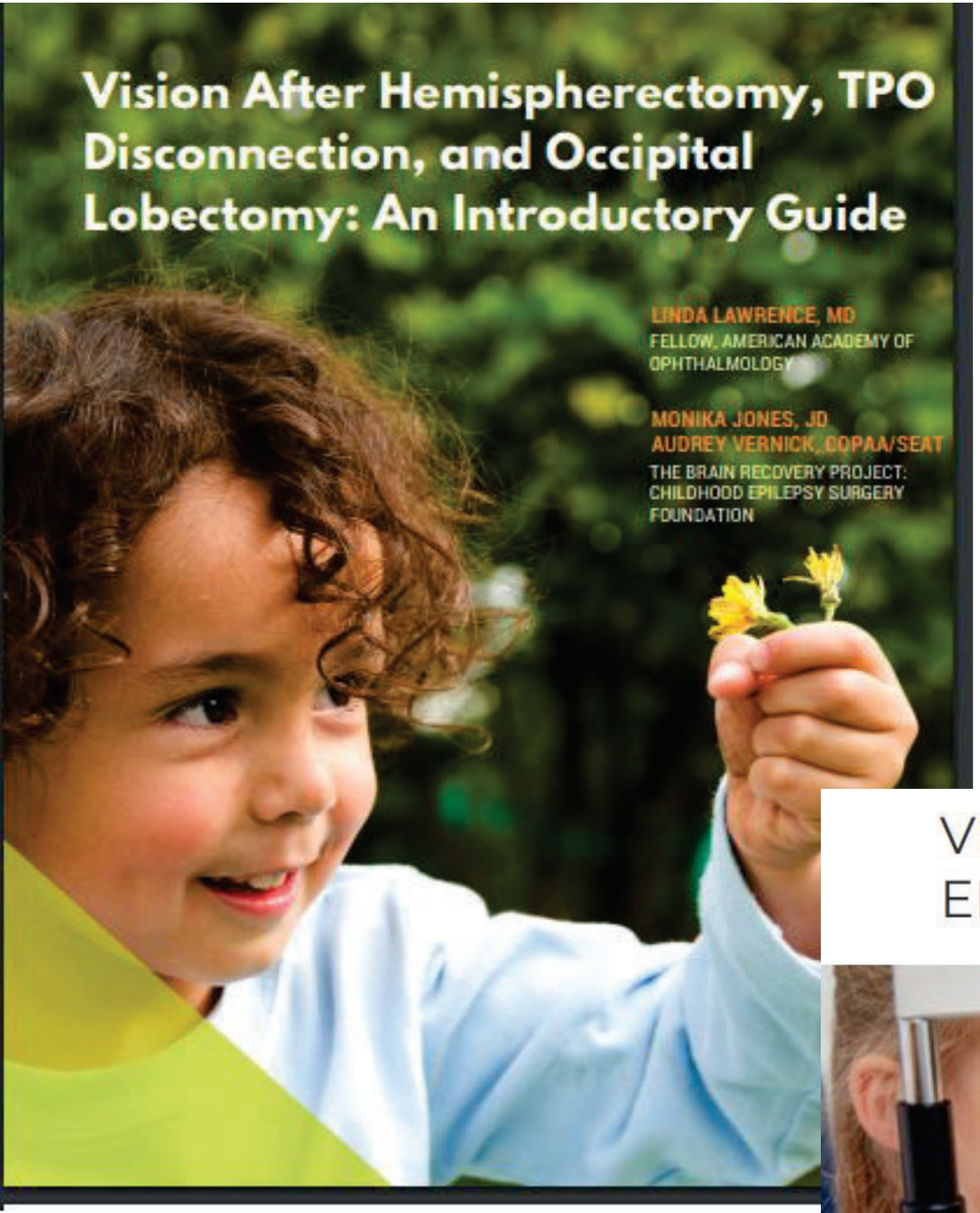
Epilepsy and Vision

Linda Lawrence MD

Salina, Kansas



Brainrecoveryproject.org

What caused the epilepsy?

- Important question because the reason for the epilepsy may affect the brain/visual pathways even if the seizures are controlled

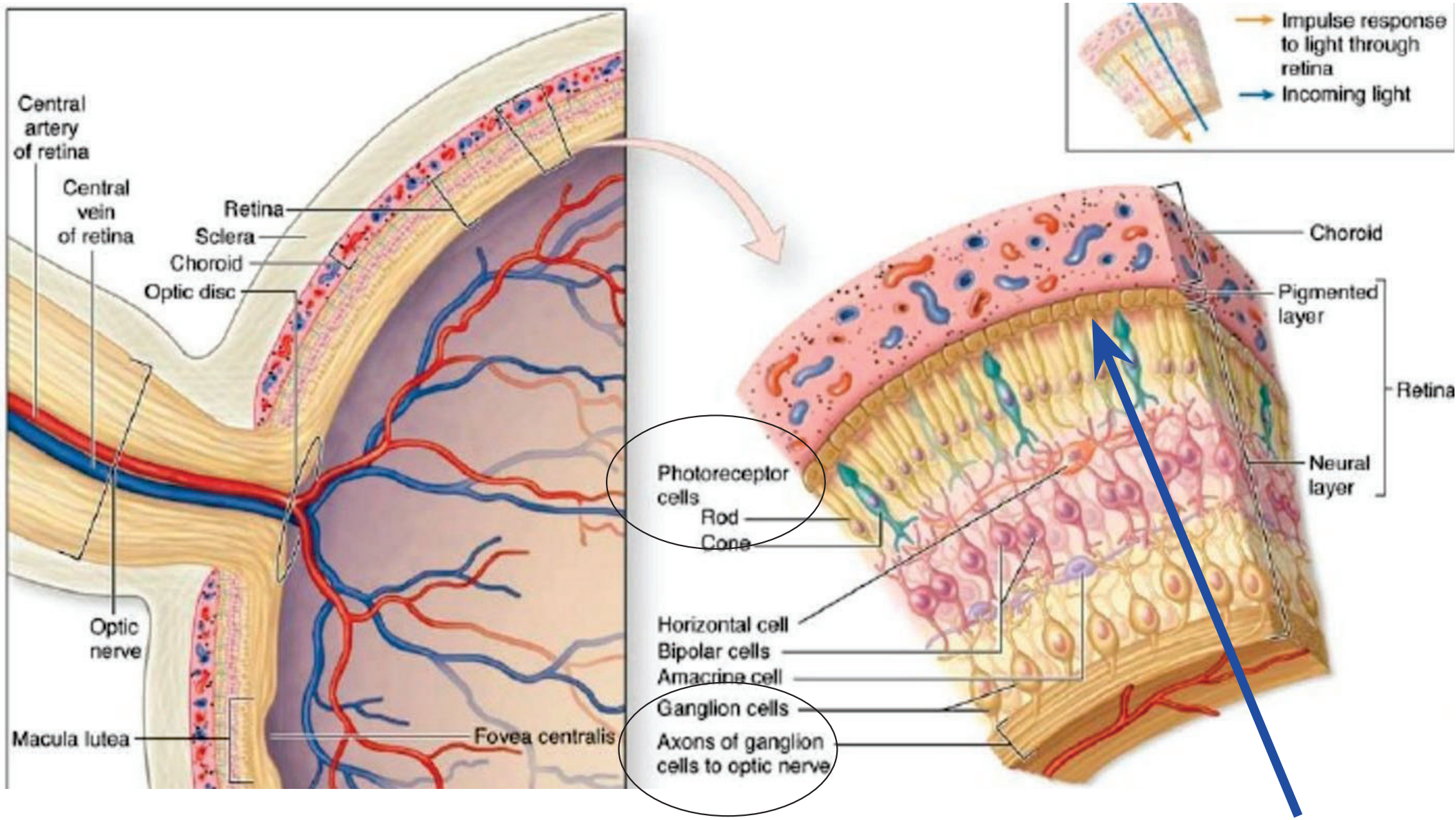
Seizure

"spontaneous abnormal synchronized hyper-excitation of the brain" or seizure

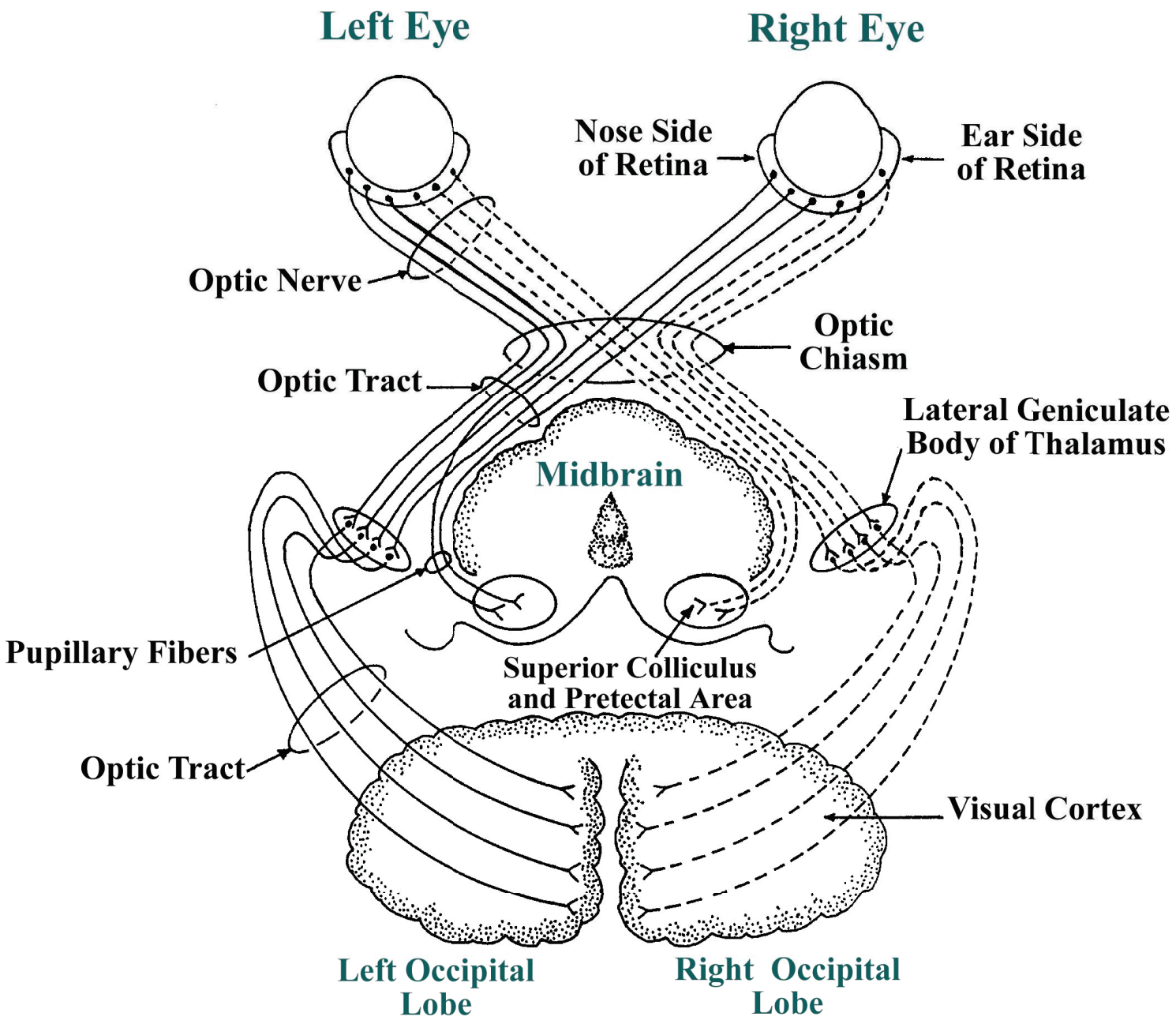
Can arise from almost anything that damages the brain

- Trauma
- Stroke
- Infection
- Tumor
- Inherited genetic mutations
- Epileptic seizure can lead to brain damage

