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Etiology of Vestibular/Balance Disorders in Children

Prof Soumit Dasgupta

MBBS DLO MS FRCS MSc FIAOHNS FRCP

Consultant Audiovestibular Physician and Clinical Lead

Alder Hey Children's NHS Foundation Trust, Liverpool, UK

Honorary Visiting Professor, Otology and Skull Base Surgery, University of Siena, Italy

Honorary Senior Clinical Lecturer, University of Liverpool, UK

Honorary Lecturer, University of Manchester, UK

Special considerations in children to diagnose aetiology

- History may not be forthcoming so 'vestibular behaviour' from parents/carers need to be obtained
- Testing children is an art and must incorporate fun activities and improvisations
- Often a second tester or a distractor required especially in young children
- Tests selected according to the developmental age of the child
- Laboratory norms for tests used in adults are **not established** in children – every paediatric vestibular laboratory must have its own norms
- Aetiology and vestibular phenotypes are markedly different in children as compared to adults that must be borne in mind and objective of assessment is also to figure out a cause for decompensation

- Remember the neurology and neurotology interface is far more close than what you will find in the adult population

- The approach to paediatric vestibular medicine is holistic and a good knowledge in paediatric neurology, developmental paediatrics, paediatric ophthalmology and paediatric medical specialities is required as paediatric vestibular phenotypes span across specialities and contribute to overall development in children

- Given the cerebral plasticity in children, vestibular rehabilitation has a better functional outcome in children than in adults, thus, diagnosis is crucial

- Therefore, to practice vestibular medicine in children, a thorough holistic knowledge is required in paediatrics with dedicated training and insight and it is inappropriate to extrapolate the adult algorithm to children

- One third of children with hearing loss will also present with a vestibular deficit

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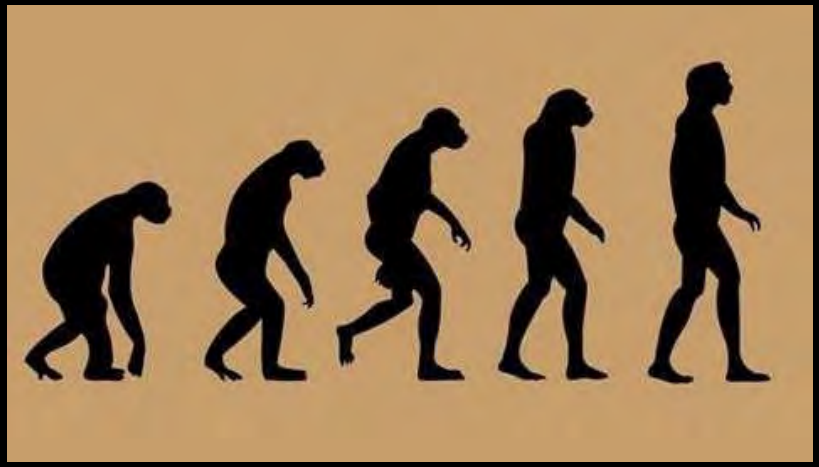
Development



In utero

- Vestibular complex fully formed
- Synapses/neuronal connections established
- Ossification of bony labyrinth complete
- Otoconial mechanotransduction established but canals not functional
- Genetically controlled targeted development is complete regulated by 38 identified genes

After birth

- Follows a critical period when experience of external information is needed for normal development of function
- This is the period of stimulus controlled development process that follows a temporal pattern
- Dependant on neurotransmitter expression and regulation of synaptic connections

Innate differences between child and adult metabolism

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Physiology	Aetiology correlate
Higher cellular metabolism and mitotic rate demanding high energy	Acute viral vestibular neuritis half as rare as in adults
Cross talk between metabolism and immune system higher in children	Acute viral vestibular neuritis half as rare as in adults
Priming of immune system generates expended repertoire of immune cells	Acute viral vestibular neuritis half as rare as in adults
Otolith anchorage proteins mature in childhood and then degenerate	Idiopathic BPPV rare
Stria vascularis and spiral ligament shows more integrity due to high metabolic rates	Idiopathic MD rare
Labyrinthine trauma behaves differently due to cerebral perfusion, anatomy and intracranial pressure	Variable and unpredictable labyrinthine damage following trauma
Synaptic transmission and neuronal circuitry in a state of high activity	Random firing more common explains VM as so common in children

Glynn, J.R., Moss, P.A.H. Systematic analysis of infectious disease outcomes by age shows lowest severity in school-age children. Sci Data 7, 329 (2020). https://doi.org/10.1038/s41597-020-00668-y
Huang S and Qian S(2022) Advances in otolith-related protein research. Front. Neurosci. 16:956200. doi: 10.3389/fnins.2022.956200
Figaji AA. Anatomical and Physiological Differences between Children and Adults Relevant to Traumatic Brain Injury and the Implications for Clinical Assessment and Care. Front Neurol. 2017 Dec 14;8:685. doi: 10.3389/fneur.2017.00685
Wang C et al. Pediatric Meniere's disease. Int J Pediatr Otorhinolaryngol. 2018; 105:16-19

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Paediatric vestibular disorders

Inspired by Children

Aetiology	O'Reilly 2007 (chair/calorics)	Vacher 2008 (chair/calorics)	Hamilton 2015 (vHIT)	Sommerfleck 2016 (vHIT)	Dasgupta series 2017 (vHIT)
Peripheral vestibular	29.5%	18%	40%	22%	20.3%
Migraine and BPVC	24.2%	45%	24%	49%	18.5%
Traumatic head injury	9.8%	10%	6%	6.8%	3.7%
Central	9.1%	<5%	3%	2%	3.7%
Third window	<1%	<1%	6%	<1%	26%
Genetic	N/A	N/A	N/A	N/A	12.9%
Idiopathic	N/A	N/A	N/A	N/A	12.9%
Others	26.4%	21%	21%	19.2%	5.7%

A.I. duPont Hospital for Children, Wilmington, Delaware
Alder Hey Children's Hospital, Liverpool

Aetiology

- Peripheral vestibulopathy/third window
- Vestibular migraine
- Motor/developmental delay
- Traumatic brain injury
- CNS structural lesions
- Behavioural/psychogenic
- Idiopathic
- Movement disorder/neurodegenerative
- Encephalopathy
- Vascular
- Peripheral neuropathy
- Oculomotor abnormality

Prevalence of 8 – 18% between 1 to 15 years
35% of paediatric balance disorders

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Congenital/genetic vestibular disorders

Structural deformities

- Complete aplasia (Michel)
- Rudimentary otocyst
- Incomplete partition of cochlea/vestibule
- Third windows
- Canal/otolith dysplasia
- Arnold Chiari

The SNHL group

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- Highly heterogenous phenotypes and genotypes
- Majority AD inheritance but those causing AD may be AR
- Associated with SNHL
- AD usually post lingual

