

5th Congress of the European Academy of Neurology

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Teaching Course 15

**Eye movements and vestibular function in critical care,
emergency, and ambulatory neurology (Level 2)**

**Eye Movements in muscles, nerves,
neuromuscular junction, and functional
neurological disorders**

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Eye movements and vestibular function in critical care, emergency, and ambulatory neurology

Eye Movements in nerves, muscles, neuromuscular
junction, and
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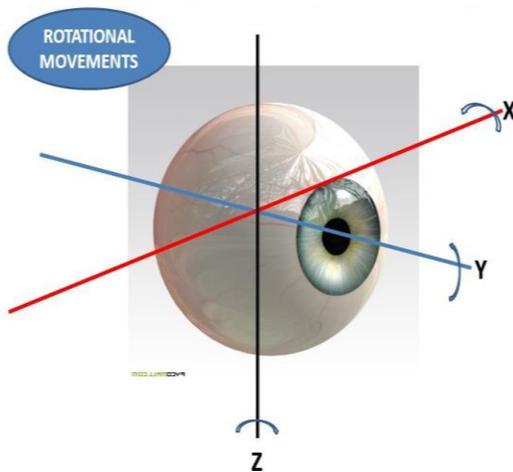
Conflict of Interest



In relation to this presentation and manuscript:

the Author has no conflict of interest in relation to this manuscript.

Globe Rotates around the Three Axes



FICK'S AXES

- X AXIS: NASAL-TEMPORAL
 - Y AXIS: POSTERIOR-ANTERIOR
 - Z AXIS: SUPERIOR-INFERIOR
-
- These axes intersect at the centre of rotation where also passes an imaginary coronal plane: the listing plane
 - Globe rotates right and left (adduction/abduction) on vertical axis Z
 - Globe rotates up and down (elevation /depression) on orizontal axis X
 - Globe makes torsional movements (intorsion/extorsion) on the antero-posterior axis Z

Agonist

Any particular EOM producing specific ocular movement (right LR abduction)

Synergists

Muscles of the same eye that move the eye in the same direction (Right SR and IO for elevation)

Antagonists

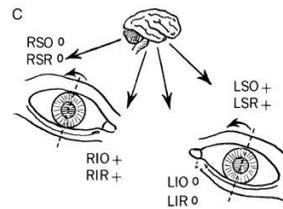
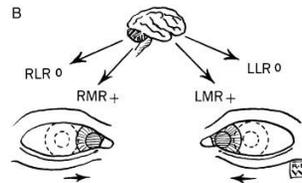
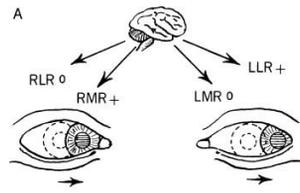
A pair of muscles in the same eye that move the eye in opposite direction (Right LR and MR)

Yoke Muscles

Pair of muscles one in each eye, that produce conjugate ocular movements (right LR and left MR in destroversion).

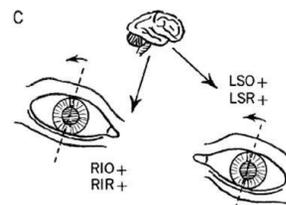
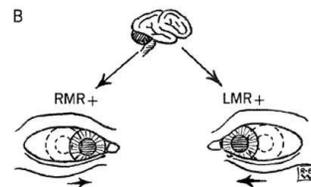
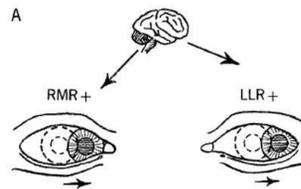
Sherrington law
of the reciprocal innervation

whenever an agonist receives an input to contract, an equivalent inhibitory impulse is sent to the antagonist muscle



Hering law
of equal innervation or motor correspondence.

Whenever an impulse for performing an eye movement is sent out, corresponding muscles of each eye, receive the same innervation to contract or relax



Listing's plane

Tweed, Cadera & Vilis 1990

Listing Law

All achieved eye orientations can be reached starting from a specific primary position, then rotating about an axis that lies within a plane orthogonal to the primary orientation direction (line of sight/visual axis)

The plane is the Listing plane

According to listing law cycloverision is 0

Position of Gaze

- Primary
- Secondary
- Tertiary

Secondary position

Primary position

Tertiary position

Tertiary position

Secondary position

Tertiary position

Nerve	Muscle	Primary action	Secondary action	Tertiary action
III CN	MR	ADDITION		
	SR	ELEVATION	INTORTION	ADDITION
	IR	DEPRESSION	EXTORSION	ADDITION
	IO	EXTORSION	ELEVATION	ABDUCTION
IV	SO	INTORSION	DEPRESSION	ABDUCTION
VI	LR	ABDUCTION		

Superior muscles (SR and SO) are incycloductors; Inferior muscles (IR and IO) are excycloductors; Vertical Rectus Muscles (SR and IR) are Adductors; Oblique muscles (IO and SO) are Abductors