Normal Retinal and Optic Nerve Anatomy



OPTIC NERVE PATHWAY IN THE BRAIN

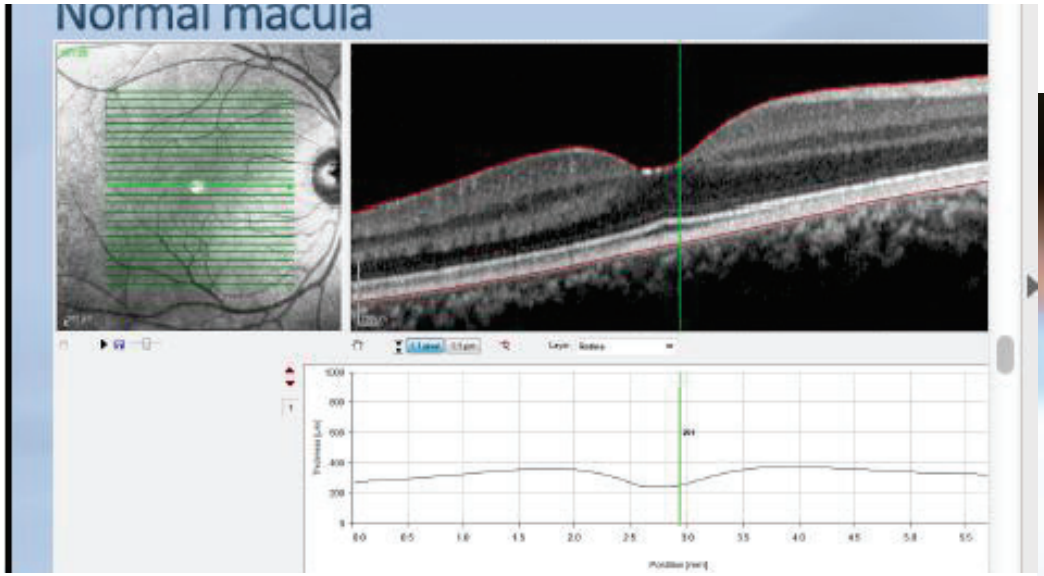


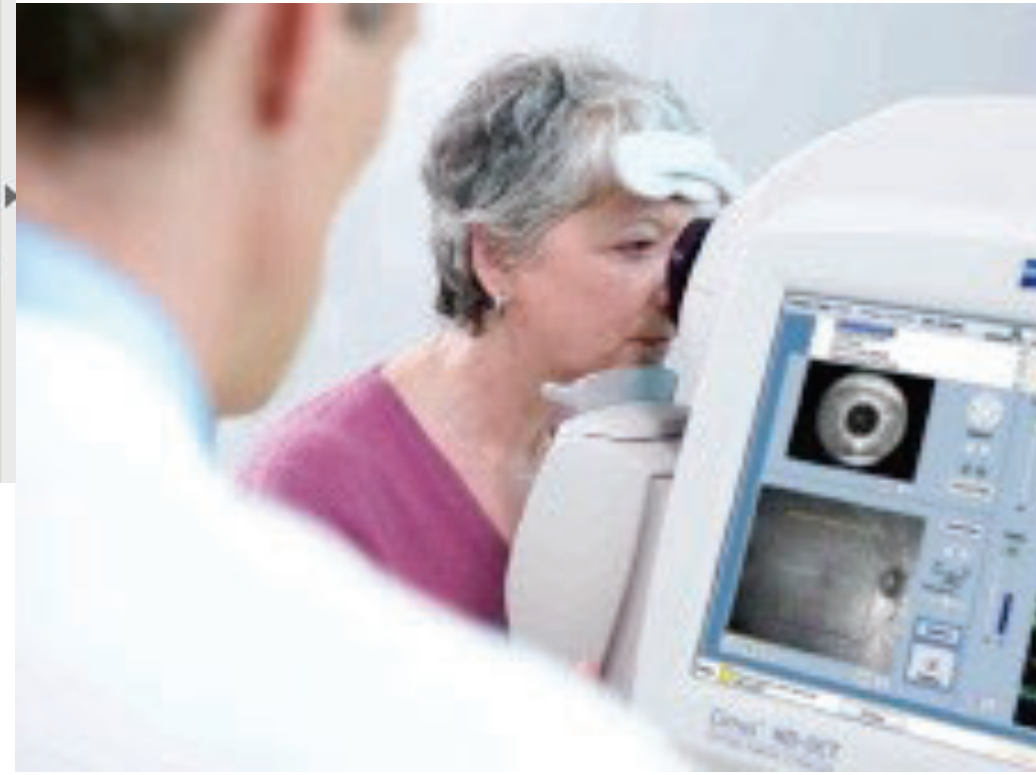
Inflammatory reaction

- Inflammatory reaction in brain following seizure
- Immune response includes damaging and restorative mechanism
- We can study this in the retina
- Retina is extension of the brain….
- Retinal inflammation may be a marker of seizure burden

Widespread white and grey matter involvement has already been shown in epilepsy.
Evidence of trans-synaptic degeneration in the human central nervous system has already been shown in previous studies using OCT.

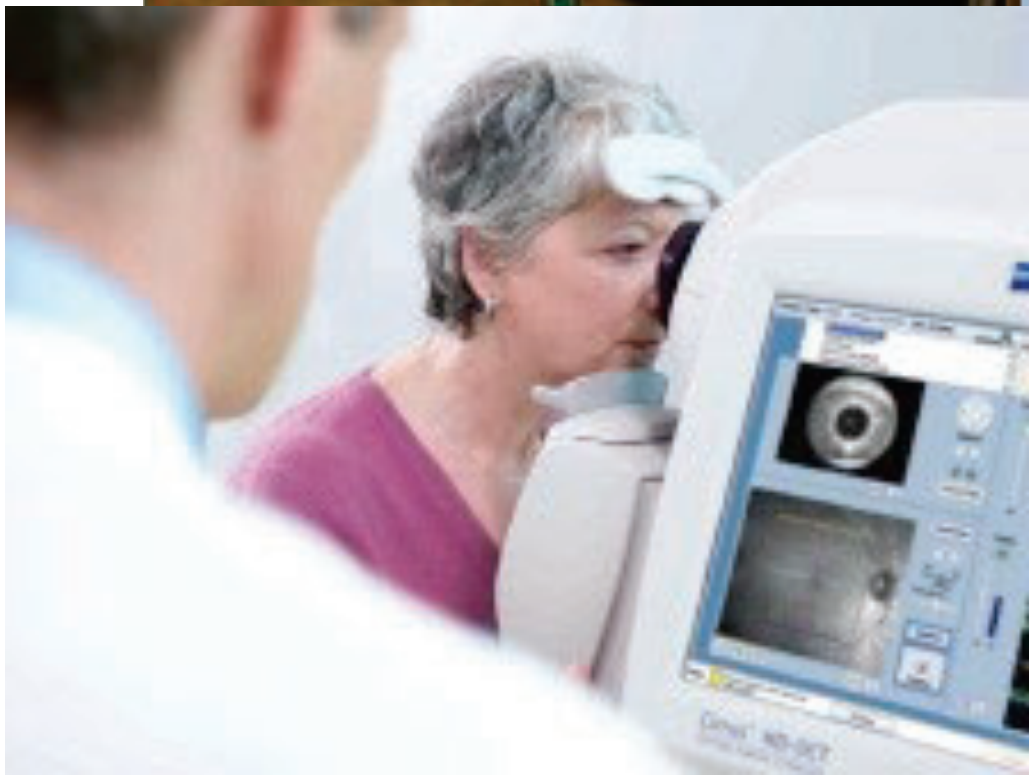
RNFL thickness could be advanced as a reliable, inexpensive and easily assessed complementary surrogate marker for exploration of whole-brain cerebral processes, such as potential neurodegenerative processes, in human epilepsy.





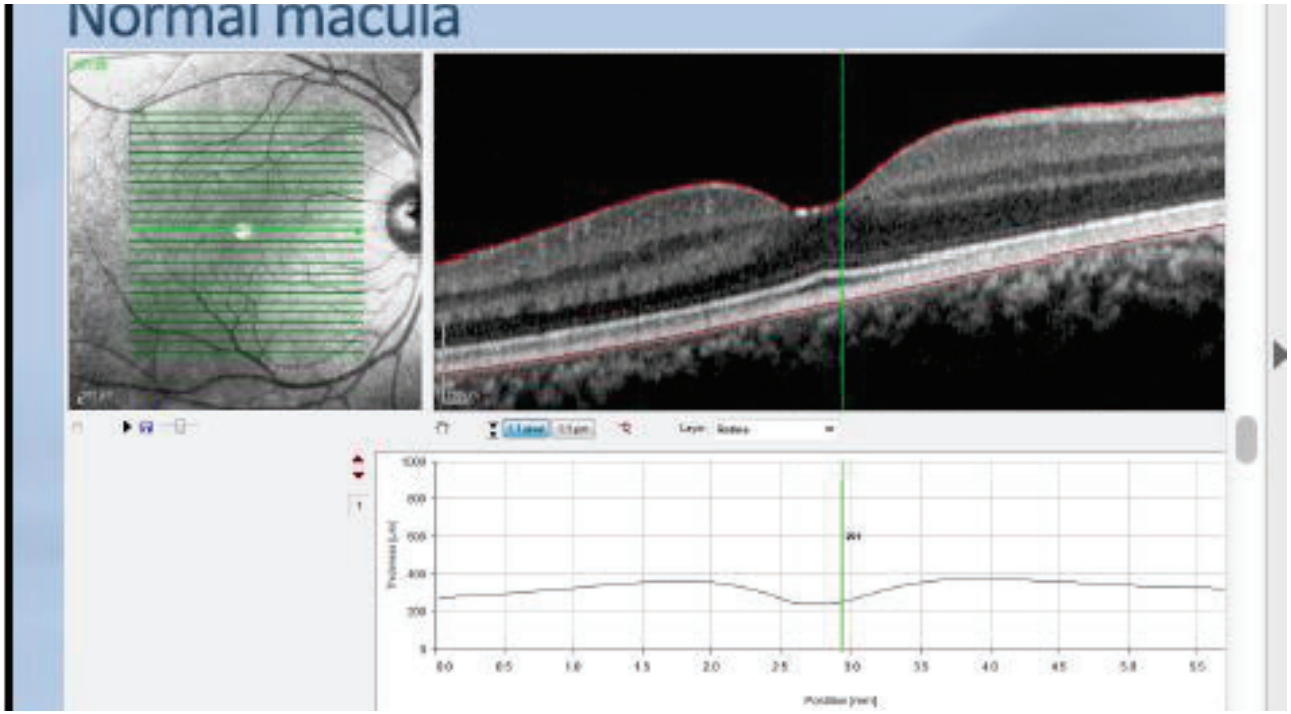
Technical challenges in Kids

- No official norms for kids: soon
- Difficult technically in kids, nystagmus, fixation
- Hand held expensive
- Built for adults

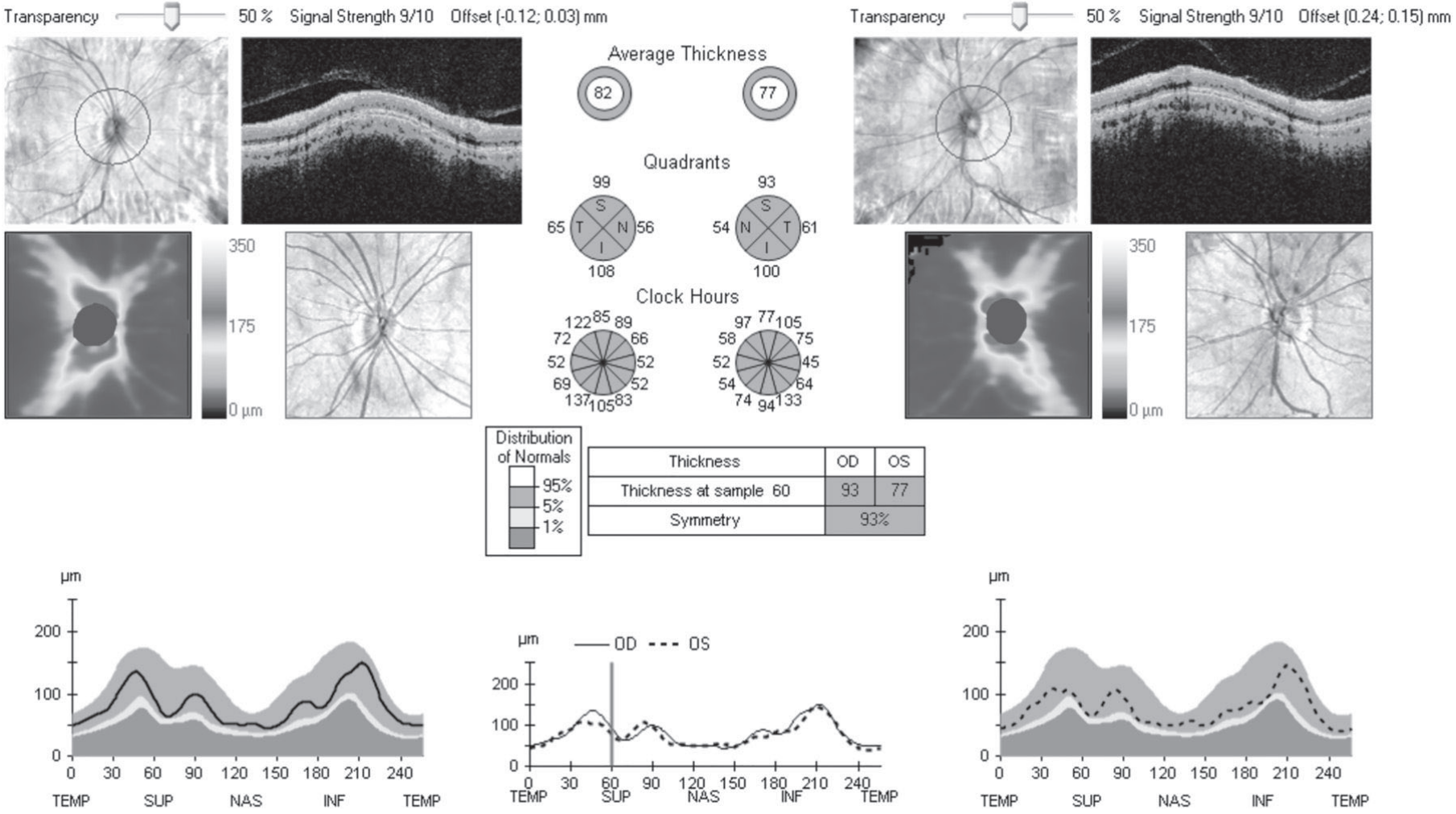


Normal Retina

Vitreous
Inner retina
  Internal limiting membrane
  Nerve fiber
  Ganglion cell
Central retina
  inner plexiform
  inner nuclear
  outer plexiform
  outer nuclear
Outer Retina
  external limiting membrane
  rods and cones
  retinal pigment epithelial
  Bruch's membrane
Choroid
  choriocapillaris/choroid



Sample optical coherence tomography report of retinal nerve fibre layer (RNFL) thickness taken from a healthy control with normal visual fields showing normal RNFL thickness with an average RNFL thickness of 82 µm in the right eye and 77 µm in the left eye.



