Comparative Neuro-Ophthalmology

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The Cranial Nerves

- Olfactory nerve fibers (I)
- Optic nerve (II)
- Oculomotor nerve (III)
- Trochlear nerve (IV)
- Trigeminal nerve (V)
- Abducens nerve (VI)
- Facial nerve (VII)
- Vestibulocochlear nerve (VIII)
- Glossopharyngeal nerve (IX)
- Vagus nerve (X)
- Accessory nerve (XI)
- Hypoglossal nerve (XII)

Pons
Medulla
Cranial Nerves

“12 pairs of cranial nerves pass through skull foramina, fissures, or canals distribute their innervation to respective structures in the head and neck”

Numbered in the order in which they arise from the brain

- **Afferent** = sensory input from a receptor
- **Efferent** = motor output
  - *Somatic* to skeletal muscle (voluntary or reflexive)
  - *Visceral* to smooth muscle and glands (reflexive)

- **General** = components that are carried by cranial as well as spinal nerves
- **Special** = components that are carried by cranial nerves only
The Cranial Nerves

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*parasympathetic nuclei
## Cranial Nerves Relevant to the Eye

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<th>Modality</th>
<th>Function Related to Eye</th>
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<td>Motor to 4 extraocular mm. and levator m.</td>
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<td>Somatic afferent</td>
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<td>*Autonomic</td>
<td>*Distributes parasympathetics and sympatheticns to eye, adnexa, orbit</td>
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<td>Abducens Nerve (CN VI)</td>
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<td>Visceral efferent</td>
<td>Parasympathetics to lacrimal gland</td>
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<tr>
<td>Vestibulo-cochlear nerve (CN VIII)</td>
<td>Somatic afferent</td>
<td>Sensory input from vestibular system to CN III, IV, VI</td>
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Somatic Afferent = sensory (input)
Efferent = motor (effect) can be somatic (skeletal mm) or visceral (smooth muscle, gland or striated muscles of branchial origin)
Autonomic Nervous System: Eye

- Controls smooth muscle and glands, regulated by hypothalamus

- Parasympathetic nuclei of Oculomotor nerve (CN III) and Facial nerve (CN VII)

- Synapse in ganglia:
  - pre and post ganglionic fibers
  - ciliary and pterygopalatine ganglion (parasympathetic)
  - cranial cervical ganglion (sympathetic)

- Distributed to eye, adnexa and orbit through terminal branches of Trigeminal nerve (CN V)

- Parasympathetic postganglionic neurotransmitter = acetylcholine
- Sympathetic postganglionic neurotransmitter = norepinephrine
Disclaimer for Neuro-ophthalmology Lectures

- Some of this material is somewhat esoteric for veterinary ophthalmologists

- Esoteric slides marked with E

- However, all of it is fascinating and should be of interest to the well rounded comparative ophthalmologist
Neuro-ophthalmology

I. The Pupil
II. Visual Pathways
III. Eye Movement
IV. Eyelid and Nictitans Movement
V. Lacrimation
The Pupil

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The Pupil

Relevant Cranial Nerves

- Optic nerve (CN II) - somatic *afferent* from retina

- Oculomotor nerve (CN III) - visceral *efferent* to intrinsic muscles of iris; somatic *efferent* to 4 extraocular muscles

- Trigeminal nerve (CN V) – distributes *parasympathetic and sympathetic efferent; axon reflex*
Pupillary Light Reflex (PLR)

- CN II and CN III
- Only autonomic nervous system reflex that is readily evaluated

- Direct PLR:
  - response in illuminated eye

- Indirect or consensual PLR
  - response in the opposite eye
  - best to donate by response FROM OD TO OS or vice versa
Anatomic Pathways:
Afferent (Input) Arm of PLR

- Retina
- Optic nerve
- Optic chiasm
- Optic tract
- Pretectal nuclei

Diagram showing:
- Retina
- Optic Nerve
- Optic Chiasm
- Optic Tract
- LGB
- PTN
- CNIII parasympathetic nuclei
AFFERENT ARM OF PLR: RETINA:

- rod/cone photoreceptors
- retinal bipolar cells
- retinal ganglion cells (RCGs) and axons
- intrinsically photosensitive RGCs*
Afferent Arm of PLR: Optic Chiasm

