Pupil Testing
Back to the Basics

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Financial Disclaimer

• Speaker for Shire Ophthalmic
Overview

- Pupil anatomy and physiology
- Pupil testing
- Commonly encountered pupil disorders and how to detect them
Why evaluate the pupils

One of few objective reflexes that detect and quantify abnormalities of the retina, optic nerve, optic chiasm, optic tract, midbrain, and/or peripheral nerves
Why evaluate the pupils

● Pupil abnormalities can:
  ○ Reveal serious neuro-ophthalmic and retinal disease
  ○ Help aid in diagnosis and management of many conditions
  ○ Should be incorporated into every optometric examination
Eye and Pupil Anatomy
Pupil Anatomy and Physiology

- Hole in center of iris

- *Involuntarily* controls how much light enters the eye
• Improves vision by preventing irregular refraction from peripheral cornea

• Allows passage of aqueous from posterior to anterior chamber
Pupil Anatomy and Physiology

- Iris contains 2 groups of smooth muscle
  - Sphincter pupillae → circularly oriented
  - Dilator pupillae → radially oriented
• Dim light → sympathetic superior cervical ganglion stimulated → constriction of radial dilator pupillae muscles → pupil gets bigger
Bright light → parasympathetic short ciliary nerve
innervated → constriction of circular sphincter
pupillae muscles → pupil gets smaller
Pupil Anatomy and Physiology

- Average pupil size in normal illumination ~3.5mm
  - Range 1.0 - 10.0 mm
    - <2mm considered mitotic
    - >7mm considered mydriatic
  - Decrease with age due to senile miosis
    - Higher rate of atrophy of dilator muscle vs. constrictor muscles
  - Difference of >0.4mm is clinically significant
Pupil Anatomy and Physiology

- In a normal pupil, amount of light entering the eye governs the size of the pupil

- Pupil size governed by
  - Amount of light entering the eye
  - Where patient is focusing
  - Mood
  - Drug use
Vocabulary Review

- Anisocoria - difference in pupil size between eyes
- Mydriasis - dilation of pupil
- Miosis - constriction of pupil
- Hippus - small constant changes in pupil size
- Afferent - signals going from the eye to the brain
- Efferent - signals going from the brain to the eye
- Bifurcation - divide into 2 equal branches
Vocabulary Review

- Light-Near Dissociation - pupil constricts to accommodation much more than to a light stimulus
- Afferent Pupil - pupil that responds poorly or not at all to a direct light but has a normal consensual response when light is shone into opposite eye
Pupillary Function
Pupil Anatomy and Physiology

- Pupil size is dependent on a balance between the sympathetic and parasympathetic innervation of the iris muscles.
Parasympathetic Innervation

- Controlled by the parasympathetic system:
  - Pupil’s response to light (miosis / light response)
  - Pupil’s response to how close things are (near response/constriction)
Afferent Pupillary Pathway

light impulse → retinal photoreceptors → optic nerve → optic chiasm (bifurcation of fibers) → optic tract
Afferent Pupillary Pathway

after optic tract, fibers break off to go to

- Lateral geniculate nucleus (90%) $\rightarrow$ visual cortex
- Hypothalamus $\rightarrow$ circadian rhythm
- Superior colliculus $\rightarrow$ saccades
- Pretectum $\rightarrow$ pupil
Afferent Pupillary Pathway

After optic tract, fibers break off to bilaterally stimulate the pretectal nuclei in the midbrain
Internuclear Pathway

pretectal nuclei → **bifurcate again** → Edinger-Westphal nuclei of the oculomotor nerve (CN III)
Efferent Pupillary Pathway

Edinger-Westphal nuclei of the oculomotor nerve (CN III) →
travel back towards orbit to the ciliary ganglion

- 97% innervate ciliary body → accommodation
- 3% innervate iris sphincter → pupil constriction
Pupillary Reaction to Near Response

- Fixation at near causes
  - Convergence
  - Accommodation
  - Pupillary constriction / Miosis
- If the direct pupillary light reaction is normal, the pupillary near response is always intact
Sympathetic Innervation