Simona Balestrini et al. J Neurol Neurosurg Psychiatry 2016;87:396-401

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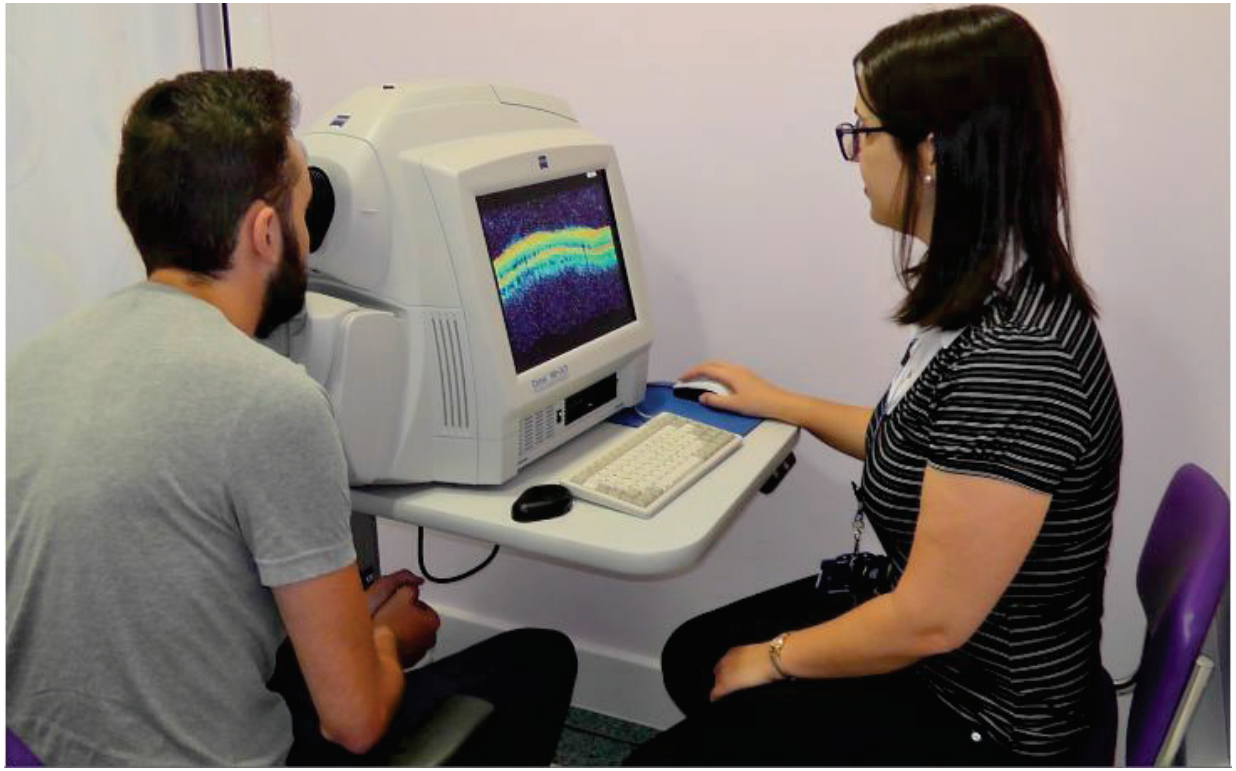
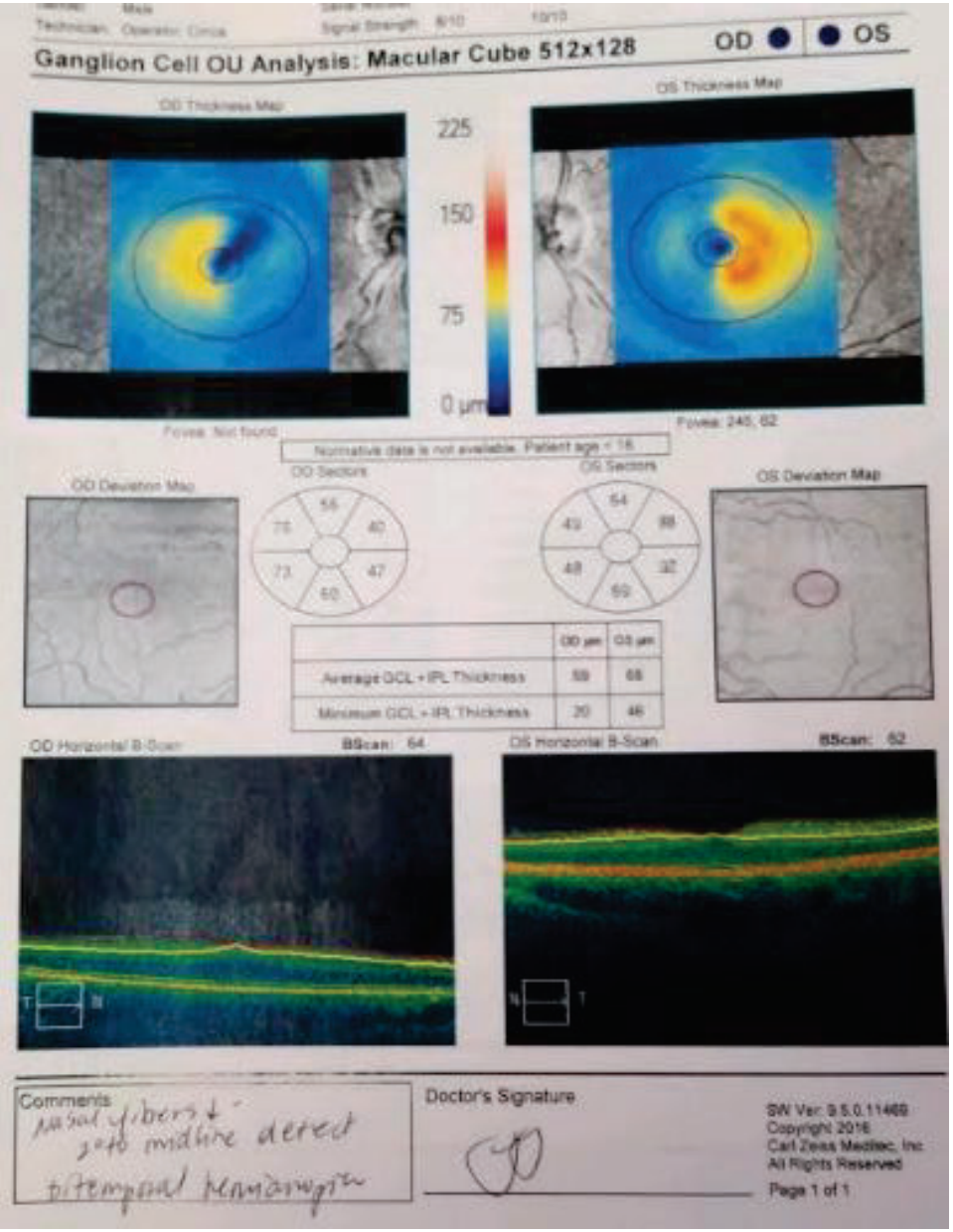
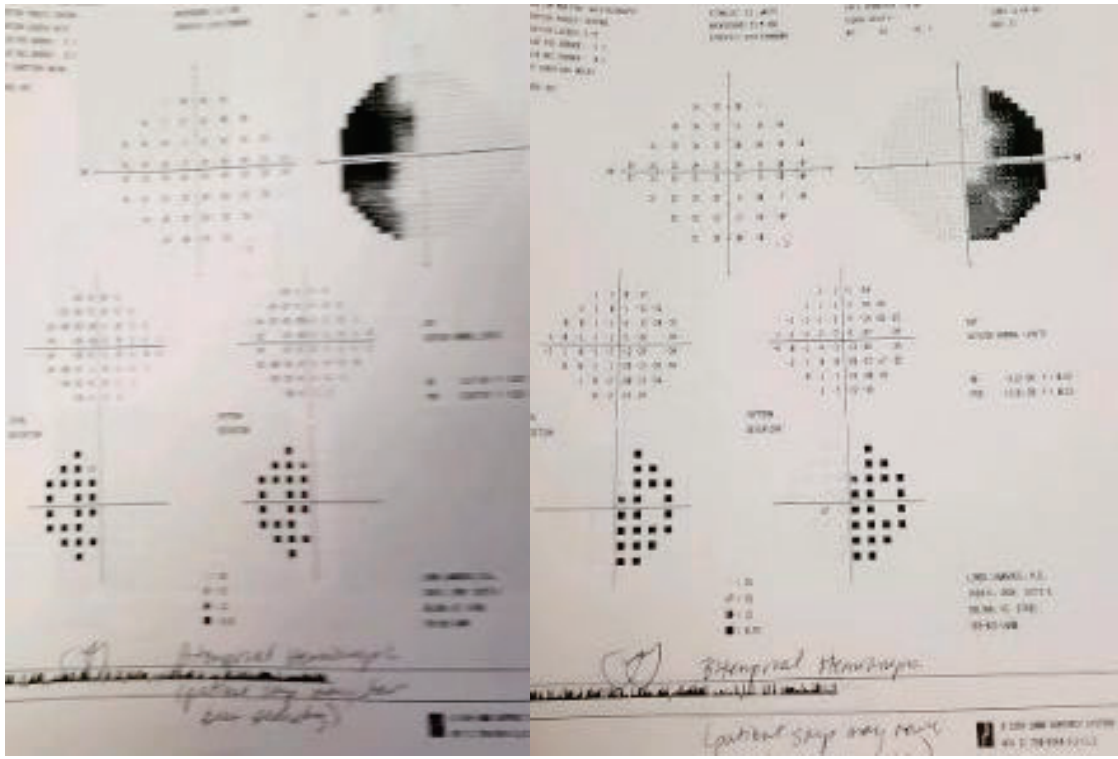
JNNP

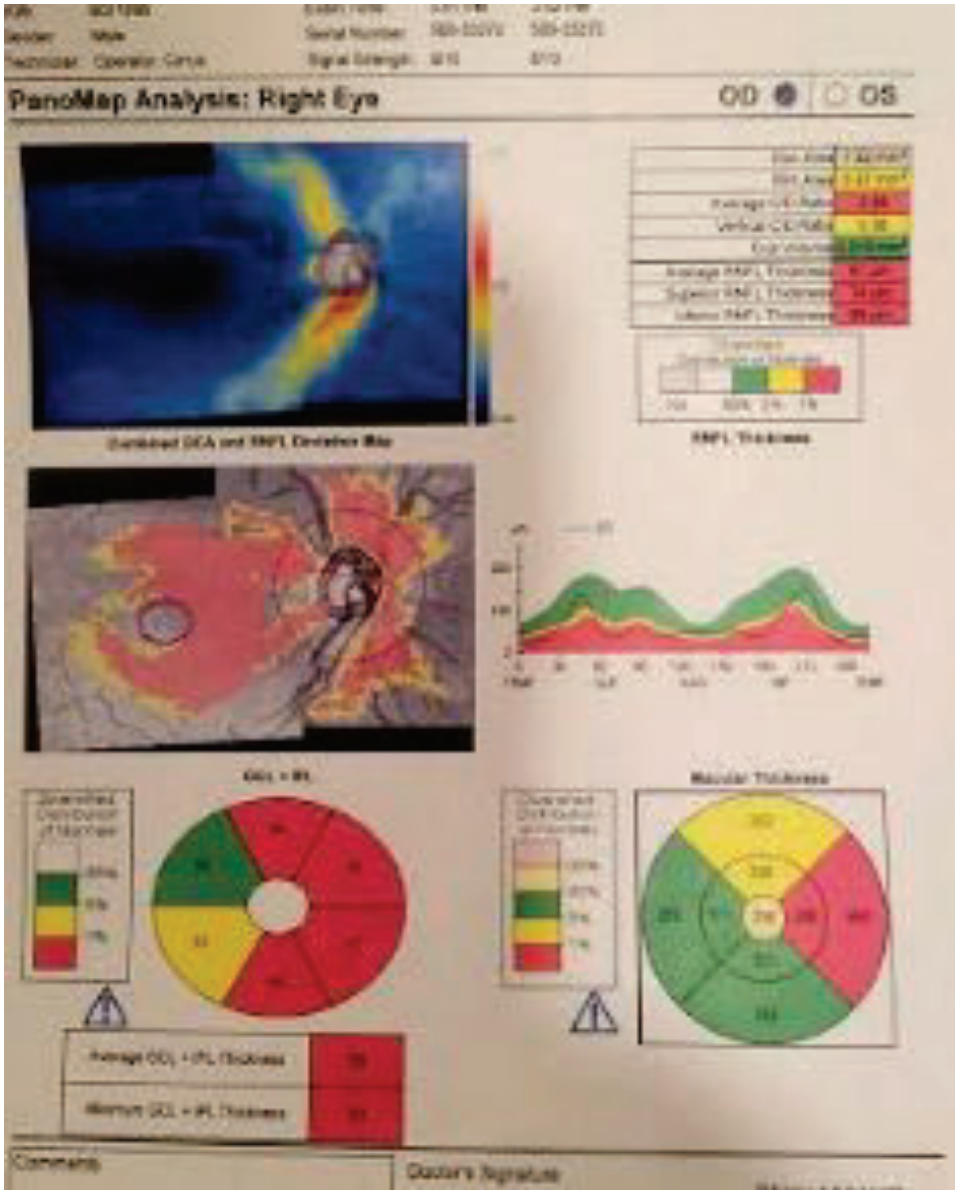
- Perimetry is a subjective test
- OCT may be more reliable
- In study of 250 persons, 65% who could not do perimetry, could do OCT

