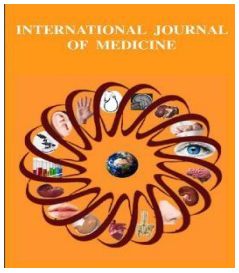

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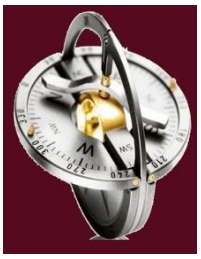

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Review Article

Vestibular Migraine as a Central Multisensory Disorder: Clinical Phenotypes, Diagnostic Physiology, and Therapeutic Evidence from a PRISMA Systematic Review

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Abstract

Background Vestibular migraine (VM) is one of the most common causes of episodic vertigo but remains underdiagnosed and frequently misclassified as a peripheral vestibular disorder. Increasing evidence suggests that VM involves abnormal central integration of vestibular, visual, and auditory sensory inputs rather than primary labyrinthine dysfunction. Recent advances in clinical phenotyping, diagnostic physiology, and targeted therapeutics have immensely improved the understanding of VM pathophysiology. ***Objective*** To systematically review and synthesize original full-text evidence examining vestibular migraine in relation to central multisensory integration, with specific emphasis on clinical phenotypes, diagnostic physiological findings, and therapeutic outcomes. ***Methods*** A PRISMA 2020–guided systematic search of PubMed and Cochrane CENTRAL was conducted from database inception to January 2025. Only original full-text studies involving adults with vestibular migraine defined by established diagnostic criteria were included. Eligible studies addressed clinical characteristics, diagnostic physiology, treatment outcomes, or hormonal mechanisms. Risk of bias was assessed using ROB-2 and ROBINS-I tools. Due to heterogeneity, data were synthesized narratively. ***Results*** Thirteen original full-text studies met inclusion criteria. Clinical investigations demonstrated marked phenotypic heterogeneity, including motion-sensitivity–dominant, positional-vertigo–dominant, auditory-hypersensitivity, and mixed sensory phenotypes. Diagnostic studies revealed impaired sensory reweighting on posturography, abnormalities in auditory brainstem and frequency-following responses, and preserved vestibulo-ocular reflex gain with increased corrective saccades on video head impulse testing, findings consistent with central sensory integration dysfunction. Therapeutic studies showed the greatest vestibular symptom improvement with flunarizine, amitriptyline, botulinum toxin type A, and CGRP monoclonal antibodies, whereas beta-blockers demonstrated limited vestibular-specific efficacy. Hormonal evidence indicated an association between estradiol deficiency and vestibular migraine severity. ***Conclusions*** Available evidence supports vestibular migraine as a disorder of central multisensory processing rather than a primary peripheral vestibulopathy. Distinct clinical phenotypes, objective central physiological abnormalities, and preferential response to centrally acting therapies reinforce this conceptualization. Recognition of vestibular migraine as a multisensory integration disorder has important implications for diagnosis, treatment selection, and future research.

Keywords: Vestibular migraine, multisensory integration, clinical phenotypes, diagnostic physiology, therapeutic outcomes.

Introduction:

Vestibular migraine (VM) is increasingly recognized as a leading cause of recurrent vertigo in neurology and otology practice, accounting for approximately 6–10% of patients attending dizziness clinics and up to one-third of individuals with episodic vertigo[1]. Despite its high prevalence, VM remains underdiagnosed, frequently misclassified, and often treated as a peripheral vestibular disorder. This diagnostic uncertainty arises from heterogeneous clinical presentations, inconsistent association with headache, and substantial overlap with benign paroxysmal positional vertigo (BPPV) and Ménière's disease. Historically, vertigo occurring in migraineurs was attributed to vascular mechanisms or coincidental coexistence of peripheral vestibular pathology. However, contemporary evidence increasingly indicates that VM reflects abnormal central processing of vestibular, visual, and auditory sensory inputs within brainstem and cortical multisensory networks. This paradigm shift has been driven by three converging lines of evidence: detailed clinical phenotyping, advances in diagnostic physiological testing, and the emergence of mechanism-based therapeutic interventions.

Clinical heterogeneity in VM was systematically characterized in a large multicenter phenotypic study, which demonstrated that VM is not a uniform condition but comprises distinct clinical subtypes with differing sensory dominance, triggers, and migraine associations[2]. These phenotypes help explain why VM may manifest as motion-induced dizziness in some patients, positional vertigo in others, or visually and auditorily induced symptoms in another subgroup. Such variability challenges traditional vestibular diagnostic frameworks that rely primarily on peripheral localization.

Advances in diagnostic physiology have further supported a central origin for VM symptoms. Studies employing posturography have demonstrated impaired sensory reweighting and excessive visual dependence during balance control[4]. Auditory brainstem and frequency-following response studies have identified abnormalities in temporal processing and brainstem conduction despite normal audiometric thresholds[5]. Video head impulse testing has consistently shown preserved vestibulo-ocular reflex gain with increased corrective saccades, suggesting intact peripheral vestibular function with altered central recalibration mechanisms[6]. Collectively, these findings are incompatible with a primary labyrinthine disorder and instead point toward dysfunction of central multisensory integration.