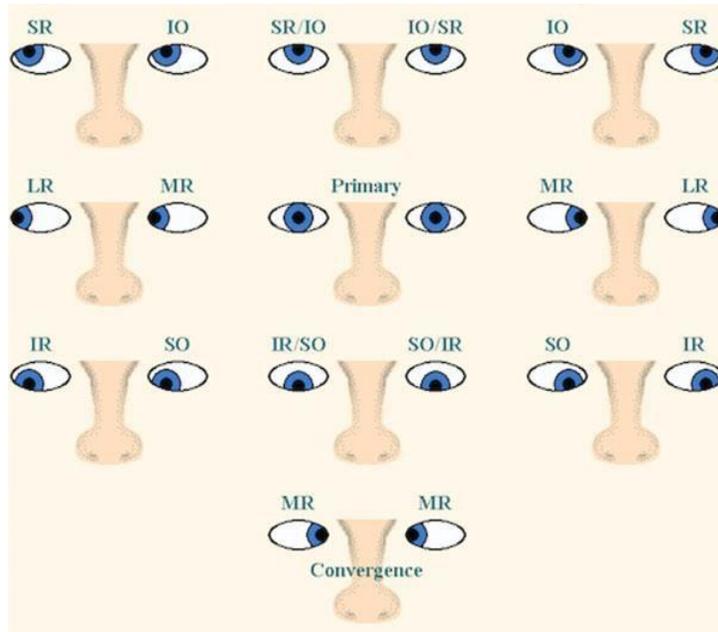
CLINICAL EXAMINATION

VERSIONS

DUCTIONS

VERGENCE

VERSIONS

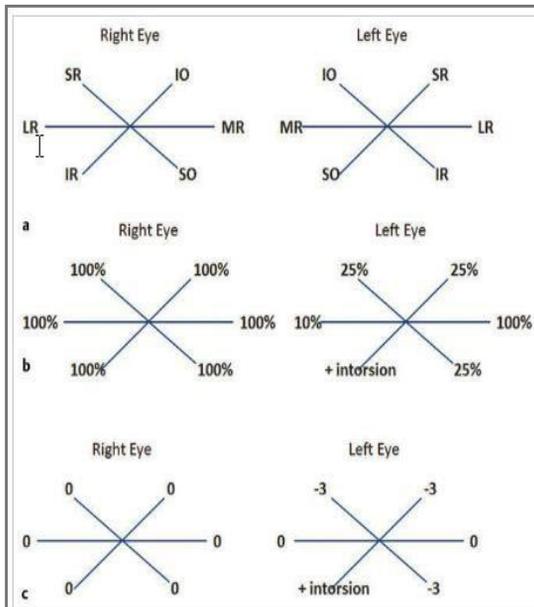


DUCTIONS

Clinical Testing

Muscle tested	Movement
SR	Looks laterally and upwards
IR	Looks laterally and downwards
LR	Looks laterally
MR	Looks medially
IO	Looks medially and upwards
SO	Looks medially and downwards

Diagram for the Transcription of Eye Movement Functions (Clinical Examination)



% of EOMs Function

IIICN

0 to -4 scale of muscle hypofunction

Eye Movements in Infranuclear Disorders

below the level of cranial nerve nuclei

- Cranial Nerve
- Neurogenic EOM palsies
- Neuromuscular Junction
- Synptogenic EOM defects
- Extraocular Muscles
- Myogenic pareses or plegias

NORMAL BINOCULAR VISION DISRUPTION

Ophthalmoparesis Ophthalmoplegia

First of all decide if there is a pattern of Cranial Nerve Deficit, if Yes, serch for Neurological Associated Abnormalities

Neuromuscular Junction and Myopathic defects affect all EOM based on structural or metabolic criteria. Ptosis is often prominent!

PEARLS

Paretic Strabismus

The angle of deviation is smaller when the unaffected eye is fixating (Primary deviation)

The angle of deviation is larger when affected eye is fixating (Secondary deviation).

The hallmark of paretic strabism is the **INCOMITANCE** (variable angle of deviation) increasing with movement into the field of action of the paretic muscle and decreasing with movement into the field of action of its antagonist.

also true for myogenic or synaptogenic disorders.

Causes of incomitant misalignment:

- Extraocular muscle disease
- Myasthenia gravis
- Third, fourth or sixth nerve palsy
- Internuclear ophthalmoplegia
- One-and half syndrome
- Miller Fisher

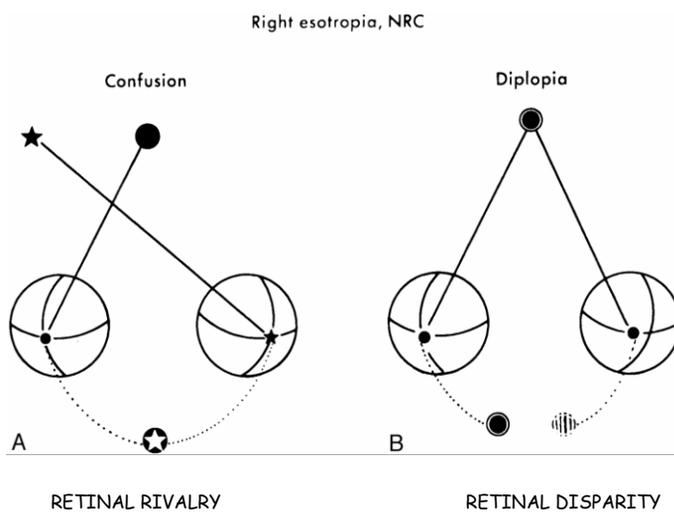
Causes of comitant misalignment:

- Early childhood strabismus
- Loss of fusion (severely decreased vision in one eye)
- Acquired vergence disturbance (convergence, divergence)
- Long standing sixth nerve palsy
- Skew deviation

Normal Binocular Vision Requires Fusion

motor and sensory fusions allow an image laying in corresponding retinal points of each eye, being perceived as single

Sensory Consequence of Ocular Misalignment is Diplopia or Confusion



Assesment of Diplopia

Monocular: ocular problem

Binocular: 5 simple questions!

1. Is horizontal or Vertical?
2. Is for distance or near?
3. In which direction of gaze is the diplopia worse?
4. Is associated to face turn?
5. Is there a head tilt?
6. Is pain associated?
7. Is there a change during the day or with fatigue?