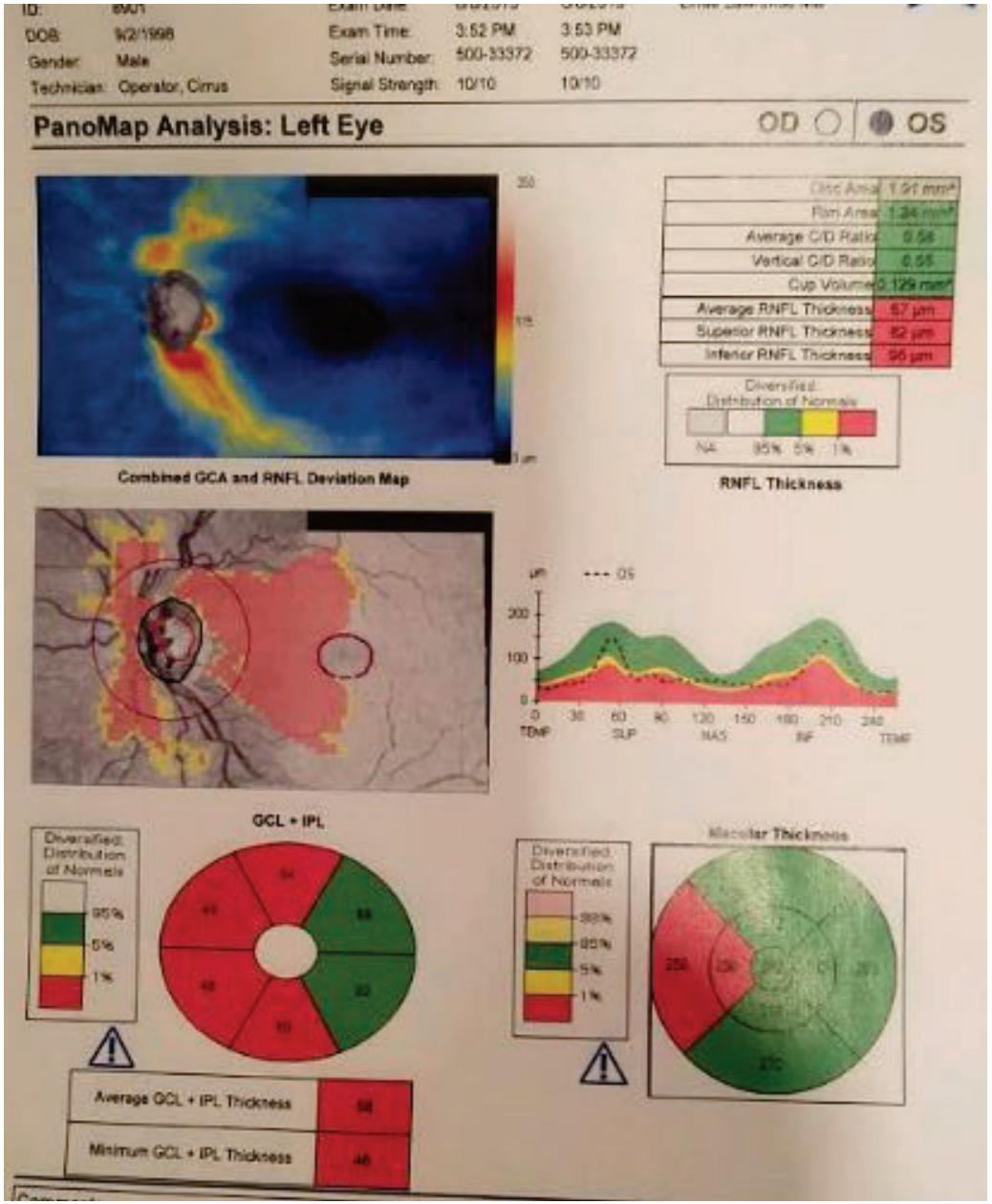






Nerve fiber layer los correlates with visual field defect


PanoMap Analysis: Right Eye
OD
OS
Combined GCA and RNFL Deviation Map
RNFL Thickness
GCL + IPL
Macular Thickness
Average GCL + IPL Thickness
Minimum GCL + IPL Thickness
Comments
Doctor's Signature


DOB: 9/2/1998
Exam Time: 3:52 PM 3:53 PM
Gender: Male
Serial Number: 500-33372 500-33372
Technician: Operator, Cirrus
Signal Strength: 10/10 10/10
PanoMap Analysis: Left Eye
OD
OS
Average C/D Ratio 0.58
Vertical C/D Ratio 0.55
Cup Volume 0.129 mm³
Average RNFL Thickness 57 µm
Superior RNFL Thickness 82 µm
Inferior RNFL Thickness 96 µm
Combined GCA and RNFL Deviation Map
RNFL Thickness
GCL + IPL
Macular Thickness
Average GCL + IPL Thickness 58
Minimum GCL + IPL Thickness 46

What about medications?

Vigabatrin

In 2003, vigabatrin was shown by Frisén and Malmgren to cause irreversible diffuse atrophy of the retinal nerve fiber layer in a retrospective study of 25 patients

This has the most effect on the outer area (as opposed to the macular, or central area) of the retina

Vigabatrin

- Visual field loss attributable to vigabatrin was first described in 1997 (Eke *et al.*, 1997)
- The prevalence estimates range from 14 to 90% (Stefan *et al.*, 1999; Besch *et al.*, 2002) but the most probable figure is in the region of 40% (Kalviainen *et al.*, 1999)
- The field defect exhibits differing levels of severity but the common feature is an eventual bilateral concentric constriction with varying extents of temporal field preservation (Wild *et al.*, 1999) (Fig. 1)

In all cases, the field loss is present in the nasal field

Epilepsy Research (2013) 105, 262–271

ELSEVIER

journal homepage: www.elsevier.com/locate/epilepsyres

Evolution of visual field loss over ten years in individuals taking vigabatrin

Lisa M. Clayton[a], William M. Stern[a], William D. Newman[b,c], Josemir W. Sander[a,d,e], James Acheson[c], Sanjay M. Sisodiya[a,d,*]

Vigabatrin

- Fundoscopy shows non-specific abnormalities, including arterial narrowing, epiretinal membrane formation, irregular sheen, abnormal pigmentation, retinal epithelial abnormalities and optic atrophy (Miller *et al.*, 1999)
- The abnormalities are either subtle or not evident until the field loss is severe
- **A pathophysiological model is proposed that involves the lengths of intraocular (unmyelinated) retinal ganglion cell axons.**

Vigabatrin and OCT

- First licensed in UK in 1989
- Within 8 years noted that 45% of person experiencing loss of visual field
- After 10 years, 93% experience VF loss
- Peripapillary retinal nerve fiber layer thinning may be a more objective tool

Clayton, LM, et al, 2011, Retinal nerve fiber layer thickness in vigabatrin exposed patients. Ann. Neurol. 69 (5), 845-854

Topiramate (Topamax)

- Used for variety of neurological disease including epileptic seizures and infantile spasms
- Topiramate-induced glaucoma is due to ciliochoroidal effusion resulting in forward displacement of iris-lens diaphragm cusing shallowing of anterio chamber and subsequent elevated intraocular pressure
- Choroidal thickening as early as one week

Medications

Antiepileptic medications

- Eye movement disorders resulting from neurologists' prescriptions will usually be from antiepileptic medications, especially phenytoin or carbamazepine (Remler *et al.*, 1990)

- Eye movements may be affected by therapeutic or toxic doses of antiepileptic drugs, or by idiosyncratic reactions

Medications

- Disturbances of all functional classes of eye movements – saccades, smooth pursuit, vestibulo-ocular reflex, fixation, vergence and gaze-holding mechanisms – occur with many drugs which act upon the central nervous system.

Medications

- Phenytoin, carbamazepine and phenorbarbitone commonly cause diplopia and gaze-evoked nystagmus (Rashbass, 1959; Umeda and Sakata, 1977; Riker *et al.*, 1978), but only rarely downbeat nystagmus (Berger and Kovacs, 1982; Chrousos *et al.*, 1987), periodic alternating nystagmus (Campbell, 1980), and partial or total gaze palsy (Mullaly, 1982; Fredericks *et al.*, 1986)

- The likelihood of adverse effects on eye movements increases with antiepileptic polytherapy
- The newer antiepileptic drugs, including gabapentin, lamotrigine, topiramate and vigabatrin, may also cause diplopia and nystagmus (Bartlett and Jaanus, 1989)
- Carbamazepine has been implicated as the cause of oculogyric crisis as an idiosyncratic reaction (Berchou, 1979

Medications

- The greatest concern of cognitive side effects in the new generation of AEDs is seen with topiramate (**Topamax**) (Martin et al., 1999; Meador et al., 2005; Salinsky et al., 2005; Thompson et al., 2000) and, to a smaller degree, zonisamide (Zonegran) (Akaho, 1996; Berent et al., 1987)
- Topiramate-induced acute myopia is probably caused by anterior rotation of the ciliary body. The myopia usually resolves after stopping topiramate

Medications

Cognitive Side Effects of Antiepileptic Drugs in Children

- David W. Loring, Ph.D.
- *Psychiatric Times* September1, 2005 Vol. XXII Issue 10

Medications

Phenobarbital (Luminal, Solfoton) of carbamazepine (Equetro, **Tegretol**), phenytoin **(Dilantin**) and valproate sodium (**Depacon**) are comparable and associated with modest psychomotor slowing accompanied by decreased attention and memory (Meador, 2005

Side effects

- Sedation and hypnosis are the principal side effects of phenobarbital
- Central nervous system effects like dizziness, nystagmus and ataxia are also common.
- in children, it may result in paradoxical hyperactivity

Medications

Gabapentin **(Neurontin**)

- in studies of young adults,children 3–12 years of age were observed to be susceptible to mild-to-moderate mood swings, hostility, concentration problems, and hyperactivity and objective cognitive impairment

Medications

Lamotrigine (**Lamictal**)

- Cognitive side effects are common with doses over 50mg qid
- Stevens-Johnson syndrome
- Lennox-Gastaut syndrome (LGS) is a severe form of epilepsy. Typically developing before 4 years of age, LGS is associated with developmental delays

Medications

Levetiracetam (**Keppra**)

associated with some reports of irritability and aggression,

favorable cognitive side-effect profile

In an open-label study in autism

beneficial effects on attention, hyperactivity and mood instability

Side effects

Somnolence, ataxia, dizziness, vertigo, diplopia

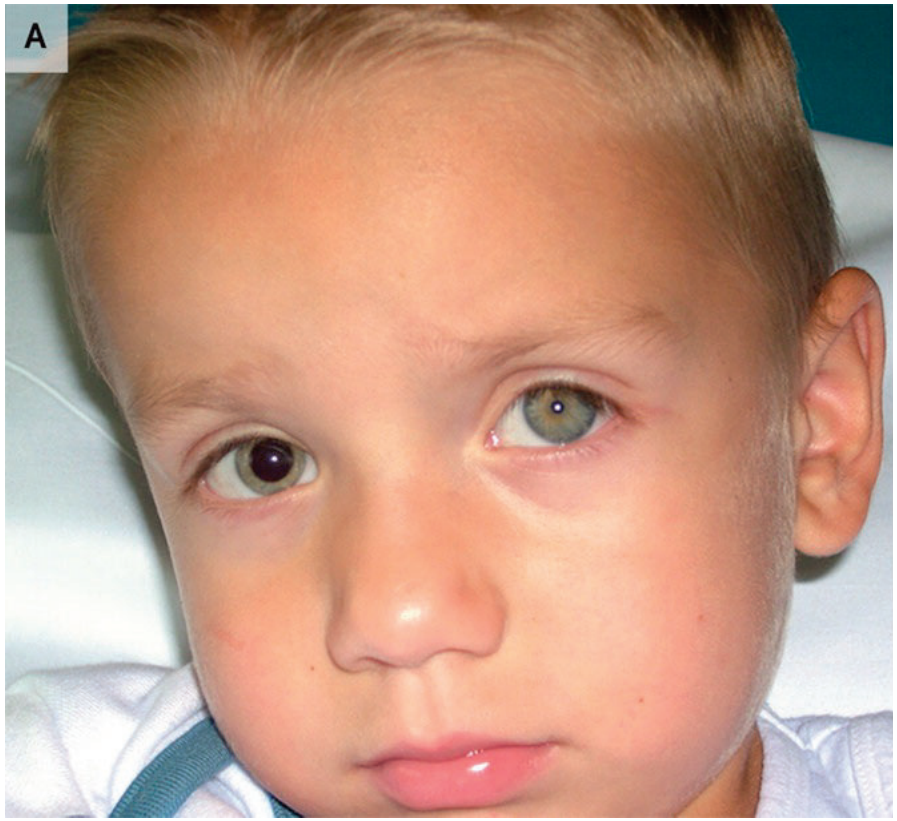
Glycopyrrolate

- anticholinergic
- *Robinul, Robinul Forte, Cuvposa*
- Reduces secretions
- Used to reduce drooling in children ages 3-16 usually with cerebral palsy