Genetic syndromic with cochleovestibular dysplasia

- Branchiotorenal spectrum - EYA1, SIX1, SIX5 AD
- CHARGE – CHD7 AD
- Goldenhar - Unknown
- Pendred – SLC26A4 AR with thyroid disorder
- Trisomy 13, 18, 21
- Noonan/Turner's – XO sporadic and mosaic
- Wildervanck
- Craniofacial syndromes -Apert (FGFR2), Crouzon (FGFR2), Pfeiffer (FGFR2), Saethre Chotzen (TWIST1),Treacher Collins syndrome (TCOF1) AD

Genetic syndromic without otic structural deformities

- JLN (cardiological) – KCNQ1 AR
- Alport (renal) – COL4A3 AD
- Alstorm (cardiological, eyes, DM) – ALMS1 AR
- Usher (Eyes) – Type 1 - MYO7A, USH1C, CDH23, PCDH15, USH1G, CIB2 variab
  Type 3 - CLRIN1
- Chromosomal aberrations
- The ataxia group (SCA, EA, ARASCS - cerebellum)
- The HSMN group (CMT)

Genetic non syndromic with SNHL without structural deformities

- DFNA 9 – COCH AD
- DFNA 11 – MYO7A AD
- DFNA 12 – TECTA AD
- DFNA 15 – POU4F3 AD
- DFNA 28 – GRHL AR
- DFNB1 – GJB2 and GJB6 AR
- DFNB 4 – MYO7A AR, atypical USH1B
- DFNB 12 – ATPB2/CDH23 AR
- DFNAB 103 – CLIC5 AR

Genetic non syndromic with SNHL with structural deformities

- DFNB4- KCNJ10, FOXI1 AR with EVA
- X linked gusher – POU3F4 gene X linked with incomplete partition and vestibular dysplasia

Other genetic

- Familial MD (MICA)
- Motion sickness (PVRL3)
- Metabolic conditions (XLHR)
- Von Hippel Lindau syndrome (TSG)
- DIDMOAD (Wolfram)
- ANSD (otoferlin, pejvakin)
- Meniere's disease (FAM136, DTNA, COCH, OTOG)
- Vestibular migraine (CACNA1, TRPM7)

Congenital disorders - phenotype

- Motor developmental delay
- Hearing loss – a third of congenital hearing losses with vestibular loss as well
- Unsteadiness and ataxia
- Incoordination and navigational difficulties
- Cognitive delay
- Behavioural difficulties especially in play grounds
- Syndromic stigmata
- Unilateral or bilateral vestibular diagnostic markers
- Learning problems
- Muscle hypotonia

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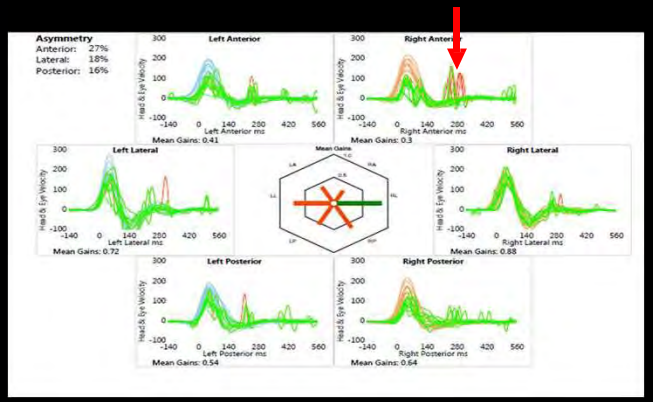
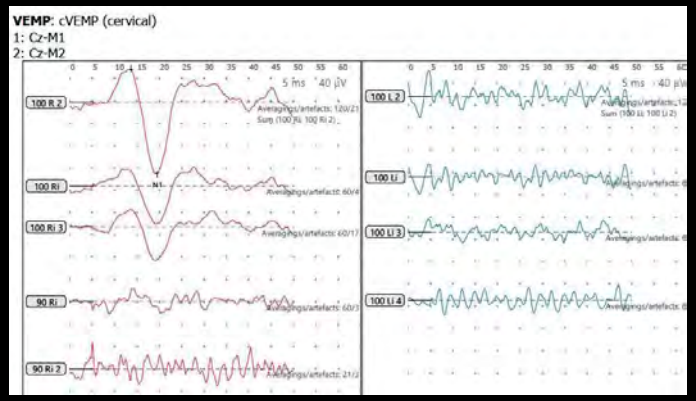
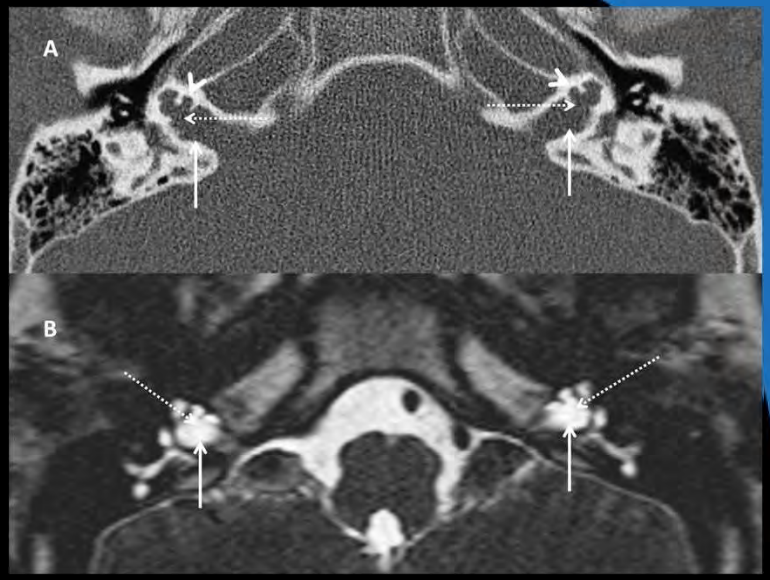
Congenital disorders – example 1







- Child with late onset mixed HL
- Motor development delay
- Neurodevelopmental issues/incoordination; ASD
- Apprehensive with physical activities
- Learning deficits
- Excellent results with rehabilitation

