

PUPILLARY PERILS FOR THE PRIMARY CARE PRACTITIONER

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OBJECTIVES

- Review neuroanatomical pathways
- Review pupil testing methods
- DDx of pupillary disorders

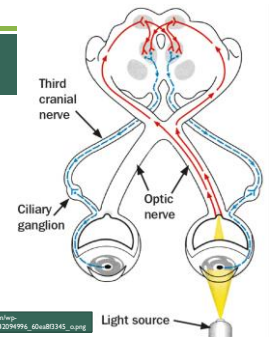


NEURO-ANATOMICAL PUPIL PATHWAYS



AFFERENT PUPILLARY PATHWAY

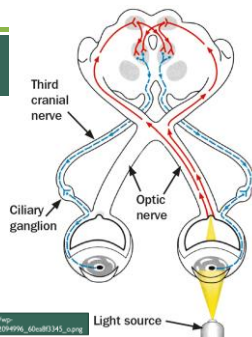
- Retinal ganglion cells send light information back through CN II (optic nerve)
- Decussate at chiasm, continue through optic tracts
 - Pupil fibers leave ~3/4 of the way back before LGN
 - ~80% go to LGN, 20% to pretectal nucleus
- Hemidecussate in pretectal nucleus
- Afferent pathway terminates at EW nucleus



http://i160131.gdimages.com/wp-content/uploads/2013/04/9442094996_60aa80345_c.jpg

PARASYMPATHETIC EFFERENT PATHWAY

- Begins in the EW nucleus
- Fibers travel through CN III
 - Inferior division of oculomotor nerve
- Synapse in ciliary ganglion
- Post-synaptic fibers enter globe via short ciliary nerves



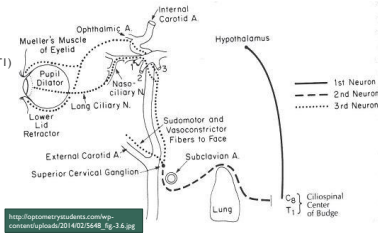
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PARASYMPATHETIC EFFERENT PATHWAY: POINTS OF INTEREST

- The 2nd order neuron (after synapse in ciliary ganglion) holds ~30 near response fibers for every light response fiber
 - i.e. The near response is MUCH stronger than the light response (30:1 ratio)
 - ~97% of parasympathetic axons go to accommodation
- There is no instance where near motor response is affected when light is not affected

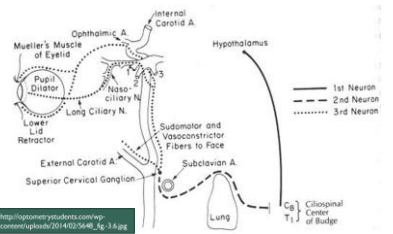
SYMPATHETIC PUPILLARY PATHWAY

- 1st order
 - Posterior hypothalamus
 - Ciliospinal center of Budge (C8-T1)
- 2nd order
 - Ciliospinal center of Budge
 - Superior Cervical Ganglion
- 3rd order
 - Superior Cervical Ganglion
 - Dilator muscle of iris



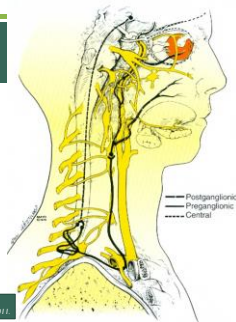
SYMPATHETIC PATHWAY: POINTS OF INTEREST

- 3rd order neurons run with ICA
 - Sympathetic pathway travels through cavernous sinus
- Bifurcation of ECA and ICA
 - Fibers for eye and lid follow ICA
 - Fibers for facial sweating follow ECA



SYMPATHETIC PATHWAY: POINTS OF INTEREST

- 2nd order neurons run along the surface of the apex of the lung and can be affected by Pancoast tumor
- The cervical chain of lymph nodes run through the neck near the sympathetic chain
- Lymph node/neck surgery may damage those sympathetic fibers and give rise to Horner's syndrome



Bernignoni, L. Clinical Anatomy and Physiology of the Visual System, 3rd ed. 2011.

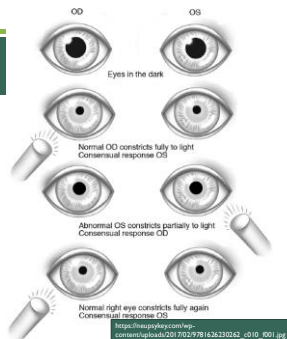
KEEPING MY EYES OPEN



PUPIL EVALUATION

PUPIL EVALUATION

- Size/Anisocoria
- Direct and consensual response
- Near reaction
- RAPD/Reverse RAPD



https://www.youtube.com/watch?v=.../4262310242_c010_0001.jpg

DDX OF PUPILLARY DEFECTS



DDX OF PUPILLARY DEFECTS

- Anisocoria
 - Essential Anisocoria
 - Fixed Pupil
- Light-Near Dissociation
 - Argyll-Robertson Pupil
 - Dorsal Midbrain Syndrome (Parinaud's)
- Afferent Pupillary Defects
 - Efferent Pupillary Defects
 - Adie's Tonic Pupil
 - Horner's Syndrome
 - CN III Palsy (w/ pupil involvement)

