Cours d'été de la SSORL
Sommerschule SGORL

Bettlach, 27 août 2011

The Vestibular System: from the periphery to the cortex

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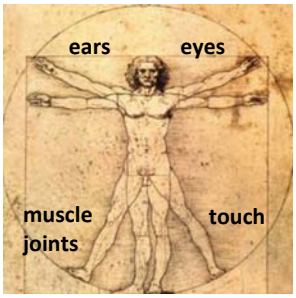
Equilibrium : complex function



Sensory inputs

vestibular

visual

proprioceptive

Equilibrium : vestibular system

multimodal system (6th sense)

Immediate CNS integration of bilateral multisensory informations

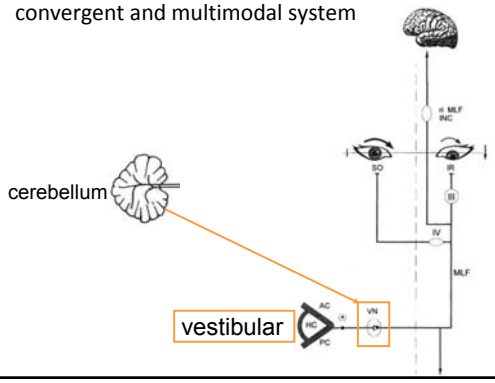
- at the subcortical level
  - vestibular nuclei
  - cerebellum
  - thalamus
- at the cortical level
  - multiple vestibular areas

Vestibular system : functions

- **Stabilization motor reflexes**
  - eye : maintenance of gaze stability during head / visual scene movements
  - body : maintenance of posture
- **Spatial orientation:**
  perception of verticality
  perception of self-motion

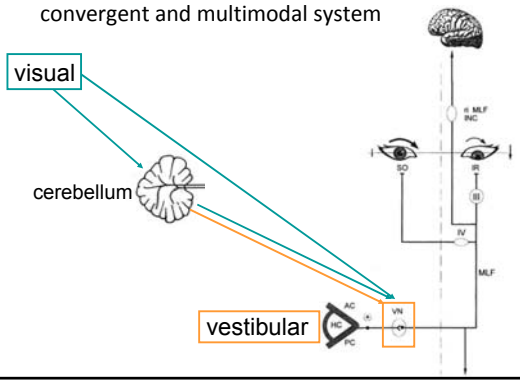
Vestibular system

convergent and multimodal system



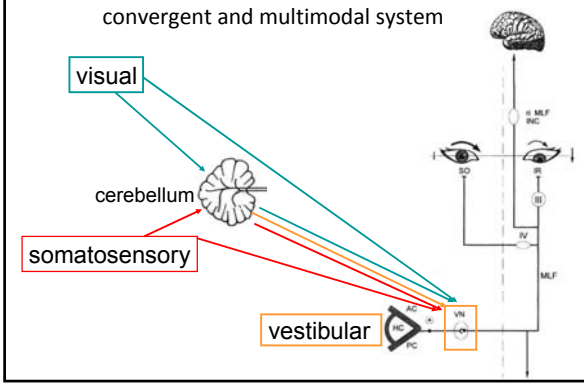
Vestibular system

convergent and multimodal system



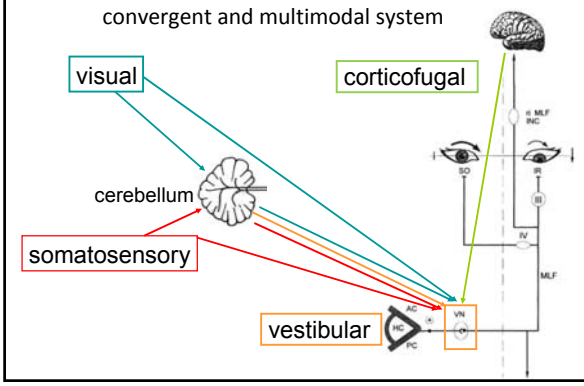
Vestibular system

convergent and multimodal system



Vestibular system

convergent and multimodal system



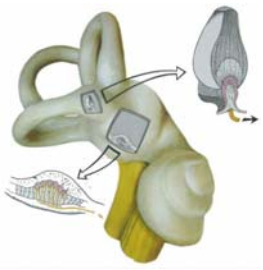
Vestibular system

Multimodal integration at the subcortical level

- vestibular nuclei
- cerebellum: nodulus, uvula, fastigial nucleus
- thalamus

→ common frame of sensory processing (eye-head-body coordination)