The goals of the evaluation of the diplopic patient are to:

- 1-Recognize the ocular misalignment
- 2-Characterize the misalignment:
 - Deviation: esotropia, exotropia, hypertropia
 - Quantify the misalignment (prisms)
 - Comitant (same amount of deviation in all directions of gaze)
 - Incomitant (varies from one direction of gaze to another)
 - Maps to a cranial nerve or suggests a muscle (or neuro-muscular junction) lesion
- 3-Describe the pupils, visual acuity, fundus
- 4-Look for orbital signs
- 5-Look for associated neurological signs

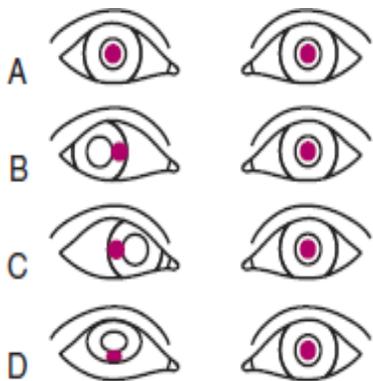
These findings allow you to: => Localize anatomically the lesion responsible for the diplopia => Make hypotheses regarding the mechanism of the lesion
=> Obtain further testing to confirm your clinical impression

Evaluation of Diplopia

Tropias manifest deviations

Forias latent deviations

(Hirshberg Test) Corneal Light Reflex



B) the eye outward, exotropia (XT)

C) the eye inward, esotropia (ET)

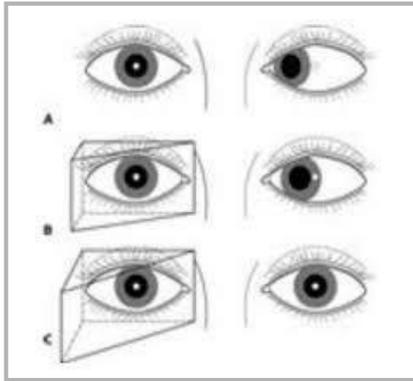
D) the eye higher, hypertropia (HT)

The ocular deviation can be quantified by estimating the decentration of the corneal light reflex (1 mm decentration corresponds to 7 degrees of ocular deviation=14 prism diopters),



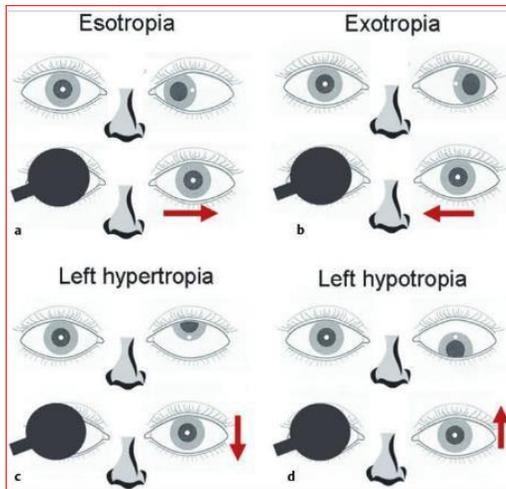
Deviation of the corneal reflex from the centre of the pupil to the limbus

The deviation is measured by placing **prisms** of increasing power before the fixating eye until the light reflex is centered in the deviating eye (**prism reflex test of Krimsky**). The prism with sufficient power to achieve centration of light reflex indicates the magnitude of the deviation.



left eye **ESOTROPIA**. A prism (base out) is placed in front of the fixating eye (right eye). The power of the prism is increased until the light reflex is centered in the deviated eye (left eye).

COVER UNCOVER TEST



-Outward movements denote convergent misalignment, **ESOTROPIA** is corrected with **Prism base OUT**

-Inward movements denote divergent misalignment, **EXOTROPIA** is corrected with **Prism base IN**

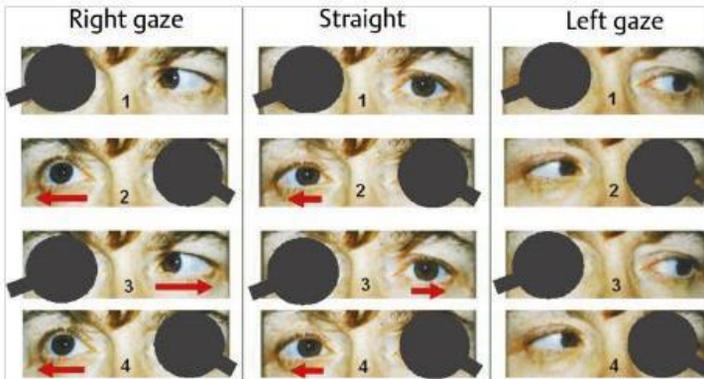
-A downward movement denotes **HYPERTROPIA** Prism base **UP**

-An upward movement denotes **HYPOTROPIA** Prism base **DOWN**

The type of misalignment in primary position, right, left, up, and downgaze should be noted.

CROSS COVER TEST stimulates alternate fixational movements. One observes if the eye being uncovered is shifting alternatively his position

The objective is to bring out any latent misalignment that may be suppressed by fusional mechanisms operating in binocular vision

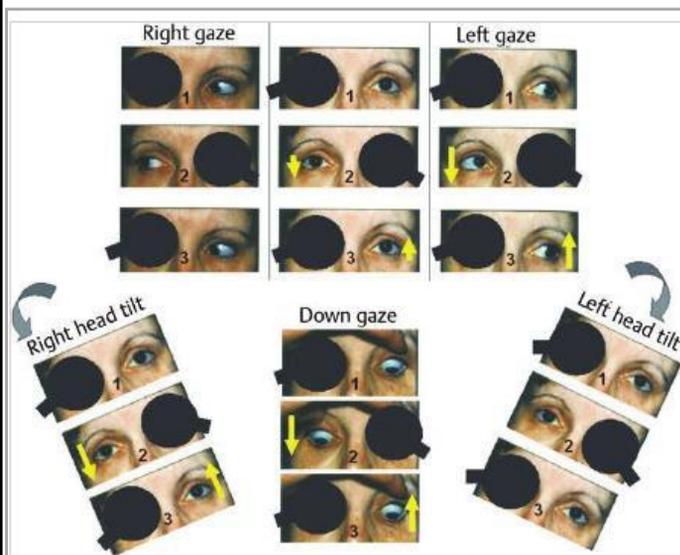


Right Abduction deficit

The refixation movement is greater in right gaze and absent in left

Right Superior Oblique Paresis IV n Palsy: The three step test Bielshowsky

Alignment is measured in straight ahead gaze (Step One), right and left gaze (Step Two) and in straight ahead gaze with the head tilted right and then left (Step Three).