X linked POUF4 mutation

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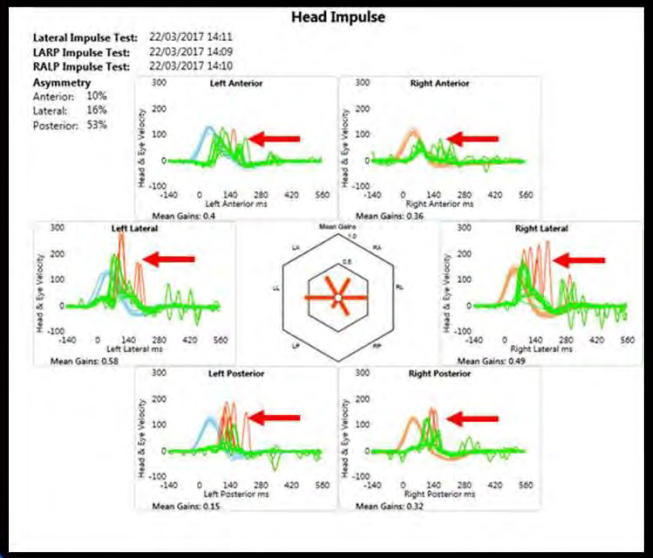
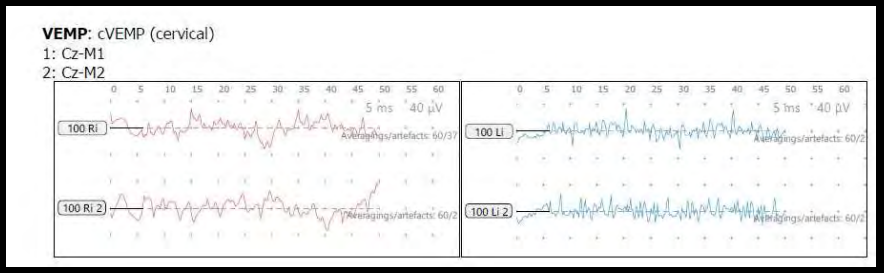
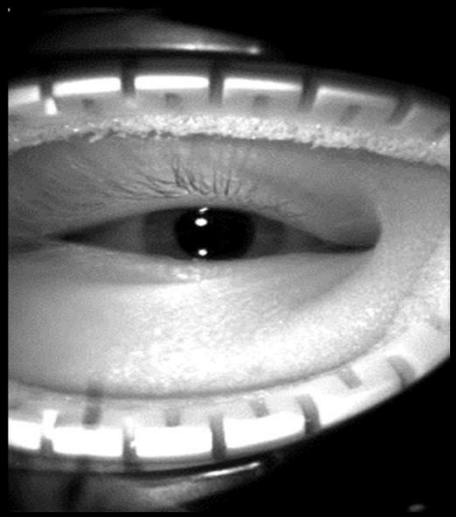
Congenital disorders – example 2

- Child with late development of motor skills and unsteadiness- bilateral moderate SNHL, scans normal, travel sickness and acrophobia; severe vestibular weakness
- Avoidance and withdrawal behaviour in playgrounds leading to poor social peer interaction
- Excellent results with customised vestibular rehabilitation







Bilateral cochleovestibular involvement, genetic MYO7A mutation

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Other peripheral vestibular disorders

Inspired by Children

Paediatric balance disorders – otological disorders

- Infective/ inflammatory – OME, CSOM, other middle ear, labyrinthitis, neuritis, meningitis, AIED
- Ototoxicity – Aminoglycosides, cisplatin, diuretics, antimalarials
- Traumatic – head injury, perilymph fistula, iatrogenic
- Third window disorders
- Miscellaneous – Endolymphatic hydrops, BPPV
- Metabolic conditions – DM, thyroid disorders, vitamin D deficiency, electrolyte imbalances

Otological disorders – acute vestibular events

- Acute vestibular viral neuritis is much less common than adults due to increased metabolic rate of the developing system
- An acute vestibular event in children is usually secondary to space occupying lesions, autoimmune ear disorder, a bacterial labyrinthitis following middle ear disorder, meningitis or sepsis, ototoxicity, intracranial radiation, secondary endolymphatic hydrops, hyperviscosity syndromes due to any reason (for example leukemias, sickle cell crisis)
- The phenotype is characterised by sudden onset of dizziness with or without HL followed by near total recovery within a few weeks and then recurrent vestibulopathy if decompensated
- An OME can generate either an acute phenotype or a chronic one due to ionic alterations in endolymphatic fluid

Otological disorders – recurrent vestibulopathy

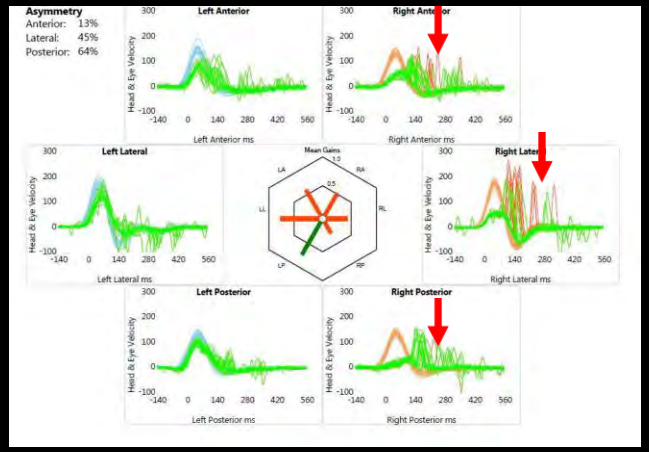
- Chronic presentation with episodic periods of decompensation
- Vestibular phenotype with dizziness on provocation or movement or positional change
- Usually short lasting and can be frequent attacks
- Visual vertigo, recent onset travel sickness and acrophobia may be present
- Usually a defined factor for decompensation present that needs to be diagnosed
- May cause a significant limitation and restriction in life
- If untreated may lead to a chronic condition but this is rare as cerebral plasticity is robust

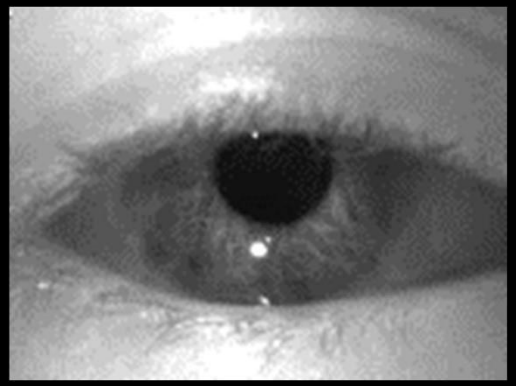
Otological disorders – inflammation and infection

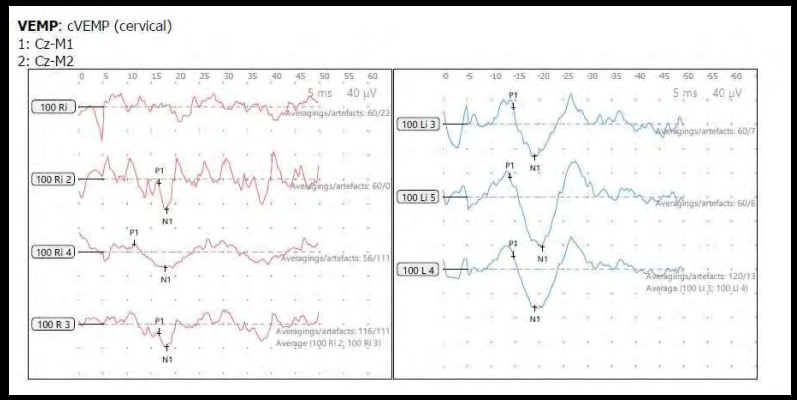
- Phenotype can be acute or chronic with vestibular symptoms
- Bacteria include the organisms causing meningitis, sepsis, CSOM and Borrelia
- Virus include herpes group, HIV and CMV
- Spirochaetes include syphilis
- Autoimmune ear disorder syndromic in systemic autoimmune disorder (SLE, RA, PAN, Bechet's, coeliac, thyroiditis, DM) or non syndromic de novo type AIED
- May extend to recurrent vestibulopathy and thus lifestyle is affected