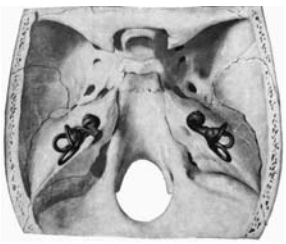
Vestibular end organs

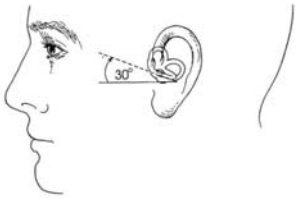


3 semi-circular canals respond to angular acceleration: rotation

2 otoliths (utricle, saccule) respond to linear acceleration: gravity, translation

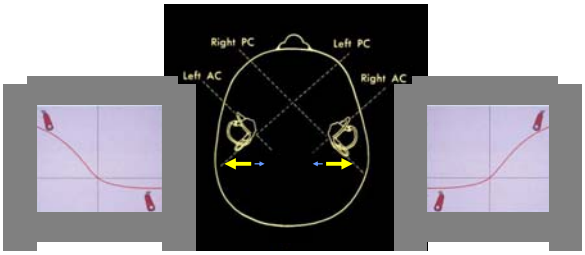
Labyrinth : anatomical orientation





Semi-circular canals: Ewald's 2nd law

Asymmetry of response

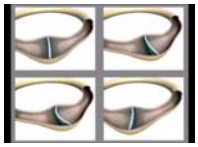


loss of gaze stabilisation (towards bad-side)
especially for fast head movements

Courtesy of H. Kingma

Semi-circular canals: frequency dependence

Phase (timing)



I ~ mass
B ~ friction (visc)
K ~ elasticity

Courtesy of H. Kingma

Semi-circular canals: frequency dependence

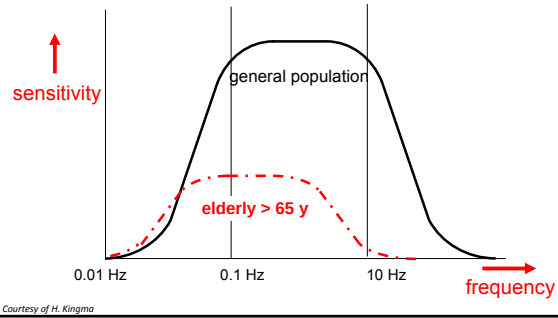
Gain

I ~ mass
B ~ friction (visc)
K ~ elasticity

Courtesy of H. Kingma

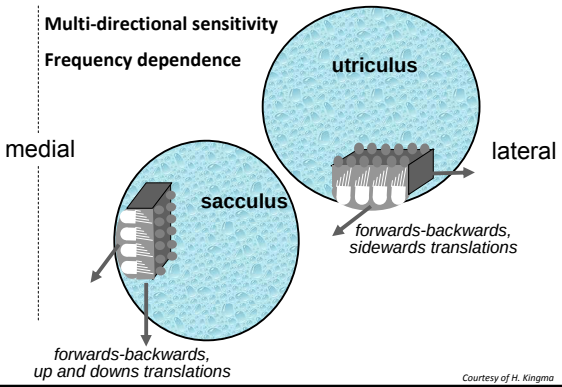
Semi-circular canals: frequency dependence

ageing (> 60 y) decrease in sensitivity and gain

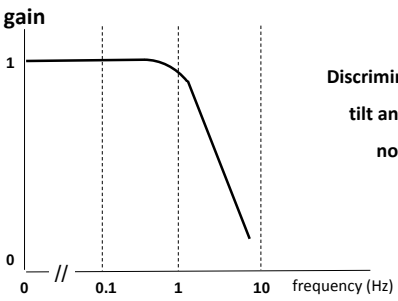


Courtesy of H. Kingma

Otolith organs



Otolith organs

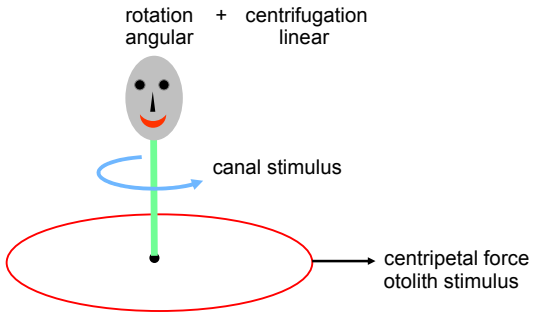


Discrimination between

tilt and translation

not possible

Otolith organs: also stimulated by rotations



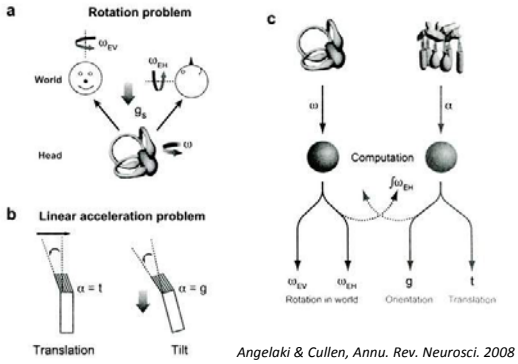
Problem of vestibular receptors

Anatomically fixed in the head
→ head-centered reference frame

- rotation problem
  axis of motion relative to the world
- linear acceleration problem
  distinction between tilt and translation

