MIGRAINE: CLINICAL PHENOTYPE, RARE VARIANTS, AND MIGRAINE EQUIVALENTS

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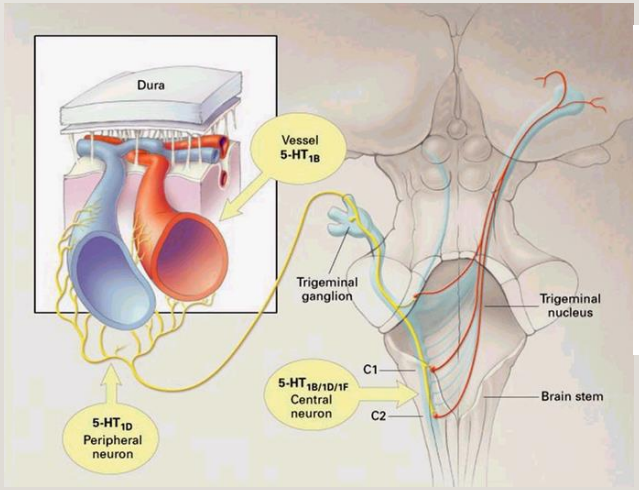
OBJECTIVES

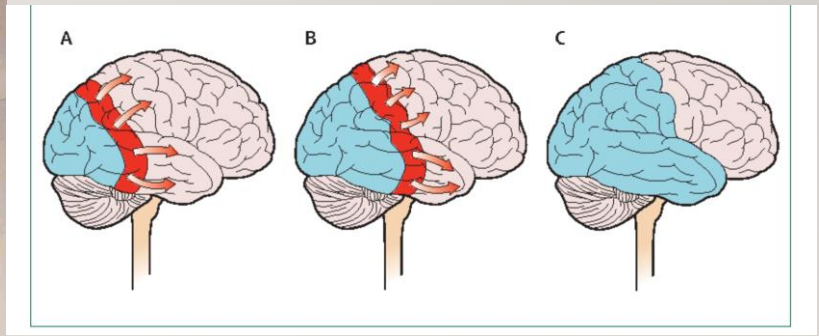
- Understand the clinical phenotype of migraines, including canonical and non-canonical symptoms.
- Explore other migraine symptoms: premonitory, aura, cranial autonomic symptoms and postdrome.
- Review rare migraine variants and equivalents, with a focus on diagnosis.
- Discuss brain-fog and dizziness (vestibular migraine).

WHAT IS MIGRAINE?

- Greek *hēmikrania*, from *hēmi-* 'half' + *kranion* 'skull'.
- Chronic neurological disorder with recurrent headaches and associated symptoms.
- Affects ~15% of adults, higher prevalence in women (3:1 ratio).
- Common in children (5-10% prevalence), often underdiagnosed.
- Pathophysiology: Cortical spreading depression,

trigeminovascular activation,
hypothalamus,
thalamus,
Peripheral/ central,
network problem/ connectivity,
CGRP, PACAP





Goadsby *et al*. New Eng J Med 2002;346:257

CANONICAL MIGRAINE SYMPTOMS

- **Headache** (hallmark):
  - Unilateral, pulsating, moderate-to-severe intensity.
  - Lasts 4-72 hours (untreated).
  - Aggravated by physical activity.
- **Associated Symptoms**:
  - Nausea and/or vomiting.
  - Photophobia (light sensitivity).
  - Phonophobia (sound sensitivity).
- Meets ICHD-3 criteria

Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition. Cephalalgia. 2018;38(1):1-211

NON-CANONICAL BUT TYPICAL SYMPTOMS

- **Allodynia**:
  - Heightened sensitivity to touch (e.g., scalp, skin) or to light (photic allodynia).
  - Occurs in ~70% of migraineurs during attacks.
  - Related to central sensitization.
- **Osmophobia**
- **Vertigo**:
  - Up to 40-50% of migraine patients, WHEN ASKED.
  - May occur in any phase.
  - Can mimic Meniere's, benign paroxysmal positional vertigo (BPPV).

