This slide encapsulates one way to think about the motility disorders. If it is unfamiliar, I strongly suggest you review the slide-set entitled ‘Motility disorders: Overview’ before proceeding. Now on with the show!
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

What does isolated mean in this context?

Isolated

Supranuclear

Nuclear

Internuclear

CN3 Nucleus

MLF

CN6 Nucleus

CN4 Nucleus

Fascicular

Subarachnoid

Cavernous sinus

Orbital

Neuromuscular junction

Extraocular muscle

MLF

Nuclear

Infranuclear
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

What does isolated mean in this context?
It means ‘absent nonocular CNS signs’

Supranuclear

Internuclear

Nuclear

Fascicular
Subarachnoid
Cavernous sinus
Orbital
Neuromuscular junction
Extraocular muscle
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

**Isolated**

What does *isolated* mean in this context?

It means ‘absent nonocular CNS signs’

Supranuclear

**Internuclear**

Nuclear

Does it also mean ‘absent CNS-related pain’?

Infranuclear

- Fascicular
- Subarachnoid
- Cavernous sinus
- Orbital
- Neuromuscular junction
- Extraocular muscle
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

What does isolated mean in this context?
It means ‘absent nonocular CNS signs’

Does it also mean ‘absent CNS-related pain’?
It does not. The sorts of CN3 palsies covered in this slide-set can be associated with pain.

- Nuclear
  - CN3 Nucleus
    - Fascicular
    - Subarachnoid
    - Cavernous sinus
    - Orbital
    - Neuromuscular junction
    - Extraocular muscle
  - Internuclear
  - Supranuclear
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Supranuclear

What does 'isolated and unilateral' imply re etiology?

Internuclear

Nuclear

CN3 Nucleus

MLF

CN6 Nucleus

CN4 Nucleus

Infranuclear

Fascicular
Subarachnoid
Cavernous sinus
Orbital
Neuromuscular junction
Extraocular muscle
Motility Disorders: Nontraumatic, **Isolated, Unilateral** CN3 Palsy

Supranuclear

What does ‘isolated and unilateral’ imply re etiology?
It implies the lesion is infranuclear, somewhere along the path from the subarachnoid to the orbital portions

Infranuclear

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Fascicular

Subarachnoid

Cavernous sinus

Orbital

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Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

What does ‘isolated and unilateral’ imply re etiology?
It implies the lesion is infranuclear, somewhere along the path from the subarachnoid to the orbital portions.

Note: It should be mentioned (because the BCSC Neuro book mentions it) that, rarely, a brainstem lesion (ie, nuclear; fascicular) can produce an isolated unilateral CN3 palsy.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

The majority of nontraumatic isolated third nerve palsy is secondary to what pathologic event?

- Microvascular injury; ie, ischemia

In which portion of the pathway does this sort of injury occur?
- The subarachnoid (although it must be noted that it could occur along the cavernous sinus portion as well)
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

**Supranuclear**

**Nuclear**

**Infranuclear**

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Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Supranuclear

Nuclear

Infranuclear

Fascicular
Subarachnoid
Cavernous sinus
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Microvascular injury; ie, ischemia

We’ll unpack this concept in detail later in the side-set
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

**Supranuclear**

**Nuclear**

**Infranuclear**

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Fascicular
Subarachnoid
Cavernous sinus
Orbital
Neuromuscular junction
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Note that this refers to a microvascular injury that just happens to occur to the cavernous sinus portion of the nerve. It is not referring to ophthalmoparesis owing to a process intrinsic to the cavernous sinus itself!

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Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

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Ophthalmoparesis owing to a cavernous-sinus process is addressed in its own slide-set (N19)
Motility Disorders: *Nontraumatic, Isolated, Unilateral CN3 Palsy*

The way you should divvy up CN3 palsies

? ?
Motility Disorders: *Nontraumatic, Isolated, Unilateral CN3 Palsy*

The way you should divvy up CN3 palsies

- Pupil-involving
- Pupil-sparing
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

What does it mean to say a CN3 palsy ‘involves the pupil’? That is, what will be abnormal about the pt’s exam?

1)

2)
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

What does it mean to say a CN3 palsy ‘involves the pupil’? That is, what will be abnormal about the pt’s exam?
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Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving \textit{versus} Pupil-sparing

What does it mean to say a CN3 palsy ‘involves the pupil’? That is, what will be abnormal about the pt’s exam?

1) The pt will have unilateral ophthalmoparesis in a pattern consistent with innervation by CN3; and
2) The pt will have anisocoria, and the \textit{larger vs smaller} pupil will be ipsilateral to the paresis
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

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Pupil-involving CN3 palsy of the right eye
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

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How much larger are we talking about here?
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

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Well, in the context of concurrent ophthalmoparesis c/w a CN3 lesion, any enlargement is concerning. But in general, the anisocoria will be a couple of millimeters, maybe a little more.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

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The opposite, actually. A pupil that large has almost always been dilated (ie, is a so-called drug pupil).
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Motility Disorders: *Nontraumatic, Isolated, Unilateral CN3 Palsy*

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*In addition to being larger, what else will be abnormal about the involved pupil?*
It will react poorly to both [word] and another word.
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*In addition to being larger, what else will be abnormal about the involved pupil?*
It will react poorly to both light and accommodation.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

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In addition to being larger, what else will be abnormal about the involved pupil?

It will react poorly to both light and accommodation.

Which portion of the nervous system controls pupil size?

The autonomic nervous system (ANS) has two components—increased input from the parasympathetic fibers causes the pupil to be smaller, and increased input from the sympathetic fibers causes the pupil to be larger.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

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Which portion of the nervous system controls pupil size?
The autonomic nervous system (ANS)

The ANS has two components—what are they, and what role does each play in determining pupil size?