- optic nerve fibers converge at chiasm
- differential decussation (crossing-over) of fibers, correlates with frontal position of the eyes:
  - primate 50%
  - feline 65%
  - canine 75%
  - equine, bovine, porcine 80-90%
  - rodents 97%
  - most submammals 100%*

Crossing of optic nerve fibers is basis for indirect or consensual PLR
Afferent Arm of PLR: Optic Tract

- Optic Tract:
  - ~80% of fibers synapse in *lateral geniculate body (LGB)* = relay center for visual fibers
  - ~20% of fibers bypass LGB:
    - many *(but not all)* synapse in *pretectal nuclei (PTN)* to generate PLR
Intrinsically Photosensitive Retinal Ganglion Cells (ipRGC)

- Subset of RCG (2%) that are photosensitive (melanopsin)

- Project to brain centers that control non-visual functions including circadian related behavior (hypothalamus), PLR (pretectal nuclei)

- RGCs regulate acute changes in pupil size; ipRGC control sustained pupil size in response to environmental light levels

Phototransduction by Retinal Ganglion Cells That Set the Circadian Clock
David M. Berson, Felice A. Dunn, Motoharu Takao
Intrinsically Photosensitive Retinal Ganglion Cells (ipRGC)

- In normal retina, input to ipRGC predominately from rod/cones (photoreceptor → bipolar cell → ganglion cell)

- ipRGC capable of generating PLR (and reportedly dazzle reflex) without rod/cone input, requires high intensity light in ~480nm wavelengths (blue)
20% Optic Tract Fibers (incl. ipRCG) Bypassing Lateral Geniculate Body

- Synapse in **hypothalamus (base of diencephalon)** to regulate circadian rhythm

- Synapse in **pretectal nuclei (at junction of diencephalon and tectum)** to elicit PLR

- Synapse in **rostral colliculi (tectum)**:
  - dazzle reflex
  - reflexive redirection of gaze and movement of head and neck in response to visual stimuli
  - reticular activating system
20% Optic Tract Fibers Bypassing Lateral Geniculate Body

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  - reticular activating system
Lateral geniculate body-vision

Pretectal nuclei-PLR

Rostral colliculi-dazzle, reflexive change of gaze, Reticular Activating System

Hypothalamus-circadian rhythm

CNII Optic Tract
Afferent Arm of PLR: Pretectal Nuclear Fibers

- At caudal commissure, some fibers stay ipsilateral, others cross over to contralateral CNIII nuclei
Afferent Arm of PLR: Pretectal Nuclear Fibers

- **Second decussation proportional to first at chiasm**
Consequences of Two, Proportional Decussations

- **Humans (50%)**:  
  - *direct PLR = indirect PLR*
  - *no anisocoria in ambient light with afferent arm defect*

- **Sub-primate mammals (>50%)**:  
  - *direct PLR > indirect PLR* ("dynamic contraction anisocoria")
  - *in dogs, indirect PLR reported as 95% of direct PLR* (Gorzdanic, IOVS 2007)
  - *so other factors modulate?*
  - *anisocoria in ambient light with unilateral afferent arm defect*
Consequences of Two, Proportional Decussations

- Most sub mammals - birds, fish, reptiles (100%):
  - *no indirect PLR*

- “Pseudo-indirect” PLR in birds:
  - *results from thin orbital septum, allows scatter illumination from stimulated eye to pass to contralateral eye, resulting in direct PLR in the contralateral eye*
Efferent Arm of PLR

- CNIII parasympathetic nuclei (Edinger Westphal nuclei)
- CNIII (visceral efferent or pupillomotor and somatic efferent or motor)
- Ciliary ganglion
- Short ciliary nerves
Preganglionic Efferent PLR Pathway

- **Pupillomotor (BLUE)** fibers originate from parasympathetic nuclei of CN III, join with *motor* fibers (PINK) of CN III and CN III courses ventrally through midbrain, through cavernous sinus and out **orbital fissure**, diverge from motor fibers in orbital cone near ciliary ganglion.
Postganglionic Efferent PLR Pathway

- Synapse in ciliary ganglion
- Short ciliary nerves
  - dog = 5-8 mixed nerves, containing parasympathetics and sensory afferent fibers (Trigeminal nerve, CN V)
  - cat = 2 short ciliary nerves (malar and nasal), only parasympathetic
- Short ciliary nerves merge with long ciliary nerves just before entering eye traverse to iris sphincter muscle
Postganglionic, Parasympathetic Cat

Ciliary Ganglion

Nasal N.