→ **otolith-canal interaction**

Otolith-canal interaction



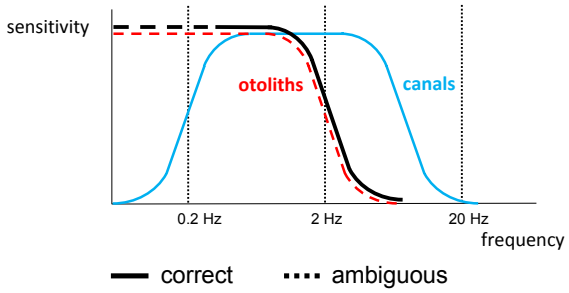
Angelaki & Cullen, Annu. Rev. Neurosci. 2008

Otolith-canal interaction

- allows adequate coding of movement relative to the world (world-centered coding)
- allows the vestibular system to function as an inertial sensor for navigation and spatial orientation

Otolith-canal interaction

Discrimination between tilt and translation

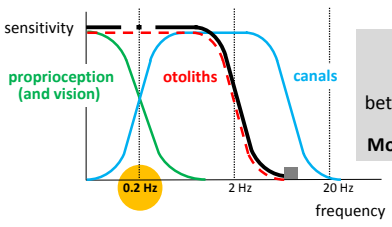


Proprioceptive-vestibular interaction

- allows body-referenced perception of motion (body-centered coding)
- distinction between active and passive movement

Proprioceptive-vestibular interaction

Discrimination between tilt and translation



0.2Hz

Persisting ambiguity between tilt and translation

Motion sickness frequency

correct ambiguous

Visual-vestibular interaction

- maintenance of gaze stability during head / visual scene movements
- maintenance of spatial perception during motion at constant velocity
- do not allow the brain to differenciate vestibular (labyrinthine) from optokinetic (visual) inputs

Gaze stability during head / visual scene movements

visual-vestibular-oculomotor system
(or vestibular-optokinetic system)

- vestibulo-ocular reflex
- optokinetic reflex

} nystagmus

- smooth pursuit (target tracking)

stabilizing gaze

Vestibulo-ocular reflex (VOR)

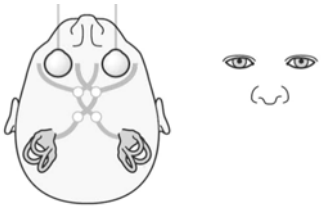
Effective : natural head movement (0.1 – 4 Hz)

- **direct pathway (rapid)**
  short latency < 8 msec
  brief, fast head movement
  small amplitude
  → **compensatory eye displacement**
  1 – 4Hz and velocity > 100°/sec : gain ≈ 1

- **indirect pathway (slow)**
  via velocity storage
  slow, continuous head movement
  large amplitude
  → **vestibular nystagmus**

stabilizing gaze

VOR : direct pathway



three-neuron chain reflex

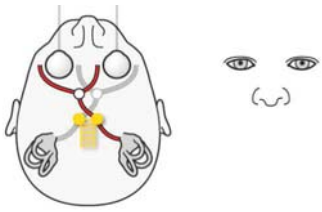
stabilizing gaze

VOR : direct pathway

Head thrust

stabilizing gaze

VOR : indirect pathway

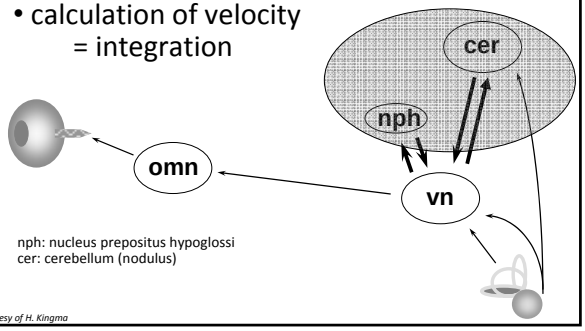


three-neuron chain + velocity storage

stabilizing gaze

VOR : velocity storage

- increase of sensitivity
- calculation of velocity
  = integration

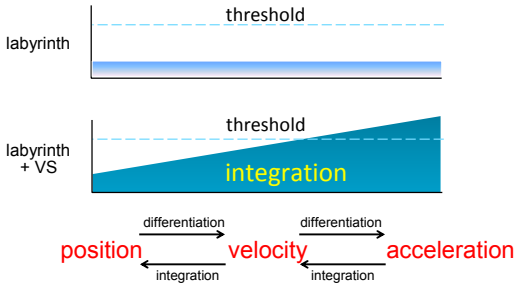


nph: nucleus prepositus hypoglossi
cer: cerebellum (nodulus)

