眩暈讀書會 - Meniere’s Disease

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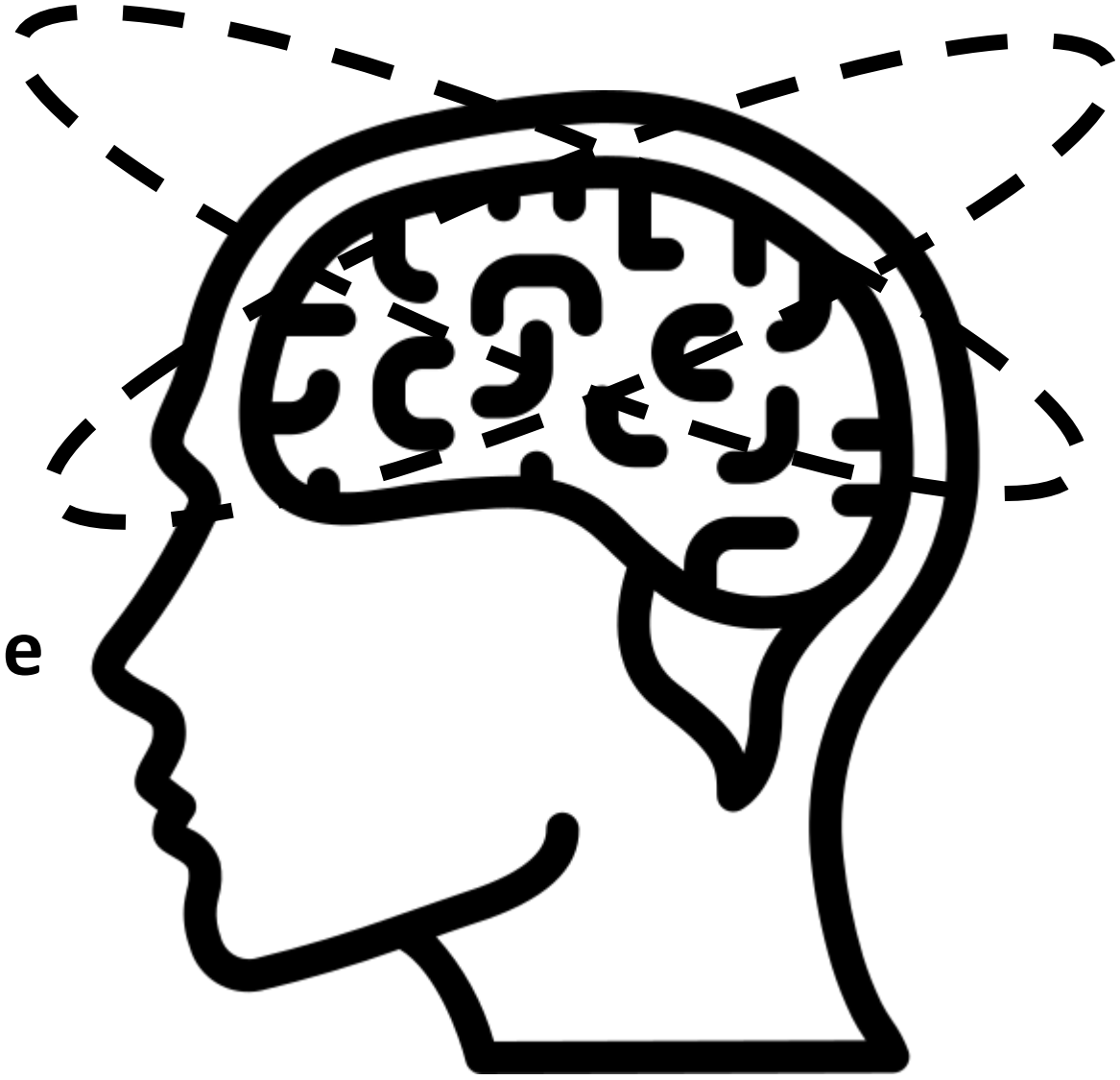


Diagnostic Criteria

Diagnostic Criteria

adapted from Lopez-Escamez et al. 2015

Box 10.1 Diagnostic Criteria of MD

MD

1. Two or more spontaneous episodes of vertigo, each lasting 20 min to 12 h
2. Audiometrically documented low- to medium-frequency sensorineural hearing loss (SNHL) in one ear
3. Defining the affected ear on at least one occasion before, during, or after one of the episodes of vertigo (± 24 h)
4. Fluctuating aural symptoms (hearing, tinnitus, or fullness) in the affected ear
5. Not better accounted for by another vestibular diagnosis

Probable MD

1. Two or more episodes of vertigo or dizziness, each lasting 20 min to 24 h
2. Fluctuating aural symptoms (hearing, tinnitus, or fullness) in the affected ear
3. Not better accounted for by another vestibular diagnosis

Diagnostic Criteria for MD

- ≥2 spontaneous vertigo, 20 mins ~ 12 hrs
- SNHL in 1 ear, mid to low frequency, audiometrically documented
- Hearing loss related to ≥1 vertigo (± 24 hrs)
- Fluctuating aural symptoms in the affected ear
  - Hearing
  - Tinnitus
  - Fullness
- No better diagnosis

Diagnostic Criteria for Probable MD

- ≥2 ~~spontaneous~~ vertigo **or dizziness**, 20 mins ~ **24** hrs
- ~~SNHL in 1 year, mid to low frequency, audiometrically documented~~
- ~~Hearing loss related to ≥1 vertigo (± 24 hrs)~~
- Fluctuating aural symptoms in the affected ear
  - Hearing
  - Tinnitus
  - Fullness
- No better diagnosis

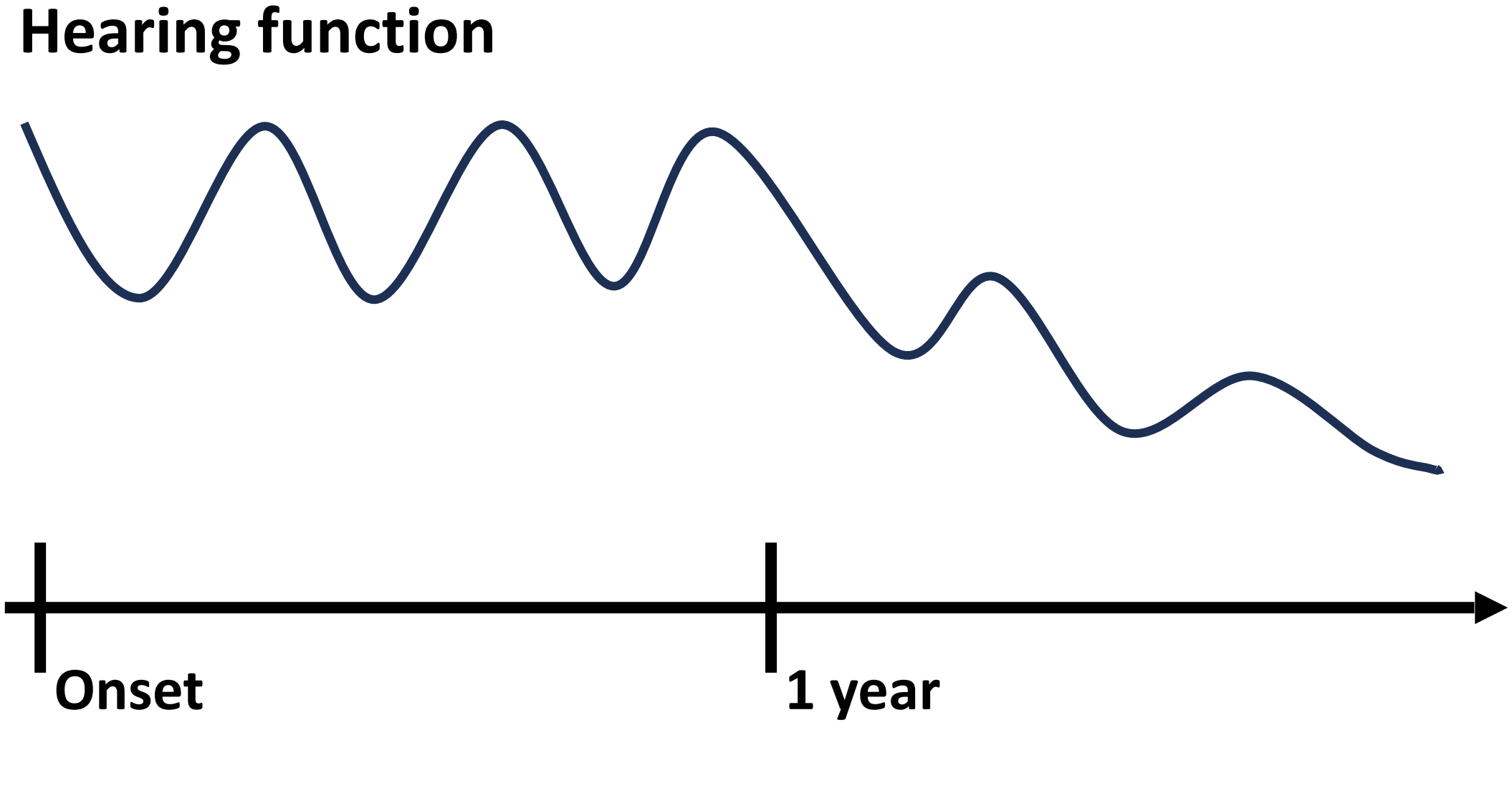
Epidemiology and Clinical Presentations

Epidemiology

- Prevalence:
  - Japan: 35/10w
  - Finland: 513/10w
- Onset age: 3rd to 7th decades
  - Korea: increase incidence rate during 2013-2017 -> aging
- Preponderance of female
  - May be due to Misdiagnosis of VM
- Higher odds: Older, white, severe obesity
- Association: migraine (2.0), arthritis (1.8), psoriasis (1.8)

