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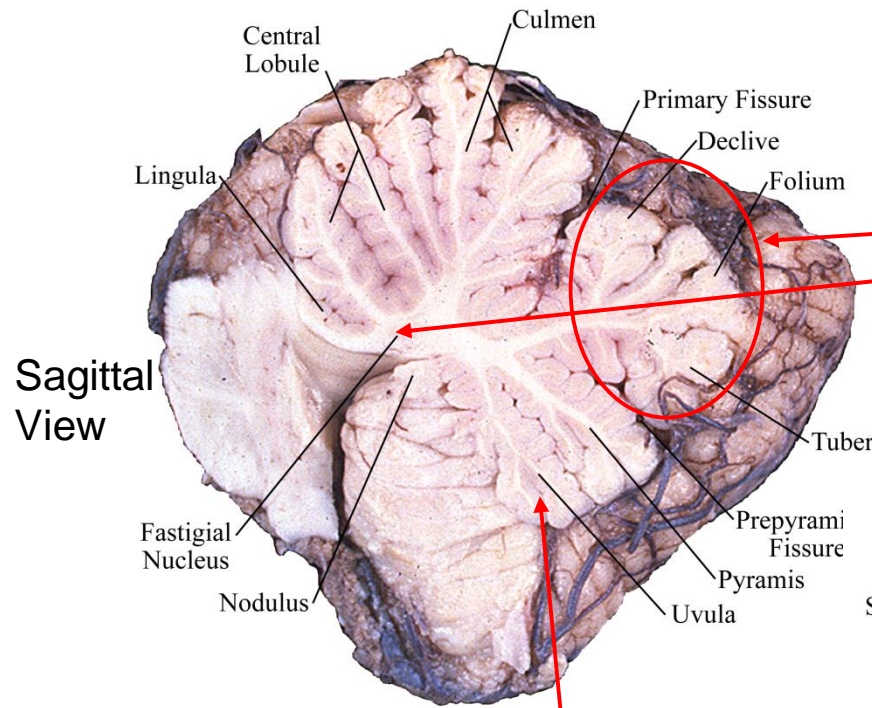


# CEREBELLAR Eye Movement Disorders: Diagnostic & Treatment Pearls for the Daily Clinic

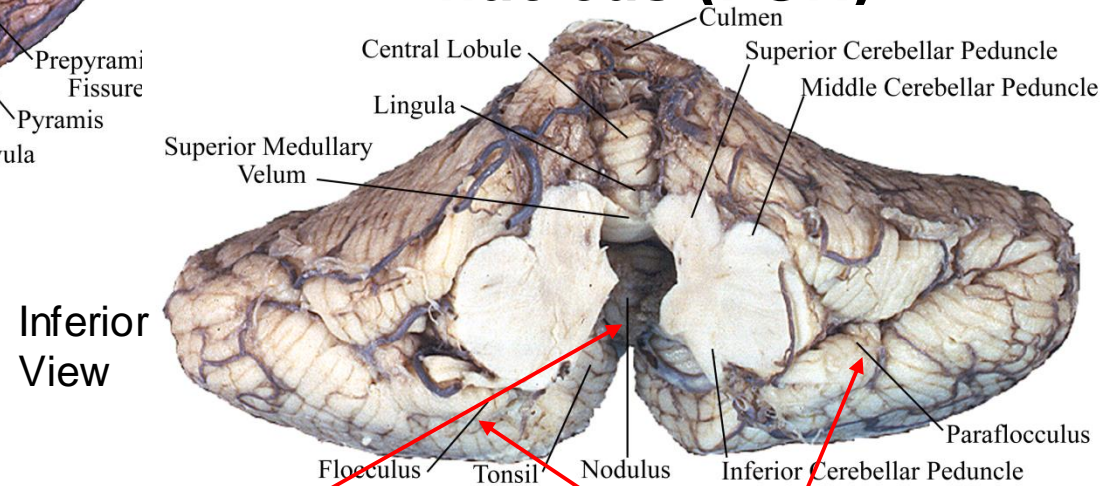
## LEARNING OBJECTIVES

- Correctly perform bedside maneuvers to elicit different types of cerebellar related ocular motor disorders.
- Localize various patterns of eye movement disorders to particular parts of the cerebellum.
- Know which drugs (off-label) might be used to treat different types of cerebellar ocular motor disorders.

# Three basic functional-anatomical cerebellar syndromes



**Syndrome of the dorsal vermis (OMV) & posterior fastigial nucleus (FOR)**

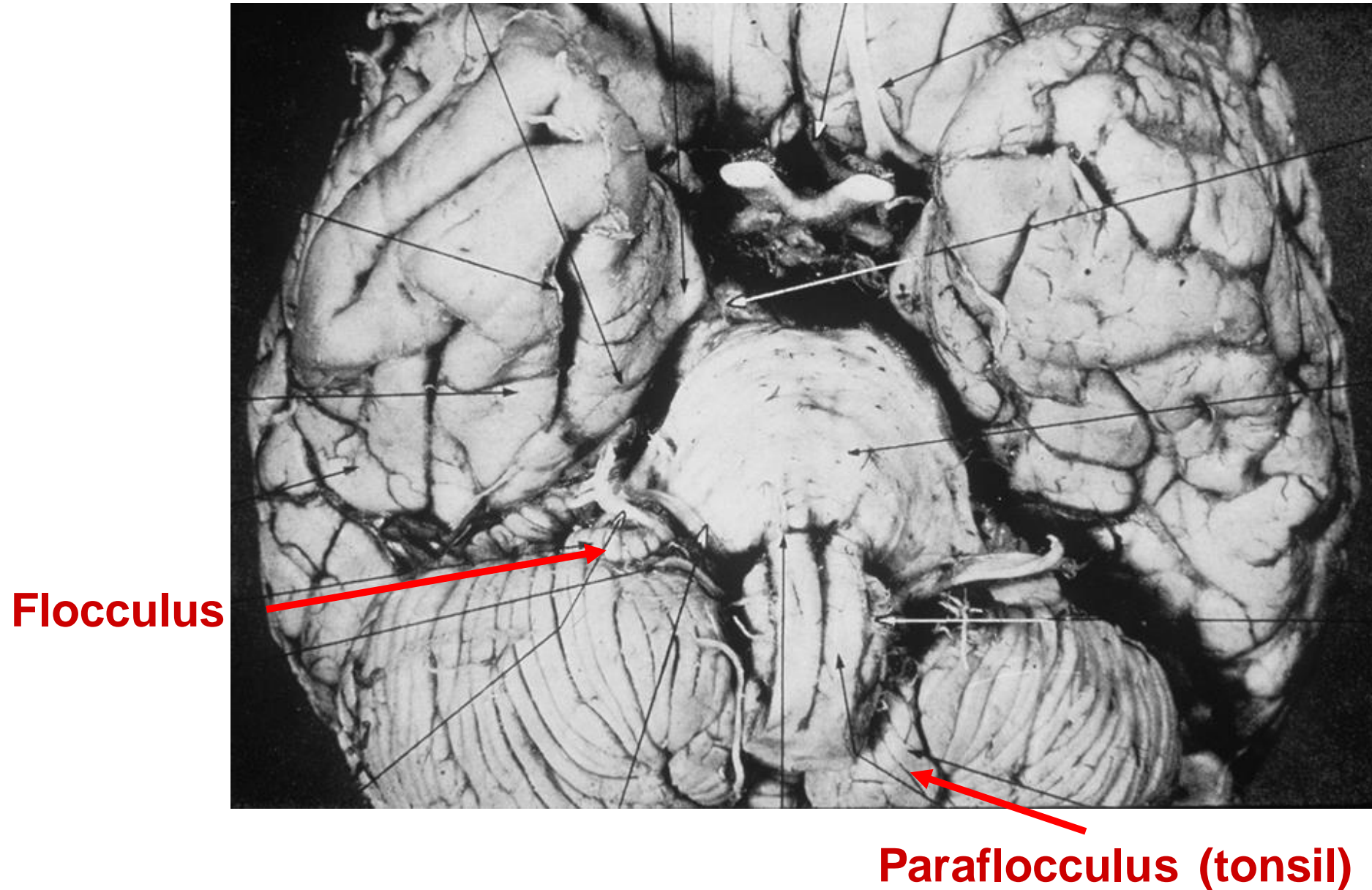


**Syndrome of the nodulus & ventral uvula**

**Syndrome of the flocculus and paraflocculus (tonsil)**



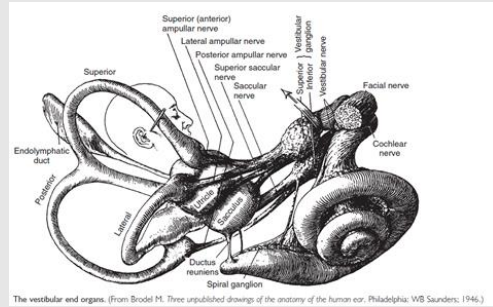
# Cerebellar flocculus and paraflocculus (tonsils)



**Flocculus**

**Paraflocculus (tonsil)**

# KEY ANATOMY OF LABYRINTH-VESTIBULO-CEREBELLAR CONNECTIONS

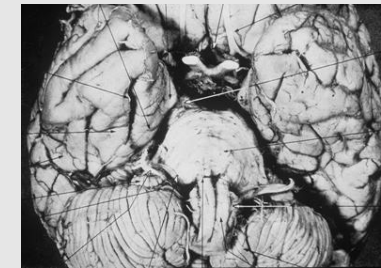


The vestibular end organs. (From Brodel M. Three unpublished drawings of the anatomy of the human ear. Philadelphia: WB Saunders; 1946.)