- In Europe “hyocine”

Atropine

- Used to treat Amblyopia

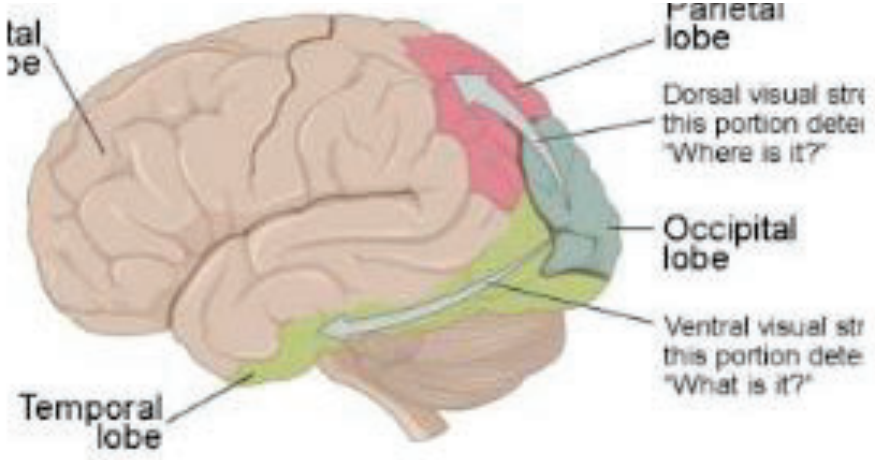


- Adverse reactions to atropine ventricular fibrillation, supraventricular or ventricular tachycardia,
- dizziness, nausea,
- blurred vision, loss of balance, dilated pupils, photophobia,,
- hallucinations, and excitation due to atropine being able to cross the blood-brain barrier.
- In overdoses, atropine is poisonous

Surgical treatment for epilepsy

- http://www.perkinselearning.org/earn-credits/self-paced/vision-after-occipital-lobectomy-and-related-surgeries

- http:/www.perkinselearningorg/



Vision After Occipital Lobectomy and Related Surgeries

Monika Jones, of the Brain Recovery Project, shares

INCIDENCE OF PEDIATRIC EPILEPSY SURGERY IN THE U.S.

Table 2. The number of surgeries by procedures over time

Type of procedures, n (%)[a]	1997	2000	2003	2006	2009
Number of cases (weighted)	375	410	589	683	706
Lobectomies, n (%)	145 (39)	135 (33)	197 (33)	194 (28)	205 (29)
Partial lobectomies, n (%)	177 (47)	223 (54)	287 (49)	376 (55)	404 (57)
Hemispherectomy, n (%)	53 (14)	57 (14)	117 (20)	130 (19)	120 (17)

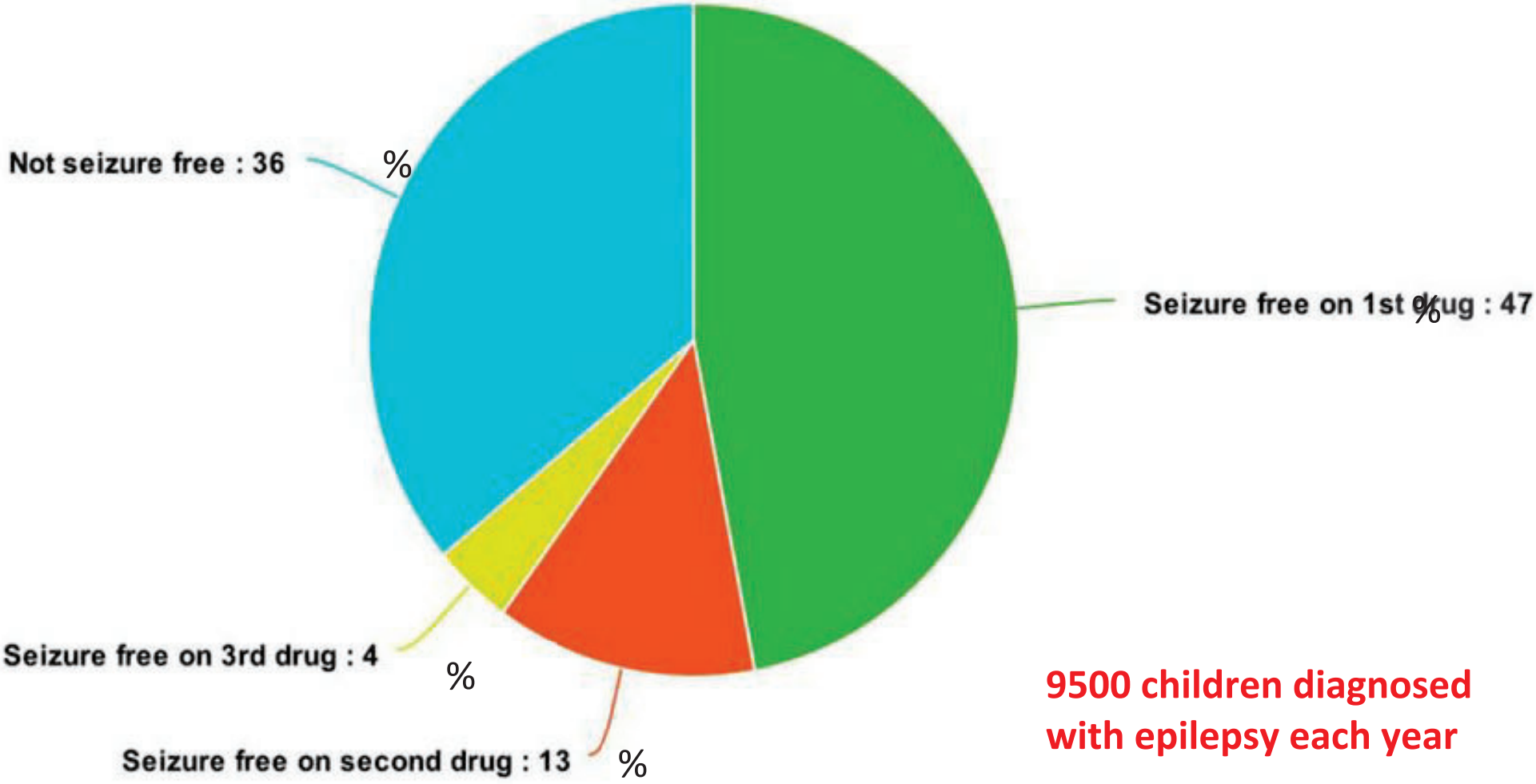
[a]Procedures may not add up to 100% due to multiple procedures in one stay.

OVERVIEW

- Why remove an occipital lobe (or more)?
- What are the resulting vision implications and how do they impact a child?
- Instruction methods, accommodations, modifications, and compensatory mechanisms to help these children succeed in school.

Epilepsy drug success

Kwan, P. Early identification of refractory epilepsy, N. Engl J of Med 2000 342:314:319



9500 children diagnosed with epilepsy each year

WHEN TO HAVE A SURGICAL EVALUATION

Failure of <u>two</u> appropriate anti-epileptic drugs … OR

Diagnosed with a “catastrophic” epilepsy … OR

Diagnosed with a condition known to be drug resistant

Cross, H. Proposed Criteria for Referral and Evaluation of Children for Epilepsy Surgery: Recommendations of the Subcommission for Pediatric Epilepsy Surgery. Epilepsia, 47(6):952–959, 2006

CATASTROPHIC EPILEPSIES

Shields, Catastrophic Epilepsy In Childhood
Epilepsia, 41(Suppl. 2):SZ-S6, 2000

Otahara syndrome

*Infantile spasms (IQ drop 4 points; CVI)

Dravet syndrome

Lennox-Gastaut syndrome

Doose syndrome

Sturge-Weber syndrome

Rasmussen's encephalitis

DRUG RESISTANT BRAIN CONDITIONS

Hemispheric malformations (hemimegalencephaly)

Rasmussen's encephalitis

In utero or post-natal stroke

Cortical dysplasia

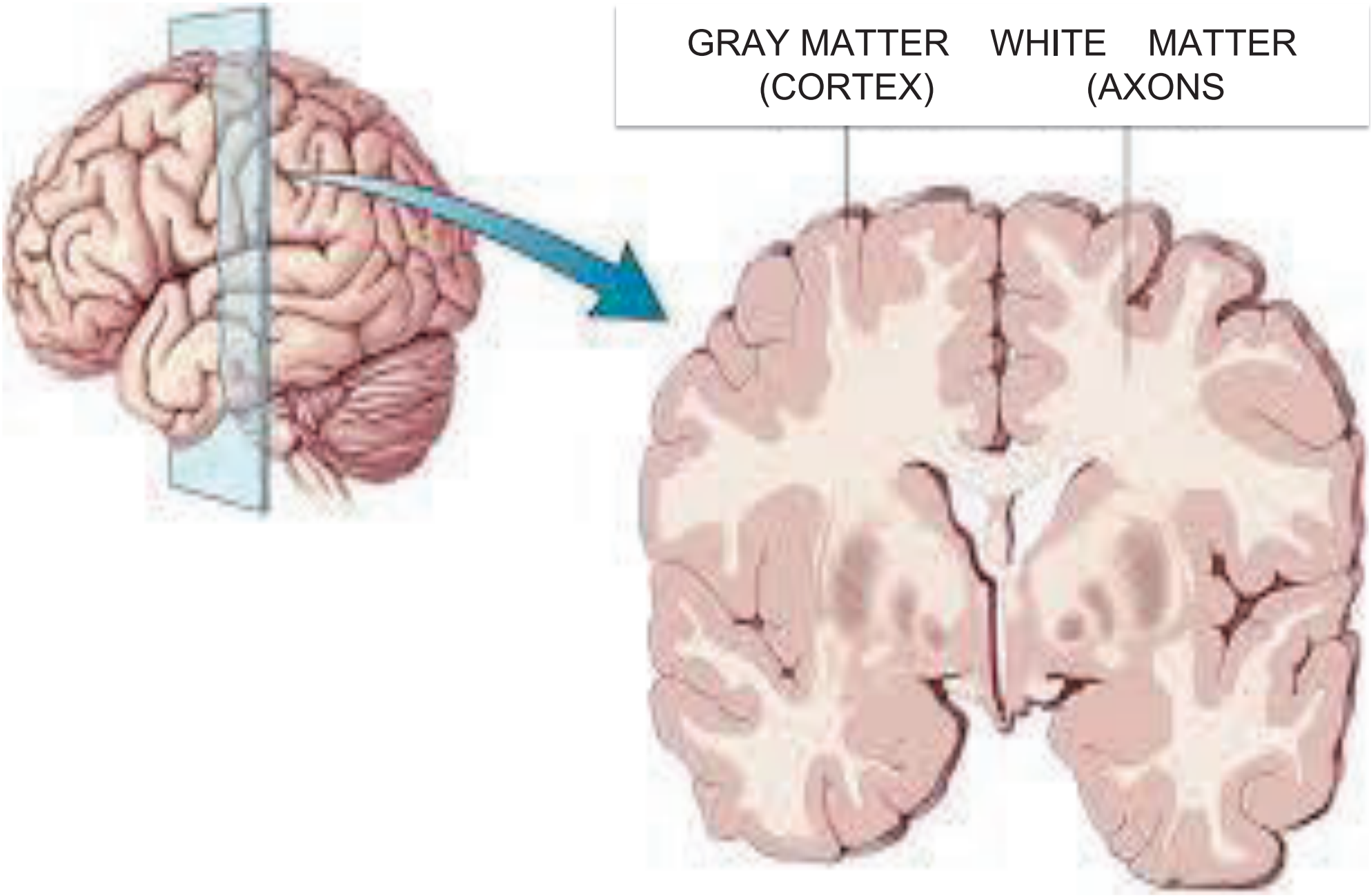
Polymicrogyria

Tuberous sclerosis complex

Hypothalmic hamartoma

Electrical status epilepticus in sleep (ESES)

Cross, H. Proposed Criteria for Referral and Evaluation of Children for Epilepsy Surgery: Recommendations of the Subcommission for Pediatric Epilepsy Surgery. Epilepsia, 47(6):952–959, 2006


GRAY MATTER
(CORTEX)
WHITE MATTER
(AXONS

What type of resection did your student have?