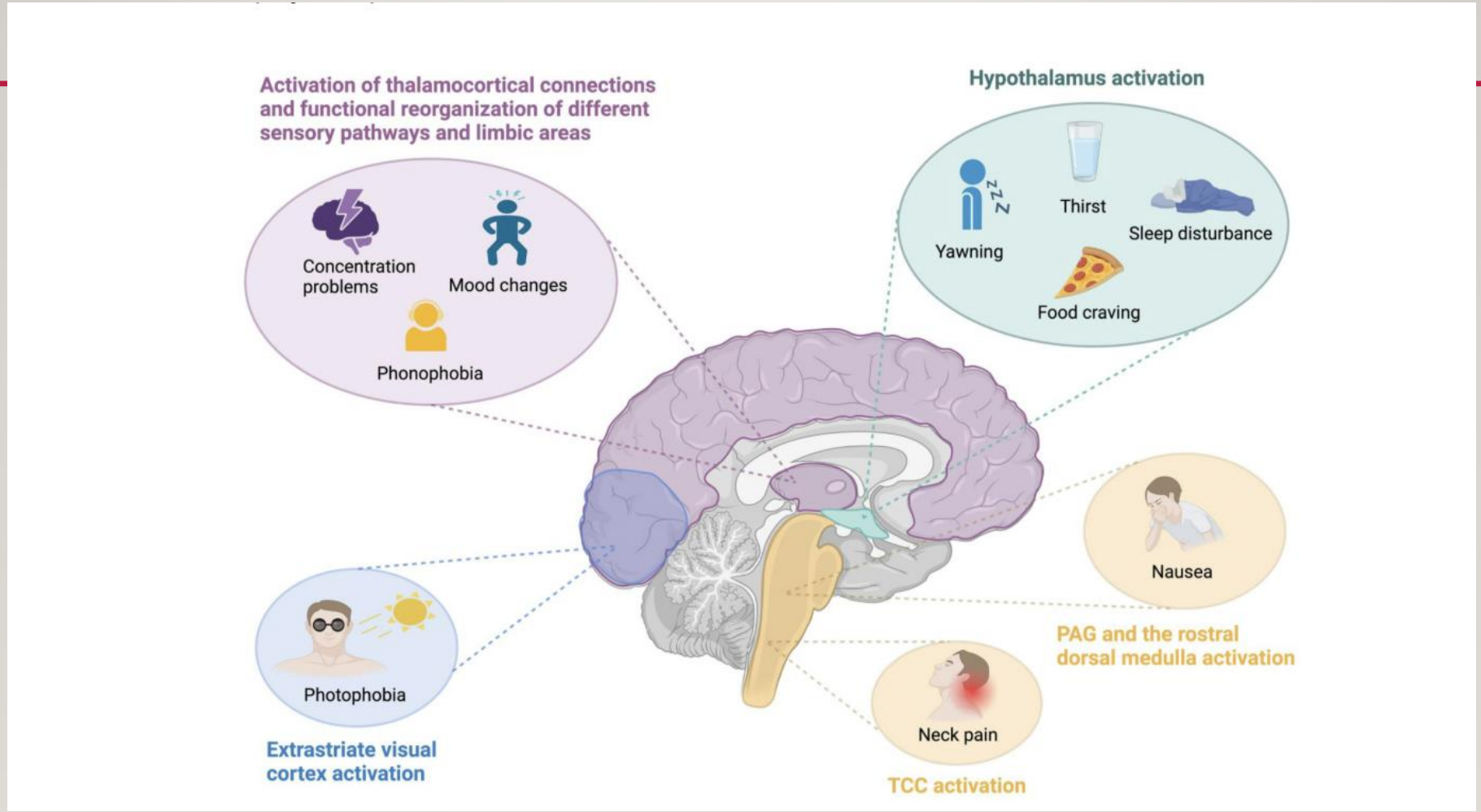
1. *After* ICHD-3 Cephalalgia 2018;38:1
2. Goadsby *et al.*, Physiol Rev 2017;97:553
3. Gowers Philadelphia; Blakiston's Son & Co 1899

