VESTIBULAR MIGRAINE

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Part 1

Patient history, Epidemiology, Course

Introduction

1. **Most frequent cause** of sEVS
2. **Current diagnostic criteria**
   1. International Bárány Society for Neuro-Otology
   2. International Headache Society, ICHD
3. In the outpatient clinic
   1. 7-12% patients of vertigo
   2. 9-30% patients of migraine
4. Terminology

   ‘Migrainous vertigo,’
   ‘migraine-associated dizziness,’
   ‘migraine-related vestibulopathy’

3. Diagnostic criteria for vestibular migraine

Go to:

Previously used terms: migraine-associated vertigo/dizziness, migraine-related vestibulopathy, migrainous vertigo.

1. Vestibular migraine

A. At least 5 episodes with vestibular symptoms[1] of moderate or severe intensity[2], lasting 5 min to 72 hours[3]
B. Current or previous history of migraine with or without aura according to the International Classification of Headache Disorders (ICHD-3)[4]
C. One or more migraine features with at least 50% of the vestibular episodes[5]:
   - headache with at least two of the following characteristics: one sided location, pulsating quality, moderate or severe pain intensity, aggravation by routine physical activity
   - photophobia and phonophobia[6],
   - visual aura[7]
D. Not better accounted for by another vestibular or ICHD diagnosis[8]

2. Probable vestibular migraine

A. At least 5 episodes with vestibular symptoms[1] of moderate or severe intensity[2], lasting 5 min to 72 hours[3]
B. Only one of the criteria B and C for vestibular migraine is fulfilled (migraine history *or* migraine features during the episode)
C. Not better accounted for by another vestibular or ICHD diagnosis[8]