Tailored

- ❑ 50-60% of the occipital lobe is devoted to central field
- ❑ Goal is to preserve central vision

Complete/Multi-Lobar

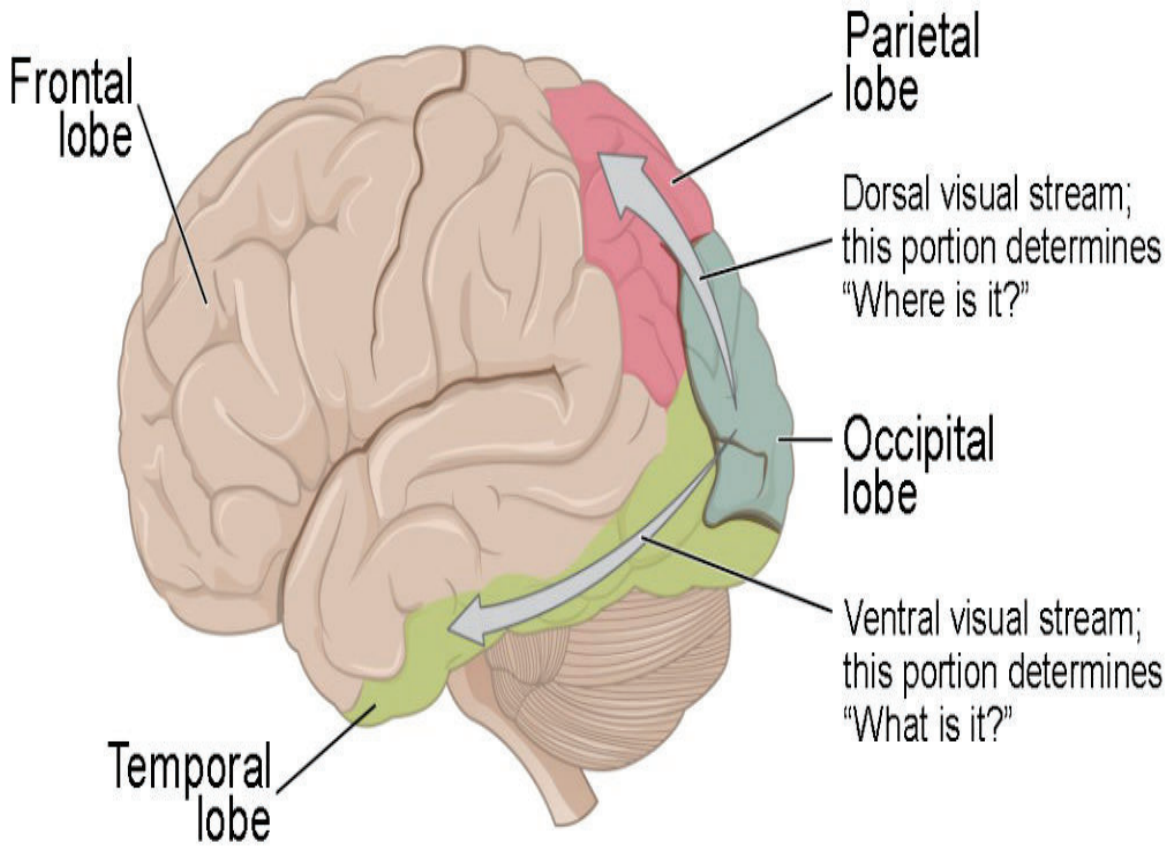
- ❑ Entire occipital lobe removed or disconnected (white matter tracts) or gray matter removed (corticectomy)
- ❑ Hemispherectomy
- ❑ Posterior quadrantic resection/disconnection
- ❑ Occipital lobectomy (w/ or w/o other lobes)

CVI?

Because the visual pathways are interrupted, homonymous hemianopia fits in the definition of CVI

Depends also on the causes of the original seizure disorder, the CVI may have existed before the surgical procedure

Post surgical complications (infection, hemorrhage, hydrocephalus) may further damage visual pathways



Case study

C-section @ 35 weeks

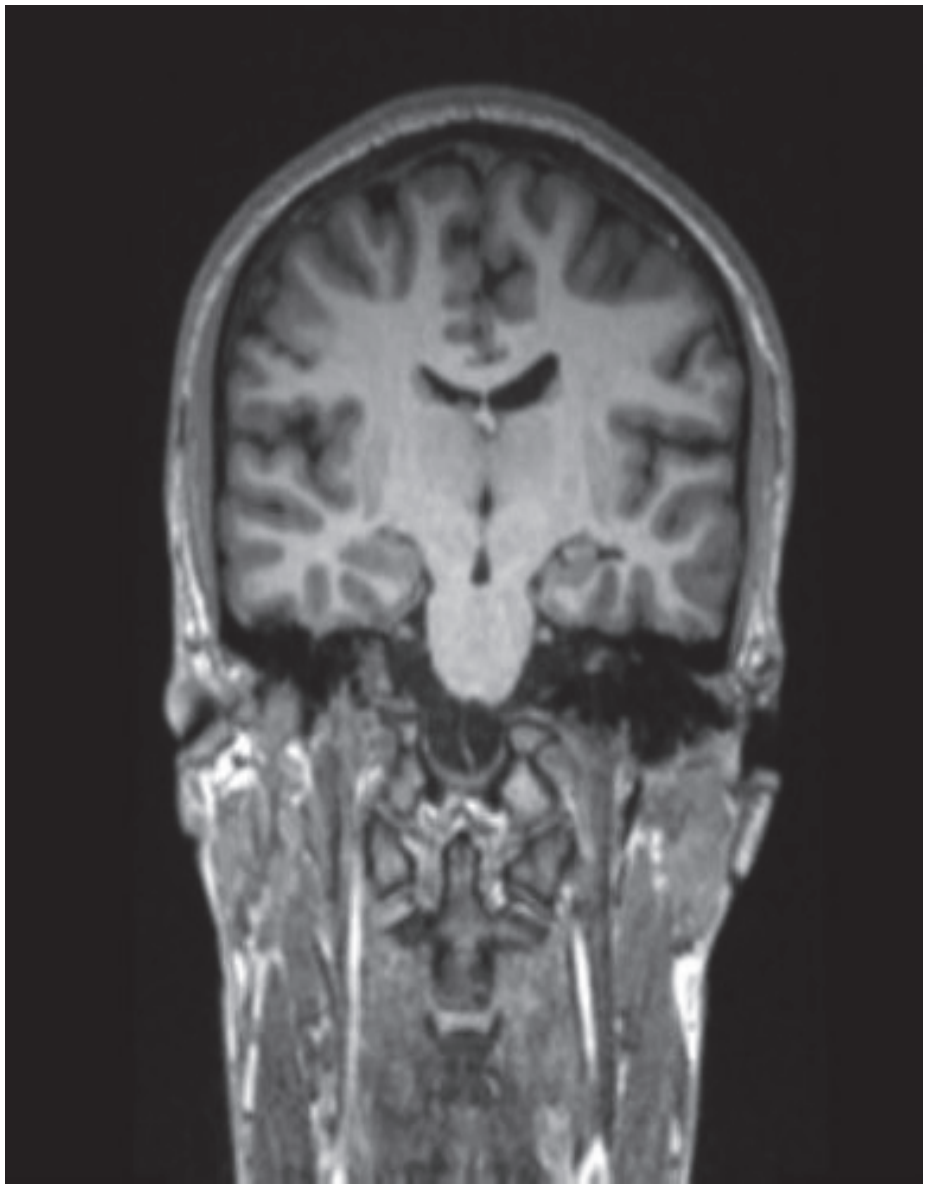
hemimegalencephaly

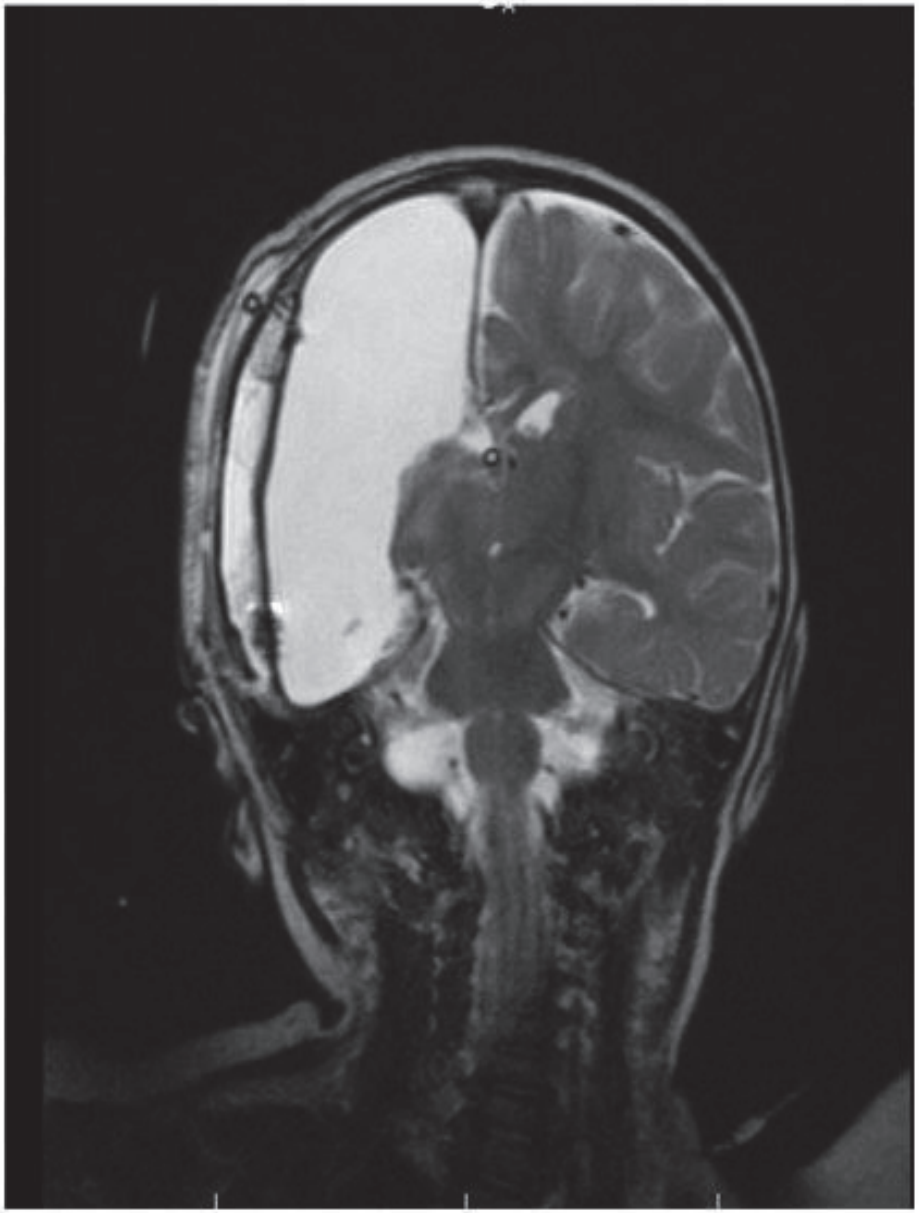
seizures in utero/at birth

infantile spasms

5 anti-epileptic drugs by three months old

Uncontrolled seizures





Hemispherectomy “+”

Hemiparesis

Auditory processing

Speech (left v. right)

Executive function/processing

Proprioception/touch

Hydrocephalus (periventricular damage?)

Seizures (71%)

Medications

IQ

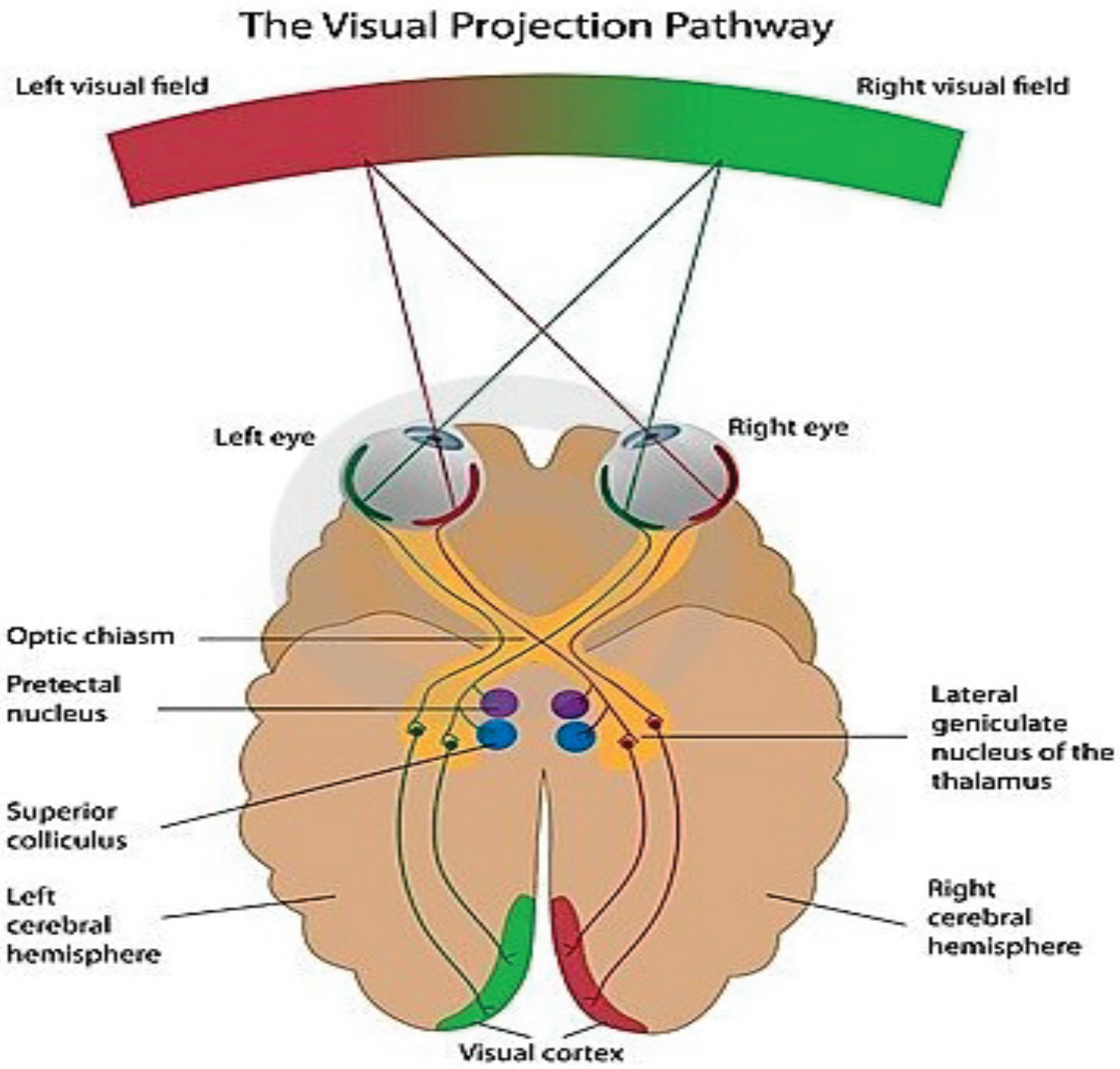
CVI (dense homonymous hemianopia and…?)