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Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

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The ANS has two components—what are they, and what role does each play in determining pupil size?

- Increased input from the parasympathetic fibers causes the pupil to be smaller.
- Increased input from the sympathetic fibers causes the pupil to be larger.

Is the opposite the case—that is, does decreased parasympathetic input lead to pupil dilation, and decreased sympathetic input lead to miosis?
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving versus Pupil-sparing

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Which portion of the nervous system controls pupil size?
The autonomic nervous system (ANS)

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Is the opposite the case—that is, does decreased parasympathetic input lead to pupil dilation, and decreased sympathetic input lead to miosis?

These are, in fact, the case. Remember, pupil size is based on the aggregate autonomic input. So if input from one component of the ANS decreases, the net effect of input from the other will be greater.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving  versus  Pupil-sparing

Is it the case that the larger pupil associated with a CN3 palsy is secondary to decreased parasympathetic input to that pupil? Yes

Decreased  larger?

Is the opposite the case—that is, does decreased parasympathetic input lead to pupil dilation, and decreased sympathetic input lead to miosis? These are, in fact, the case. Remember, pupil size is based on the aggregate autonomic input. So if input from one component of the ANS decreases, the net effect of input from the other will be greater.

The ANS has two components—what are they, and what role does each play in determining pupil size?

Increased input from the parasympathetic fibers causes the pupil to be smaller. Decreased input from the sympathetic fibers causes the pupil to be larger.
**Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy**

Pupil-involving **versus** Pupil-sparing

Is it the case that the larger pupil associated with a CN3 palsy is secondary to decreased parasympathetic input to that pupil? Indeed it is

The autonomic nervous system (ANS) has two components—what are they, and what role does each play in determining pupil size?

- Increased input from the parasympathetic fibers causes the pupil to be smaller.
- Increased input from the sympathetic fibers causes the pupil to be larger.

In addition to being larger, what else will be abnormal about the involved pupil? Decreased input from the parasympathetic fibers leads to miosis.

Is the opposite the case—that is, does decreased parasympathetic input lead to pupil dilation, and decreased sympathetic input lead to miosis?

These are, in fact, the case. Remember, pupil size is based on the aggregate autonomic input. So if input from one component of the ANS decreases, the net effect of input from the other will be greater.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

What does it mean to say a CN3 palsy ‘involves the pupil’? That is, what will be abnormal about the pt's exam?

1) The pt will have unilateral ophthalmoparesis in a pattern consistent with innervation by CN3; and 2) The pt will have anisocoria, and the larger pupil will be ipsilateral to the paresis.

In addition to being larger, what else will be abnormal about the involved pupil?

It will react poorly to both light and accommodation.

Which portion of the nervous system controls pupil size?
The autonomic nervous system (ANS)

The ANS has two components; what are they, and what role does each play in determining pupil size?

- Increased input from the parasympathetic fibers causes the pupil to be smaller.
- Increased input from the sympathetic fibers causes the pupil to be larger.

Decreased input from the parasympathetic fibers causes the pupil to be smaller? Yes

Is decreased sympathetic input leading to ipsilateral pupil miosis a thing?

It is indeed, as well.

What is the name for this condition?
Horner syndrome
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving \textit{versus} Pupil-sparing

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The autonomic nervous system (ANS)

The ANS has two components—what are they, and what role does each play in determining pupil size?

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Is the CN3 palsy \textit{involving the pupil}?

\textbf{Yes}

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It is indeed, as well.
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Which portion of the nervous system controls pupil size? The autonomic nervous system (ANS).

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--Increased input from the parasympathetic fibers causes the pupil to be smaller
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Next we will take a side-trip to cover the sympathetic and parasympathetic pupil pathways. These are important topics, so unless you know them cold, you should probably come with…
Sympathetic pathway:
First-order neurons

Second-order neurons

Third-order neurons

(No question—just get your bearings, then proceed)
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

**Sympathetic pathway:**

First-order neurons
--Originates in hypothalamus

Second-order neurons
--Originate at Budge center
--Exits spinal cord
--Travels in sympathetic chain
--Synapses in superior cervical ganglion

Third-order neurons
--Originates in superior cervical ganglion
--Travels with internal carotid artery into cavernous sinus
--Hops onto VI, then V1 to enter orbit
Sympathetic pathway:
First-order neurons
--Originate in hypothalamus

Second-order neurons

Third-order neurons
Sympathetic pathway:
First-order neurons
--Originate in hypothalamus
--Travel in spinal cord

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Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy
Sympathetic pathway:
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--Originate in hypothalamus
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Third-order neurons
Motility Disorders: *Nontraumatic, Isolated, Unilateral CN3 Palsy*

**Sympathetic pathway:**

First-order neurons
--Originate in hypothalamus
--Travel in spinal cord
--Synapse in the ciliospinal center of Budge

Second-order neurons

Third-order neurons
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First-order neurons
--Originate in hypothalamus
--Travel in spinal cord
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Third-order neurons
Sympathetic pathway:
First-order neurons
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Second-order neurons

Third-order neurons

At what level of the spinal cord is the center of Budge found?

Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy
**Sympathetic pathway:**
First-order neurons
--Originate in hypothalamus
--Travel in spinal cord
--Synapse in **ciliospinal center of Budge**

Second-order neurons

Third-order neurons

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**Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy**

At what level of the spinal cord is the center of Budge found?
C8-T2
Sympathetic pathway:
First-order neurons
--Originate in hypothalamus
--Travel in spinal cord
--Synapse in ciliospinal center of Budge

Second-order neurons
--Originate at Budge center
--Exit

Third-order neurons
Sympathetic pathway:
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Second-order neurons
--Originate at Budge center
--Exit spinal cord

Third-order neurons
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

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--Synapse in ciliospinal center of Budge

Second-order neurons
--Originate at Budge center
--Exit spinal cord
--Travel in two words

Third-order neurons
Sympathetic pathway:
First-order neurons
--Originate in hypothalamus
--Travel in spinal cord
--Synapse in ciliospinal center of Budge

Second-order neurons
--Originate at Budge center
--Exit spinal cord
--Travel in sympathetic chain

Third-order neurons
Sympathetic pathway:
First-order neurons
--Originate in hypothalamus
--Travel in spinal cord
--Synapse in ciliospinal center of Budge

Second-order neurons
--Originate at Budge center
--Exit spinal cord
--Travel in sympathetic chain

Third-order neurons

Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

What major structure do these fibers pass over?

The lung apex
Sympathetic pathway:
First-order neurons
--Originate in hypothalamus
--Travel in spinal cord
--Synapse in ciliospinal center of Budge

Second-order neurons
--Originate at Budge center
--Exit spinal cord
--Travel in sympathetic chain

Third-order neurons

Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

What major structure do these fibers pass over?
The lung apex
**Sympathetic pathway:**

**First-order neurons**
--Originate in hypothalamus
--Travel in spinal cord
--Synapse in ciliospinal center of Budge

**Second-order neurons**
--Originate at Budge center
--Exit spinal cord
--Travel in sympathetic chain
--Synapse in three words

**Third-order neurons**
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

**Sympathetic pathway:**

*First-order neurons*
--Originate in hypothalamus
--Travel in spinal cord
--Synapse in ciliospinal center of Budge

*Second-order neurons*
--Originate at Budge center
--Exit spinal cord
--Travel in sympathetic chain
--Synapse in superior cervical ganglion

*Third-order neurons*
Sympathetic pathway:
First-order neurons
--Originate in hypothalamus
--Travel in spinal cord
--Synapse in ciliospinal center of Budge

Second-order neurons
--Originate at Budge center
--Exit spinal cord
--Travel in sympathetic chain
--Synapse in superior cervical ganglion aka...?

Third-order neurons

By what other name is the superior cervical ganglion known?
Sympathetic pathway:
First-order neurons
--Originate in hypothalamus
--Travel in spinal cord
--Synapse in ciliospinal center of Budge

Second-order neurons
--Originate at Budge center
--Exit spinal cord
--Travel in sympathetic chain
--Synapse in superior cervical ganglion aka... the stellate ganglion

Third-order neurons
By what other name is the superior cervical ganglion known?
The stellate ganglion
Sympathetic pathway:
First-order neurons
--Originate in hypothalamus
--Travel in spinal cord
--Synapse in ciliospinal center of Budge

Second-order neurons aka...?
--Originate at Budge center
--Exit spinal cord
--Travel in sympathetic chain
--Synapse in superior cervical ganglion aka...the stellate ganglion

Third-order neurons
By what other name is the superior cervical ganglion known?
The stellate ganglion

Speaking of other names...The second-order neurons are often referred to by another name, one owing to the relationship between these neurons and the ganglion to which they are headed. What is that name?
**Sympathetic pathway:**
First-order neurons
--Originate in hypothalamus
--Travel in spinal cord
--Synapse in ciliospinal center of Budge

Second-order neurons *aka... pre-ganglionic neurons*
--Originate at Budge center
--Exit spinal cord
--Travel in sympathetic chain
--Synapse in superior cervical ganglion *aka... the stellate ganglion*

Third-order neurons
*By what other name is the superior cervical ganglion known?*
The **stellate ganglion**

*Speaking of other names... The second-order neurons are often referred to by another name, one owing to the relationship between these neurons and the ganglion to which they are headed. What is that name?*
The **pre-ganglionic** neurons
Sympathetic pathway:
First-order neurons
--Originate in hypothalamus
--Travel in spinal cord
--Synapse in ciliospinal center of Budge

Second-order neurons **aka...** pre-ganglionic neurons
--Originate at Budge center
--Exit spinal cord
--Travel in sympathetic chain
--Synapse in superior cervical ganglion **aka...** the stellate ganglion

Third-order neurons
--Originate in superior cervical ganglion

Motility Disorders: *Nontraumatic, Isolated, Unilateral CN3 Palsy*
Sympathetic pathway:
First-order neurons
--Originate in hypothalamus
--Travel in spinal cord
--Synapse in ciliospinal center of Budge

Second-order neurons aka...pre-ganglionic neurons
--Originate at Budge center
--Exit spinal cord
--Travel in sympathetic chain
--Synapse in superior cervical ganglion aka...the stellate ganglion

Third-order neurons aka...?
--Originate in superior cervical ganglion

Likewise, the third-order neurons are also referred to by a term owing to their relationship with the stellate ganglion. What is that term?
Sympathetic pathway:
First-order neurons
--Originate in hypothalamus
--Travel in spinal cord
--Synapse in ciliospinal center of Budge

Second-order neurons *aka...pre-ganglionic neurons*
--Originate at Budge center
--Exit spinal cord
--Travel in sympathetic chain
--Synapse in superior cervical ganglion *aka...the stellate ganglion*

Third-order neurons *aka...post-ganglionic neurons*
--Originate in superior cervical ganglion

*Likewise, the third-order neurons are also referred to by a term owing to their relationship with the stellate ganglion. What is that term? Post-ganglionic neurons*
Sympathetic pathway:
First-order neurons
--Originate in hypothalamus
--Travel in spinal cord
--Synapse in ciliospinal center of Budge

