What if?... The Pupil Showed This

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Weill Cornell Medical College

2

We have no

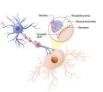
relevant to this

presentation

financial disclosures

What are we really covering?

- Anatomy
- Neurotransmitters
- Autonomic nervous system



Goal: you should be able to

- Describe the autonomic nervous system (ANS)
- Sympathetic nervous system (SNS)
- Parasympathetic nervous system (PNS)





4

you should be able to

• Give an overview of the pupil pathway • Differentiate Afferent from Efferent pathways







Goal: You should be able to

Describe how location and local structures directs your differential diagnosis

"perilous pupil" tailored to the findings and location

6



• VITAMIN

- · Vascular: aneurysm, malformation
- Infectious: Syphilis, TB
- Tumor: anything taking up space
- Anatomic: variation from the norm
- Metabolic: Thyroid
- Inflammatory: Sarcoid
- · Neoplastic: primary or metastatic

To understand neural pathways, simplify...

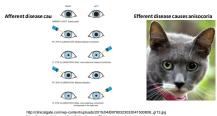
- Stimulus (light) is received by the retina
- Retina transmits message to brain by
- "Relay station" between neurons is a synapse

 Afferent neurons: eye to brain
- Efferent pathway: brain to end organ Iris sphincter
 Extra-ocular muscles



9

Afferent, Efferent: 2 different pathways



If you find afferent and efferent, the patient has TWO lesions

Repeat your pupil exam

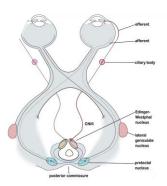


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8

Afferent system = APD

- Remember the Chiasm
- Prechiasmal Ipsilateral
- Post-chiasmal APD
- Contralateral
- 53% of fibers cross



Two types of Afferent fibers

- Vision fibers
- Pupil fibers



11

Afferents



Vision fibers

Synapse: lateral geniculate nucleus (LGN)



Pupil fibers

Bypass the LGN without synapse Synapse first in midbrain (pretectal nucleus)

Synapse again <u>bilaterally</u>

• Edinger-Westphal nuclei; CNIII

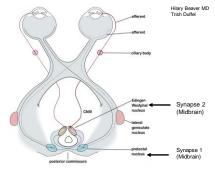
• Neuron between these synapses

After the interneuron: Efferent fibers

- Bilateral post-synaptic fibers return to both eyes
- Same impulse sent to both pupils
 Explains the equal direct and consensual re
- Neural impulse causes pupil response



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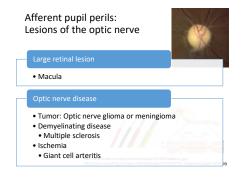


Afferent disease: sites for pupil perils

- Interruption of impulse from retina to midbrain
- Damage causes afferent pupillary defect (APD)
 - Large retinal lesion
 - Lesion of optic nerves, optic tracts
- Lesion of isolated pupil fibers all the way to midbrain
- May retain good vision or have vision loss
- RAPD not covered in PERRLA!
- You must test for and document relative afferent pupillary defect (RAPD)

15 16

> 5mm 3mm No P< APD 5mm 3mm No



18

3

Pupil perils: nerve compression



- Orbital disease
 - Graves disease
- Tumors
- Brain tumors: malignant or benign
 - Meningioma
 - Frontal, olfactory groove, sphenoid ridge
 Foster-Kennedy Syndrome
 - Pituitary (apoplexy, tumor)







Courtesy of AG Lee, MD

Pupil perils: Inflammatory/infectious involvement to chiasm

Sarcoidosis



Courtesy of AG Lee, MD

19

The forgotten afferents

Optic tracts, Midbrain



The forgotten afferents

Optic tracts

20

- 53% pupil fibers cross (vs 47% = 6% difference)
- Unequal crossing = unequal tract innervation
 53% Tract lesion causes contralateral APD
- Post chiasmal lesion
- If Visual defect, then homonymous hemianopsia



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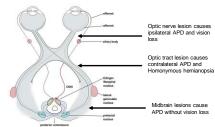
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The most forgotten pretectal afferents

- · Lesion as far back as the midbrain
 - Pupil fibers don't synapse until midbrain
 Presynaptic damage causes APD
- Pupil fibers have separated from vision fibers
 Bypass the LGN
 - Therefore no associated vision loss



Afferent pupillary defect anywhere along afferent pathway



Enough with the Afferents

On to the Efferents!