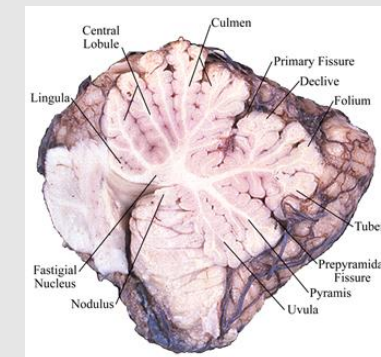
## The Labyrinth

Semicircular Canals / Otoliths project to

**FLOCCULUS, AICA**



**TONSIL, NODULUS/VENTRAL UVULA,  
PICA**



**AICA** = anterior inferior cerebellar artery

**PICA** = posterior inferior cerebellar artery

# Flocculus/Paraflocculus syndrome: Downbeat, gaze-evoked and rebound nystagmus in cerebellar atrophy



Cerebellar atrophy: SCA6



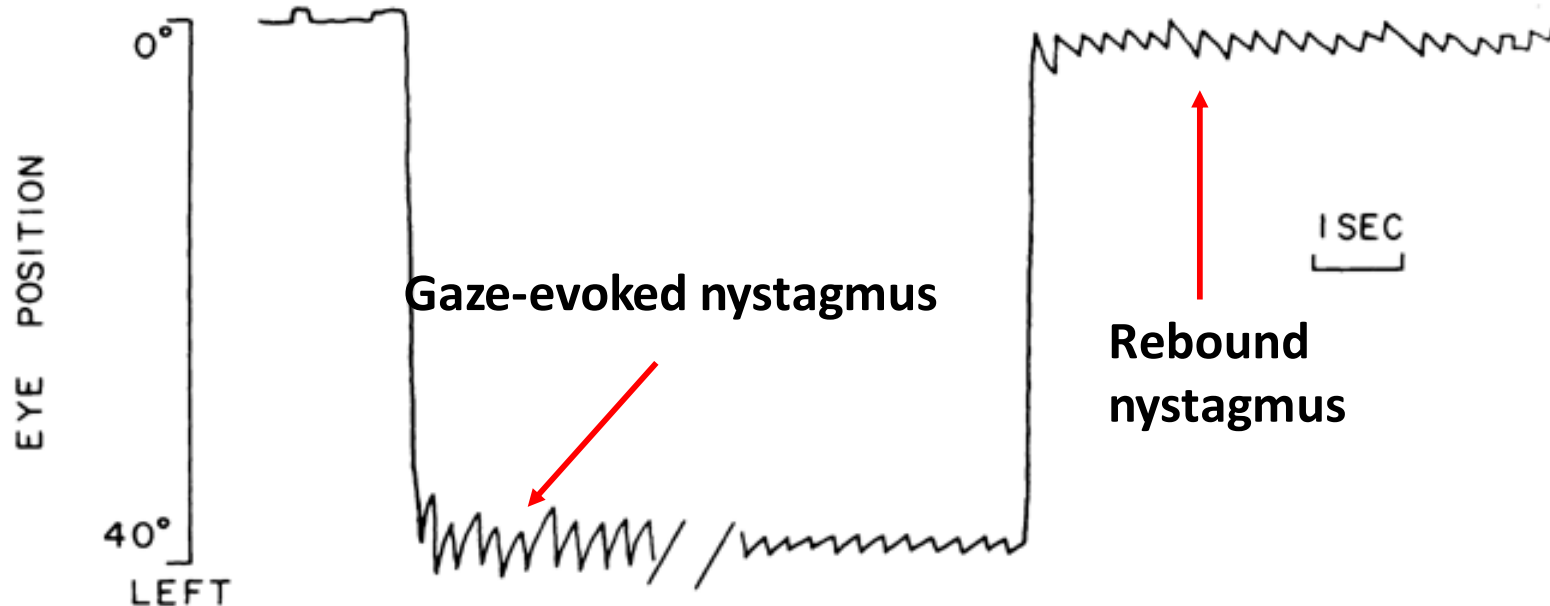
## Flocculus/Paraflocculus syndrome

Impaired pursuit and vestibuloocular reflex (VOR) cancellation (fixation suppression)

**Pursuit and VOR  
cancellation**



## Downbeat (DBN), gaze-evoked (GEN) and rebound nystagmus (RBN) in cerebellar atrophy



**PEARL: As eccentric gaze is maintained:**

**Gaze-evoked nystagmus (GEN) gets**

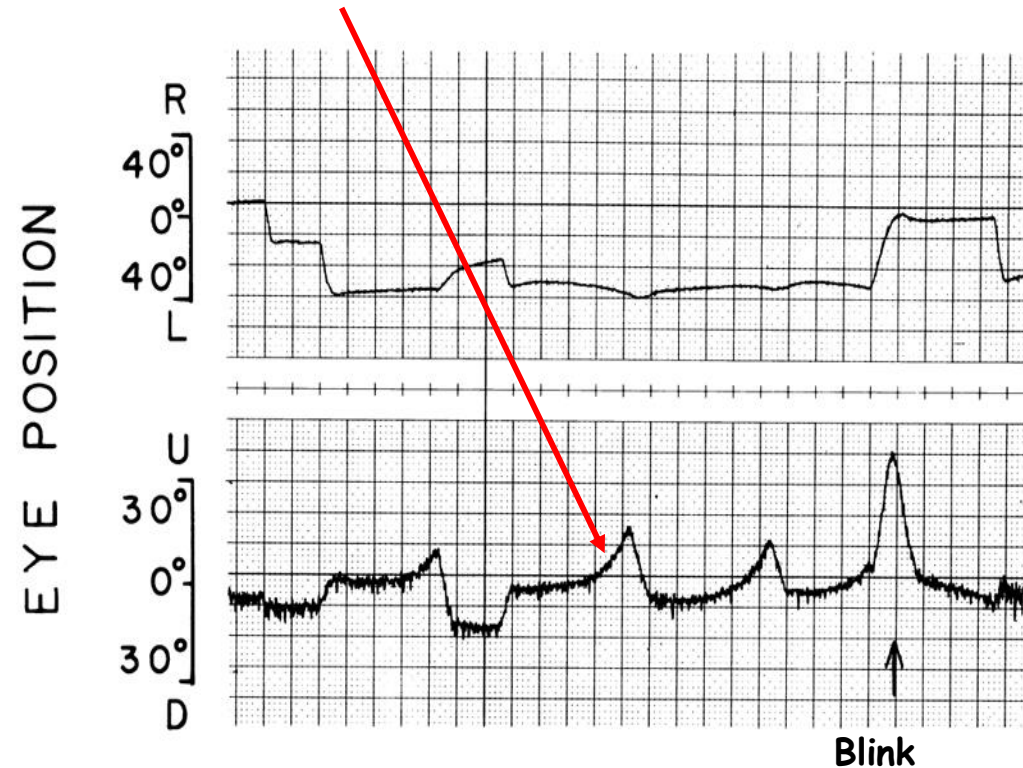
- Less with cerebellar disease, and RBN occurs
- More with myasthenia gravis, and RBN occurs
- Little change with infantile (congenital) nystagmus, and ??RBN



**Middle aged woman with a few months of rapidly progressive ataxia, No alcohol or medications, negative FH, normal MRI**



## Velocity-increasing slow phase



**PEARL: Velocity-increasing slow phases imply gaze-holding integrator is unstable.**

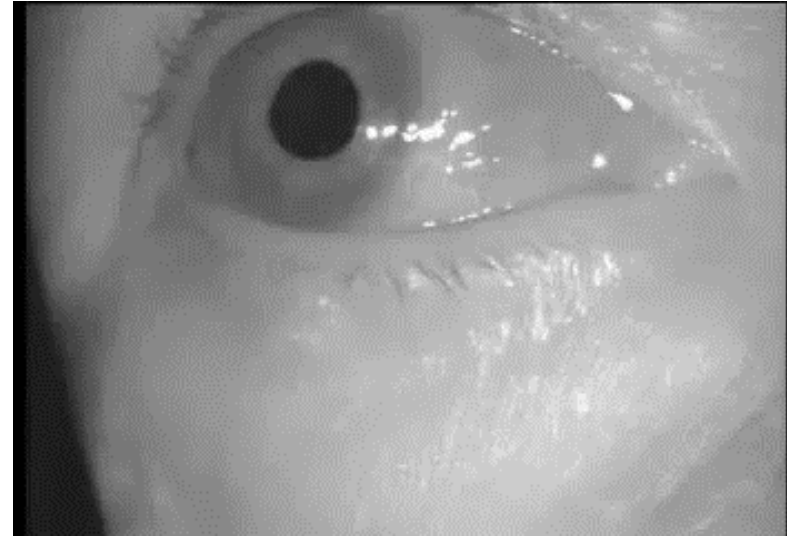
**Downbeat Nystagmus will intensify in UP-gaze (anti-Alexander's Law)**

