

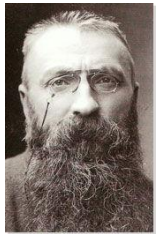
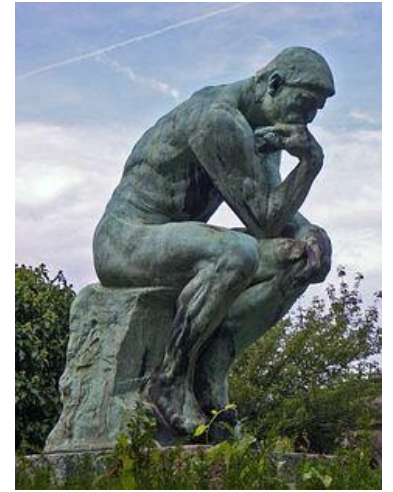
Nystagmus and other ocular oscillations: A video tutorial

OR, Lets make nystagmus **GREAT** again!



BEFORE WE START:

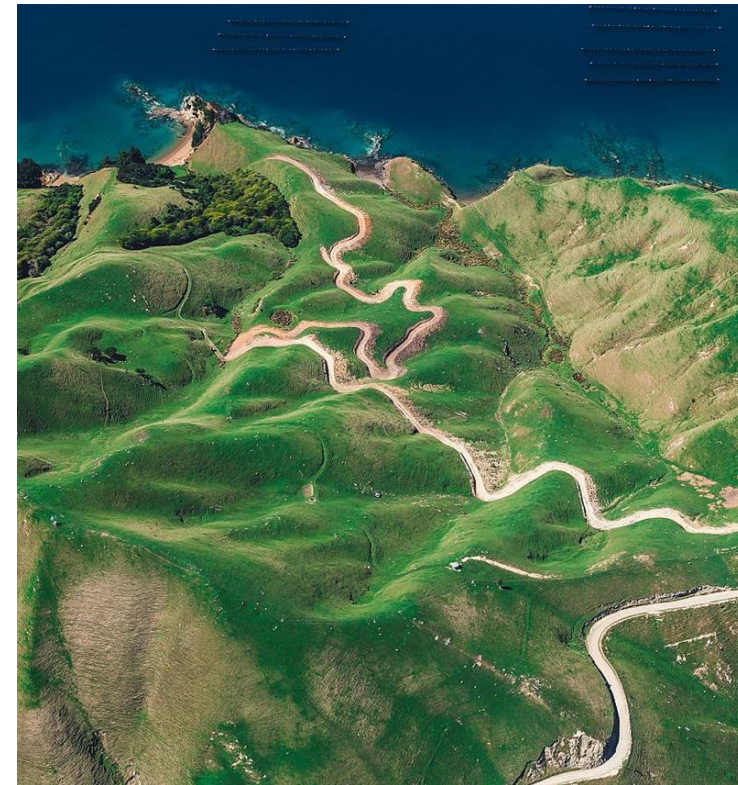
- **Is NYSTAGMUS complex?**
 - YES, highly complex, and it can be **OVERWHELMING**
- **But can we extract from the anatomy and physiology easy to use, easy to remember, practical principles for our clinics?**
 - YES, WITHOUT A DOUBT!
- **Do we need fancy equipment and detailed quantitative analysis to evaluate nystagmus?**
 - **ABSOLUTELY NOT!** The focused history and careful, ordered bedside exam usually points us to the diagnosis, and always directs us down the correct path for management. (Testing of course helps to confirm our diagnoses and provides data for research BUT)



Auguste Rodin

A Road Map for Today

- Historical perspectives and organizing one's thoughts about nystagmus
- A flow chart for diagnosis and wave-form analysis
- Key anatomy
- Major types of jerk nystagmus:
 - Peripheral vestibular
 - Brain stem and cerebellum
- Major types of pendular nystagmus: multiple sclerosis and ocular palatal tremor syndromes
- A few unusual types of nystagmus to recognize
- Saccadic intrusions, with and without an intersaccadic interval: square-wave jerks, flutter and opsoclonus
- Treatment options





A NOTE ON OSCILLOPSIA (symptom):

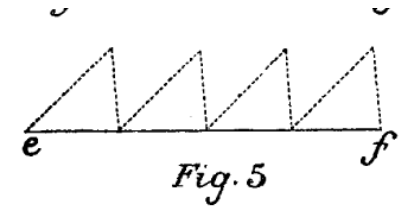
- Illusory movement of the visual world: Usually with a back and forth, jerk, or wiggle sense
- *Latin oscillo, to swing, + the Greek opsis, vision*
- If with the head still, usually due to a spontaneous nystagmus or other uncalled for eye movements
- If with the head moving, usually related to an abnormality in the amplitude or direction of compensatory slow phases of the vestibulo-ocular reflex.

How to think about nystagmus (without nightmares)

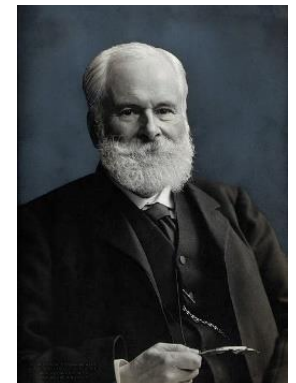
Greek origin of the word (νυσταγμός, drowsiness, nodding, dozing)



Eduard Hitzig (1871)



Crum Brown 1878



A MECHANISTIC APPROACH TO PATHOLOGICAL NYSTAGMUS

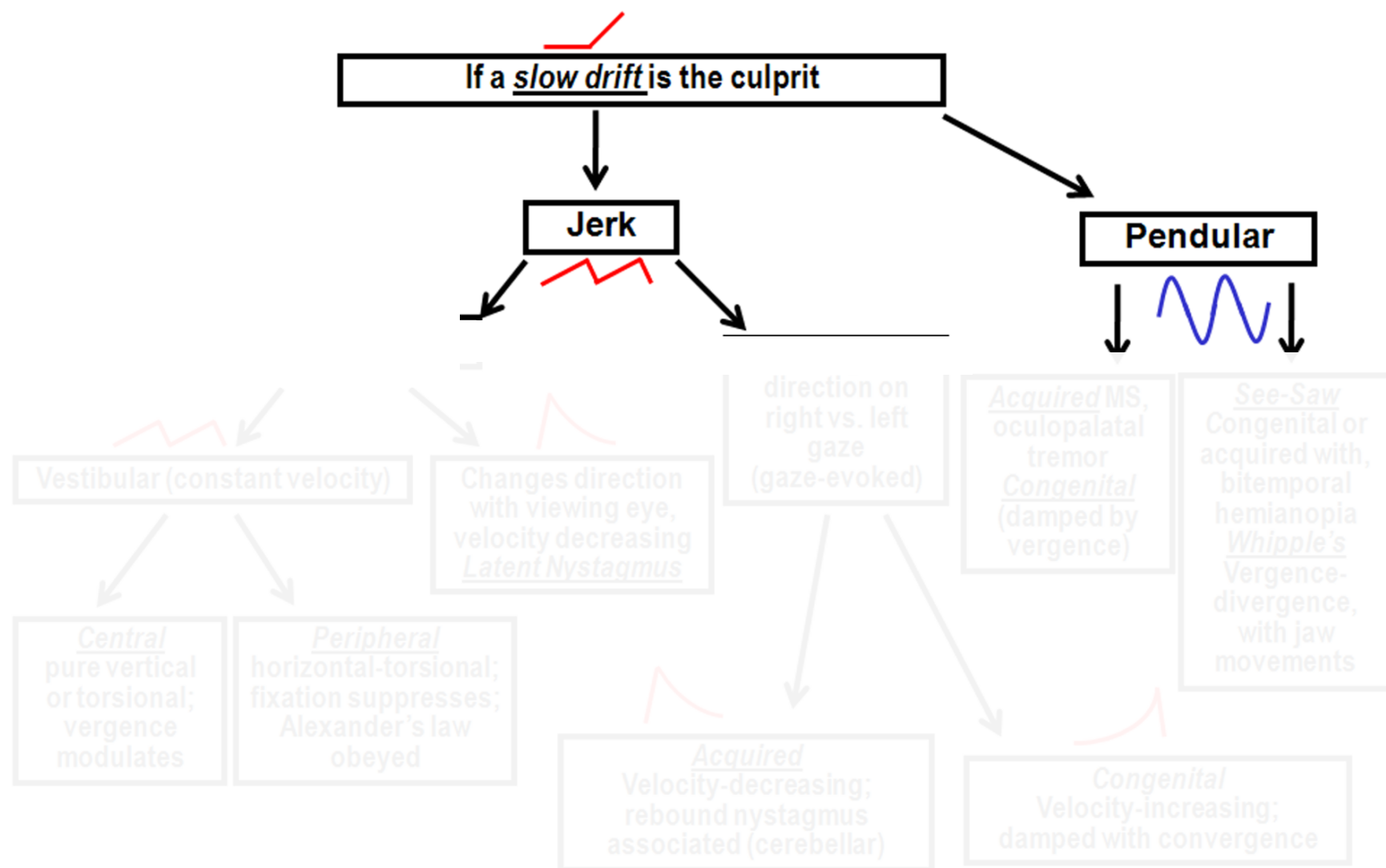
1. As a disorder of mechanisms that hold the eyes still

- Vestibular (peripheral or central)
- Gaze-holding (brainstem and cerebellum)
- Mechanisms that keep eye movements calibrated (maladaptation and sensory deprivation (nystagmus of the blind))
- Developmental disorders (motor and sensory, e.g., congenital and latent nystagmus)

2. Waveforms (slow phase) and pattern recognition (e.g., seesaw)

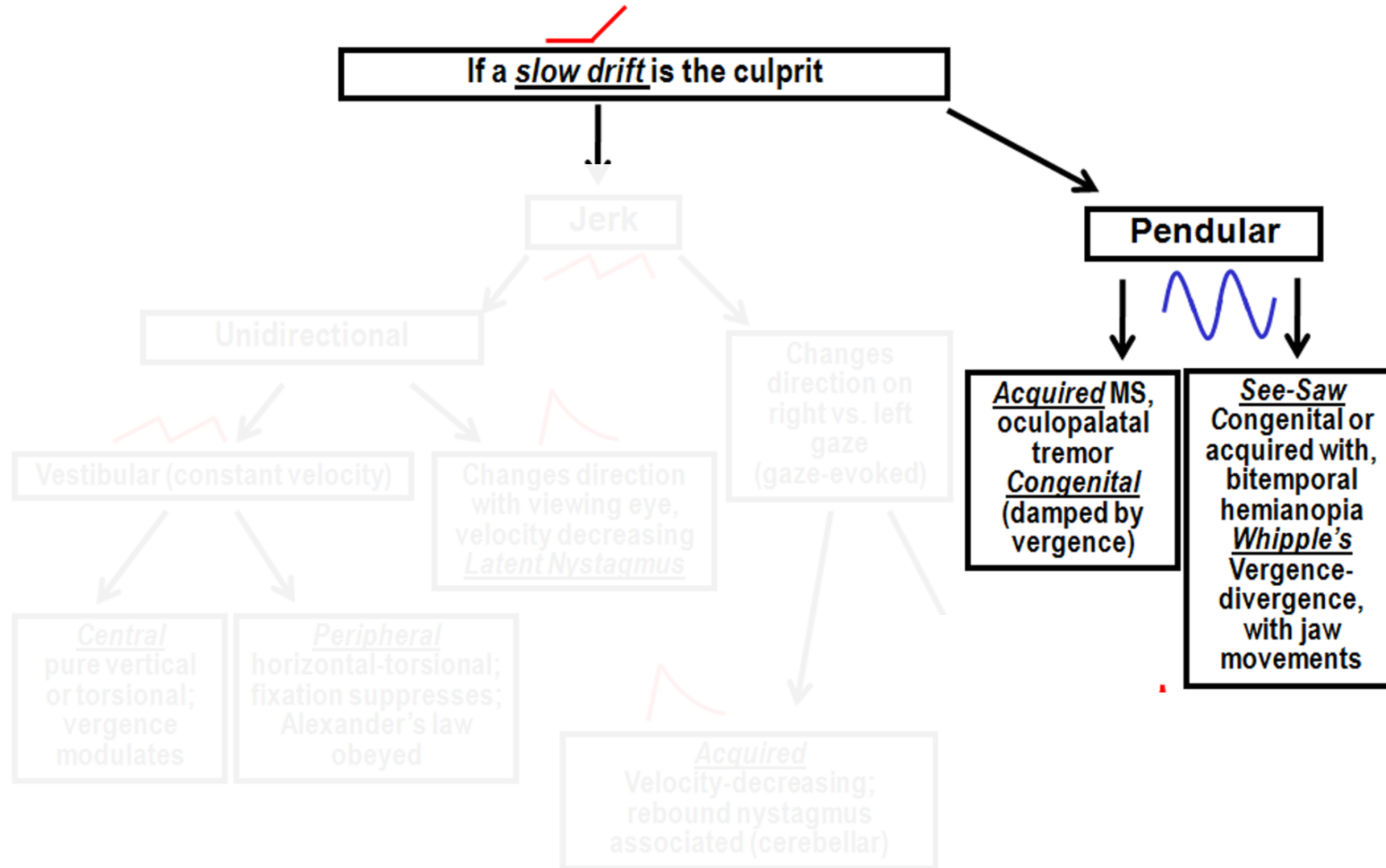
A Flow Chart to Aid Classification of Nystagmus

Is fixation impaired because of a *slow drift*, or an *intrusive saccade*, away from the target?



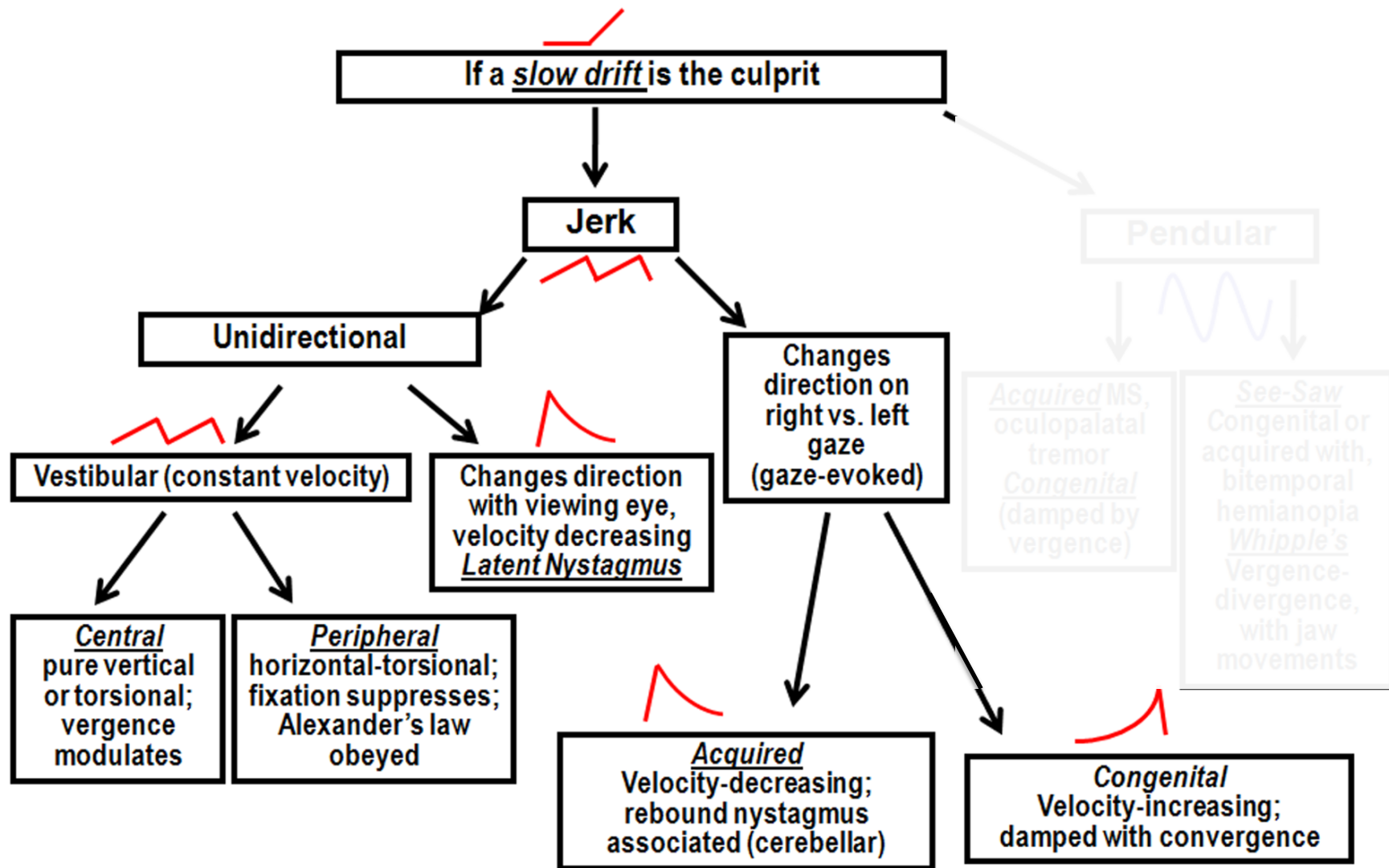
A Flow Chart to Aid Classification of Nystagmus

Is fixation impaired because of a *slow drift*, or an *intrusive saccade*, away from the target?



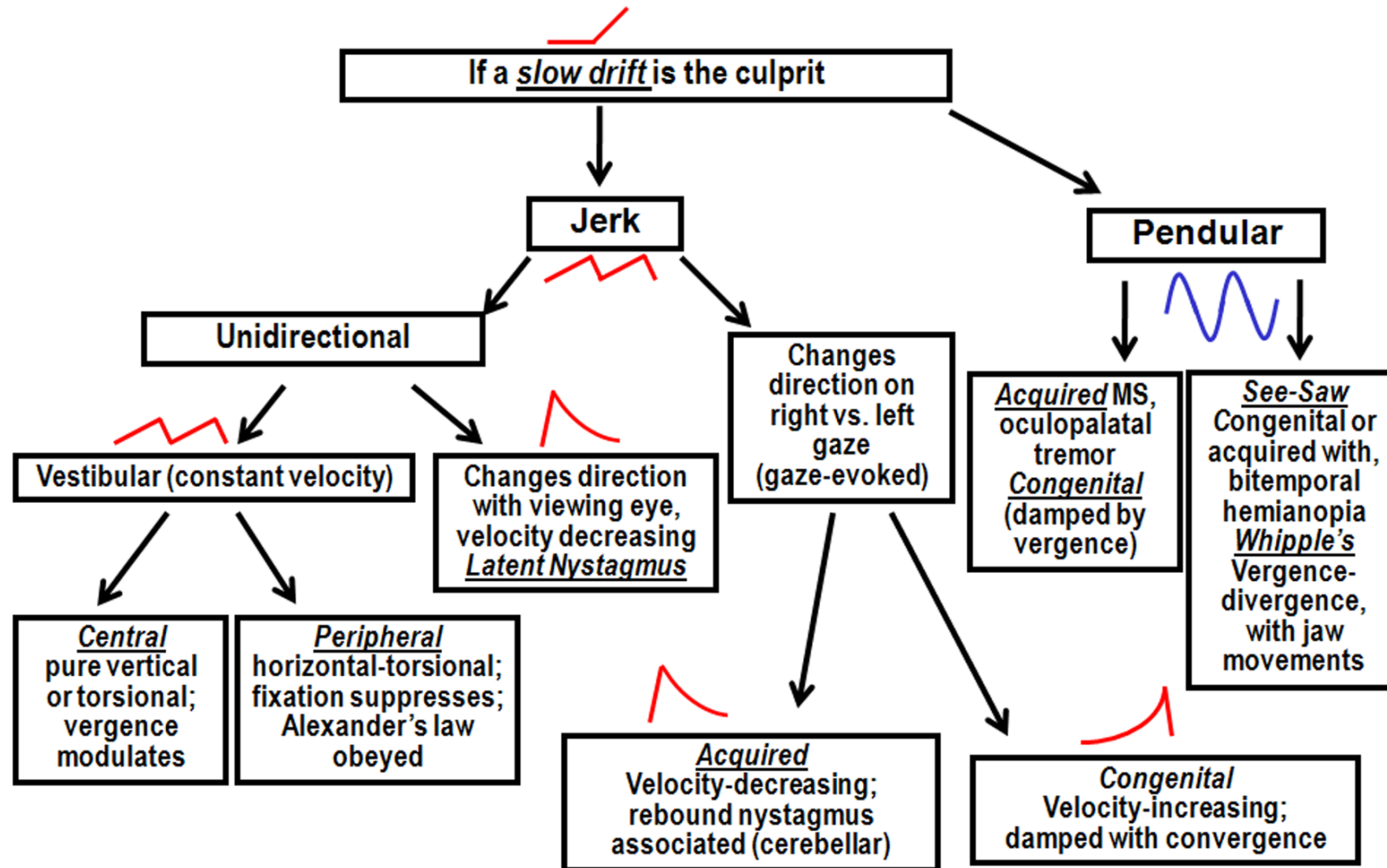
A Flow Chart to Aid Classification of Nystagmus

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A Flow Chart to Aid Classification of Nystagmus

Is fixation impaired because of a *slow drift*, or an *intrusive saccade*, away from the target?

