.59 per 10000
- Orsaken är huvudsakligen CVI hos de nya överlevarna, framför allt prematurfödda

Vid CVI ofta

- Subnormal synskärpa
- Inskränkt synfält och/eller subnormal känslighet i synfältet
- Problem att hålla fixation och att göra adekvata ögonrörelser och adekvat ackommodation
- Dorsal and ventral stream dysfunktion

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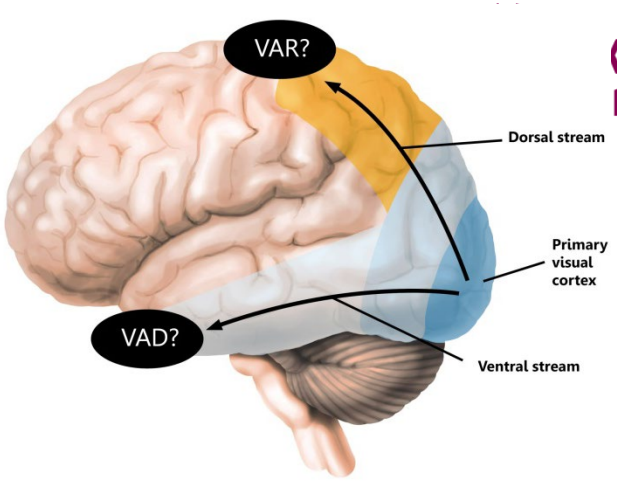
Ögonmotoriska problem vid cvi pga periventrikulär vit substansskada

- ackommodations-svaghet
- nystagmus
- skelning
- instabil fixation
- dysmetriska sackader
- inga följerörelser
- paroxysmala deviationer

Vid CVI ofta



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The ‘Tree’ of Visual Perception and Cognition