1. 1

無預兆偏頭痛

Migraine without aura

1

A. 至少有五次發作符合基準 B-D

B. 頭痛發作持續 4-72 小時 (未經治療或治療無效)

C. 頭痛至少具下列四項特徵其中兩項：

- **單側**
- **搏動性**
- **疼痛程度中或重度**
- **日常活動會使頭痛加劇或避免此類活動 (如走路或爬樓梯)**

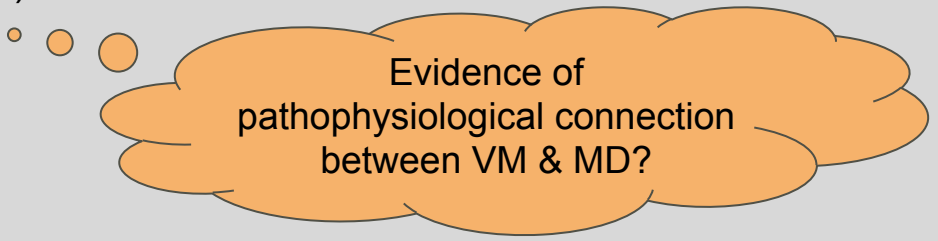
D. 當頭痛發作時至少有下列一項：

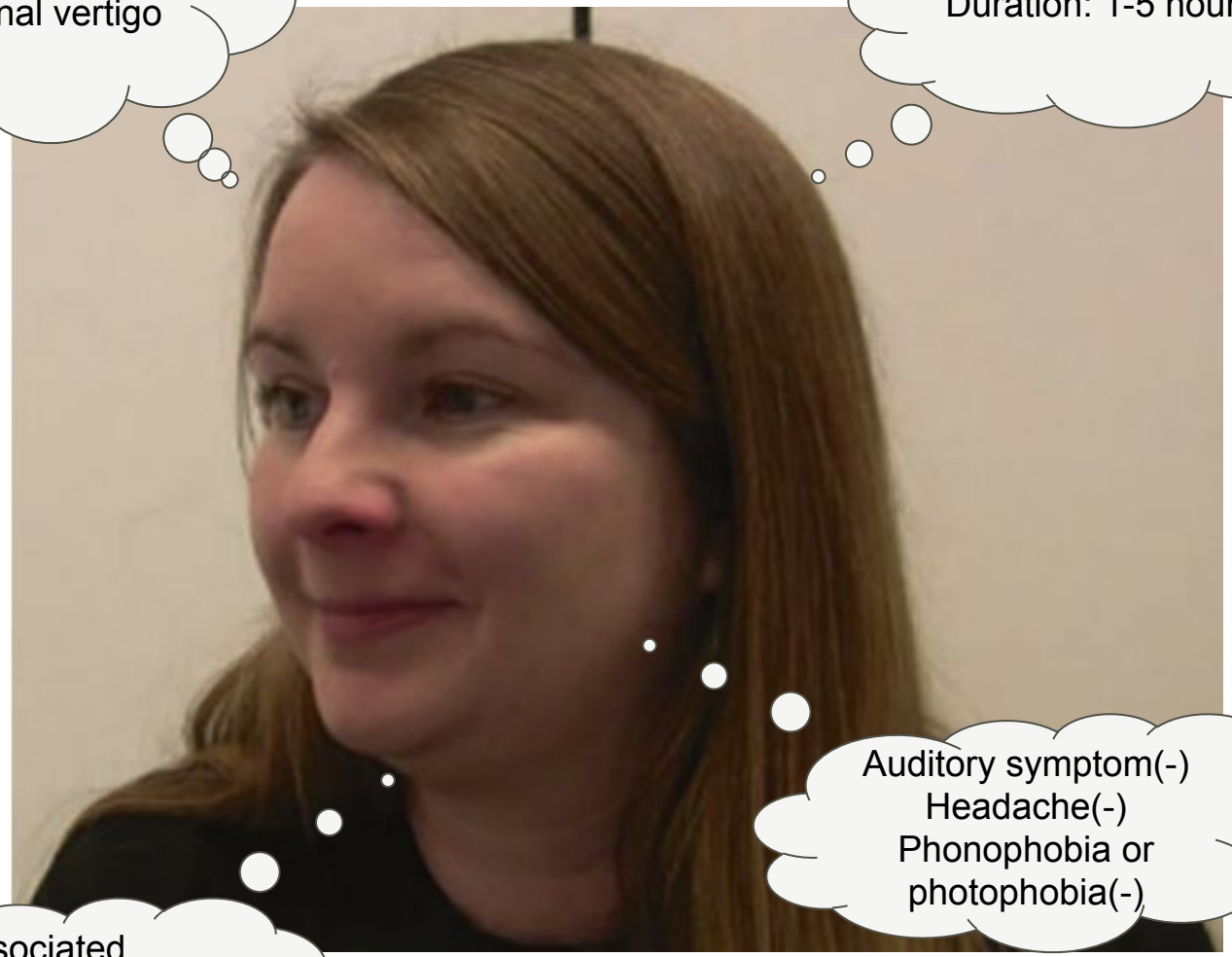
- **噁心 及 / 或 嘔吐**
- **畏光及怕吵**

E. 沒有其他更合適的 ICHD-3 診斷。

Patient history

- Main symptoms
  - **Recurring attacks** of various combinations of vertigo, dizziness, and imbalance of stance and gait
  - Visual disorders (**oscillopsia** or visual aura)
  - Accompanied or followed by primarily **occipital head pressure or headache**
    - **More rarely unilateral localization**
  - Nausea and vomiting
  - Photophobia and phonophobia
- Associated **hearing symptoms**
  - Only dizziness/vertigo (monosymptomatic attack in 75% VM)
  - Hearing disorder, tinnitus, or ear pressure
- Family history
  - Rare familial form (AD type)





Probable vestibular migraine

- Duration:
  - 5 minute to 72 hours
- Severity
  - Moderate to severe
- One of below
  - History of migraine
  - 50% attack with
    - Migraine-type headache
    - Photophobia
    - Phonophobia
    - Visual aura

Vestibular migraine

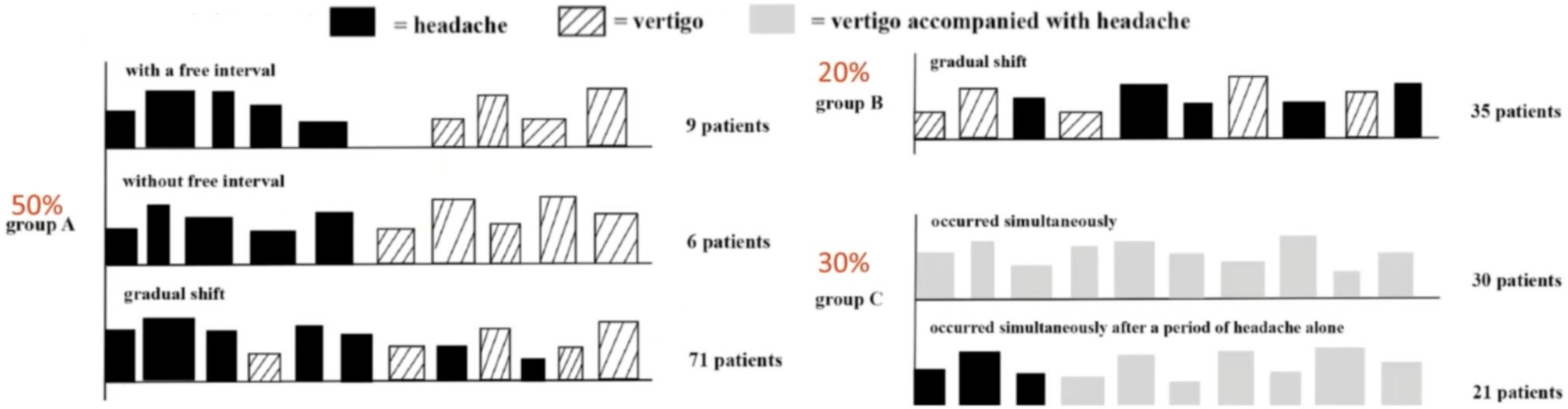
- Duration:
  - 5 minute to 72 hours
- Severity
  - Moderate to severe
- Both of below
  - History of migraine
  - 50% attack with
    - Migraine-type headache
    - Photophobia
    - Phonophobia
    - Visual aura

Epidemiology

- Lifelong prevalence
  - Vertigo 7%; migraine 16%
  - Vertigo + migraine 3.2%
    - Various vertigo syndromes
    - VM 1% (**F > M**, 3.65 times)
- 1-year prevalence
  - 2.7% in USA
  - 7-11% in dizziness clinic; >9% in headache clinic
- Age
  - **2 peak: younger age & 60-70 y/o**
  - 8.4 years for correct diagnosis (2001)
    - Currently better (Maybe?)
  - Transformation from migraine to single vertigo at **menopause age**

Temporal patterns of migraine and vertigo in VM

Group A: Headache → Vertigo
Group B: Vertigo → Headache
Group C: Vertigo/Headache simultaneously



Vertigo & dizziness in childhood

1. Attack between **1-4 y/o**
2. Seconds to minutes
3. Disappear in a few year

Migraine

- The **most frequency cause** in children
- Monosymptomatic course
  - Hard to differentiate with →
- Terminology
  - ‘Benign paroxysmal vertigo’
    - ICHD-3
    - Equivalent to migraine?
  - ‘Recurrent vertigo of childhood’
  - ‘Vestibular migraine of childhood’
  - ‘Probable vestibular migraine of childhood’
    - Barany Society 2021
  - ‘Paroxysmal vertigo of childhood’

Benign paroxysmal vertigo

Description:

A disorder characterized by recurrent brief attacks of vertigo, occurring without warning and resolving spontaneously, in otherwise healthy children.

Diagnostic criteria:

A. At least five attacks fulfilling criteria B and C

B. Vertigo[1] occurring without warning, maximal at onset and resolving spontaneously after minutes to hours without loss of consciousness