Malar N.

lateral

medial
Iris Musculature Neurophysiology

- **Mammals:**
  - Smooth muscle
  - Sphincter mm. = parasympathetic, *acetylcholine*
  - Dilator mm. = sympathetic, *norepinephrine*
  - *Reciprocal innervation with inhibition of antagonist iris mm.*

- **Most sub-mammals:**
  - Skeletal muscle
  - Degree of voluntary control of pupillary movement
  - Parasympatholytic mydriatics not effective
Lens accommodation – parasympathetic efferent using same pathway as PLR

“Translational” accommodation in some carnivores
Other Pupillary Reflexes: Accommodation Reflex

- “Accommodation-convergence reflex” or “near reflex”
- Stimuli = focusing on near object

- Afferent = CN II
- Efferent = CN III (also inhibition of Abducens n, CN VI)
- Effect =
  - accommodation (change in lens shape)
  - constriction of pupil (increase depth of focus)
  - medial convergence of eyes (medial rectus with inhibition of lateral rectus)

Video
Other Pupil Reflexes: Axon “Reflex”

- “Sensory activity ascends a branch of nerve until bifurcation, then retrograde transmission, causing a neuroeffector response without passing through the brain stem or spinal cord” i.e. a “reflex” through a single nerve with no synapse

Prodromic axoplasmic flow/transmission
Antidromic axoplasmic flow/transmission
Axon “Reflex” - Reflex Uveitis

- Relevant cranial nerve – Trigeminal nerve (CN V) somatic afferent

- Stimulation of CN V of cornea, conjunctiva, eyelids
  - prodromic transmission until bifurcation at iris/ciliary body
  - antidromic transmission to iris/ciliary body

- Effect = release of prostaglandins, substance P, vasoactive compounds, other inflammatory mediators

- Outcome = miosis, uveal vasodilation, disruption of blood-aqueous barrier, ciliary body spasm, ocular hypertension in some species
“Reflex” Uveitis
Species Considerations

- rabbit > horse > dog > cats > humans


*Prey species have developed (evolved) a more profound ocular inflammatory response and liable blood ocular barrier as a preparatory phase to corneal perforation (sealing of wound with fibrin) that allows preservation of the eye for motion (prey) detection....this would be detrimental in predator species who need higher visual acuity to capture prey and as such have developed other ocular protective features*
Other Factors Modifying the Pupil and PLR

- PLRs present at opening of eyelids, but may be sluggish until maturation of retina (28 days dog)

- direct adrenergic input from catecholamine release (fear)

- supranuclear (from cortex) inhibition of parasympathetic nuclei of CN III:
  - descending, inhibitory pathways from cortex to CN III parasympathetic nuclei
  - this inhibition lost with sleep, anesthesia, opioids (dogs), extensive cerebral cortical lesion....resulting in miosis
Key Points of Previous Section

- Somatic afferent (input) fibers through CN II:
  - two, proportional decussation of fibers at chiasm and caudal commissure that are species-specific and affect nature of direct and indirect PLR
  - includes axons from intrinsically photosensitive retinal ganglion cells

- Visceral efferent (effect) fibers through CN III
  - which also has somatic efferent or motor component
  - synapse in ciliary ganglion
  - short ciliary nerves in cat v. dog

- Axon reflex entirely through CN V
  - causes “reflex” uveitis, severity of which is species-specific

- Other factors can influence PLR and pupil size
Evaluating Pupillary Light Reflexes

- Evaluate resting pupil size in ambient light
- Swinging Flashlight Test and Cover/Uncover Test
- Chromatic PLR testing (ipRGCs)
- Dark adaptation testing
Swinging Flashlight Test

- Light alternately shifted from one pupil to other, with 2-3 seconds of direct stimulation in each eye

- Normal...both pupils constrict to equal degree when stimulated, illuminated eye produces slightly more constriction (direct PLR slightly > indirect PLR)
Swinging Flashlight Test

- **Efferent (CN III) lesion**...when light is shifted to the affected side, the pupil is dilated and stays dilated.