Step 1) small right hyperdeviation

Step 2) large right hyperdeviation in left gaze

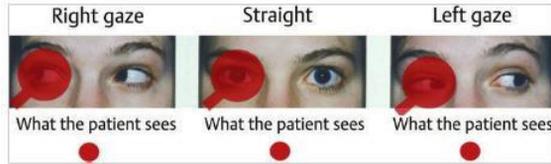
Step 3) in head tilted to the right the hyperdeviation is maximal

RED GLASS TEST

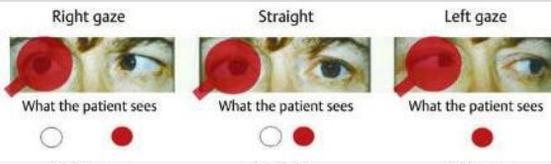
By convention the red filter is placed in front of the right eye

The patient has to report the location of two different-colored lights..

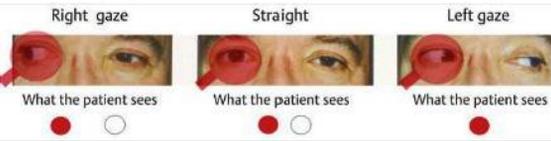
The misalignment is described as one white and one red light. The extent of separation of images horizontally and vertically is determined.



orthophoric

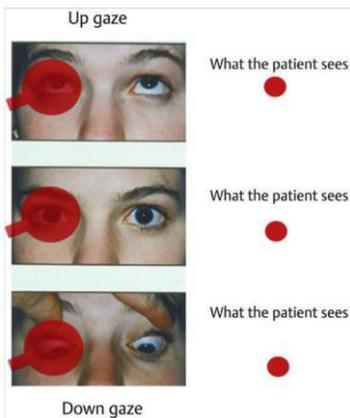


Right **abduction** deficit

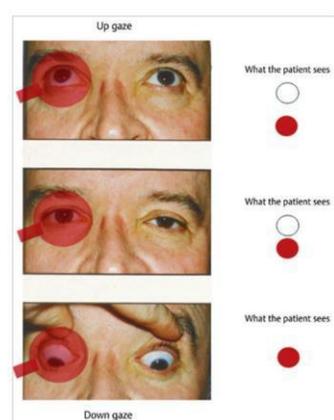


Left **adduction** deficit

Red Filter in Vertical Gaze



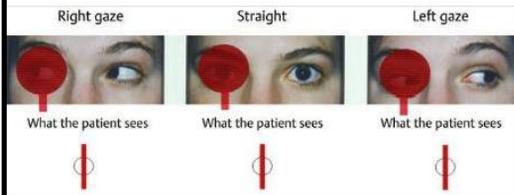
orthophoric



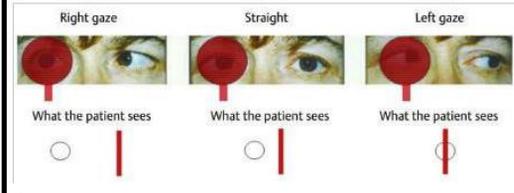
right hypertropia

The Maddox rod

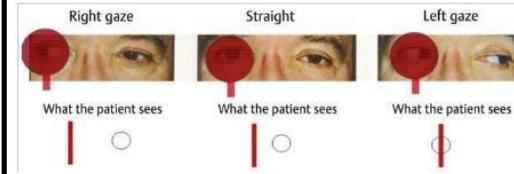
transparent red plastic cylinders. When placed between a light source and the eye, it produces an image of a straight red line oriented at 90 degrees to the axis of the cylinders.



Orthophoric

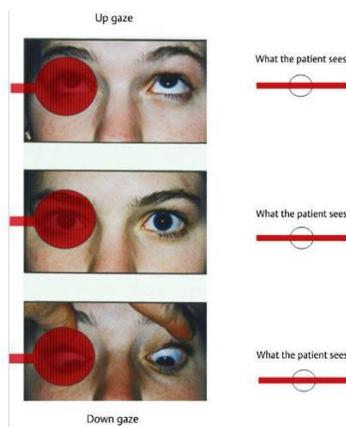


Right **abduction** deficit
ESOTROPIA = UNCROSSED DIPLOPIA

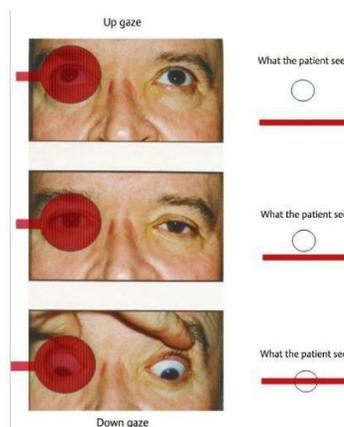


Left **adduction** deficit
EXOTROPIA = CROSSED DIPLOPIA

Maddox Rod in Vertical Misalignment



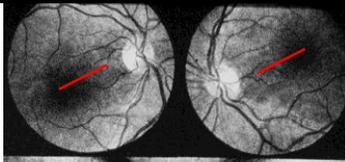
Orthophoric



Right hypertropia

A special case: SKEW

Counterroll



Skew



Patients with cerebellar ataxia may show
Ocular Tilt Reaction (OTR) -acute
imbalance of static utricular righting
reflexes