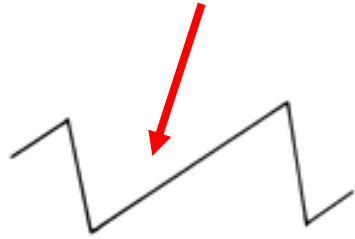


From Leigh and Zee, NEM, 5th edition, 2015

Waveforms of Nystagmus

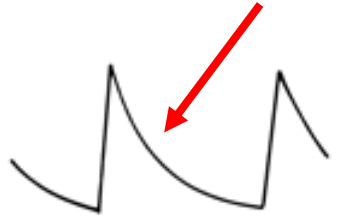
EYE POSITION

A



Jerk or linear
(vestibular)

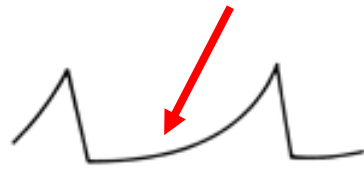
B



Velocity decreasing

- acquired, gaze-evoked
- congenital, latent

C



Velocity increasing

- horizontal, usually congenital
- vertical, usually acquired

D

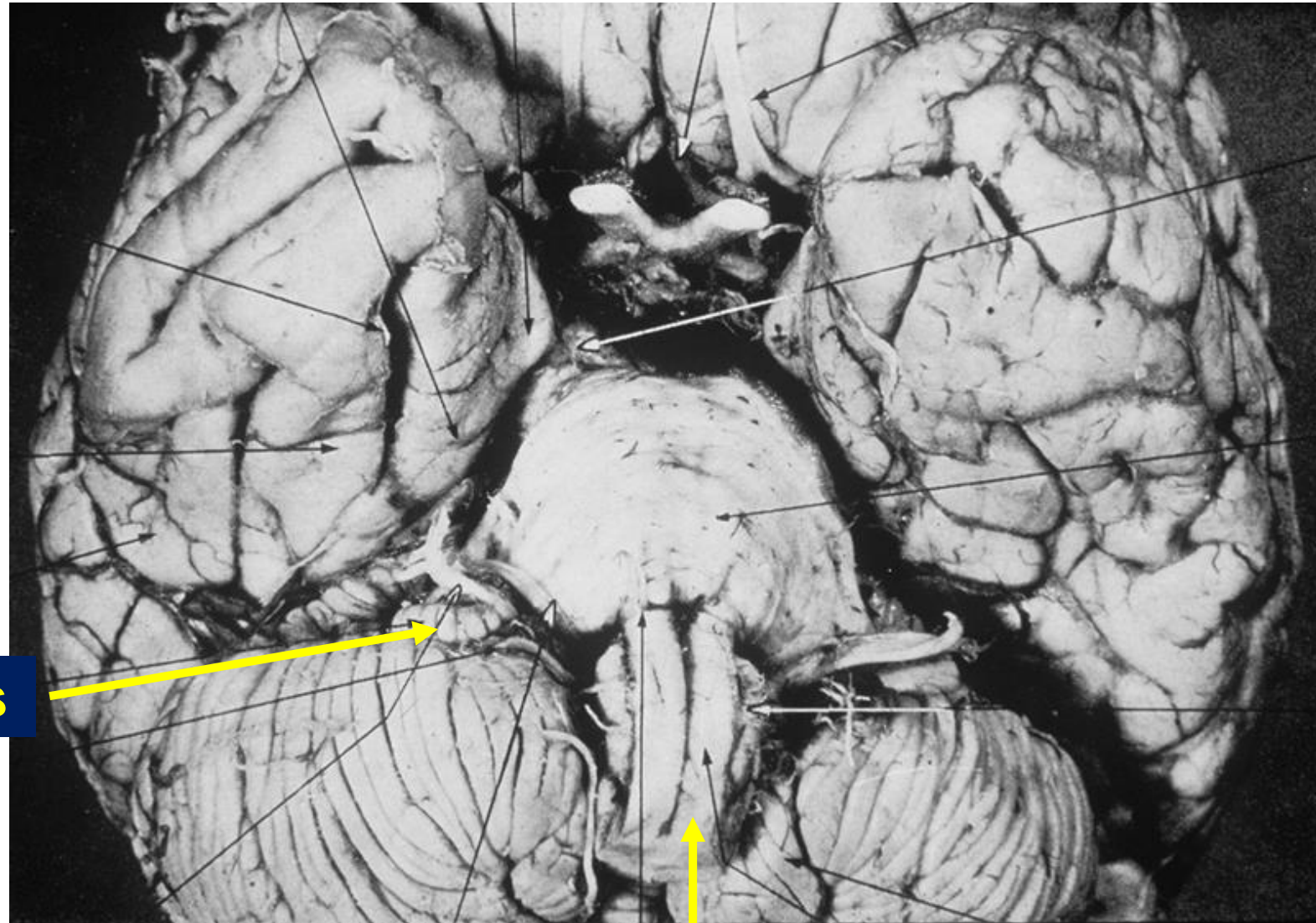


Pendular
(acquired or congenital)

TIME



KEY ANATOMY: GAZE-HOLDING networks in the cerebellum



Flocculus

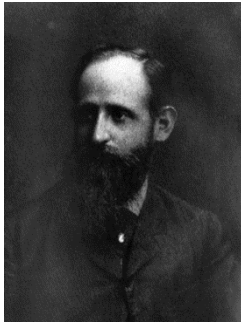
Paraflocculus (Tonsils)



Ewald



Flourens



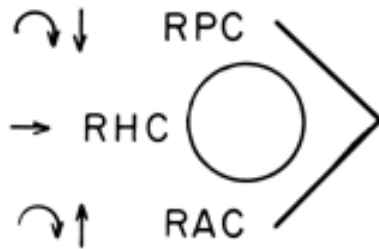
Breuer

KEY PHYSIOLOGY from three 19th Century Giants



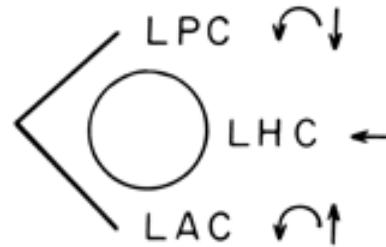
What happens when you stimulate one semicircular canal?

YOU GET NYSTAGMUS: A slow phase, which is the compensatory response to labyrinthine stimulation, and a quick phase, which is the resetting movement.

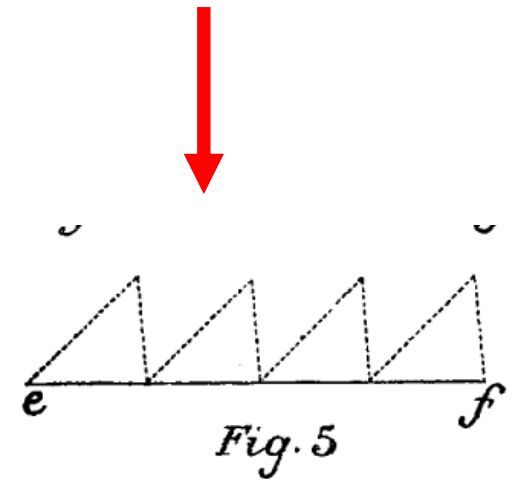


OCCIPUT

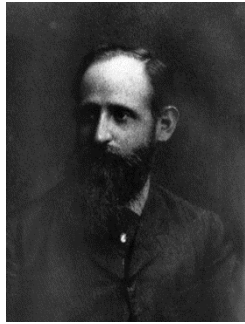
BROW



Arrows indicate direction of slow phase with stimulation



Crum Brown 1878



KEY PHYSIOLOGY from three 19th Century Giants

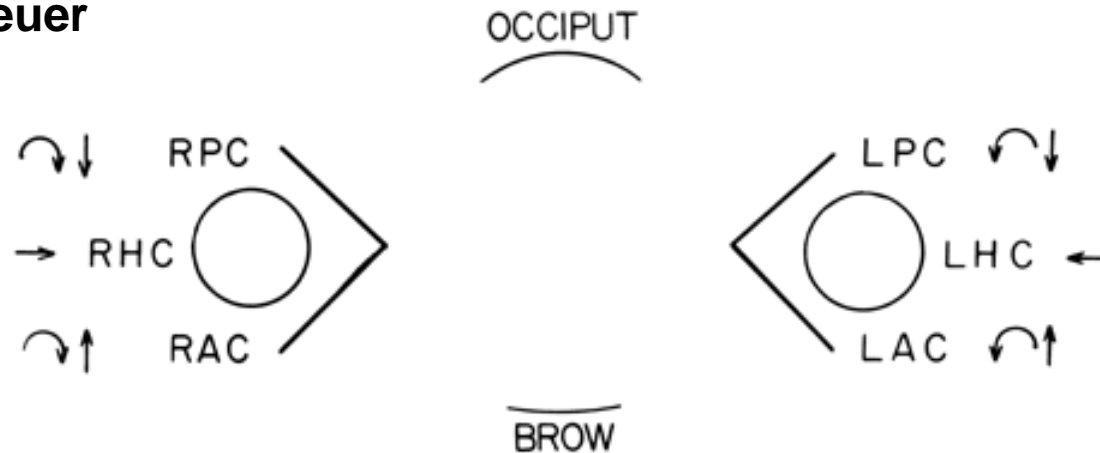


What happens when you stimulate a single semicircular canal?

Ewald

Flourens

Breuer



Arrows indicate direction of slow phase with stimulation

Ewald's First Law: Eyes (head) rotate in a plane parallel to that of head (detected by the SCC in that plane) and so stabilizes gaze (eye-in-space) around all three axes of head rotation.

Ewald's Second Law: The lateral SCC are stimulated better by *ampullopetal* (excitation) than by *ampullofugal* (inhibition) fluid flow.

Ewald's Third Law: The vertical SCC are stimulated better by *ampullofugal* (excitation) than by *ampullopetal* (inhibition) fluid flow.

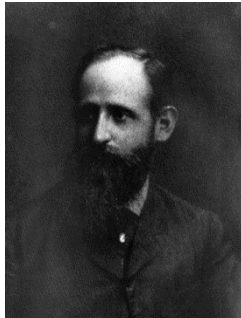
****The excitatory direction of a canal is always when you turn or tilt your head toward that side.**



Ewald



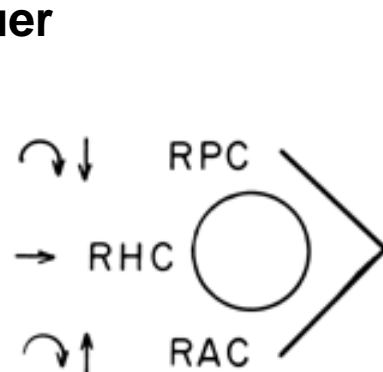
Flourens



Breuer

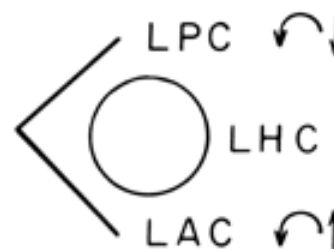
KEY PHYSIOLOGY from three 19th Century Giants

What does this scheme tell the clinician?



OCCIPUT

BROW



Arrows indicate direction of slow phase with stimulation

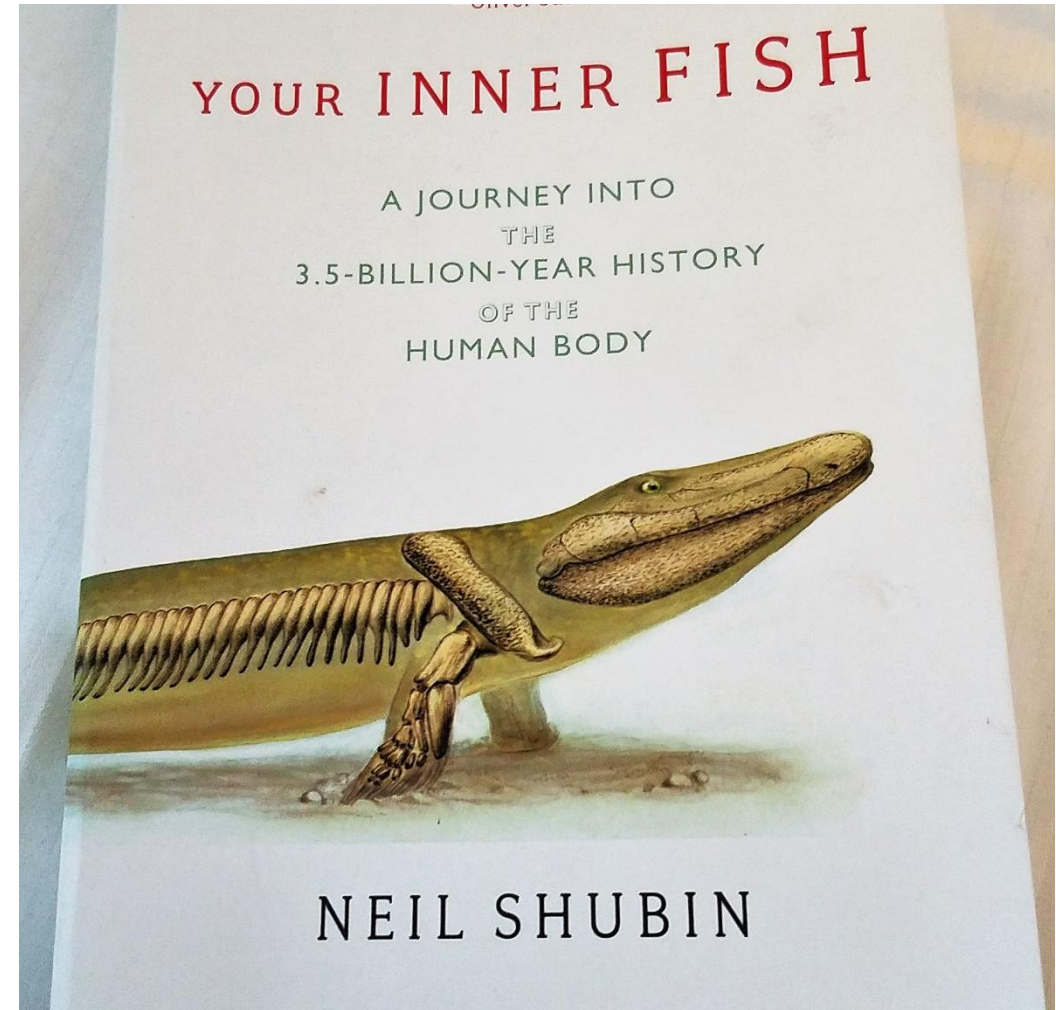
- Pure vertical and pure torsional nystagmus are central signs
- Mixed horizontal-torsional nystagmus is a peripheral sign
- Mixed vertical-torsional nystagmus comes from stimulation of a single vertical SCC and is usually a peripheral sign

**BUT we (and many other predators) are frontal-eyed.
Does the pigeon scheme work for us?**



<https://www.bbc.com/future/article/20141013-why-do-your-eyes-face-forwards>

**Not only is there a pigeon but there is a rabbit
and a fish in all of us!**



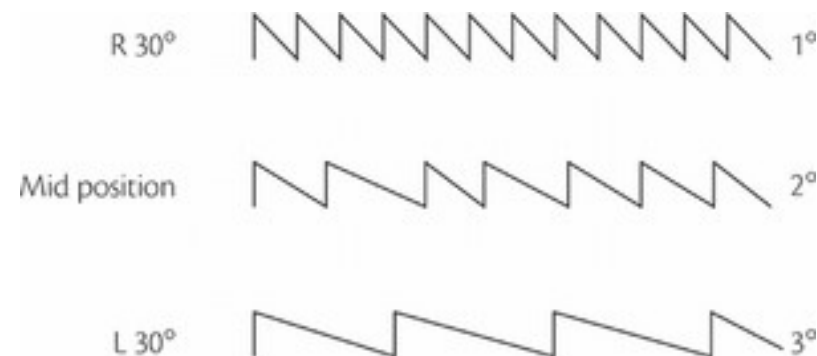
Gustav
Alexander



MORE KEY PHYSIOLOGY from another 19th Century Giant



The effect of gaze on the intensity of a spontaneous nystagmus

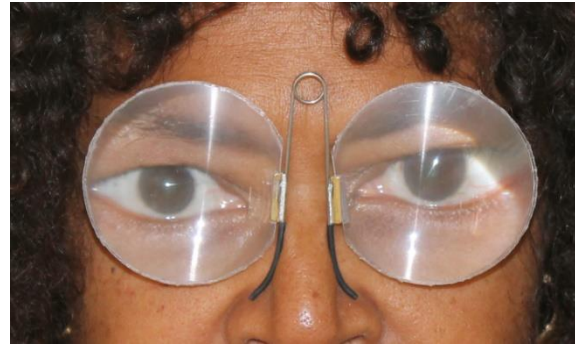
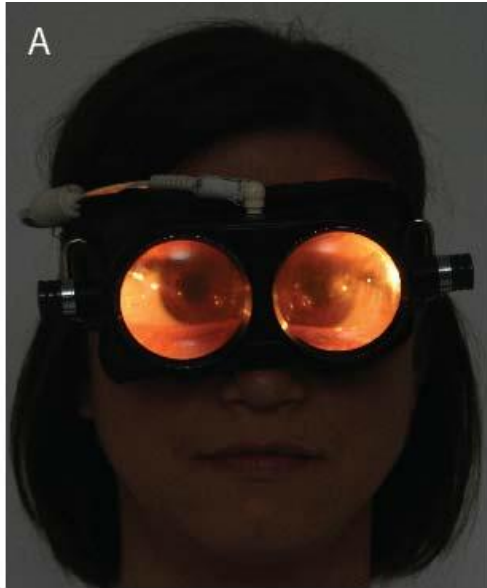


ALEXANDER'S LAW: The intensity of a jerk nystagmus increases when you look in the direction of the quick phase.

CLINICAL LOCALIZATION

- Alexander's law is true for a peripheral vestibular nystagmus but not always for a central vestibular nystagmus.
- If the intensity of a jerk nystagmus increases when you look in the direction of the slow phase (anti-Alexander's law), the localization is central. usually medulla or cerebellum

Look for nystagmus: with and without fixation (clinical dictum: fixation suppression of vestibular nystagmus is impaired in central lesions)

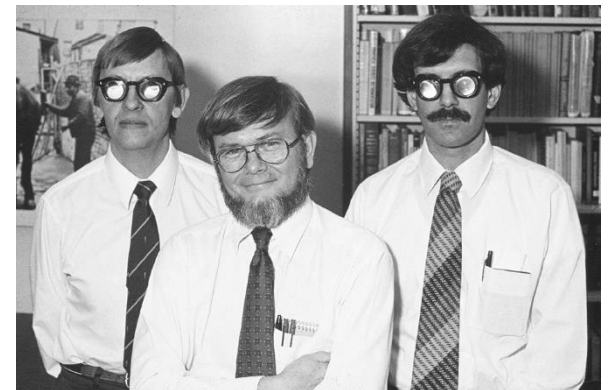


Strupp, Neurology, 2014

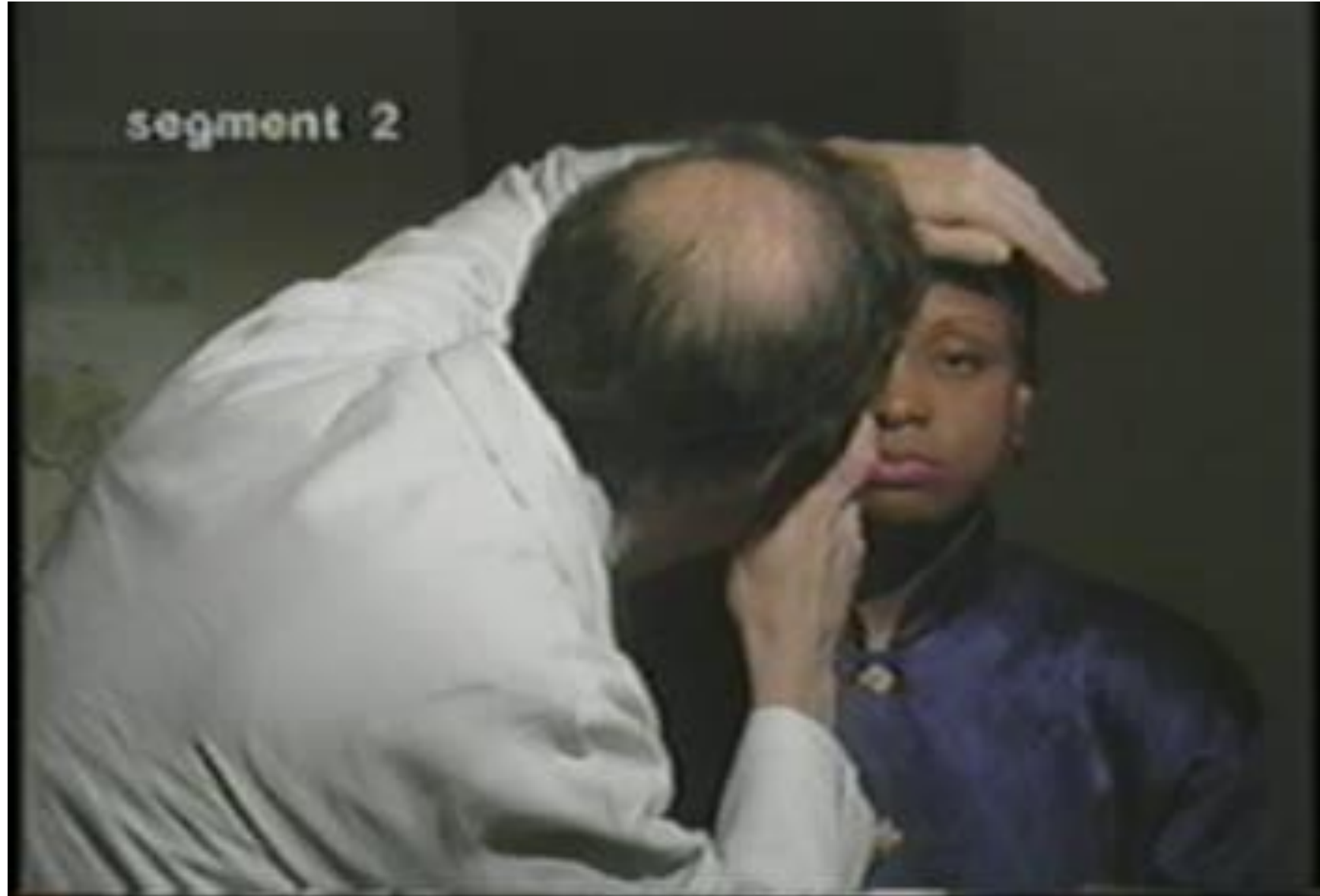


Frenzel goggles, ebay

**Frenzel Lenses (*best used*
with room lights off) to
remove fixation**



Ophthalmoscope and spontaneous nystagmus and other oscillations



Young man develops acute vertigo, nausea, vomiting, imbalance, without hearing symptoms.



- **Peripheral vestibular nystagmus is increased or brought out by removal of fixation**
- **Alexander's Law: Peripheral vestibular nystagmus increases in intensity when looking in the direction of quick phase**

Unidirectional spontaneous nystagmus (vestibular bias) and a gaze-evoked nystagmus (changes direction on left vs. right gaze)

Bruns Nystagmus



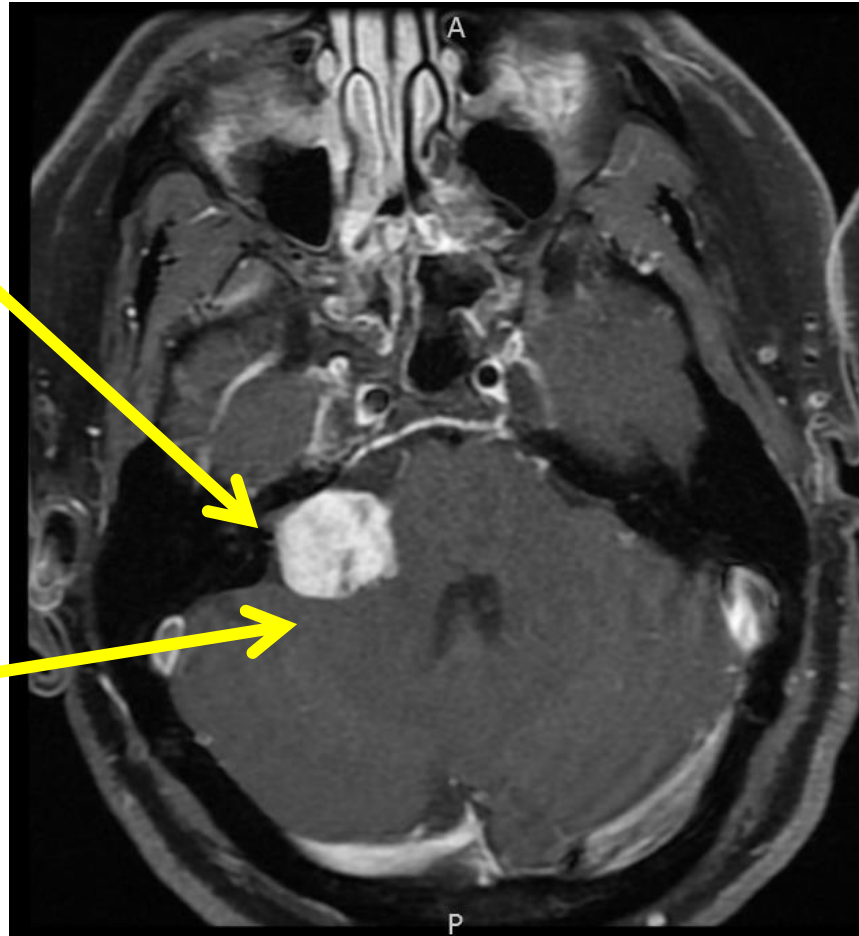
Ludwig Bruns



BRUNS NYSTAGMUS

VIII Nerve lesion causing an *ipsilateral* slow-phase vestibular bias

Cerebellar lesion causing an ipsilateral gaze-holding deficit with *contralateral* slow phases



L

R

This is the same pattern one can see with an AVS (acute vestibular syndrome) due to a CENTRAL lesion

HINTS algorithm for diagnosing posterior fossa stroke

Nystagmus which changes direction with gaze left vs gaze right is CENTRAL



Pointing to a PERIPHERAL lesion

- Nystagmus is increased or brought out by removal of fixation (Romberg sign of VOR)
- Mixed horizontal-torsional pattern is characteristic for complete unilateral loss of function
- Nystagmus intensifies when looking in the quick-phase direction (Alexander's Law)
- Nystagmus obeys Ewald's 1st Law: Eye rotates in a plane parallel to the stimulated canal no matter what the position of the eye in the orbit

(E.g., in Benign Paroxysmal Positional Vertigo (BPPV) of the posterior canal (due to detached otoconia in the canal) the nystagmus is more vertical when looking away from side of the affected labyrinth and more torsional when looking toward the side of the affected labyrinth).



