

PUPILLARY PERILS FOR THE PRIMARY CARE PRACTITIONER

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OBJECTIVES

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

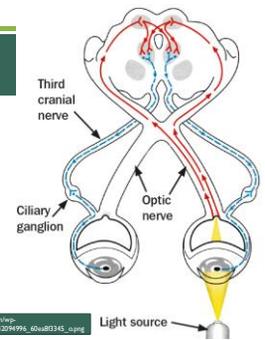


NEURO-ANATOMICAL PUPIL PATHWAYS



AFFERENT PUPILLARY PATHWAY

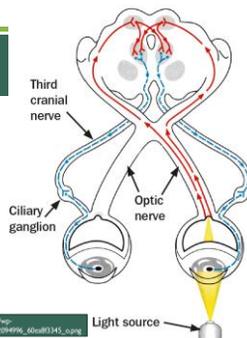
- Retinal ganglion cells send light information back through CN II (optic nerve)
- Decussate at chiasm, continue through optic tracts
 - Pupil fibers leave ~3/4 of the way back before LGN
 - ~80% go to LGN, 20% to pretectal nucleus
- Hemidecussate in pretectal nucleus
- Afferent pathway terminates at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



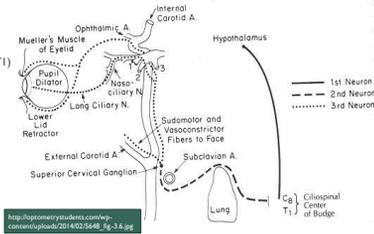
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PARASYMPATHETIC EFFERENT PATHWAY: POINTS OF INTEREST

- 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

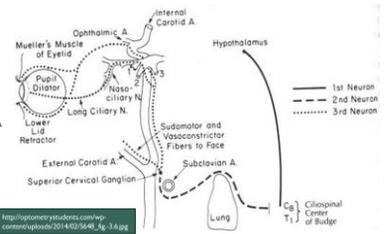
SYMPATHETIC PUPILLARY PATHWAY

- 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



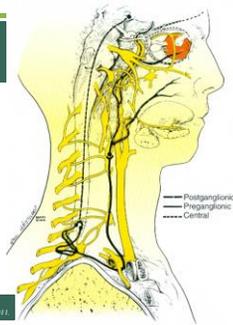
SYMPATHETIC PATHWAY: POINTS OF INTEREST

- 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



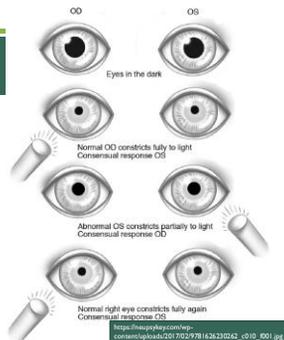
KEEPING MY EYES OPEN



PUPIL EVALUATION

PUPIL EVALUATION

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



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

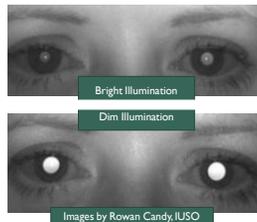
- Normal or physiological variant
 - Can be episodic
 - Can switch between eyes
- Disturbance in parasympathetic or sympathetic pathways
- Disturbance in iris itself



<https://i.stabovision.com/conditions/2017/anisocoria-bowie-1200x800.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

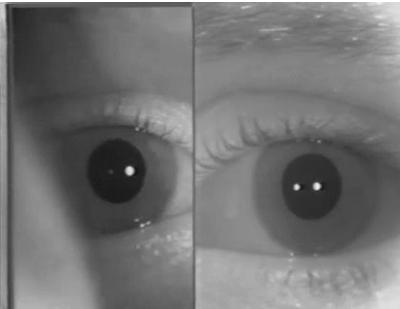
- ND filters in 0.3 log unit steps
- Place over unaffected eye
- Perform swinging flashlight test until defect disappears/reverses
- Re-"bleach" eyes between each test

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

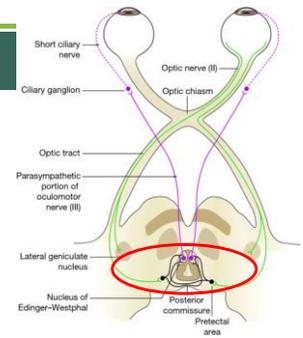
- Argyll-Robertson pupil
- Dorsal Midbrain Syndrome (aka Parinaud's Syndrome)
- Encephalitis/meningitis
- Demyelination
- Pretectal lesions (e.g. Pineal gland tumor)
- Diabetes
- Aberrant regeneration of CN III
- Bilateral afferent disease

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

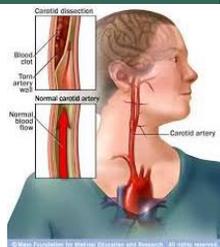
- 3:1 ratio of saline:2.5% phenylephrine
- Denervation sensitivity of 3rd order neuron
- Dilation: 3rd order (postganglionic)
- No dilation: 1st or 2nd order (preganglionic)

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