- **EFFERENT ONLY** system
  - Modulates pupil dilation via constriction of radial dilator muscles of iris
    - Less during drowsiness and sleep
      - During sleep pupils are partially constricted but still reactive to light
    - More during intense concentration, fright, and arousal
Sympathetic Innervation

- Hypothalamus 1st order neuron → descends through brainstem on each side (no bifurcation)
  → 1st synapse at ciliospinal center at C8 - T1 level
Sympathetic Innervation

- 2nd order neuron exit spinal cord → pass over apices of the lungs → synapse at superior cervical ganglion
- synapse at superior cervical ganglion → 3rd order neuron form a plexus around internal carotid artery → run along the internal carotid artery into the cavernous sinus
● Neurons traveling with ophthalmic artery → Mueller’s muscle (eyelid control)
● Neurons traveling with V1 → through long ciliary ganglion → iris dilator (mydriasis)
● Neurons traveling to sweat glands of face
Sympathetic Innervation

- Pupil dilation
- Eyelid elevation
- Facial sweating

Interruption of ocular sympathetic pathway at any level will result in
  - Miosis
  - Ptosis
  - Facial anhidrosis
Pupillary Testing
Pupil Testing

Can objectively measure integrity of afferent and efferent pupillary pathways
Pupil Testing

- Comprehensive and detailed case history is key to reach appropriate diagnosis
  - Recent contact with medications or agents that can affect pupil size
  - History of trauma
  - History of surgery
  - Ocular history of inflammation
  - Use old photos to evaluate possible onset and duration
Pupil Testing

- Purpose is to evaluate pupil:
  - Symmetrical Size (bright and dim)
  - Symmetrical Shape (round)
  - Similar Location (central)
  - Strength of *direct* pupillary light response compared to strength of *consensual* pupillary light response - the in the same eye
Pupil Testing

- Pupils should be round
  - Non-round pupillary shape can be due to

<table>
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<tr>
<th>Surgery</th>
<th>Iris atrophy from age</th>
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<td>Trauma</td>
<td>Ischemia</td>
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<td>Inflammation</td>
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<td>Posterior synechiae</td>
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Pupil Testing

● Pupils should be
  ○ Symmetrical in Size
    ■ Anisocoria - unequal size between pupils
  ● Physiologic anisocoria
    ○ 20% of people, benign
    ○ Difference in pupil diameter less than 1.0mm
    ○ Difference is same in dark and bright illumination
Pupil Testing

- Pupils should be Symmetrical
  - Pupillary inequality (anisocoria) usually results from an *iris innervation* (efferent) problem
    - But can also be due to trauma, inflammation, synechiae
  - Must check iris sphincter and iris dilator muscles - best in slit lamp
Pupil Testing

- Remove glasses
- Fixate on a non-accommodative distance target (or pupils constrict)
- Stand off to the side
- Observe pupils in light
- Then perform in dim room (able to visualize pupils)
Pupil Testing

- Measure using a mm ruler
  - Some new auto refractors
  - Pupillometer
    - Keep below visual axis to avoid accommodation and miosis
- Can use O-scope to simultaneously observe red reflexes-easier to evaluate symmetry of pupil size
Anisocoria worse in dim light
Anisocoria Testing - too small

- Small Pupil is the problem
  - Anisocoria greater in the dark (unable to dilate in the dark)
  - Impairment of oculo-sympathetic system
Anisocoria Testing - too small

- Small Pupil is the problem
  
  Pharmacologic
  
  Horner’s syndrome
  
  Argyll-Robertson
Anisocoria Testing - too small

- Pharmacologic constriction
  - Morphine, Heroin, Codeine, Oxycodone
    - usually bilateral
  - Cholinergic agonist / Anticholinesterase
    - Antipsychotics, antidepressants, MAOI
    - Clonidine and tetrahydrozoline (for HTN)
    - Pilocarpine, flea/tick control products
- Spray or patch
Anisocoria Testing - too small

- Horner’s Syndrome / Oculo-sympathetic paresis
  - Interruption along oculo-sympathetic pathway between hypothalamus (origin) and iris dilator (destination)
  - Classic triad - Ipsilateral
    - Unilateral ptosis
    - Miosis
    - Facial anhidrosis
Anisocoria Testing - too small