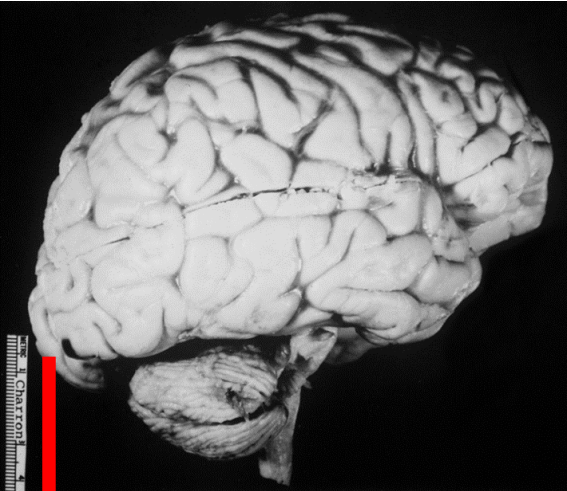
Pointing to a CENTRAL lesion

- Fixation suppression of nystagmus usually impaired
(Caveat: May not be impaired with unilateral brainstem or cerebellar lesions)
- Pure vertical or pure torsional nystagmus, and which remains so on eccentric gaze
- Nystagmus considerably modulated with vergence
- Nystagmus that diminishes when looking in the direction of the quick phase
(anti-Alexander's law)

(Caveat: Nystagmus that obeys Alexander's law or Ewald's 1st Law can be CENTRAL if it involves the central projections of the semicircular canals)

Gaze-holding failure and gaze-evoked nystagmus

(Cerebellar flocculus/paraflocculus(tonsil) are also involved in gaze holding)



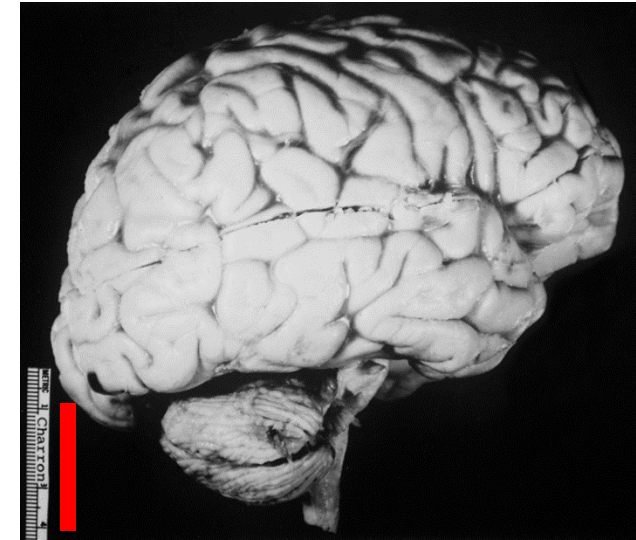
**Cerebellar
atrophy: SCA6**



Pathology and anatomy of cerebellar ocular motor abnormalities



Cranial-cervical junction: Chiari

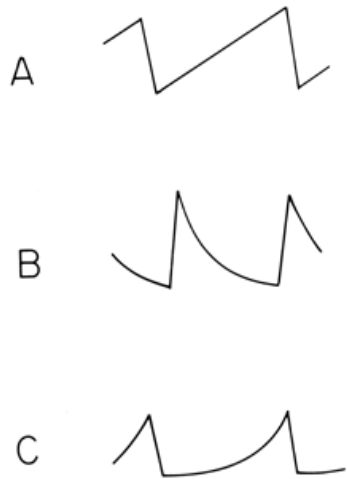


**Cerebellar atrophy:
SCA6**

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

What is the slow-phase waveform?

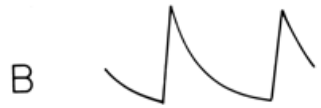
- A. Constant velocity?**
- B. Velocity decreasing?**
- C. Velocity increasing?**



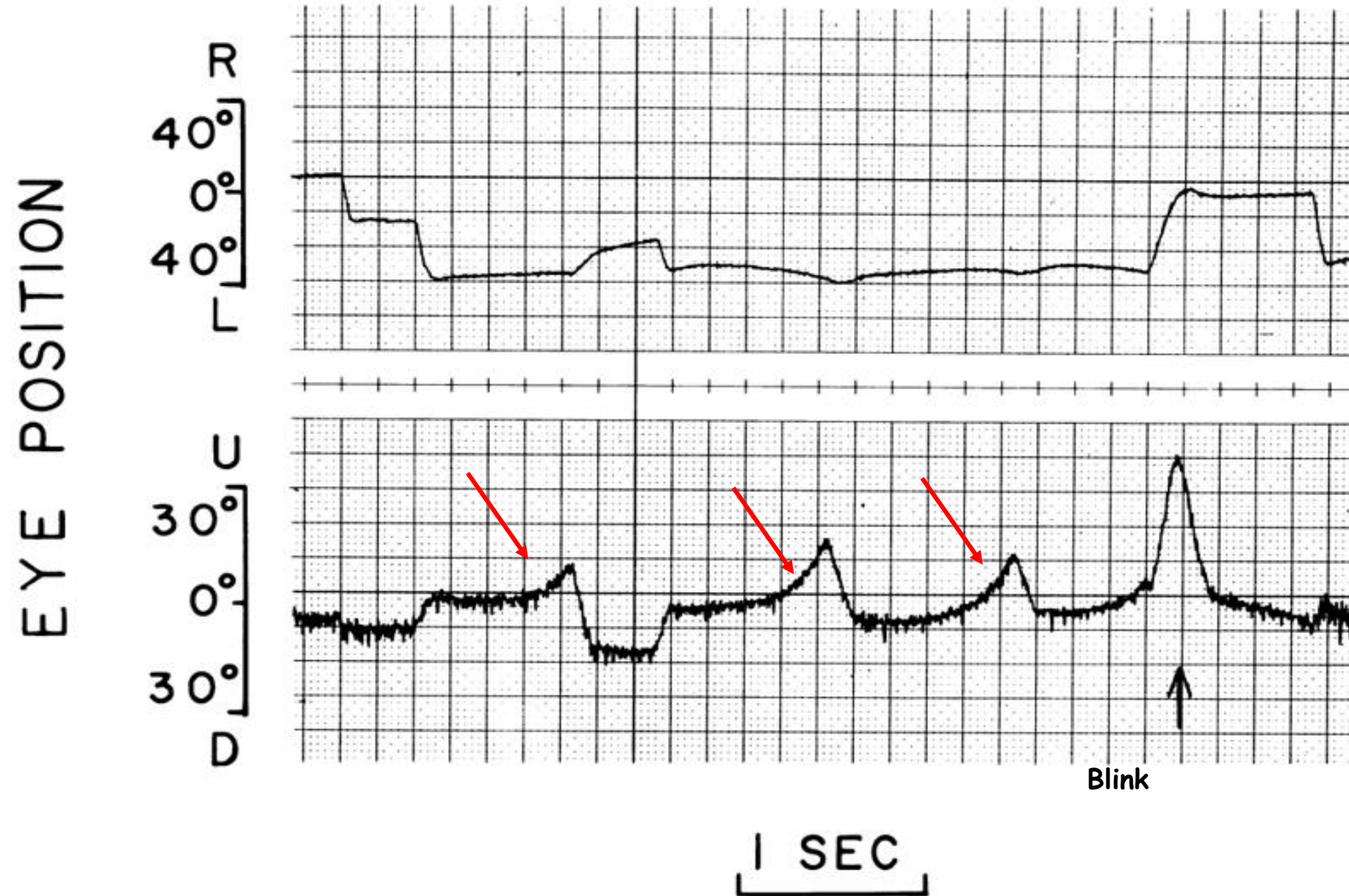
HX: A few months of rapidly progressive ataxia

What is the slow-phase waveform?

- A. Constant velocity?**
- B. Velocity decreasing?**
- C. Velocity increasing?**



Velocity-increasing slow phase



Velocity-increasing slow phase

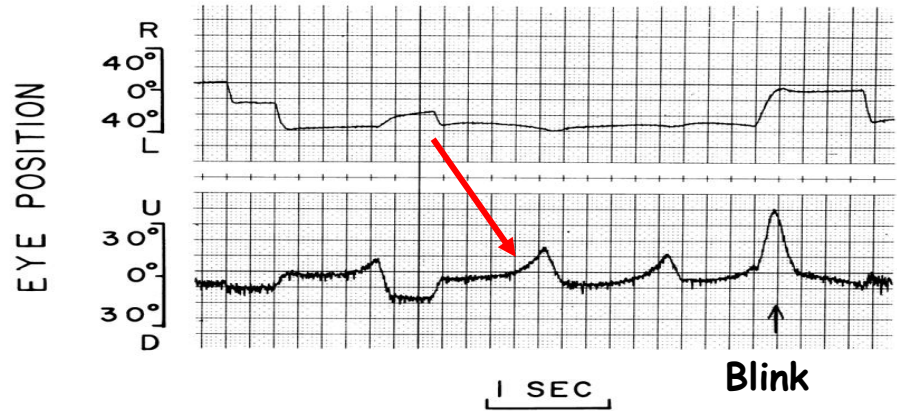


HX: A few months of rapidly progressive ataxia, normal MRI, negative FH

AND THE DIAGNOSIS IS?

- 1. Alcoholic cerebellar degeneration**
- 2. Nutritional (B1, B12) cerebellar degeneration**
- 3. Paraneoplastic degeneration**
- 4. Late-onset cerebellar degeneration (LOCA)**
- 5. Anticonvulsant intoxication**

Velocity-increasing slow phase



HX: A few months of rapidly progressive ataxia, normal MRI, negative FH

AND THE DIAGNOSIS IS?

1. Alcoholic cerebellar degeneration
2. Nutritional (B1, B12) cerebellar degeneration
3. **PARANEOPLASTIC DEGENERATION**
4. Late-onset cerebellar degeneration (LOCA)
5. Anticonvulsant intoxication

Velocity-increasing slow phase



HX: A few months of rapidly progressive ataxia, normal MRI, negative FH

AND THE DIAGNOSIS IS?

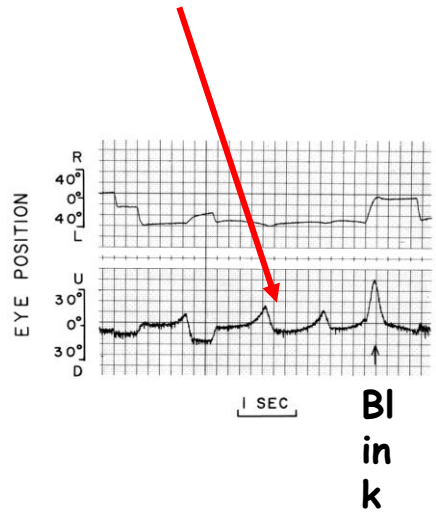
PARANEOPLASTIC DEGENERATION

OVARIAN CARCINOMA, ANTI –YO

PEARLS



Velocity-increasing
slow phase



- Velocity-increasing slow phases implies gaze-holding networks (neural integrators) are unstable.
- If unstable, DB Nystagmus intensifies in up-gaze or UB Nystagmus intensifies in down-gaze (anti-Alexander's Law)

(Recall Alexander's law; nystagmus intensity increases when looking in direction of the quick phase (e.g., peripheral vestibular nystagmus)).
- Velocity-increasing slow phases occur in acquired lower-brainstem (e.g., B1 deficiency in Wernicke's encephalopathy) or in cerebellar floccular lesions.
- Velocity-increasing slow phases are often a feature of CONGENITAL NYSTAGMUS (usually horizontal).

**Young woman, pregnant, incessant vomiting, imbalance
and gaze-evoked nystagmus**



POSSIBLE DIAGNOSES?

- 1 Labyrinthitis**
- 2 Brainstem stroke**
- 3 B12 deficiency**
- 4 Onset cerebellar degeneration**
- 5 B1 deficiency**
- 6 Acute attack MS**
- 7 Area Postrema Syndrome NMO**

Young woman, pregnant, incessant vomiting, imbalance
and gaze-evoked nystagmus



POSSIBLE DIAGNOSES?

- 1 Labyrinthitis
- 2 Brainstem stroke
- 3 B12 deficiency
- 4 Onset cerebellar degeneration
- 5 **B1 DEFICIENCY**
- 6 Acute attack MS
- 7 Area Postrema Syndrome NMO

**Vitamin B1 (Thiamine) deficiency (Wernicke's encephalopathy)
in a patient with hyperemesis gravidarum**



Wernicke's Disease – Upbeat Nystagmus

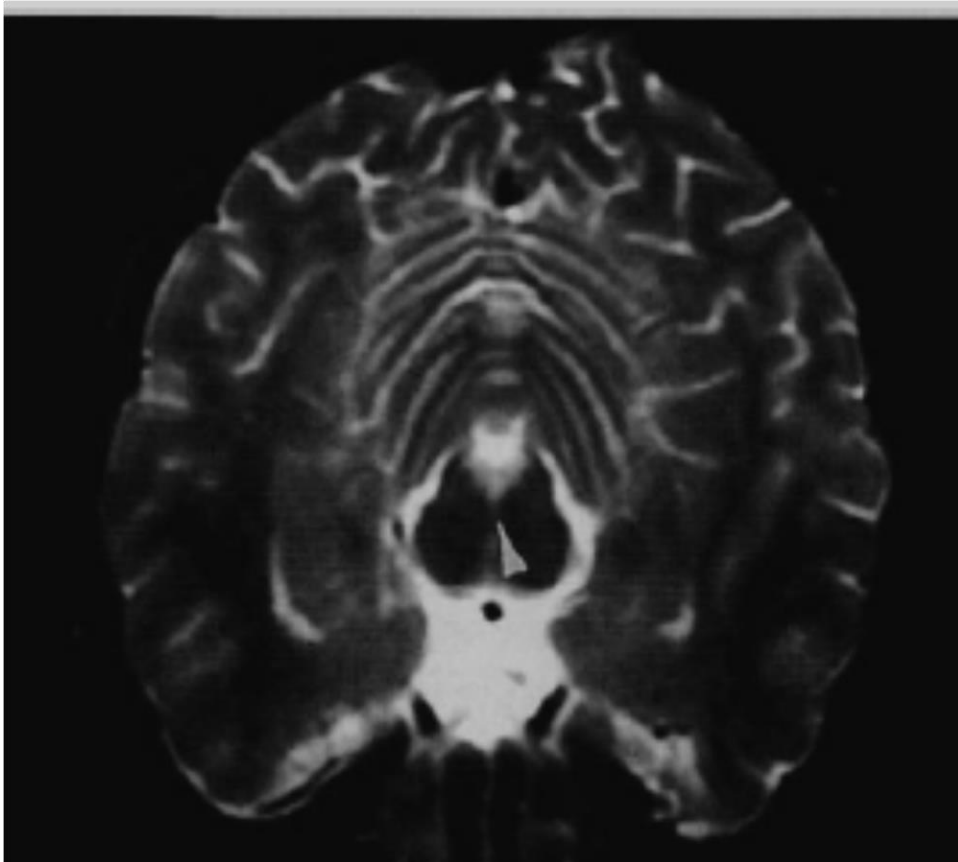


**ANOTHER KEY FEATURE OF Wernicke's Encephalopathy –
Absent horizontal (spared vertical) VOR slow phases**

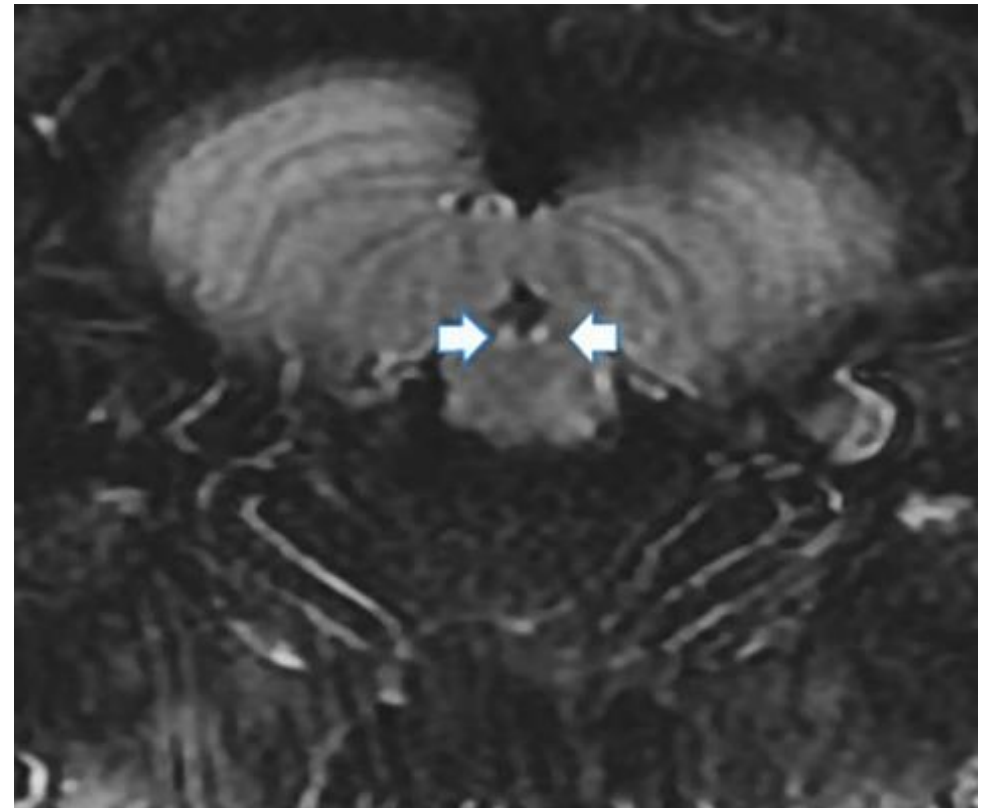


WERNICKE'S ENCEPHALOPATHY

Lesions in the medial vestibular nuclei (MVN) and nucleus prepositus hypoglossi (NPH), part of the horizontal gaze-holding network AND mediates horizontal VOR

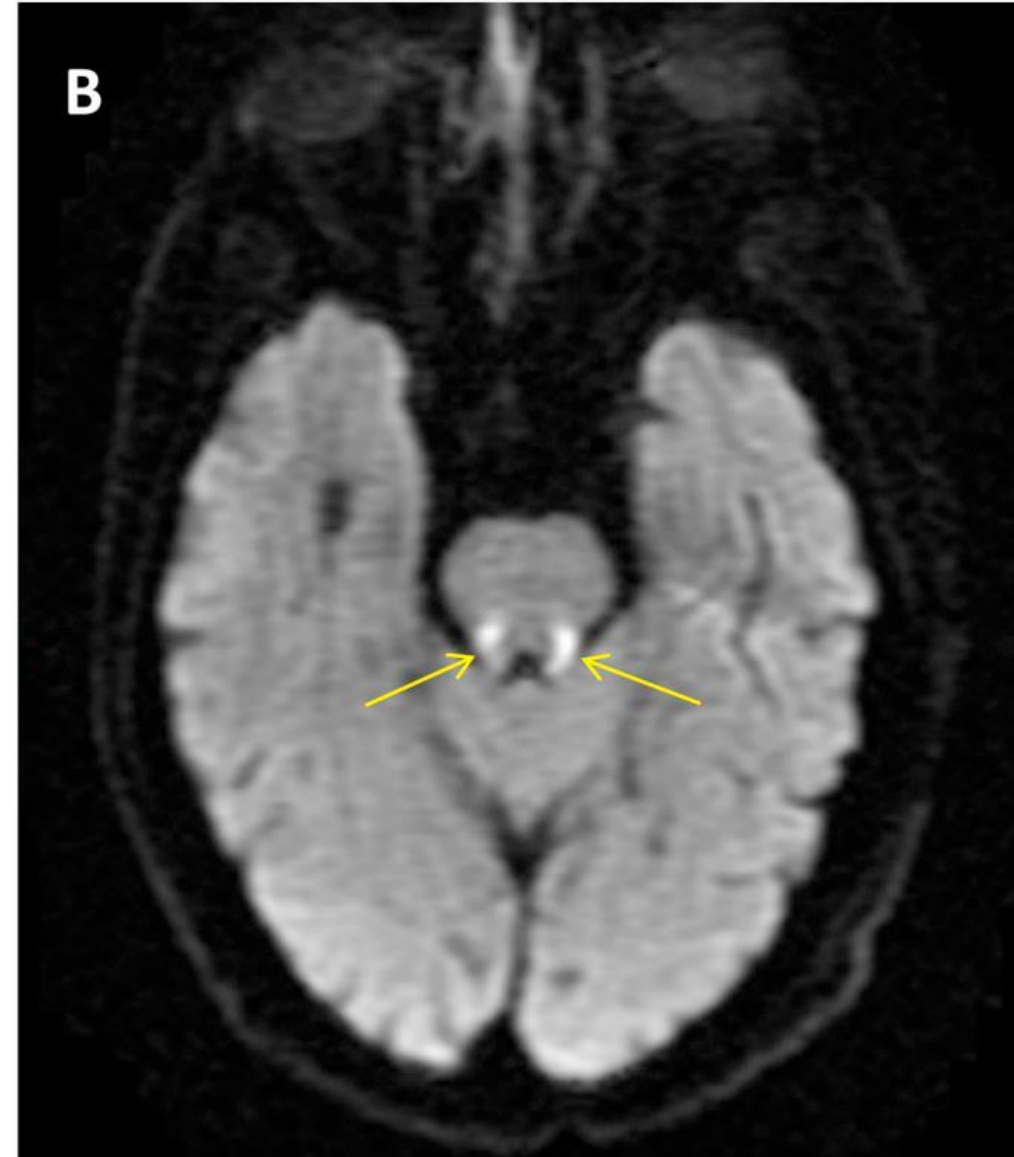
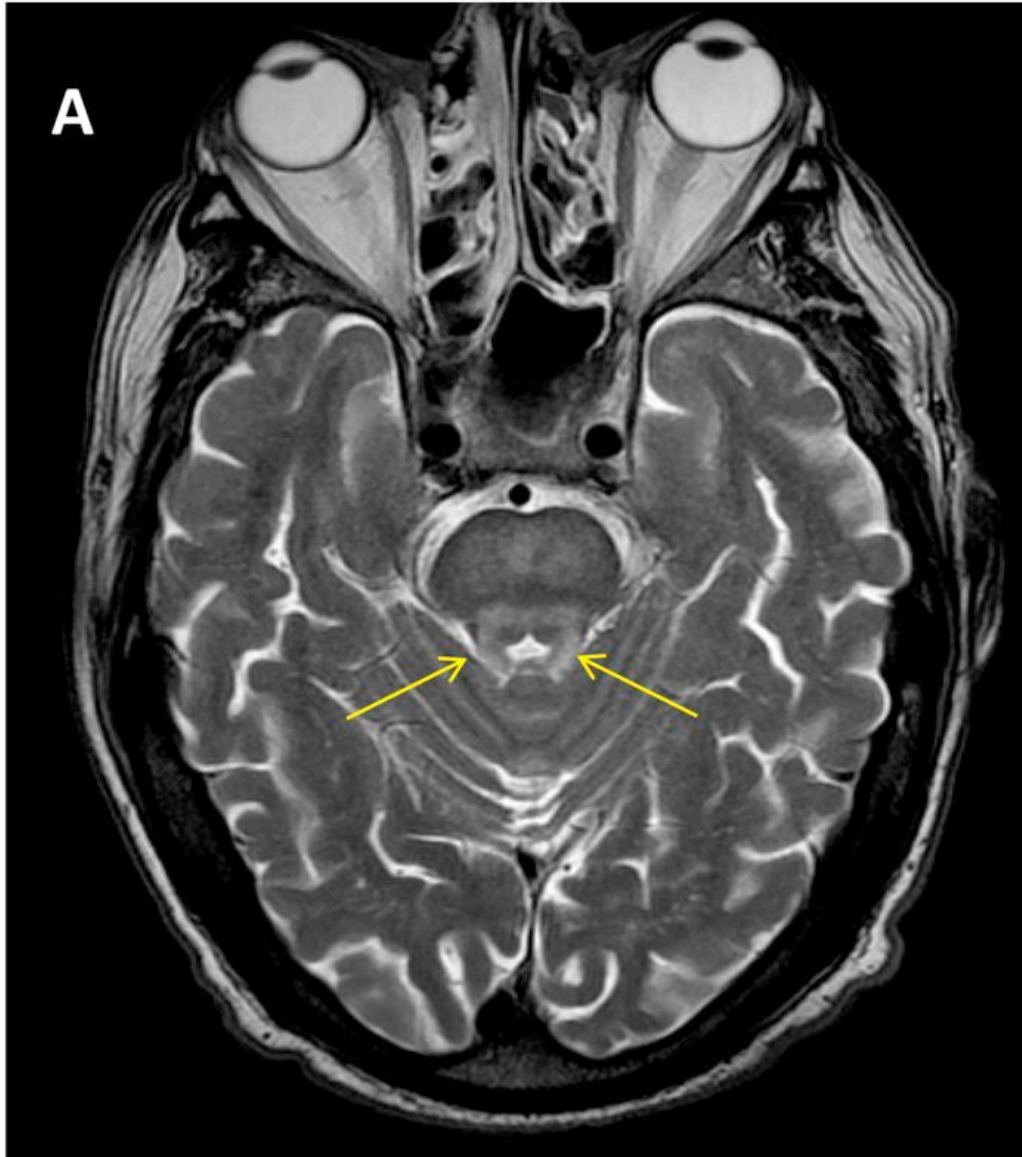