C. At least one of the following five associated symptoms or signs:

1. nystagmus
2. ataxia
3. vomiting
4. pallor
5. fearfulness

D. Normal neurological examination and audiometric and vestibular functions between attacks

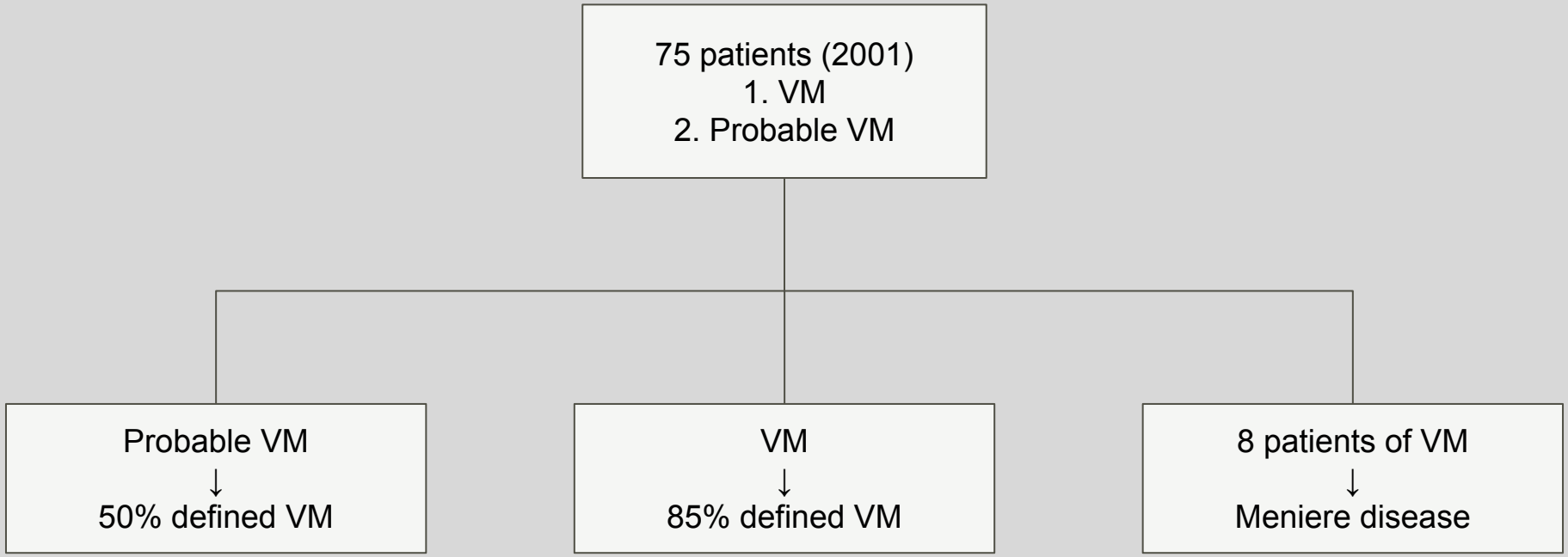
E. Not attributed to another disorder[2].

Notes:

1. Young children with vertigo may not be able to describe vertiginous symptoms. Parental observation of episodic periods of unsteadiness may be interpreted as vertigo in young children.
2. In particular, posterior fossa tumours, seizures and vestibular disorders have been excluded.

International Headache Society		Bárány Society
Included	**Confirmed**	**Included**
Benign Paroxysmal Vertigo	**Vestibular Migraine**	**Probable Vestibular Migraine**
A. At least five attacks fulfilling criteria B and C B. Vertigo occurring without warning, maximal at onset and resolving spontaneously after minutes to hours without loss of consciousness C. At least one of the following five associated symptoms or signs 1. Nystagmus 2. Ataxia 3. Vomiting 4. Pallor 5. Fearfulness D. Normal neurological examination and audiometric and vestibular functions between attacks E. Not attributed to another disorder.	A. At least 5 episodes with vestibular symptoms of moderate or severe intensity, lasting 5 min to 72 hours B. Current or previous history of migraine with or without aura according to the International Classification of Headache Disorders (ICHD-3) C. One or more migraine features with at least50% of the vestibular episodes: 1. Headache with at least two of the following characteristics: one sided location, pulsating quality, moderate or severe pain intensity, aggravation by routine physical activity 2. Photophobia and phonophobia 3. Visual aura D. Not better accounted for by another vestibular or ICHD diagnosis	A. At least 5 episodes with vestibular symptoms of moderate or severe intensity, lasting 5 min to 72 hours B. Only one of the criteria B and C for vestibular migraine is fulfilled (migraine history or migraine features during the episode) C. Not better accounted for by another vestibular or ICHD diagnosis

Course


75 patients (2001)
1. VM
2. Probable VM
Probable VM
↓
50% defined VM
VM
↓
85% defined VM
8 patients of VM
↓
Meniere disease

Part 2

Characteristics of Attacks, Clinical examination, Technical examination

Characteristics of Attacks

- Onset
  - **Spontaneous** 67% *(21-83%)*
  - Position-dependent vertigo attacks 24% *(17-65%)*
  - Viewing moving objects (Oscillopsia) or imbalance
- Accompanied symptom
  - Instability of stance 91%
  - Imbalance 82%
  - Rotating vertigo 57%
- Duration
  - **From seconds to hours**
  - 5-60 minutes 10-30%

Characteristics of Attacks

- Associated with **headache**
  - Often present but **not in every time**
  - Variation between patients or between attack, even in same patient
  - Time
    - Less than 59% **vertigo + headache**
    - 16% Vestibular symptom + headache
    - 10% Preceding
    - 3% Prodromal
    - 6% isolative vertigo + headache
- Other symptoms
  - Occipital head pressure
  - Light or sound hypersensitivity
  - Positive family history
  - Tired after attack
  - Urge to urinate??
  - Aural symptoms (mild and transient dysfunction)

Clinical examination

- During the attack interval (inter-ictal)
  - **Slight central ocular motor disorder** (8.6-63%)
    - Gaze-evoked nystagmus (sometimes dislocated)
    - A saccadic smooth pursuit beyond age normal (especially vertical)
    - A spontaneous horizontal or vertical nystagmus or fixational nystagmus (downbeat nystagmus)
    - A central positional nystagmus
  - **Increasing over the time (more while older)**
    - Slowing down by migraine prophylaxis
  - Peripheral vestibular alterations
    - Unilateral (8-22%) or bilateral (up to 11%)
  - Mild(!) hearing loss
    - 57% VM patients with auditory symptoms
    - Unilateral (3-12%) or bilateral (18%)
    - hearing deficits in the lower frequency range
    - Lower thresholds of otoacoustic emissions
    - A prolonged peak V of acoustic brainstem potentials

Clinical examination

- During the attack
  - **Pathological nystagmus** (70%)
    - **Central origin** 50%
      - Central positional nystagmus
    - Peripheral origin 15%
    - Unknown 35%
  - **Ear symptoms** (38%)
    - Tinnitus & mild hearing loss
    - Pressure in the ears (most bilaterally)
  - **Hypersensitive to movement** (31-77%) & motion sickness
    - A sensory neuron overexcitability

Up to 97%

Cocholar migraine?