Head Tilt



Halmagyi, 1979

Diplopia in ataxia: Skews vs Superior Oblique Palsies



David Zee's collection

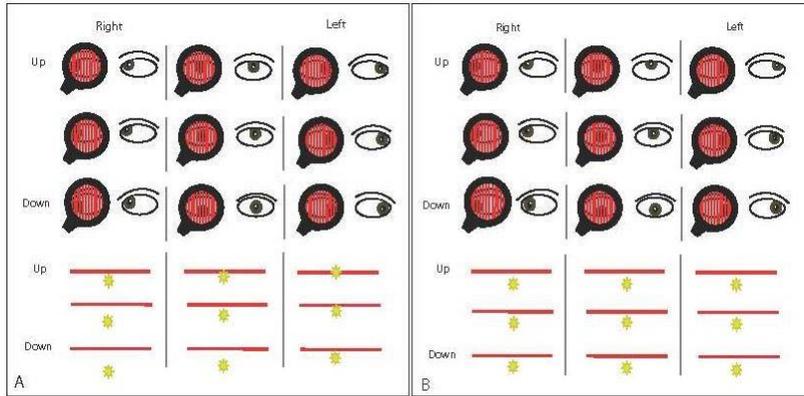
Left, Right, Up, Down Gaze



Head tilt test



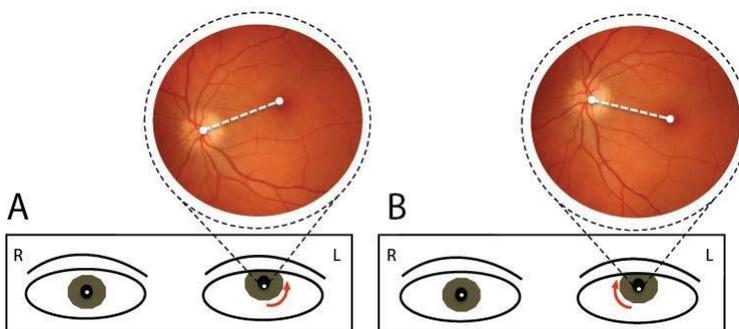
Superior Oblique Palsy versus Skew Deviation



SOP
NONcomitant, paralytic,
deviation changes with orbital
position

Skew
Comitant, nonparalytic,
deviation independent of
orbital position

Ocular fundus torsion



Skew
Higher eye
intorted

SOP
Higher eye
extorted

Differentiating unilateral superior oblique palsy (SOP) from Skew

- Skews are more comitant (less change with eye position in the orbit).
- The higher eye is INTorted with a skew and EXTorted with a SOP.
- Skews may diminish with going from upright to supine.
- The vertical deviation of SOP changes with lateral head tilt (Bielschowsky).
- SOP shows a V pattern esodeviation (more eso on down gaze due to loss of abducting action of SO muscle)

III Cranial Nerve Palsy

Signs Symptoms

- Unilateral ptosis (or bilateral: nuclear)
- Diplopia when manually open the lid
- Position is Down and Out: Non comitant exotropic hypotropic eye position
- Limitation or absence of elevation depression and adduction
- Pupil may be dilated and no reactive to the light
- Often patient is old and affected by hypertension diabetes



From the Stanford School of Medicine video collection

III CN Fascicular Lesions

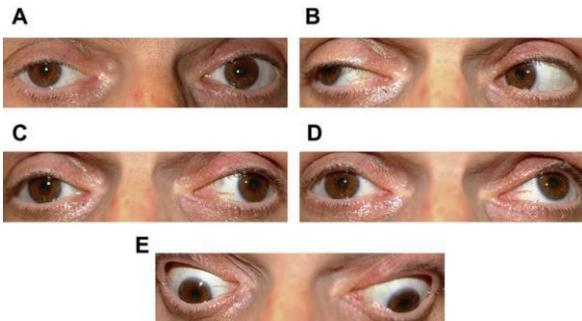


Claude S 54 yom right ptosis and limitation of vertical movements pupil spearing. MRI Infarction of the right mesencephalon involving III cn Fascicle and Superior cerebellar peduncle

- **Nothnangel S** (superior cerebellar peduncle) ipsilateral cerebellar ataxia
- **Benedict S** (red nucleus) ipsilateral III n contralateral hemytremor
- **Weber S** (cerebral peduncle) ipasilateral III contralateral hemiparesis
- **Claude S** (superior cerebellar Peduncle red nucleus) contralataeral cerebellar ataxia and limb tremor

Infiltrative-Ischemic-Inflammatory

III CN Troncular Lesions



Uncal herniation
(dilated and fixed pupil)

ICA Aneurism (pupil involvement)

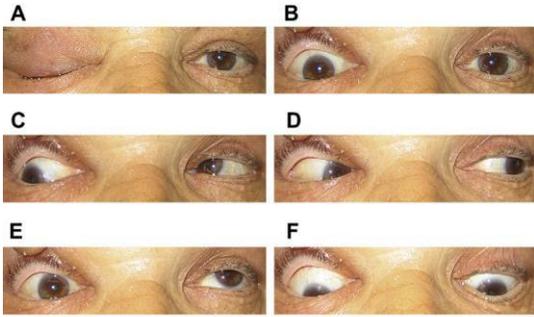
Cavernous Sinus Syndrome (pupil usually spared)

Orbital Apex Syndrome (superior and inferior division)

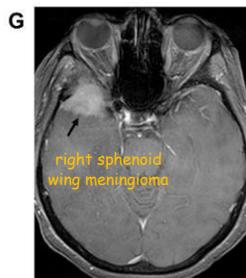
55 YO man diabetes and hypertension. RE III cn palsy Pupil spearing

Pupil Sparing **Ischemic**
Pupil Involvement **Compressive**

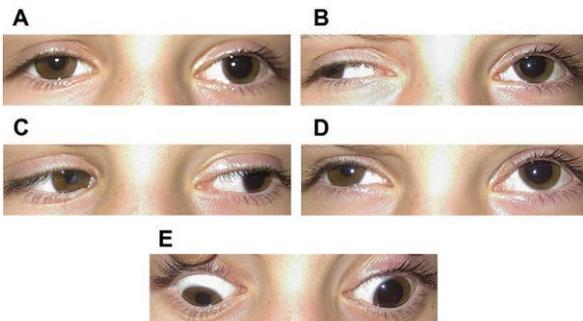
III CN Superior Division Palsy



63-year-old woman with right superior divisional third nerve palsy following resection of right sphenoid wing meningioma, causing isolated dysfunction of the levator palpebrae and superior rectus muscles.