## **Downbeat nystagmus in adults**

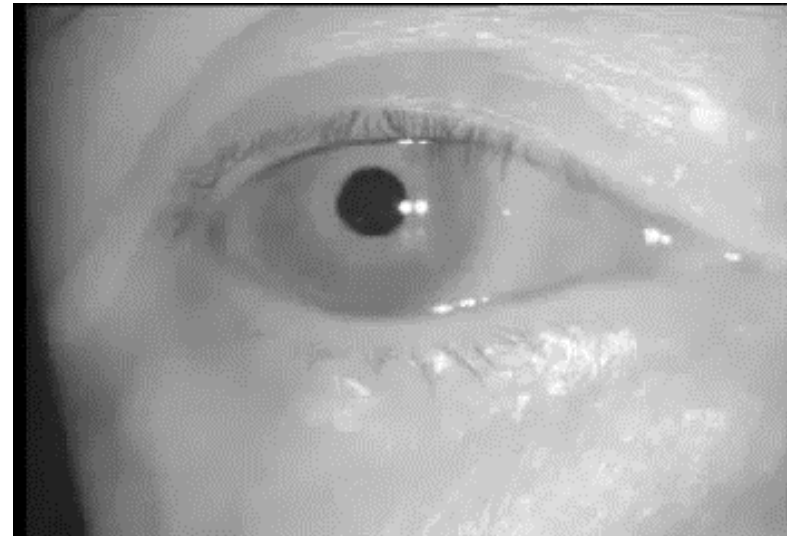
- **Paraneoplastic syndrome (anti-yo in women (gyn tumors), anti-hu, anti-gad, anti-ma/ta. Note anti-ri is associated with opsoclonus)**
- **Lithium, carbamazepine, amiodorone**
- **Cerebellar degeneration**
- **Cranio-cervical junction anomalies**
- **Wernicke's encephalopathy (often converts to upbeat with convergence or vice versa)**
- **TREATMENT – 4-aminopyridine. Note also some evidence this works in upbeat nystagmus and in EA2 (episodic ataxia type 2). Other choices, though less consistently helpful, include clonazepam and baclofen. (Note upbeat nystagmus is produced by nicotine)**

# Drug Treatments – Aminopyridines

- **3,4-diaminopyridine**
- **4-aminopyridine (more effective and less side effects).**
- **Improve Purkinje cell function via blocking K channels (Kalla, Brain, 2007; Strupp, Prog Br Res 2008)**
- **NOTE may also lessen gaze-evoked nystagmus**



Downbeat\_Before34DAP



Downbeat\_After34DAP

Videos courtesy of Dr. Michael Strupp

Strupp M, Schuler O, Krafczyk S, Jahn K, Schautzer F, Büttner U, Brandt T (2003) Neurology 61:165-170



# HEAD IMPULSE RESPONSE



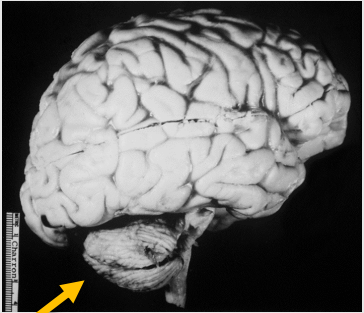
**Testing of the VOR: Head impulse sign in a unilateral  
peripheral labyrinthine lesions**



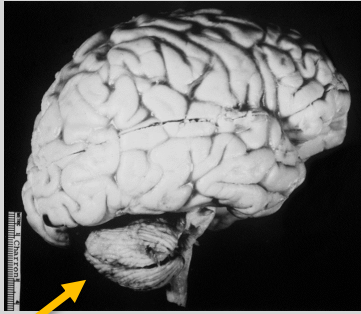
**Catch-up saccade  
during brief, high-  
acceleration,  
head rotation  
(left-sided loss)**

**Head-impulse  
sign in unilateral  
labyrinthine loss**

**Abnormal VOR in cerebellar disease: Abnormal direction**



## Abnormal VOR in cerebellar disease: Increased gain



**Corrective saccades IN THE DIRECTION of head rotation (opposite the slow phase) during fixation of a stationary target indicate a HYPERACTIVE VOR**

**Corrective saccades OPPOSITE THE DIRECTION of head rotation (same as slow phase) during attempted fixation of a target indicate a HYPOACTIVE VOR**



# Head-shaking induced nystagmus (HSN) in peripheral labyrinthine disease



# Head-shaking nystagmus (HSN) in cerebellar disease

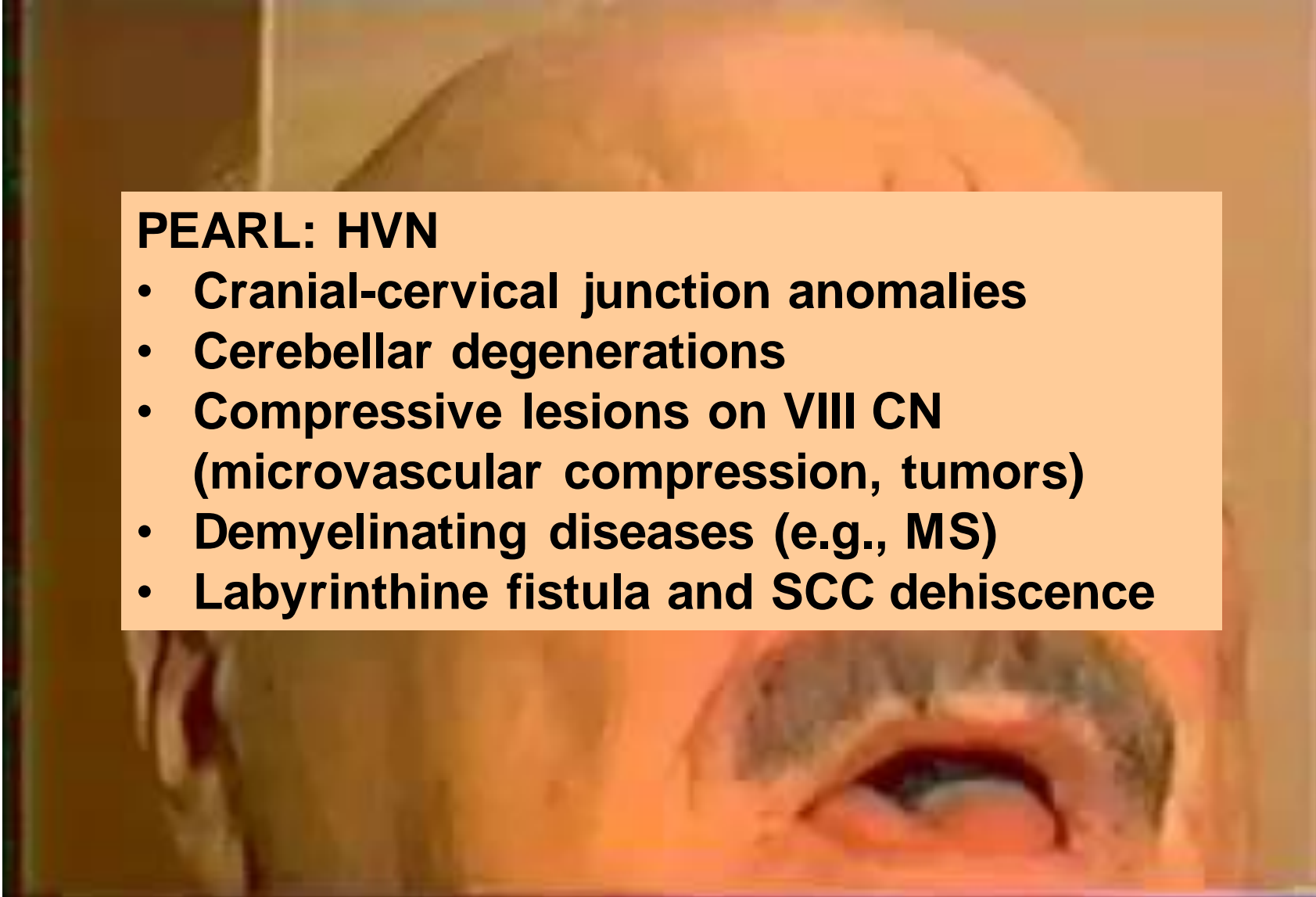
**PEARL: Think central if HSN is**

- **Directed DIFFERENTLY than head motion (cross-coupled), e.g, vertical nystagmus with horizontal head-shaking.**
- **Directed opposite to spontaneous nystagmus**
- **If there is a reversal of the direction of HSN that is early and strong**

## Hyperventilation-induced (HVN) downbeat nystagmus

### **PEARL: HVN**

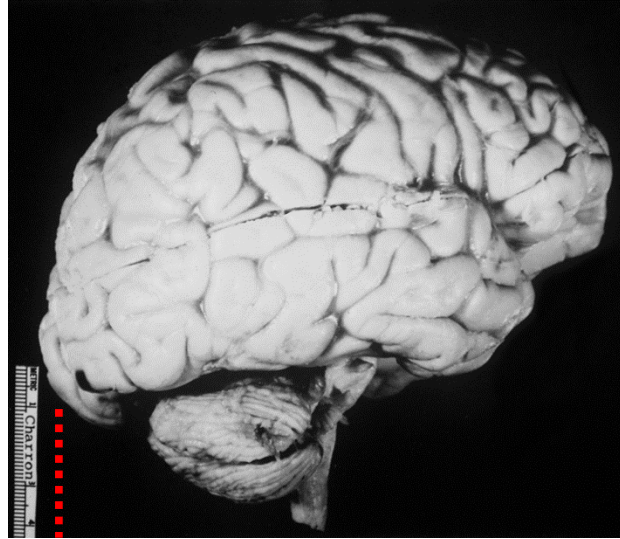
- **Cranial-cervical junction anomalies**
- **Cerebellar degenerations**
- **Compressive lesions on VIII CN**  
(microvascular compression, tumors)
- **Demyelinating diseases (e.g., MS)**
- **Labyrinthine fistula and SCC dehiscence**