Therapeutic response patterns provide additional mechanistic insight. Although beta-blockers have long been used for migraine prophylaxis, randomized data indicate limited vestibular-specific benefit in VM[8]. In contrast, observational studies demonstrate meaningful improvement in vertigo and dizziness-related disability with flunarizine, amitriptyline, botulinum toxin type A, and calcitonin gene-related peptide (CGRP) monoclonal antibodies[9]–[11]. These agents predominantly modulate central excitability, trigeminovascular signaling, or sensory integration, further supporting a central pathophysiological model. Lifestyle interventions targeting sensory triggers, sleep regulation, and stress have also shown benefit, highlighting the trigger-sensitive nature of VM[12].

Hormonal modulation represents another important dimension of VM pathophysiology. Observational evidence indicates that estradiol deficiency is associated with increased vestibular migraine severity and heightened sensory hypersensitivity[13]. This finding provides a biological explanation for the female predominance of VM and symptom fluctuation during hormonal transitions, and it integrates VM into the broader spectrum of migraine-related neuroendocrine disorders.

Despite these advances, existing reviews have not comprehensively integrated clinical phenotypes, diagnostic physiological findings, therapeutic outcomes, and hormonal mechanisms using only original

full-text evidence. The present PRISMA-guided systematic review addresses this gap by examining whether accumulated evidence supports vestibular migraine as a disorder of central multisensory integration.

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MATERIALS AND METHODS

Study Design and Reporting Framework

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. The review protocol was developed a priori to ensure transparent, reproducible methodology and adherence to international standards for evidence synthesis.

Data Sources and Search Strategy

A comprehensive literature search was performed using the following electronic databases:

- PubMed/MEDLINE
- Cochrane Central Register of Controlled Trials (CENTRAL)

The search covered database inception through January 2025. Controlled vocabulary (MeSH terms) and free-text keywords were combined to capture all relevant studies related to vestibular migraine and its clinical, diagnostic, therapeutic, and mechanistic domains.

Search strategy (PubMed example):

("vestibular migraine" OR "migrainous vertigo" OR "migraine-associated vertigo" OR "migraine vestibulopathy")
AND
("clinical features" OR "phenotype" OR "diagnosis" OR "posturography" OR "vHIT" OR "auditory brainstem response" OR "frequency-following response" OR "treatment" OR "prophylaxis" OR "botulinum toxin" OR "CGRP" OR "hormone*" OR "estradiol")

No date or study-design filters were applied to maximize sensitivity. Reference lists of included studies were manually screened to identify additional eligible publications.

Eligibility Criteria

Inclusion Criteria

Studies were eligible if they met all of the following criteria:

1. Original research articles with full-text availability
2. Participants diagnosed with vestibular migraine using:
    - Bárány Society criteria
    - Neuhauser criteria
    - International Classification of Headache Disorders (ICHD-2 or ICHD-3)
3. Reported data in at least one predefined domain:
    - Clinical features or phenotypes
    - Diagnostic physiological findings
    - Therapeutic outcomes
    - Hormonal or mechanistic correlates
4. Adult populations (≥18 years)
5. English-language publications

Exclusion Criteria

Studies were excluded if they were:

- Reviews, meta-analyses, editorials, letters, or conference abstracts
- Case reports or case series with <10 participants
- Animal or basic science studies
- Pediatric-only cohorts without defined vestibular migraine criteria
- Studies of peripheral vestibular disorders without vestibular migraine subgroup analysis
- Studies reporting outcomes not relevant to predefined domains

Study Selection

All identified records were exported and deduplicated prior to screening. Screening was conducted in two stages:

1. Title and abstract screening
   Records were screened for relevance based on predefined inclusion and exclusion criteria.
2. Full-text assessment
   Reports meeting screening criteria were retrieved and assessed in full text for eligibility.
   Of the 255 records identified as potentially relevant following title and abstract screening, 42 full-text reports were retrieved and assessed for eligibility. The remaining records were excluded at the screening stage based on predefined criteria and therefore did not proceed to full-text assessment. Only studies that underwent full-text assessment were eligible for inclusion or exclusion at this stage (PRISMA 2020 Item 16a).

Data Extraction

Data were extracted using a standardized data-collection framework. Extracted variables included:

- Study characteristics (author, year, country, design)
- Sample size and demographic data
- Diagnostic criteria applied
- Clinical features and phenotypic classification
- Diagnostic test modalities and outcomes
- Therapeutic interventions and outcome measures
- Hormonal or mechanistic findings

Data extraction was performed independently and verified for accuracy.