- **Afferent (retina or CN II) lesion**...when light is shifted to affected side, the pupil is initially constricted, then dilates.
  - "positive" (abnormal) test or "Marcus Gunn pupil"
  - unilateral prechiasmal lesion (optic nerve or retina) in humans
  - can be associated with either pre- or post-chiasmal afferent arm lesions in sub-primate mammals (see notes for proof)
Swinging Flashlight Test

if pupil dilates after initial constriction:
- slight amount can be normal (adaptation of stimulated retina)
- may result from incomplete unilateral, afferent arm lesion....results from scatter illumination entering the contralateral, normal eye causing an initial indirect PLR in the illuminated, abnormal eye
Normal
Partial lesion
Normal

"Pupillary Escape" From Scatter Illumination
“Cover-Uncover” Test

- Therefore, equivocal “positive” swinging flashlight test is followed by “cover-uncover” test.

- Cover each eye with hand…. ambient light rather than penlight is stimuli, this eliminates influence of scatter illumination.
Chromatic PLR Testing
(intrinsically photosensitive retinal ganglion cells)
Evaluation of Retinal Status Using Chromatic Pupil Light Reflex Activity in Healthy and Diseased Canine Eyes

Sinisa D. Grozdanic,1 Milan Matic,1 Donald S. Sakaguchi,2 and Randy H. Kardon3

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Slide Courtesy of Dr. Andras Komaromy
Chromatic PLR Testing

- **Normal:**
  - Positive PLR with bright red light (photoreceptors normal)
  - Positive PLR with bright blue light (iPR ganglion cells normal)

- **Photoreceptor disease (SARDS, PRA, acute retinal detachment):**
  - Negative PLR with red light (photoreceptors abnormal)
  - Positive PLR with blue light (ganglion cells normal and still functioning)

- **Retinal ganglion cell disease (optic neuritis, ON neoplasia, ON hypoplasia, ON avulsion, chronic panretinal degeneration from any cause):**
  - Negative PLR with red light (ganglion cells necessary for signal to be transmitted from photoreceptors to brainstem)
  - Negative PLR with blue light (ganglion cells abnormal)

*White light contains all wavelengths in visible spectrum incl. blue….some degree of PLR with *bright* white light does not rule out photoreceptor disease*
Assessment of Rod, Cone, and Intrinsically Photosensitive Retinal Ganglion Cell Contributions to the Canine Chromatic Pupillary Response

Connie Y. Yeh,1,2 Kristin L. Koehl,1 Christine D. Harman,1 Simone Iwabe,2 Jose M. Guzman,2 Simon M. Petersen-Jones,1 Randy H. Kardon,3,4 and Andras M. Komaromy1,2

Invest Ophthalmol Vis Sci. 2017;58:65–78. DOI:10.1167/iovs.16-19865

More to follow from Dr. Komaromy!
Dark Adaptation Test

- assessment of pupillary size after 5 minutes in dark

- examine with direct ophthalmoscope at an arm’s distance, turned on immediately prior to assessment so as not to stimulate PLR
Dark Adaptation Test

- normal = both pupils dilate fully and symmetrically
- afferent (CN II) and efferent (CN III) lesions = both pupils dilate
Dark Adaptation Test

- anterior uveitis = affected pupil does not fully dilate
- posterior synechiae = affected pupil fails to dilate
- Horner syndrome = affected pupil fails to dilate, anisocoria accentuated by dark adaptation

The dark adaptation test is the single most useful test to diagnosis Horner syndrome, esp. incomplete cases.
“Positive” (bad) swinging flashlight test, where illuminated pupil dilates, indicates afferent arm lesion. Follow equivocal positive test with cover-uncover test to eliminate influence of scatter illumination.

Chromatic PLR testing can differentiate outer retinal disease (negative red light, positive blue light) from inner retinal/optic nerve disease (neg. both red and blue light).