Courtesy of H. Kingma

stabilizing gaze

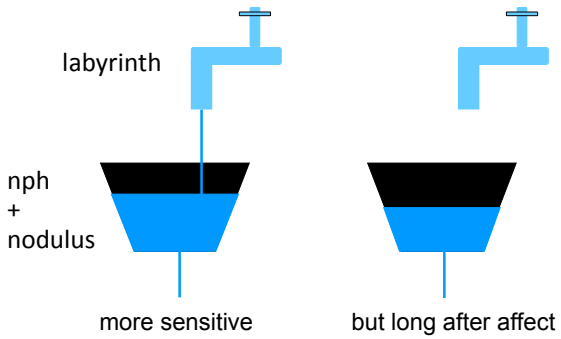
VOR : velocity storage



Courtesy of H. Kingma

stabilizing gaze

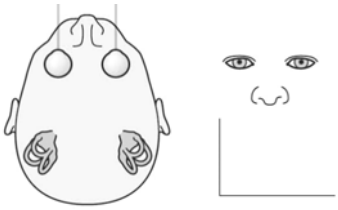
VOR : velocity storage



Courtesy of H. Kingma

stabilizing gaze

VOR : velocity storage

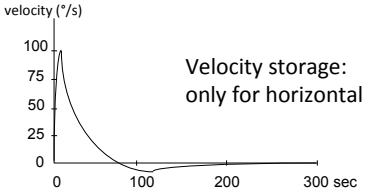


Impulse (velocity step)

prolonged time discharg with time constant

stabilizing gaze

VOR : velocity storage



Velocity storage:
only for horizontal canals

Duration (≈ 3x time constant)

$duration_{deflection\ cupula}$ = 6 ms

$duration_{cupula\ back}$ = 20 s

$duration_{velocity\ storage}$ = 60 s

$duration_{central\ adaptation}$ > 300 s
>100 s

Time constant (τ)

τ_{cupula} ≈ 2 ms

τ_{canal} ≈ 6 s

$\tau_{velocity\ storage}$ ≈ 20 s

$\tau_{central\ adaptation}$

stabilizing gaze

Optokinetic system

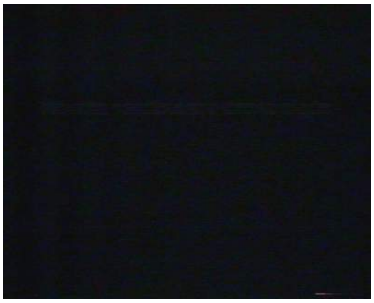
Effective : slow image slip on retina
< 1Hz ; velocity < 100°/sec

- **direct pathway = smooth pursuit**
  fast, foveal, volontary (cortical)
  → target tracking
  → visual suppression of vestibular nystagmus

- **indirect pathway**
  slow, extrafoveal, unvolontary (subcortical)
  via velocity storage
  → optokinetic nystagmus

stabilizing gaze

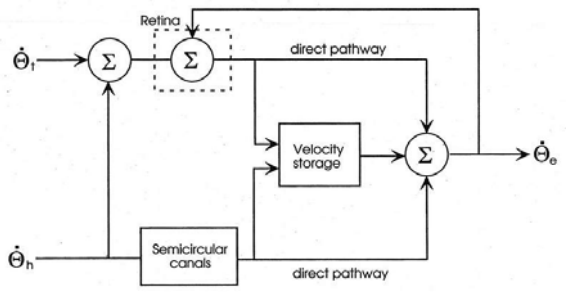
Low frequency < 1Hz



Visual suppression of vestibular nystagmus

stabilizing gaze

Visual-vestibular interaction



In : *Clinical neurophysiology of the vestibular system*
Baloh & Honrubia, 3e ed, CNS, 2001

Vestibular system

Multimodal integration at the cortical level

- multisensory vestibular cortex

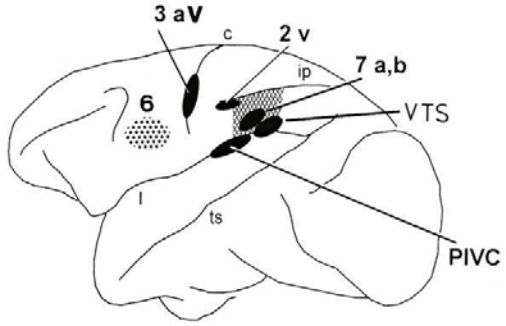
  → fusion of the different sensory inputs (multisensory coding)

  → internal representation of space in unique 3-D map

Multisensory vestibular cortex

- no primary vestibular cortex
- multiple vestibular cortex areas
  - ↳ parieto-insular cortex
  - ↳ multisensory neurons
    respond to vestibular, optokinetic and somatosensory stimuli