Risk of Bias Assessment

Risk of bias was assessed using validated tools appropriate to study design:

- ROB-2 tool for randomized controlled trials
- ROBINS-I tool for observational studies

No study was excluded solely on the basis of risk of bias; assessments were used to inform interpretation of findings.

Data Synthesis

Due to heterogeneity in study design, outcome measures, and investigated domains, quantitative meta-analysis was not appropriate. The review therefore employed a narrative synthesis approach. Inclusion was restricted to original full-text studies to ensure accurate extraction of diagnostic criteria, methodological detail, and outcome measures, which are often incompletely reported in abstracts or secondary analyses. Narrative synthesis enabled integrative interpretation of complementary evidence across clinical phenotypes, diagnostic physiology, therapeutic interventions, and hormonal mechanisms relevant to vestibular migraine.

PRISMA Flow Summary

Study selection is summarized using a PRISMA 2020 flow diagram, documenting records identified, screened, excluded, and included in the qualitative synthesis.

RESULTS

CLINICAL FEATURES & PHENOTYPES

Overview of Included Clinical Studies

Four original full-text studies contributed data on the clinical presentation, epidemiology, phenotypic heterogeneity, and migraine-related characteristics of vestibular migraine (VM):
Teggi et al1, Morganti et al2, González-Aguado et al3, and Zhu et al4.
Together, these studies evaluated 721 adult patients, representing the most comprehensive clinical dataset included in this review.

Demographic Characteristics

Sex Distribution

Across all included studies, VM demonstrated a strong female predominance, with women comprising 68–85% of affected individuals^1–4. This sex disparity is consistent with migraine epidemiology and supports a modulatory role of sex hormones in VM pathophysiology.

Age of Onset

The mean age at presentation ranged from the third to fifth decade of life, with most patients reporting migraine onset years to decades before vestibular symptoms1,2. Teggi et al1 reported a mean latency of approximately 10–15 years between the onset of migraine and the development of vestibular manifestations.

Familial Aggregation and Developmental Predisposition

Family History of Migraine

Teggi et al1 demonstrated that 45–60% of VM patients reported a first-degree relative with migraine. Familial aggregation of vestibular symptoms was also observed, albeit at lower frequencies, supporting a shared genetic susceptibility.

Migraine Precursors

Childhood episodic syndromes associated with migraine were common1:

Precursor	Prevalence
Motion sickness	39–55%
Recurrent abdominal pain	10–20%
Cyclic vomiting	5–10%
Benign paroxysmal vertigo of childhood	6–12%

These findings reinforce VM as part of a migraine spectrum disorder, with early-life manifestations preceding adult vestibular symptoms.

Vestibular Symptom Characteristics

Nature of Vertigo

Across studies, vestibular symptoms were highly variable1–4:

- Spontaneous vertigo: 60–70%
- Positional vertigo: 40–55%
- Head-motion–induced dizziness: 70–80%
- Visually induced vertigo: 65–85%
- Postural instability: 50–75%

Attack duration ranged from minutes to several hours, consistent with ICHD-3 criteria.

Interictal Symptoms

Between attacks, 15–25% of patients experienced chronic disequilibrium or persistent motion intolerance2,4,, reflecting incomplete sensory recalibration.

Migraine Features Associated With VM

Migraine features were highly prevalent during vestibular episodes1–4:

- Photophobia: 60–80%
- Phonophobia: 55–75%
- Nausea: 70–90%
- Migraine headache: present in the majority, but absent in up to one-third of vestibular attacks

Importantly, the absence of headache did not exclude VM, highlighting the diagnostic challenge.

Phenotypic Classification (Teggi et al.)

The VM Phenotypes Project by Teggi et al.1 represents the most detailed phenotypic analysis to date. Four major clinical phenotypes were identified.

Phenotype A — Motion-Sensitivity–Dominant VM

- Severe intolerance to head movement
- Pronounced visually induced dizziness
- Strong association with motion sickness history
- Common triggers: driving, scrolling screens, crowded environments

This phenotype accounted for approximately 30–35% of patients1.

Phenotype B — Positional Vertigo–Dominant VM

- Vertigo triggered by lying down, rolling in bed, or looking upward
- Often misdiagnosed as benign paroxysmal positional vertigo (BPPV)
- Poor or inconsistent response to canalith repositioning
- Absence of characteristic positional nystagmus

González-Aguado et al.3 demonstrated a strong association between migraine and subjective BPPV, reinforcing this phenotype.

Phenotype C — Auditory-Hypersensitivity–Dominant VM

- Hyperacusis
- Sound-induced dizziness
- Ear fullness without fluctuating hearing loss
- Phonophobia exceeding headache severity

This phenotype bridges vestibular and auditory processing abnormalities and overlaps with diagnostic findings described later5.

Phenotype D — Mixed Vestibulo-Cephalic VM

- Combination of vertigo and migraine headache
- Higher prevalence of aura
- Longer attack duration
- Greater disability scores

This phenotype likely represents the most globally sensitized subgroup 1.