III cn Inferior Division Palsy

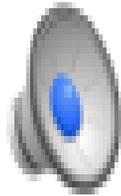


An 8-year-old girl with postviral left inferior divisional III cn palsy.

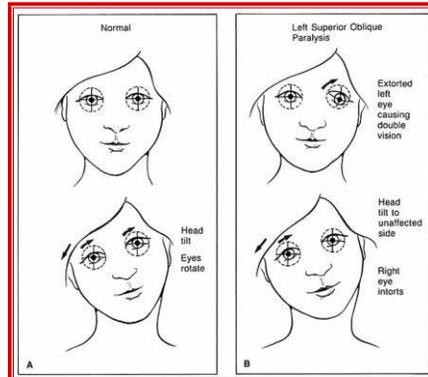
MR-IR and PUPIL involvement

IV Cranial Nerve Palsy

The only crossed nerve !!!



Midbrain



Vertical diplopia
 Eye extortion
 Head tilting toward the unaffected side
 Weakness in depression and abduction

NUCLEAR

- Almost never isolated, if complete: downward gaze palsy with associated midbrain signs.
MSS, Infarction, Infiltrative, Infectious

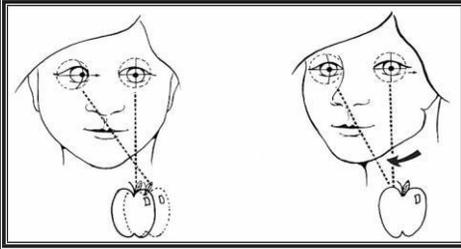
FASCICULAR

- The contralateral eye. Often traumatic or post infective

TRONCULAR

- Long course and thin caliber.
Trauma, infections, venous sinus syndrome

VI Cranial Nerve Palsy



•Loss of Abduction Toward the side of the lesion

•Double vision even in primary position that worsen looking toward the direction of action of the paretic muscle

•Head turned in the opposite direction



Horizontal diplopia grater on leftward gaze

35 yo man with acute onset horizontal diplopia. Large Cardiac Right to Left Shunt

A



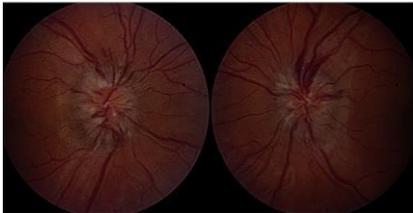
B



C



D



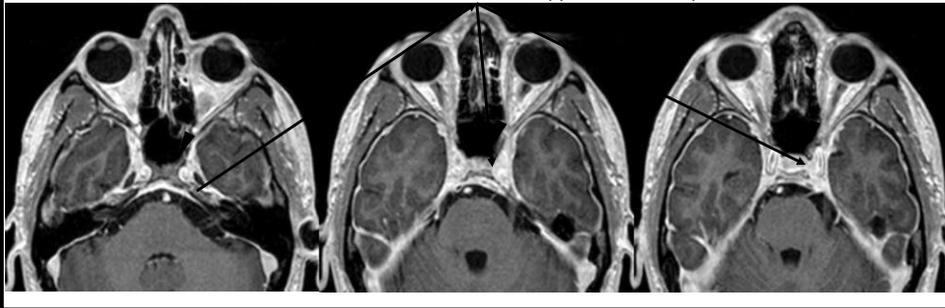
VI CN palsy in Intracranial Hypertension

A 29-year-old woman with left sixth nerve palsy due to pseudotumor cerebri following pregnancy. Brain MRI, MR venogram, and CSF constituents were normal.



M, 27 y-o, T-ALL presenting headache, and horizontal diplopia due to left VI cranial nerve palsy 5 days after diagnostic and therapeutic lumbar puncture

Arrowheads: prominent left retroclival dural thickening
Arrows: left VI cranial nerve showing gadolinium-enhancement in its medium and upper cisternal portions



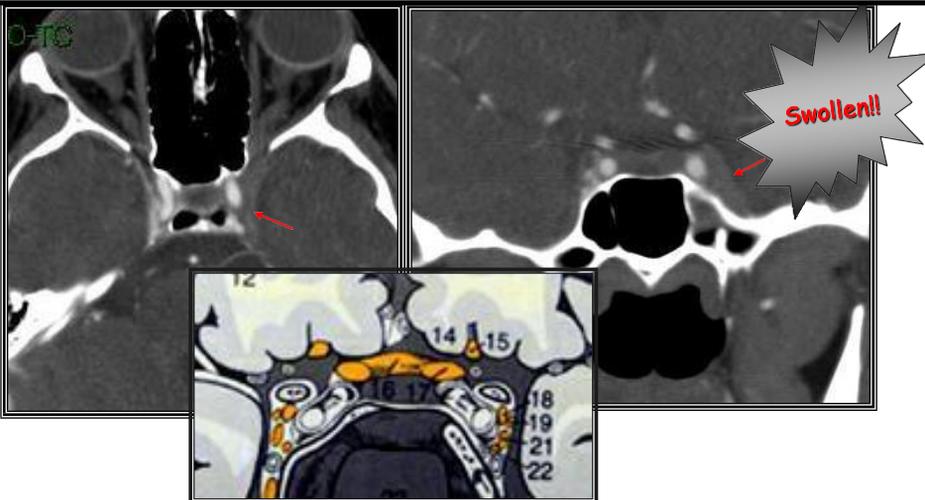
More than One Cranial Nerve Involvement

Male 35 y-o in good health



- **Acute Onset: 2 weeks**
- **Acute Pain:** orbital and temporal (left)
- **Deficit in adduction depression and elevation**
- Since **10 days** complete ptosis
- **Mild Proptosis**
- **V nerve (I and II)**
- **abduction deficit.**