Vestibular cortex (monkey)



Brandt & Dieterich, Ann. NY Acad. Sci. 1999

Parieto-insular vestibular cortex (PIVC)

- **Afferents** (via vestibular nuclei and thalamus)
  semi-circular canals and otoliths
  optokinetic
- **Efferents** (corticofugal feed-back)
  direct projection to vestibular nuclei

PIVC : functions

- perception of verticality
- perception of self-motion
- internal representation of space and body orientation in unique 3-D coordinates

  unified visual-vestibular-somatosensory map

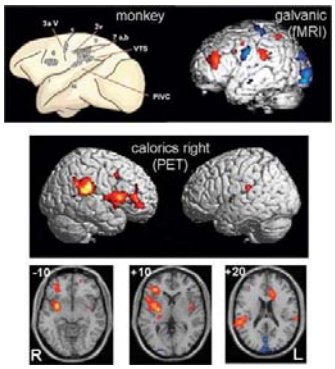
  ↳ egocentric (body-centered)

  ↳ exocentric (world-centered)

PIVC

- bilateral activation
- right hemispheric dominance (non-dominant hemisphere)
- interaction with primary visual cortex

Illustration of the normal activation-deactivation pattern during unilateral vestibular stimulation in healthy volunteers (activations in yellow-red, deactivations in blue)

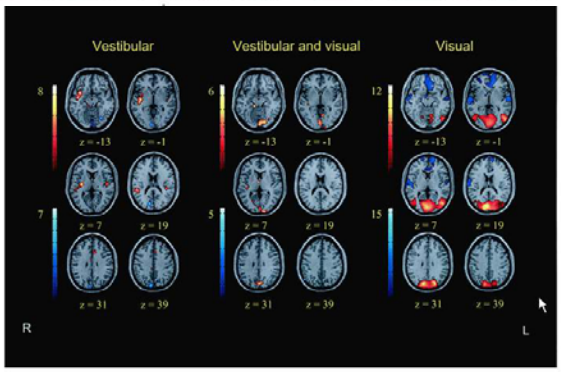


Dieterich, M. et al. Brain 2008 131:2538-2552

Self-motion perception

Mechanism of reciprocal inhibitory visual-vestibular interaction

- optokinetic deactivates the vestibular cortex
- vestibular stimulation deactivates the visual cortex



Brandt et al. Ann N.Y. Acad Sci 956: 230-241 (2002)

Reciprocal inhibitory visual-vestibular interaction

- prevents sensory mismatch and perceptual ambiguity
- allows the brain to link the perception of self-motion to the dominant input:
  - vestibular (head acceleration)
  - visual (constant velocity)
  - both

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Management of vertigo

PD Dr Raphaël Maire
Unité d'Otoneurologie et Audiologie
Service d'ORL, CHUV, Lausanne

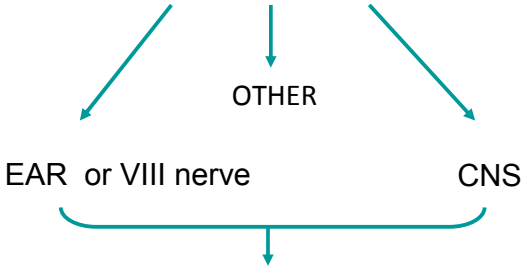
Acute vertigo : main diagnosis

- Benign paroxysmal positional vertigo
- Acute unilateral peripheral vestibular loss
- Menière's attack
- Orthostatic hypotension
- Transient ischemic attacks, Stroke
  - brainstem, cerebellum
- Head trauma
  - temporal bone fracture, perilymph fistula
- Intoxication (drugs, alcohol)

Chronic (*or recurrent)* vertigo : main diagnosis

- uncompensated unilateral peripheral vestibular loss
- Menière's disease
- recurrent vestibulopathy (vestibular Menière?)
- vestibular migraine
- fistula / superior canal dehiscence syndrome
- tumor (vestibular schwannoma, meningioma, glioma)
- vestibular paroxysmia (neuro-vascular compression)
- bilateral vestibulopathy
- post traumatic syndrome
- central vestibular (neurological), drugs side effects
- immune-mediated inner ear diseases, metabolic disorders
- psychophysiologic (sensory ambiguity perception)
  - space and motion discomfort, chronic subjective dizziness, visual vertigo
  - anxiety, phobic disorder

ORIGIN OF VERTIGO



OTONEUROLOGICAL EXAMINATION

Evaluation of the dizzy patient

History

Examination of the vestibular system

- ear examination, including hearing test
- static posture, walking tests
- neurological evaluation
- labyrinthine evaluation

neurovestibular examination

- ± cardiovascular examination

Neurovestibular examination

1) Neurological evaluation

- cranial nerves
- cerebellar tests
- sensory /motor deficit
- state of consciousness