Technical examination

- **VM is a clinical diagnosis**
- Posturography
- Measure of SVV
  - Normal value
- **VEMP**
  - Delayed, lost, or reduced in amplitude (or normal)
  - cVEMP can differentiate MD with VM
    - Higher asymmetry ratio of cVEMP amplitudes in MD
    - In MD, cVEMP > oVEMP

Part 3

Differential diagnosis and clinical problem

Differential diagnosis

- Differential diagnosis
  - Meniere disease
  - Vestibular paroxysmia
  - Episodic ataxia type 2
  - Transient ischemic attack (vascular problem)
- Comorbidities
  - Benign paroxysmal positional vertigo
  - Functional dizziness

Meniere disease

- Pathophysiologic combination in VM & MD
- Symptoms
  - Predominantly vestibular symptoms
  - Equal prevalence **in men and women**
    - Not in the earlier time
- **MD + migraine 56%**
  - > Normal control 25%
- Fulfilling both criteria is possible
  - **Overlapping syndrome**

Benign Paroxysmal Positional Vertigo

- **3 times more frequent** in migraineur
- A relapsing inner ear dysfunction (??)
  - The form of vasospasm (??)
  - Pathoetiology unknown
- The same manege of idiopathic BPPV

Episodic ataxia type 2

- **Autosomal dominant** disease
  - Mutation: **CACNA1** (calcium channel)
    - Impaired function of cerebellar Purkinje cells
- Symptoms
  - Episodic attack of dizziness
  - Ataxia
  - Ocular motor disturbances
    - Central nystagmus (downbeat nystagmus)
    - Even in attack-free interval
- Therapy
  - 4-aminopyridine
  - **Acetazolamide**

Episodic ataxia

1. Type 1-6
2. Type 1
   a. Mutation gene: KCNA1
   b. Symptom:
   episodic ataxia, myokymia, neuromyotonia

Functional dizziness

- **Importance of an early differential diagnosis of VM**
  - Development to functional dizziness more often
  - Comorbidities up to 65% with psychiatric disorder (anxiety and depression)
  - Vestibular symptoms much more strongly
    - Anxiety ↑↑↑
  - More impaired daily life
- Symptoms
  - Postural or diffuse dizziness
- Additional symptoms
  - Motivation and concentration disorders
  - Decline of performance
  - **Subjectively experienced restrictions** in professional and everyday activities
  - **Vegetative symptoms** that accompany the dizziness
    - tachycardia, nausea, profuse sweating, dyspnea, fear of suffocating, loss of appetite, weight loss
  - Disorders of mood
  - Sleep disorder
  - Symptoms of anxiety

Vascular event

- **Transient ischemic attacks in the vertebrobasilar system**
- Basilar artery thrombosis
- Brainstem/cerebellar hemorrhage
  - **Rapid development**
  - Vigilance disorders that can worsen until coma
  - Increasing deficits of the cranial nerves
  - Pareses or sensory deficits in the extremity
- **Vertebral artery dissection**
  - After trauma or chiropractic maneuver
  - Symptoms
    - Occipital head and nuchal pain, nuchal pressure
    - Dizziness
    - Brainstem ischemia
  - Important differential diagnosis of first migraine attack!!!

Part 4

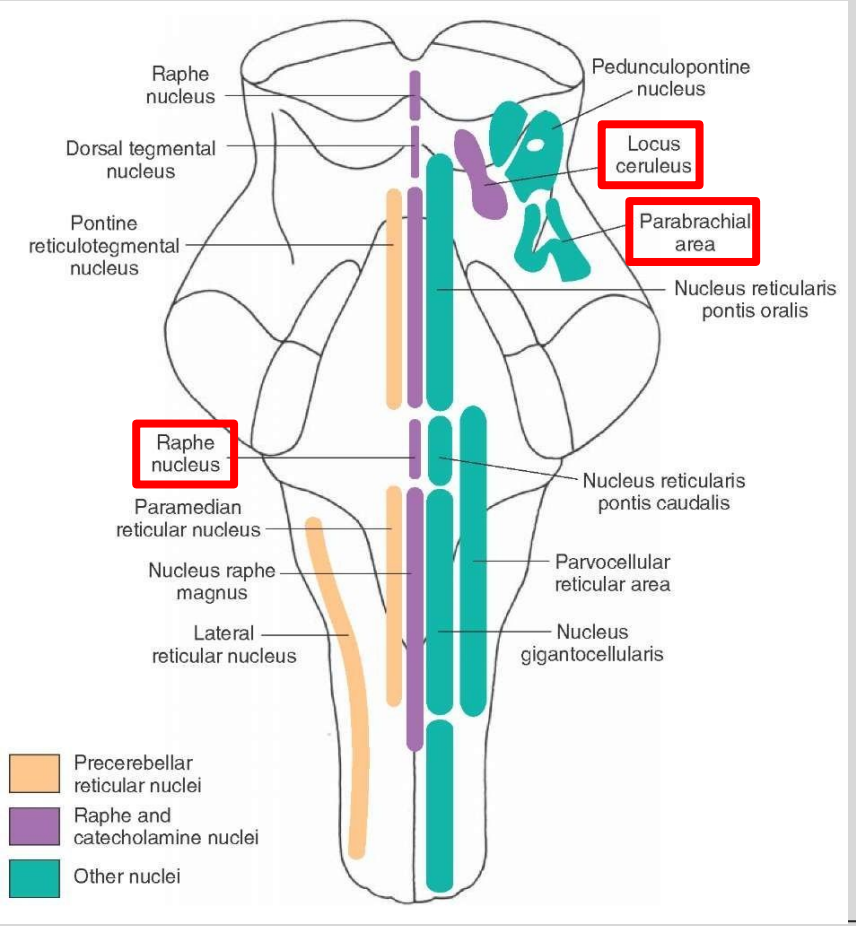
Pathophysiology and therapeutic principle

Pathophysiology

- Basic mechanism of vestibular dysfunction
  - **Not clear**
- Hypotheses
  - A simultaneous activation of vestibular and cranial nociceptive connections
  - Neuronal function disorders in the brainstem
    - Neuroinflammation & ischemia in the labyrinth
  - Gene for hemiplegic migraine (channelopathies?)
  - Cortical ‘spreading depression’

Vestibular & cranial nociceptive connections

- Same transmitters
  - **Trigeminal & vestibular ganglia**
  - Serotonin, capsaicin, & purinergic receptors
- Brainstem structure
  - **Modulation of sensitivity of nociceptive pathways**
    - Parabrachial nucleus
    - Nucleus raphe
    - Locus coeruleus
  - Development of anxiety