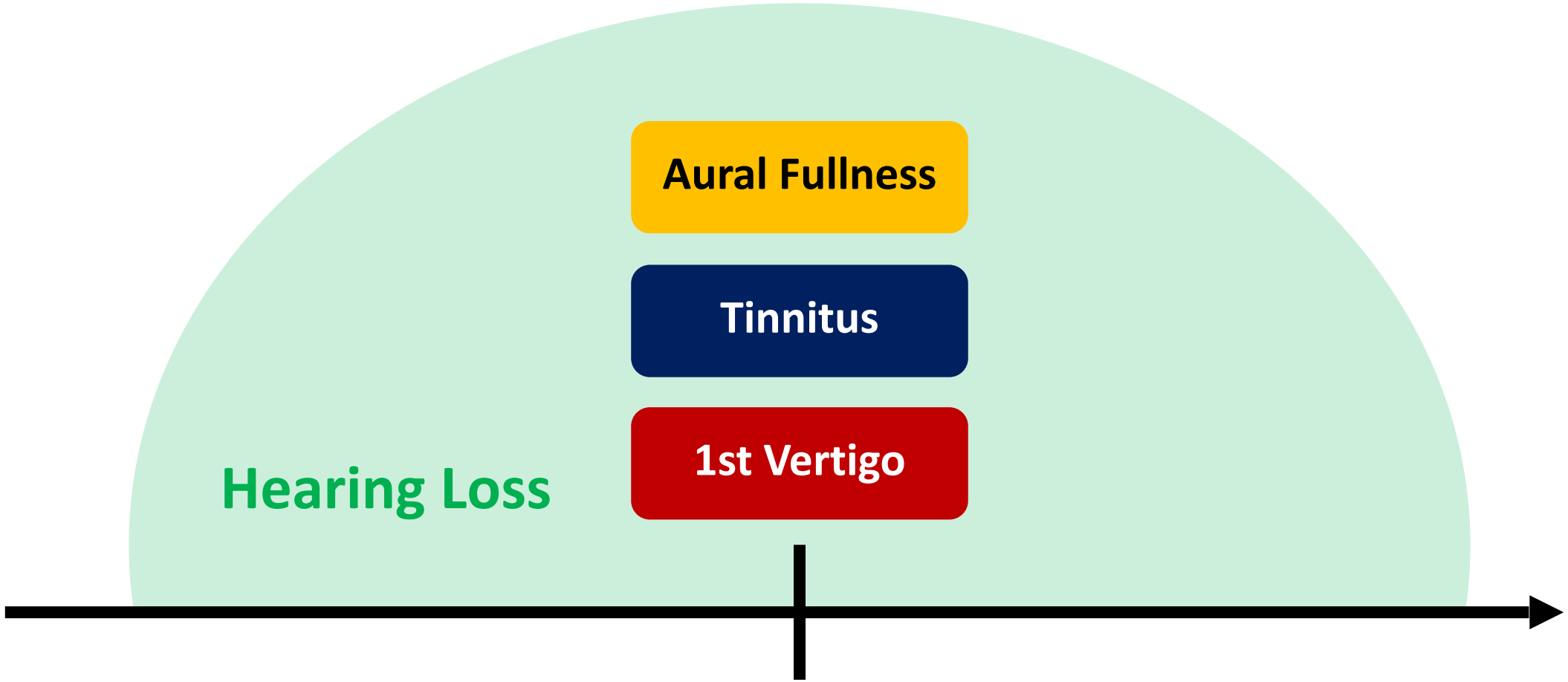
Patient History

- No any provoking factors
- Duration: the time that the patient has to be at rest and cannot move.
  - If < 20 mins or > 12 h, other disorders should be considered
  - May have residual symptoms, ex: postural imbalance, gait impairment
- 1st year, hearing fluctuates considerably.
- After recurrent episodes of vertigo, there is often a progression of hearing loss which persists.
- Then, vertigos are often no longer associated with other ear symptoms.


Hearing function
Onset
1 year

Patient History (Cont'd)

- Monosymptomatic pure vestibular or pure cochlear episodes may occur at the beginning of the disease.
- Episodic vertigo may precede the onset of hearing loss by several weeks or months, but **tinnitus** or **aural fullness** is usually associated with the first episode of vertigo.
- Conversely, **sensorineural hearing loss** may **precede** the onset of vertigo episodes by several months or years. -> **Delayed MD**


Aural Fullness
Tinnitus
1st Vertigo
Hearing Loss

Subgroup of MD

Box 10.2 Clinical Subgroups of Patients with MD (Frejo et al. 2017)

Unilateral MD

- Type 1 Sporadic MD (if concurrent migraine, autoimmune disease, or familial MD is observed, patients do not belong to this subgroup)
- Type 2 Delayed MD (hearing loss precedes vertigo attacks by months or years)
- Type 3 Familial MD (at least two patients in the first or second degree)
- Type 4 Sporadic MD with migraine (temporal relationship not required)
- Type 5 Sporadic MD with an autoimmune disease

Bilateral MD

- Type 1 Unilateral hearing loss becomes bilateral
- Type 2 Sporadic, simultaneous hearing loss (usually symmetric)
- Type 3 Familial MD (most families have bilateral hearing loss, but unilateral patients may coexist in the same family)
- Type 4 Sporadic MD with migraine
- Type 5 Sporadic MD with an autoimmune disease

Patient History (Cont'd)

- Tumarkin's otolithic catastrophe (Vestibular drop attacks)
  - Sudden loss of vestibulospinal tone
  - Lasting a few seconds
  - Most often without LOC. If occurs -> vestibular syncope
- MD may also develop **symptoms of the third mobile windows**
  - Tullio phenomenon: changes in pressure or low-frequency sounds induce short attacks lasting seconds to minutes
  - Pronounced endolymphatic hydrops brings the endolymphatic labyrinth close to the stapes footplate

Disease Course

- The longer one follows these patients, the more often one sees a bilateral involvement
  - 2 yrs: 15% bilateral
  - 10 yrs: 35% bilateral
  - 20 yrs: 47% bilateral
- The second most frequent cause of bilateral vestibulopathy
- Lower incidence of bilateral MD in Asian population
- The frequency of attacks declines in the first 5-10 years.

Examinations

Clinical Examination - Attack-free interval

- Hearing Tests
  - Finger rub
  - Rinne
  - Weber
  - Audiometry
- Otoscopy: exclude zoster, otitis media
- NE
  - **HIT often normal** despite **reduced caloric irrigation**

Clinical Examination - During an attack

- Unilateral transient vestibular excitation (mins)
  - Nystagmus, fast phase beating toward the affected labyrinth
- Subsequently, longer-lasting vestibulocochlear inhibition (many mins)
  - Nystagmus, **reversal of direction**, fast phase beating toward the non-affected labyrinth

Nystagmus of an attack in MD

Initial phase of an acute attack in MD:
nystagmus beats towards the affected side

https://doi.org/10.1007/000-95q

Late phase of an attack in MD:
nystagmus beats towards the non-affected side

https://doi.org/10.1007/000-95n

Clinical Examination - During an attack

- Helpful diagnostic tools
  - Video of eye movement during attack
  - Audio app to document hearing

Application of Protable Audiomtery

› Otol Neurotol. 2019 Feb;40(2):e130-e134. doi: 10.1097/MAO.0000000000002080.