- Horner’s Syndrome / Oculo-sympathetic paresis
  - 33% are idiopathic
  - 4 - 13% are congenital
    - Iris heterochromia - lighter iris = affected eye
Anisocoria Testing - too small

- Horner’s Syndrome / Oculo-sympathetic paresis
- Acquired causes - central (1st order)
  - Stroke
  - Trauma to neck
  - Surgery
  - Aortic or carotid artery dissection
  - Otitis media
Anisocoria Testing - too small

- Horner’s Syndrome / Oculo-sympathetic paresis
- Acquired causes
  preganglionic (2nd order)
  - Pancoast tumor
  - Tuberculosis
  - Neck trauma or surgery
  - Thyroid surgery/neoplasm
Anisocoria Testing - too small

- Horner’s Syndrome / Oculo-sympathetic paresis
- Acquired causes - postganglionic (3rd order)
  - Trauma /surgery
  - Raeder’s syndrome
    - painful cluster migraine
  - Giant cell arteritis
  - Cavernous sinus/superior orbital fissure lesion
  - Nasopharyngeal carcinoma
Anisocoria Testing - too small

- Horner’s Syndrome / Oculo-sympathetic paresis

  Detailed history and diagnostic imaging can help with differential diagnosis
Anisocoria Testing - too small

- Horner’s Syndrome / Oculo-sympathetic paresis
  - Evaluation
    - Look for ‘dilation lag’ - Horner’s pupil will be delayed in its dilation in dim illumination
    - Anisocoria most evident 4-5 seconds after turn off lights and will equalize 10-15 seconds after
Anisocoria Testing - too small

- Horner’s Syndrome / Oculo-sympathetic paresis
  - In most instances, imaging takes precedence over localization via drops
    - Diplopia
    - Cranial nerve palsy
    - Numbness
    - Headache
    - Pain
Anisocoria Testing - too small

- Horner’s Syndrome / Oculo-sympathetic paresis
  - Pharmacologic testing can help localize lesion and aid in differential diagnosis
  - apraclonidine / Iopidine (Alcon)
    - Alpha-adrenergic receptor agonist
    - One drop of 0.5% or 1% will dilate a Horner’s pupil with no/minimal effect on normal pupil
    - Must have 1.0mm or more dilation after 30-45 minutes
Anisocoria Testing - too small

- Allow 48 hours for lopedine to dissipate
  - Two drops of 1% hydroxyamphetamine (Paredrine)
    - Akorn - difficult to obtain
    - Will dilate first or second order neuron lesion and normal pupils only
      - Release stored norepinephrine from postganglionic axon terminals into neuromuscular junction at iris dilator
      - Can not differentiate between first or second order lesions
Right Horner’s

Horner’s due to first or second order neuron lesions

Raredrine OU

Horner’s due to 3rd order
Anisocoria Testing - too small

- Horner’s Syndrome / Oculo-sympathetic paresis
  - No treatment for Horner’s itself
  - Resolution is often possible if/when underlying cause is cured
    - Few weeks to few months
  - Can use 2.5% phenylephrine to resolve anisocoria
Anisocoria Testing - too small

- Argyll-Robertson Pupils
  - Asymmetrically, bilateral small and irregular pupils that
    - Respond poorly to light
    - Respond poorly to dilation
  - Light-Near Dissociation = pupil constriction to near response markedly better than to light response
Argyll-Robertson Pupils

- Due to lesion in the Edinger-Westphal nucleus
- Associated with chronic syphilis, MS, DM, wernicke’s encephalopathy
  - Bloodwork indicated
    - CBC
    - FTA-Abs
    - RPR/VDRL
Anisocoria worse in bright light
Pupil Testing

- Anisocoria - worse in bright light
  - Larger pupil is not constricting properly
  - Parasympathetic problem
    - Pharmacologic dilation
    - Trauma
    - Cranial nerve III palsy
    - Adie’s tonic pupil
Anisocoria Testing - too big