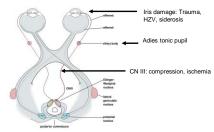


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Efferent disease Iris innervated by Autonomic Nervous System
 Constrictor muscle
 Parasympathetic fibers: midbrain to pupil Dilator muscle
 Sympathetics, covered later Present with anisocoria Patients have good vision, intact retinas and normal optic nerves (no RAPD)

26

Efferent pupillary defect = anisocoria



27

Pupil path autonomic nervous system

- You don't have to think for them to function • Autonomic nervous system works while you

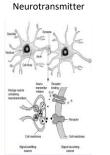
- Sympathetic nervous system (SNS)
- Parasympathetic nervous system (PNS)

- Activation (stimulation)
- Suppression (inhibition)

28

Components of the ANS

- Sympathetic nervous system
- Neurotransmitter: epinephrine, norepinephrine
- Ex.: Fight or flight response
- · Increased heart rate and blood pressure
- "Wide eyed with fright"- opens pupil and lid
- Parasympathetic nervous system
 Neurotransmitter: acetylcholine
 Ex.: Digestion
 Pupil constriction



Chemical released at synapse Passes the excitation from one nerve to another nerve or Runners passing baton

pubs.niaaa.nih.gov

29 30



Parasympathetics constrict pupil

- Sphincter muscle
- Contraction constricts pupil
- Purse string effect
- PNS defect = dilated pupil



Sympathetics dilate pupil

- Dilator muscle- like spokes on wheel
- Contraction dilates pupil
- SNS defect = small pupil





31 32



Applied science: Locate lesion using anisocoria

 Pinpoint which neuron by pharmacologic testing



33 34



Localize anisocoria by pupil responses: 3 choices

- Asymmetry equal in light and dark
- Asymmetry greater in dark
 One pupil cannot dilate
- Asymmetry greater in light
 One pupil cannot contract

Asymmetry equal in light and dark

• Physiologic or simple anisocoria
• 20% of normal people
• Benign, variable by day
• Example
• Dark: 5 mm OD, 4 mm OS
• Light: 4 mm OD, 3 mm OS



Patient presents with anisocoria: Localize by the pupil responses

- Asymmetry equal in light and dark
 Physiologic or simple anisocoria
- Asymmetry greater in dark Pupil cannot dilate
- Asymmetry greater in light

Asymmetry greater in dark: the little pupil is abnormal

- Pupil cannot dilate
- Dilator not being stimulated (SNS problem)
- Most marked immediately after lights out
 - Dilation lag



37 38

SNS does more then just pupils

- Elevates lid (Mueller's muscle)
- Dilates pupil
- Facial sweating
- Loss of these function = Horner syndrome



http://4.bp.blogspot.com/-M-gG_XF814/TzFbBPfYFJI/AAAAAAAAAAAAAnc/Axthh-it6N8/s16001Horners_syndrome.jpg

Don't forget upside down ptosis





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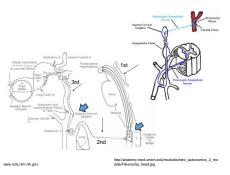


39



- First order neuron
 - Hypothalmus, runs down spinal column
 - Synapse in C7-T2 cord
- Second order neuron
 Leaves spine, ascend outside spine
 - Over lung apex
 - Synapse near jaw
 Superior cervical ganglion
- Third order neuron
 Within wall of carotid into skull





• External carotid- **sweat glands** of lower face Internal carotid- Into skull Sympathetic • Cavernous sinus- rides CN VI then third order • In orbit on ciliary nerves • Pupil dilator muscle • On ophthalmic artery branches
• Muller's muscle (lid) neuron Lower eyelid retractors • Frontal sweat glands



• Do not touch or drop the eye! • Makes subsequent testing unreliable • Cocaine 10% (Compounding pharmacy) • Prevents synaptic reuptake of norepinephrine Horner test Step • Iris dilator muscle • Excess norepinephrine floods iris dilator receptors Normal pupil dilates
 ****If SNS not functioning, no baseline release of norepinephrine so no dilation = Horner syndrome

• Postcocaine anisocoria > 1mm is Horner

45

Traditional: Step two

43

- Go home- you've had step one, which makes further same day testing
- Hydroxyamphetamine 1% (Compounding pharmacy)
 - Stimulates intact nerve to release norepinephrine
 - Released norepinephrine stimulates dilator muscle