Dark adaption test is useful to diagnosis Horner syndrome.
Characteristics of PLR Pathway Lesions

- **Afferent Arm:**
  - pre-chiasmal (retina, optic nerve)
  - optic tract

- **Efferent Arm:**
  - pre-ganglionic
  - post-ganglionic
Unilateral Prechiasmal (Retina/Optic Nerve) Lesion

- anisocoria in room light with ipsilateral larger pupil (sub primates)
- deficit of direct PLR in affected eye and indirect PLR FROM affected eye TO fellow eye
- positive (abnormal) swinging flashlight test and cover-uncover test in affected eye
- normal dark adaptation test
- remember effects of ipRGCs....PLRs can persist with advanced photoreceptor disease
- visual, dazzle reflex deficits in affected eye

Enrofloxacin toxicosis
Optic neuritis
Unilateral Optic Tract Lesions (Anterior to Lateral Geniculate Body)

- similar to unilateral prechiasmal lesion but more dilated pupil contralateral to lesion

- more subtle anisocoria vs. prechiasmal lesion (afferent fibers from both eyes affected)

- positive swinging flashlight test contralateral to lesion in non-humans (*see notes for proof)

- more miotic pupil persists in the same eye (ipsilateral to lesion) regardless of which eye is stimulated

- abnormal visual field contralateral to affected tract
Bilateral Retina, Optic Nerve or Tract, Optic Chiasm or Caudal Commissure Lesions

- bilateral mydriasis, PLR deficits, visual deficits commiserate with severity of lesion

- lesions in both retinas more common than (> chiasm > bilateral optic nerves > bilateral caudal commissure > bilateral optic tracts
Unilateral Efferent Arm (CN III) Lesions

- Ipsilateral dilated pupil, anisocoria more pronounced than afferent arm lesion

- Negative direct PLR, negative indirect PLR from normal eye to affected eye….i.e. the affected pupil does not respond to light stimuli from either eye

- Normal dark adaptation test

- Normal vision
**Efferent Arm Lesions**

- **Preganglionic:**
  - most often pupillomotor and motor fibers affected

- **Postganglionic:**
  - pupillomotor fibers only, as motor fibers diverge from pupillomotor fibers in orbit before ciliary ganglion
Internal Ophthalmoplegia

- “Impairment of pupillary function” (sphincter m, atropine, parasympathetic innervation)

- Parasympathetic efferent denervation (pupillomotor fibers), ocular movement (motor fibers) unaffected

- Generally post-ganglionic, may be idiopathic and self-resolving (analogous to “Adie Tonic Pupil” in humans)

- D or reverse D shaped pupil in cats if only one short ciliary nerve affected

- Pupillomotor fibers superficial (medial) and smaller in diameter than motor fibers in CN III
  - In humans, may be preferentially affected with compressive lesions (e.g. aneurism, mass) OR preferentially spared with microvascular diseases (e.g. diabetes, hypertension)

www.davidwilliams.org.uk
External Ophthalmoplegia

- Motor denervation of CNIII

Head rotated up, paralysis of ocular movement
Total Ophthalmoplegia

- internal and external ophthalmoplegia (pupillomotor and motor)
- by definition, a preganglionic lesion (re: ciliary ganglion),
  - almost always, intracranial lesion, as pupillomotor and motor fibers of the ventral ramus of CN III diverge ~mid-orbit
  - i.e. intraorbital cause of total ophthalmoplegia rare and caused by lesion in caudal orbit
Key Points from Previous Section

- **Afferent (retina, CN II) lesion:**
  - pre-chiasmal = direct PLR affected and positive swinging flashlight test *ipsilateral* to lesion
  - post-chiasmal = direct PLR more affected and positive swinging flashlight test *contralateral* to lesion
  - vision concurrently affected if before lateral geniculate body

- **Efferent (CN III) lesion:**
  - obvious anisocoria
  - ipsilateral direct PLR and indirect PLR *from* normal side affected
  - preganglionic (before ciliary ganglion) = motor and pupillomotor affected, generally intracranial
  - postganglionic = only pupillomotor affected, possible D-shaped pupil in cats
Pharmacologic Localization of Autonomic Diseases of Eye

- Direct testing stimulates receptor (apply exogenous neurotransmitter e.g. pilocaripine, epinephrine)
- Indirect testing affects release or reuptake of neurotransmitter (e.g. acetylcholinesterase inhibitor or hydroxyampethamine)
Pharmacologic Localization of Lesions of Autonomic Innervation to Eye

- Often evaluates for the presence of **denervation hypersensitivity**:
  - receptors deprived of neurotransmitter will increase in number and affinity for that neurotransmitter causing an exaggerated effect
  - denervation hypersensitivity generally > with postganglionic lesions
Limitations/Caveats in Pharmacologic Testing for Autonomic Disorders