Second-order neurons aka...pre-ganglionic neurons
--Originate at Budge center
--Exit spinal cord
--Travel in sympathetic chain
--Synapse in superior cervical ganglion aka...the stellate ganglion

Third-order neurons aka...post-ganglionic neurons
--Originate in superior cervical ganglion
--Travel with three words to enter the two words

Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy
**Sympathetic pathway:**

**First-order neurons**
--Originate in hypothalamus
--Travel in spinal cord
--Synapse in ciliospinal center of Budge

**Second-order neurons** *aka*...pre-ganglionic neurons
--Originate at Budge center
--Exit spinal cord
--Travel in sympathetic chain
--Synapse in superior cervical ganglion *aka*...the stellate ganglion

**Third-order neurons** *aka*...post-ganglionic neurons
--Originate in superior cervical ganglion
--Travel with internal carotid artery to enter the cavernous sinus
**Sympathetic pathway:**

**First-order neurons**
--Originate in hypothalamus
--Travel in spinal cord
--Synapse in ciliospinal center of Budge

**Second-order neurons** *aka...pre-ganglionic neurons*
--Originate at Budge center
--Exit spinal cord
--Travel in sympathetic chain
--Synapse in superior cervical ganglion *aka...the stellate ganglion*

**Third-order neurons** *aka...post-ganglionic neurons*
--Originate in superior cervical ganglion
--Travel with internal carotid artery to enter the cavernous sinus
--In the sinus, hop onto cranial nerve # then cranial nerve # to enter orbit
**Sympathetic pathway:**

- **First-order neurons**
  --Originate in hypothalamus
  --Travel in spinal cord
  --Synapse in ciliospinal center of Budge

- **Second-order neurons aka...pre-ganglionic neurons**
  --Originate at Budge center
  --Exit spinal cord
  --Travel in sympathetic chain
  --Synapse in superior cervical ganglion aka...the stellate ganglion

- **Third-order neurons aka...post-ganglionic neurons**
  --Originate in superior cervical ganglion
  --Travel with internal carotid artery to enter the cavernous sinus
  --In the sinus, hop onto cranial nerve 6, then cranial nerve V₁ to enter orbit
Sympathetic pathway:
First-order neurons
--Originate in hypothalamus
--Travel in spinal cord
--Synapse in ciliospinal center of Budge

Second-order neurons
aka...pre-ganglionic neurons
--Originate at Budge center

Third-order neurons
aka...post-ganglionic neurons
--Originate in superior cervical ganglion
--Travel with internal carotid artery to enter the cavernous sinus
--In the sinus, hop onto cranial nerve 6, then cranial nerve V₁ to enter orbit

Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

For a more detailed review of the postganglionic sympathetics pathway and Horner syndrome, see slide-set N3
**Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy**

**Sympathetic pathway:**
First-order neurons
--Originate in hypothalamus
--Travel in spinal cord
--Synapse in ciliospinal center of Budge

Second-order neurons *aka*... **pre-ganglionic neurons**
--Originate at Budge center
--Exit spinal cord
--Travel in sympathetic chain
--Synapse in superior cervical ganglion

Third-order neurons *aka*... **post-ganglionic neurons**
--Originate in superior cervical ganglion
--Travel with internal carotid artery to enter the cavernous sinus
--In the sinus, hop onto cranial nerve 6, then cranial nerve V₁ to enter orbit

Note that the sympathetic pre-ganglionic neurons are relatively **short** (the Budge center and stellate ganglion are very close to one another), whereas the post-ganglionic neurons are relatively **long** (they have travel the length of the ICA, then the length of the orbit). We shall see that this is not the case with the parasympathetics.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

*Parasympathetic pathway*

And now, the *parasympathetic portion of the pathway*
Parasympathetic pathway:
First-order neurons?

Second-order neurons?

Third-order neurons?

Speaking of: Is the parasympathetic pathway similarly divided into 1st, 2nd and 3rd order neurons?
*Parasympathetic pathway:*

First-order neurons: ‘Top’ inputs

Second-order neurons?

Third-order neurons?

*Speaking of: Is the parasympathetic pathway similarly divided into 1st, 2nd and 3rd order neurons?*

No. The ‘top’ inputs that influence parasympathetic innervation of the pupil are widely distributed, and cannot reasonably be conceptualized as a unitary ‘first-order neuron.’ (Note: I made up the term ‘top inputs’ for illustrative purposes; it is not used in practice.)
Parasympathetic pathway:

First order neurons  ‘Top’ inputs

Second order neurons

Third order neurons

Speaking of: Is the parasympathetic pathway similarly divided into 1st, 2nd and 3rd order neurons? No. The ‘top’ inputs that influence parasympathetic innervation of the pupil are widely distributed, and cannot reasonably be conceptualized as a unitary ‘first-order neuron.’ (Note: I made up the term ‘top inputs’ for illustrative purposes; it is not used in practice.) It follows that if there are no 1st-order neurons, the terms second- and third-order neurons are not applicable.
Parasympathetic pathway:
- First order neurons  ‘Top’ inputs
- Second order neurons
- Third order neurons

Pre-ganglionic neurons
- Second order neurons

Post-ganglionic neurons
- Third order neurons

Speaking of: Is the parasympathetic pathway similarly divided into 1\textsuperscript{st}, 2\textsuperscript{nd} and 3\textsuperscript{rd} order neurons? No. The ‘top’ inputs that influence parasympathetic innervation of the pupil are widely distributed, and cannot reasonably be conceptualized as a unitary ‘first-order neuron.’ (Note: I made up the term ‘top inputs’ for illustrative purposes; it is not used in practice.) It follows that if there are no 1\textsuperscript{st}-order neurons, the terms second- and third-order neurons are not applicable. For this reason, pre- and post-ganglionic are the preferred terms for these neurons.
Parasympathetic pathway:

- **First-order neurons**
  - ‘Top’ inputs
  - Originate (mainly) in the pretectal nuclei
  - Travel in spinal cord
  - Synapse in ciliospinal center of Budge

- **Second-order neurons**
  - Originate at Budge center
  - Exit spinal cord
  - Travel in sympathetic chain
  - Synapse in superior cervical ganglion

- **Third-order neurons**
  - Originate in superior cervical ganglion
  - Travel with internal carotid artery to enter the cavernous sinus
  - In the sinus, hop onto cranial nerve 6, then cranial nerve V to enter orbit

Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy
Parasympathetic pathway:
- First-order neurons: 'Top' inputs
  - Originate (mainly) in the pretectal nuclei

Pre-ganglionic neurons
- Second-order neurons

Post-ganglionic neurons
- Third-order neurons
**Parasympathetic pathway:**

- **First order neurons** — ‘Top’ inputs — origin in the **pretectal nuclei**
- **Second order neurons** — origin at Budge center, exit spinal cord, travel in sympathetic chain, synapse in superior cervical ganglion
- **Third order neurons** — origin in superior cervical ganglion, travel with internal carotid artery to enter the cavernous sinus, then onto cranial nerve 6 and cranial nerve V to enter orbit

**Where are the pretectal nuclei located?**

- **Pretectal nuclei** — located in the **dorsal midbrain**

- **Damage to the pretectal nuclei of the dorsal midbrain** produces the eponymous syndrome:
  - **Parinaud syndrome** (aka dorsal midbrain syndrome, aka pretectal syndrome)
Parasympathetic pathway:

First order neurons -- Originate (mainly) in the pretectal nuclei -- Travel in spinal cord -- Synapse in ciliospinal center of Budge

Second order neurons -- Originate at Budge center -- Exit spinal cord -- Travel in sympathetic chain -- Synapse in superior cervical ganglion

Third order neurons -- Originate in superior cervical ganglion -- Travel with internal carotid artery to enter the cavernous sinus -- In the sinus, hop onto cranial nerve 6, then cranial nerve V to enter orbit

Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Where are the pretectal nuclei located?
The dorsal midbrain
Parasympathetic pathway:

First-order neurons
--Originate (mainly) in the pretectal nuclei
--Travel in spinal cord--Synapse in ciliospinal center of Budge

Second-order neurons
--Originate at Budge center--Exit spinal cord--Travel in sympathetic chain--Synapse in superior cervical ganglion

Third-order neurons
--Originate in superior cervical ganglion--Travel with internal carotid artery to enter the cavernous sinus
--In the sinus, hop onto cranial nerve 6 , then cranial nerve V to enter orbit

Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Where are the pretectal nuclei located?
The dorsal midbrain

Damage to the pretectal nuclei of the dorsal midbrain produces what eponymous syndrome?
Parasympathetic pathway:
First-order neurons
--Originate (mainly) in the pretectal nuclei
--Travel in the spinal cord--Synapse in the ciliospinal center of Budge

Second-order neurons
--Originate at Budge center--Exit spinal cord--Travel in the sympathetic chain--Synapse in the superior cervical ganglion

Third-order neurons
--Originate in the superior cervical ganglion--Travel with the internal carotid artery to enter the cavernous sinus--In the sinus, hop onto cranial nerve 6, then cranial nerve V to enter the orbit

Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Where are the pretectal nuclei located?
The dorsal midbrain

Damage to the pretectal nuclei of the dorsal midbrain produces what eponymous syndrome?
Parinaud syndrome (aka two words syndrome, aka two words syndrome)
**Parasympathetic pathway:**

- **First order neurons** -- Originate (mainly) in the pretectal nuclei -- Travel in spinal cord -- Synapse in ciliospinal center of Budge

- **Second order neurons** -- Originate at Budge center -- Exit spinal cord -- Travel in sympathetic chain -- Synapse in superior cervical ganglion

- **Third order neurons** -- Originate in superior cervical ganglion -- Travel with internal carotid artery to enter the cavernous sinus -- In the sinus, hop onto cranial nerve 6, then cranial nerve V to enter orbit

---

**Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy**

*Where are the pretectal nuclei located?*
The dorsal midbrain

*Damage to the pretectal nuclei of the dorsal midbrain produces what eponymous syndrome?*
Parinaud syndrome (aka dorsal midbrain syndrome, aka pretectal syndrome)
**Parasympathetic pathway:**

First order neurons -- Originate (mainly) in the pretectal nuclei

‘Top’ inputs

Second order neurons -- Originate at Budge center -- Exit spinal cord -- Travel in sympathetic chain -- Synapse in superior cervical ganglion

Third order neurons -- Originate in superior cervical ganglion -- Travel with internal carotid artery to enter the cavernous sinus -- In the sinus, hop onto cranial nerve 6, then cranial nerve V to enter orbit

**Motility Disorders:** Nontraumatic, Isolated, Unilateral CN3 Palsy

Where are the pretectal nuclei located?
The dorsal midbrain

Damage to the pretectal nuclei produces what eponymous syndrome?
Parinaud syndrome (aka dorsal midbrain syndrome, aka pretectal syndrome)

What are the cardinal features of Parinaud syndrome?
--?
--?
--?
--?
Parasympathetic pathway:

**First order neurons**
- Originate (mainly) in the pretectal nuclei
- Travel in spinal cord
- Synapse in ciliospinal center of Budge