Neurovestibular examination

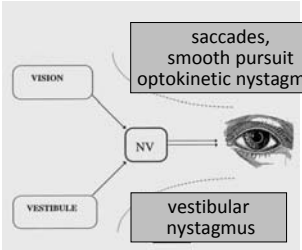
2) Balance (vestibulospinal reflexes)

- Romberg
- Unterberger (Fukuda)
- walking tests

Neurovestibular examination

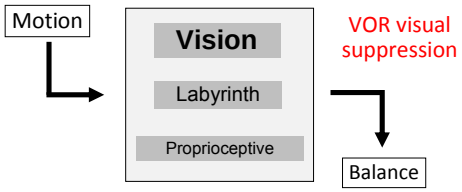
3) Visual-vestibular pathways

Vestibulo-ocular reflex
Optokinetic reflex



Visual-vestibular interaction: hierarchy

- low frequency (<1Hz) : vision > labyrinth

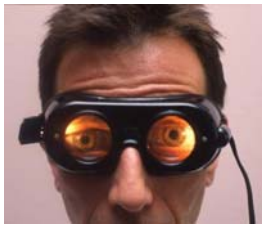


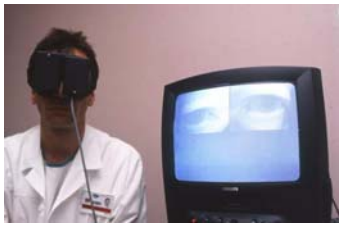
- high frequency (1–4Hz) : labyrinth > vision

Visual-vestibular pathways examination

- at light
- in condition preventing fixation
  - darkness
  - Frenzel glasses
  - infrared videoscopy

Test visual suppression of nystagmus





Neurovestibular examination

4) Labyrinthine evaluation

- bithermal binaural caloric testing
  ⟶ low frequency VOR evaluation (<0.1Hz)
- Head-thrust test (Halmagyi)
  ⟶ high frequency VOR evaluation (>1Hz)
- fistula/dehiscence test (Politzer, Valsalva, Tullio)
- rotational testing

Types of pathologic nystagmus

- spontaneous (eyes in primary position)
- gaze-evoked
- head-shaking
- positional / positioning
  - direction fixed, direction changing
- congenital

Pathologic nystagmus

origin	characteristics
peripheral	conjugate (binocular) ↓ by fixation
central	conjugate / disconjugate not ↓ or ↑ by fixation

Spontaneous nystagmus (primary gaze)

- peripheral
  - combined horizontal-torsional, unidirectional
  - asymmetric loss of peripheral vestibular tone (labyrinth or vestibular nerve)
- central
  - often pure horizontal, vertical or torsional
  - may change direction
  - imbalance in central vestibular tone (brainstem or cerebellum)

Acute peripheral vestibular loss

- Vestibular neuritis (idiopathic)
- Labyrinthitis or neurolabyrinthitis
  - herpes zoster oticus
  - complication of otitis media
- Labyrinthine concussion
  - head trauma, temporal bone fracture
- Labyrinthine infarction

Acute peripheral vestibular loss

Effect on the vestibular system

- acute imbalance in central vestibular tone (vestibular nuclei)
- oculomotor, postural and perceptual deficits

Acute peripheral vestibular loss

Clinical signs :

- spontaneous nystagmus towards healthy ear, ↓ by fixation
- head tilt towards affected ear
- tonic eye deviation towards affected ear
- postural deviation towards affected ear
- partial/total caloric weakness of affected ear
- pathologic head thrust towards affected ear (Halmagyi sign)
- no central neurological signs

Acute peripheral vestibular loss

spontaneous

nystagmus

beating

towards healthy side

Acute peripheral vestibular loss

Symptoms :

- rotatory vertigo
- perceptual tilt towards affected side
- postural deviation towards affected side
- nausea ± vomiting

Acute peripheral vestibular loss

Evolution :

- decrease of signs and symptoms with central compensation (3 to 6 weeks)

→ recovery of central vestibular tone (vestibular nuclei)

→ re-equilibration of low frequency VOR (velocity storage)

Central vestibular compensation

Lacour M 1992 – 2010

maximum compensation is reached within 3-12 months

- stimulated by movement and fastened by betahistine
- reduced by immobility and vestibular sedation

STATIC components of compensation are good (at rest)

- powerful neuroplasticity in VN

DYNAMIC components of compensation are poor (during movement)

- impaired automatization of gait and balance
- impaired image stabilization
- hypersensitivity to optokinetic stimuli
- impaired spatial orientation