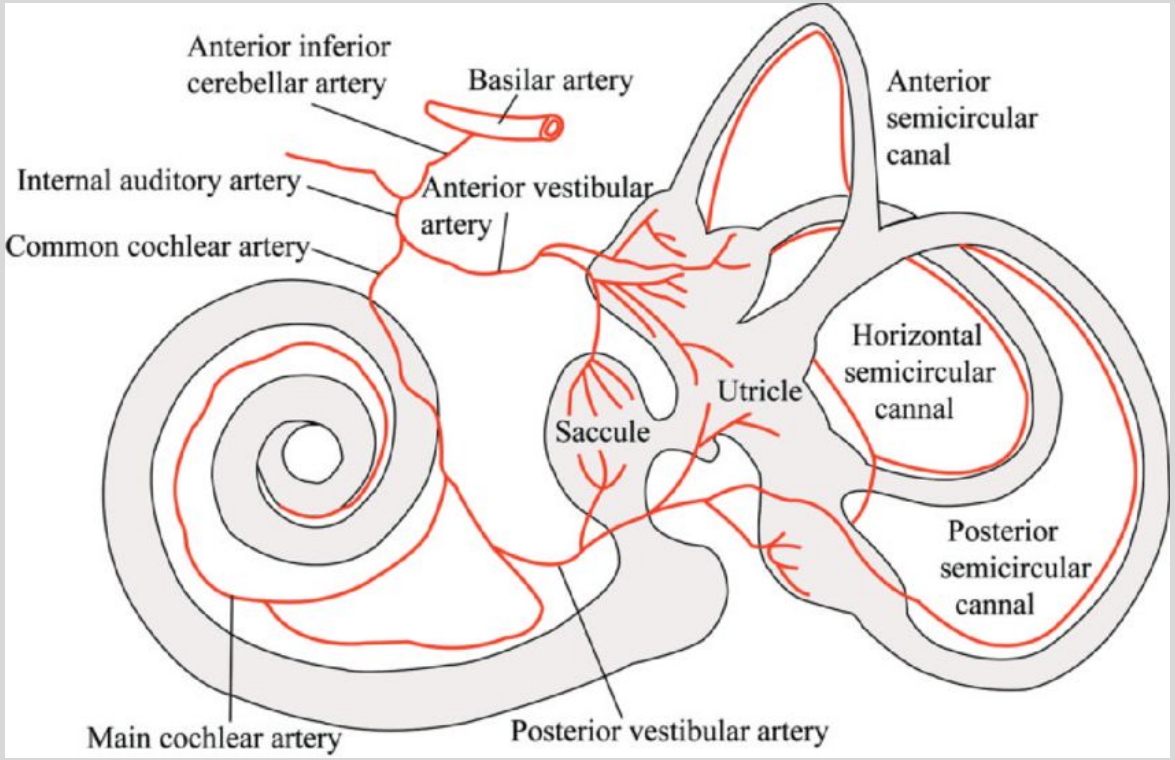


Neuronal functional disorders in the brainstem

- **Locus coeruleus**
  - Most important central core of the **noradrenergic system**
  - **Modulator of the cerebral blood flow**
    - Via trigeminovascular system
    - Primarily neurovascular headache syndrome
    - Animal model
- Serotonergic **dorsal raphe nucleus**
  - PET evidence
  - Activated immediately after successful treatment of a migraine attack
    - Not during the symptom-free interval
  - Modulating the processing in the vestibular nuclei
    - Central amygdaloid nucleus
    - With Non-serotonergic dorsal raphe nucleus

Role of trigeminal nerve

- **A dense sensory innervation**
  - Cerebral, basilar, and meningeal blood vessels
  - Inner ear arteries
    - AICA
  - Cochlea & the vestibular labyrinth
    - **Ophthalmic branch (V-1)**
    - Parasympathetic innervation to the basilar artery & AICA



Neuroinflammation & ischemia in the labyrinth

Activation of CN V

Releasing CGRP & substance P

migraine

Local neuroinflammation

Vasodilation

Permeability change

Edema

Endolymphatic hydrop (EH)

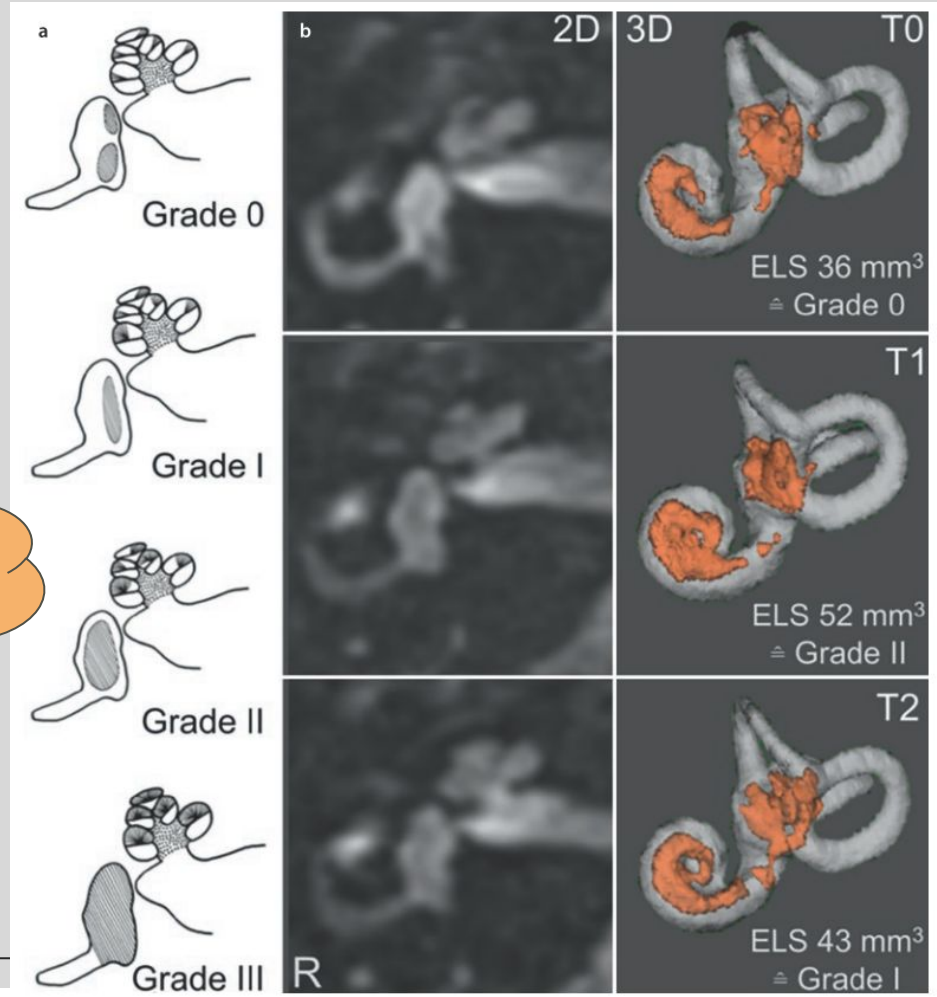
More difficult to differentiate between VM & MD

inability to auto-regulate

Migraine-associated vasculopathy

Persisting EH

Inner ear ischemia



A little difference?