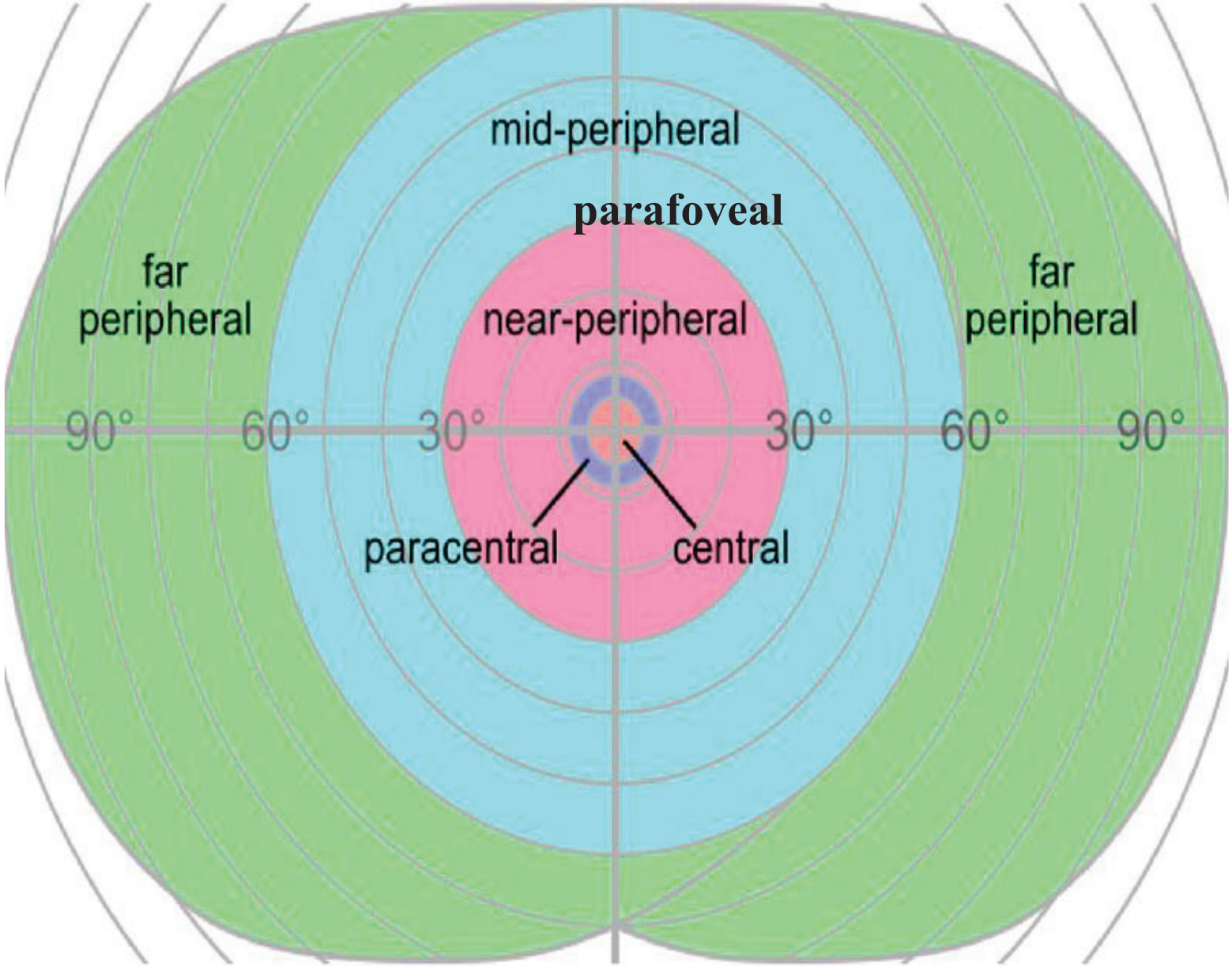
Oculomotor control

Strabismus/Exotropia (corrected?)

Nystagmus?

Optic nerve damage?


The Visual Projection Pathway
Left visual field
Right visual field
Left eye
Right eye
Optic chiasm
Pretectal nucleus
Superior colliculus
Left cerebral hemisphere
Lateral geniculate nucleus of the thalamus
Right cerebral hemisphere
Visual cortex

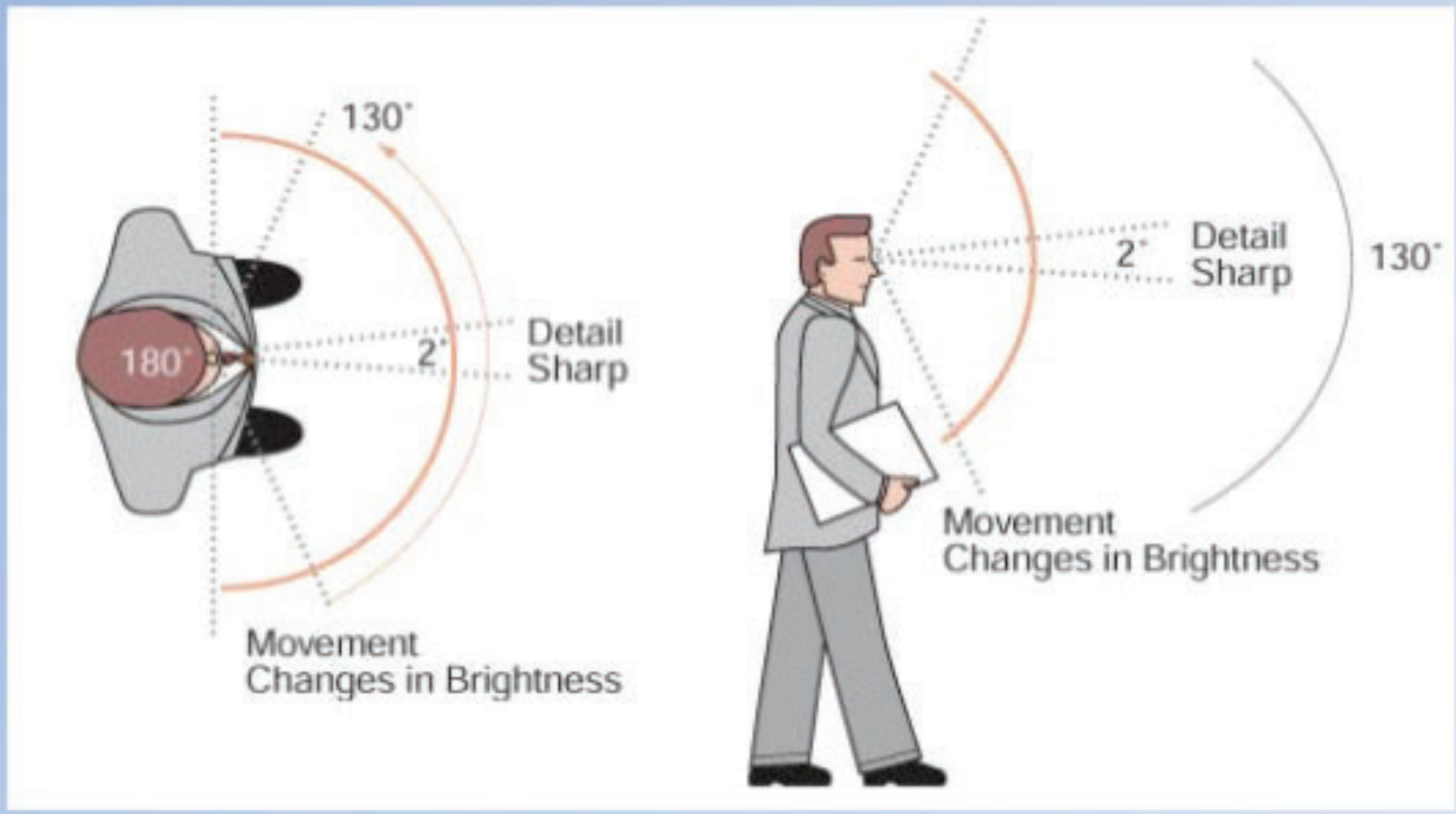

mid-peripheral
parafoveal
far
peripheral
near-peripheral
far
peripheral
90°
60°
30°
30°
60°
90°
paracentral
central

- Fovea is only 2-5 degrees of the total visual field - about the size of two times the thumbnail viewed at arms length
- Fovea represents 50% of the visual cortex (occipital lobe)
- Views detail. Only part of the retina where 20/20 vision possible.
- If object large, eyeballs must move around to view the object in detail.

Krantz, John H. (1 October 2012). "Chapter 3: The Stimulus and Anatomy of the Visual System" (PDF). *Experiencing Sensation and Perception*. Pearson Education. ISBN 978-0-13-097793-9.

Fairchild, Mark. (1998), *Color Appearance Models*. Reading, Mass.: Addison, Wesley, & Longman, p.7. ISBN 0-201-63464-3