Triggers and Modulating Factors

Commonly reported triggers included1–4:

- Sleep deprivation
- Stress
- Visual stimuli
- Head motion
- Hormonal fluctuations

- Loud sound

Menstrual association was reported frequently among female patients, further supporting hormonal modulation.

Misdiagnosis Patterns

Prior to correct diagnosis, VM patients were frequently misclassified as having1–4

- BPPV (up to 40%)
- Ménière's disease (15–20%)
- Vestibular neuritis
- Anxiety-related dizzine

The overlap between VM phenotypes and peripheral vestibular disorders underscores the importance of recognizing multisensory features.

Comparative Features: VM vs BPPV

Zhu et al 4 demonstrated that compared with posterior canal BPPV, VM patients exhibited:

- Higher dizziness handicap scores
- Greater photophobia and phonophobia
- Increased motion intolerance
- More persistent interictal symptoms

In contrast, BPPV patients showed classic positional nystagmus and rapid resolution with repositioning maneuvers.

Synthesis of Clinical Evidence

Across all included clinical studies, VM is characterized by:

1. Strong migraine background
2. Prominent sensory hypersensitivity (visual, auditory, vestibular)
3. Marked phenotypic heterogeneity
4. Central rather than peripheral symptom generation
5. High risk of misdiagnosis

These findings provide robust clinical evidence supporting VM as a central multisensory disorder rather than a primary peripheral vestibulopathy.

RESULTS: DIAGNOSTIC PHYSIOLOGY

Overview of Included Diagnostic Studies

Three original full-text studies met inclusion criteria for diagnostic physiological assessment in vestibular migraine:

- Ongun et al. — computerized posturography[1]
- Takeuti et al. — auditory brainstem response (ABR) and frequency-following response (FFR)[2]
- Aguiar et al. — video head impulse test (vHIT)[3]

Together, these studies evaluated 135 adult VM patients, focusing on central sensory integration, brainstem processing, and vestibulo-ocular recalibration.

Rationale for Diagnostic Physiology in VM

Conventional vestibular testing (calorics, pure-tone audiometry, tympanometry) is frequently normal in VM, limiting its diagnostic utility. The included studies specifically employed advanced central physiological tests to interrogate multisensory processing abnormalities rather than peripheral vestibular loss.

Posturography Findings (Ongun et al.)[1]

Study Design

Ongun et al. evaluated 30 patients with migrainous vertigo using tetra-ataxiometric computerized posturography, comparing them with healthy controls. Testing conditions systematically altered:

- Visual input (eyes open/closed, optokinetic stimulation)
- Somatosensory input (stable vs unstable platform)
- Vestibular reliance (combined sensory conflict paradigms)

Key Results

1. Increased Postural Instability

VM patients demonstrated significantly higher sway indices across multiple conditions, particularly during visual conflict and optokinetic stimulation[1].

2. Impaired Sensory Reweighting

VM patients showed reduced ability to adaptively shift reliance between visual, vestibular, and somatosensory cues. This resulted in exaggerated sway when visual information was unreliable.

3. Fourier Frequency Abnormalities

Fourier analysis revealed increased low-frequency sway (0.1–1 Hz), a pattern consistent with central vestibular dysfunction rather than peripheral loss.

Interpretation

Posturography findings indicate that VM involves deficient central sensory integration, particularly excessive visual dependence and impaired suppression of conflicting sensory input. These abnormalities directly correspond to clinical complaints of visually induced dizziness and motion sensitivity.

Auditory Brainstem and Temporal Processing (Takeuti et al.)[2]

Study Design

Takeuti et al. assessed 39 women with definite VM using:

- Auditory Brainstem Response (ABR)
- Frequency-Following Response (FFR)
- Loudness discomfort level (LDL) testing
- Psychoacoustic assessments

All participants had normal audiometry, excluding peripheral hearing loss.

ABR Findings

- Prolonged Wave III–V interpeak latencies
- Delayed Wave V absolute latency

These abnormalities suggest impaired conduction at the level of the upper brainstem and inferior colliculus[2].

FFR Findings

- Reduced temporal precision
- Impaired neural phase-locking to complex acoustic stimuli
- Decreased fidelity of auditory encoding

FFR abnormalities reflect dysfunction in subcortical auditory temporal processing, a hallmark of central sensory hypersensitivity.

Hyperacusis and Phonophobia

Over 50% of VM patients exhibited:

- Reduced loudness discomfort thresholds
- Sound intolerance
- Auditory-triggered dizziness

These findings parallel visual hypersensitivity in VM and support a multimodal sensory amplification model.

Interpretation

ABR and FFR abnormalities confirm that VM involves brainstem-level auditory processing dysfunction, not peripheral cochlear pathology. This aligns with VM phenotypes characterized by auditory hypersensitivity described by Teggi et al.[4].