Otological disorders - example of inflammation

- Child with acute imbalance, joint pain, hearing loss almost overnight seen by paediatrics, very reliant on visual sensors, head movements very difficult, walking with support with a veering gait, very difficult to ambulate in the dark; balance improved over a period of days but hearing remains severely affected







- Raised ESR, CRP and IgG; CT/MRI normal
- Severe SNHL on the right
- Treated with steroids followed by vestibular rehabilitation with favourable outcome

- Autoimmune ear disorder with acute labyrinthitis on the right
- Eventually proven to be juvenile rheumatoid arthritis

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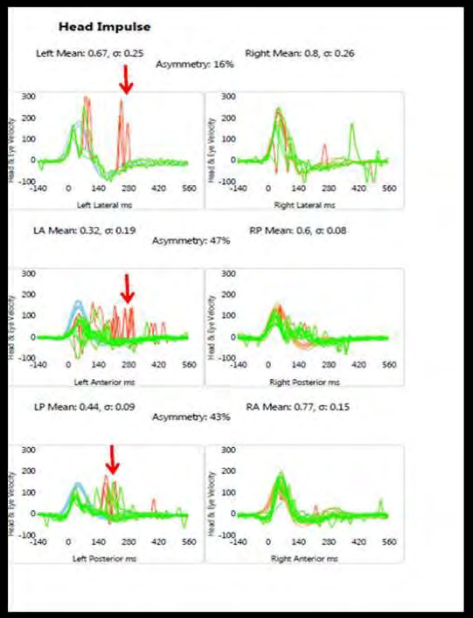
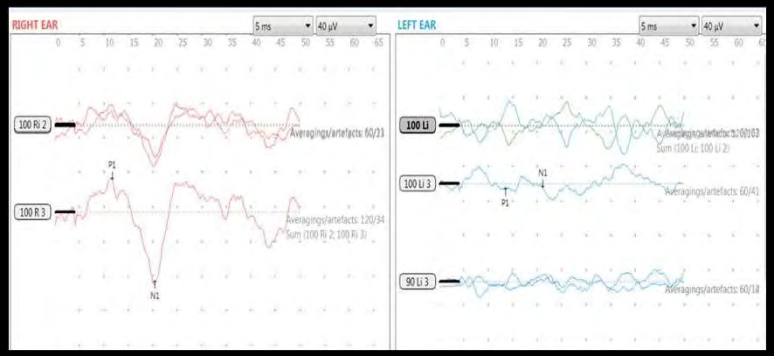
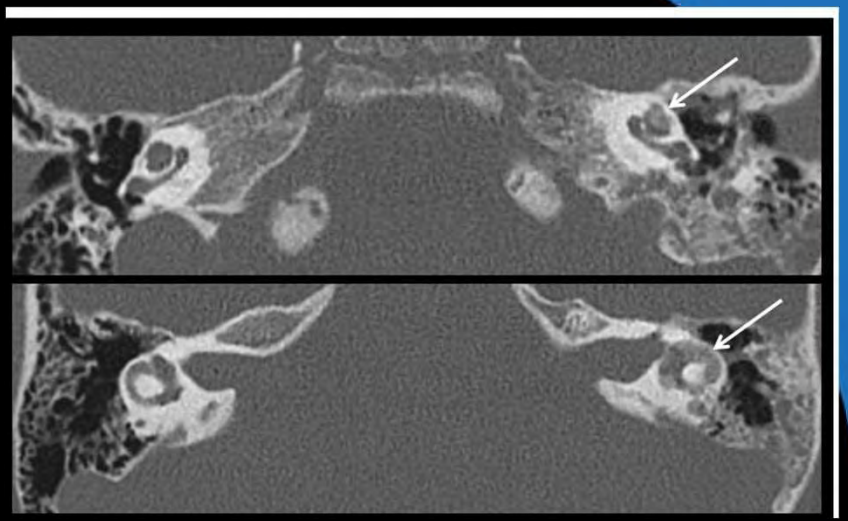
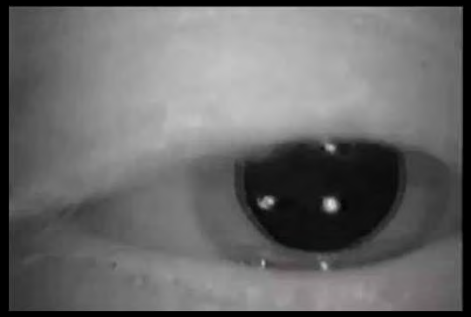
Otological disorders – example of infection









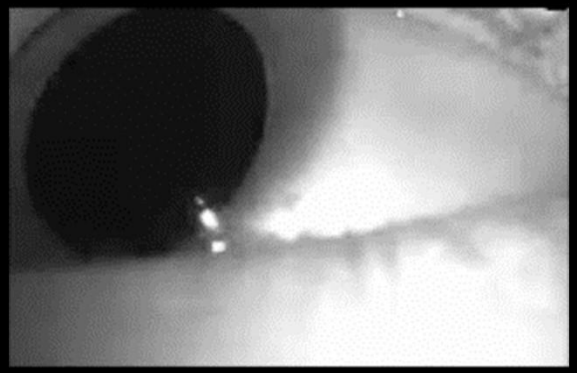
Acute left labyrinthits probably provoked by past PBT

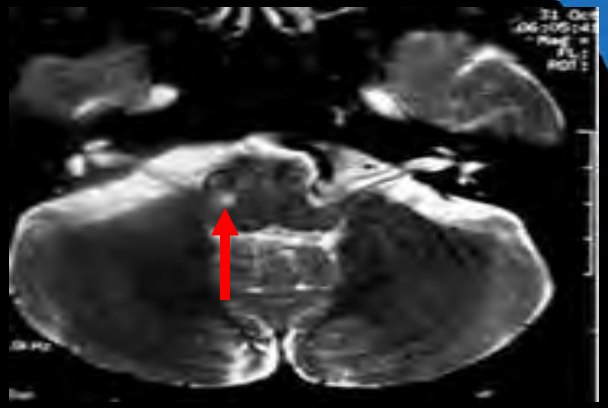
- Child with treated EAC cancer with high fever and raised septic inflammatory markers
- Acute SNHL and severe dizziness and loss of balance years after PBT
- Complete recovery within 4 weeks
- Asymptomatic from vestibular aspect

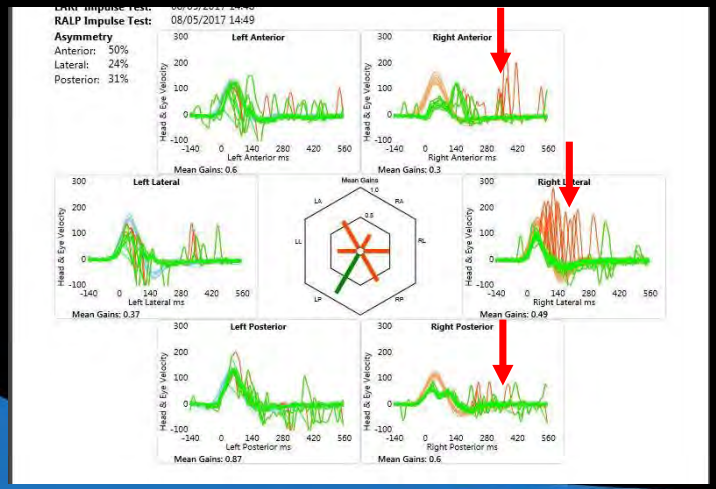
Otological disorders – Space occupying lesions