MIGRAINE PHASES

- Migraine is a multiphase disorder:
  - Premonitory phase
  - Aura phase (in ~25-30% of cases) (MIGRAINE WITH/ WITHOUT AURA)
  - Headache phase
  - Postdrome phase
- Each phase has distinct symptoms, aiding diagnosis

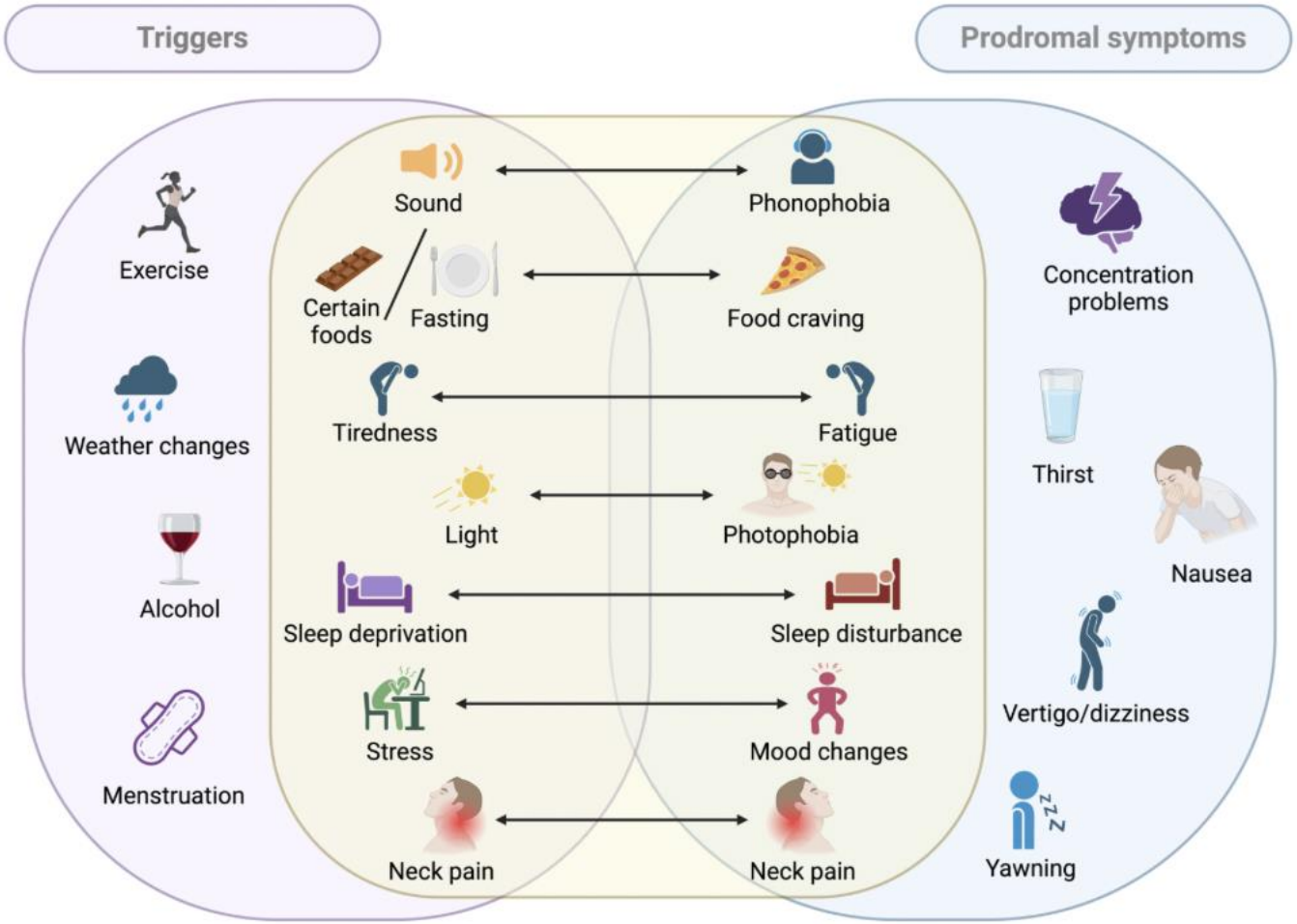
Giffin NJ, et al. Premonitory symptoms in migraine: an electronic diary study. Neurology. 2016;87(9):939-944.