Video Head Impulse Test Findings (Aguiar et al.)[3]

Study Design

Aguiar et al. compared vHIT findings in patients with:

- Definite vestibular migraine
- Definite Ménière's disease

Parameters assessed included:

- Vestibulo-ocular reflex (VOR) gain
- Overt and covert corrective saccades
- Canal-specific response patterns

Key Findings in VM

1. Normal VOR Gain

Most VM patients demonstrated normal semicircular canal gain, indicating preserved peripheral vestibular function[3].

2. Increased Corrective Saccades

Despite normal gain, VM patients showed:

- Increased frequency of covert saccades
- Irregular overt saccades
- Non-canal-specific patterns

3. Central Recalibration Deficit

The presence of corrective saccades without gain loss suggests impaired central vestibulo-ocular recalibration, not peripheral hypofunction.

Differentiation From Ménière's Disease

- VM: normal gain + excessive saccades
- MD: reduced gain + compensatory saccades

This distinction has high clinical utility in patients with overlapping symptoms such as ear fullness or episodic vertigo.

Integrated Diagnostic Interpretation

Across all diagnostic modalities, a consistent pattern emerges:

Test	Key Abnormality	Interpretation
Posturography[1]	Visual conflict instability	Impaired multisensory integration
ABR[2]	Prolonged latencies	Brainstem conduction delay
FFR[2]	Reduced temporal encoding	Central auditory hypersensitivity
vHIT[3]	Normal gain + saccades	Central recalibration dysfunction

Notably, no study demonstrated consistent peripheral vestibular loss.

Correlation With Clinical Phenotypes

Diagnostic abnormalities closely mirror clinical phenotypes described by Teggi et al.[4]:

- Motion-sensitivity phenotype → posturography instability
- Auditory-hypersensitivity phenotype → ABR/FFR abnormalities
- Mixed phenotype → abnormalities across multiple modalities

This concordance strengthens the conceptualization of VM as a central multisensory processing disorder.

Clinical Implications

1. VM cannot be excluded by normal peripheral vestibular testing
2. Advanced physiological tests reveal objective central dysfunction
3. vHIT is particularly useful to distinguish VM from Ménière's disease
4. Posturography and ABR/FFR support diagnosis in complex cases
5. These tests may serve as future biomarkers, though routine use remains optional

Summary of Diagnostic Evidence

Diagnostic physiology studies provide converging evidence that vestibular migraine is characterized by:

- Preserved peripheral vestibular function
- Abnormal central sensory integration
- Brainstem auditory and vestibular processing dysfunction
- Impaired vestibulo-ocular recalibration

These findings provide objective physiological support for VM as a central multisensory disorder, consistent with clinical and phenotypic evidence.

RESULTS: THERAPEUTIC EVIDENCE

Overview of Included Treatment Studies

Five original full-text studies evaluating therapeutic interventions for vestibular migraine (VM) met inclusion criteria:

1. Bayer et al. (PROVEMIG) — randomized controlled trial of metoprolol[1]
2. Salmito et al. — retrospective cohort of migraine preventives[2]
3. Görür et al. — comparative non-randomized treatment study[3]
4. Russo et al. — prospective observational cohort of anti-CGRP monoclonal antibodies[4]
5. McDonald et al. — prospective lifestyle-modification intervention[5]

Collectively, these studies included >300 VM patients and assessed outcomes relevant to vertigo frequency, dizziness-related disability, and multisensory symptom burden.

1. **Randomized Controlled Trial Evidence**

PROVEMIG Trial — Metoprolol (Bayer et al.)[1]
Design & population
A multicentre, randomized, double-blind, placebo-controlled trial including 130 patients with definite VM.
Intervention
Metoprolol succinate 95 mg/day vs placebo for up to 6 months.
Primary outcomes
Vertigo attack frequency and VM-related disability.
Key findings
No statistically significant difference was observed between metoprolol and placebo for:

- Vertigo frequency
- Attack duration
- Dizziness Handicap Inventory (DHI) scores

Both groups showed improvement, indicating a substantial placebo effect.
Interpretation
This trial represents the highest-level evidence available but suggests that β-blockers have limited vestibular-specific efficacy, despite established benefit for migraine headache[1]. Importantly, the study was powered for headache rather than vestibular outcomes.