 - If pupil dilates, then 3rd order nerve is intact
 Thus 3rd order not the problem
 Therefore is a 1st or 2nd order lesion

New kid on the block: apraclonidine (Iopidine)

• Iris receptors

44

46

- · Alpha 1: dilates
- Alpha 2: constricts
- Apraclonidine primarily alpha-2 agonist
 - Constricts normal pupils (glare post lasik)
 • Weak alpha-1 activity
- But.... Horner syndrome Denervation supersensitivity after 5-7 day

Denervation supersensitivity

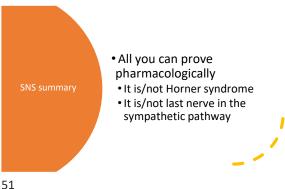
- Apraclonidine normally alpha-2 agonist
- Horner: denervation supersensitivity (α -1)
- Small pupil dilates (alpha-1)
 Ptotic lid elevates (alpha-1)
- Reversal of anisocoria
- Easy to obtain drop
 Easy to read result



BEFORE APRACLONIDINE DARK

Apracionidine test (inferior image) confirmed suspected diagnosis of Horner syndrome. González Martín-Moro et al. Horner Syndrome, a New Complication. J Oral Maxillofac Surg 2009.

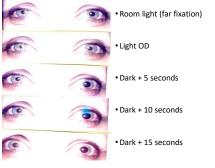
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30 year old WF presents with 4 months of anisocoria

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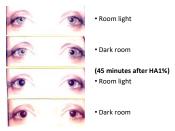
Saw chiropractor-resolved



1 hour after cocaine 10% • Room light Dark room • Mild ptosis, miosis, dilation lag, poor response to cocaine = Horner syndrome

53 54

Hydroxyamphetamine 1%

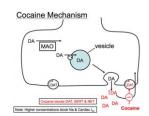


• DX: Preganglionic Horner (brachial plexus trauma)

How to remember the sympathetics?

- People like stimulation
 - Cocaine and amphetamine thus drugs of abuse
 - Stimulation dilates pupil (wide eyed
- with fright)

 Cocaine is a stimulant and will dilate pupils
 - Inhibits reuptake of neurotransmitter
 Sympathetic pathway must be intact
- Amphetamine forces release of neurotransmitter $\underline{\text{if}}$ third order neuron is intact



56

Where is the "Peril"? 3rd order neuron lesion



- Dissection (splitting apart) Blood within wall
- Post traumatic
- Roller coaster, whiplash, chiropractic manipulation
- . Stroke risk: Carotid occlusion or clot

57

59

55

Neck dissection, endarterectomy

Preganglionic "Perils"?

- 2nd order neuron lesion

 - Apical lung cancer (Panonast tumor)
 Beware Homer in snoken!
 Metastasis-Sentinel nodes in neck
 Chest lesion: aortic aneurysms, brachial plexus syndrome, surgery
- 1st order neuron lesion
- Brain and spinal cord- stroke, tumor, disc dx
 Rarely isolated as is tight space



58

Infant with Horner syndrome

- Congenital lesion along the sympathetic chain
- Birth trauma to brachial plexus
- · Associated with iris heterochromia
- Neuroblastoma
- Malignant but treatable childhood tumor
- "Baby gram" MRI scan of the sympathetic chain
- Chest lesion



Patient presents with anisocoria: Localize by the pupil responses

- Asymmetry equal in light and dark
 Physiologic or simple anisocori
- Asymmetry greater in dark
 Sympathetic N.S. defect
- Asymmetry greater in light
 Pupil cannot constrict

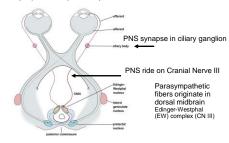
Anisocoria greater in light; Problem is the dilated pupil

- Pupil can't constrict- big pupil abnormal
 Sphincter muscle not getting stimulated
 Nerve defect: parasympathetic pathway
 - Iris muscle damage: slit lamp exam
- Differential diagnosis
 - Pupil involved CN III lesion
- Adie's tonic pupil
 Pharmacologic dilation