**Second order neurons**
- Originate at Budge center
- Exit spinal cord
- Travel in sympathetic chain
- Synapse in superior cervical ganglion

**Third order neurons**
- Originate in superior cervical ganglion
- Travel with internal carotid artery to enter the cavernous sinus
- In the sinus, hop onto cranial nerve 6, then cranial nerve V to enter orbit

Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

**Parinaud syndrome**
- Damage to the pretectal nuclei of the dorsal midbrain produces what eponymous syndrome (aka dorsal midbrain syndrome, aka pretectal syndrome)

**Cardinal features of Parinaud syndrome**
- Impaired upgaze
- Lid retraction
- Convergence-retraction nystagmus
- Light-near dissociation

Where are the pretectal nuclei located?
- The dorsal midbrain

What are the cardinal features of Parinaud syndrome?
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Parasympathetic pathway:

First order neurons
--Originate (mainly) in the pretectal nuclei
--Travel in spinal cord--Synapse in ciliospinal center of Budge

Second order neurons
--Originate at Budge center--Exit spinal cord--Travel in sympathetic chain--Synapse in superior cervical ganglion

Third order neurons
--Originate in superior cervical ganglion--Travel with internal carotid artery to enter the cavernous sinus
--In the sinus, hop onto cranial nerve 6, then cranial nerve V to enter orbit

Nontraumatic, Isolated, Unilateral CN3 Palsy

Pre-ganglionic neurons

Damage to the pretectal nuclei of the dorsal midbrain produces what eponymous syndrome?

Parinaud syndrome (aka dorsal midbrain syndrome, aka pretectal syndrome)

Where are the pretectal nuclei located?
The dorsal midbrain

What are the cardinal features of Parinaud syndrome?
--Impaired upgaze
--Lid retraction
--Convergence retraction nystagmus

Light-near dissociation

What is light-near dissociation?
**Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy**

**Parasympathetic pathway:**
- First order neurons: 'Top' inputs -- Originate (mainly) in the pretectal nuclei -- Travel in spinal cord -- Synapse in ciliospinal center of Budge
- Second order neurons: -- Originate at Budge center -- Exit spinal cord -- Travel in sympathetic chain -- Synapse in superior cervical ganglion
- Third order neurons: -- Originate in superior cervical ganglion -- Travel with internal carotid artery to enter the cavernous sinus -- In the sinus, hop onto cranial nerve 6, then cranial nerve V to enter orbit

**Where are the pretectal nuclei located?**
The dorsal midbrain

**Damage to the pretectal nuclei produces what eponymous syndrome?**
Parinaud syndrome (aka dorsal midbrain syndrome, aka pretectal syndrome)

**What are the cardinal features of Parinaud syndrome?**
- Impaired upgaze
- Lid retraction
- Convergence retraction nystagmus

- **Light-near dissociation**

**What is light-near dissociation?**
A phenomena in which pupils miose less robustly in response to light than they do as part of the near response
Parasympathetic pathway:

First-order neurons
--Originate mainly in the pretectal nuclei

Second-order neurons
--Originate in the Edinger-Westphal nucleus--Travels with CN3 into cavernous sinus (CS)--Exit CS with inferior division of CN3--Synapse in ciliary ganglion

Third-order neurons
--Originate in superior cervical ganglion--Travel with internal carotid artery to enter the cavernous sinus--In the sinus, hop onto cranial nerve 6, then cranial nerve V to enter orbit

Pre-ganglionic neurons
--Originate in the nucleus

Post-ganglionic neurons
**Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy**

**Parasympathetic pathway:**
- **First-order neurons**  'Top' inputs
  --Originate mainly in the pretectal nuclei

- **Second-order neurons**  
  --Originate in the Edinger-Westphal nucleus

- **Third-order neurons**
  --Originate in the superior cervical ganglion
  --Travel with internal carotid artery to enter the cavernous sinus
  --In the sinus, hop onto cranial nerve 6, then cranial nerve V to enter orbit

**Pre-ganglionic neurons**

**Post-ganglionic neurons**
Parasympathetic pathway:
- First order neurons -- ‘Top’ inputs
  -- Originate mainly in the pretectal nuclei

Pre-ganglionic neurons
- Second order neurons
  -- Originate in the Edinger-Westphal nucleus

Post-ganglionic neurons
- Third order neurons

Where in relation to the CN3 nuclear complex is the Edinger-Westphal nucleus located?
Parasympathetic pathway:
- First order neurons -- ‘Top’ inputs
  -- Originate mainly in the pretectal nuclei

Pre-ganglionic neurons
- Second order neurons
  -- Originate in the Edinger-Westphal nucleus

Edinger-Westphal nucleus

Where in relation to the CN3 nuclear complex is the Edinger-Westphal nucleus located?
It is a part of the complex
**Parasympathetic pathway:**

- **First-order neurons** -- 'Top' inputs
  -- Originate mainly in the pretectal nuclei

**Pre-ganglionic neurons**

- **Second-order neurons**
  -- Originate in the Edinger-Westphal nucleus
  -- Travels with CN3 into the important intracranial space

**Post-ganglionic neurons**

- **Third-order neurons**
**Parasympathetic pathway:**

- **First order neurons** — *‘Top’ inputs*
  --Originate mainly in the pretectal nuclei

- **Pre-ganglionic neurons**
  --Originate in the Edinger-Westphal nucleus
  --Travels with CN3 into the cavernous sinus (CS)

- **Post-ganglionic neurons**
  --Third order neurons
Parasympathetic pathway:
First order neurons -- 'Top' inputs
-- Originate mainly in the pretectal nuclei