Effect of betahistine on central compensation after vestibular neurectomy

Cats *Tighilet B et al (jan. 1995) J Vestibular Research*

placebo: recovery in 6 weeks*

betahistine (50mg/kg/day): recovery in 3 weeks*

*posture and locomotor balance

Meniere patients *Redon C et al (apr. 2011) J Clin Pharmacology*

placebo: recovery in ≥ 3 months

betahistine (2x24mg/day): recovery in ≈ 1 month*

* postural stability, subjective visual vertical, head orientation

Acute peripheral vestibular loss

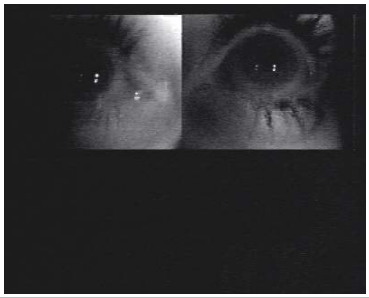
General treatment recommendations

- mobilization and rehabilitation as soon as possible
- avoid immobility and vestibular sedation
- betahistine 48-72mg/day 4-12 weeks
- ± prednisone 1mg/kg/day 7-10 days (according to authors)

Head shaking nystagmus

Indicates asymmetry in the velocity storage system

Usually due to uncompensated unilateral peripheral vestibular loss



Acute peripheral vestibular loss

Evolution :

- if severe lesion :
  persisting high frequency VOR deficit
  towards affected side (Halmagyi sign)

→ oscillopsia, reduced dynamic visual acuity

mechanism : retinal slip due to VOR loss

Severe peripheral vestibular loss

Persisting high frequency VOR deficit

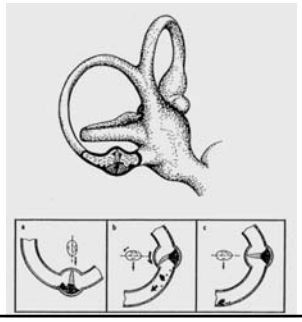
pathologic

head-thrust

(Halmagyi sign)

Benign paroxysmal positional vertigo (BPPV)

Mechanism : canalo / cupuloliothiasis



BPPV

Most frequent cause of vertigo

Localization: posterior canal : 80-90%
horizontal canal: 10-20%
anterior canal: rare

Symptoms

brief episodes of vertigo (< 1min) with position change:

- getting in and out of bed
- turning over in bed
- straightening up
- extending the neck to look up

BPPV: etiology of canalo/cupulolithiasis

- disturbance in otolith metabolism (vascular, ageing, Ca^{2+} metabolism/osteoporosis)
- head trauma (otolith detachment)
- bed rest (clot formation in canals)
- vestibular neuritis, labyrinthitis
- ear surgery
- idiopathic (most frequent)

BPPV: classical positioning manoeuvre

Dix-Hallpike modified Dix-Hallpike

Diagnostic manœuvre for posterior BPPV
(or contralateral anterior BPPV)

Posterior BPPV

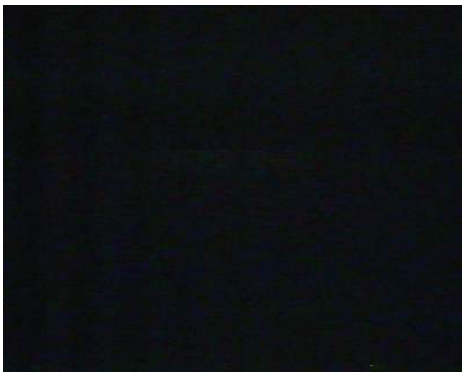
Typical features:

- latency : 1-30 sec
- duration: < 1 minute (paroxysmal)
- characteristic positioning nystagmus:
  upward vertical and torsional
- fatigability: nystagmus decreases with repeated positioning

Posterior BPPV

Typical nystagmus induced by rapidly moving the patient from sitting to sidelying position

Right posterior BPPV



Posterior BPPV

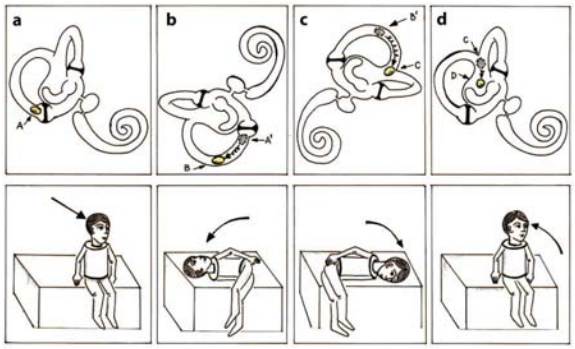
Treatment

- Liberatory manoeuvre (Epley, Semont)
  move the patient around the plane of posterior canal
- Surgery
  - singular neurectomy (Gacek)
  - posterior canal occlusion (Parnes)