- requires normal, control eye
- quantity of absorbed drug affected by volume, integrity of corneal epithelium, etc.
- prior drug action (wait 24 hours minimum between tests)
- acute lesion, denervation hypersensitivity may not have yet developed
- partial lesions, partial denervation hypersensitivity
- pre-ganglionic lesion, partial denervation hypersensitivity
Pharmacologic Testing with Parasympathetic Denervation

- 0.5% physostigmine:
  - indirect parasympathomimetic, acetylcholinesterase inhibitor….allows buildup of acetylcholine at synaptic fissure
  - postganglionic = no constriction of pupil
  - preganglionic = constriction of pupil
Post-ganglionic Lesion
0.5% Physostigmine (Acetylcholinesterase inhibitor)

Acetylcholine not present at synaptic terminal, physostigmine has no effect

Postganglionic fiber affected

Short ciliary nerves

Ciliary ganglion
Acetylcholine present at synaptic terminal, physostigmine allows buildup of AcH, constriction of pupil.

Preganglionic fiber affected, postganglionic fiber unaffected.

Pre-ganglionic Lesion

0.5% Physostigmine (Acetylcholinesterase inhibitor)
Pharmacologic Testing with Parasympathetic Denervation

- Direct testing with 2% pilocarpine (direct parasympathomimetic):
  - wait 24 hours post indirect agent testing
  - postganglionic lesion constricts sooner than normal eye (denervation hypersensitivity)
  - preganglionic lesion constricts similar timeframe to normal eye**

- some clinicians use 0.05% pilocarpine, no effect on normal eye
- failure to respond to both tests indicates pharmacologic blockade or iridal disease (atrophy, synechia)
Denervation hypersensitivity develops causing exaggerated response, rapid constriction of pupil

Postganglionic axon affected

Short ciliary nerves

Ciliary ganglion

Post-ganglionic Lesion

2% Pilocarpine (Acetylcholine-like drug)
No or minimal denervation hypersensitivity develops, constriction of pupil similar to normal eye

Pre-ganglionic Lesion

2% Pilocarpine (Acetylcholine-like drug)
Oculosympathetic Pathway

- Sympathetic efferent:
  - central (1st order)
  - preganglionic (2nd order)
  - postganglionic (3rd order)

Diagram:
- Lateral tectotegmentospinal tract
- Cranial cervical ganglion
- Vagosympathetic trunk
- 1
- 2
- 3

Labels:
- A. Iris sphincter
- B. Iris dilator mm.
Sympathetic Efferent Pathway: 1st Order Neurons

- hypothalamus
- lateral tectotegmentospinal tract
- descend ipsilaterally through brain stem and lateral funiculus of spinal cord
- synapse in preganglionic cell bodies in gray matter of intermediolateral column of spinal cord T1-T4
Sympathetic Efferent Pathway: 2nd Order Neurons

- rami communicans through ventral roots
- vagosympathetic trunk (with vagus nerve, carotid artery)
- synapse in cranial cervical ganglion (caudomedial to tympanic bullae) with postganglionic sympathetic neurons
Sympathetic Efferent Pathway: 3rd Order Neurons (Postganglionic)

- join tympanic branch of glossopharyngeal nerve (CN IX) to form caroticotympanic nerves

- over promontory of middle ear

- exit middle ear, nerve of pterygoid canal (with parasympathetics to lacrimal gland) and enter cavernous sinus

- **join relevant cranial nerve – Trigeminal nerve (CN V)**

  - most fibers pass through *ophthalmic division of CN V*, to *nasociliary nerve* (to levator m, smooth m of orbit) and then continue into globe via the *long ciliary nerves* in the suprachoroidal space to iris dilator m

  - some fibers through *maxillary division of CN V* to *infraorbital/zygomatic nerve* to supply lower eyelid and nictitans
Sympathetic Efferent Pathway: 3rd Order Neurons

*Always evaluate eyelid and corneal sensitivity with Horner syndrome*
Horner Syndrome

- protrusion of nictitans
- ptosis and reverse ptosis
- miosis
- enophthalmos

All four of these clinical findings are not always present**
Horner Syndrome

- peripheral vasodilation on affected side = conjunctival hyperemia
Efferent Sympathetic: Horner Syndrome

- ptosis and "reverse ptosis"