Foveal vs. Peripheral vision



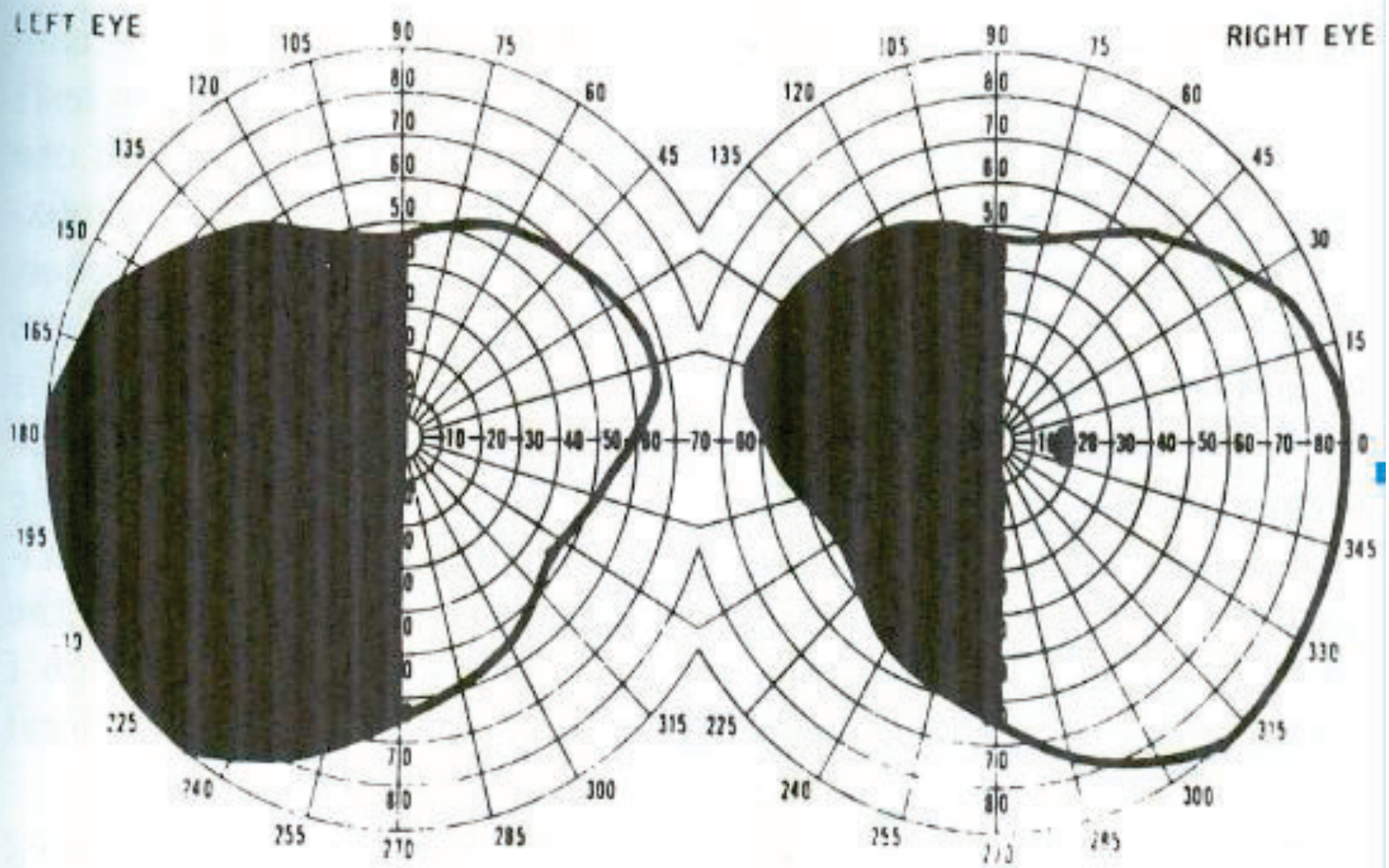
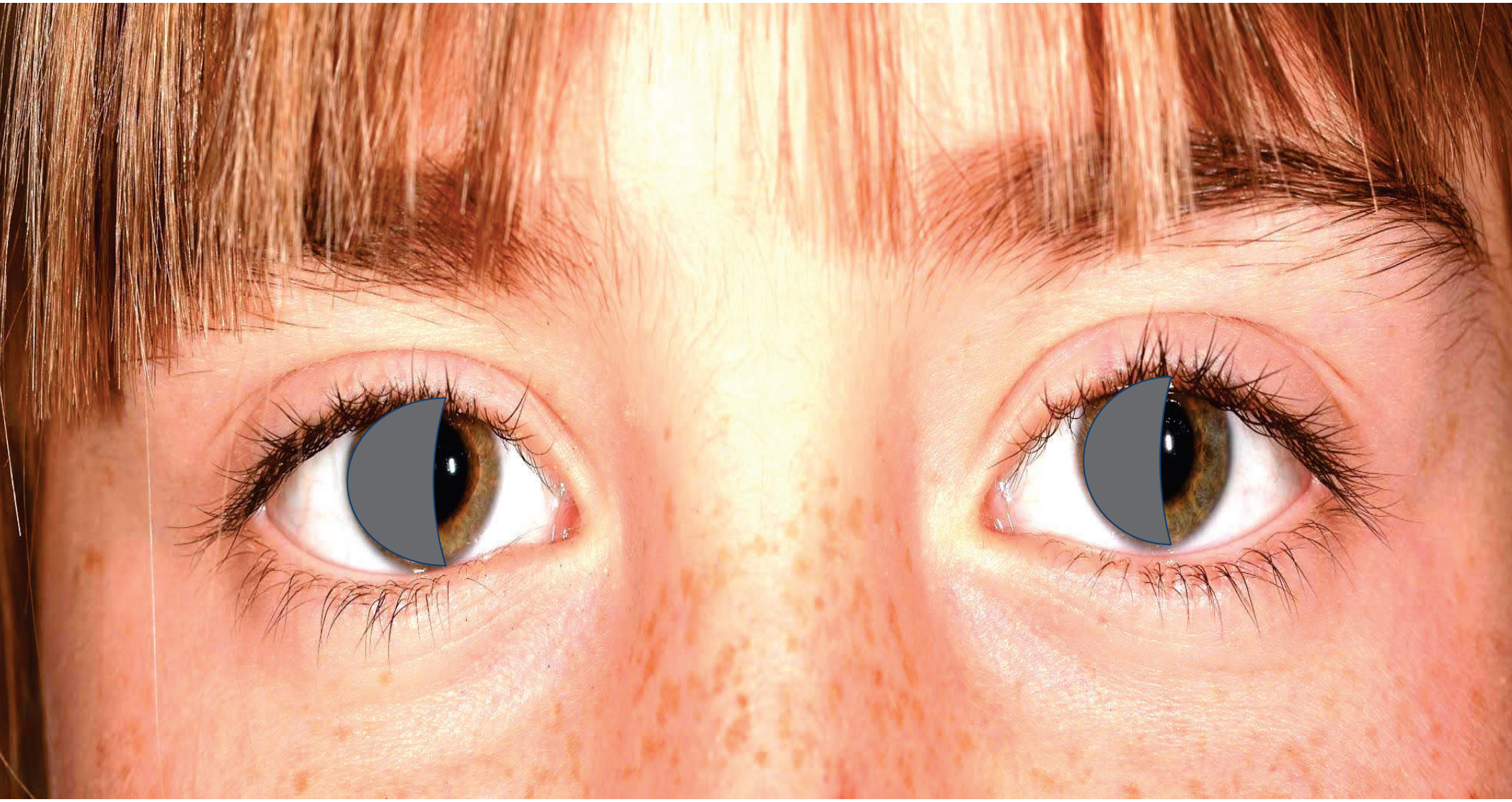
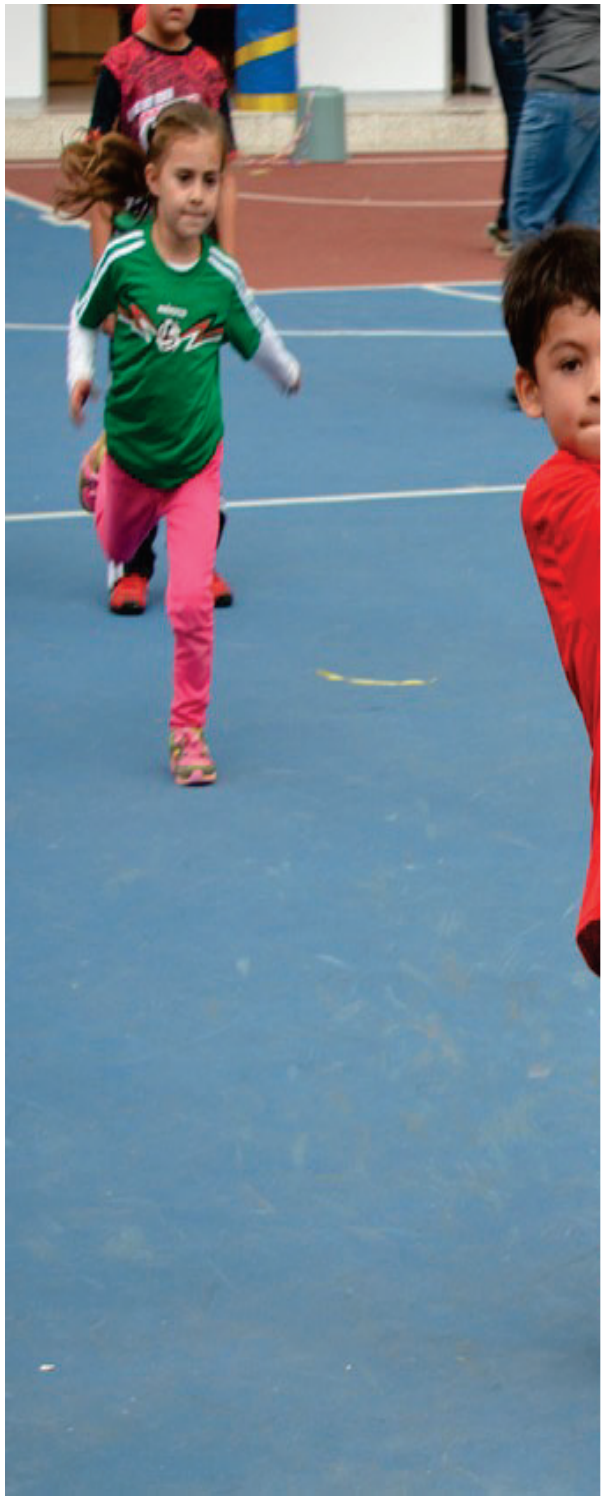


FIG 3–19.
Classic left homonymous hemianopia on peripheral visual field test.

Instruction Methods, Accommodations, and Helpful Strategies






Goal Setting
Honesty
Self-Esteem

ORIENTATION AND MOBILITY

CHALLENGES

bump into people and objects

trip and fall/stairs

pouring beverages

reduced participation in social life, sports, recess

50% states prohibit driving

visual neglect

INTERVENTIONS/TRAINING

Comprehensive eval (static/dynamic/familiar/unfamiliar)

cane?

spontaneous saccades to the blind side

mark crucial features

consistent furniture placement

Hemianopsia.net


PHOTO & DIGITAL
SPECIALISTS
INSTANT

How does the child accommodate?

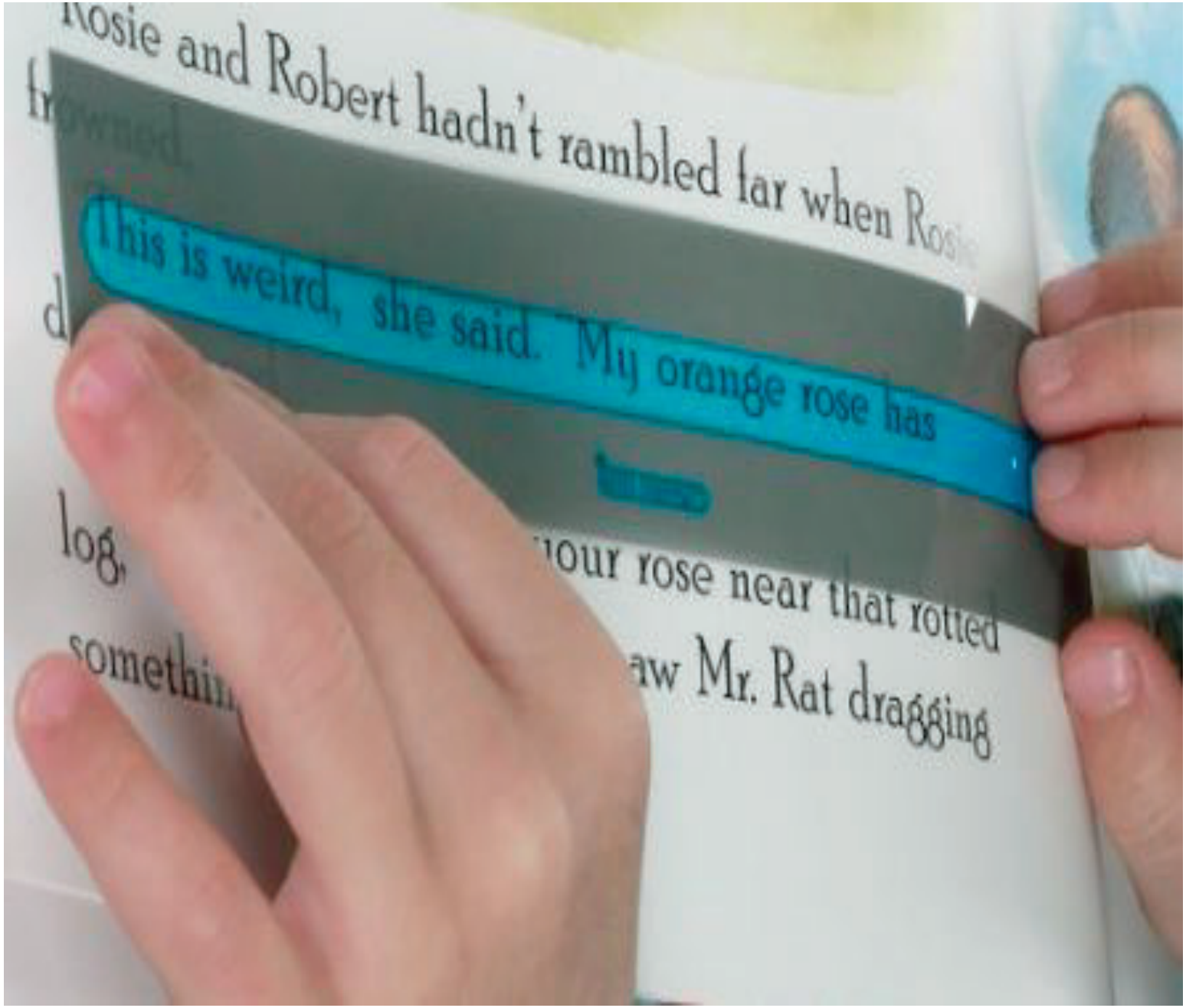
- Head tilt
- Face turn and eye gaze into hemifield (...is it autism?)
- Exotropia (but what about binocular vision)

Sma t

Large text

Last letter cancellation therapy involves teaching the child to see the end of a word by making a slash mark at the end of each word first, and then learning to read to the slash mark.

PRESENTING
TEXT
IN
A
COLUMN
RATHER
THAN
A
LINE


Rosie and Robert hadn't rambled far when Ros
This is weird, she said. My orange rose has
our rose near that rotted
aw Mr. Rat dragging

Other strategies

Teach the child to scan the page first

When reading a line of text, help the child understand the sequence of words by **moving your finger underneath** each word and down each line

Classroom seating - toward the back in the blind field (unless acuity issues, but also beware of auditory processing). Requires **continuous evaluation**

A NOTE ABOUT THE INDIVIDUALS WITH DISABILITIES EDUCATION ACT

Diagnosis is not enough to trigger IEP services

In order to be “identified” as a child with a visual impairment, the child must require “specialized instruction.”

If you don’t know what specialized instruction the child needs, the child will not qualify as visually impaired!

For more information

www.brainrecoveryproject.org