# Pathology and anatomy of ocular motor abnormalities with cerebellar disease

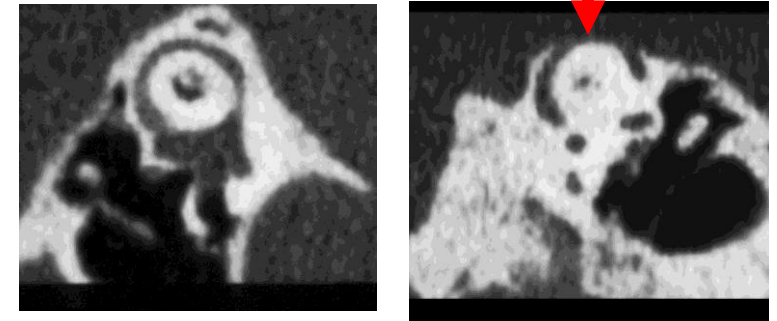


**Cranial-cervical junction:  
Chiari**



**Cerebellar atrophy:  
SCA6**

## Superior Semicircular Canal dehiscence

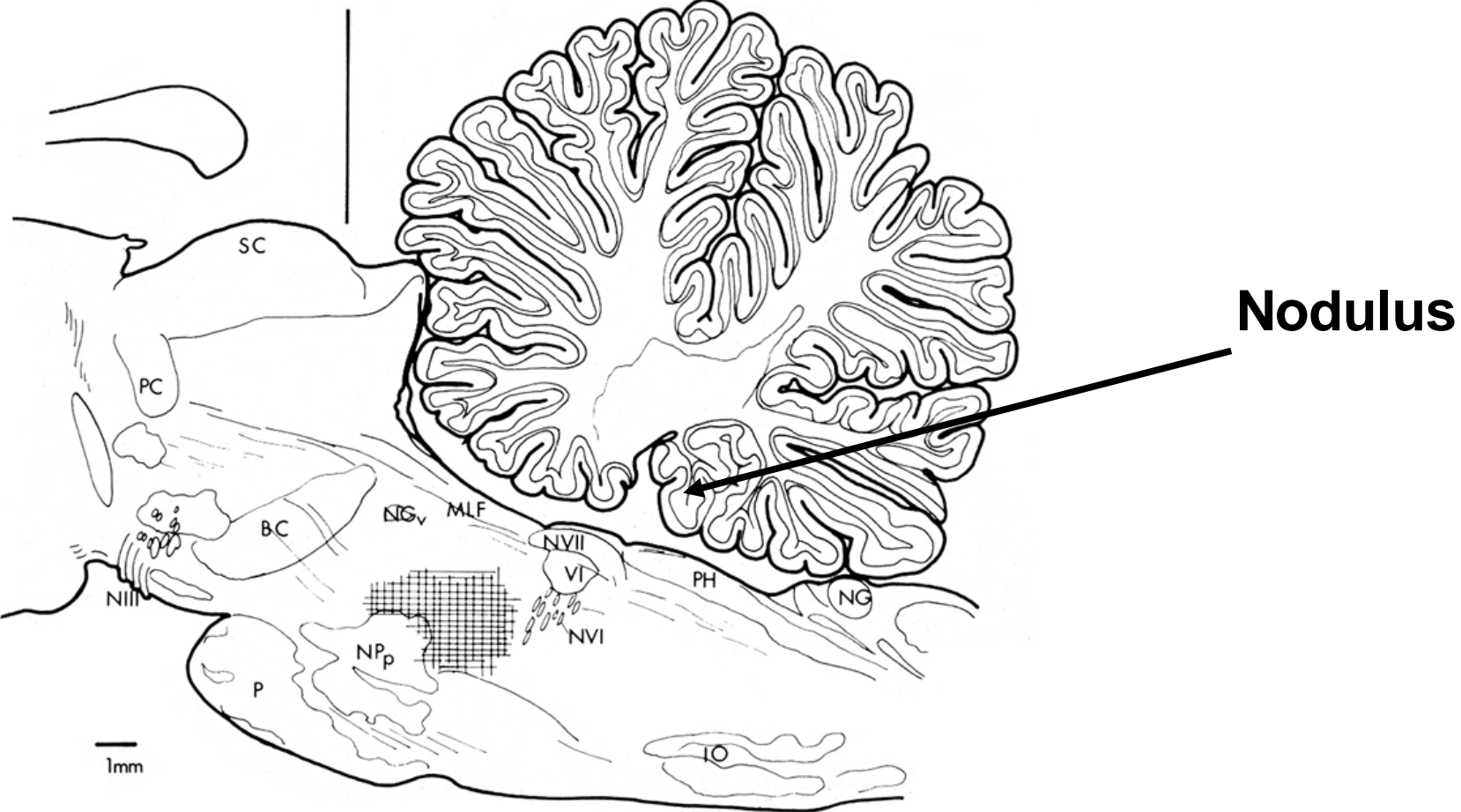


**PEARL: Remember Valsalva-induced vertigo with cranial-cervical junction anomalies and with labyrinthine fistula and SCC dehiscence**





**Ocular motor disorders with nodulus lesions:  
Periodic Alternating Nystagmus and Central Positional Nystagmus**



# PAN: Pathogenesis and Treatment

## Two key normal mechanisms

- **Central velocity storage mechanism** located within the vestibular nuclei that improves the ability of the vestibular system to respond to low-frequency (sustained) head motion by **perseverating** peripheral vestibular signals.
- **Adaptation mechanism** that acts to **null** any sustained unidirectional nystagmus (which in natural circumstances is always due to a lesion)

## PAN: Pathogenesis and Treatment

- In PAN, instability in velocity storage is produced by **loss of (gaba-mediated) inhibition** from the Purkinje cells of the nodulus onto the vestibular nuclei.
- Short-term adaptation (which is working normally) causes **reversals of nystagmus** leading to sustained oscillation.
- **Baclofen (GABA-b)\*** provides the missing inhibition and stops the nystagmus.
  - Usually need only 10 mg PO TID.
  - Avoid precipitous discontinuation.
  - Does not work as well in congenital PAN.
  - Memantine\* may be of help.



## **Nodulus lesions and positional nystagmus**

- **Young woman suddenly developed positional vertigo with nausea and vomiting, without other neurological symptoms or signs. Thought to have BPPV**
- **Positional nystagmus noted. All eye movement exam and general neurological exam is normal except for findings with positional testing and head shaking.**

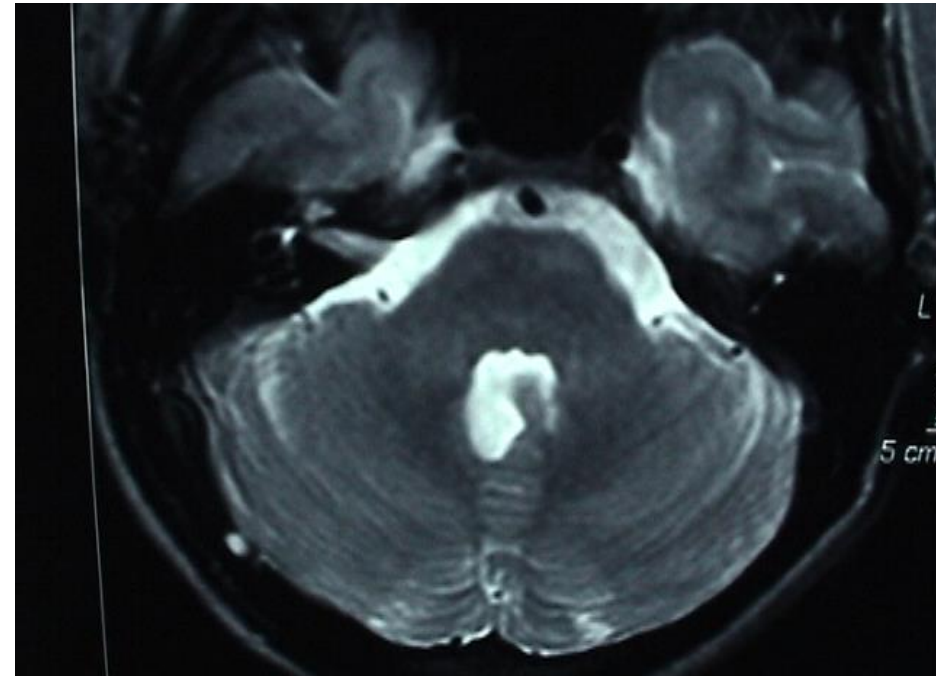
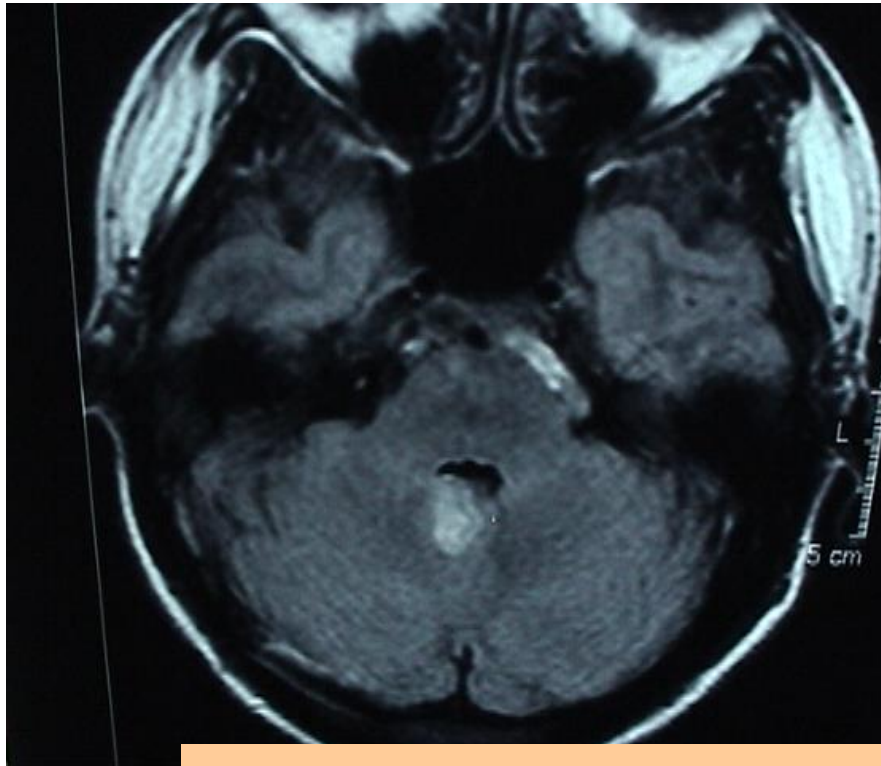