61

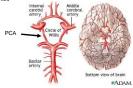
Parasympathetic pathway



62

PNS lesion: CN III lesion

- Ride on Cranial Nerve III
 - \bullet Ride on \boldsymbol{top} of third nerve
 - Nerve travels **below** posterior communicating artery
 Circle of Willis



CN III "perils"



- PNS Ride on top Cranial Nerve III
 Under posterior communicating artery (PCA)
 Aneurysm of the PCA compresses the top of CN III and PNS
- * Enter cavernous sinus
 * Tumor, vascular, inflammatory, or infectious disease
 * Enter orbit on inferior division CN III
- Tumor, inflammatory or infectious disease



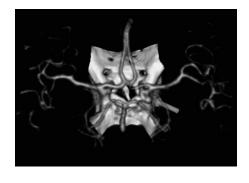
- Ride on inferior oblique division of CN III
- Innervates pupil sphincter

63

64



65 66



Unilateral dilated pupil: Is it a CN III palsy?



- Ptosis: Partial or complete
- Noed to lift the lid for drops?
 Stop and reassess
 Exotropia: Partial or complete
 Cannot adduct, elevate, depress
 Lateral rectus (CNVI) unopposed
 - - Out Down

s.wordpress.com/2012/07/down-and-out.jpg

67

Your role

- If you need to lift the lid to instill drops, Stop!
- Note pupil findings with abnormal motility
- The issue in diagnosing a dilated pupil
 Is this a pupil involved third nerve palsy???
- Life or death encounter

Pupil involved CN III

- MRI/CTA- emergent
- Arteriogram
- 1% risk of morbidity and mortality Neuroradiology/neurosurgery consult
- Coiling/clipping of aneurys



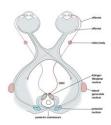
Courtesy of AG Lee, MD

12

70

Relax: more benign causes of pupil dilation

- Adie's tonic pupil
- Pharmacologic dilation
- · Iris muscle damage



Adie's tonic pupil PNS lesion at the ciliary ganglion Post viral, young female predominance
 4% bilateral Segmental iris de-innervation
 Parts of sphincter contract, iris writhes Vermiform movements Light-near dissociation Iris supersensitivity to neurotransmitter
 Acetylcholine receptors

72 73



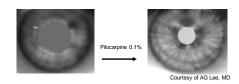
- Aneurysm of PCA compresses pupil fibers
- Associated with third nerve findings
 May be partial CN III, partial pupil
- Pupil is key to diagnosis
- Alternative diagnosis if pupil sparing, complete CN III (ischemic)
 Expanding PCA aneurysm ruptures

- 50% mortality
 50% severe neurologic damage

69

Look for vermiform movements

• Infared pupilometry: segmental transillumination defects of the pupil sphincter



74

Is the pupil supersensitive • Has this been there a long time? • Pilocarpine 1/8% (1/10%) • Normal pupil won't react • Adie's pupil will constrict Near response greater then light Supersensitivity to dilute pilocarpine Courtesy of AG Lee, MD

Other causes: Isolated dilated pupil

- Pharmacologic
- Inadvertent contamination
 - Scopolamine patch
 - Naturally occurring alkaloids
 Jimson weed
 - Angels trumpet
- Contralateral alpha agonist for glaucoma (Alphagan, Iopidine)
- Intentional dilation
 - Non-organic disease

Is the pupil pharmacologically dilated (had no response to pilo 1/8%)

• Pilocarpine 1%

75

77

79

- Normal pupil constricts
- Pharmacologically dilated pupil will not
- Clue:extreme dilation, suspect pharmacologic





76

Iris causes

- Trauma
- Sphincter rupture- pupil irregular
- Acute post-traumatic mydriasis
- Surgical: retinal laser, post cataract surgery
- Inflammation
- Posterior synechiae
- Iris atrophy
 - Herpetic eye disease
 - SimplexZoster



Traumatic mydriasis OS

Afferent summary

- Afferent disease: APD
- $\bullet\,\mbox{Impulse}$ blocked from retina to midbrain
- May have vision loss
 - Ipsilateral loss: large retinal lesion, optic nerve • Homonymous hemianopsia: optic tracts- LGN
- May have good vision
 - Even with lesions listed above
- Lesions posterior to LGNNot covered in PERRLA!
- Must test for afferent pupillary defect (APD)