- Pharmacologic Dilation - bi or unilateral
  - Anticholinergics
    - Scopolamine - motion sickness patches
    - Permethrin - insecticide
  - Plants
    - Angel’s trumpet, jimson weed, belladonna
  - OTC products
    - Phenylephrine - antihistamines, ‘get the red out’ drops, anti-itch creams, nose spray
Anisocoria Testing - too big

- Pharmacologic Dilation
  - Recreational drugs
    - Alcohol
    - Stimulants - cocaine, crack, methamphetamines
    - Ecstasy, LSD, Acid, Hallucinogens
    - Marijuana, inhaled propellants
Anisocoria Testing - too big

- Pharmacologic Dilation
  - Fixed or sluggish and dilated
  - Will not constrict to 1% pilocarpine
Anisocoria Testing - too big

- Trauma
  - Trauma / surgery to circular iris sphincter at edge of pupil
    - Can be full or sectoral
Anisocoria Testing - too big

- Cranial Nerve III Palsy
  - CN III palsy signs
    - Moderate-Large ptosis
      - levator palpebrae
    - Exotropia and hypotropia (down and out)
      - Medial, superior, inferior recti, inferior oblique
        - Eye does not adduct on EOM testing
  - Pupil dilation
  - Unilateral accommodative dysfunction
Anisocoria Testing - too big

- Cranial Nerve III Palsy
  - Pupillary fibers are close to surface of CN III → susceptible to compression via mass or aneurysm at or close to CN III
    - Inability for pupil to constrict
    - Poor accommodation
Anisocoria Testing - too big

● Cranial Nerve III Palsy
  ○ Posterior communicating artery aneurysm presents with a CN III palsy 30-60% of the time
  ○ Other causes:
    ● Tumor
    ● Trauma
Anisocoria Testing - too big

● Cranial Nerve III Palsy
  ○ Ptosis, down and out eye, with pupil involvement
  ■ IMMEDIATE ER / Neuro consult with neuroimaging and angiography
● Notify hospital by phone of incoming patient
Anisocoria Testing - too big

- Cranial Nerve III Palsy
  - A CN III palsy with *no* pupil involvement is usually ischemic in nature (DM, HTN)
  - Pupil-sparing may become pupil-involving over time
    - 14% of CN III palsies due to aneurysm may not have pupil involvement in early stages
    - Follow very closely with neurologist
Anisocoria Testing - too big

- Adie’s Tonic Pupils
  - Lesion to ciliary ganglion or short posterior ciliary nerve which innervate iris constrictor
  - Most common cause is postviral denervation of pupil sphincter
    - Orbital trauma
    - Virus
    - Diabetes
    - Giant cell arteritis
    - Syphilis
    - Varicella-Zoster
Anisocoria Testing - too big

- Tonic Pupils
  - Adie’s tonic pupil
    - Idiopathic tonic pupil found in 20-40yo females
    - Markedly diminished or absent deep tendon reflexes in knee and ankle frequently found
Anisocoria Testing - too big

- Tonic Pupils
  - Unilateral
  - Can become bilateral at rate of 4% / year
  - Anisocoria diminishes with time as larger tonic pupil becomes more miotic with age
    - Long standing Adie’s pupil will be miotic and remain constricted
Anisocoria Testing - too big

- Characteristic findings
  - Sluggish, segmental pupillary sphincter palsies
  - Light-near dissociation
    - Better (but still poor) pupil constriction to near with slow redilation
      - Vs. Argyle-Robertson where the constriction to near is quick and normal
  - Denervation hypersensitivity - supersensitive constriction to diluted pilocarpine (0.125%)
Anisocoria Testing - too big

- Tonic Pupils
  - No treatment available
  - Mild miotics may help for symptomatic glare
    - Brimonidine
    - Low-dose pilocarpine
  - Bifocal for accommodation
  - Cosmetic CL for aniso
Defects of Pupillary Light Response
Pupillary Light Response

- Observe pupils before introducing light for anisocoria
- Use transilluminator or light from BIO (penlight too dim) shone ~1 inch away
- Dim room, patient fixates at distance with glasses off
- Point light directly into eye
  - Stray light can cause non-tested pupil to constrict
- Hold light for 2-4 seconds
  - Observe both tested and non-tested pupil response
Swinging Flashlight / Marcus Gunn Test