**Downbeat positional nystagmus**

**Torsional nystagmus after *horizontal* head shaking**



# Central positional nystagmus and abnormal head shaking nystagmus due to a nodulus lesion (glioneuronal tumor)



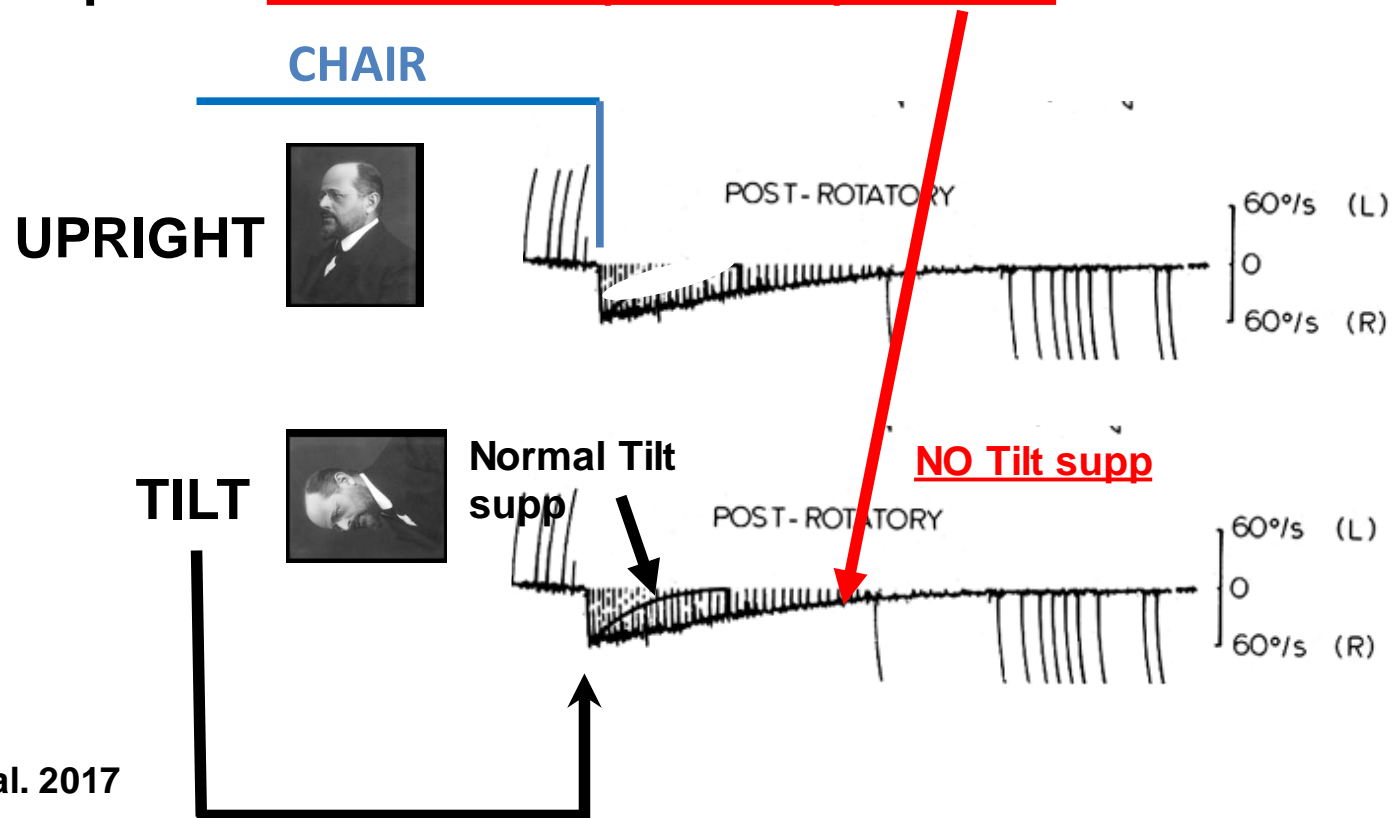
## IMPERATIVE

- Tell the radiologist where to look
- Look yourself

# SOMETHING 'NEW' FOR THE ACUTE VERTIGO PATIENT

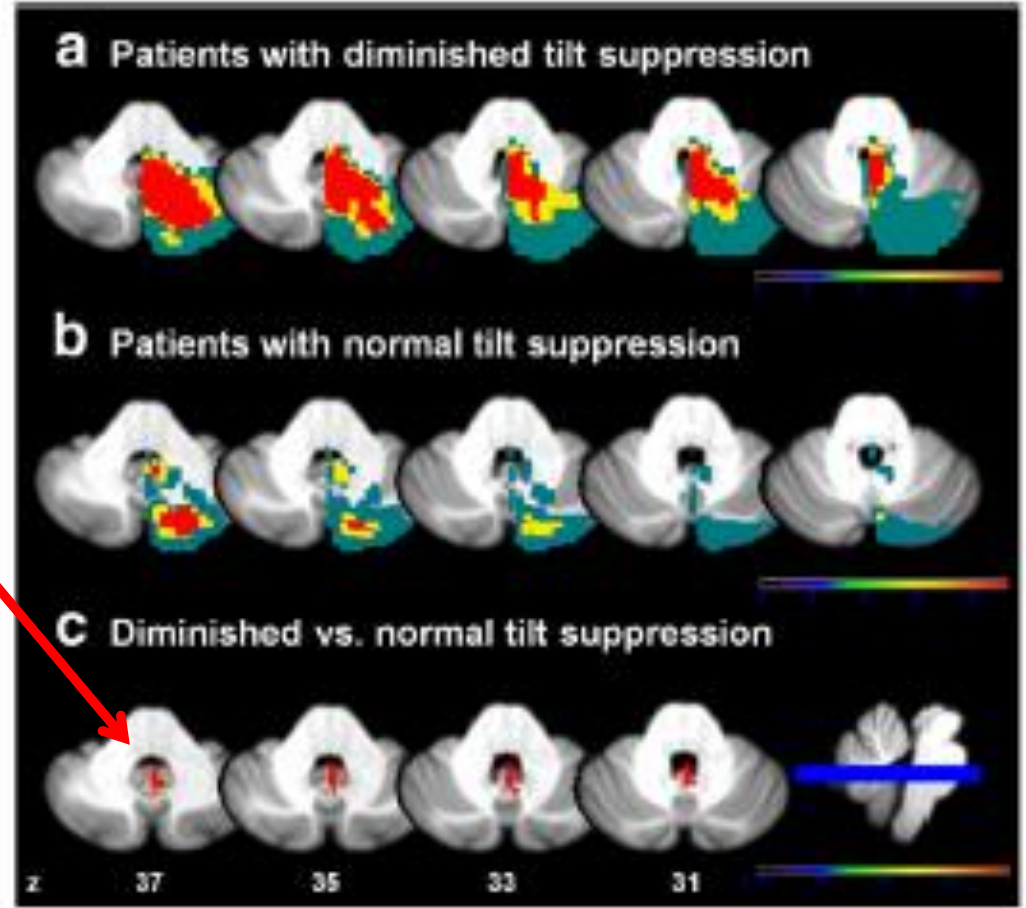
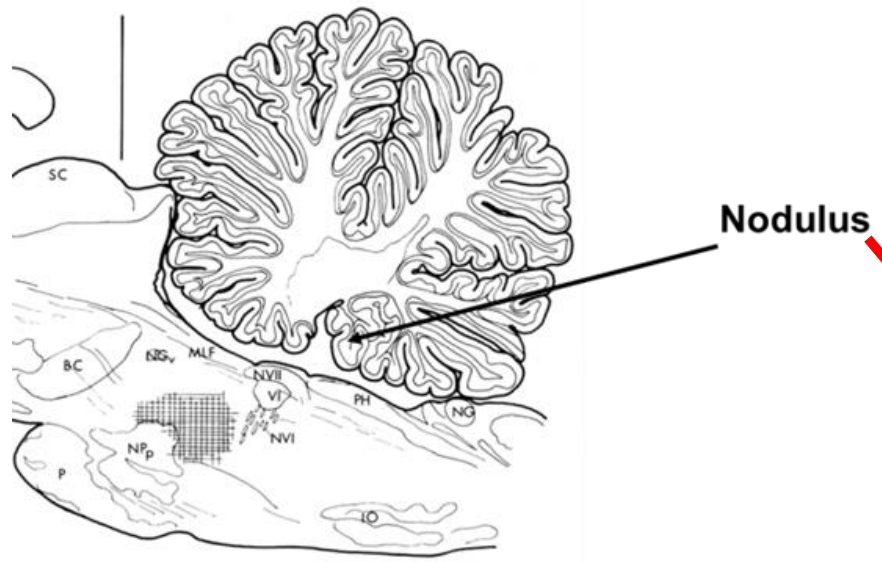
Tilt suppression (Tilt supp) of post-rotatory nystagmus after a sustained constant-velocity rotation.  
(Note the head is tilted just when the **CHAIR** stops moving)