Novel Use of Portable Audiometry to Track Hearing Fluctuations in Menière's Disease: A Pilot Study

Darren Tse [1], Tim Ramsay [2 3], Daniel A Lelli [4]

Affiliations + expand

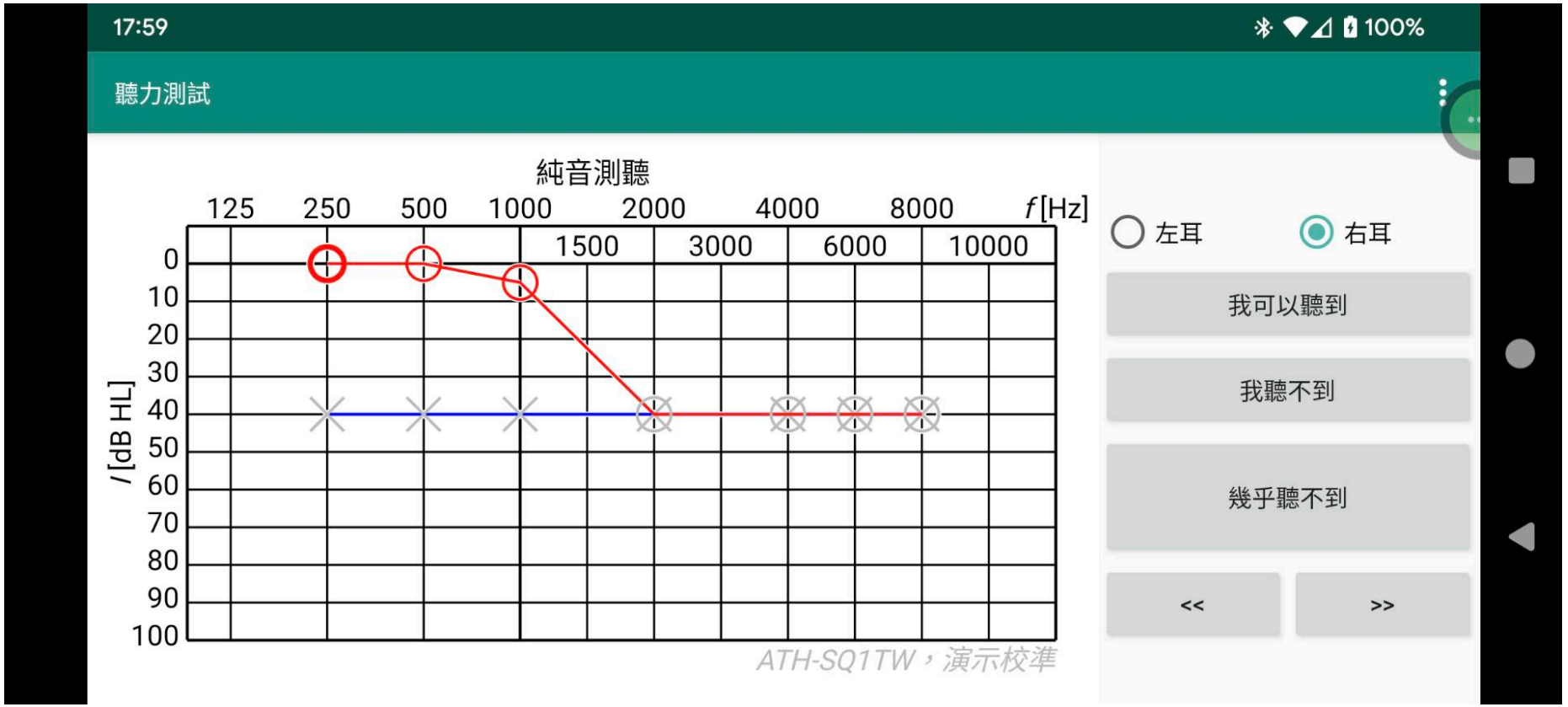
PMID: 30614898 DOI: 10.1097/MAO.0000000000002080

Active MD (1 episode within 4 wks), protable audiogram QD for 3 months
Manually track vertigo

4F + 1M, age 49.8y, disease duration 4mo to 5yrs, 72 tests (45 - 102)
Affected ear (2.5 - 25dB) (IQR)
Unaffected ear (0 - 6.25dB) (IQR)


聽力測試
e-audiologia.pl
解除安裝
開啟


聽力測試
聽力閾值測試
進行新的純音測聽測試
語音清晰度測試
進行新的噪點清晰度測試
瀏覽測試
瀏覽以前的測試


17:59
100%
聽力測試
純音測聽
125
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ATH-SQ1TW，演示校準
左耳
右耳
我可以聽到
我聽不到
幾乎聽不到
<<
>>

17:30
100%
聽力測試
2024年1月24日
17:29:45
PTA
純音測聽
125
250
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輕度聽力損失
中度聽力損失
嚴重聽力損失
耳聾
ATH-SQ1TW，演示校準

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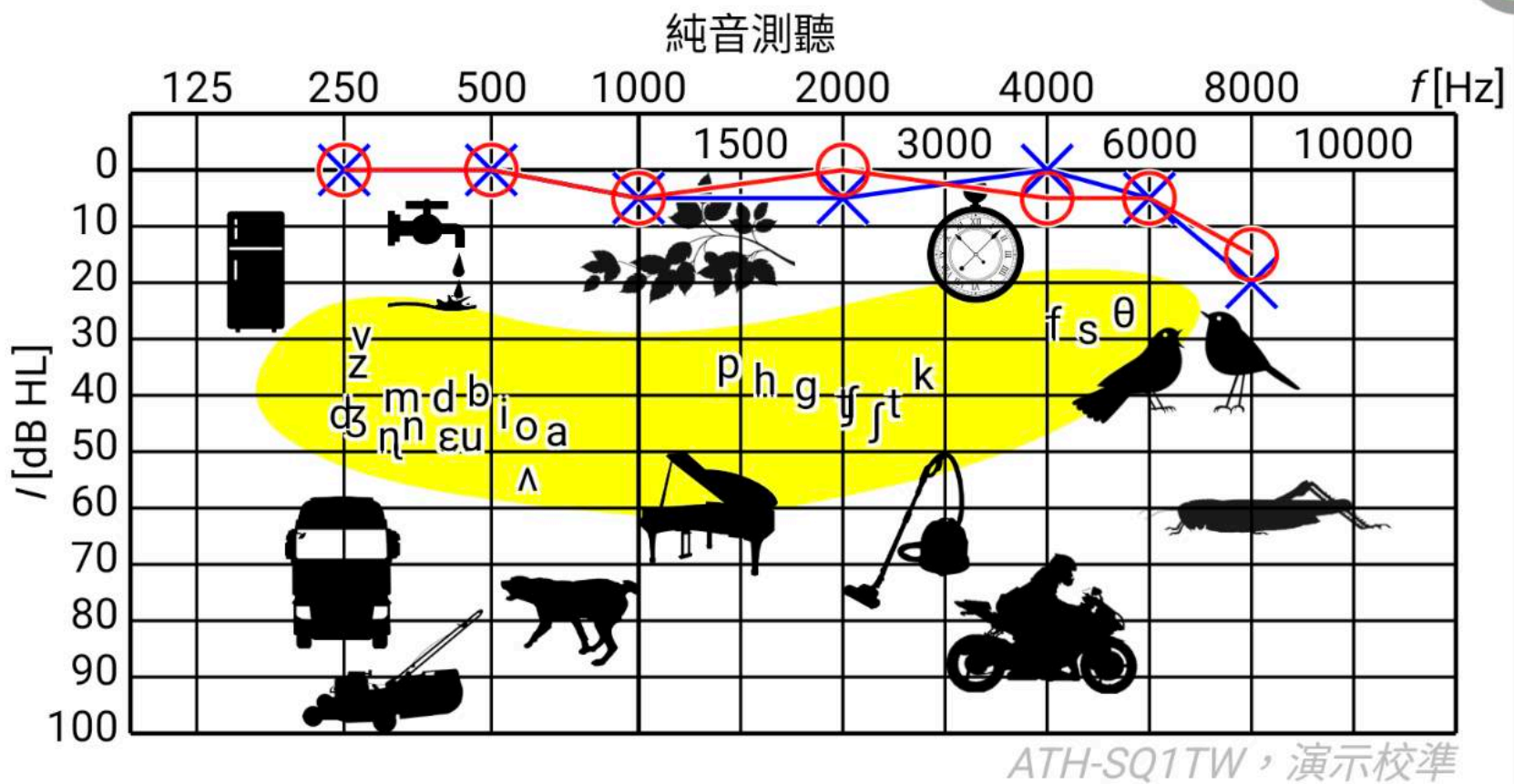
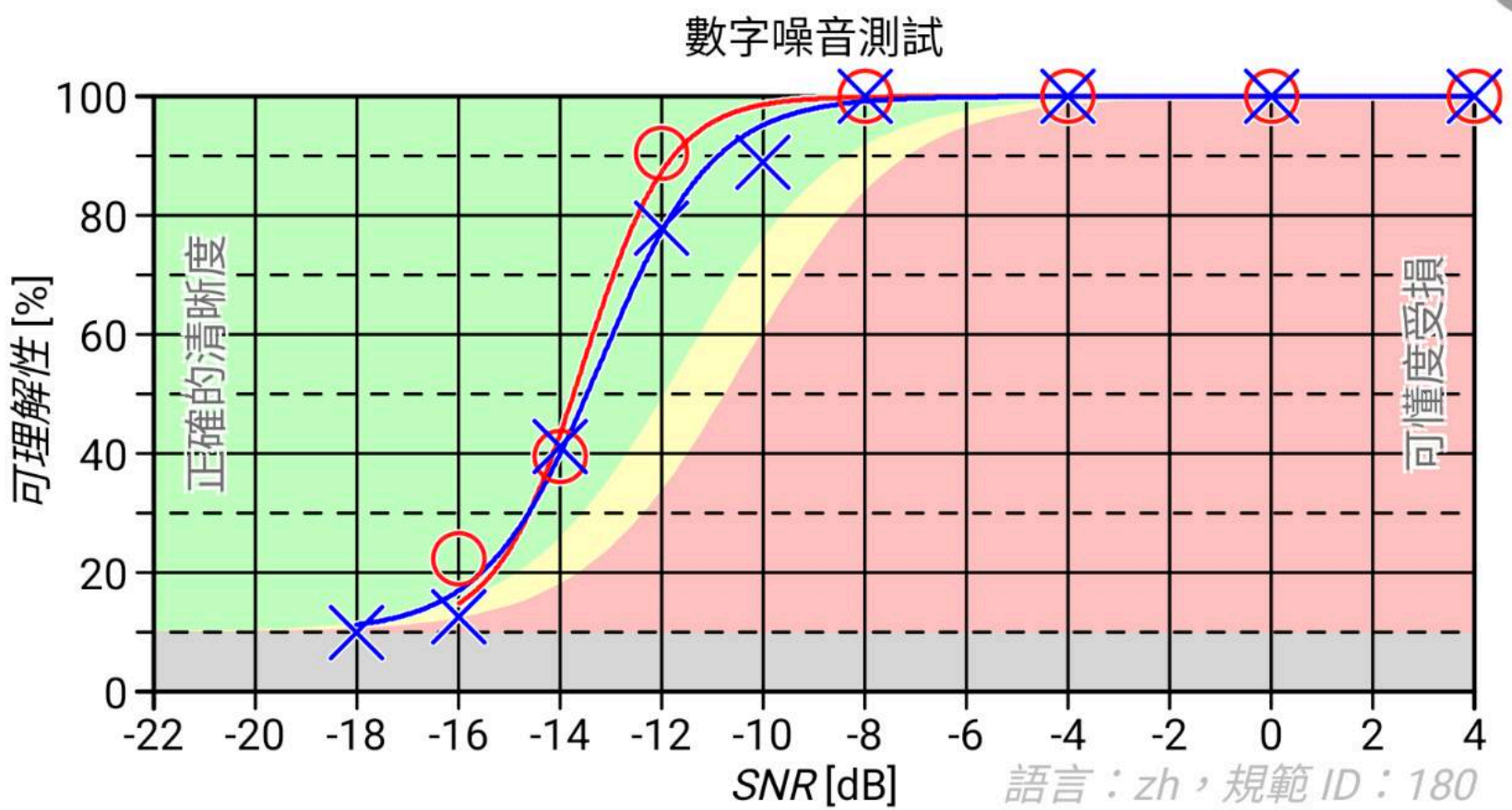
聽力測試

