

Upbeat Nystagmus a clinical and pathophysiological aid

PRODUCT INSIGHTS

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DEFINITION AND CLINICAL CHARACTERISTICS

Upbeat nystagmus (UBN) is a form of central nystagmus characterized by a slow downward drift of the eyes followed by a corrective quick phase upward (figures 1 and 2).

It may present as spontaneous, gaze-evoked, or be influenced by head or body position. Clinically, patients frequently report symptoms such as oscillopsia (illusory movement of the visual environment), vertical diplopia, postural unsteadiness, or balance disturbances. In some cases, however, UBN may remain asymptomatic and is discovered incidentally during routine neurological or vestibular examinations.

Etiology

UBN is typically associated with lesions affecting the central vestibular pathways, particularly those within the brainstem and cerebellum. Etiologies include ischemic or hemorrhagic strokes, demyelinating diseases (e.g., multiple sclerosis), neoplasms, structural malformations (e.g., Arnold-Chiari malformation), neurodegenerative conditions, and vestibular cerebellar dysfunctions. The localization of the lesion often correlates with the specific circuitry involved in vertical gaze holding and vestibular integration.

Symptoms and Visual Consequences

The clinical hallmark of Upbeat Nystagmus Syndrome (UBNS) is oscillopsia, perceived as vertical motion of the visual field due to involuntary upward eye movements. This occurs because the slow phase of the nystagmus shifts the retinal image downward, without a corresponding motor command (i.e., no efference copy), leading to a perceptual mismatch and illusion of scene movement. Interestingly, this illusion is often less intense than the actual eye movement might suggest, possibly due to a central reduction in visual motion sensitivity as a compensatory mechanism to minimize visual discomfort.

A **secondary consequence** of oscillopsia is postural imbalance, particularly along the sagittal plane. The vestibulo-spinal reflex (VSR), activated to compensate for perceived backward body tilt (due to downward eye drift), may induce anterior–posterior sway or retropulsion. The body responds as if it were tilting backward, even in the absence of actual motion, resulting in an inappropriate forward lean or instability. However, this compensatory pattern may vary, and some patients paradoxically exhibit backward falls like those observed in downbeat nystagmus.

PATHOPHYSIOLOGICAL MECHANISMS

UBN arises from an imbalance between neural systems controlling upward and downward vertical eye movements. Since gravitational forces naturally promote downward drift, upward gaze requires tonic facilitatory activity from specific excitatory pathways. Disruption of these systems unmasks the gravity-facilitated downward drive, resulting in the observed nystagmus.

1. Crossing Ventral Tegmental Tract (CVTT)

- The CVTT is a key excitatory pathway responsible for upward eye movements. It originates in the **superior vestibular nucleus (SVN)**, crosses in the pons and midbrain, and terminates in the **oculomotor nucleus (III)**.
- Afferents to the SVN include inputs from the **anterior semicircular canals (ASCCs)**, **maculae**, the **flocculus**, and **caudal medullary structures** such as the **nucleus of Roller (RN)** and the **intercalated nucleus of Staderini (SIN)**.
- The CVTT functions as an **anti-gravity system**, continuously modulating oculomotor output based on head orientation and gravitational input, particularly from the otolith organs.
- Lesions affecting the CVTT or its upstream modulators impair upward gaze facilitation, leading to a relative dominance of downward drift and resulting in UBN.
- Data from altered gravity experiments (e.g., spaceflight, parabolic flight) support the existence and functional importance of this pathway in vertical gaze stabilization.

2. SVN–RN/SIN–Flocculus Feedback Loop

- This **feedback loop** regulates tonic output from the SVN via inhibitory-excitatory interactions among the **RN**, **SIN**, and **flocculus**.
- **Nucleus of Roller (RN)**: Located near the hypoglossal nucleus, it receives excitatory

projections from the SVN and sends inhibitory output to the flocculus. The flocculus, in turn, inhibits the SVN. Lesions of the RN result in floccular disinhibition, excessive suppression of the SVN, and ultimately UBN due to impaired activity in upward gaze muscles (superior rectus, inferior oblique).