- Normal with peripheral lesions
- Impaired with central (nodulus) lesions



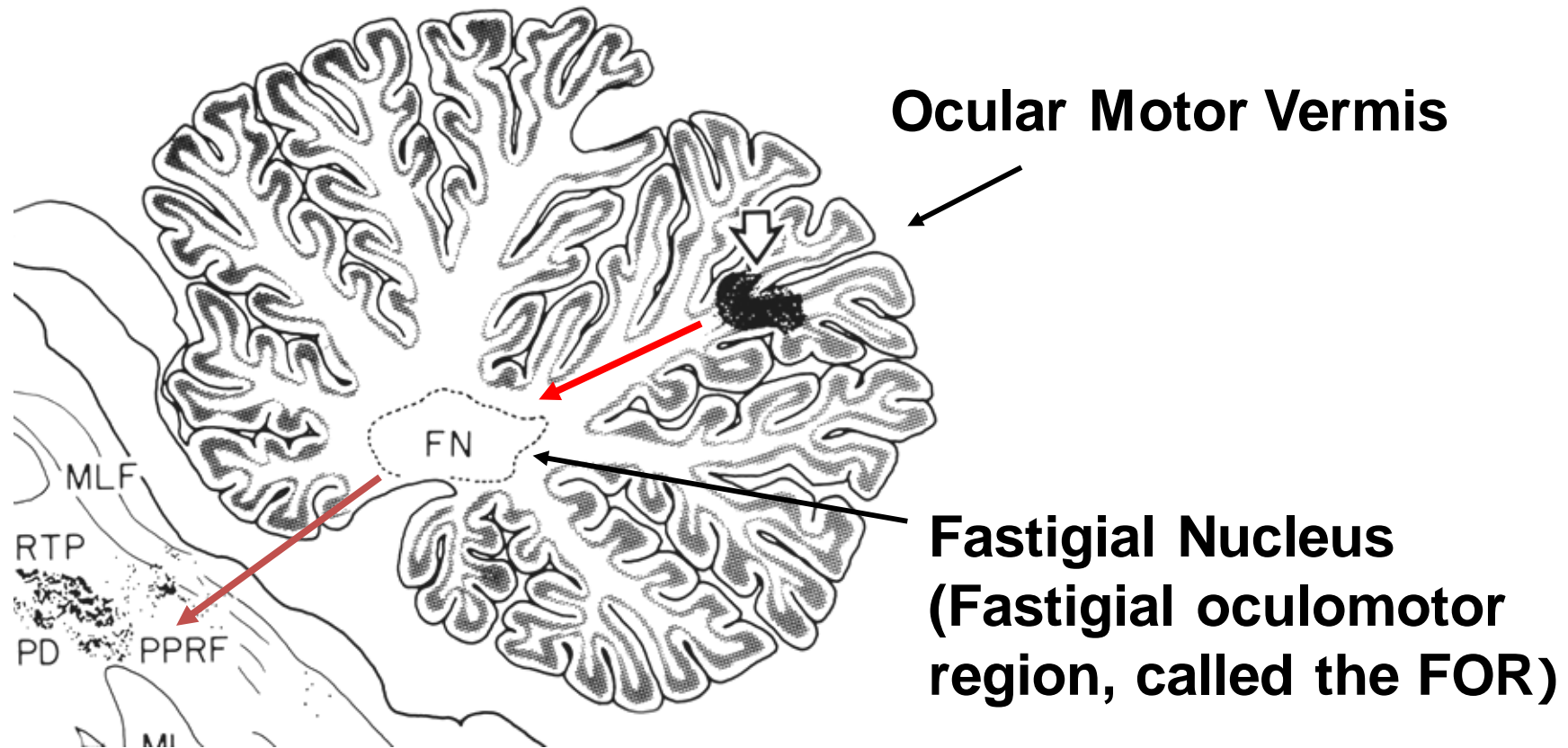


# Location of lesions in cerebellar patients who have impaired tilt suppression of post-rotatory nystagmus: The nodulus





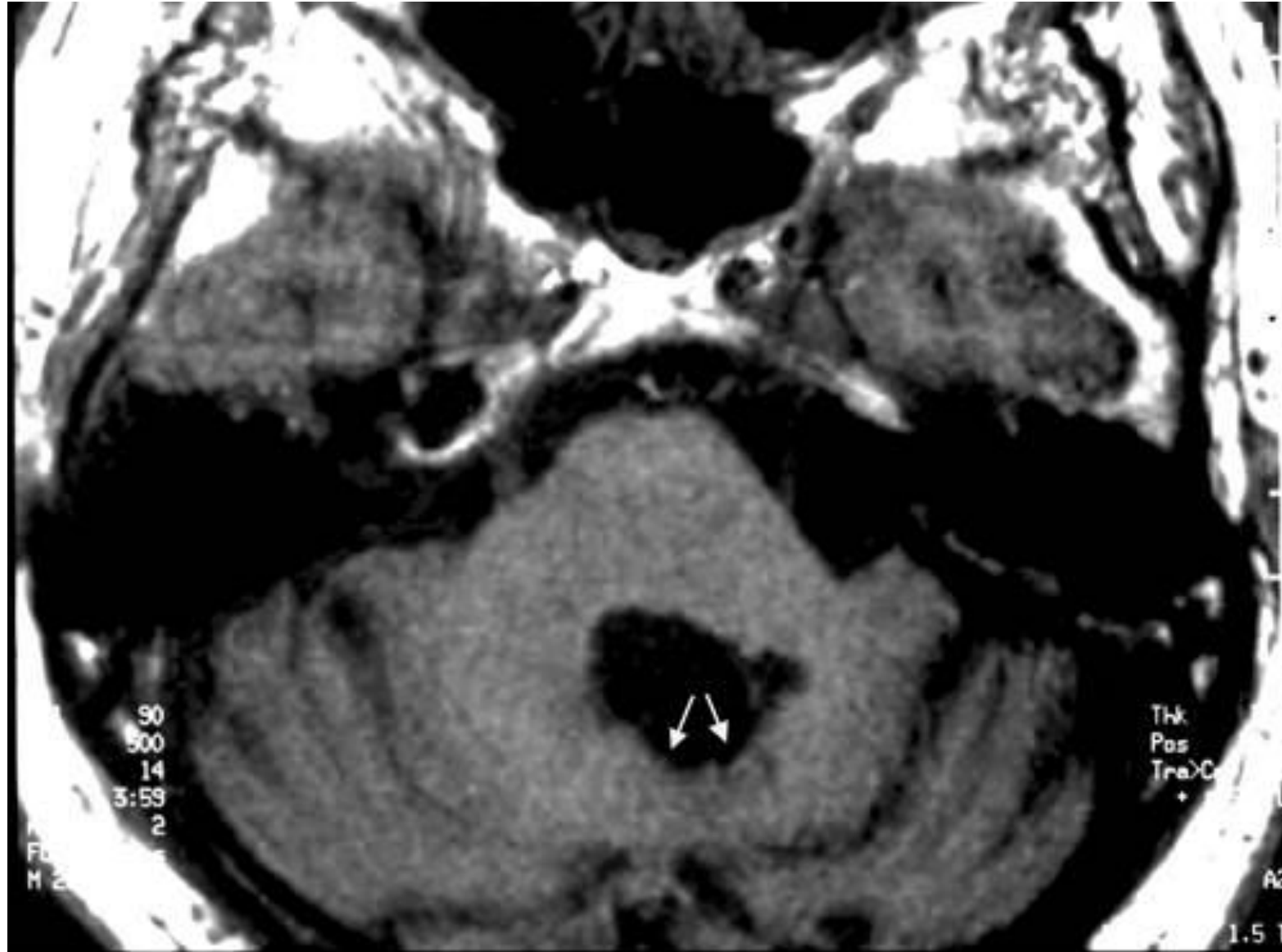
# Cerebellum and saccades



**REMEMBER: 1) The vermis contains Purkinje cells and they INHIBIT their target neurons in the deep nuclei (FOR)  
2) Each FOR normally stops ipsilateral saccades**