2024年1月24日
17:29:45 PTA



2024年1月24日
17:50:35 DIN

2024年1月24日
17:29:45 PTA

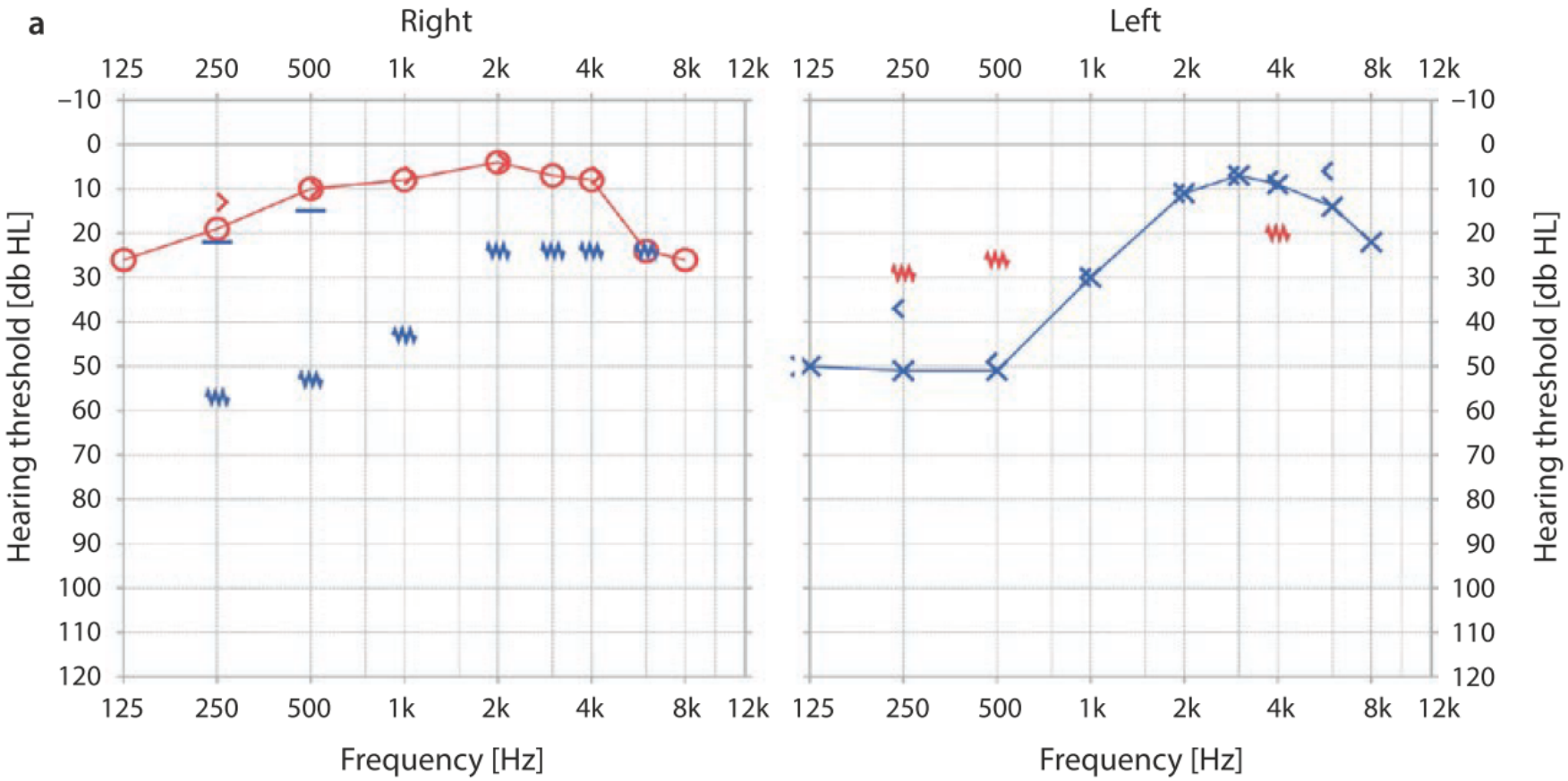


Lab Examination

- Audiometry:
  - Unilateral SNHL

    BC worse than unaffected ear by **at least 30dB** at each of **2 contiguous frequencies below 2000 Hz**.
  - Bilateral SNHL

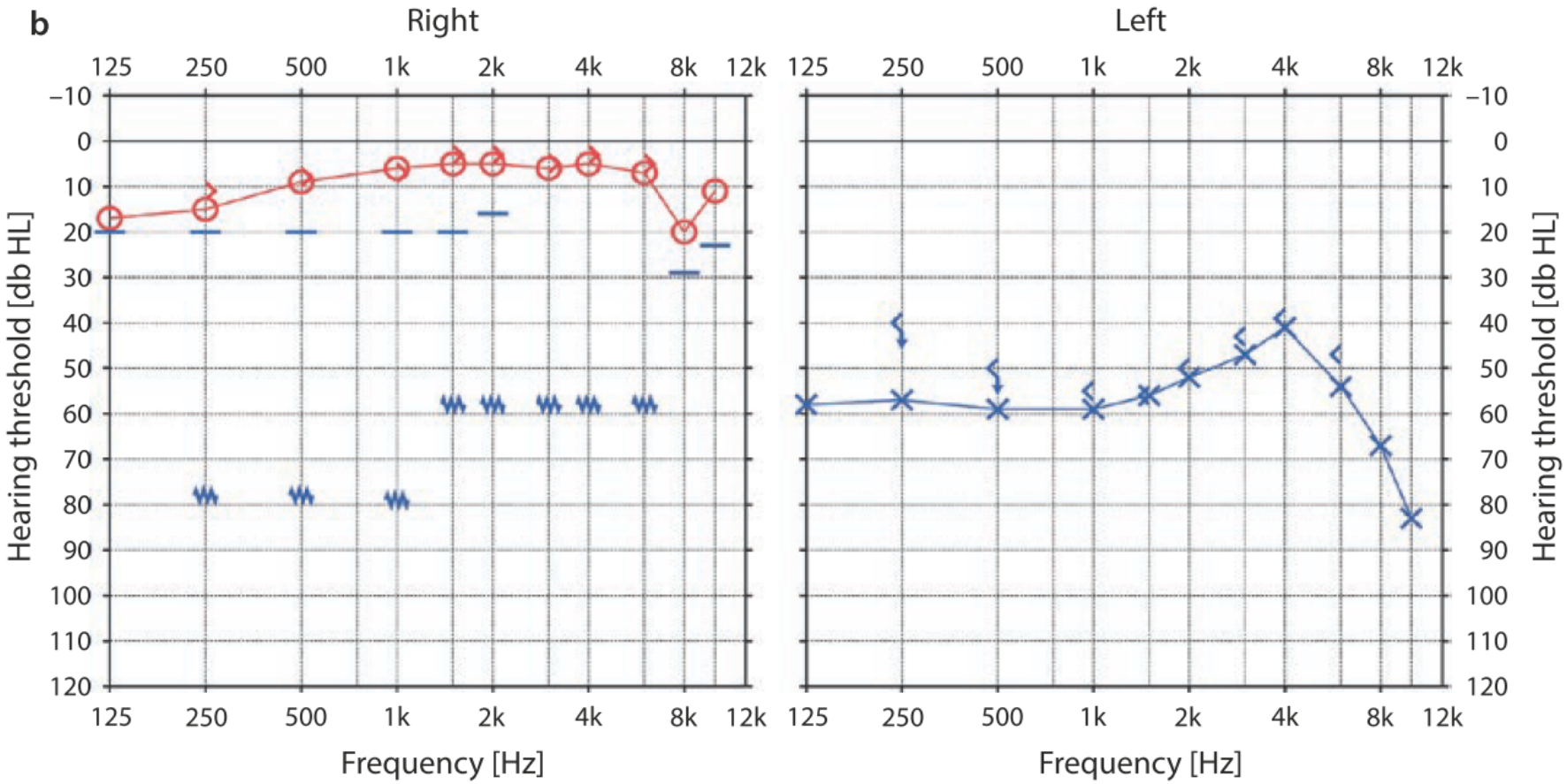
    BC absolute threshold **at least 35dB** at each of **2 contiguous frequencies below 2000 Hz**.