PREMONITORY PHASE



Sebastianelli G, et al (IHS-iHEAD). Insights from triggers and prodromal symptoms on how migraine attacks start: The threshold hypothesis. Cephalalgia. 2024 Oct;44(10):33310242412872 24

PREMONITORY PHASE OR TRIGGERS?



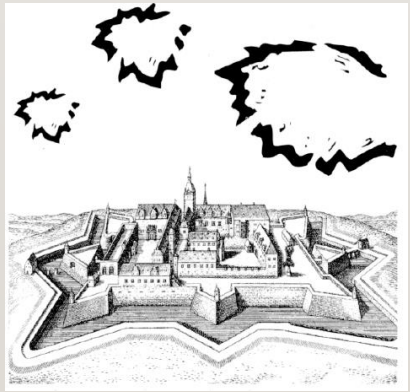
Patient-reported trigger[3]	Corresponding potential premonitory symptom	Percentage agreement (%)
Relaxation from stress	Elation	**91**
Physical exertion	Movement sensitivity	**83**
Meal skipping	Hunger/cravings	**81**
	GI discomfort	**85**
Bright light	Photophobia	**66**
Loud sounds	Phonophobia	**79**
Under sleeping	Fatigue	34
Dehydration	Thirst	55

Sebastianelli G, et al (IHS-iHEAD). Insights from triggers and prodromal symptoms on how migraine attacks start: The threshold hypothesis. Cephalalgia. 2024 Oct;44(10):33310242241287224

AURA SYMPTOMS

- Visual (e.g., scintillating scotoma, zigzag lines) – most common.
- Sensory (e.g., tingling, numbness).
- Motor (e.g., weakness in hemiplegic migraine).
- Speech/language disturbances, vertigo, loss of consciousness (brainstem aura).

- Occurs in migraine with aura; may occur without headache (acephalgic migraine).