- Vestibular migraine
  - Rarely observed endolymphatic hydrop
- Meniere disease
  - Cochlear hydrops
  - +/- vestibular hydrops
  - Also happen in VM + MD
- Migraine pathomechanisms
  - Causative factor of inner ear dysfunction
  - Common final pathway of hydrops
  - **Overlapping syndrome**

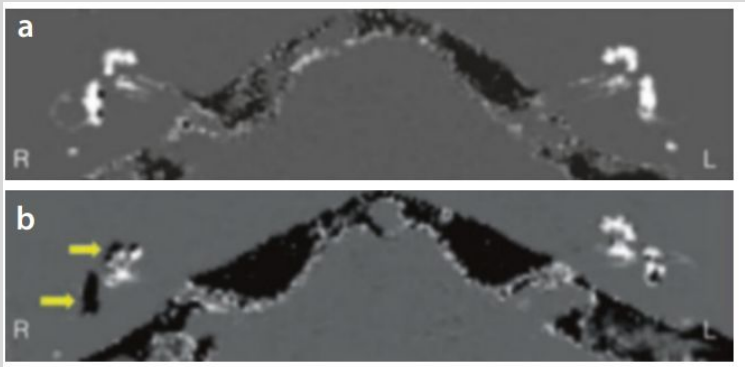


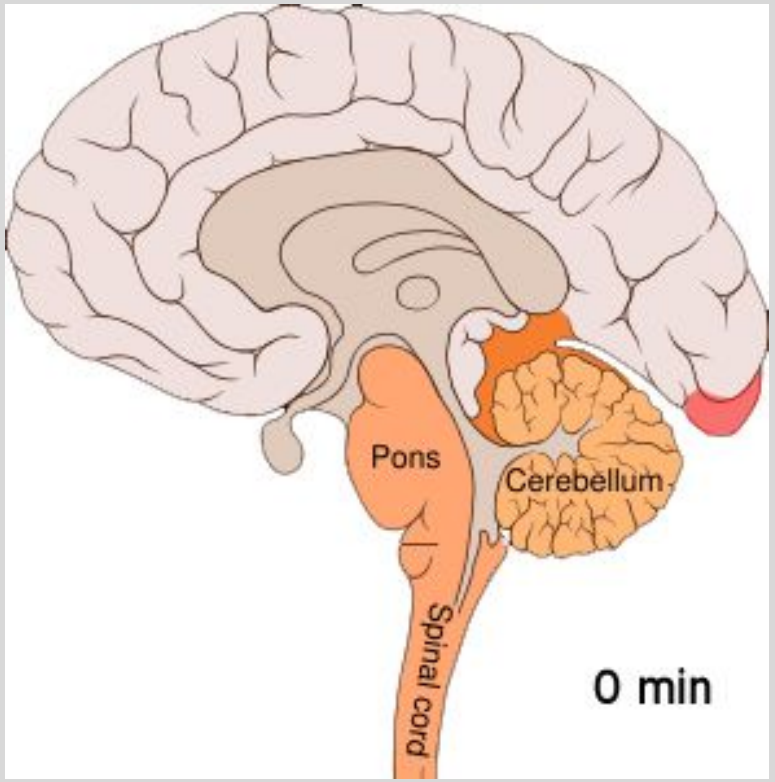
Fig. 14.5 MRI images 4 h after i.v. contrast enhancement of VM and Meniere's disease patients' inner ears. Black structures indicate endolymphatic hydrops (EH) by an absence in the perilymph space that can be identified by the contrast enhancement (white). **a** A 53-year-old female patient with pure VM. EH is not seen in the cochlea and vestibulum on both sides. **b** A 69-year-old male patient with pure Meniere's disease. The right inner ear shows severe EH in both the cochlea and the vestibulum (yellow arrows). There is no EH in the left inner ear. Area ratio of the endolymphatic space to the total fluid space constitutes 67% of the vestibulum on the right side and 13% of the vestibulum on the left side. (Oh et al. 2021)

Gene of hemiplegic migraine?

- From episodic ataxia type 2
- Mutation of the PQ calcium channel gene
  - 19p13
  - Disease
    - Familial hemiplegic migraine (FMH) type 1
    - Episodic ataxia type 2
    - Spinocerebellar ataxia type 6
    - Vestibular migraine?
      - No correlation so far
- Question?
  - Hereditary neuronal function disorders in the brainstem nuclei (channelopathies?)

Cortical spreading depression

- Cause of aura
  - Brainstem aura
    - **Vestibular syndrome**
    - Ataxia (not attributable to sensory deficit)
    - Tinnitus
    - Hypacusis
    - Dysarthria
    - Diplopia
    - Decreased level of consciousness (GCS < 13)
- Migraine-induced ischemia
  - Changes in the local brain circulation
  - Because of vasospasm



Aspect from functional and structure image

- A relevant overlap of vestibular and nociceptive pathway
  - Cortex
    - **Volume reduction**
      - Superior, inferior, and middle **temporal gyri**, medial cingulum, dorsolateral prefrontal cortex, parietal and occipital cortex areas, & the insular region
      - Nociceptive, visual, vestibular processing
      - **Reduced threshold of signal transmission**
    - During attack
      - Hyperactive in thalamus and temporo-parieto-insular region bilaterally
      - Bilateral cerebellar activation
        - Adaptive processes aiming for a downregulation of a hyperactive vestibular system
      - Deactivation of the bilateral occipital cortex
        - Reciprocal inhibition of the visual and vestibular systems
  - Thalamus
  - Brainstem