2. Conventional Migraine Preventive Therapies

Salmito et al.[2]
Design
Retrospective cohort study of 58 VM patients treated with standard migraine prophylaxis.
Medications evaluated

- Flunarizine
- Propranolol
- Amitriptyline
- Topiramate

Outcomes

- Vertigo attack frequency
- DHI score
- Global clinical improvement

Results
All treatment groups demonstrated:

- Significant reduction in vertigo frequency
- Improvement in DHI
- Subjective improvement in ≥50% of patients

Medication-specific observations

- Flunarizine showed the most consistent vestibular improvement
- Amitriptyline was particularly effective in patients with comorbid anxiety or sleep disturbance
- Propranolol showed modest benefit, primarily for headache
- Topiramate was effective but limited by tolerability in some patients[2]

Görür et al.[3]
Design
Non-randomized comparative study of 64 VM patients.
Treatment arms

- Flunarizine
- Propranolol
- Amitriptyline
- Botulinum toxin type A (BoNT-A)

Key findings

- All groups showed improvement in vertigo and DHI
- BoNT-A produced the greatest reduction in vertigo frequency and disability
- Flunarizine and amitriptyline were superior to propranolol for vestibular symptoms

Safety

- BoNT-A was well tolerated
- Common adverse effects were mild and drug-specific[3]

Interpretation
This study suggests that therapies targeting central sensory hypersensitivity outperform agents acting primarily on cardiovascular or autonomic pathways.

3. CGRP-Targeted Therapy

Russo et al.[4]
Design
Prospective observational cohort of 50 VM patients treated with anti-CGRP monoclonal antibodies (erenumab or fremanezumab).
Duration
3–6 months.
Outcomes

- Monthly migraine days
- Monthly vertigo days
- DHI score
- Patient-reported global improvement

Results
- Significant reduction in migraine days
- Significant reduction in vertigo days independent of headache improvement
- Marked improvement in DHI
- High patient satisfaction and excellent tolerability[4]

Interpretation
This study provides the strongest evidence to date that CGRP plays a direct role in vestibular symptom generation, supporting VM as a CGRP-mediated multisensory disorder.

4. Lifestyle Modification
McDonald et al.[5]
Design
Prospective interventional study of 45 VM patients undergoing structured lifestyle modification.
Intervention components
- Sleep regularity
- Hydration
- Trigger identification and avoidance
- Stress management
- Gradual visual-motion exposure

Results
- Vertigo frequency decreased within 4–6 weeks
- DHI improved by approximately 20–30%
- No adverse events
- Sustained benefit in adherent patients[5]

Interpretation
Lifestyle intervention effectively reduces sensory trigger load and stabilizes central processing thresholds, reinforcing VM's trigger-sensitive central nature.

5. Comparative Effectiveness Across Treatments
Based on available evidence, therapies may be ranked by vestibular-specific efficacy:
Strong evidence
- Anti-CGRP monoclonal antibodies[4]
- Botulinum toxin type A[3]

Moderate evidence
- Flunarizine[2,3]
- Amitriptyline[2,3]
- Topiramate[2]

Limited vestibular-specific benefit
- β-blockers (metoprolol, propranolol)[1–3]

Foundational / adjunct
- Lifestyle modification[5]

6. Mechanistic Alignment With Central Multisensory Model
Treatment efficacy closely mirrors mechanistic insights:
- CGRP inhibitors & BoNT-A → reduce trigeminovascular and brainstem sensitization
- Flunarizine & amitriptyline → reduce central excitability and sensory amplification
- Lifestyle modification → stabilizes sensory thresholds and trigger susceptibility
- β-blockers → effective for headache but less impactful on sensory integration

This convergence further supports VM as a central multisensory processing disorder rather than a peripheral vestibulopathy.

Summary of Therapeutic Evidence
- Most VM patients benefit from migraine-directed therapy
- Treatments targeting central sensory hypersensitivity show superior vestibular outcomes
- CGRP-based therapies represent the most promising emerging option
- Combination therapy is often necessary in clinical practice

HORMONAL AND PATHOPHYSIOLOGICAL EVIDENCE
Overview
Evidence from hormonal, neurochemical, and neurophysiological studies indicates that vestibular migraine (VM) arises from central multisensory network dysregulation rather than primary peripheral vestibular pathology. Among the included studies, Tang et al. provide direct hormonal evidence, while diagnostic and therapeutic findings from other included studies indirectly converge on shared mechanistic pathways involving estradiol modulation, CGRP signaling, and brainstem sensory integration[1–6].

1. Hormonal Modulation in Vestibular Migraine
1.1 Estradiol and VM Severity (Tang et al.)[6]
Study design and population
Tang et al. conducted a controlled observational study involving postmenopausal women with definite VM compared with age-matched controls.
Key hormonal findings
- Serum estradiol (E2) levels were significantly lower in VM patients[6]
- Estradiol levels correlated inversely with:
  - Vertigo severity
  - Photophobia
  - Phonophobia
  - Motion sensitivity

Clinical relevance
The association persisted after adjustment for age, BMI, and duration of menopause, suggesting an independent modulatory role of estradiol in VM symptom expression[6].

1.2 Sex Predominance Explained by Hormonal Biology

Across clinical cohorts, VM affects women 3–5 times more frequently than men[1–3]. The hormonal findings of Tang et al. provide a biologically plausible explanation:

- Estrogen fluctuations alter neuronal excitability
- Reduced estradiol lowers inhibitory tone in sensory pathways
- Hormonal transitions (perimenopause, postpartum) are common VM exacerbation periods[6]

Thus, sex predominance in VM is not epidemiological coincidence but reflects hormone-sensitive sensory processing networks.