ANISOCORIA

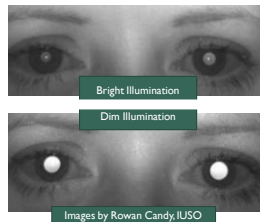
- Normal or physiological variant
 - Can be episodic
 - Can switch between eyes
- Disturbance in parasympathetic or sympathetic pathways
- Disturbance in iris itself



<https://i.stabovision.com/conditions/2017/anisocoria-bowie-1200x632.jpg>

ESSENTIAL ANISOCORIA

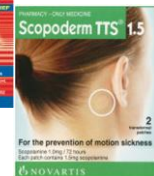
- AKA "physiological" or "benign" anisocoria
- ~20% of normal population
- More obvious when pupils are small
- Inequality is the same in ALL lighting conditions
- May be episodic or switch sides



Images by Rowan Candy, IUISO

FIXED PUPIL

- No rxn to light or near
- Possible etiologies:
 - Pharmacologic (reduced near VA)
 - Trauma or inflammatory
 - Blunt trauma (traumatic mydriasis)
 - Posterior synechia
 - Acute angle closure glaucoma
 - Structural abnormalities
 - Adie's tonic pupil
 - Drugs



FIXED PUPIL: DIAGNOSIS

- 1% pilocarpine will constrict a compressive or tonic pupil, but not all pharmacologically induce pupils
- With any pharmacological testing, instill drops in both eyes to compare reaction between eyes



AFFERENT PUPILLARY DEFECTS – APD OR RAPD

- Impaired function of sensory retina or optic nerve
 - Unilateral or Asymmetrical
- Less stimulation is received by EW nucleus when light is directed to affected eye
- Diagnosed by swinging flashlight test
 - Look at direct/consensual reaction
 - "Reverse" RAPD
- Graded on I-4 scale
- Measured with neutral density filter over "better" eye

RAPD VIDEO: RIGHT EYE

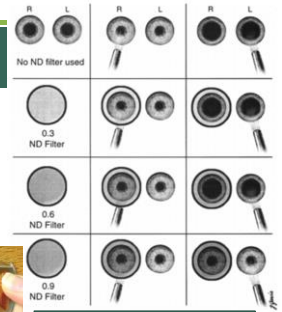


Video Credit: <https://www.youtube.com/watch?v=...>

QUANTIFICATION OF RAPD

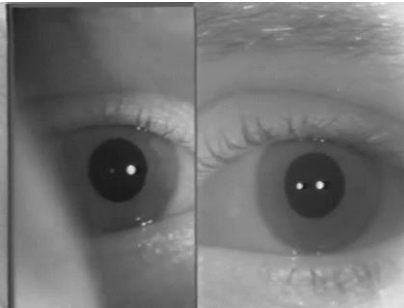
- ND filters in 0.3 log unit steps
- Place over unaffected eye
- Perform swinging flashlight test until defect disappears/reverses
- Re-"bleach" eyes between each test

- Can also be used as "RAPD Double-Check"



<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3080071/BHL-NOVELAC/SOPFA11972/figure/F1933.pdf>

QUANTIFICATION OF RAPD



Video Credit: <https://www.youtube.com/watch?v=...>

RAPD: POSSIBLE ETIOLOGIES

- Optic Nerve Disease
 - Optic neuritis (90% past or present)
 - Ischemic optic neuropathy
 - Traumatic optic neuropathy
 - Compressive optic neuropathy
 - Optic Nerve Drusen
 - Asymmetric Glaucoma
- Retinal Disease
 - Retinal detachment or significant macular disease
 - CRAO
- Conditions that **DO NOT** cause RAPD
 - Refractive error/Amblyopia
 - Media opacities (corneal, lenticular, vitreal)
 - Malingering

LIGHT-NEAR DISSOCIATION

- Occurs when afferent fibers are disrupted in the pretectal nucleus
- Light response is diminished, near response is preserved
 - 30:1 ratio of near:light fibers
 - Near response bypasses pretectal; straight to EW nucleus
- Present with unequal mid-dilated pupils
 - Exception: Argyll-Robinson pupils

LND: POSSIBLE ETIOLOGIES

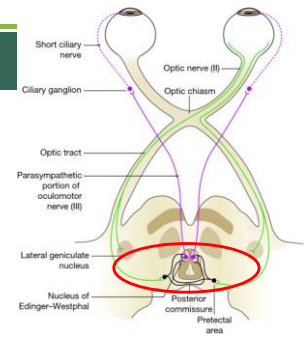
- Argyll-Robertson pupil
- Dorsal Midbrain Syndrome (aka Parinaud's Syndrome)
- Encephalitis/meningitis
- Demyelination
- Pretectal lesions (e.g. Pineal gland tumor)
- Diabetes
- Aberrant regeneration of CN III
- Bilateral afferent disease