Ming, 1998



Kattah 2017

Dracula's teeth (superior cerebellar peduncle) in Wernicke's Encephalopathy



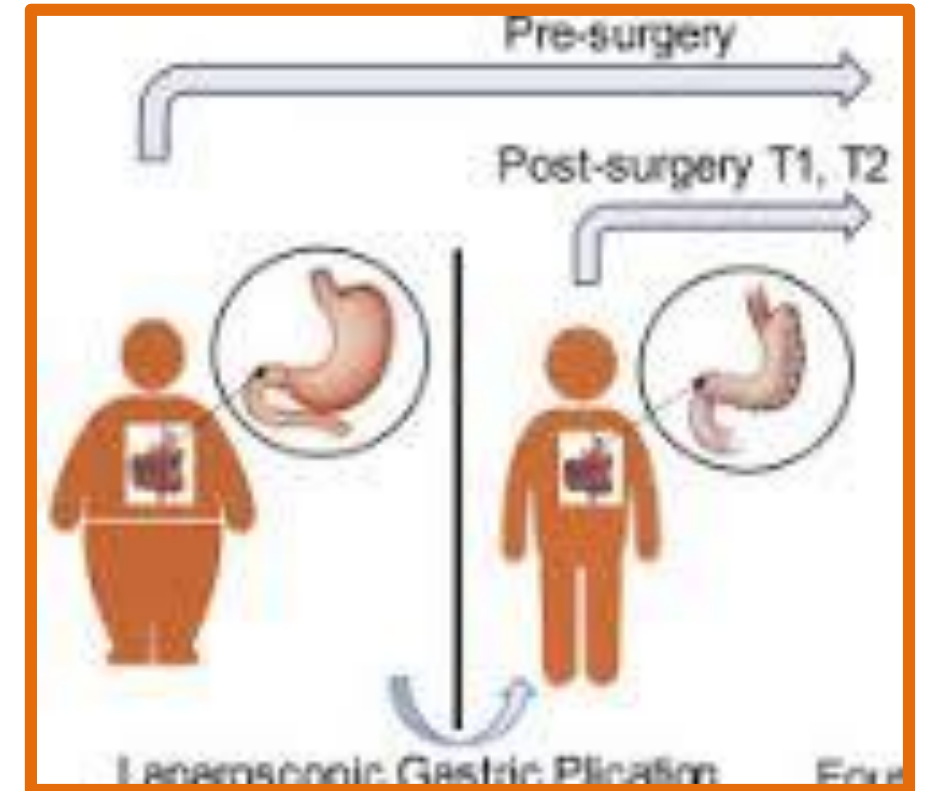
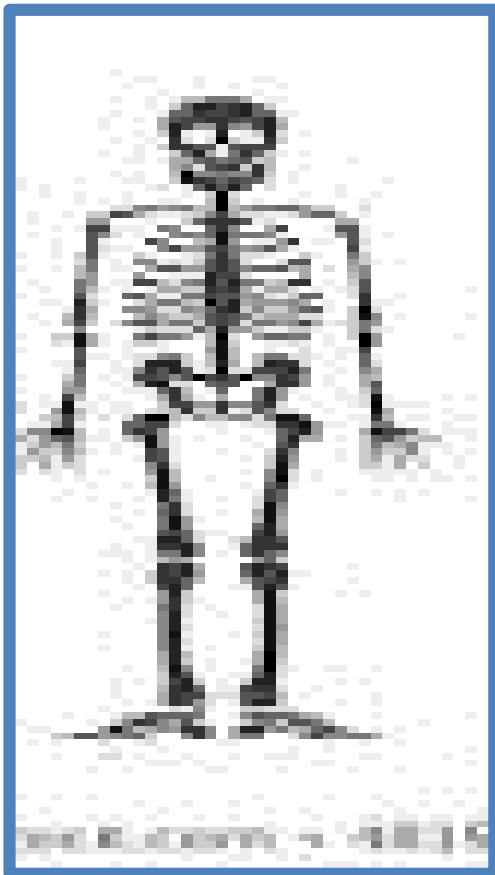
Wernicke's Disease: **AN ABSOLUTE EMERGENCY**

- Wernicke's syndrome can show ophthalmoplegia, nystagmus of virtually any type (horizontal, vertical), gaze palsies and internuclear ophthalmoplegia
- B1 deficiency occurs in the setting of MALNUTRITION
 - alcoholism
 - eating disorders (bulimia, anorexia nervosa, bizarre diets)
 - excess vomiting (hyperemesis gravidarum, chemotherapy),
 - B1 deficient formula
 - post gastric diversion
 - social isolation
 - precipitated by a glucose load
- Treat with IV 500mg B1, Magnesium if necessary.



WERNICKE'S ENCEPHALOPATHY

THINK NUTRITION AND VITAMINS!



Upbeat nystagmus in Multiple Sclerosis

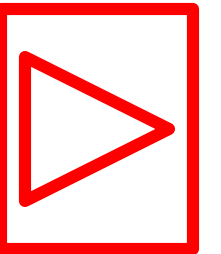


Medulla

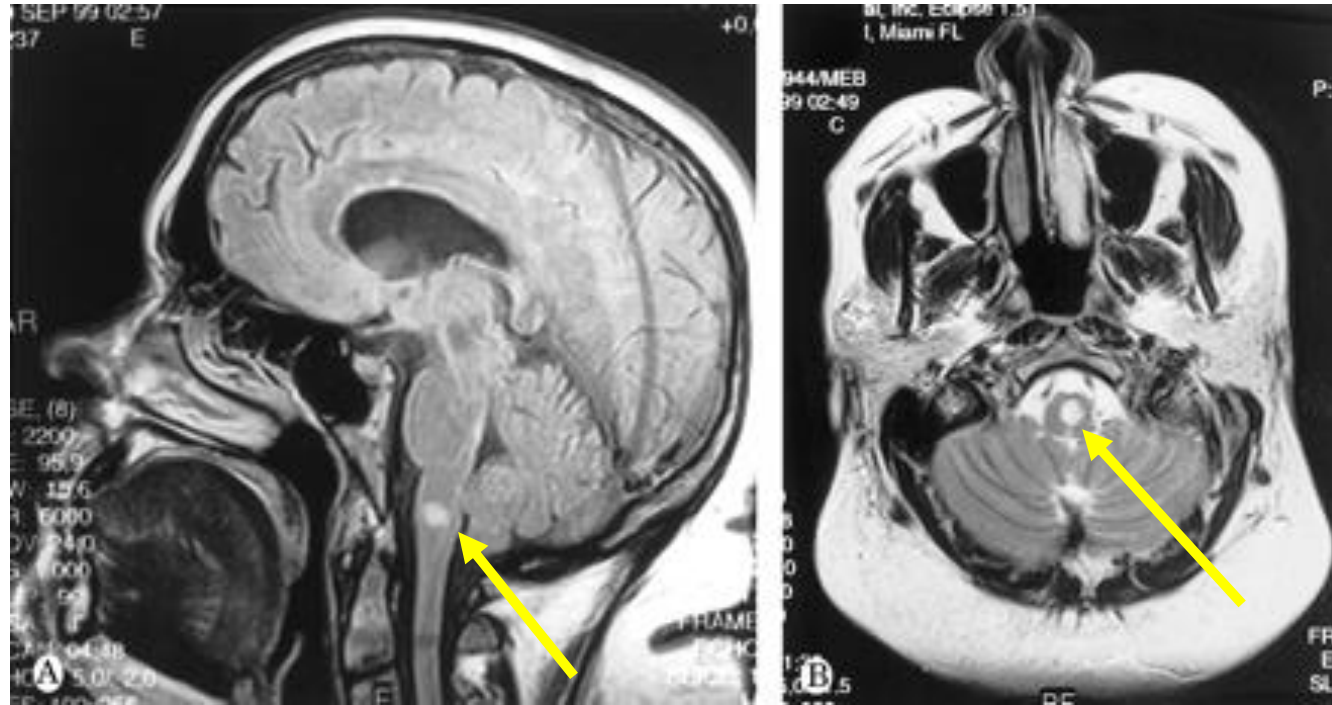
Where is the lesion??



Upbeat nystagmus: effect of convergence



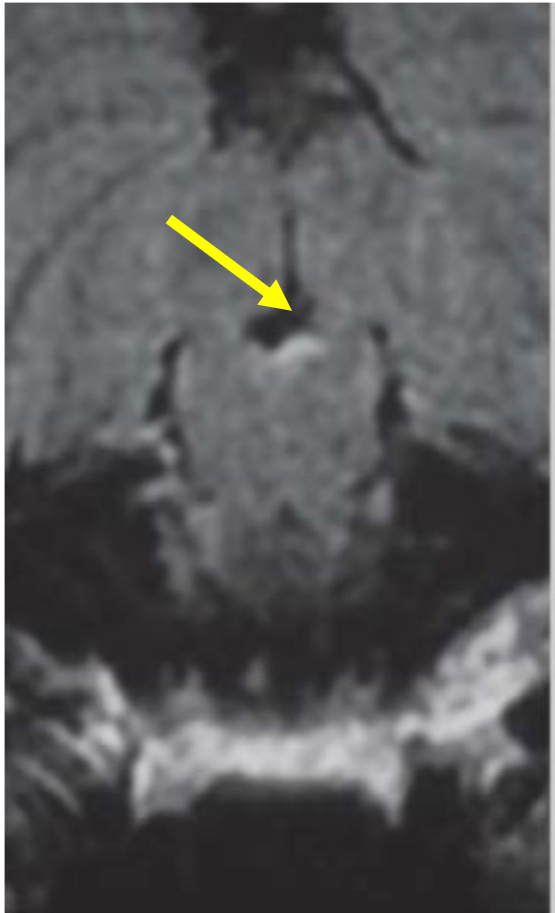
Upbeat nystagmus and the nucleus intercalatus and nucleus of Roller (perihypoglossal nuclei) in the MEDULLA.



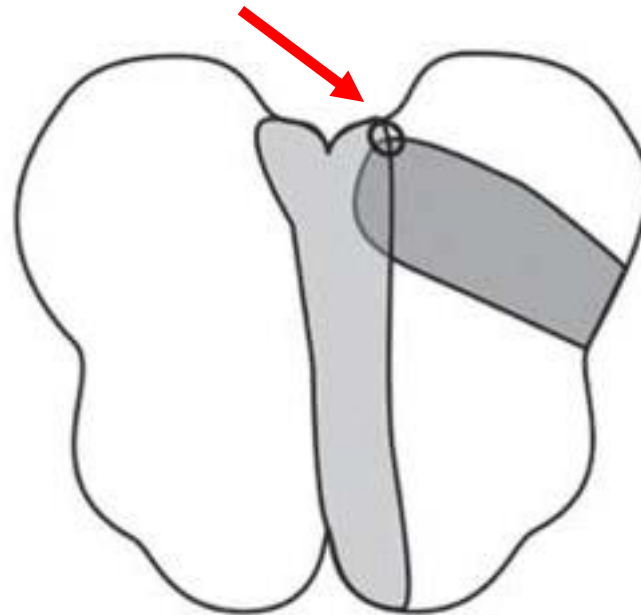
Minagar et al. Neurology 2001

Pierrot-Deseilligny and Milea, 2005

Upbeat Nystagmus with lesion in the nucleus intercalatus (Staderini) in the medial medulla underneath the floor of the IV ventricle



(Saito, 2010 Arch Neurol)



Olszewski-Baxter, 2014

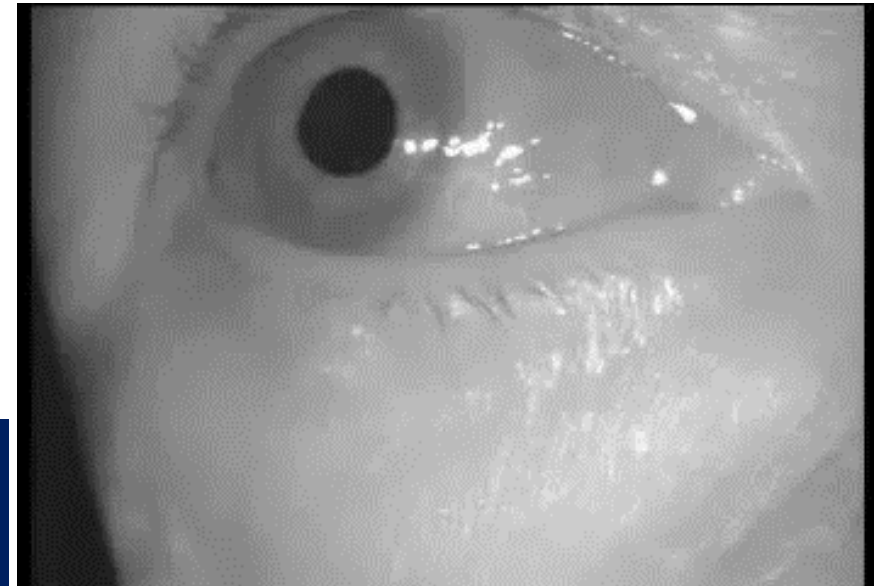
SOME FEATURES OF CENTRAL NYSTAGMUS

- Spontaneous UPBEAT nystagmus is often damped or converted to DOWNBEAT nystagmus with convergence
- Spontaneous DOWNBEAT nystagmus is often enhanced with convergence.
- Large changes in amplitude or direction of VERTICAL nystagmus with convergence or with changes in the horizontal line of sight probably reflect abnormal modulation based on the requirements for the translational VOR (tVOR). The tVOR depends on where the fovea points.
- Congenital horizontal nystagmus remains horizontal on up and down gaze and is usually suppressed with convergence.

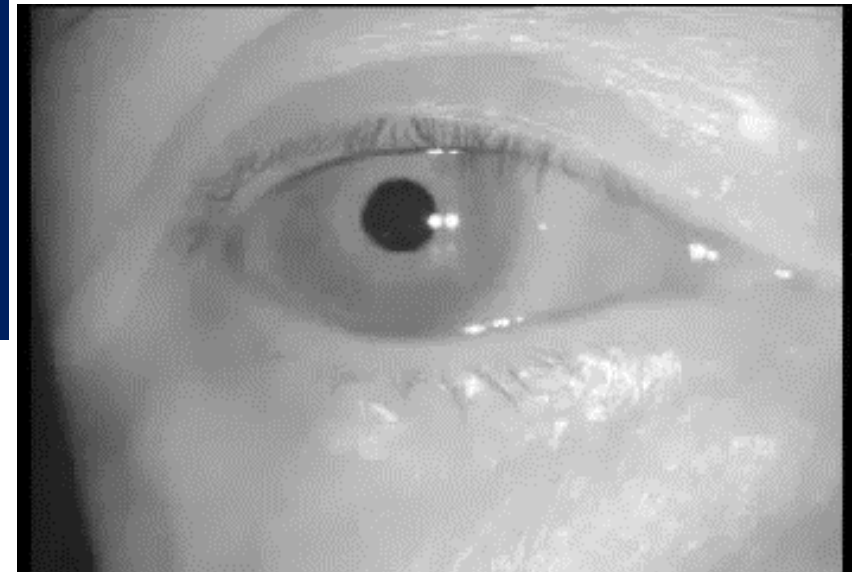
Drug Treatments

- 4-aminopyridine (ampyra) (Compounding Pharmacy)
- NOTE may stop downbeat nystagmus and also lessen gaze-evoked and upbeat nystagmus, improve pursuit and balance

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



Downbeat_Before34DAP

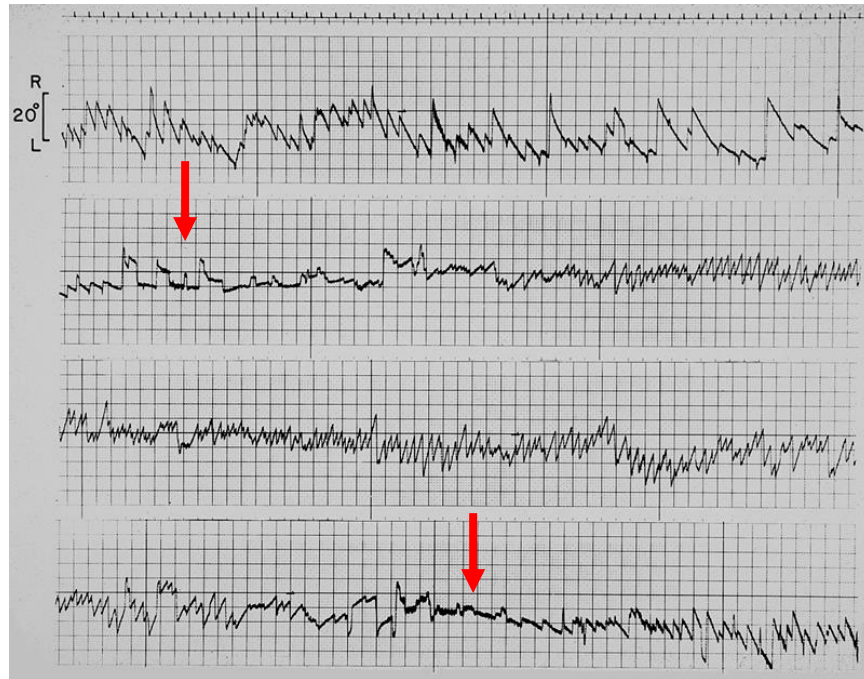


Downbeat_After34DAP



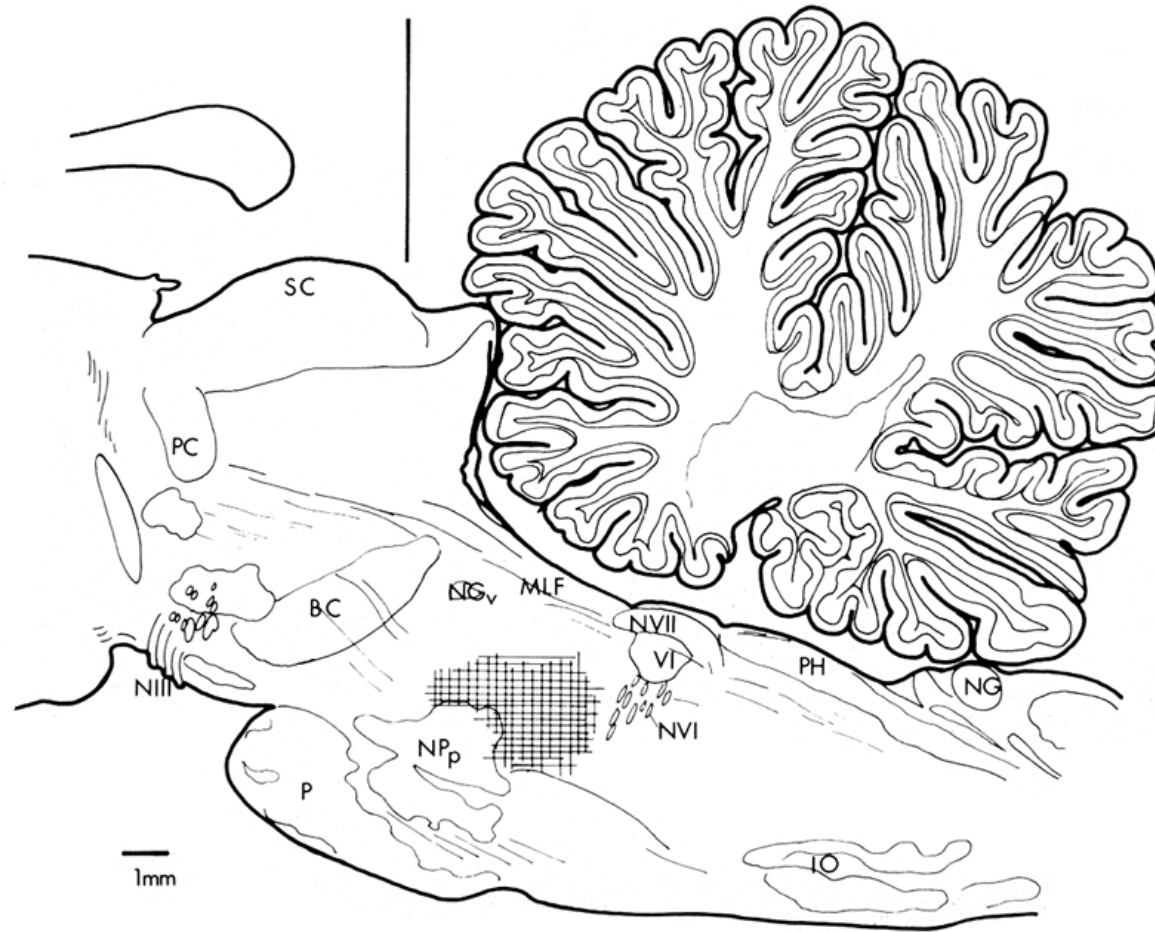
WHAT IS THIS CALLED??