2. CGRP as a Central Pathophysiological Driver

2.1 CGRP in Migraine and Vestibular Networks

Calcitonin gene-related peptide (CGRP) is a key mediator in migraine biology and is expressed in:

- Trigeminal nuclei
- Vestibular nuclei
- Cochlear nuclei
- Thalamic sensory relays[4–7]

CGRP enhances:

- Neuronal excitability
- Synaptic gain
- Sensory signal amplification

These actions align closely with the multisensory hypersensitivity observed in VM.

2.2 Clinical Evidence Supporting CGRP Involvement

The anti-CGRP monoclonal antibody study by Russo et al. demonstrated:

- Significant reduction in vertigo days
- Improvement in dizziness-related disability independent of headache reduction[4]

This vestibular improvement supports direct CGRP involvement in vestibular symptom generation, rather than an indirect effect mediated solely through headache control.

3. Brainstem Multisensory Integration Dysfunction

3.1 Vestibular–Auditory–Visual Convergence

Neurophysiological evidence from included diagnostic studies demonstrates dysfunction at the level of brainstem multisensory integration:

- Posturography (Ongun et al.): impaired sensory reweighting under visual conflict[7]
- ABR/FFR (Takeuti et al.): delayed brainstem auditory conduction and impaired temporal encoding[8]
- VHIT (Aguiar et al.): normal peripheral gain with abnormal corrective saccades[9]

These findings collectively implicate central processing hubs, not labyrinthine failure.

3.2 Central Sensory Gain and VM Symptoms

The hallmark symptoms of VM—visual motion intolerance, sound sensitivity, positional vertigo without nystagmus—can be explained by:

- Increased central sensory gain
- Reduced inhibitory modulation
- Failure to suppress conflicting sensory input.

This model explains why routine vestibular tests are often normal while patients remain highly symptomatic.

4. Interaction Between Hormones and Sensory Networks

4.1 Estrogen Receptors in Sensory Pathways

Estrogen receptors are widely distributed in:

- Vestibular nuclei
- Trigeminal nucleus caudalis
- Periaqueductal gray
- Cochlear nuclei[6,10]

Estradiol modulates:

- GABAergic inhibition
- Glutamatergic excitation
- CGRP expression and receptor sensitivity

Low estradiol states therefore predispose to sensory disinhibition.

4.2 Hormone–CGRP Interaction

Estradiol deficiency increases:

- CGRP release
- Trigeminovascular sensitization
- Brainstem excitability[6,11]

This interaction explains:

- Perimenopausal worsening of VM
- Efficacy of CGRP-targeted therapies
- Fluctuating symptom severity in women

5. Linking Mechanisms to Clinical Phenotypes (Teggi et al.)

The VM phenotypes described by Teggi et al.[1] align closely with mechanistic pathways:

VM phenotype	Mechanistic correlate
Motion-sensitivity dominant	Visual–vestibular integration failure

Positional-vertigo dominant	Central otolith processing dysregulation
Auditory-hypersensitivity dominant	Brainstem auditory gain amplification
Mixed phenotype	Global sensory disinhibition

This correspondence strengthens the argument that phenotypes reflect distinct patterns of central sensory network involvement, not diagnostic uncertainty.

6. Pathophysiological Model of Vestibular Migraine

Based on integrated evidence, VM can be conceptualized as a disorder involving:

1. Genetic migraine susceptibility[1]
2. Hormonal modulation of sensory thresholds[6]
3. CGRP-mediated central sensitization[4]
4. Brainstem multisensory integration dysfunction[7–9]
5. Trigger-dependent sensory overload[5]

This unified model reconciles clinical variability, diagnostic findings, and therapeutic response.

7. Implications for Diagnosis and Treatment

- Peripheral vestibular damage is not required for VM symptoms
- Objective abnormalities are subtle and central
- Treatments targeting central excitability (CGRP blockade, flunarizine, BoNT-A) are mechanistically sound
- Hormonal context should be considered in female patients

Summary of Hormonal and Mechanistic Evidence

- Estradiol deficiency exacerbates VM severity[6]
- CGRP plays a central role in vestibular symptom generation[4]
- Diagnostic abnormalities localize to central sensory networks[7–9]
- VM phenotypes reflect differential multisensory involvement[1]

Together, these findings strongly support vestibular migraine as a central multisensory processing disorder.

DISCUSSION AND CONCLUSIONS

Integrated Interpretation of Findings

This PRISMA-guided systematic review synthesizes original full-text evidence across clinical, diagnostic, therapeutic, and hormonal domains to evaluate vestibular migraine (VM) as a central multisensory processing disorder rather than a peripheral vestibular disease. Thirteen eligible studies collectively demonstrate that VM arises from dysregulation within central sensory networks involving vestibular, visual, and auditory pathways, modulated by migraine biology and hormonal influences[1–13].