- Direct light into right eye
- Hold 2 - 4 seconds
- Quickly move light to left eye in a “U” motion
  - Avoid stimulating accommodation
- Hold 2 - 4 seconds
- Repeat 3 - 4 times
- Magnitude and duration must be constant
Swinging Flashlight / Marcus Gunn Test

Direct → Consensual → Swinging Flashlight
Pupillary Light Response

- Light pointed into right eye
- Measuring afferent pathway of right eye
  - Observe direct response of right eye
  - Observe consensual response of left eye
- Constriction amount (quantity), rapidity (quality), and time to release should be the same
Pupillary Light Response

- Light pointed into left eye
- Measuring afferent pathway of left eye
  - Observe direct response of left eye
  - Observe consensual response of right eye
- Similar quantity, quality, and release
Normal pupil response
Swinging Flashlight / Marcus Gunn Test

- RAPD alone does not cause anisocoria
  - Due to consensual response pupils will look the same size
  - Anisocoria is due to an efferent, traumatic, mechanical, or pharmacological etiology
Swinging Flashlight / Marcus Gunn Test

- Afferent Pupillary Light Reflex - Optic Nerve and Tract
  - Strength of direct pupillary light response compared to strength of consensual pupillary light response in the SAME EYE - a RELATIVE comparison
- Relative Afferent Pupillary Defect (RAPD)
  - Damage at or before the Pretectum / Midbrain
Swinging Flashlight / Marcus Gunn Test

- Relative Afferent Pupillary Defect
  - *Consensual* response of an eye is greater than *direct* response of the same eye
  - Unilateral or asymmetric damage to anterior visual pathway (afferent) on that side
Left AD
Swinging Flashlight / Marcus Gunn Test

- Consensual Response
  - Only one functioning pupil or one visible pupil needed to test for RAPD in *either* eye
    - Surgical / traumatic / pharmacologic pupil
    - Obscured view of pupil
    - Anisocoria
Swinging Flashlight / Marcus Gunn Test

- Consensual Response
  - Perform as usual but observe ONLY the VISIBLE / REACTIVE pupil
    - Compare *that* eye’s direct response to *that* eye’s consensual response
    - If working pupil constricts more with direct illumination than with consensual, RAPD is present in the *opposite*, unreactive or unobservable eye
Pupil with no APD/MG (fixed due to medication or synechia)

Look only at the left pupil's response
*do not spend longer on one eye than the other*
Swinging Flashlight / Marcus Gunn Test

- Grading an APD can help identify
  - Subtle defects
  - Monitor progression
- Visual acuity does not necessarily correlate with RAPD
  - However, always look carefully for an APD in cases of reduced BCVA in one eye
Swinging Flashlight / Marcus Gunn Test
Grading Scale of RAPD

- Grade 1+: weak initial pupillary constriction followed by greater redilation
- Grade 2+: initial pupillary stall followed by greater redilation
- Grade 3+: immediate pupillary dilation
- Grade 4+: no reaction to light (amaurotic)
Swinging Flashlight / Marcus Gunn Test

- Neutral density filter

Dim amount of light entering the ‘better’ eye until the afferent responses are equal and RAPD is resolved
P.E.R.R.L.A (+ / - RAPD / MG)

- PE: pupils are equal
- R: pupils are round
- RL: pupils are equally reactive to light  
  ■ Direct and Consensual
- A: pupils are responsive to accommodation
- + or - relative afferent pupillary defect  
  ■ Note grade and which eye if positive
Conclusion

- Pupillary testing is an important component of every comprehensive eye examination.
- Careful observation may reveal important information about the anterior visual pathway as well as the autonomic nervous system.
Conclusion

A comprehensive history can be key in proper diagnosis

Loss of vision / BCVA
Loss of visual field
Pain
Diplopia
Ptosis / Proptosis
Color vision / Red desat

Surgical history
Trauma history
Medication history
Medical history
tumor, aneurysm, HA, ear
infection, inflammation
Thank You

Questions?

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