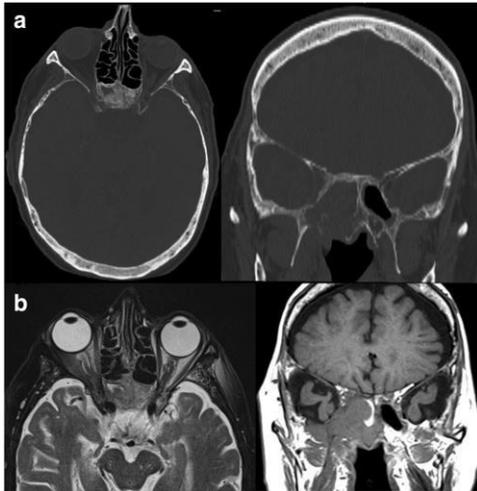
What do you Think



CT Scan

Venous Phase

Cavernous Sinus Thrombosis



a 78 yo man experienced acute painless H diplopia and right partial ptosis (2y history of MM responsive to specific therapy) chronic cerebrovascular disease, hypertension.

Neurological Examination :

EOM Right ptosis and functional limitation of the superior rectus and ipsilateral abducens nerve palsy

Vision was normal
Pupils symmetric and normally reactive to light and near

Fundoscopy retinal signs of hypertension

Where the lesion is ? Which kind of lesion?

Neuromuscular Junction Diseases

- 1) Myasthenia Gravis postsynaptic (pupil Spared)
- 2) Lambert Eaton presynaptic
- 3) Botulism (pupil Involvement)

OCULAR SIGNS in MG

1. Variability of muscle involvement and range of limitation
2. Fatigability
3. Cogan's Lid twitch= excessive twitch of the upper lid upon return of the eyes to central position after sustained down gaze.
4. Enhanced Ptosis: following the Hering law of equal innervation, the sign consists of development of ptosis in a less or non paretic eyelid upon the manual elevation of the more ptotic lid.

Diagnostic Bedside Testing

1. Ice and Rest test
2. Edrophonium Chloride or Tensilon Test (a reversible Acetylcholinesterase inhibitor that slow breakdown of Ach in the Neuromuscular Junction synaptic cleft, thereby improving neuromuscular transmission.

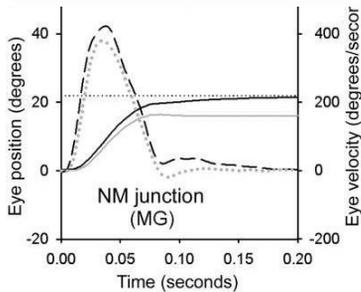


ICE TEST



MG may mimic any pupil spearing eye movement deficit

64 yo with horizontal diplopia
Pseudo VI cn Palsy



A Serra and J Leigh Archive

40 YO with intermittent diplopia
initially diagnosed with INO



1. Large saccades followed by dissociated NY
2. Abducting saccades faster than adducting
3. Adducting saccades smaller and with onward drift
4. Initial high speed of saccade

65 YO man complained rapidly progressive facial weakness, diplopia and ptosis, fatigue, dysphagia



Anti MUSK positivity. In this form facial muscles are primarily affected. This patient had a good response to 5 days of plasmapheresis therapy

Extraocular Muscle Anatomy

Orbital layer :

- Fast myofibrills
- SIFs innervation 80%
- ATPase activity
- Oxidative capacity
- Mitochondria
- Resistant to fatigue



Keep the tone of the extraocular muscles in each position

Global layer:

- Fast myofibrills
- SIFs innervation 80%
- ATPase activity
- Oxidative capacity
- Mitochondria
- Resistant to fatigue



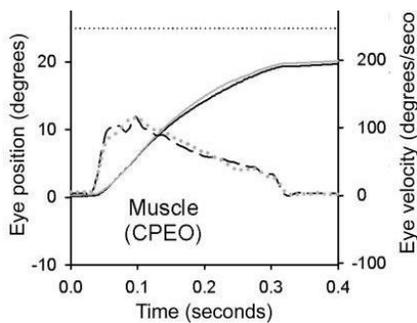
Activated during saccades



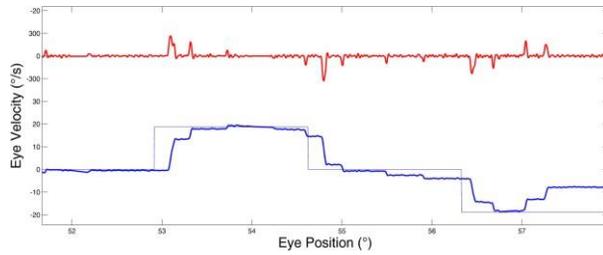
-Scott AB, Collins CC. Division of labor in human extraocular muscle. Arch Ophthalmol 90, 319-322, 1973

Chronic Progressive External Ophthalmoplegia CPEO

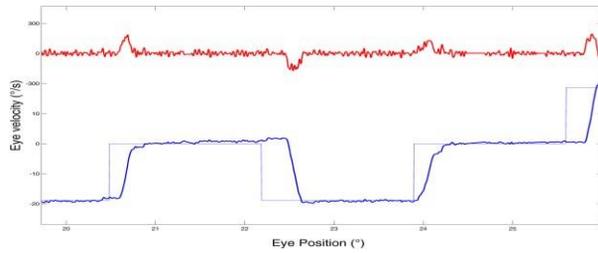
- Nuclear and mitochondrial DNA mutations
- Ptosis
- Slow and hypometric saccades
- Limitation of the range of eye movements H/V
- No diplopia
- RRF at muscle biopsy