**Cerebellar fastigial nucleus lesions produce  
saccade *hypermetria***

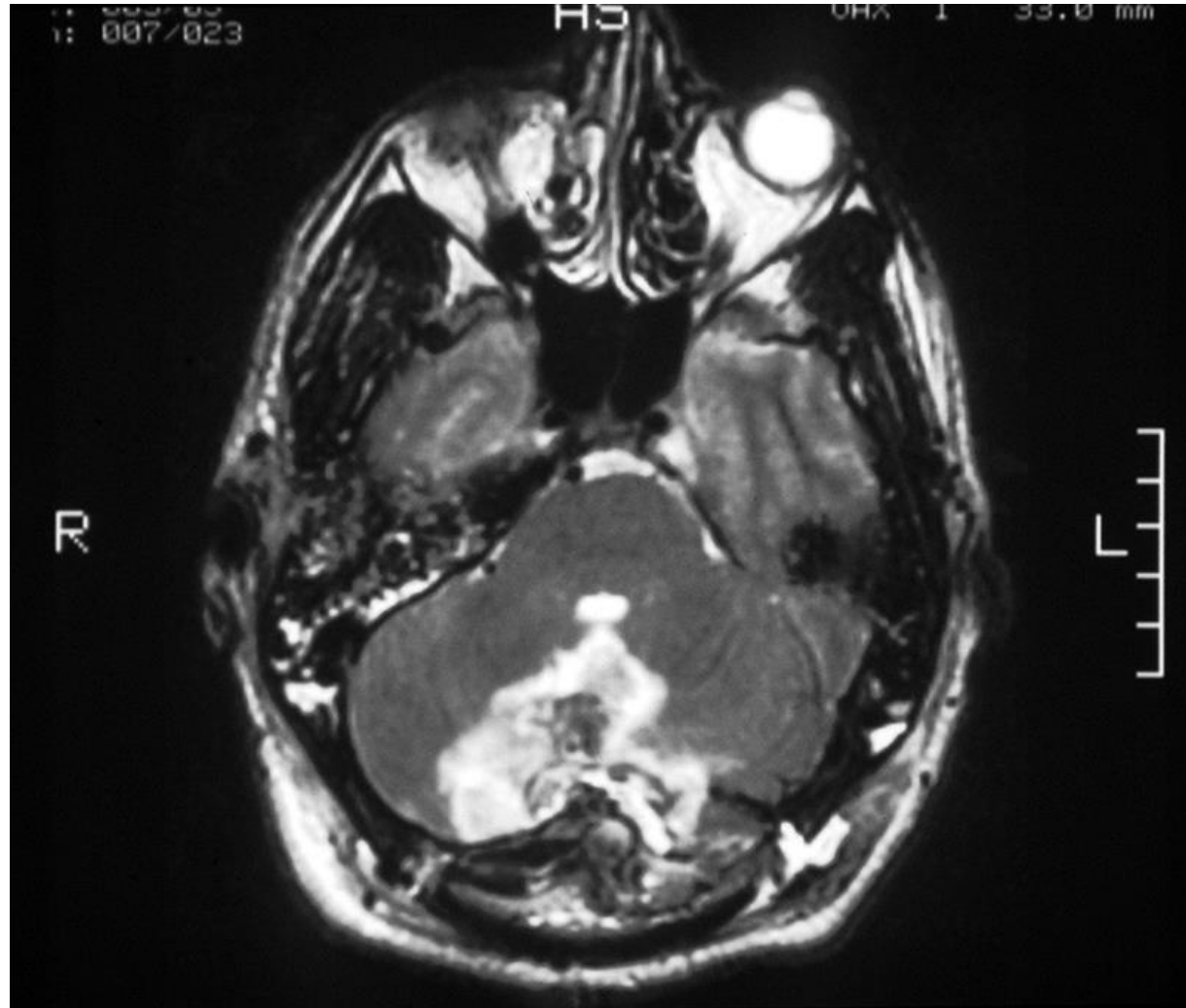






**Cerebellar dorsal vermis lesions  
produce saccade *hypometria***

**Hemangiopericytoma  
Involving dorsal  
vermis**





## CLINICAL POINT

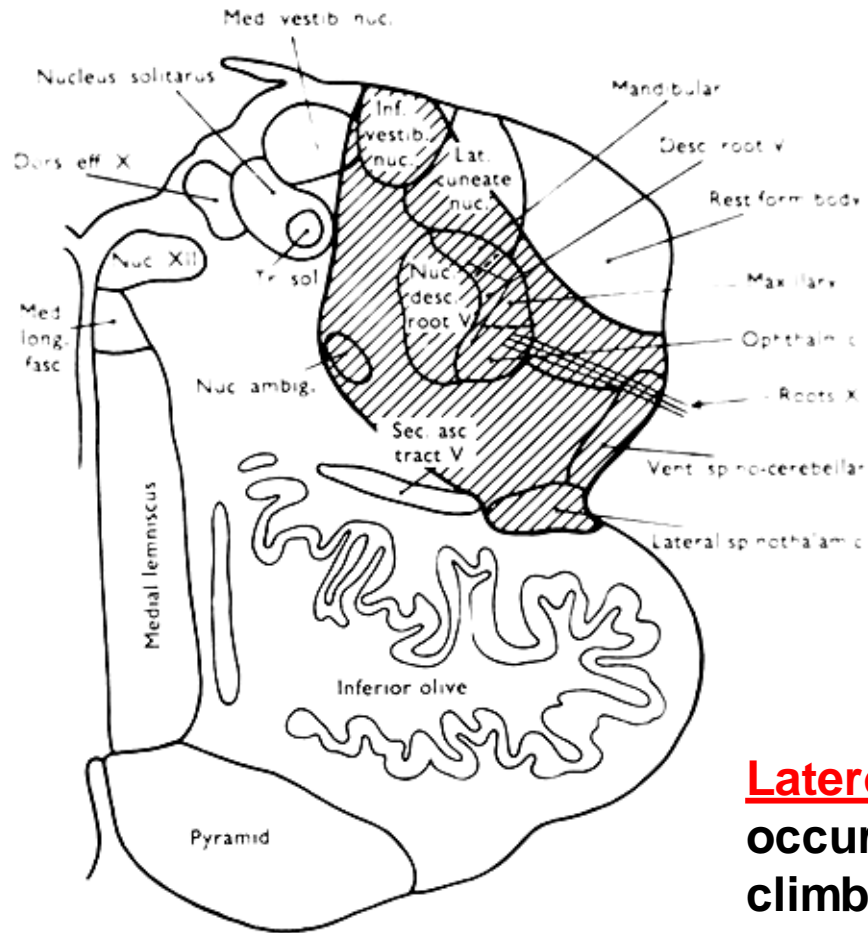
- Each Fastigial Oculomotor Region (FOR) sends its axons through the contralateral FOR before projecting to the brainstem alongside the superior cerebellar peduncle (hooked bundle of Russell, uncinate fasciculus). Each FOR acts to STOP ipsilateral saccades.
- A structural UNILATERAL lesion of the FOR is not possible.
- A functional UNILATERAL lesion of the FOR is possible: Wallenberg's syndrome in which one FOR is inhibited by excessive Purkinje cell activity (from decreased climbing fiber activity and increased mossy fiber activity) causing IPSI-pulsion (ipsilateral hypermetria of saccades).
- Functional UNILATERAL overactivity of one FOR is possible when there is a unilateral lesion of the overlying oculomotor vermis. This produces CONTRA-pulsion (contralateral hypermetria of saccades).



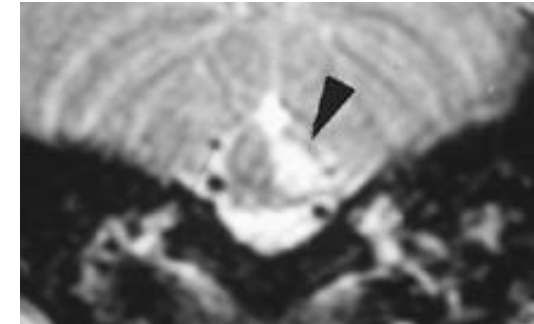
**Dysmetria of saccades: *Overshoot* to one side, *undershoot* toward the other, called *lateropulsion* of saccades**



# Wallenberg's Syndrome – Posterior Inferior Cerebellar Artery distribution infarct involving the dorsolateral medulla



**Restiform body (ICP)**



**Lateropulsion (IPSIPULSION) of saccades occurs because of an interruption of climbing fiber input thru the ICP which causes INCREASED activity of Purkinje Cells in the dorsal vermis and INCREASED inhibition of the underlying fastigial nucleus**

# THE ALIGNMENT CHANGES IN PATIENTS WITH CEREBELLAR DISEASE



• Esodeviation (eyes turn in with distance viewing, mimics a divergence paralysis)

• 'Skew' (vertical misalignment (alternating hyperdeviation, usually abducting eye is higher))