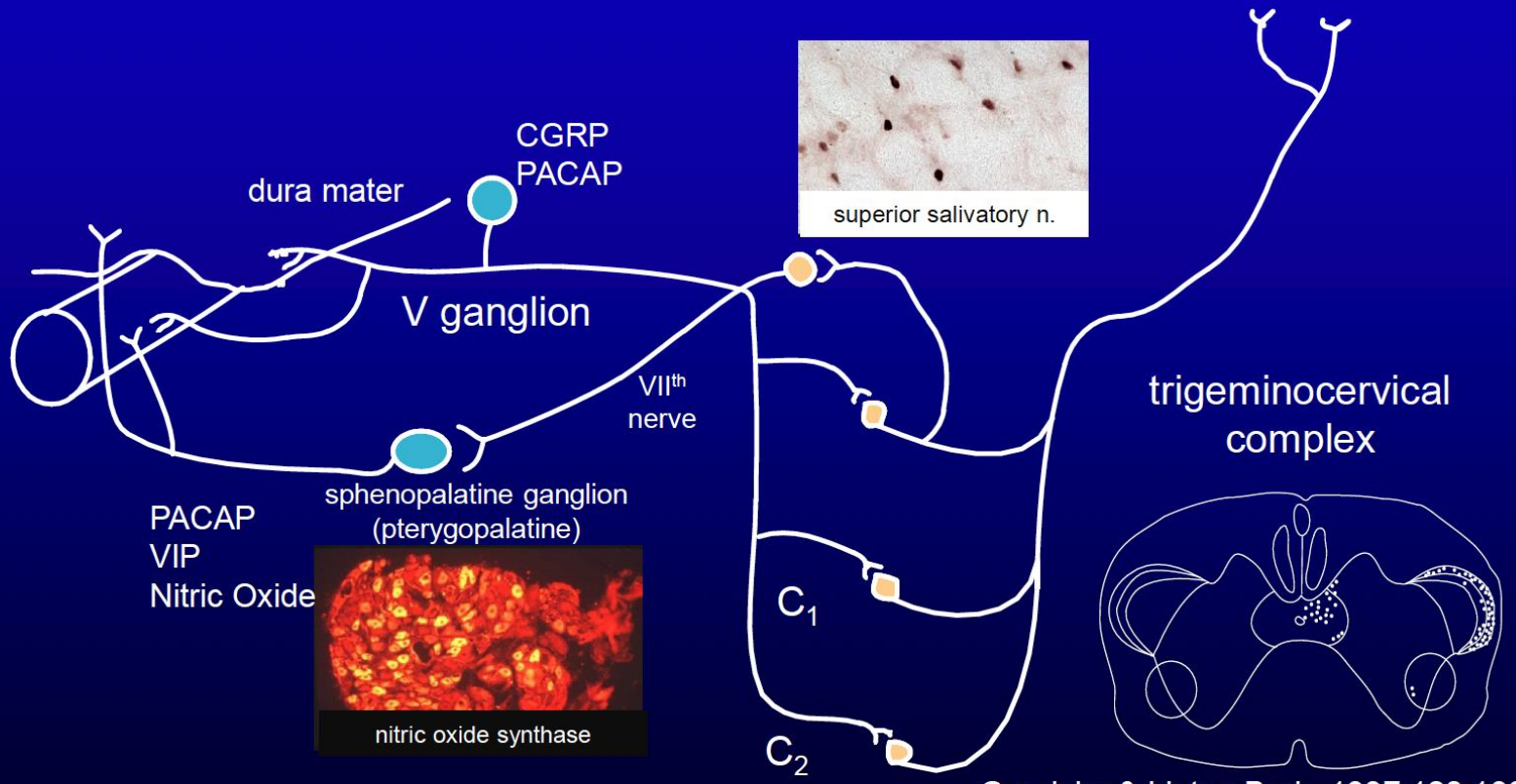
Viana M, et al. Clinical features of migraine aura: results from a prospective diary-aided study. Cephalalgia. 2017;37(10):979-989.

CRANIAL AUTONOMIC SYMPTOMS

Cranial Autonomic Symptoms

1. Conjunctival injection, lacrimation, or both
2. Nasal congestion, or rhinorrhoea, or both
3. Eyelid oedema
4. Forehead and facial sweating
5. Forehead/facial flushing
6. Sense of fullness in the ear
7. Miosis, or ptosis, or both

Trigeminal-autonomic reflex



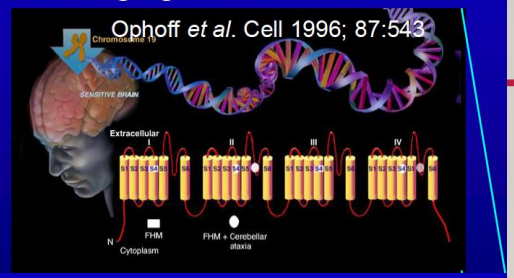
Goadsby & Lipton Brain 1997;120:193

CGRP- calcitonin gene-related peptide
PACAP- pituitary adenylate cyclase activating peptide

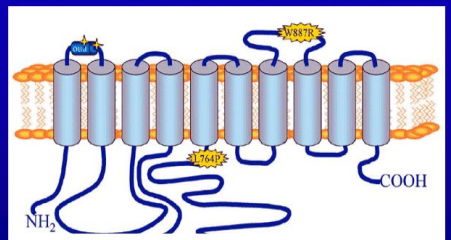
RARE MIGRAINE VARIANTS

- **Hemiplegic Migraine**:
  - Temporary unilateral weakness/paralysis (SPREADS).
  - Familial (FHM) or sporadic (SHM)
  - Genetic mutations (e.g., CACNA1A, ATP1A2)
- **Retinal Migraine**:
  - Monocular visual loss or scintillations
  - Lasts minutes, may precede headache
- **Brainstem Aura**
  - Bilateral symptoms (e.g., vertigo, dysarthria, ataxia)
  - Rare, requires careful diagnosis