Evolution

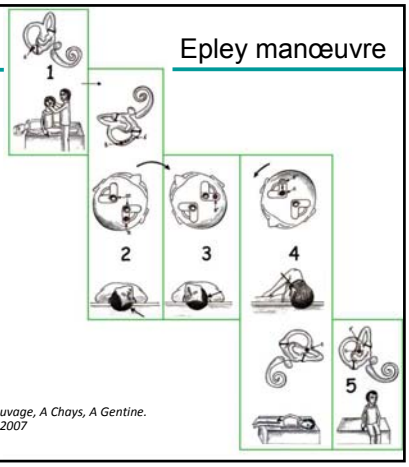
- good prognosis
  most BPPV spontaneously disappear within 2 to 10 weeks
- common recurrences

Posterior BPPV: Semont manoeuvre



In: « vertiges positionnels » JP Sauvage, A Chays, A Gentine. Société française d'ORL, éditeur, 2007

Posterior BPPV — Epley manœuvre



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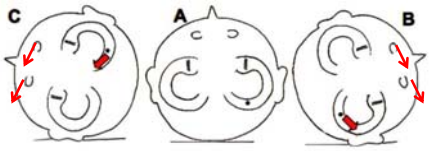
Horizontal BPPV: positioning nystagmus

Canalolithiasis

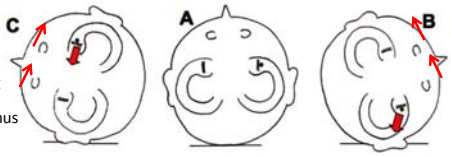
Direction-changing **geotropic** horizontal nystagmus



Supine position

Cupulolithiasis

Direction-changing **apogeotropic** horizontal nystagmus



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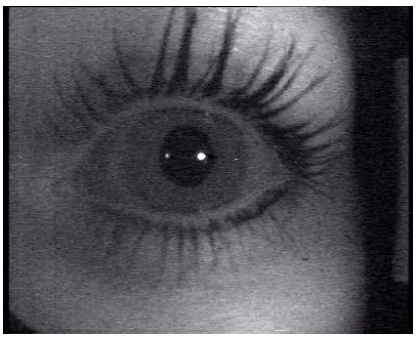
hor BPPV: direction-changing horizontal nystagmus



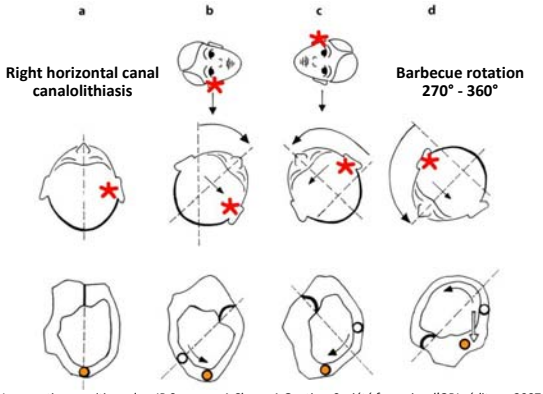
Horizontal BPPV

- **canalolithiasis** — geotropic, transient nystagmus; greater intensity towards affected side
- **cupulolithiasis** — apogeotropic, persistent nystagmus; greater intensity towards healthy side
- nystagmus not fatigable with repeated positioning
- frequency: canalolithiasis > cupulolithiasis

Evolution — good prognosis
canalolithiasis quickly disappears < 2 weeks
common recurrences

Treatment — liberatory manoeuvre
Lempert (barbecue rotation), Gufoni
sustained position ≈ 12 hours on healthy side (Vannucchi)

Horizontal BPPV: Lempert manoeuvre



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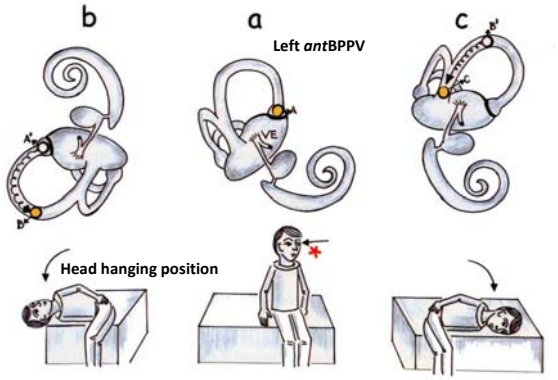
Horizontal BPPV: Gufoni manoeuvre

geotropic *h*BPPV variant: towards unaffected side
apogeotropic *h*BPPV variant: towards affected side

Anterior BPPV

- same general features than other canals BPPV
  latency, duration < 1 minute
- characteristic positioning nystagmus after Dix-Hallpike manœuvre with strong head hanging position
  downward vertical ± torsional
- rare: spatial orientation of anterior canal allows spontaneous evacuation of clot into the utricle just by sitting up

Anterior BPPV: liberatory manoeuvre



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