Saccades MG vs CPEO



MG



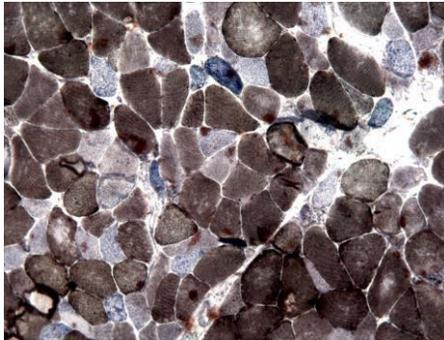
CPEO

Kearns-Saure Syndrome

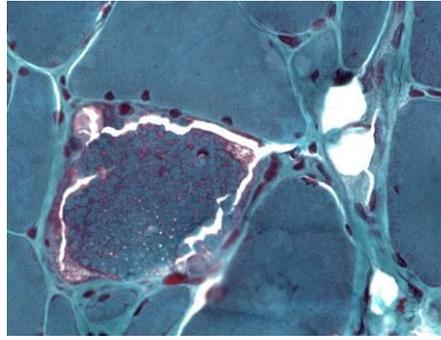
CPEO early onset
Pigmented retinopathy
Heart block
Hearing loss
Cranial muscle weakness
Diabetes
Peripheral neuropathy
Cerebellar ataxia
RRFs



Muscle biopsy in a mitochondrial myopathy



Modified Gomori Staining
Ragged red fibers

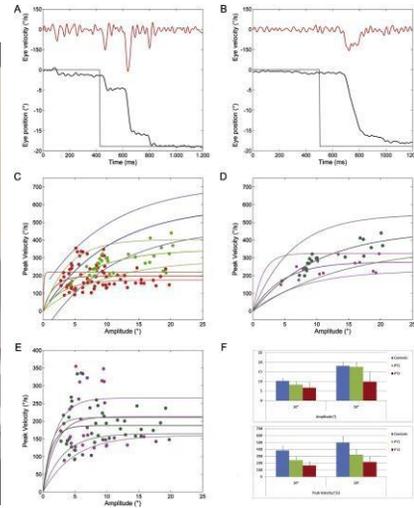


Cox-sdh staining high
percentage of cox negative
fibers

Mitochondrial Neurogastrointestinal Encephalomyopathy (MNGIE)

- Autosomal recessive disease
- Deletions and depletion of mitochondrial (mt) DNA in skeletal muscle
- **Gene ECGF I** (chromosome 22) encoding **Tyridine phosphorylase (TP)**.
- **Clinical manifestations** : external ophthalmoplegia ,gastrointestinal dysmotility, cachexia, anemia leucoencephalopathy, peripheral neuropathy .
- **Onset** before age 20years.
- **Bone marrow transplantation**

44 yo gastrointestinal dismotility, cachexia (Body Max Index 14,6) and anemia, increased blood levels of piruvate and lactate gait ataxia, severe muscle weakness, severe external ophthalmoplegia. abnormalities of mtDNA and mitochondrial respiratory chain enzymes in muscle biopsy



Saccades of two patients with MINGIE
adduction slower than abduction

Thyroid's Myopathy



Grave's disease is an autoimmune disorder

Bilateral asymmetric

Exophthalmos

Chemosis

Lid retraction

Diplopia

Loss of vision

MR and IR most affected

Surgical decompression of orbital irradiatio

Functional Eye Movement Abnormalities

7 YO Girl suddenly started with very rapid horizontal oscillations and reading problems.



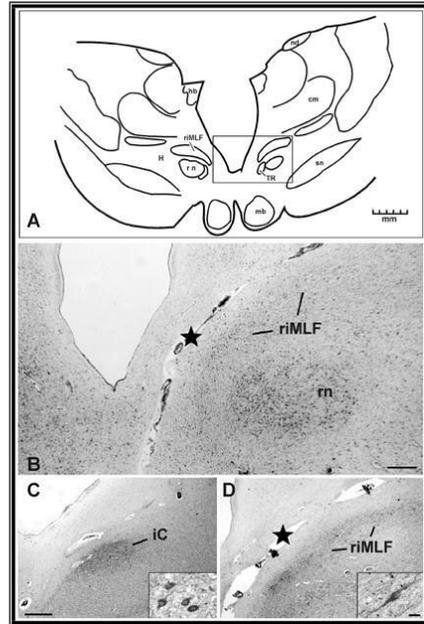
11 YO girl presenting with Voluntary tonic gaze deviations



Thank you for your attention

Anatomy

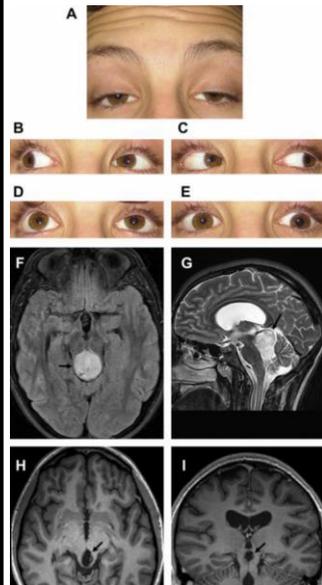
- Nucleus dorsal mesencephalon
- Fasciculus in the brainstem parenchyma
- Nerve in the subarachnoid space; cavernous sinus; orbital fissure: sup inf division



III Cranial Nerve (Oculomotor)

Nuclear

*Dorsal mesencephalon. Isolated lesions extremely rare!!
Usually associated with other neurological signs*



- Bilateral Ptosis
- Bilateral SR Paresis
- Pupil Light and Near