Periodic Alternating Nystagmus (PAN)



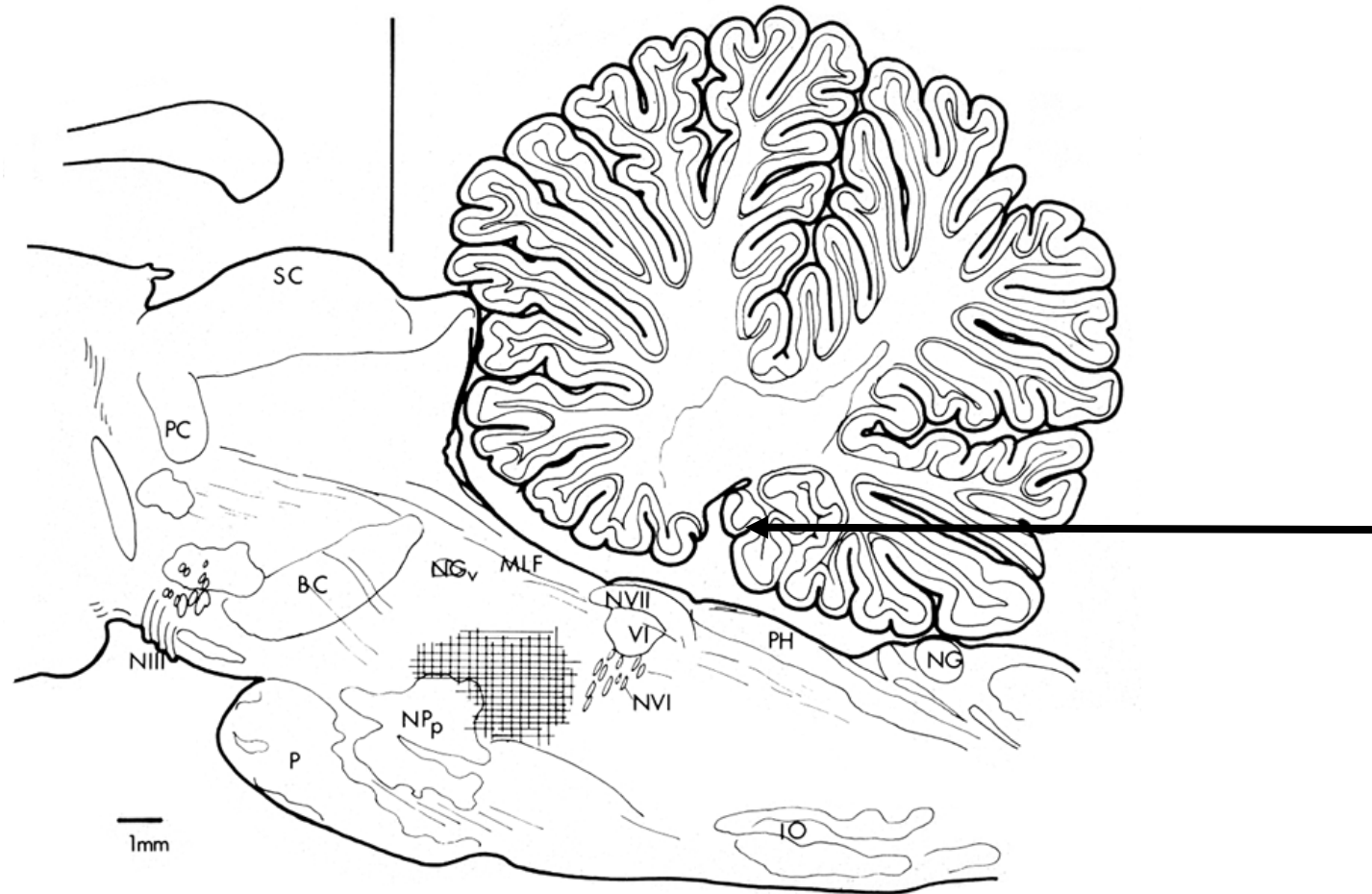
Null every two minutes

Anatomical Locus of Period Alternating Nystagmus (PAN)?



1. Flocculus
2. Tonsil
3. Dorsal vermis
4. Nodulus
5. Medial vestibular nucleus

Anatomical Locus of Period Alternating Nystagmus (PAN)



1. Flocculus
2. Tonsil
3. Dorsal vermis
4. NODULUS
5. Medial vestibular nucleus

PAN: Treatment

- **Baclofen (GABA-b)** provides the missing inhibition and stops the nystagmus.
 - Usually need only 10 mg PO TID.
 - Avoid precipitous discontinuation.
 - May work synergistically with memantine
 - Baclofen does not work as well in congenital PAN.

Treatment of Periodic Alternating Nystagmus

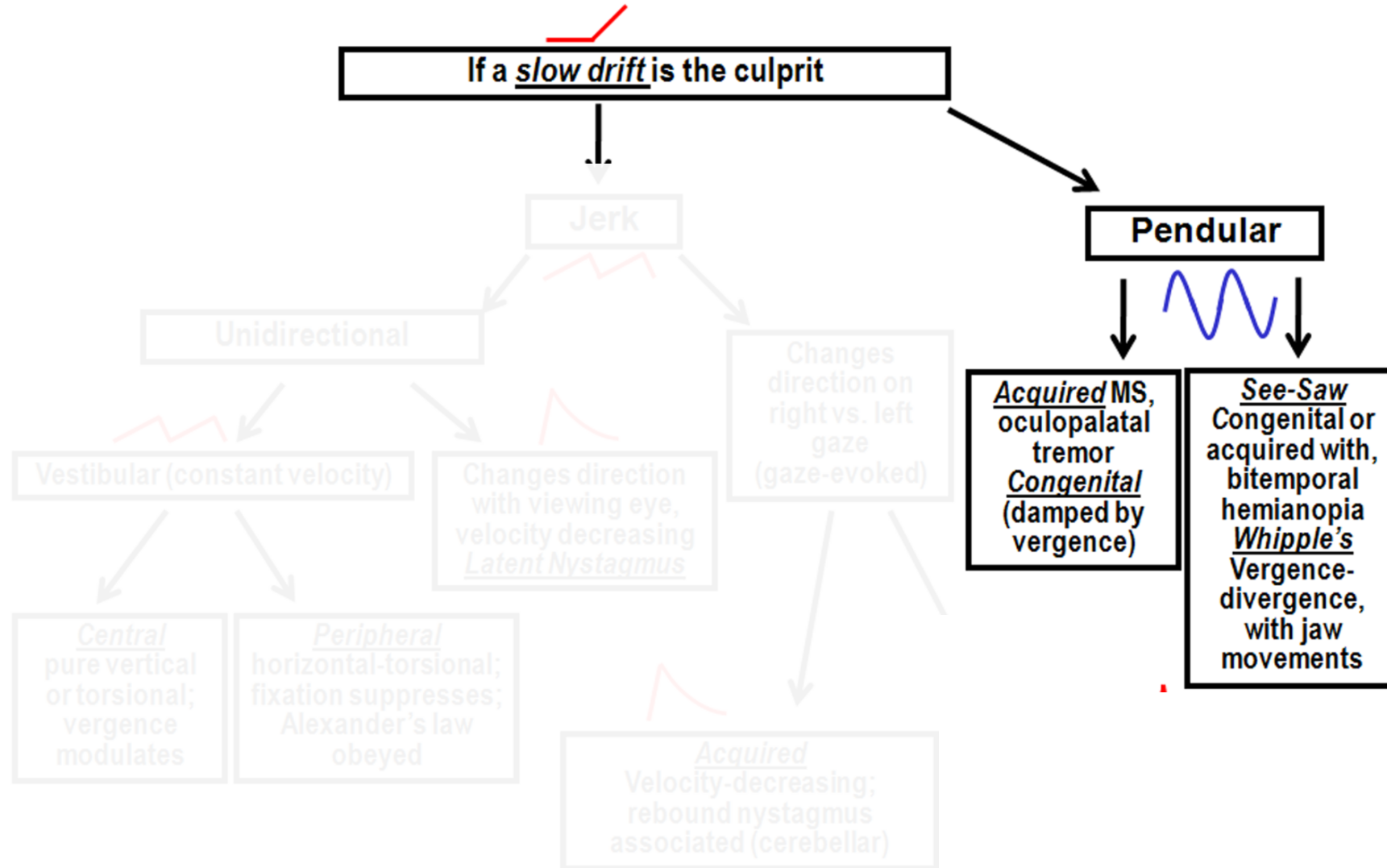
G. Michael Halmagyi, MB, Peter Rudge, MRCP, Michael A. Gresty, PhD,
R. John Leigh, MD, and David S. Zee, MD

Two patients with longstanding acquired periodic alternating nystagmus (PAN) were treated with baclofen, 30 mg/day. Baclofen abolished the PAN and relieved oscillopsia in both patients but was ineffective in another patient with congenital PAN.

Halmagyi GM, Rudge P, Gresty MA, et al: Treatment of periodic alternating nystagmus.
Ann Neurol 8:609–611, 1980

A Flow Chart to Aid Classification of Nystagmus

Is fixation impaired because of a *slow drift*, or an *intrusive saccade*, away from the target?



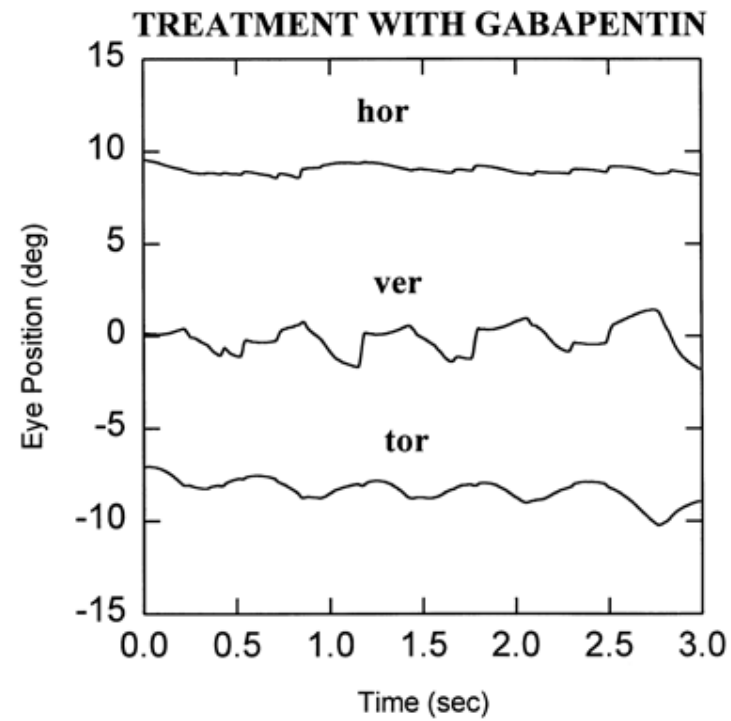
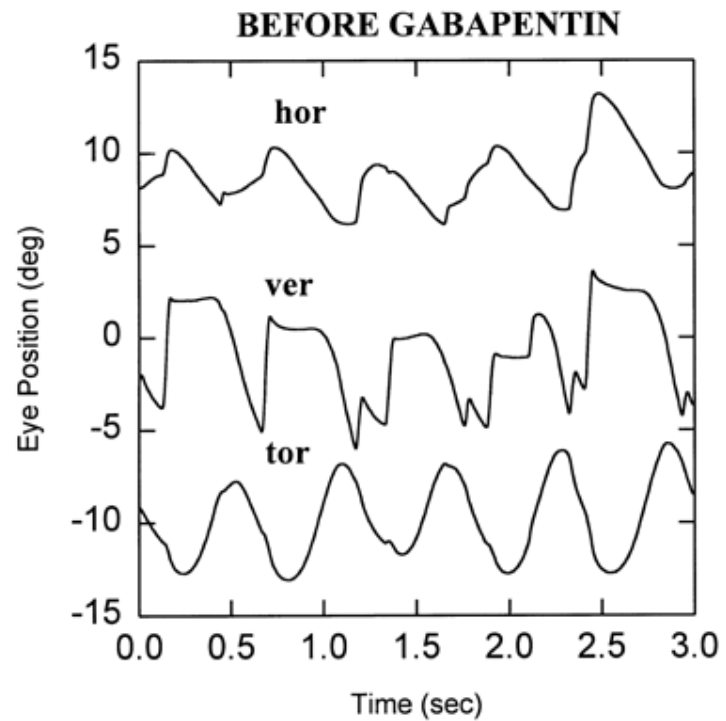
Elliptical Nystagmus



Effects of saccades and blinks on pendular nystagmus



Rx of pendular nystagmus



Irregular pendular oscillations

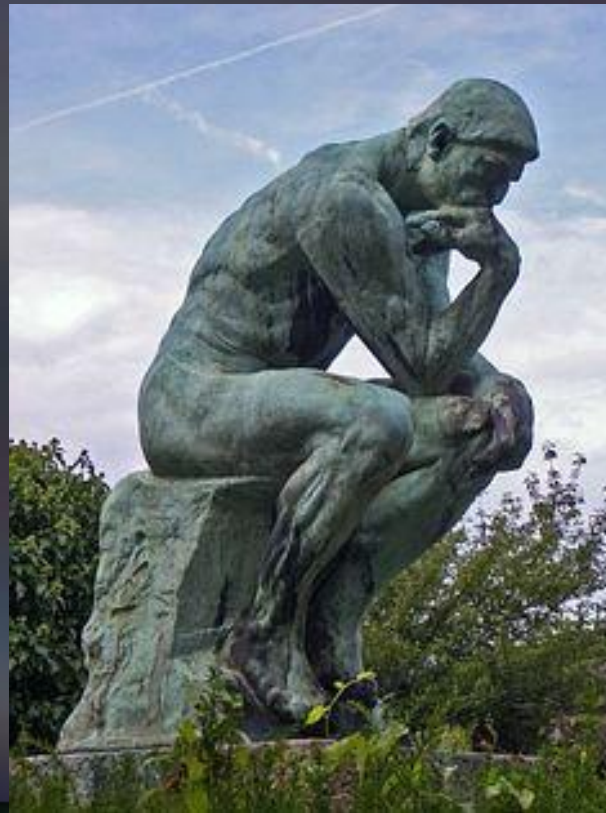


Pendular oscillations

Use your
ophthalmoscope
to evaluate
nystagmus



What do I examine next after seeing this type of pendular nystagmus??

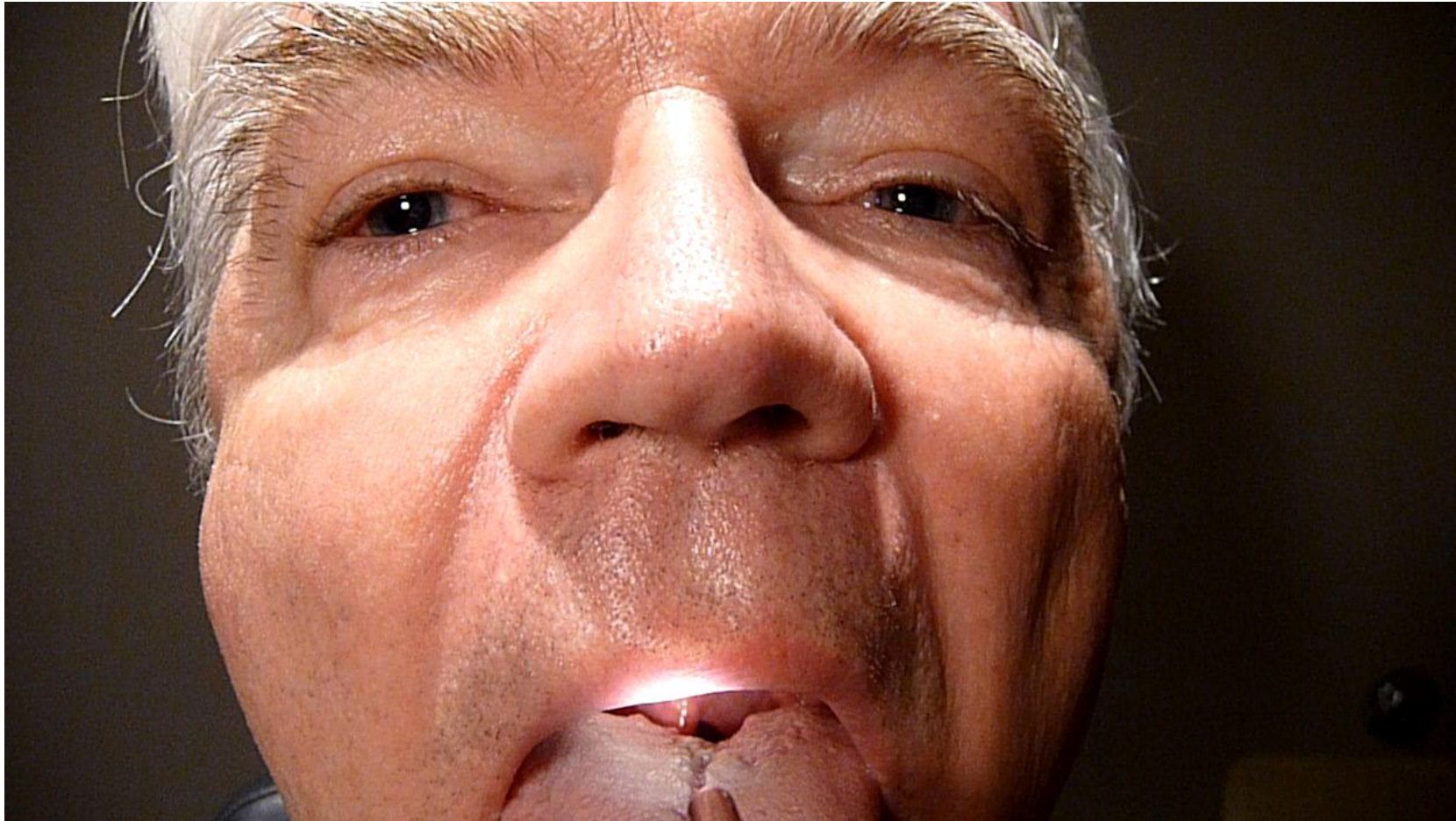


And this syndrome is called??

Oculopalatal tremor (myoclonus)



EYE CLOSURE (of the patient not the examiner) may bring out pendular nystagmus and other ocular oscillations (saccadic oscillations such as opsoclonus and flutter)





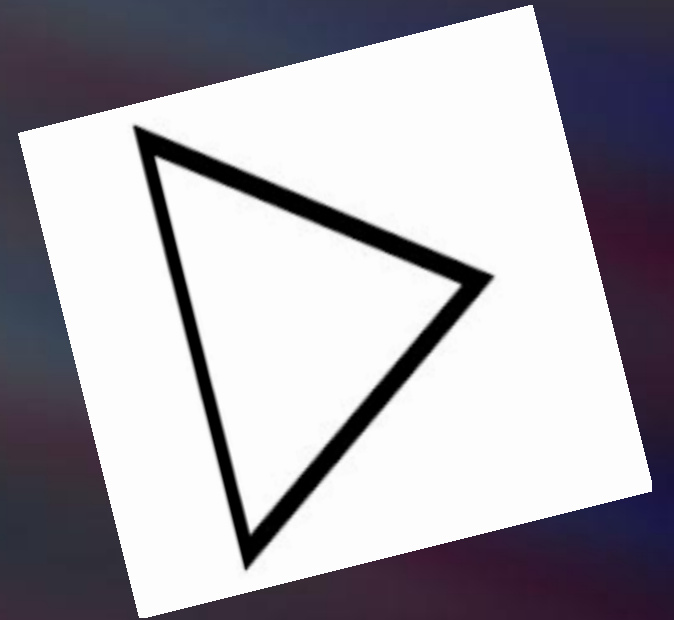
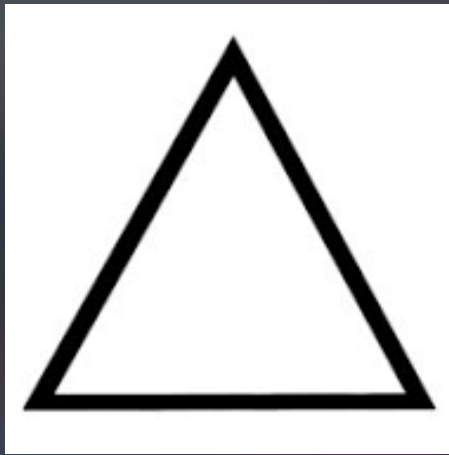
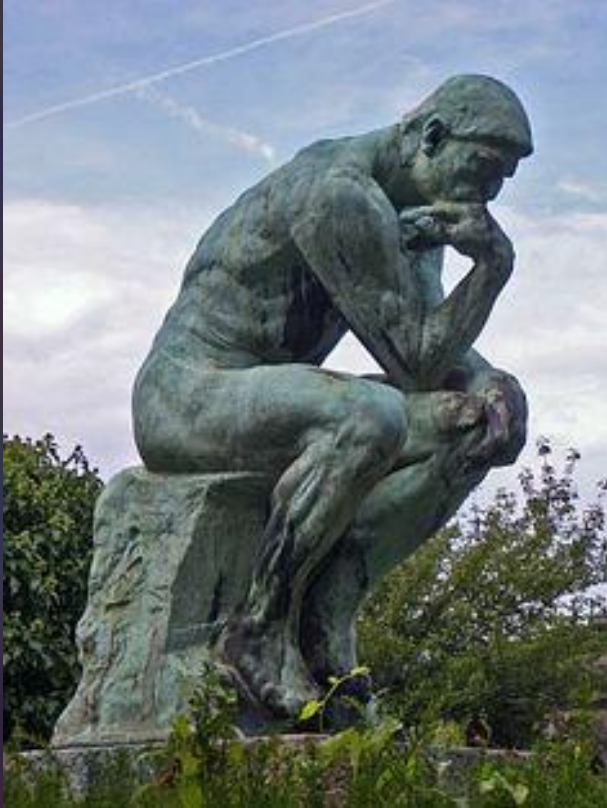
**LOOK at the
palate in all
patients with
pendular
nystagmus or
ataxia**