- Commonest CPA tumour is vestibular schwanomma associated with NF2
- Other tumours are meningioma and lipoma
- SOLs include epidermoid cysts, arachnoid cysts, granulomas, cross arterial compression syndromes with vestibular paroxysmia (brief lasting spells in seconds due to provocation' HVIN positive) and AVMs
- Malignant tumours in 10%
- Presentation may be acute or chronic and affects balance and causes dizziness
- SOL maintains decompensation
- HL might not be present

Space occupying lesions - example







- Child with acute presentation with CPA syndrome including cochleovestibular symptoms
- VFT severely deranged
- Recurrent vestibulopathy with vestibular neuralgia

CPA AVM with acute bleeding - compressive vestibular neuralgia, excellent response with carbamazepine and stereotactic gamma knife debulking

Otological disorders – Ototoxicity

Agents

- Aminoglycosides
  Gentamycin, Tobramycin,
  Sterptomycin
- Platinum compounds
- Diuretics Frusemide
- Antimalarials Chloroquin
- Antiepileptic Phenytoin

Risk factors

- Genetic susceptibility
- Poor nutrition and anaemia
- Renal compromise
- Hypoalbuminemia
- May be dose related
- Extremes of age
- Synergism with other drugs
- Cranial irradiation
- Pre existing hearing losses
- Previous noise damage

Acute or delayed presentation with balance problems and recurrent vestibulopathy; always bilateral symmetrical unless posterior fossa tumours

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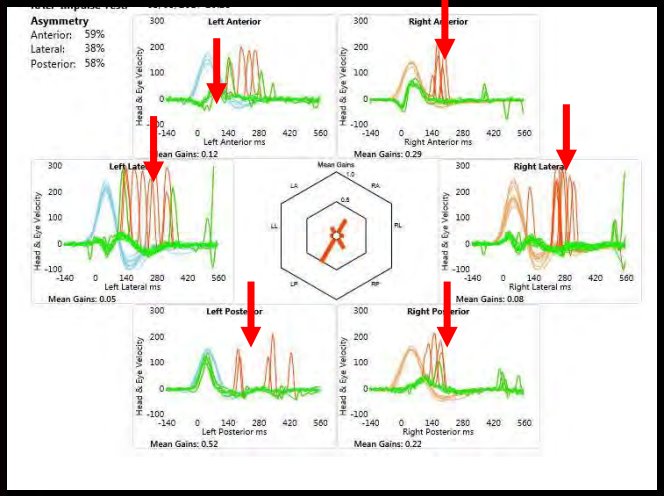
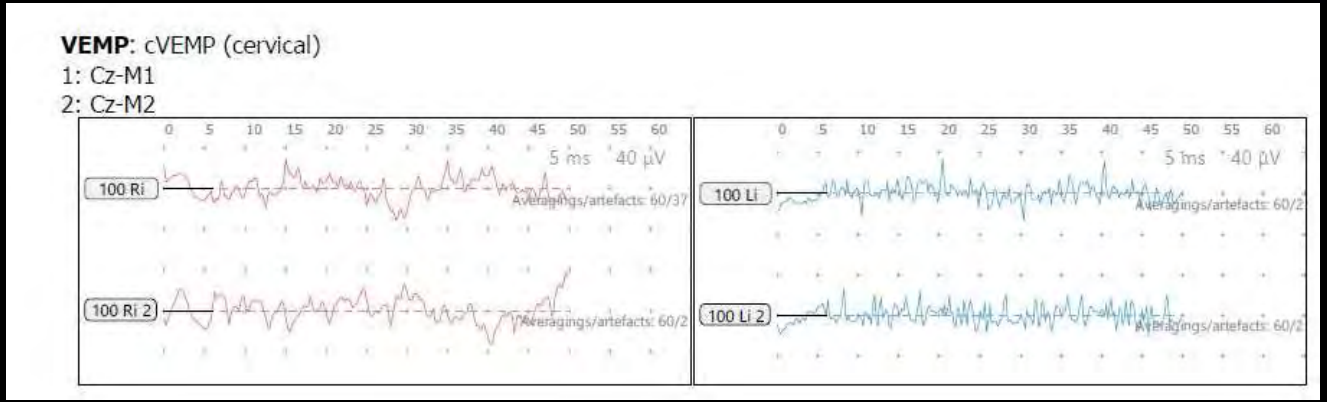
Ototoxicity - example





- Child with severe unsteadiness after second cycle of chemotherapy for medulloblastoma with cisplatin; SIOP 2
- Ototoxicity rescue
- Left with recurrent vestibulopathy affecting childhood
- Excellent results with customised vestibular rehabilitation

Acute bilateral vestibulototoxicity following cisplatin

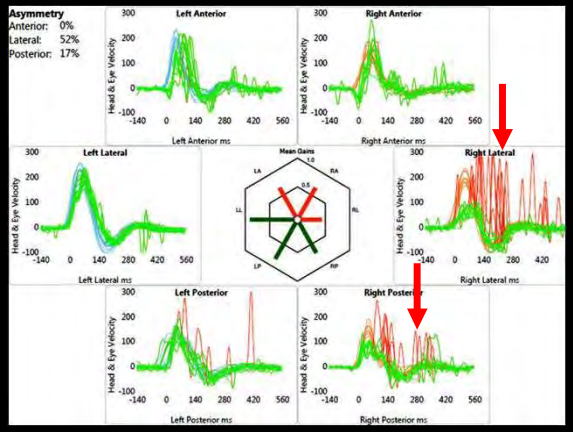
Otological disorders – Trauma

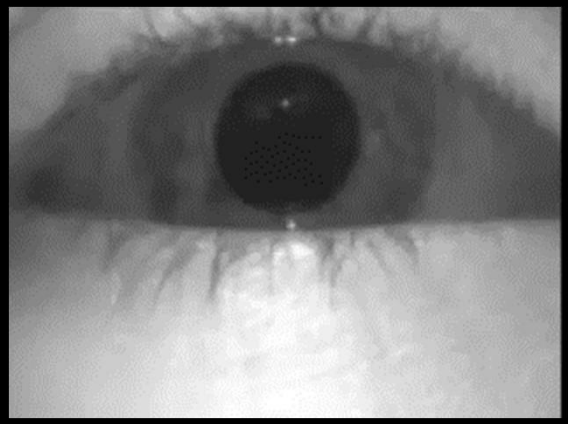
- Up to 80-100% subjects with an acute traumatic head injury will show labyrinthine concussion and up to 50% shows a permanent labyrinthine dysfunction at 5 years of which 25% remain undiagnosed, hearing loss is observed in up to 50% of traumatic HI
- Direct blow or acceleration/deceleration injuries encountered
- Often misdiagnosed, underdiagnosed or not diagnosed but has huge implications to life style – children may be asymptomatic in unilateral afflictions
- There is a strong legal implication to any head injury and the vestibular component may lead to a significant financial compensation package
- The force of the injury is not related to labyrinthine damage and trivial trauma can cause vestibular damage