- **Nucleus intercalatus of Staderini (SIN)**: Located adjacent to the dorsal vagal nucleus, SIN functions similarly to RN, sharing inputs and outputs with the flocculus and possibly contributing to **vertical gaze holding**. UBN has been documented in SIN lesions secondary to stroke, multiple sclerosis, and brainstem cavernomas. However, some debate remains over whether SIN is directly involved in gaze-holding or primarily modulates tonic vestibular activity.

3. Paramedian Tract (PMT) Cell Groups

- The **PMT system** comprises small nuclei along the midline of the medulla and pons. These structures receive input from premotor gaze centers and project to the cerebellar flocculus, paraflocculus, and vermis.
- They act as a **relay and integration hub**, transmitting efference copies and eye position signals to the vestibulocerebellum.
- In particular, the **nucleus paraphales** relays vertical gaze information from the **interstitial nucleus of Cajal** to the cerebellum. Lesions of this nucleus may produce UBN or **gaze-evoked vertical nystagmus (GEN)**.

4. Brachium Conjunctivum (BC)

- Historically considered part of the excitatory pathway for upward gaze, the BC projects from the SVN to the oculomotor nucleus. However, its distinct role has been questioned as it closely overlaps anatomically with the CVTT.

- Lesions confined to the BC tend to produce **downbeat nystagmus** or gaze-evoked downbeat nystagmus, rather than UBN, suggesting it may not be a primary facilitator of upward gaze.
 - In some cases, UBN associated with BC-region lesions is likely due to concurrent damage to the cerebellar vermis, rather than the BC itself.
5. Medial Longitudinal Fasciculus (MLF)
- The MLF is a critical conduit for vestibulo-ocular signals, particularly in the vertical plane.
 - Clinical studies in patients with MLF lesions reveal that upward VOR gain is often relatively preserved, suggesting the existence of extra-MLF pathways (e.g., CVTT) for upward gaze.
 - These patients commonly exhibit upbeat gaze-evoked nystagmus, supporting the idea that MLF damage deprives the interstitial nucleus of Cajal (a vertical neural integrator) of necessary vestibular input.
 - UBN due to MLF lesions likely results from selective involvement of upward gaze fibers with relative sparing of the downward VOR circuitry.

TREATMENT OPTIONS

Management strategies for UBN can be etiology-driven (treating the underlying condition) or symptomatic, aiming to reduce nystagmus intensity and its visual consequences.

- First-line medications include baclofen, 4-aminopyridine (4-AP), and memantine. These can be used individually or in combination if monotherapy is insufficient.
- Carbamazepine, although less commonly used, has shown occasional benefit.
- The choice of therapy should be tailored based on the presumed lesion site, patient tolerance, and response.

CONCLUSION

UBN serves as a distinctive clinical marker of dysfunction in the brainstem–cerebellar networks responsible for upward gaze control. Most commonly, it reflects disruption in circuits such as the CVTT and the SVN–RN/SIN–flocculus loop, which normally integrate vestibular, visual, and gravitational inputs to maintain vertical ocular stability. Recognition of the affected anatomical pathway is essential not only for accurate localization and diagnosis but also for guiding appropriate therapeutic strategies aimed at restoring visual and postural stability in affected patients.