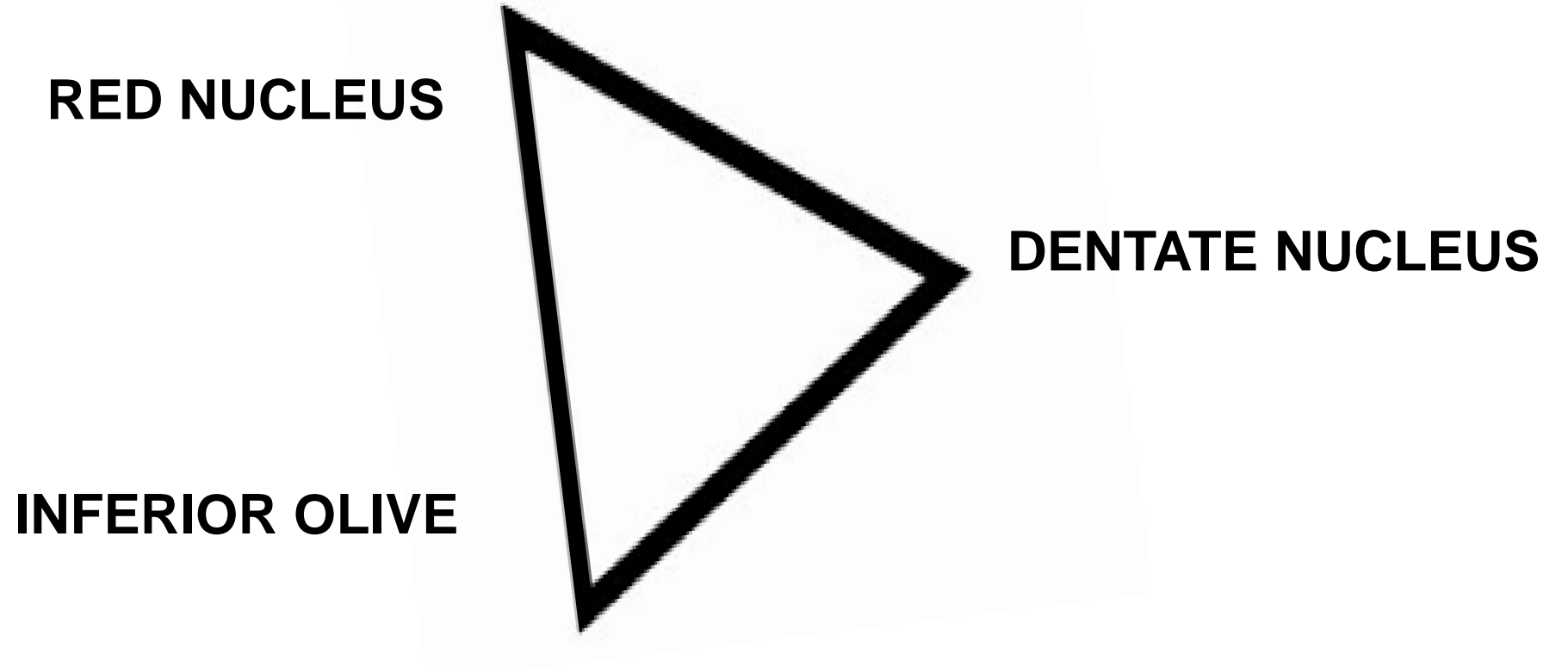
Courtesy JS Kim

Courtesy JS Kim

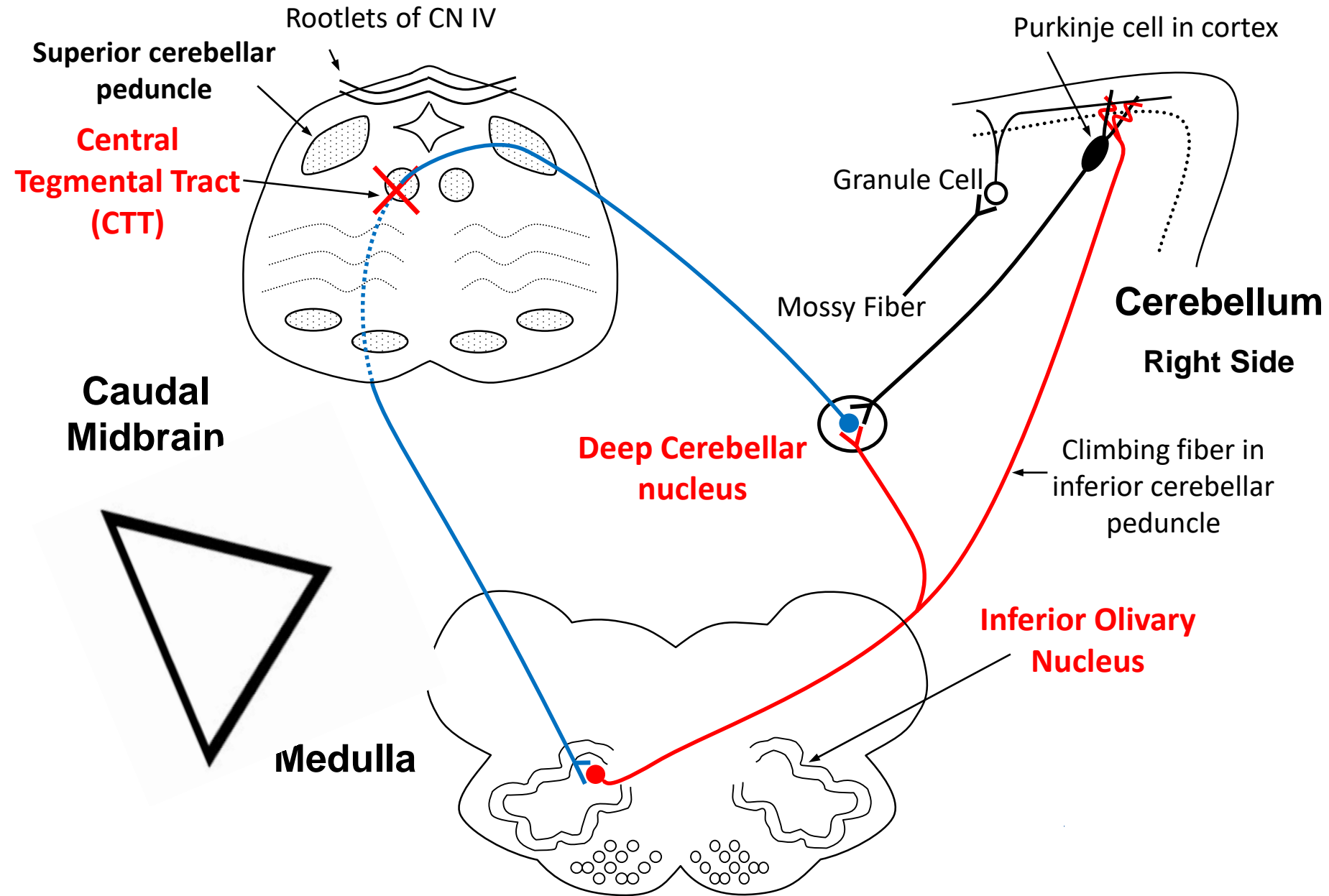
Where is the lesion in ocular-palatal tremor??



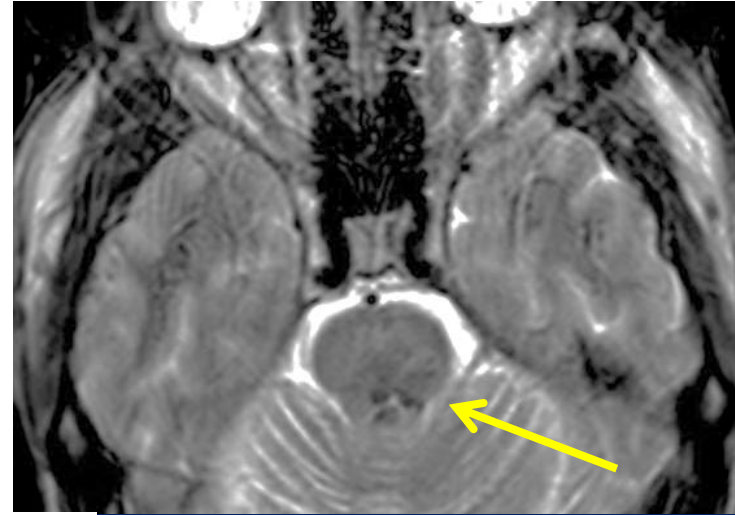
GUILLAIN-MOLLARET TRIANGLE



Guillain-Mollaret Triangle (Dentate nucleus, Red nucleus, Inferior Olive)

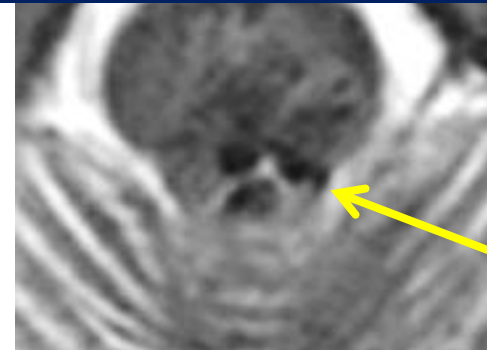


PATIENTS WITH OCULOPALATAL TREMOR SYNDROME

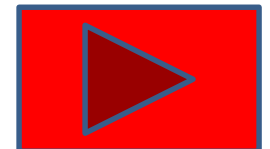


CAREFULLY LOOK AT INFERIOR OLIVE ON MRI IN ALL PATIENTS WITH ATAXIA OR NYSTAGMUS

**Inferior olivary hypertrophy
with increased signal in olive**



**Iron due to old
hemorrhage in AVM**



Oculopalatal tremor (OPT)



Abnormal signal and hypertrophy in Inferior Olive

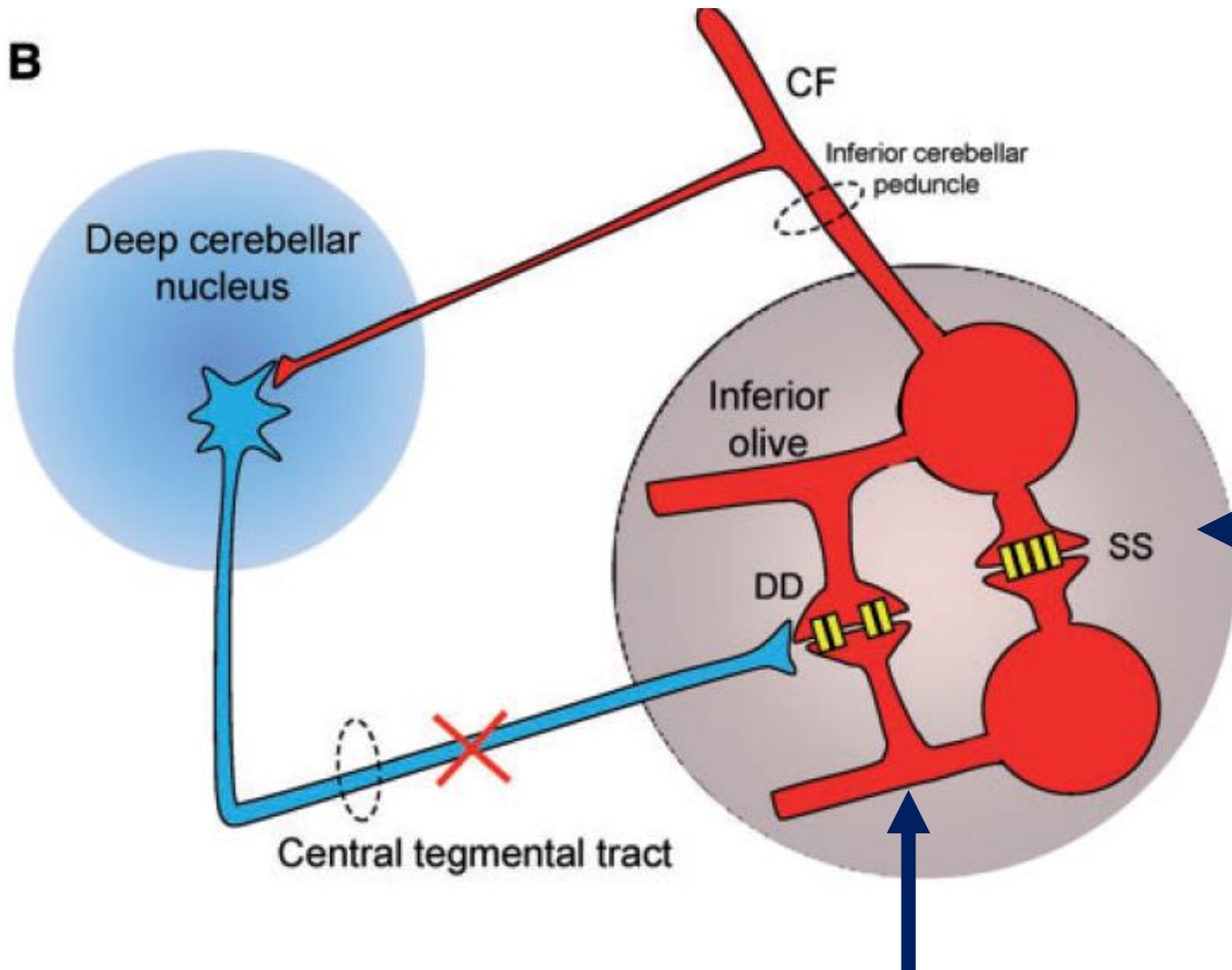
Partial Differential Diagnosis

- Acquired structural lesions (often hemorrhage) in Guillain-Mollaret triangle
- PAPT (progressive ataxia palatal tremor syndrome)
- Alexander's disease
- POLG (mitochondrial mutations)
- Whipple's disease
- SCA20

Pathophysiology of OPT

- Interruption of inhibitory inputs to inferior olive leads to transsynaptic degeneration with hypertrophic change.
- Olivary neurons balloon and soma contact each other.
- Electrotonic conduction via gap junction (channels are composed of connexins) normally occurs in IO between dendrites (DD).
- When IO neurons balloon there is soma-soma (SS) electrotonic conduction which leads to global synchronized activity and consequent tremor.

B



When Inferior olive neurons balloon after deafferentation there is soma-soma (SS) electrotonic conduction via gap-junctions which leads to global synchronized activity and consequent tremor.

Shaikh, 2010

Normal dendrite-dendrite (DD) electrotonic conduction via gap-junctions.

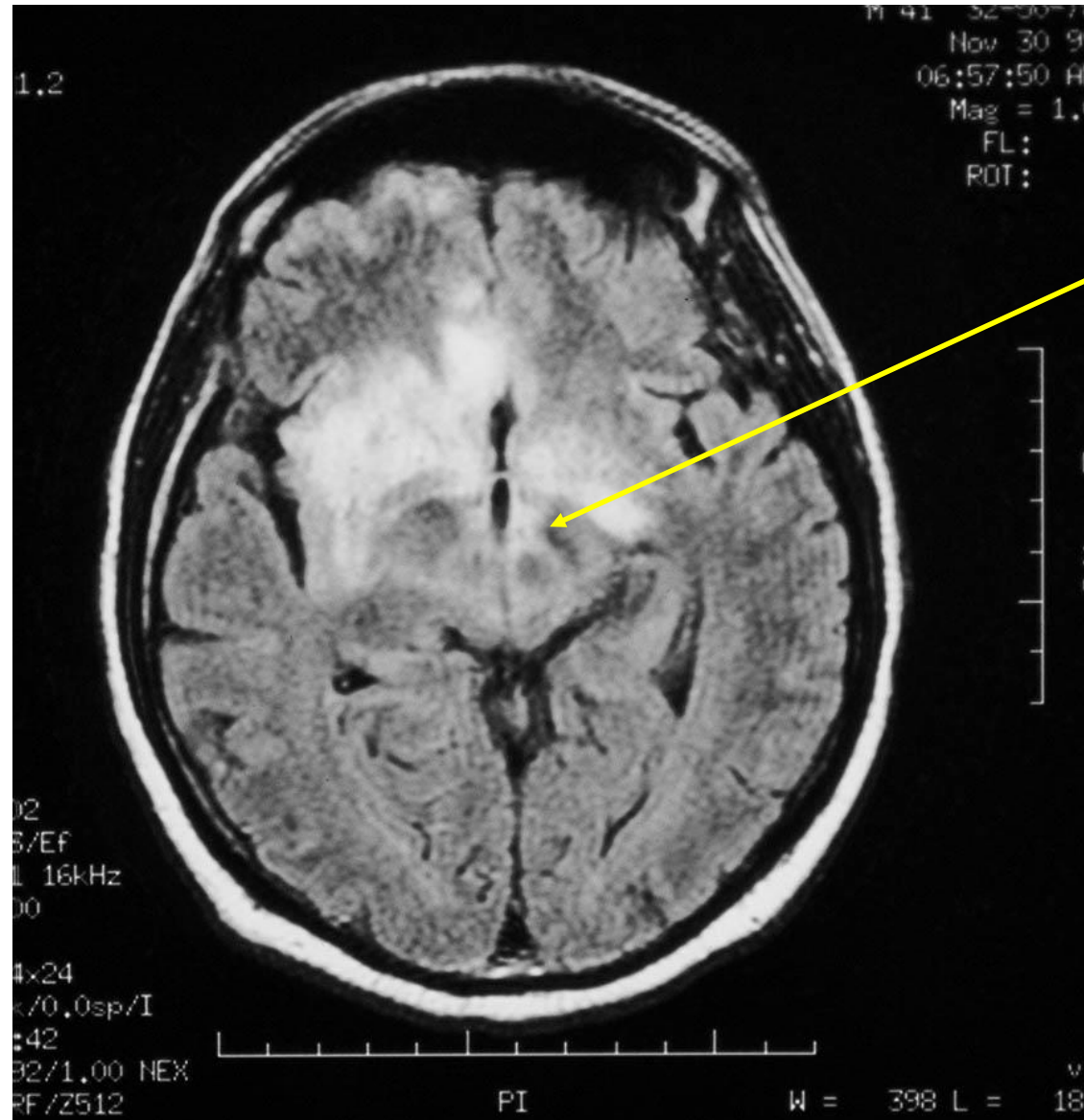
Pathophysiology of OPT

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- Electrotonic conduction via gap junction (channels are composed of connexins) normally occurs in IO between dendrites.
- When IO neurons balloon there is soma-soma electrotonic conduction which leads to global synchronized activity and consequent tremor.
- Note: Connexin 36 knockout mouse has low synchrony, supporting this potential mechanism for OPT.
- **Potential treatment: Connexin blockers (quinine and antimalarials), memantine, clonazepam**



Courtesy Jack Selhorst

Whipple's Disease



Rostral Midbrain

Whipple's Disease

- Cognitive Disorder
- Myoclonus
- *Supranuclear ophthalmoplegia (vertical)*
- *Convergence (and other forms of) pendular nystagmus*
- *Myorhythmia of masticatory muscles (and limbs)*
- Uveitis
- Systemic (GI, joints, rash)
- Abnormal CSF
- Abnormal MRI
- PCR positive (blood and csf)



Convergence-retraction nystagmus (dorsal midbrain lesions)



Convergence-retraction nystagmus

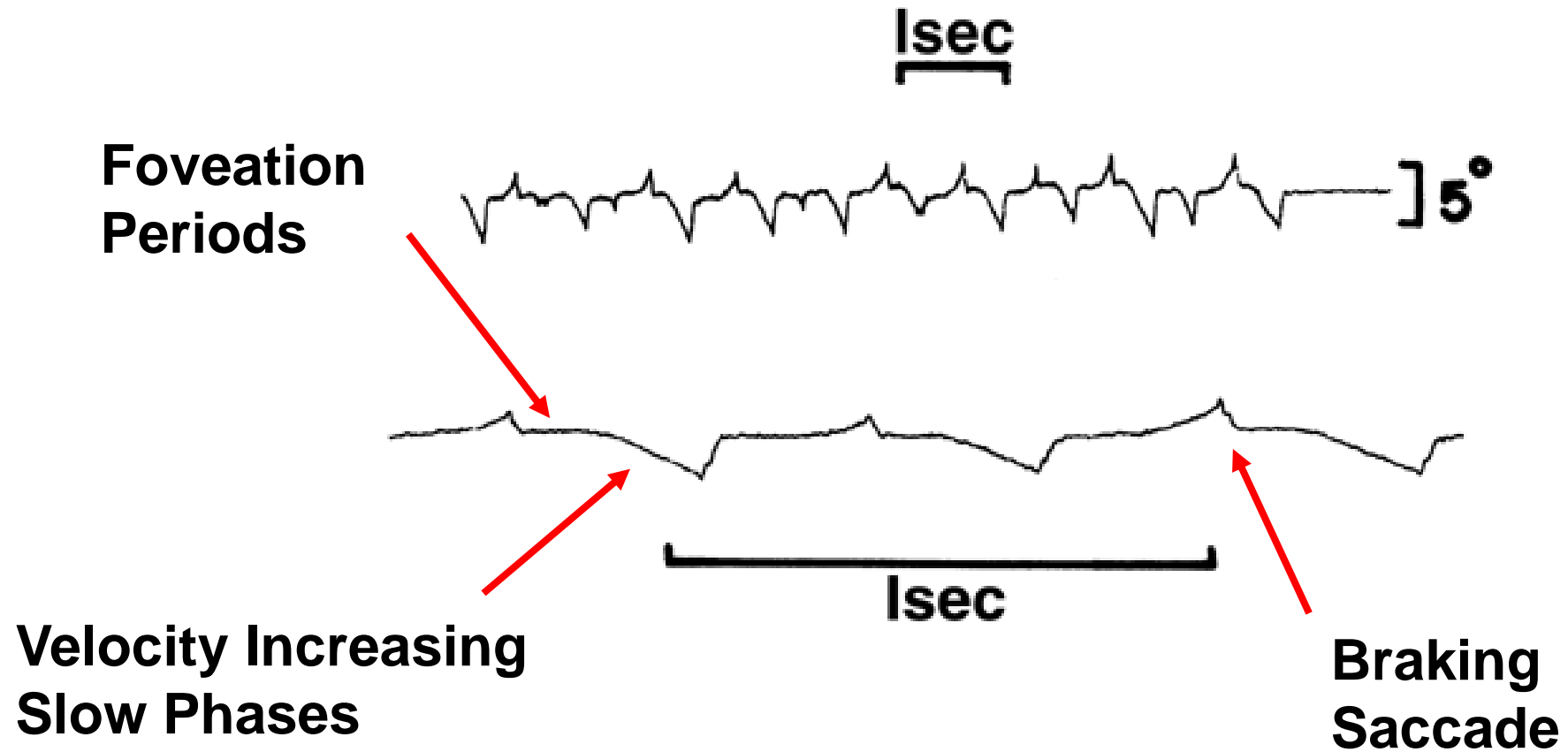


Congenital (Infantile) Nystagmus

Young woman referred
for headaches and
evaluation of abnormal
eye movements



Congenital Nystagmus



Congenital (infantile) nystagmus



- Horizontal (may have torsion), often increased on lateral gaze and stays horizontal on up and downward gaze
- Conjugate, increasing slow-phase velocity waveforms
- Pendular or jerk or mixed
- Red flags for a sensory deficit
 - High frequency, pendular or with a vertical component
 - Photophobia, high myopia, paradoxical pupil (constricts in darkness, after a few seconds)
- Null, head turn, head tremor