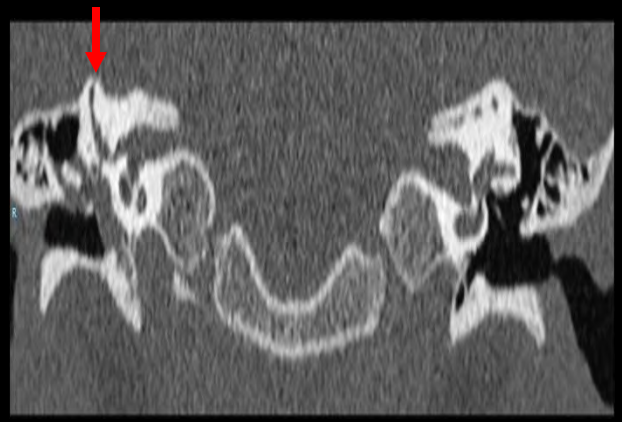
Legacies of trauma

- Chronic vestibular syndrome with intermittent decompensating episodes (up to 50%)
- BPPV (up to 60%)
- Vestibular migraine and classical migraine (up to 40%)
- Vestibular processing syndromes (up to 50%)
- Post traumatic Meniere's disease (up to 25%)
- Traumatic third window lesions – PLF, SCD,
- Isolated otolith damage
- Complete/incomplete transection of the VIII nerve in temporal bone fractures

Trauma - example







- Trivial injury in child, fall and hitting side of head on the right; GCS 15/15
- Complete SNHL on right; no vestibular symptoms; near total cochleovestibular loss on the right
- No intervention needed

Labyrinthine injury following trauma with right sided SCDS

Otological disorders – Third windows

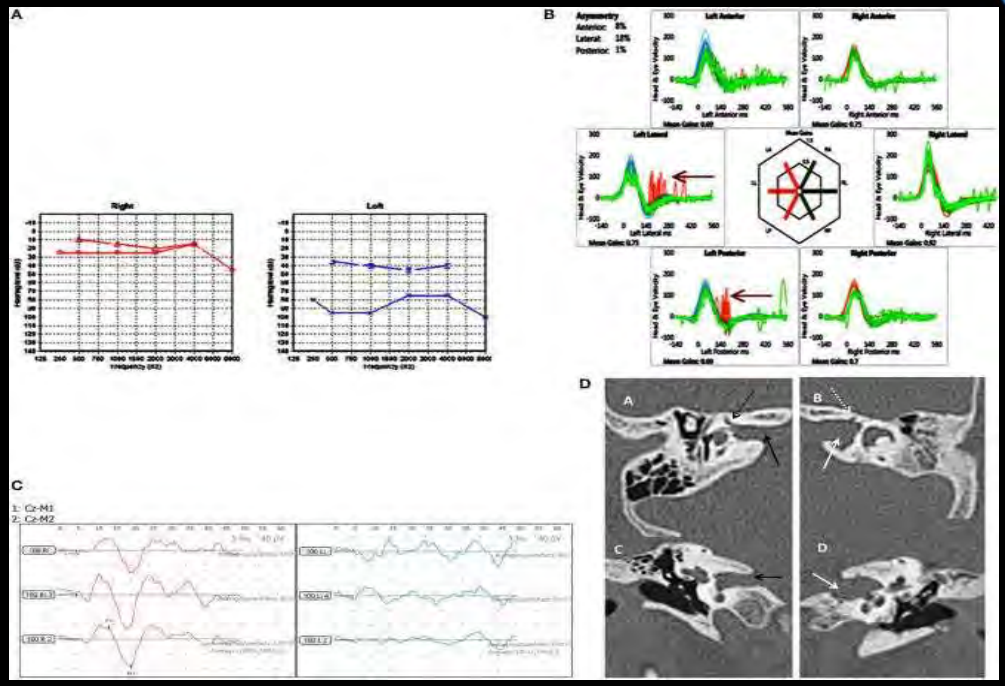
- Third windows in children do not have the same phenotype as that of adults and are often missed
- Commonest narrated symptom if possible is conductive dysacusis, misophonia, pulsatile tinnitus and autophony – hearing loss ranges from CHL, mixed and SNHL – vestibular assessment shows VEMP and vHIT abnormalities
- Final diagnosis by HRCT – thinning rather than a frank dehiscence can generate a similar phenotype
- Commonest is enlarged vestibular aqueduct (EVA)
- Symptoms may generate a significant emotional reaction due to their oddity and not infrequently children sent to mental health services due to a lack of awareness

Third windows examples

- Superior, posterior, and lateral semicircular canal dehiscence
- Cochlea-facial nerve dehiscence
- Cochlea-internal carotid artery dehiscence
- Cochlea-internal auditory canal dehiscence
- X linked gusher syndrome
- Perilymph fistula
- Facial nerve canal dehiscence
- Wide vestibular aqueduct in children
- Dilated internal auditory meatus
- Posttraumatic hypermobile stapes footplate
- Otosclerosis with internal auditory canal involvement
- Bone dyscrasias for example Paget's disease of the bone and osteogenesis imperfecta
- Endolymphatic hydrops

Third window - example

- Autophony, misophonia and disequilibrium
- Strong emotional reaction, referred to mental health
- Left sided vestibular dysfunction with left mixed HL
- Excellent results with CBT and vestibular rehabilitation, no surgery needed



Left dilated internal auditory meatus with left facial nerve canal dehsicence

Otological disorders – Meniere's syndrome and BPPV

Meniere's syndrome

- Rare in children, usually secondary endolymphatic hydrops
- May coexist with vestibular migraine
- Usually normal VFT
- 0.4% to 6% of children

BPPV

- Rare in children, usually post concussion
  May coexist with vestibular migraine
- Usually normal VFT

Parameter	Children	Adults
Pathogenesis	More stria vascularis integrity	Less stria vascularis integrity
Anamnesis	Difficult to elicit to fit criteria	Easier to elicit to fit criteria
Hearing loss	Variable, may be normal	Usually low frequency to start with
Vestibular function tests	Variable	Up to 80% abnormal
Aetiology	Almost always secondary	Majority idiopathic
Progression	Slow over several years	May be fast over months