Second order neurons
-- Originate in the Edinger-Westphal nucleus
-- Travels with CN3 into the cavernous sinus (CS)

Third order neurons
-- Originate in superior cervical ganglion
-- Travel with internal carotid artery to enter the cavernous sinus
-- In the sinus, hop onto cranial nerve 6, then cranial nerve V to enter orbit

Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pre-ganglionic neurons

With respect to the cross-sectional organization of CN3, in what aspect of the nerve do the pre-ganglionic fibers run?
**Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy**

**Parasympathetic pathway:**
- First order neurons – ‘Top’ inputs
  -- Originate mainly in the pretectal nuclei

**Pre-ganglionic neurons**
- Second order neurons
  -- Originate in the Edinger-Westphal nucleus
  -- Travels with CN3 into the cavernous sinus (CS)

*With respect to the cross-sectional organization of CN3, in what aspect of the nerve do the pre-ganglionic fibers run?*
They run superficially, ie, on the outermost surface of the nerve
Parasympathetic pathway:
- First-order neurons — ‘Top’ inputs
  -- Originate mainly in the pretectal nuclei

Pre-ganglionic neurons
- Second-order neurons
  -- Originate in the Edinger-Westphal nucleus
  -- Travels with CN3 into the cavernous sinus (CS)

With respect to the cross-sectional organization of CN3, in what aspect of the nerve do the pre-ganglionic fibers run?
They run superficially, i.e., on the outermost surface of the nerve.

Take note: This is going to be really important in a few slides!
Parasympathetic pathway:
- First-order neurons: ‘Top’ inputs
  -- Originate mainly in the pretectal nuclei

Pre-ganglionic neurons
- Second-order neurons
  -- Originate in the Edinger-Westphal nucleus
  -- Travels with CN3 into the cavernous sinus (CS)

As ocular-motor nerves go, is CN3 large, or small?
Parasympathetic pathway:
- First order neurons — ‘Top’ inputs
  -- Originate mainly in the pretectal nuclei

Pre-ganglionic neurons
- Second order neurons
  -- Originate in the Edinger-Westphal nucleus
  -- Travels with CN3 into the cavernous sinus (CS)

As ocular-motor nerves go, is CN3 large, or small?
Quite large, with over \# fibers (contrast that with the itty-bitty CN4 and its \# fibers)
**Parasympathetic pathway:**
- First order neurons — 'Top' inputs
  -- Originate mainly in the pretectal nuclei

**Pre-ganglionic neurons**
- Second order neurons
  -- Originate in the Edinger-Westphal nucleus
  -- Travels with **CN3** into the cavernous sinus (CS)

---

As *ocular-motor nerves go, is CN3 large, or small?*
Quite large, with over 15,000 fibers (contrast that with the itty-bitty CN4 and its 2000 fibers)
Parasympathetic pathway:
- First-order neurons: ‘Top’ inputs
  -- Originate mainly in the pretectal nuclei

Second-order neurons
- Originate in the Edinger-Westphal nucleus
- Travels with CN3 into the cavernous sinus (CS)
- Exit CS with inferior division of CN3
- Synapse in the ciliary ganglion

Third-order neurons
- Originate in the superior cervical ganglion
- Travel with the internal carotid artery to enter the cavernous sinus
- In the sinus, hop onto cranial nerve 6, then cranial nerve V to enter the orbit

Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pre-ganglionic neurons
- Second-order neurons
  -- Originate in the Edinger-Westphal nucleus
  -- Travels with CN3 into the cavernous sinus (CS)

As ocular-motor nerves go, is CN3 large, or small?
- Quite large
  - with over 15,000 fibers (contrast that with the itty-bitty CN4 and its 2000 fibers)

Take note part deaux: The fact that CN3 is a relatively large nerve will come up again as well!
Parasympathetic pathway:
First order neurons  ‘Top’ inputs
--Originate mainly in the pretectal nuclei

Pre-ganglionic neurons
Second order neurons
--Originate in the Edinger-Westphal nucleus
--Travels with CN3 into the cavernous sinus (CS)

Post-ganglionic neurons
Third order neurons
--Originate in superior cervical ganglion--Travel with internal carotid artery to enter the cavernous sinus
--In the sinus, hop onto cranial nerve 6 , then cranial nerve V to enter orbit

Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

CN3 undergoes an important conformational change while inside the CS. What is this change?
Parasympathetic pathway:
- First order neurons: ‘Top’ inputs
  -- Originate mainly in the pretectal nuclei

Pre-ganglionic neurons
- Second order neurons
  -- Originate in the Edinger-Westphal nucleus
  -- Travels with CN3 into the cavernous sinus (CS)

Post-ganglionic neurons
- Third order neurons
  -- Travels with internal carotid artery to enter the cavernous sinus
  -- In the sinus, hops onto cranial nerve 6, then cranial nerve V to enter orbit

Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

**CN3** undergoes an important conformational change while inside the CS. What is this change?

It divides into two divisions: The ______, and the ______
Parasympathetic pathway:
- First order neurons — ‘Top’ inputs
  -- Originate mainly in the pretectal nuclei

Pre-ganglionic neurons
- Second order neurons
  -- Originate in the Edinger-Westphal nucleus
  -- Travels with CN3 into the cavernous sinus (CS)

Post-ganglionic neurons
- Third order neurons
  It divides into two divisions: The Superior, and the Inferior
**Parasympathetic pathway:**
- First order neurons  ‘Top’ inputs
  --Originate mainly in the pretectal nuclei

**Pre-ganglionic neurons**
- Second order neurons
  --Originate in the Edinger-Westphal nucleus
  --Travels with CN3 into the **cavernous sinus** (CS)

CN3 undergoes an important conformational change while inside the CS: What is this change?