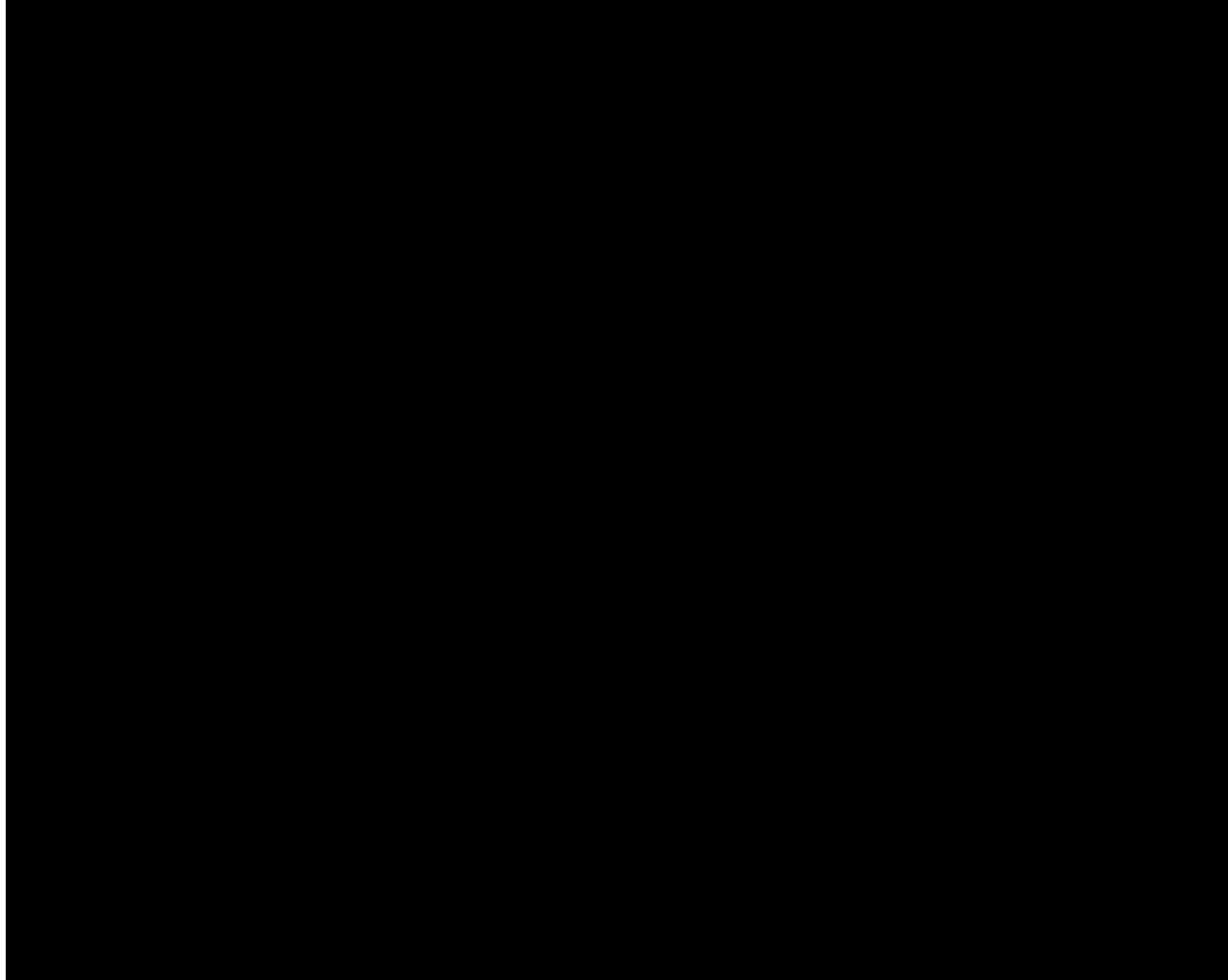
Congenital (infantile) nystagmus



- Damped by convergence and by eye closure
- Reversed pursuit and optokinetic nystagmus
- Commonly an absence of oscillopsia
- Foveation periods
- Evolution over first few years of life -- triangular > pendular > jerk
- Associations -- albinism, cone and other retinal abnormalities, optic nerve abnormalities, etc.
- Treatment:
 - memantine/gabapentin/clonazepam/baclofen
 - muscle surgery
 - contact lens
 - prisms, for convergence and head turns
 - systemic and topical carbonic anhydrase inhibitors

Rx of CN with memantine

McLean et al, 2007



Seesaw nystagmus (III ventricle, rostral midbrain lesions)

TO SEE IF THE EYE
MOVEMENTS ARE
DISCONJUGATE LOOK AT
THE BRIDGE OF THE
NOSE, NOT AT EACH EYE
INDIVIDUALLY.

LET YOUR PARAFOVEAL
PERIPHERAL VISION
MAKE THE DECISION
ABOUT CONJUGACY



Seesaw nystagmus



Seesaw nystagmus

- Congenital and acquired forms
- Achromatic Belgian sheep dogs and achromatic humans (septo-optic dysplasia)
- Associated with third ventricle tumours (bitemporal hemianopia) and upper midbrain lesions
- Occasionally associated with palatal tremor
- Possibly related to mechanisms that produce the ocular tilt reaction and dissociated vertical deviation (DVD)



EYE MOVEMENTS OF THE BLIND

Congenital/Infantile form, due to sensory deprivation with lack of calibration.

Adult, acquired blindness

May occur with partial loss of vision, especially when due to retinal disease (windmill nystagmus)

Eye movements similar to cerebellar disease since the cerebellar repair shop, which keeps motor responses calibrated, is in the “dark”.



Tullio's phenomenon — noise-induced vertigo

**Superior
Semicircular
Canal dehiscence**



Valsalva-induced vertigo



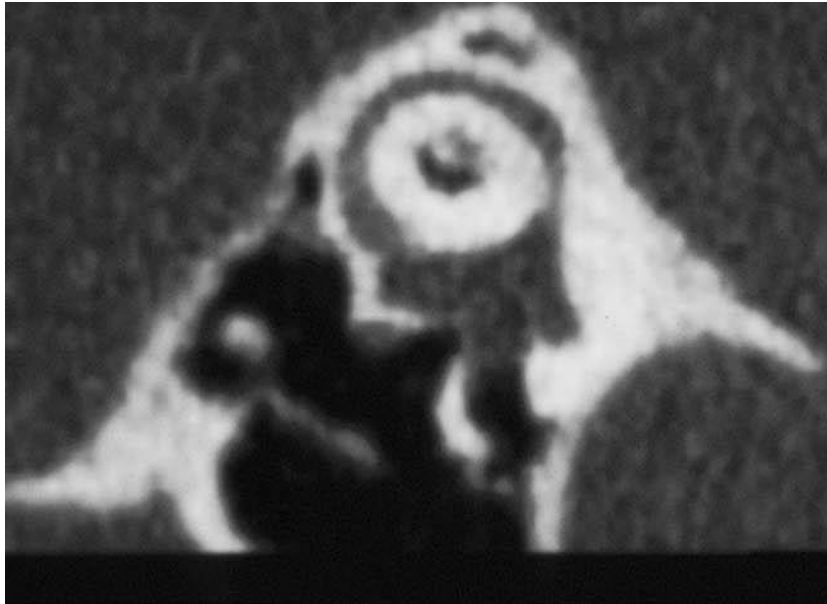


Fistula due to dehiscence of the roof of the superior SCC

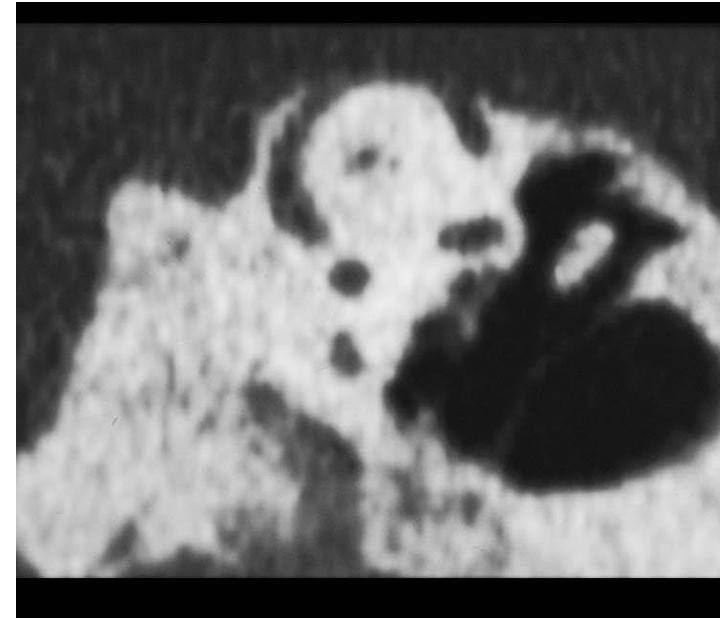
Intact side



**Lloyd
Ninor**



Abnormal side



Pharmacological Rx of Nystagmus (off label)

EFFECTIVENESS

+++++

Drug therapy for jerk nystagmus

++++

- baclofen (periodic alternating nystagmus)

+++

- 4-aminopyridine (downbeat nystagmus), (acetazolamide for episodic ataxias)

+

- clonazepam, chlorzoxazone (downbeat nystagmus)

Drug therapy for pendular nystagmus

++

- memantine, gabapentin

+

- levetiracetam, clonazepam

+

- Drug therapy for congenital nystagmus:
 - memantine, baclofen, clonazepam

+

NYSTAGMUS: A FEW MORE TAKE AWAY MESSAGES

- **Keep your eyes (and brains) open in the clinic**
- **Post the diagnostic algorithm and waveform charts of nystagmus in your clinic**
- **If you see pendular nystagmus LOOK in the mouth for palatal tremor**
- **Look under closed lids for nystagmus (pendular) and other oscillations (opsoclonus)**

NEVER MISS THE TREATABLE FORMS OF NYSTAGMUS (EXAMPLES INCLUDE)

- **Wernicke's disease**
- **Paraneoplastic syndromes, usually causing downbeat nystagmus but many eye oscillations including opsoclonus and flutter. FIND the tumor**
- **Whipple's disease**
- **Intoxications and medication side effects (e.g., amiodarone)**
- **Pendular nystagmus in multiple sclerosis (memantine, gabapentin)**
- **Downbeat nystagmus (4 aminopyridine, diamox for Episodic Ataxia)**
- **Monocular nystagmus (spasmus nutans) in children. LOOK for a tumor**

Exam Time!

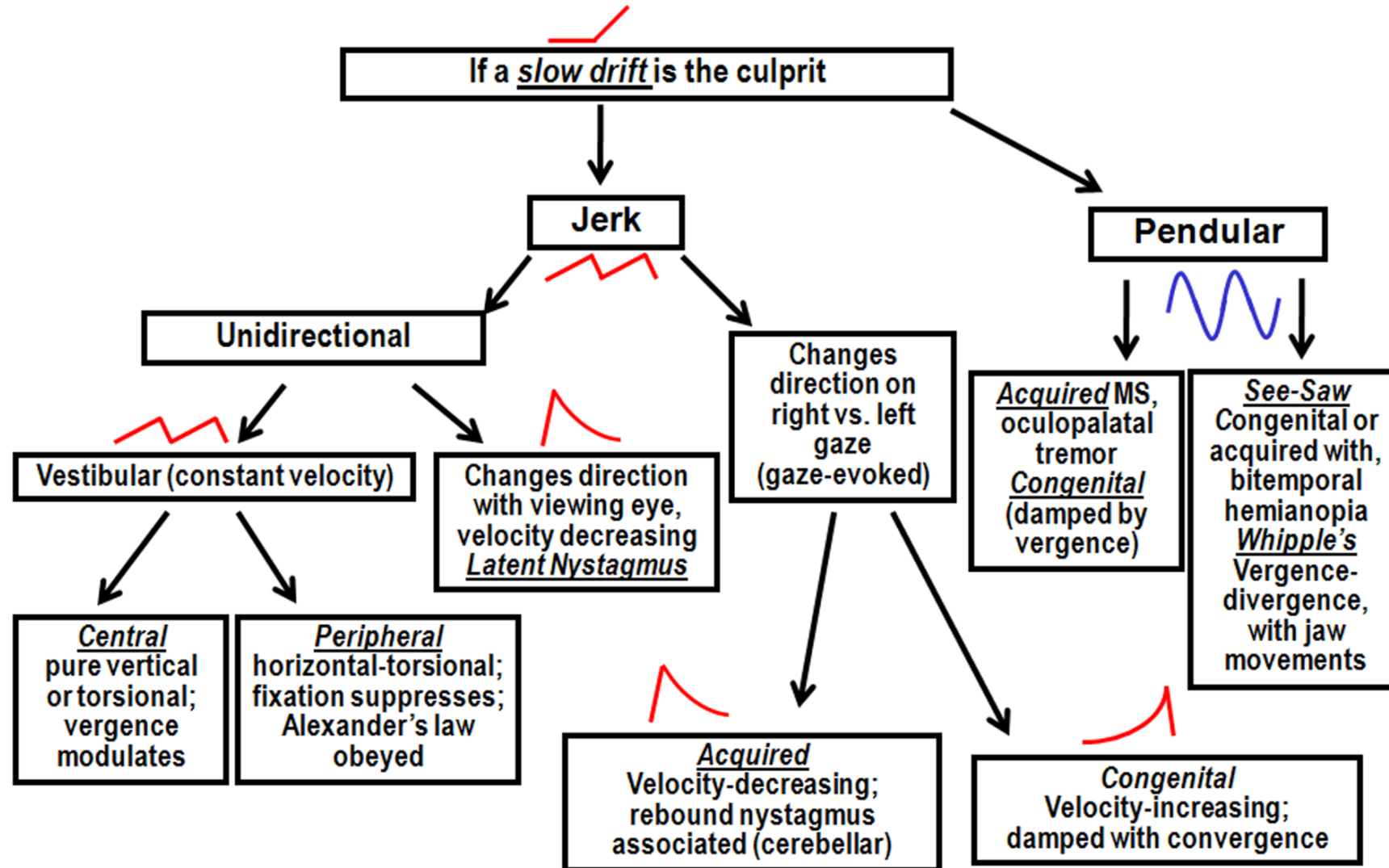
**Voluntary saccadic oscillations (“voluntary nystagmus”),
often familial and frequency-specific within a family!**

What is the Dx?



A Flow Chart to Aid Classification of Nystagmus


Is fixation impaired because of a *slow drift*, or an *intrusive saccade*, away from the target?



From Leigh and Zee, NEM, 5th edition, 2015

A Flow Chart to Aid Classification of Saccadic Intrusions

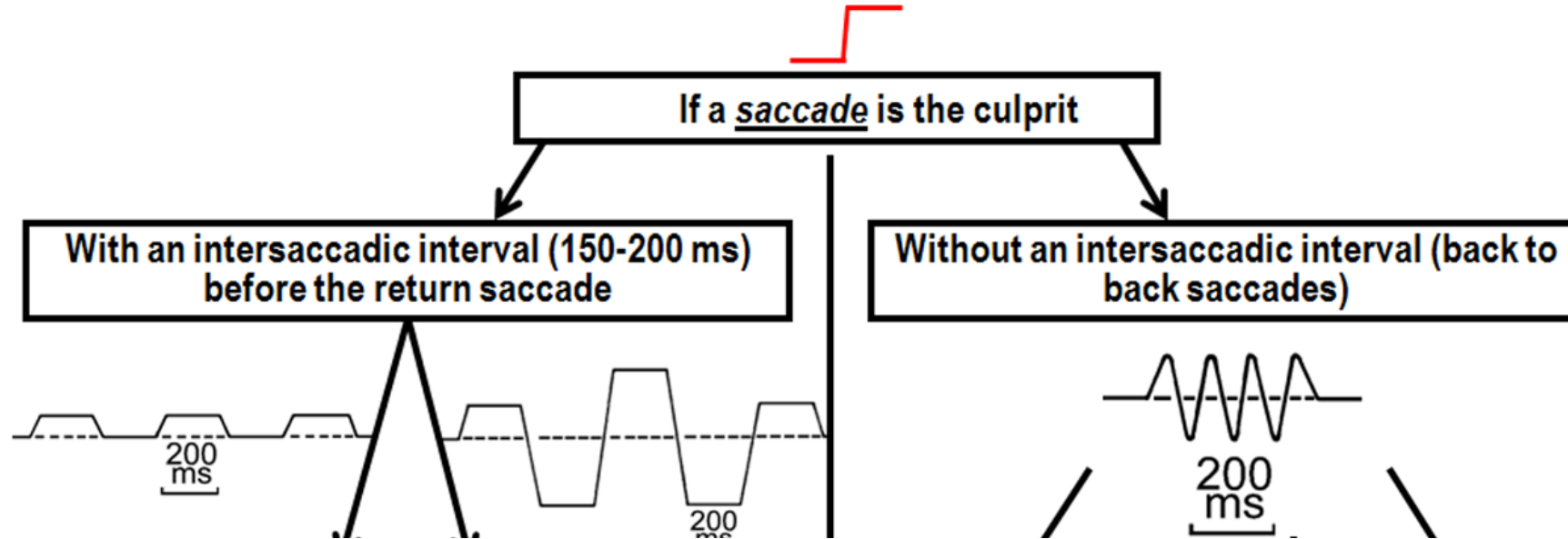
Is fixation impaired because of a *slow drift*, or an *intrusive saccade*, away from the target?



If a saccade is the culprit

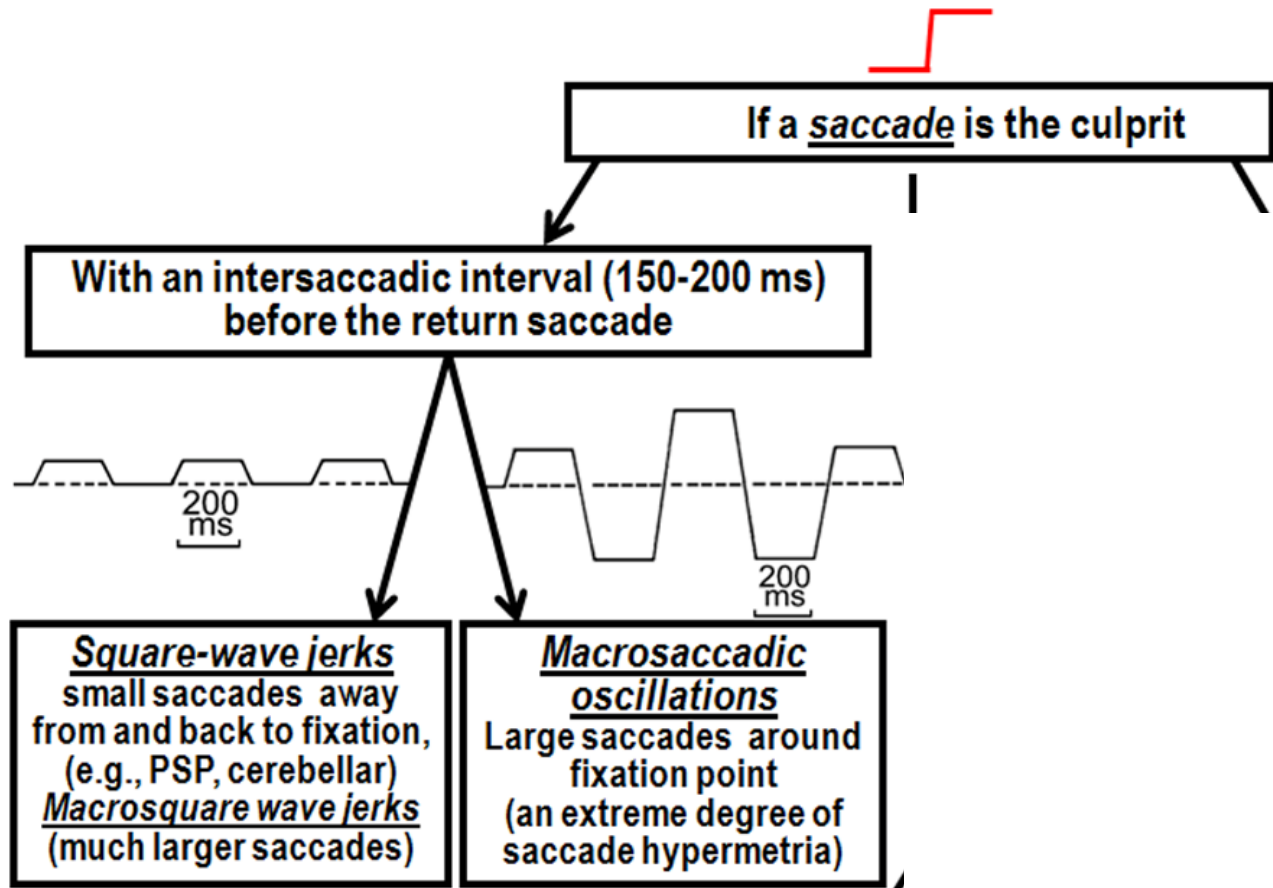
A Flow Chart to Aid Classification of Saccadic Intrusions

Is fixation impaired because of a *slow drift*, or an *intrusive saccade*, away from the target?



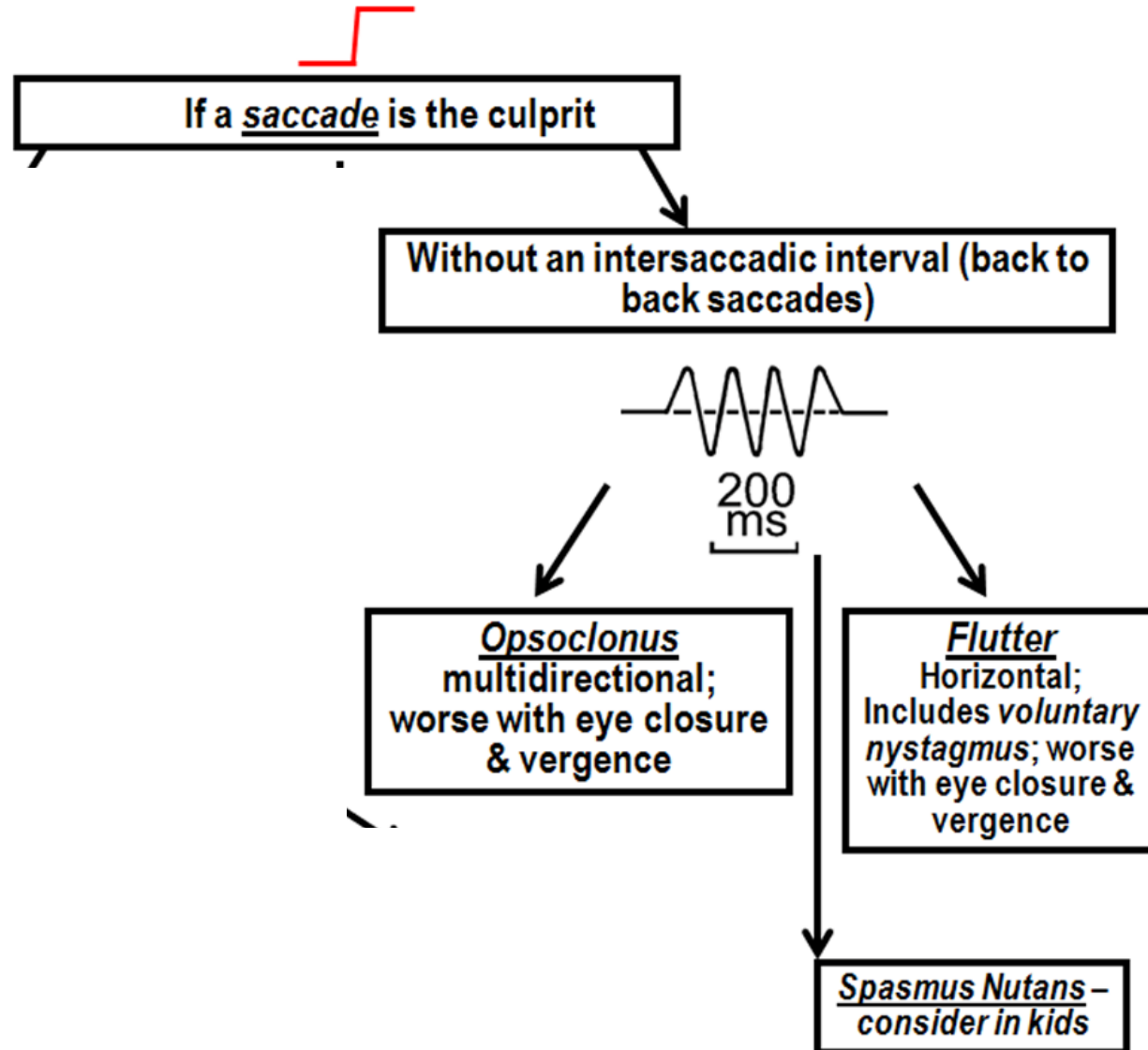
A Flow Chart to Aid Classification of Saccadic Intrusions

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A Flow Chart to Aid Classification of Saccadic Intrusions

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A Flow Chart to Aid Classification of Saccadic Intrusions

Is fixation impaired because of a *slow drift*, or an *intrusive saccade*, away from the target?