Efferent summary: anisocoria

- Physiologic anisocoria
- Pupil asymmetry equal in light and dark
- Sympathetic lesion (Horner syndrome)
- Asymmetry greater in dark
- Anisocoria > 1 mm after cocaine 10%
- 3rd order neuron (postganglionic) damage •No dilation with hydroxyamphetamine 1%
- Beware with trauma, vasculopathic, or smokers
- Congenital- evaluate for neuroblastoma

Parasympathetic summary

- Ptosis: Stop!
- No drops or tonometry
- If you must lift lid- reassess



- Third nerve palsy
- Look carefully for partial palsy
 Dilating aneurysms are at risk for rupture

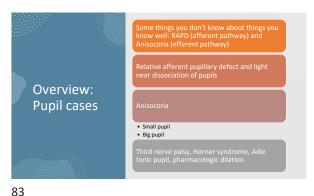


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Parasympathetics, continued

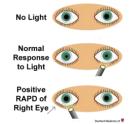
- Adie's tonic pupil
- Young women, post viral
- Vermiform movements
- 1/8 % pilocarpine supersensitivity
- Parasympathetic mimics
- $\bullet \ \, \text{Pupil damage: trauma, surgery, inflammation} \\$
- Pharmacologic (prove with pilocarpine 1%)
 - Accidental
- Intentional



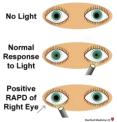


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Relative afferent pupillary defect (RAPD) OD: Which side is the lesion?



Relative afferent pupillary defect (RAPD) OD: Which pupil dilates with an RAPD OD?



84 85

How do we check RAPD in an ipsilateral pupil involved third nerve palsy?



https://www.atlasophthalmology.net/photo.jsf?node=5830&locale=en

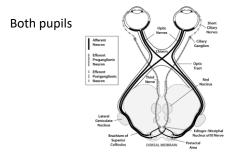
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Panel questions

- What would you ask?
- What would you do on exam?
- What tests or imaging would you do and when?
- Should you admit to hospital?
- What would make you admit?
- What is the treatment and prognosis?

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https://www.cambridge.org/core/books/abs/neuro dilation/ED4F21E059F6CB01FEF4645A5EBD470B

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Bilateral light near dissociation

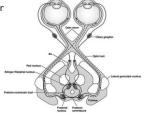




Panel questions

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Bilateral light near dissociation



https://www.cambridge.org/core/books/abs/neurologic-differential-diagnosis/pupil-dilation/ED4F21E059F6CB01FEF4645A5EBD470B

91

15

"PERRLA" ≠ NORMAL



Panel questions

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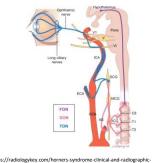
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Apraclonidine test (inferior image) confirmed suspected diagnosis of Horner syndrome. González Martín-Moro et al. Horner Syndrome, a New Complication. J Oral Maxillofac Surg 2009.

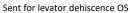


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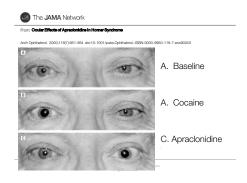


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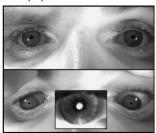








Bilateral small to pinpoint without tonic near OU



Panel questions

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98 99

Pilocarpine 1/10% and pilocarpine 1% do not constrict pupil



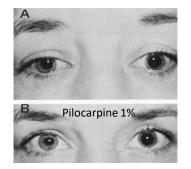


http://mmcneuro.wordpress.com/2013/02/

Panel questions

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100 101



What if....



102 103

Panel questions

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104



107

What if....



Panel questions

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106

Panel questions

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108

Panel questions

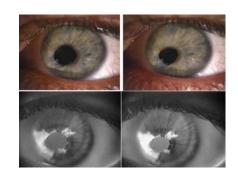
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109 110

What if....







111 112

Panel questions

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What if...



113 114

Panel questions

- What would you ask?
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Different days



115 116

Panel questions

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What if....



117 118

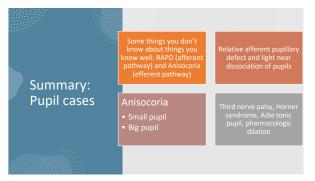
What if it was non-traumatic and there was a family history of scalloped pupil and amyloid?



Panel questions

- What would you ask?
- What would you do on exam?
- What tests or imaging would you do and when?
- Should you admit to hospital?
- What would make you admit?
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119 120



Thanks for your time & attention















122 123