Aspect from functional and structure image

- A relevant overlap of vestibular and nociceptive pathway
  - Cortex
    - The **prefrontal cortex**, insular-opercular region, and the inferior parietal and supramarginal gyri
    - Negatively correlation with Dizziness Handicap Index
  - Thalamus
    - Antero-ventral thalamus
    - During caloric stimulation
      - **Increased activity in the thalamus only in the patient with VM**
  - Brainstem

Part 5

Pragmatic treatment

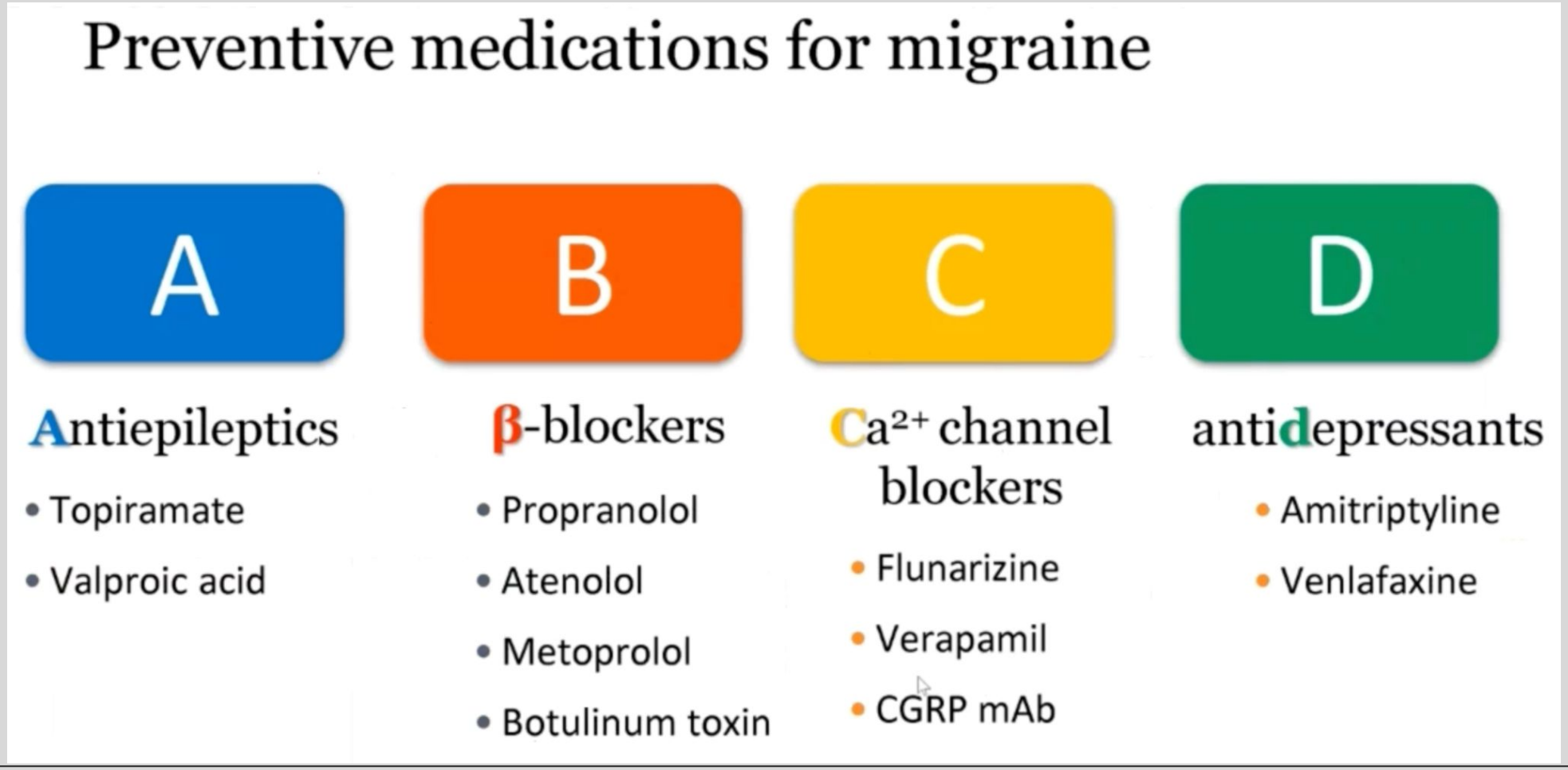
Treatment of acute attack

- **Non-steroid anti-inflammatory agent**
- An analgesic
- Combination with **antiemetic drug**
- Triptan in some patients (?)
  - 5-HT1B/1D receptors of the arteries
  - Not enough evidence