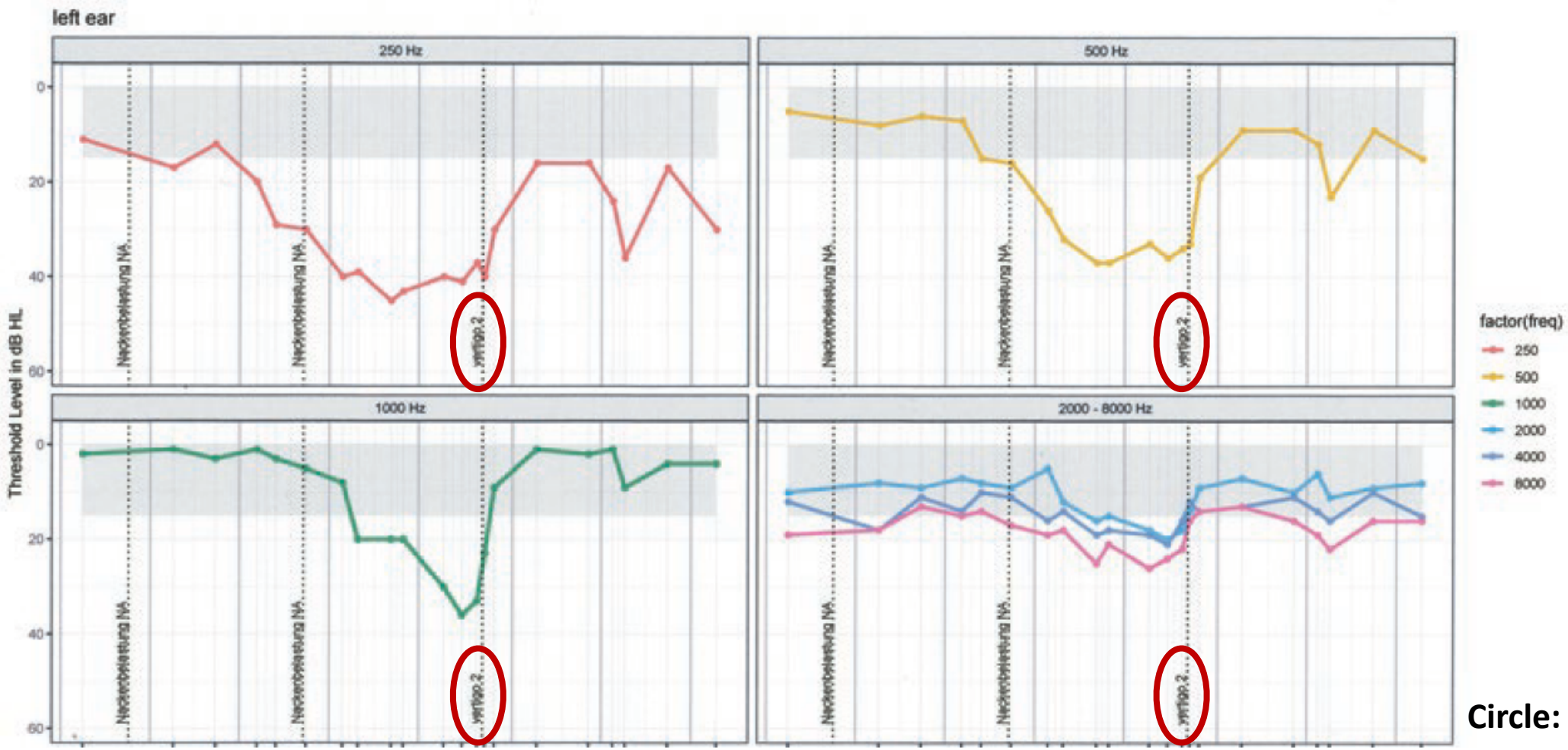
a Left-sided sensorineural hearing loss in the low-frequency range. There must be a reduction of hearing of at least 30 dB in two neighboring frequencies below 2000 Hz.

Lab Examination

- Audiometry:
  - Recovery of SNHL in low frequency at some point in time supports the diagnosis of MD.
  - PTA allows a differentiation between MD and VM, but there is **a clear overlap**
  - Bilateral synchronous SNHL -> consider **autoimmune inner ear disease**
  - After several episodes, MD can also involve **medium** and **high** frequencies.



b Left-sided sensorineural pantonal hearing loss.



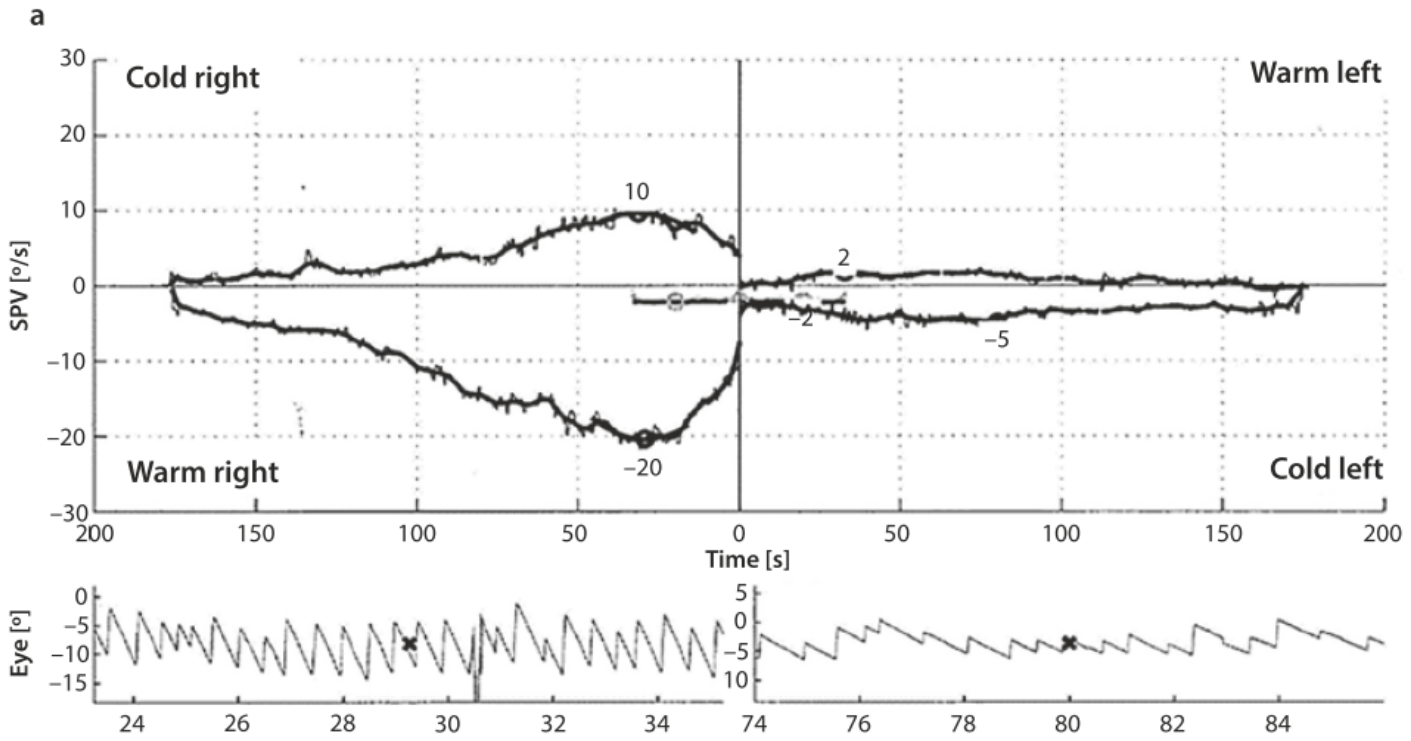
Circle: vertigo

Audiogram for four different frequency spectra recorded by a patient using an **audio app** before, during, and after an attack. There was a decrease of hearing in the low-frequency range before and during the attack with an improvement after the attack.