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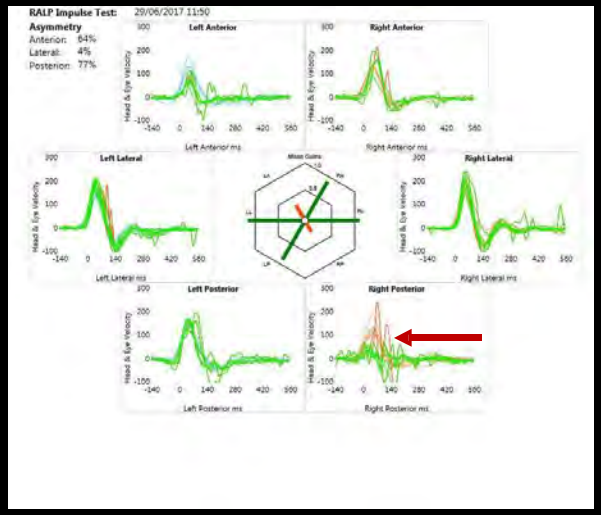
Meniere's syndrome - example



- Child fulfilled Barany criteria for definite MD
- Unsteady and dizzy
- Also fulfilled Barany VM criteria
- VFT mild left sided weakness, LFHL
- Sudden drop of hearing salvaged successfully
- Steroid responsive AIED
- Symptom free with medical management

Paediatric balance disorders – neurological disorders

Spectrum

- Migraine and migraine variants (BPT, BPV, hemiplegic, CV)
- Motion sickness
- Neoplastic and SOL – Brain tumours
- Cerebellum ataxia syndromes (SCA, EA)
- Epilepsy
- CVAs
- Demyelinating disorders
- Hereditary sensory motor ataxias
- Hypoxic ischaemic encephalopathies
- Neurodegenerative conditions
- Neurodevelopmental disorders – autism, ADHD, development coordination disorder
- Post infective conditions – sepsis, meningitis/encephalitis

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Paediatric balance disorders – neurological disorders

Phenotype

- Variable neurological features
- Movement disorders and incoordination
- Variable dizziness that can be continuous
- Dizziness may improve with eye closure
- Fatigue, headache and cognitive symptoms
- Fainting episodes
- Positional dizziness
- Central oculomotor eye movement - abnormalities are highly site specific
- Navigational difficulties
- Cognitive/psychological difficulties

Neurological disorders – vestibular migraine

- Commonest vestibular affliction in child upto 16 years (25% of all vestibular disorders)
- Phenotype qualification by Barany's criteria especially the 3rd and 4th as history might not be forthcoming
- Significant drain in quality of life and education
- Variable vestibular function test results – peripheral and central signs both encountered
- May coexist with ELH, BPPV

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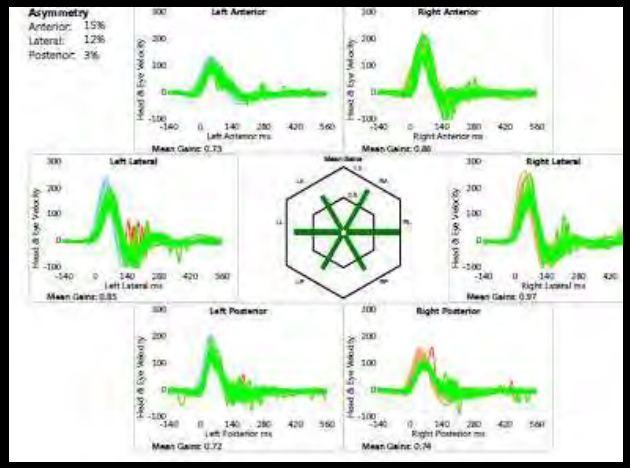
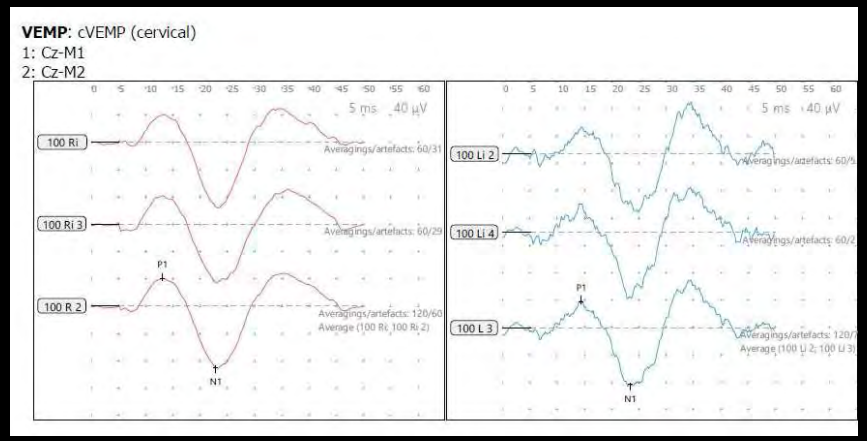
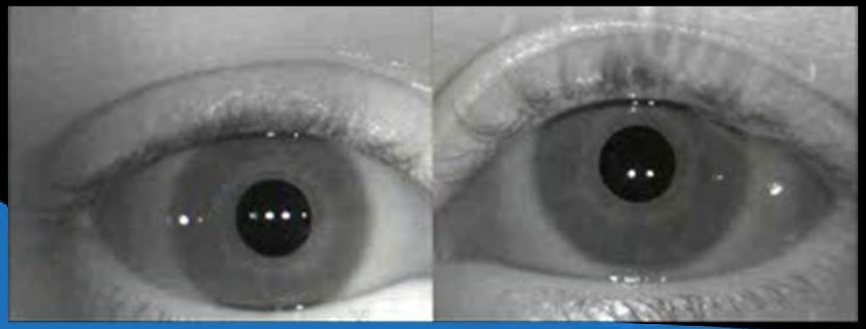
Vestibular migraine - example

- Child with an acute dizzy spell followed by recovery but persistence of episodic spells lasting for hours with photophobia and phonophobia; difficulties in quick head movements
- Severe reduction on confidence and avoidance of school





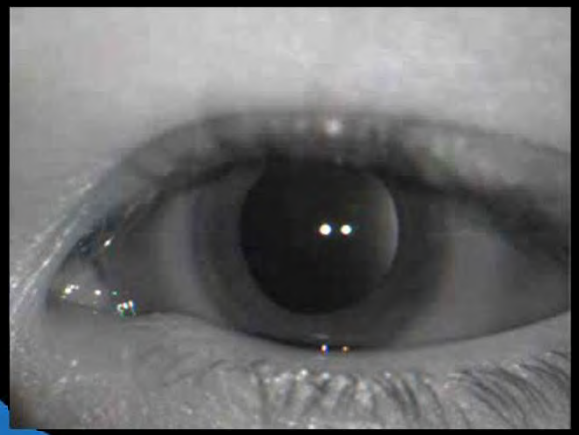
- High VOR gain in some canals
- All other tests normal
- Scan normal
- Abnormal central sign
- Treated with propranolol with excellent results, normal life style



Vestibular migraine

Neurological disorders – example 1

- Child with undiagnosed proximal myopathy; severe ataxia; positional dizziness with every change of posture; feels better in the dark; frequent falls; tinnitus and auditory processing problems; chronic symptoms and developmental delay with learning deficits
- Migraine features with headache and autonomic symptoms
- Obesity and some endocrine abnormalities; normal hearing
- Simultaneous vestibular migraine