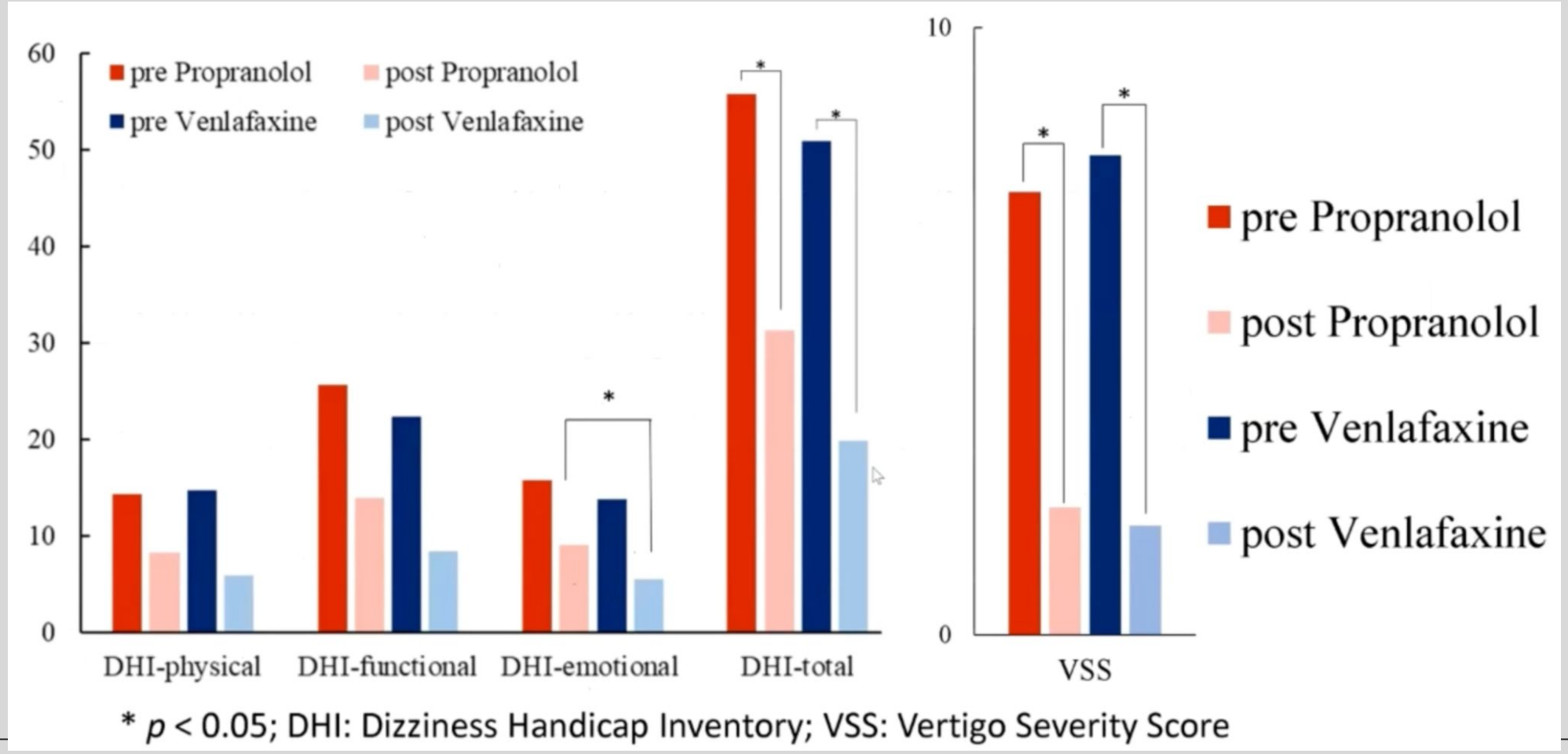
Prophylactic treatment

- Lack of evidence
  - Necessary quality
  - Difficult to patient inclusion
- Treatment as migraine
  - First choice
    - **Beta-blocker** (Metoprolol 95 mg QD or Propranolol 40-80 mg BID)
  - Alternative choice
    - Topiramate 50-150 mg/day
    - Valproic acid 600-2000 mg/day
    - Flunarizine 5-10 mg/day
    - Lamotrigine 50-200 mg/day
    - Amitriptyline 25-50 mg/day
    - Venlafaxine 37.5 mg/day
- **Vestibular rehabilitation**

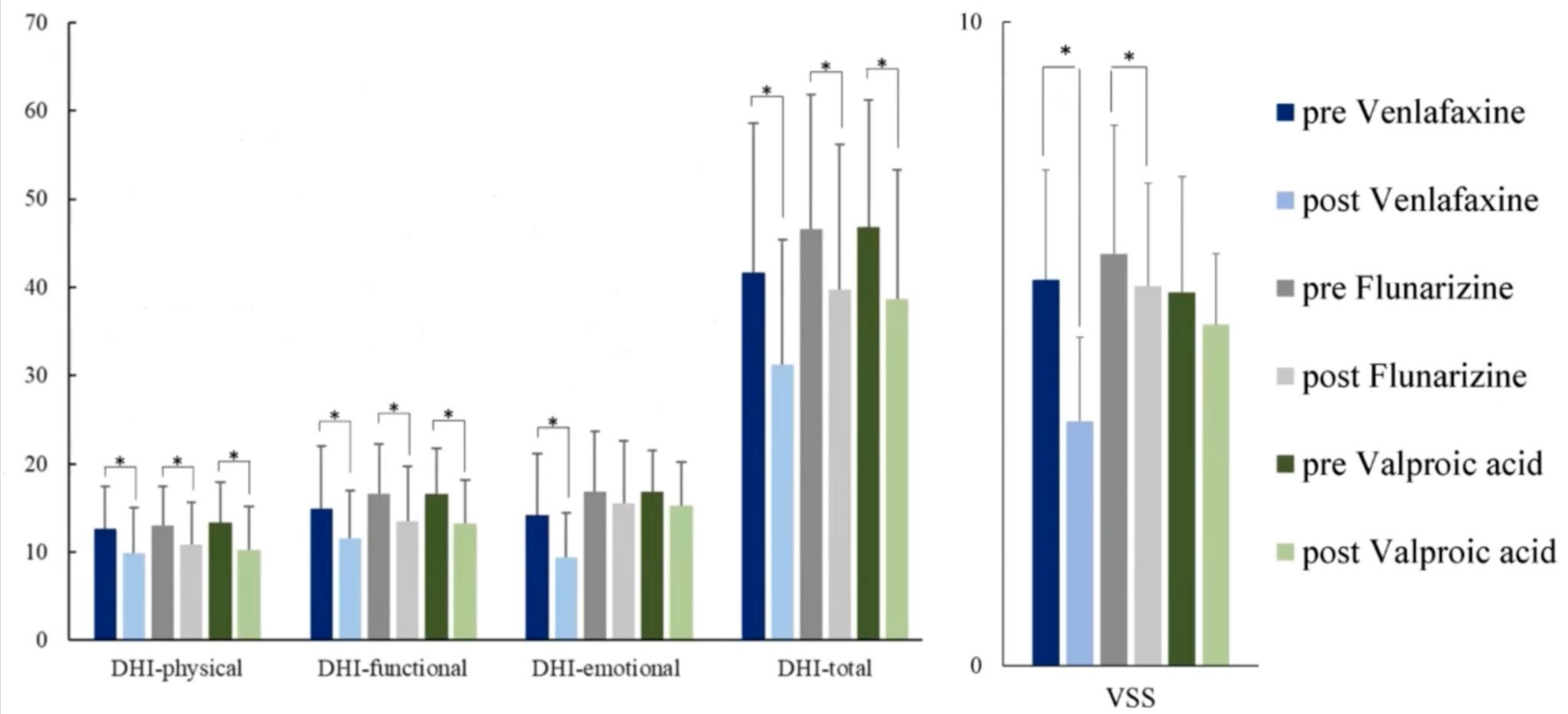
Prophylactic treatment



Prophylactic treatment



Prophylactic treatment



* $p < 0.05$; DHI: Dizziness Handicap Inventory; VSS: Vertigo Severity Score

Thank for your listening