Complementary Tests

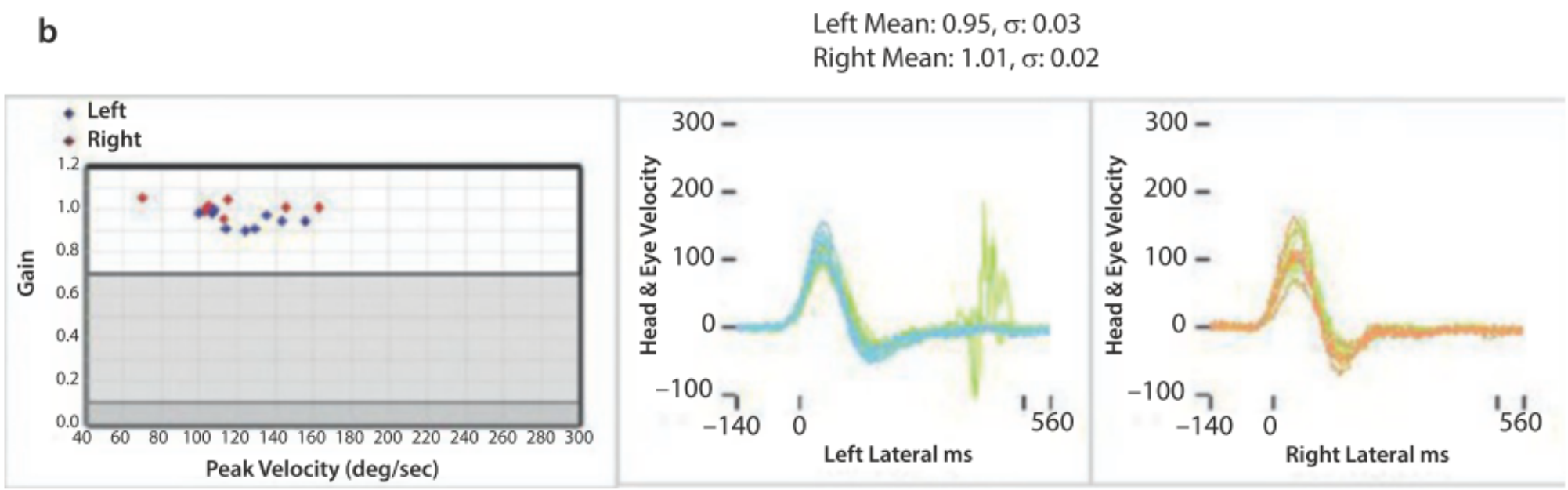
- Pathological caloric but pseudo-normal vHIT
  - Causes are not yet completely understood
  - Increase of the diameter of the endolymphatic space with a change in the hydrodynamics, leading to a pseudo-normal HIT
- VEMP is less often impaired

Caloric Test



Partial deficit on the left side in the low-frequency range

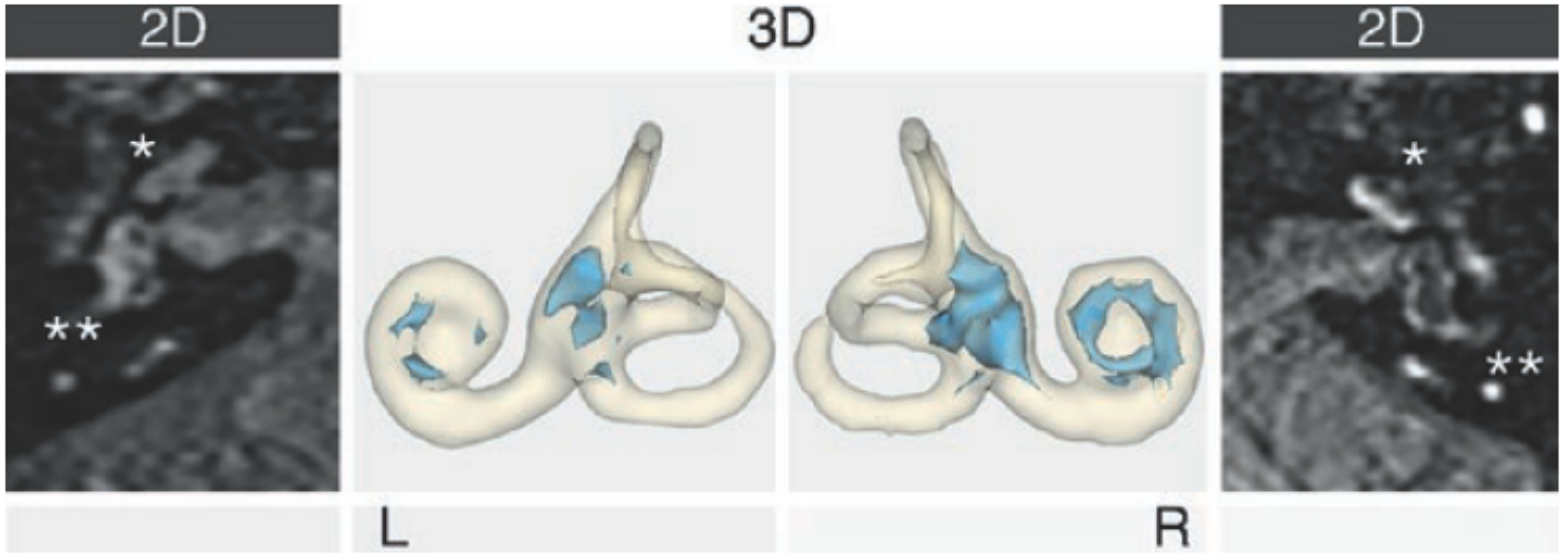
Video-HIT



Normal (or pseudo-normal) VOR gain in the high frequency range.

Imaging

- High resolution MRI of inner ear with Gd: **endolymphatic hydrops (ELH)**



asymmetrical ELH on the right side (R) with normal findings on the left (L). Gadolinium diffuses into the perilymphatic space only (white, *cochlea, **labyrinth), which explains why ELH is only indirectly visualized by contrast sparing. 3D reconstruction (middle) can demonstrate the whole extent of the ELH (blue) (Kindly provided by V. Kirsch)

Imaging

- Data supportive of ELH
  - Se 84.6%, Sp 92.3%
- Data against ELH
  - ELH also found in healthy subjects
  - ELH correlated with hearing impairment, but not the vestibular deficit
  - 10% in sacculus, 40% of SNHL > 45dB without vestibular symptoms
  - VM with auditory symptoms: 20% with ELH
  - Study 1: 99.4% of MD, 31% of healthy, 28.1% of VM, 25.9% of vestibular schwannoma
  - Study 2: 80% of MD, 25% of MD+VM, 8% of VM

Imaging (Cont’d)

- ELH is a necessary but not sufficient condition for the diagnosis of MD.
- **Brain MRI+C** should, **of course**, be performed to exclude other pathologies (especially vestibular schwannoma).

Differential Diagnosis

- Patients can fulfill the criteria for both MD and VM.
- Supportive features of VM:
  - No evidence of hearing impairment < 2000Hz
    - Mild hearing disturbance in VM:
      - Unilateral 3-12%
      - Bilateral 18%
  - Typical migrainous symptoms during > 50% of the attacks
  - Migraine history
  - Mild-to-moderate central ocular motor dysfunction in the attack-free interval (60%)
  - Convincing response to migraine acute and prophylactic treatment

Box 10.3 Important Differential Diagnoses for MD (in Alphabetical Order)

- Autosomal dominant sensorineural hearing loss
- Autoimmune inner ear disease
- Benign recurrent vestibulopathy
- Cerebrovascular disease (stroke/TIA in the vertebrobasilar system, namely AICA territoty) (see ► Chap. 13)
- Cogan's syndrome
- Endolymphatic sac tumor
- Meningiomas and other masses of the cerebellopontine angle
- Otosyphilis
- Susac syndrome (low-frequency hearing loss, tinnitus, visual loss, and/or central neurological/psychiatric symptoms due to an autoimmune microangiopathy)
- Syndrome of the third mobile windows (see ► Chap. 12)
- Vestibular migraine (see ► Chap. 14)
- Vestibular paroxysmia (see ► Chap. 11)
- Vestibular schwannoma

Differential Diagnosis (Cont'd)

- Supportive features of AUVP
  - Duration > 24hrs
- Cogan's syndrome
  - Impaired vestibular function, SNHL, interstitial keratitis
  - Typically bilateral
  - Inflammation: ESR, CRP, WBC
  - Treatment: IV MTP 1000mg QD x 5 days
  - Even if Cogan's syndrome is only suspected, immediate and aggressive immunosuppressive therapy is fully indicated.

Differential Diagnosis (Cont'd)

- Benign recurrent vestibulopathy
- Vestibular paroxysmia: may also be associated with audiological S/S
- For tumarkin's otolithic catastrophe:
  - Paroxysmal brainstem attack (MS?)
  - TIA in VB territory
  - Cardiovascular diseases
- AICA infarction

Diagnosis

- PTA
  - AUVP
  - AICA
- Audio apps
- Contrast MRI: exclude vestibular schwannoma
  - ELH: requires further evaluation

Discussion

- Experiences of audio apps
- Nystagmus
- VEMP?
- Is Brain MRI+C a must?