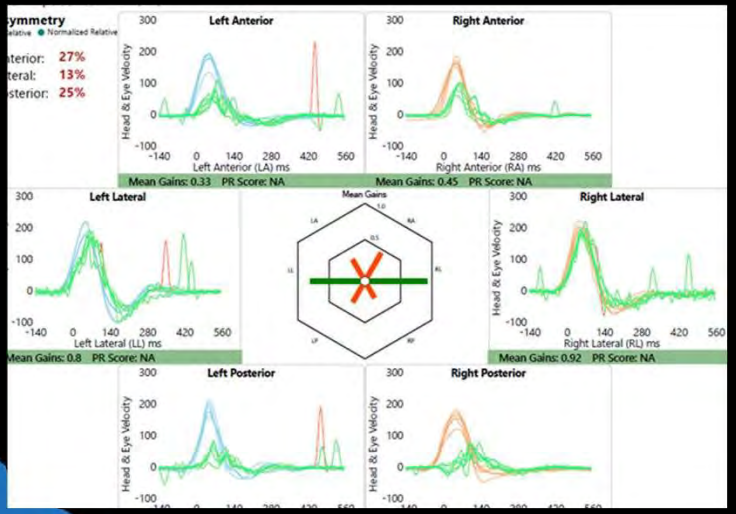


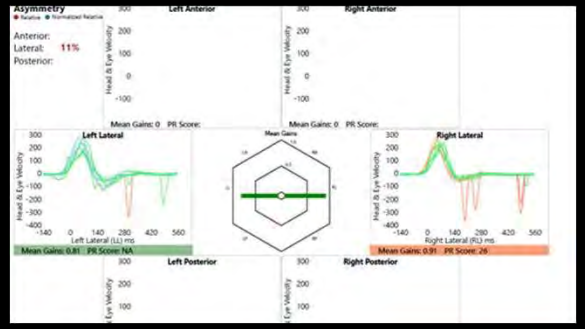
- Vestibular battery completely normal
- Macrosaccadic oscillations, perverted HSN, GEN
- Central scans normal
- Partial response to vestibular rehabilitation but more confident of balance; resolution of VM with pizotifen

A variant of cerebellar ataxia EA2 CACNA1 mutation

Neurological disorders – example 2

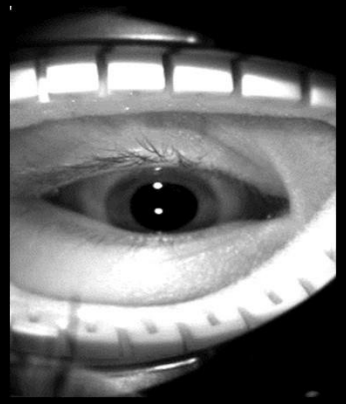
- Child with postural instability and ataxia
- Vestibular function normal
- Positional dizziness
- Partial response with vestibular rehabilitation and neurophysiotherapy



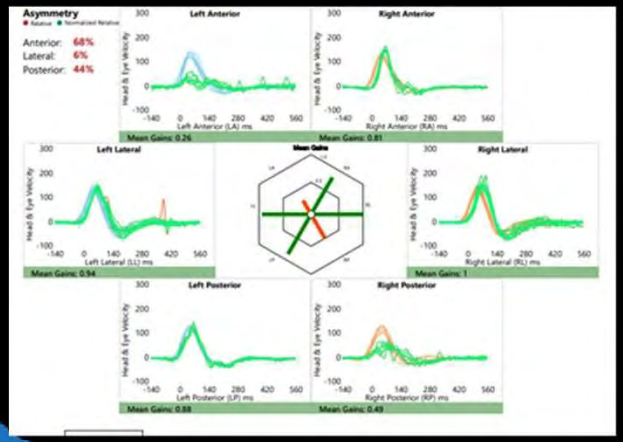


Cerebellar demyleination

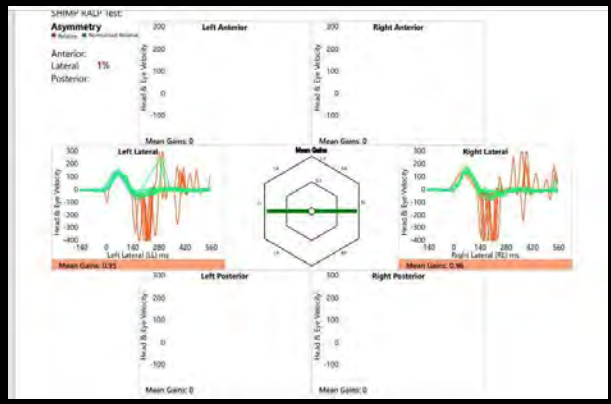
Neurological disorders – example 3



- Child fulfilling Barany's criteria for VM
- Has a PVP for intractable hydrocephalous
- Vestibular function normal, but low PSV in SHIMPS
- Positional dizziness
- Response to antimigraine medication



Parinaud's syndrome with dorsal mid brain stenosis of aqueduct of Sylvius



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Paediatric balance disorders – non peripheral/central vestibular disorders

Cardiovascular disorders
- Long QT syndromes
- Structural abnormalities
- Orthostatic hypotension
- Vasovagal syncope

Metabolic disorders
- Diabetis, electrolyte imbalances, thyroid disorders, anaemia, hyperviscosity syndromes

Musculoskeletal disorders
- Lower limb biomechanical abnormalities and orthopaedic conditions
- Myopthies and muscle dystrophies

Ocular abnormalities
- Refractive disorders, strabismus, vergence disorders

Psychogenic disorders
- Anxiety disorders, panic attacks

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Conclusions

Inspired by Children

The art of rational thinking and inductive reasoning

Inspector Gregory: Is there any point to which you wish to draw my attention?

Holmes: To the curious incident of the dog in the night-time.

Gregory: The dog did nothing in the night-time.

Holmes: That was the curious incident.

- Diagnosing balance disorders and detecting an aetiology in children is challenging, stimulating and rewarding as it is so complex
- The paediatric vestibular physician is required to possess wide knowledge in paediatric medicine especially neurology
- Awareness is very limited in paediatric general and subspecialties; in a recent survey even in balance specialists, awareness is limited to 30% or less
- Aetiology, phenotypes, natural history of pathology, laboratory norms and treatment are different in children as compared to adults

International Pediatric Vestibular Network
Promoting excellence in pediatric balance medicine

- Recently formed
- Membership open
- Website : www.ipbn.net
- Founding members

INTERNATIONAL PEDIATRIC BALANCE NETWORK
Promoting excellence in pediatric balance care

- Sylvette Vacher Wiener – Paris, France
- Leen Maes – Ghent, Belgium
- Soumit Dasgupta – Liverpool, UK
- Jacob Brodsky – Boston, USA
- Sharon Cushing – Toronto, Canada
- Ruth van Haecke – Ghent, Belgium
- Josine Widdershoven – Maastricht, Netherlands
- Kristen Janky – Boys Town, USA

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Alder Hey Children's Hospital Paediatric Audiovestibular Department presents

Alder Hey Paediatric Vestibular Course
October every year

Inspired by Children