FHM-I *CACNA1A*:
P/Q voltage-gated Ca^{2+} channel chr 19

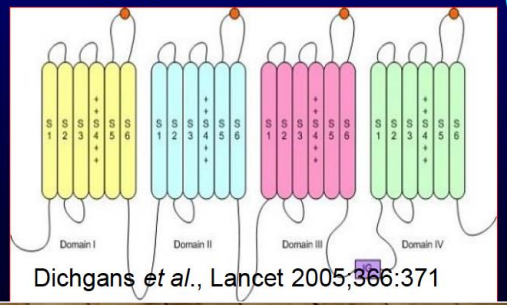


FHM-II *ATP1A2*:
Na^+/K^+ ATPase chr 1q23



De Fusco *et al*. Nat Gen 2003;33:192

FHM-III *SCN1A*:
Voltage-gated Na^+ channel chr 2



Dichgans *et al*., Lancet 2005;366:371

Russell MB, et al. Genetics of migraine: hemiplegic migraine and beyond. Cephalalgia. 2019;39(3):404-413

MIGRAINE EQUIVALENTS

- Symptoms related to migraine but without classic headache
- More common in children, may persist into adulthood.
- Reflect same neurological mechanisms (e.g., cortical spreading depression)
- Often underdiagnosed due to atypical presentation.
- Of note, paediatric migraine (age 4-17; *n*=125), more incomplete presentations, 70% have one CAS symptom.

Lagman-Bartolome AM, et al. Pediatric migraine variants: a review. Curr Neurol Neurosci Rep. 2018;18(4):16.
Gelfand *et al.*, Neurology; 2013;81:431

COMMON MIGRAINE EQUIVALENTS

- **Motion/ car sickness.**
- **Abdominal Migraine**:
  - Recurrent abdominal pain, nausea, vomiting.
  - Common in children (2-4% prevalence).
- **Cyclic Vomiting Syndrome**:
  - Intense vomiting episodes, often without headache.
- **Benign Paroxysmal Vertigo**:
  - Brief vertigo episodes in young children.
- **Benign Paroxysmal Torticollis**:
  - Head tilting episodes in infants.

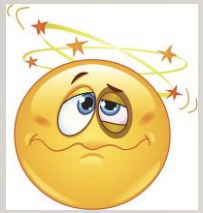
Angus-Leppan H, et al. Migraine equivalents in childhood. Arch Dis Child. 2020;105(4):395-400

BRAIN-FOG IN MIGRAINE

- Cognitive dysfunction during or between attacks
- Symptoms:
    - Difficulty concentrating, memory lapses.
    - Feeling "cloudy" or slowed thinking.
- Mechanism: Likely related to cortical dysfunction.
- Impact: Affects work/school performance, often underreported.

Gil-Gouveia R, et al. Cognitive dysfunction in migraine: a review of the literature. J Headache Pain. 2021;22(1):29.

VESTIBULAR MIGRAINE



- SPONTANEOUS
  - Internal
  - External
- POSITIONAL
- VISUALLY-INDUCED
- HEAD MOTION-INDUCED
- HEAD MOTION-INDUCED DIZZINESS WITH NAUSEA

- Main DD Ménière's.
- Pathophysiology probably related to thalamic sensitization.
- Vertigo symptoms 5 min and 72 hours.

Cantillo-Martínez M et al. Clin Med. 2025 Jul 8;14(14):4828

CLINICAL PEARLS

- Suspect migraine equivalents in children with recurrent, unexplained symptoms.
- Family history of migraine is a strong clue.
- Use diaries to track symptoms and triggers.
- Educate patients: Migraine is more than just headache.

TAKE HOME MESSAGE

- Migraine is a complex disorder with canonical (headache, nausea) and non-canonical (allodynia, vertigo) symptoms. Make sure you ask for all symptoms.
- Atypical migraine is NOT a diagnosis.
- Phases: Premonitory, aura, headache, postdrome symptoms.
- Rare variants (e.g., hemiplegic) and equivalents (e.g., abdominal migraine) require high suspicion, family history.
- Brain-fog and vestibular symptoms are significant, treatable symptoms.
- Future: tailor management to presentation.