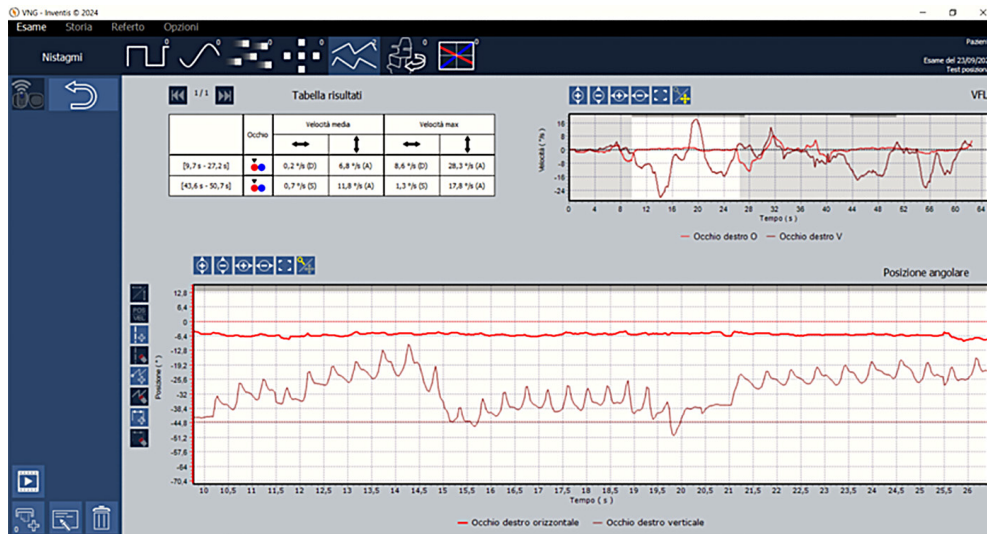


Figure 1. AT, male, 67 yo. Spontaneous upbeat nystagmus due to thiamine deficiency in patient affected by Wernicke encephalopathy.

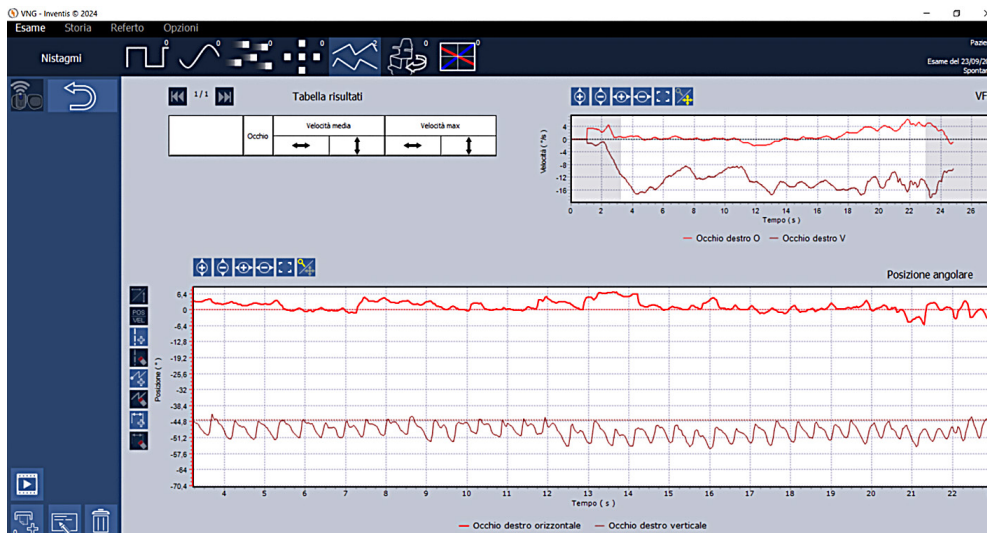


Figure 2. GDB, female, 61 yo. Very strong spontaneous upbeat nystagmus in acute medullar stroke.

Table 1. Key points of peripheral and central UBN	Peripheral	Central
Spontaneous	Rare	Frequent
Positional	Frequent	Frequent
Present in primary position	Yes	Yes
Presence of horizontal or torsional components	Frequent	Rare
Alexander law	Yes	Variable
Slow phase velocity	Linear	Linear, increasing or decreasing
Visual fixation inhibition	Yes	No
Convergence modification	No	Yes
Change vertical direction with different head positions	Only in BPPV	Often
Abnormal SP and Saccades	No	Often

Table taken from Marcelli V, Giannoni B, Volpe G, Faralli M, Marcelli E, Cavaliere M, Fetoni AR and Pettorossi VE (2025) Upbeat nystagmus: a clinical and pathophysiological review. Front. Neurol. 16:1601434. doi: 10.3389/fneur.2025.1601434.