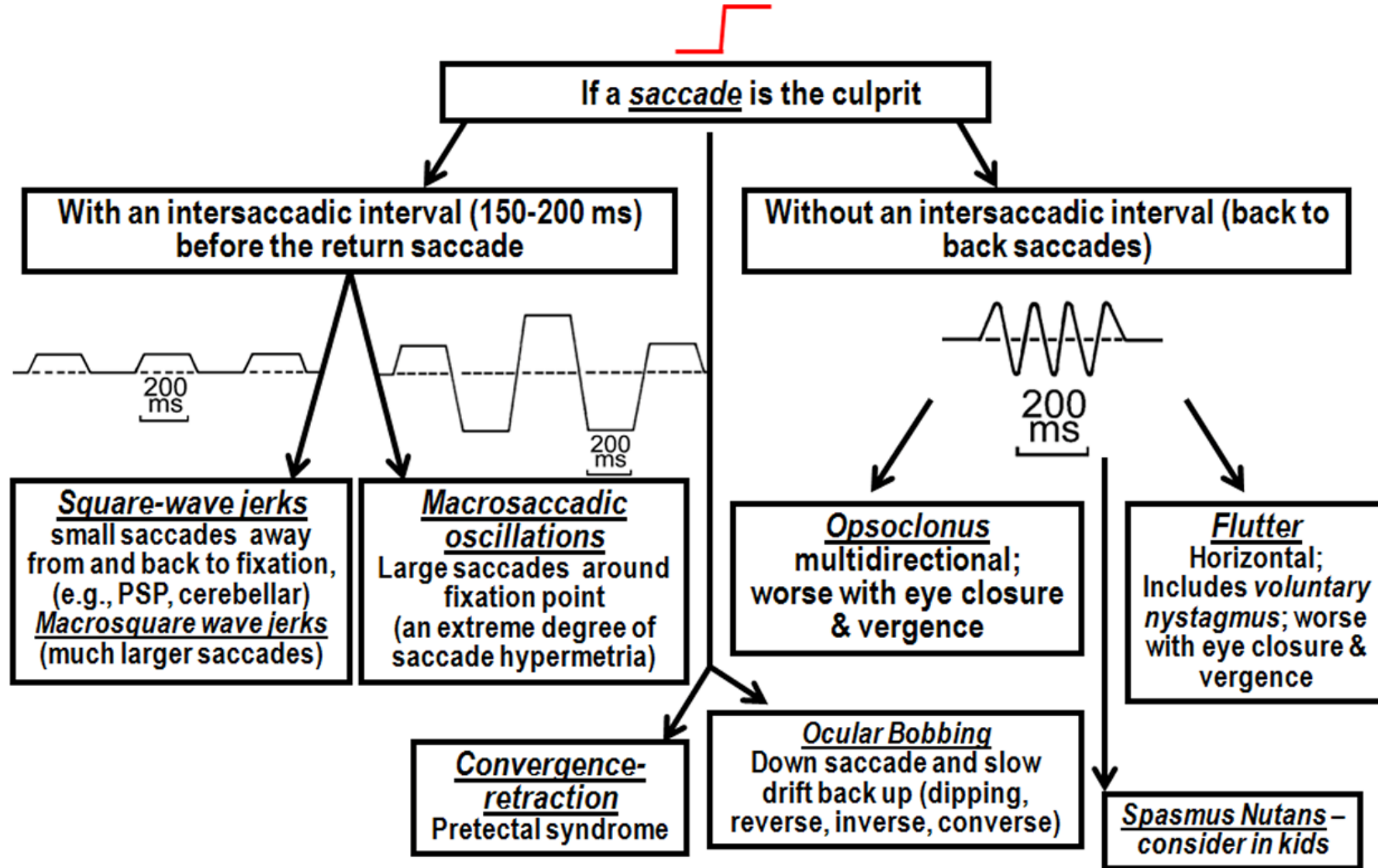
If a saccade is the culprit

Convergence-
retraction
Preectal syndrome

Ocular Bobbing
Down saccade and slow
drift back up (dipping,
reverse, inverse, converse)

A Flow Chart to Aid Classification of Saccadic Intrusions

Is fixation impaired because of a *slow drift*, or an *intrusive saccade*, away from the target?



Ocular bobbing



Ocular Bobbing

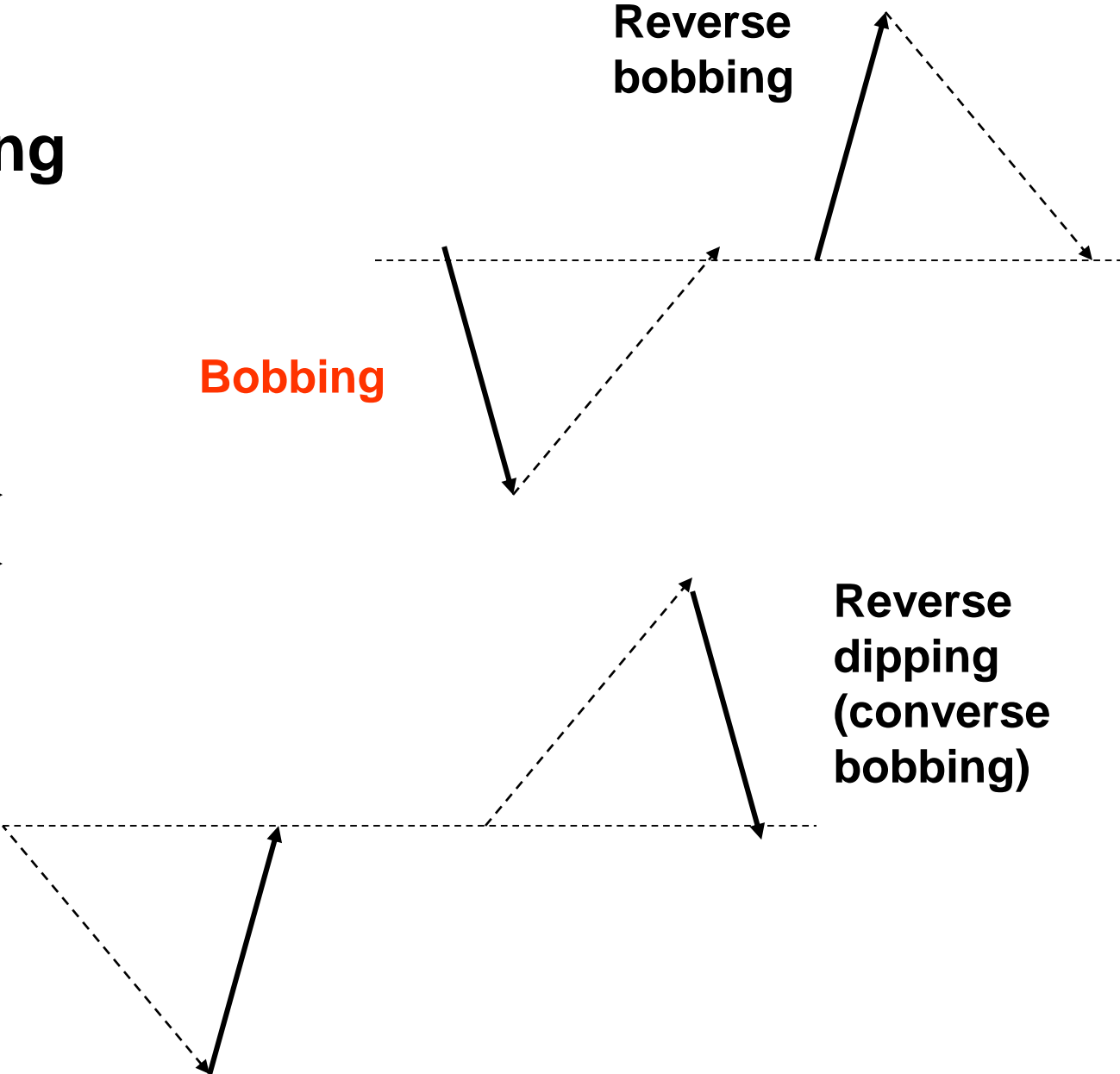
Saccade →
Slow Drift - - - - ->

Bobbing

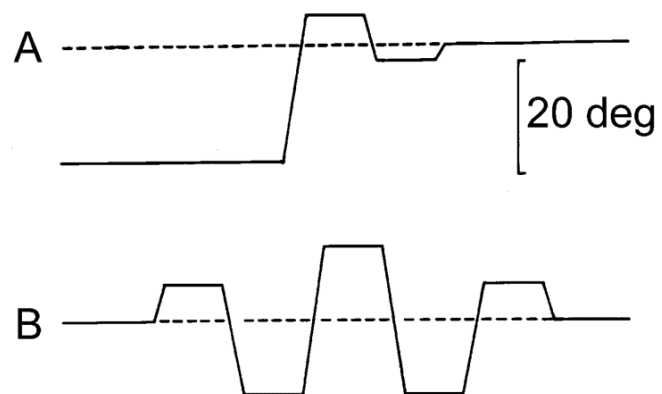
Reverse
bobbing

Dipping
(inverse
bobbing)

Reverse
dipping
(converse
bobbing)



Saccadic overshoot dysmetria with macrosaccadic oscillations

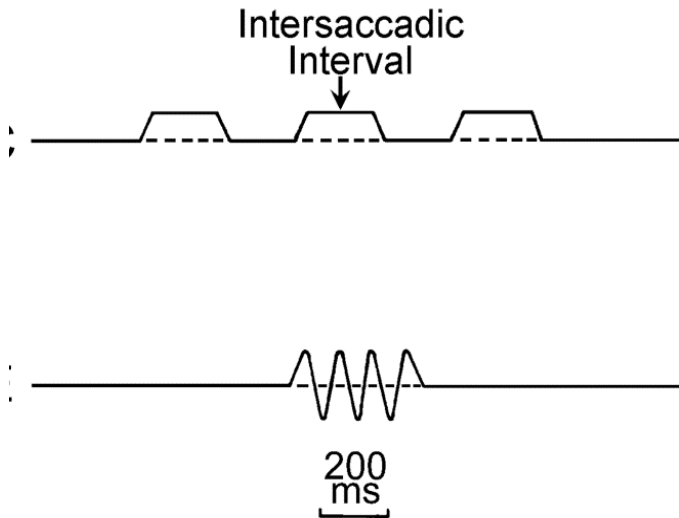


Macrosaccadic Oscillations



Friederich's Ataxia: Saccadic intrusions (Square wave jerks)

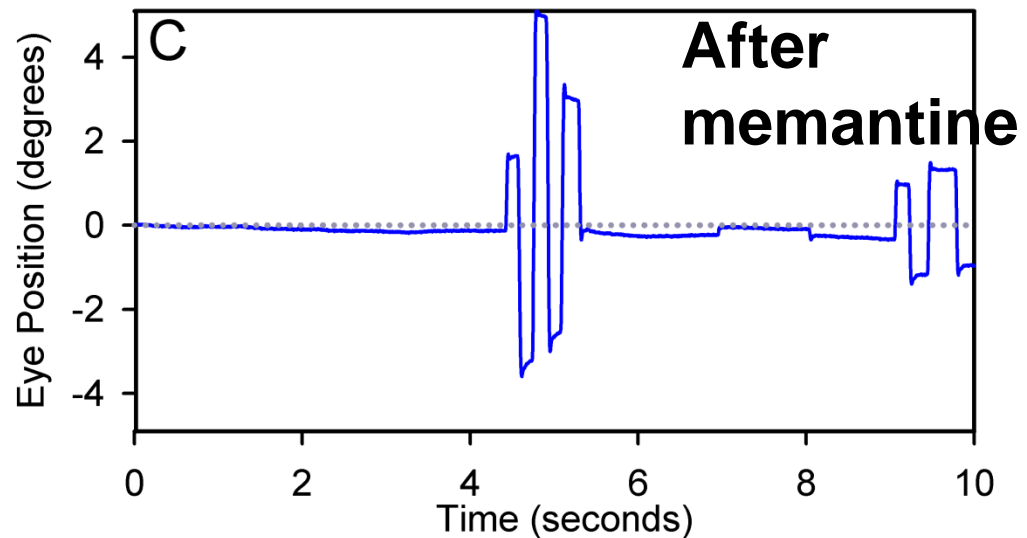
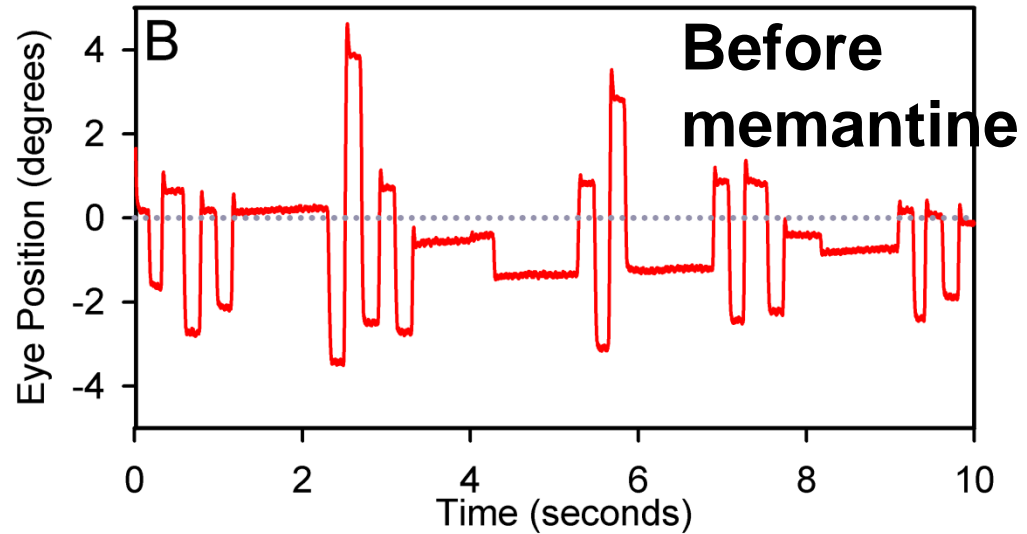
SWJ with a brief intersaccadic interval



Note: Flutter usually refers to horizontal saccade oscillations **WITHOUT** an intersaccadic interval (i.e., horizontal form of opsoclonus)



Saccadic Intrusions in SCASI: Treatment with memantine



Square-wave jerks

- **Cerebellar
disease**
- **Elderly**
- **Progressive
Supranuclear
Palsy**
- **Schizophrenia**
- **Dementing
illnesses**



Square-wave jerks

**Impaired and slow
vertical saccades**

**Intact vertical
vestibulo-ocular reflex**



Saccadic oscillations: Opsoclonus



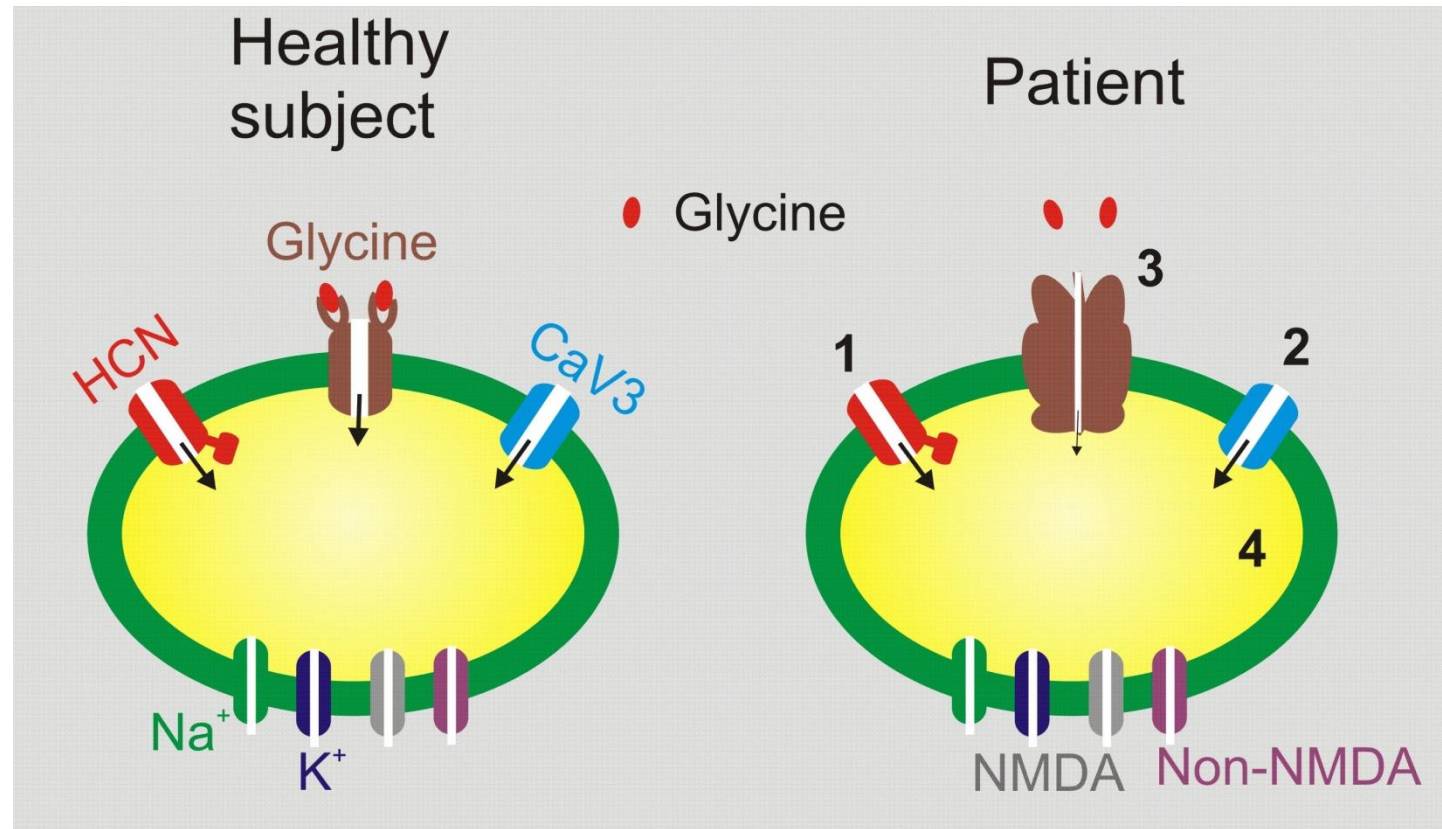


Opsoclonus



Note brief bursts of small, high-frequency oscillations

An ion channel model of opsoclonus: Defective glycine inhibition on burst neurons related to a loss of pause cell inhibition



Shaikh et al., *Brain* 130:3020-3031, 2007

Saccadic oscillations: Opsoclonus

Rapid ocular oscillations (uncalled for, back-to-back saccades with no intersaccadic interval).

Extreme cases are called *opsoclonus* (*all directions*).

Mild cases are called *flutter* (*horizontal*).

Microsaccadic flutter or microopsoclonus

Causes

Autoimmune

Post-infectious

Paraneoplastic (related to a tumor elsewhere in the body)

Toxic/metabolic

Inherited

Migraine (microflutter)

‘Voluntary’



Spasmus Nutans

- Head-nodding -- horizontal and vertical components, head tilt or turn
- Eye oscillations, intermittent, asymmetrical and dissociated (disconjugate (greatest in the abducting eye))
- High-frequency, “shimmering”, pendular like, usually horizontal
- May be provoked by near response or associated with convergence nystagmus
- Onset in the first year, usually with spontaneous resolution after a few years but sometimes longer, and tiny oscillations may persist
- Head nodding aids gaze stability, nulling the spontaneous oscillations using an indirect VOR effect
- **BEWARE** -- compressive lesions on the optic nerve and rule out retinal disease (often with upbeat nystagmus)



Spasmus nutans



Seen with
Neil Miller

When to image in infants with nystagmus??

- **Optic nerve disease**
 - Atrophy
 - Hypoplasia (chiasm or other midline defects)
- **Spasmus nutans like, dissociated or disconjugate, or vertical nystagmus**
- **Seesaw nystagmus (midline defects)**
- **Other neurological findings, especially if progressive**
 - Mitochondrial disorders
 - Cerebellar syndromes
 - Degenerative disorders



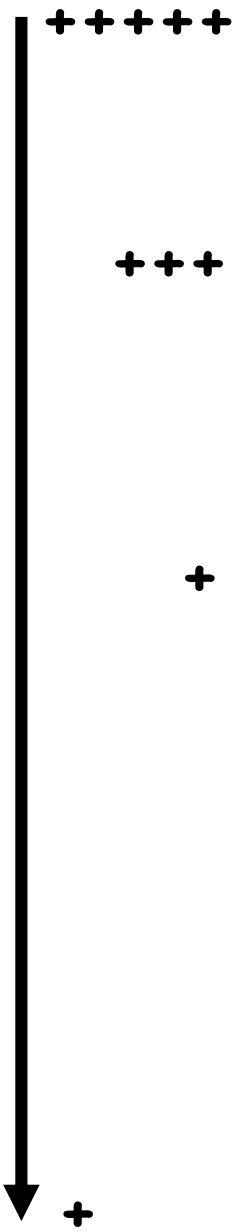
Ping-pong gaze



Seen with bilateral hemispherical lesions

EFFECTIVENESS

Pharmacological Rx of miscellaneous oscillations (off label)



- Drug therapy for ocular neuromyotonia, superior oblique myokymia and irritative nystagmus with VIII n. microvascular compression: carbamazepine, lacosamide
- Drug therapy for saccadic oscillations: memantine, betablockers, ethosuximide, clonazepam



<http://www.gamarjobat.com> **Michael R. MacAskill**, Kazuo Koga and **Tim J. Anderson**: Japanese street performer mimes violation of Hering's Law, *Neurology* 2011;76;1186
Can Unusual Convergent Gaze in "Kabuki Play" Generalize the Norm of Evaluation System for the Beauty Beyond the Individual Art?-Symmetrical or Asymmetrical- KOGA KAZUO (Nagoya Univ., Res. Inst. of Environ. Med.) *IEIC Technical Report (Institute of Electronics, Information and Communication Engineers)* VOL.105;NO.479(HIP2005 79-106);PAGE.47-50(2005)