- enophthalmos variably present......narrowed palpebral fissure (ptosis and reverse ptosis) creates impression of “apparent” enophthalmos even if not present
Horner Syndrome in Large Animals

- signs more subtle than dogs/cats
- **ptosis** most consistent finding, miosis inconsistent
- ipsilateral cutaneous facial and cervical hyperthermia

- cattle = **ipsilateral lack of sweating** (anhydrosis, detected in nose, sweating mediated by alpha adrenergic receptors), vascular engorgement of pinna

- horse = **ipsilateral sweating** (vasodilation and increased blood flow from decreased vasomotor tone)
  - entire ipsilateral head and body = first order lesion
  - ipsilateral head and neck = second or third order lesion
  - guttural pouch infection a common cause
Pourfour du Petit Syndrome
(the opposite or Horner syndrome)

- mydriasis, widened palpebral fissure, exophthalmos
- oculosympathetic hyperactivity (irritative lesion)
- reported in 3 cats following ear flushing
Pharmacologic Testing for Horner Syndrome

- 1% hydroxyamphetamine...causes norepinephrine release
  - postganglionic = no or incomplete mydriasis
  - preganglionic = normal mydriasis
Post-ganglionic axon affected

No norepinephrine at synaptic terminal, hydroxyamphetamine causes no effect

Postganglionic lesion
1% Hydroxyamphetamine (causes norepi release)
Fiber affected to ganglion, postganglionic fiber unaffected, i.e. no trans-synaptic axonal degeneration

Norepinephrine present at synaptic terminal, hydroxyamphetamine causes mydriasis

Preganglionic lesion
1% Hydroxyamphetamine (causes norepi release)
Pharmacologic Testing for Horner Syndrome

- **2.5-10% phenylephrine**
  - postganglionic = mydriasis, retraction of nictitans, resolution of ptosis in 5-8 minutes
  - preganglionic = no effect

- some clinicians use 1% phenylephrine that does not affect normal pupil
Denervation hypersensitivity causes rapid resolution of Horner syndrome signs.

Post-ganglionic axon affected

Postganglionic lesion

2.5-10% Phenylephrine (direct sympathomimetic)
Fiber affected to ganglion, postganglionic fiber unaffected, i.e. no trans-synaptic axonal degeneration

No or minimal denervation hypersensitivity, no effect

Preganglionic lesion
2.5-10% Phenylephrine (direct sympathomimetic)
Localization of Pupillary Abnormalities

Summary

- First rule out non-neurologic or ocular conditions:
  - fear – endogenous norepinephrine release
  - ocular disease – corneal ulcer, anterior uveitis, glaucoma, lens luxation
  - structural iris lesion - synechia or iris atrophy
    - if uncertain of former, dark adaptation test
    - If uncertain of latter, test with pilocarpine
  - pharmacologic blockade - prior administration of atropine (duration of action 3-7 days)
Localization of Pupillary Abnormalities
Summary

- If you have ruled out these factors:
  - evaluate direct and consensual PLR using swinging flashlight test
  - consider chromatic PLR testing to localize if retinal disease suspected
  - response to dark adaptation testing (Horner syndrome)
Localization of Pupillary Abnormalities

Summary

- Concurrently evaluate:
  - menace response and dazzle reflex (localizing for afferent arm lesion)
  - globe position and movement (localizing if concurrent motor deficit of CNIII present)
- perform funduscopic exam
- cranial nerve and neurologic exam
Special Notes on Pupil Size and PLR and Intracranial Lesions

- Cerebellar lesions may cause unilateral (contralateral) or bilateral mydriasis with normal PLR.

- Acute cerebral or brainstem swelling may cause ipsilateral or bilateral mydriasis/PLR deficit from compression of CNIII.

- Extensive cerebro-cortical lesion may be associated with bilateral miosis (loss of supranuclear inhibition of CNIII).
Key Points from Previous Section

- Pharmacologic localization of autonomic disorders of the eye may use indirect or direct acting agents, often assesses for denervation hypersensitivity, must be interpreted with caution.

- Horner syndrome may cause reverse ptosis and conjunctival hyperemia.

- Horner syndrome in large animals...ptosis most consistent finding; cows = ipsilateral lack of sweating, horses = ipsilateral sweating.

- Many PLR and pupillary abnormalities result from ocular, not neurologic, disease.