Pathology and Pathophysiology

Pathological Anatomy Etiology

- Endolymphatic Hydrops (ELH)
  - “Glaucoma of the inner ear”
  - 99.4% in MD
  - High production or low reabsorption of endolymph
  - Complex impairment of ion homeostasis: autoimmunity and genetics

Pathophysiology

Rupture of the endolymph **membrane** +/- Opening of tension-sensitive unselective **ion channels**

→ **Increase** in **potassium** concentration in the **perilymphatic** space with potassium-induced depolarization

→ Initially causes a **transient excitation**, subsequently a **conduction block**

→ Vertigo, hearing problem, direction changing nystagmus

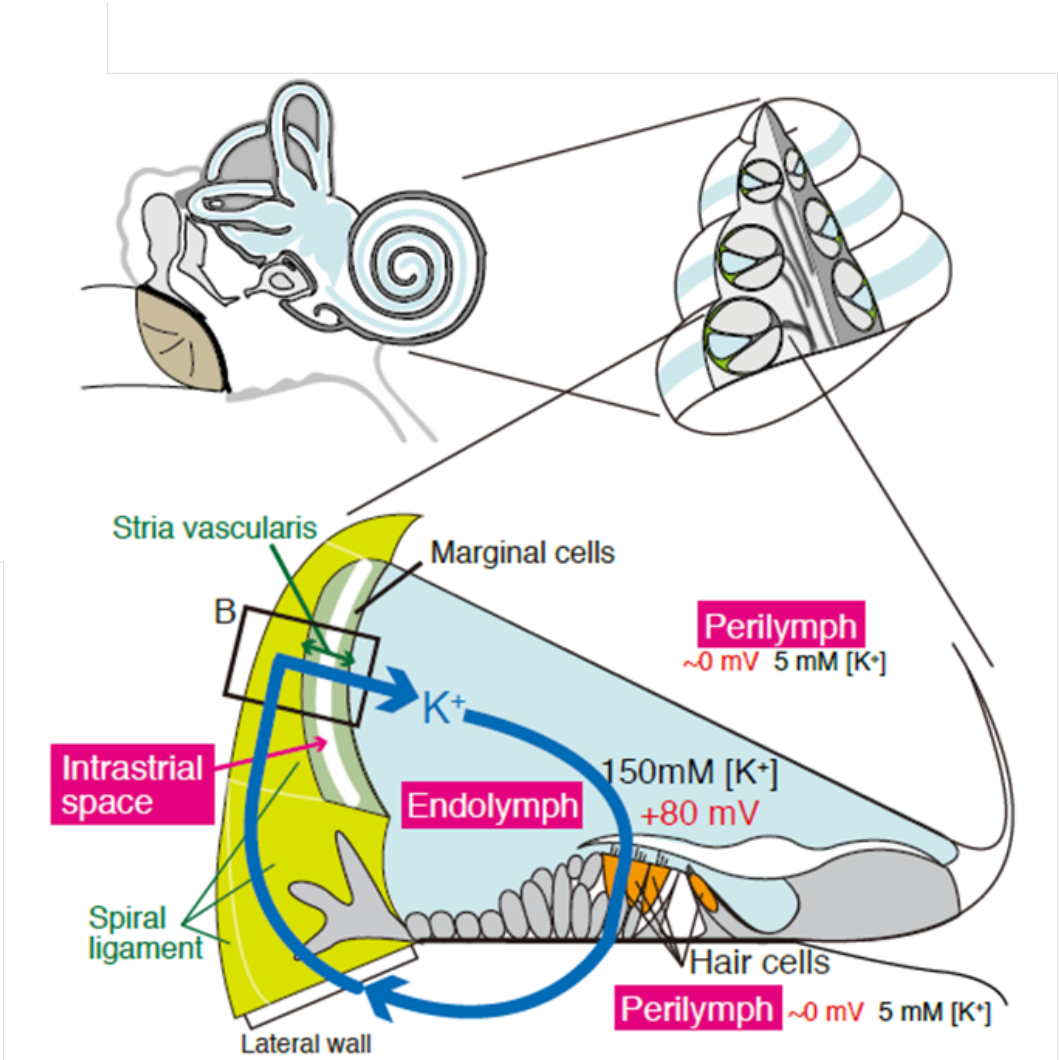


Fig. 1 The cross section of the cochlea

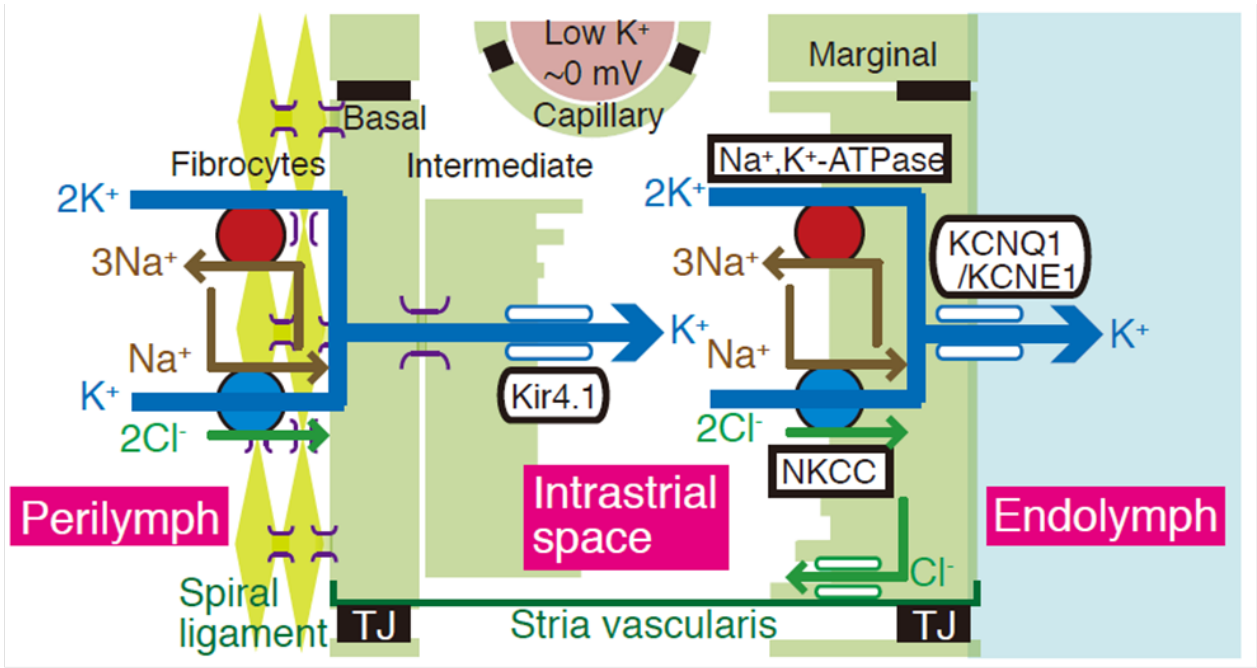


Fig.2 Functional coupling of ion channels and transporters

Treatment - Overview

Treatment - Overview

- **No evidence to date:**
  - Low-salt diet
  - Abstinence of coffee or alcohol
  - Diuretics
  - Endolymphatic sac surgery
  - Meniett device
  - Betahistine 144mg/d
  - Intratympanic dexamethasone

Treatment - Overview (Cont'd)

- **Betahistine**: weak H1 agonist and H3 antagonist
  - Weak H1 agonist: increase membrane permeability -> reduce ELH
  - H3 antagonist: dose-dependent cochlear blood flow
  - 99% PO betahistine is metabolized by MAO-B/A in GI tract -> Add MAOi (selegiline or rasagiline)
  - Evidence:
    - 48 or 144mg/d not superior than placebo (but strong placebo effect 70%)
    - Uncontrolled observational study: higher dosage
    - Bioavailability increased by 5mg selegiline by a factor of 100

Treatment - Overview (Cont'd)

- Intratympanic steroids
  - Double-blind placebo-controlled trial in 2005: 82% vs 57%
  - High-dose, 3 months dexamethasone: no difference (placebo effect 60%)
  - Pharmacokinetics of steroids are highly variable
- Intratympanic gentamicin
  - Reduce frequency of vertigo attack
  - Damage type I hair cells
  - Effect develops with a delay of weeks
  - Single injection, or Q4W FU
  - Only given to patient already with significant hearing impairment
  - However, meta-analysis concluded that there is only low evidence.
  - 47% MD develop the condition bilaterally

Treatment - Overview (Cont'd)

- Comparison of intratympanic steroids and gentamicin
  - Controversial
- Combined intratympanic therapies
  - Dexamethasone + betahistine > dexamethasone + placebo
  - Gentamicin + dexamethasone > dexamethasone alone

Treatment - Overview (Cont'd)