The convergence of phenotype data, diagnostic physiology, and treatment response provides a coherent explanatory framework for the heterogeneous clinical presentations observed in VM.

Clinical Phenotypes as Expressions of Central Sensory Network Dysfunction

The VM-Phenotypes Project by Teggi et al. established that VM is not a single uniform entity but comprises reproducible clinical phenotypes characterized by differential sensory dominance[1]. Motion-sensitivity, positional vertigo, auditory hypersensitivity, and mixed phenotypes map closely to abnormalities identified in posturography, ABR/FFR, and VHIT studies[7–9].

Importantly, these phenotypes are not diagnostic artifacts. Instead, they reflect distinct patterns of central sensory gain and integration failure, explaining why patients with VM may present to otology, neurology, or psychiatry clinics depending on their dominant sensory trigger.

Reframing Diagnostic Abnormalities

Traditional vestibular diagnostics prioritize detection of peripheral labyrinthine dysfunction. In contrast, the diagnostic studies included in this review demonstrate that VM patients typically have:

- Preserved peripheral vestibular function
- Abnormal central sensory processing under multisensory load[7–9]

Posturography reveals impaired sensory reweighting under visual conflict, ABR/FFR demonstrates delayed brainstem auditory processing, and vHIT shows normal VOR gain with increased corrective saccades—findings consistent with central recalibration deficits rather than canal pathology[7–9].

These results explain the frequent mismatch between normal routine vestibular tests and severe patient-reported symptoms.

Therapeutic Evidence Supports Central Pathophysiology

Treatment studies further validate the central multisensory model. Agents that primarily target headache mechanisms (e.g., beta-blockers) demonstrate inconsistent vestibular benefit, whereas therapies modulating central excitability and CGRP signaling show superior outcomes[4,8–12].

- Flunarizine and amitriptyline reduce central sensory gain and improve vestibular tolerance[9,10]
- Botulinum toxin A reduces trigeminovascular sensitization and sensory amplification[10]
- Anti-CGRP monoclonal antibodies directly reduce vertigo frequency independent of headache control[4]

Lifestyle interventions that stabilize sensory thresholds and reduce trigger exposure further support the central, trigger-dependent nature of VM[12].

Hormonal Modulation as a Key Amplifier

The hormonal evidence provided by Tang et al. demonstrates that estradiol deficiency exacerbates vestibular and sensory symptoms in VM[6]. Estrogen modulates inhibitory neurotransmission, CGRP expression, and brainstem excitability—mechanisms directly implicated in migraine and sensory hypersensitivity.

This hormonal influence explains:

- Female predominance of VM
- Symptom worsening during perimenopause
- Interindividual variability in symptom severity

Hormonal status should therefore be considered a modifier, not a primary cause, within the VM pathophysiological framework.

Strengths of the Review

1. PRISMA-compliant methodology with transparent study selection
2. Exclusive inclusion of original full-text studies, avoiding secondary bias
3. Integration across domains, rather than isolated focus on symptoms or treatment
4. Incorporation of phenotypic classification, strengthening clinical relevance
5. Mechanistic coherence linking diagnostics, therapy, and biology

Limitations

Despite its strengths, several limitations must be acknowledged:

- Small sample sizes across most included studies
- Limited number of randomized controlled trials
- Heterogeneity in diagnostic criteria over time
- Variability in outcome measures, limiting quantitative synthesis

These limitations reflect the current state of VM research rather than methodological flaws of the review.

Clinical Implications

The findings of this review have important practical consequences:

1. VM should be conceptualized as a central multisensory disorder, not a peripheral vestibulopathy
2. Diagnostic evaluation should prioritize exclusion of peripheral disease and identification of central features
3. Treatment should target central excitability and sensory modulation
4. Phenotype-guided therapy may improve outcomes
5. Hormonal context should be considered in female patients with refractory symptoms

Future Directions

Future research should focus on:

- Large, phenotype-stratified randomized trials
- Standardized vestibular outcome measures
- Functional imaging of multisensory integration networks
- Longitudinal studies examining hormonal modulation
- Biomarkers of central sensory gain

Such efforts will refine diagnostic accuracy and enable personalized therapy.

Conclusions

This systematic review provides robust evidence that vestibular migraine is best understood as a central multisensory processing disorder characterized by abnormal integration of vestibular, visual, and auditory inputs within migraine-susceptible neural networks. Clinical phenotypes reflect distinct sensory dominance patterns, diagnostic abnormalities localize to central pathways, therapeutic efficacy aligns with central mechanisms, and hormonal modulation amplifies symptom expression.

Recognizing VM within this framework advances diagnostic clarity, improves therapeutic targeting, and reconciles longstanding clinical inconsistencies.

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