## Alignment changes in cerebellar disease



## Alignment changes in cerebellar disease



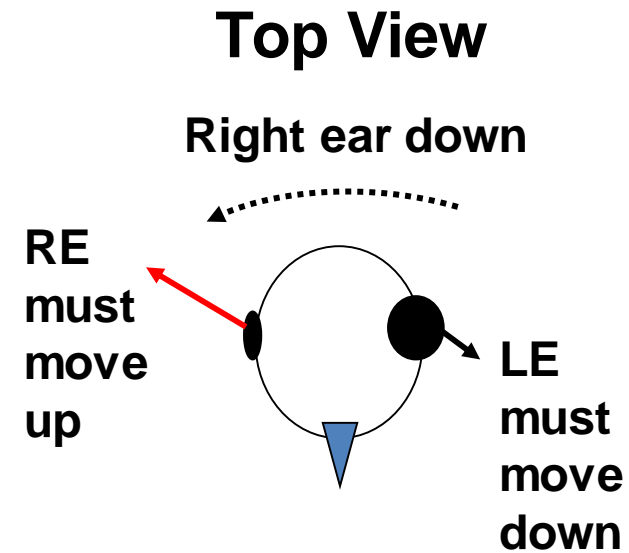
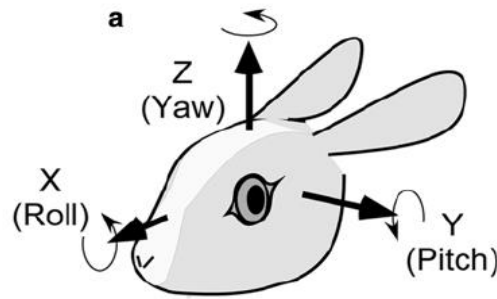
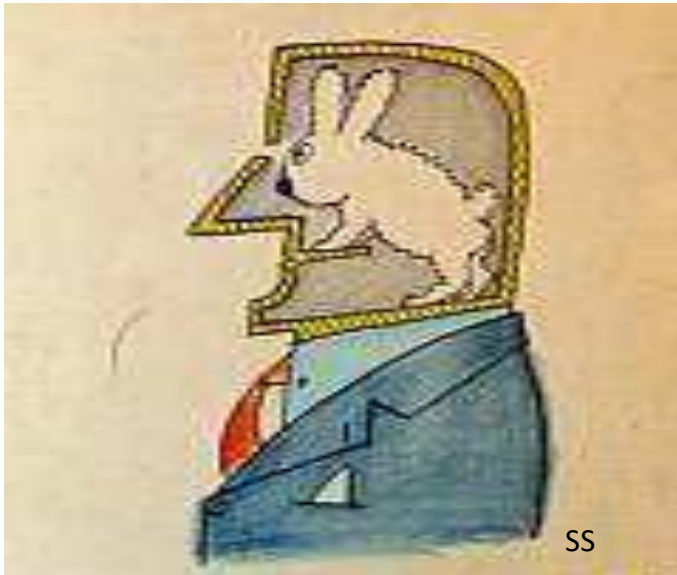


## Alignment changes in cerebellar disease





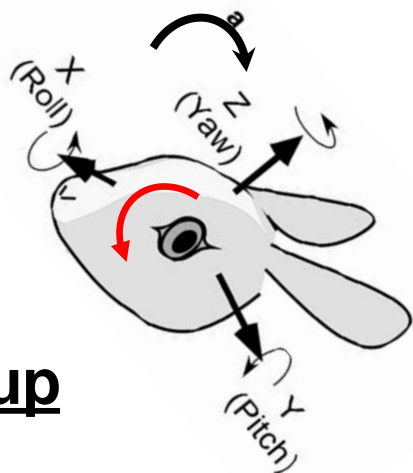
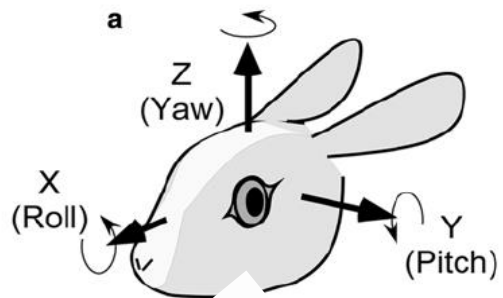
**WHY this pattern? We ALL have a lateral-eyed rabbit inside our ‘human’ brains. In the rabbit, a lateral tilt (one ear up and the other down) leads to the eyes rotating around the *roll axis* with one eye rotating down and the other eye rotating up (a physiological skew)**



**This is reflected in the Ocular Tilt Reaction (OTR) – in which (the rabbit) emerges when there is imbalance in otolith (utricle) responses**



# Alternating Skew in Cerebellar Patients: A misinterpretation of head pitch in a “lateral-eyed” animal?

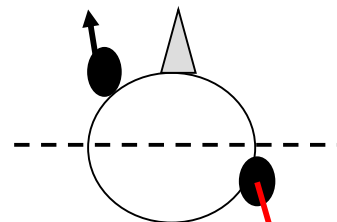


Nose up

## Top View

Nose up, eyes directed conjugately to the right

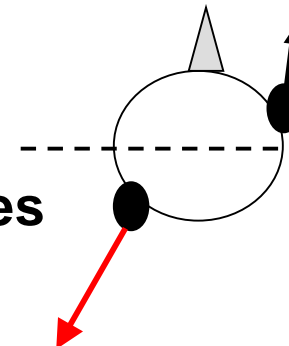
LE moves down



RE moves up

Nose up, eyes directed conjugately to the left

LE moves up



RE moves down



## CEREBELLAR Eye Movement Disorders: Diagnostic & Treatment Pearls for the Daily Clinic

LEARNING OBJECTIVES: Correctly perform key bedside maneuvers to elicit cerebellar related ocular motor disorders.

- Saccades: speed and accuracy
- Pursuit, gaze-holding, rebound
- Head impulse test
- Positional testing
- Head-shaking nystagmus
- Hyperventilation
- Eye alignment



## **CEREBELLAR Eye Movement Disorders: Diagnostic & Treatment Pearls for the Daily Clinic**

**LEARNING OBJECTIVES:** Localize various patterns of eye movement disorders to particular parts of the cerebellum

- Flocculus/Paraflocculus: Pursuit, gaze-holding, DBN, RebN
- Nodulus/ventral uvula: DBN, Positional nystagmus, PAN, impaired tilt suppression, OTR (contralateral)
- Dorsal vermis: Saccade (ipsilateral) HYPOMETRIA
- Fastigial Oculomotor Region (FOR): Saccade (ipsilateral) HYPERMETRIA) BUT structural lesions are inherently bilateral because of immediate crossing of efferent pathways





## CEREBELLAR Eye Movement Disorders: Diagnostic & Treatment Pearls for the Daily Clinic

**LEARNING OBJECTIVES:** Know which drugs (OFF-LABEL) might be used to treat different types of cerebellar ocular motor disorders.

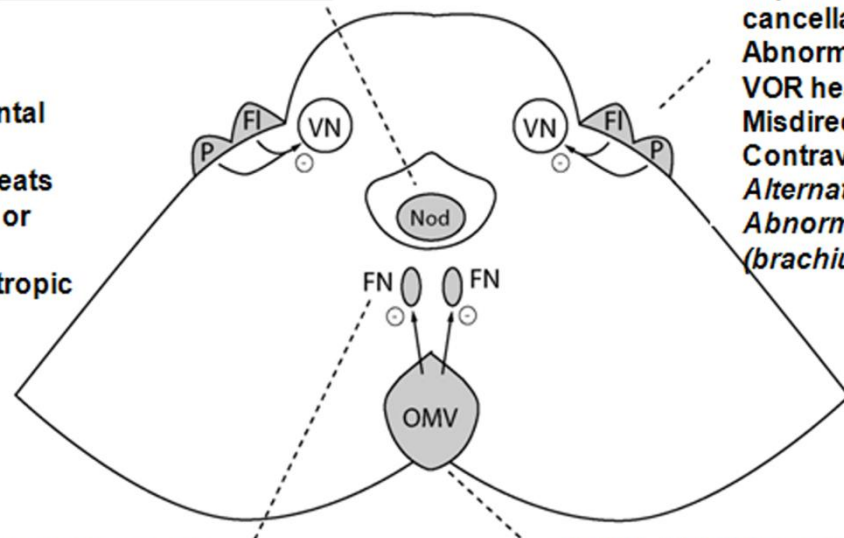
- Baclofen: Periodic alternating nystagmus (PAN)
- 4-aminopyridine: Downbeat nystagmus (DBN)
- Memantine: Excessive saccade intrusions, perhaps saccade dysmetria
- Clonazepan: DBN, pendular nystagmus
- Memantine, Gabapentin: pendular nystagmus

## Topical Localization in the Cerebellum

*(Italics, provisional localization)*

### NODULUS/UVULA

Prolonged rotational VOR  
 Periodic alternating nystagmus (PAN)  
 Impaired habituation of VOR  
 Impaired tilt suppression of post-rotatory nystagmus  
 Impaired translational VOR  
 Downbeat nystagmus  
 Impaired vertical and horizontal pursuit  
 Head-shaking nystagmus (beats ipsilesional, strong reversal or misdirected)  
 Direction changing, apogeotropic positional nystagmus  
 Contraversive OTR, skew (also dentate nucleus)  
*Alternating skew deviation*



### FLOCCULUS/PARAFLOCCULUS (TONSIL)

Downbeat, gaze-evoked, rebound, centripetal nystagmus  
 Impaired smooth pursuit and cancellation of VOR  
 Abnormal amplitude and direction of VOR head impulse response  
 Misdirected head-shaking nystagmus  
 Contraversive OTR but without skew  
*Alternating skew deviation*  
*Abnormal torsion with vertical pursuit (brachium pontis)*

### FASTIGIAL NUCLEUS (FN)

Unilateral:

Hypermetric ipsiversive saccades  
 Hypometric contraversive saccades  
 Reduced contralateral initial acceleration of pursuit

Bilateral:

Hypermetric saccades  
 Macrosaccadic oscillations  
*Normal pursuit*  
 Exophoria  
*Saccade intrusions (square wave jerks)*

### OCULAR MOTOR VERMIS (V,VI,VII)

Unilateral:

Hypermetric contraversive saccades  
 Hypometric ipsiversive saccades  
 Reduced initial acceleration of ipsilateral pursuit

Bilateral:

Hypometric saccades  
 Reduced initial acceleration of pursuit  
 Esophoria (*greater at distance, "divergence paralysis"*)

*(Globose/Emboliform – esophoria, vertical saccade dysmetria)*