LND: ARGYLL-ROBERTSON PUPIL

- Bilateral, asymmetric miosis
- Often irregular pupils
- Respond poorly to dilating agents
- Light-near dissociation
 - Virtually no response to light
 - Observable response to near
- Normal VA
- Caused by lesion in midbrain
 - "Disconnect" between afferent and efferent limbs
- Neuro-syphilis
 - Labs: VDRL and FTA-Abs
 - Treated with Penicillin
- Neuro-sarcoidosis
- Multiple Sclerosis
- Diabetes - rare

LND: DORSAL MIDBRAIN SYNDROME

- AKA: Parinaud's Syndrome
- Damage to the dorsal midbrain
 - Pretectal nucleus
 - Posterior commissure
 - Superior colliculus
- Triad of symptoms
 - LND
 - Convergence-retraction nystagmus
 - Limited up-gaze



ADIE'S TONIC PUPIL

- LND (mild)
 - Light reaction is poor or absent
 - Accommodation is slow and tonic
 - Can mimic AR when bilateral
- Slow re-dilation after accommodation
- Benign lesion of ciliary ganglion resulting in denervation of iris sphincter and ciliary body
- Presumed viral/infectious etiology

ADIE'S TONIC PUPIL

- Prevalence is ~2 per 100 people
- Female > Male (2.5 : 1)
- 2nd to 4th decade
- Unilateral 80%
- 90% have diminished or absent deep tendon reflexes
 - Particular knee or ankle

ADIE'S TONIC PUPIL

- Postganglionic denervation
 - Areas of sectoral paresis of iris sphincter and ciliary body
 - Contractions of parts of sphincter cause vermicular or "worm-like" contraction of iris border
- Abberant re-innervation
 - Resprouting of axons from damaged ciliary ganglion
 - Causes pupil to become small, even in dim light

DDX OF OTHER DILATED NONREACTIVE PUPILS

- Adie's has cholinergic super sensitivity
 - I.e. hypersensitive to weak cholinergic or parasympathomimetic agents
- 0.125% pilocarpine (8:1 saline: 1% pilo)
 - Adie's pupil will constrict
 - Normal pupil will not constrict
- 1% pilocarpine
 - Normal, CN III palsy, and Adie's will constrict
 - Pharmacologically dilated pupil will not constrict



<https://iStock.com/juniorcorle>

HORNER'S SYNDROME

- Lesion is in sympathetic pathway
- Produces miosis of affected eye
- Most notable in dim illumination
- Normal near and light reaction
- Unilateral ptosis and upsidetdown ptosis
 - Loss of Müller's muscle and loss of muscle tone



DIAGNOSIS OF HORNER'S SYNDROME

4 or 10% Cocaine

- Requires functional sympathetic pathway
- Dilates pupil by blocking reuptake of Norepinephrine
 - Will not dilate a Horner's Pupil!
- Only confirms Horner's; does not localize lesion

0.5% Apraclonidine

- α_2 adrenergic agonist
- Stimulates iris dilator muscle with denervation super sensitivity
 - Dilates a Horner's pupil, will not dilate normal pupil
- Reversal of anisocoria is a (+)ve test for Horner's Syndrome
- Only confirms Horner's' does not localize lesion

LOCALIZATION OF LESION

1% Hydroxyamphetamine

- Stimulates release of norepinephrine into synaptic space on dilator muscle
 - Must have intact 3rd order neuron
- Dilation: 1st or 2nd order (preganglionic)
- No dilation: 3rd order (postganglionic)

1% Phenylephrine

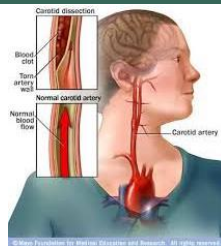
- 3:1 ratio of saline:2.5% phenylephrine
- Denervation sensitivity of 3rd order neuron
- Dilation: 3rd order (postganglionic)
- No dilation: 1st or 2nd order (preganglionic)

LOCALIZATION OF LESION

- There is no pharmacological test to differentiate between a 1st or 2nd order lesion
- First order lesions often produce other brainstem related symptoms
 - Facial pain
 - Ataxia
 - Hyperesthesia

HORNER'S SYNDROME: ETIOLOGY

- 1st order: Neoplasm, trauma, vertebral-basilar insufficiency
- 2nd order: Pancoast or thyroid tumor, neck trauma or surgery
- 3rd order: Cavernous sinus lesion, **dissecting carotid aneurysm**, cluster headaches
 - Consider dissecting carotid aneurysm in every painful Horner's patient
 - Medical emergency – ER referral
- Higher risk of malignancy with preganglionic lesions
- Testing: MRI, MRA, Chest CT



PUPIL INVOLVING CN III PALSY

- Pupil sparing CN III palsy is typically related to ischemic events (DM, HTN)
- Pupil involving CN III palsy tends to be due to compressive lesion (aneurysm, tumor)
 - 90% of aneurysmal CN III palsies have pupillary involvement
- Most common location of pupil involving CN III palsy – Posterior Communicating Artery
- Immediate MRI/MRA