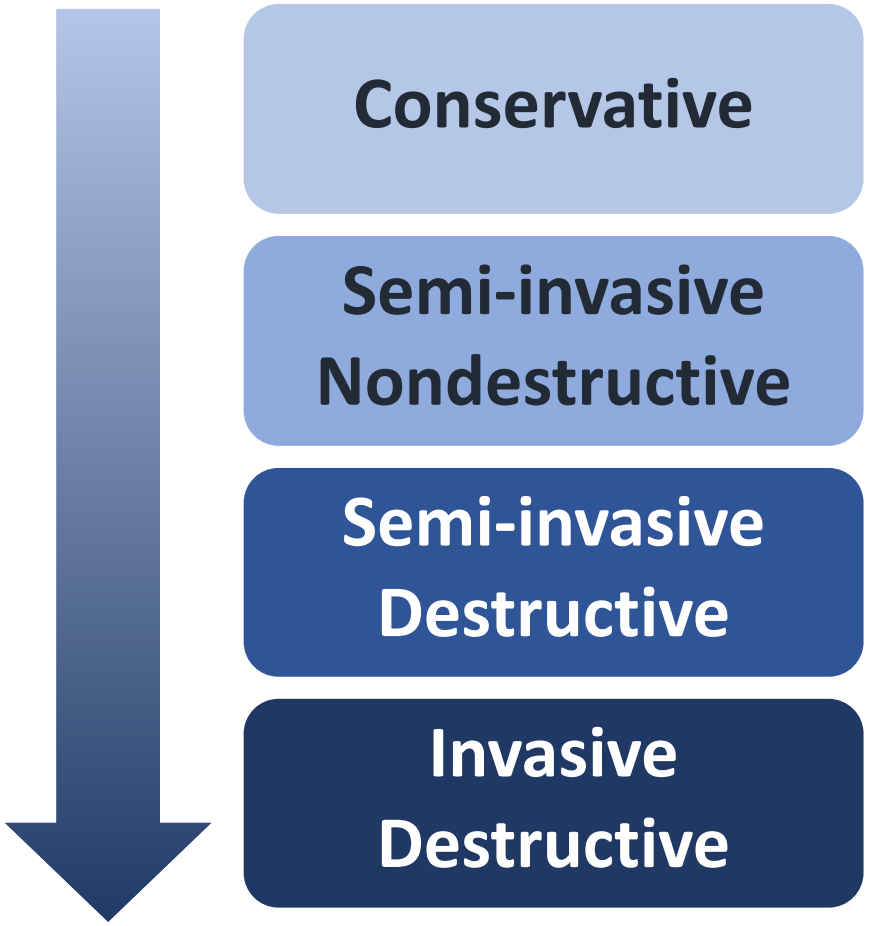
- Endolymphatic sac surgery
  - Cochrane: efficacy not proven
- Labyrinthectomy + cochlear implantation
  - For advanced MD

Treatment - Pragmatic Therapy

Symptomatic Treatment of the Attacks

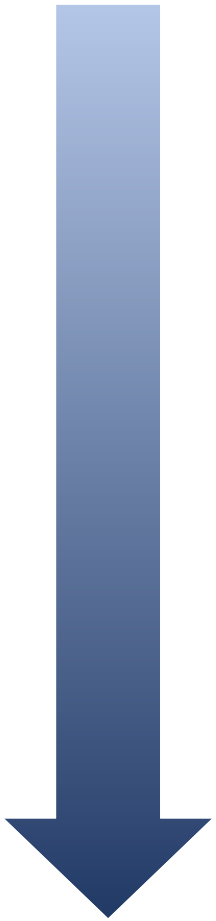
- Dimenhydrinate 50-100mg PO / Supp, or 1-3 x 100mg/day IV
- Ondansetron 4-8mg PO
- Lorazepam 0.5-1.0 sublingually

Prophylactic Therapy



Incremental Approach

Prophylactic Therapy



Conservative

Semi-invasive
Nondestructive

Semi-invasive
Destructive

Invasive
Destructive

Betahistine dihydrochloride

- ≥ 96mg TID (24mg x 4 x 3) for ≥ 12 mo
- If free of attack for 6 months
  - Taper 1 tablet every 3 months
- If frequency remains unchanged after 3-mo Rx
  - Increase to ≥ 480mg/d (24mg x 20)
- Potential alternatives
  - 4 x 48mg/d + selegiline 5mg/rasagiline 1mg

Prophylactic Therapy

Conservative

Semi-invasive Nondestructive

Semi-invasive Destructive

Invasive Destructive

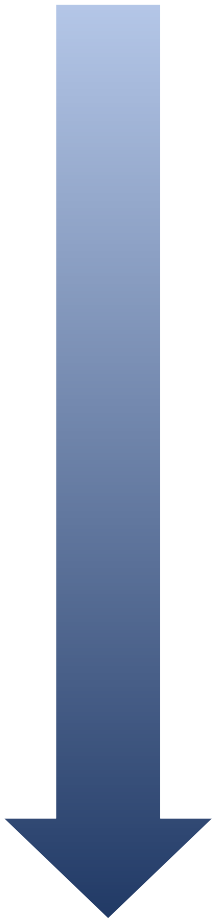
Intratympanic Glucocorticoids

- Methylprednisolone 50mg Q2W, 2 injections
- Dexamethasone 2mg Q2W, 2 injections

10.7.2.4 Intratympanic Treatment

We very rarely see an indication for intratympanic treatment. If it is indicated, one can start with glucocorticoids, which are not ototoxic: 50 mg methyl-prednisolone or 2 mg dexamethasone, two injections with a latency of 2 weeks. If this not sufficient even

Prophylactic Therapy



Conservative

Semi-invasive Nondestructive

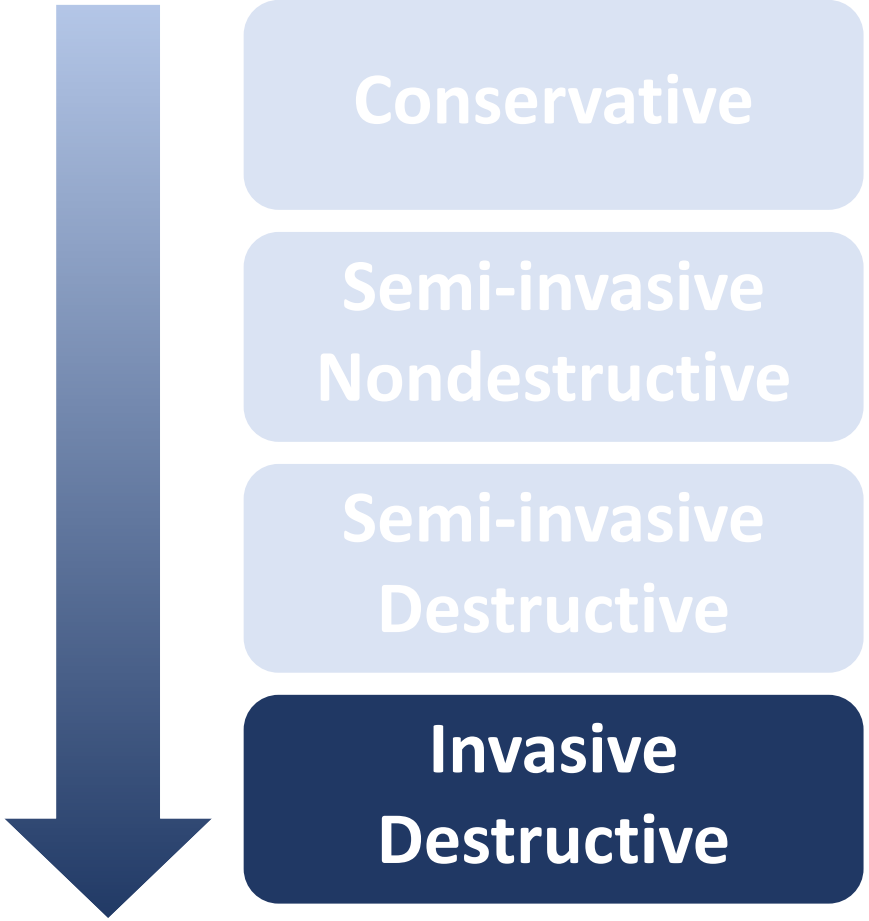
Semi-invasive Destructive

Invasive Destructive

Intratympanic Gentamicin

- Consider if
  - Prominent impairment of vestibular and audiological function
  - The affected ear can be identified certainly
  - No response to intratympanic glucocorticoids after 3 months
- Gentamicin 12-40mg single dose
  - May give additional dose after 4-8 weeks

Prophylactic Therapy



Labyrinthine destruction with simultaneous cochlear implantation

- Consider (be cautious of) the high frequency of bilateral MD

Treatment of Tumarkin's Otolithic Catastrophe

- Very high dosage of betahistine + MAOBi
- Intratympanic steroids or gentamicin
  - Identify the affected ear with various measures, including audiogram, caloric test, HIT, VEMP.
- No controlled studies on this.

Physiotherapy

- Daily and life-long training, especially in bilateral MD
- Enhancing central compensation in patients with severe attack and transient peripheral vestibular deficit

Discussion

- Dosage of betahistine
- Experience of MAOBi
- Diuretics? such as acetazolamide or hydrochlorothiazide

Take Home Message

- **Audio apps** may assist diagnosis of MD.
- **MAOBi** may enhance the effect of betahistine in prophylaxis of attacks.
- **Brain MRI with contrast** needs to be considered in patients with audiological and vestibular symptoms to exclude vestibular schwannoma.

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