It divides into two divisions: The **Superior**, and the **Inferior**

**Post-ganglionic neurons**
- Third order neurons

Which muscles are innervated by fibers in the:
  Superior division?
  Inferior division?
Parasympathetic pathway:
- First order neurons – ‘Top’ inputs
  --Originate mainly in the pretectal nuclei

Pre-ganglionic neurons
- Second order neurons
  --Originate in the Edinger-Westphal nucleus
  --Travels with CN3 into the cavernous sinus (CS)

Post-ganglionic neurons
- Third order neurons

CN3 undergoes an important conformational change while inside the CS. What is this change?

It divides into two divisions: The Superior, and the Inferior

Which muscles are innervated by fibers in the:
Superior division? Superior rectus, and the levator
Inferior division?
Parasympathetic pathway:
- First-order neurons — ‘Top’ inputs
  -- Originate mainly in the pretectal nuclei

Pre-ganglionic neurons
- Second-order neurons
  -- Originate in the Edinger-Westphal nucleus
  -- Travels with CN3 into the cavernous sinus (CS)

CN3 undergoes an important conformational change while inside the CS. What is this change?
- It divides into two divisions: The Superior, and the Inferior

Post-ganglionic neurons
- Third-order neurons
Which muscles are innervated by fibers in the:
  Superior division? Superior rectus, and the levator
  Inferior division?
**Parasympathetic pathway:**
- First order neurons  
  -- Originate mainly in the pretectal nuclei

**Pre-ganglionic neurons**
- Second order neurons
  -- Originate in the Edinger-Westphal nucleus
  -- Travels with CN3 into the **cavernous sinus** (CS)

**Post-ganglionic neurons**
- Third order neurons

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**Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy**

CN3 undergoes an important conformational change while inside the CS. What is this change?

It divides into two divisions: The **Superior**, and the **Inferior**

Which muscles are innervated by fibers in the:
- **Superior division**: Superior rectus, and the levator
- **Inferior division**: The medial rectus, inferior rectus and inferior oblique
Parasympathetic pathway:

First-order neurons: "Top" inputs
--- Originate mainly in the pretectal nuclei

Pre-ganglionic neurons
--- Originate in the Edinger-Westphal nucleus
--- Travels with CN3 into the cavernous sinus (CS)
--- Exit CS with division of CN3

Post-ganglionic neurons
--- Third-order neurons
Parasympathetic pathway:

- First order neurons: ‘Top’ inputs
  --Originate mainly in the pretectal nuclei

Pre-ganglionic neurons

- Second order neurons
  --Originate in the Edinger-Westphal nucleus
  --Travels with CN3 into the cavernous sinus (CS)
  --Exit CS with inferior division of CN3

Post-ganglionic neurons

- Third order neurons

Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy
**Parasympathetic pathway:**

- **First order neurons** — ‘Top’ inputs
  -- Originate mainly in the pretectal nuclei

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**Pre-ganglionic neurons**

- **Second order neurons**
  -- Originate in the Edinger-Westphal nucleus
  -- Travels with CN3 into the cavernous sinus (CS)
  -- Exit CS with inferior division of CN3
  -- Synapse in ganglion

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**Post-ganglionic neurons**

- **Third order neurons**
Parasympathetic pathway:

First-order neurons
- ‘Top’ inputs
  -- Originate mainly in the pretectal nuclei

Pre-ganglionic neurons
- Second-order neurons
  -- Originate in the Edinger-Westphal nucleus
  -- Travels with CN3 into the cavernous sinus (CS)
  -- Exit CS with inferior division of CN3
  -- Synapse in ciliary ganglion

Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy
Parasympathetic pathway:
- **First-order neurons**
  -- Originate mainly in the pretectal nuclei

**Pre-ganglionic neurons**
- **Second-order neurons**
  -- Originate in the Edinger-Westphal nucleus
  -- Travels with CN3 into the cavernous sinus (CS)
  -- Exit CS with inferior division of CN3
  -- Synapse in the **ciliary ganglion**

**Post-ganglionic neurons**
- **Third-order neurons**
  -- Originate in the superior cervical ganglion
  -- Travel with internal carotid artery to enter the cavernous sinus
  -- In the sinus, hop onto cranial nerve 6, then cranial nerve V to enter orbit

**Motility Disorders:** Nontraumatic, Isolated, Unilateral CN3 Palsy
- Pre-ganglionic neurons
  - ‘Top’ inputs
- Post-ganglionic neurons
  - Where is the ciliary ganglion located?
Parasympathetic pathway:
- First-order neurons -- ‘Top’ inputs
  -- Originate mainly in the pretectal nuclei

Pre-ganglionic neurons
- Second-order neurons
  -- Originate in the Edinger-Westphal nucleus
  -- Travels with CN3 into the cavernous sinus (CS)
  -- Exit CS with inferior division of CN3
  -- Synapse in the ciliary ganglion

Post-ganglionic neurons
- Third-order neurons

Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Where is the ciliary ganglion located?
At the orbital apex
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Parasympathetic pathway:

- **First order neurons**: ‘Top’ inputs
  --Originate mainly in the pretectal nuclei

**Pre-ganglionic neurons**
- **Second order neurons**
  --Originate in the Edinger-Westphal nucleus
  --Travels with CN3 until the cavernous sinus (CS)
  --Exit CS with inferior division of CN3
  --Synapse in ciliary ganglion

**Post-ganglionic neurons**
- **Third order neurons**
  --Originate in ciliary ganglion
Parasympathetic pathway:
- **First-order neurons** — ‘Top’ inputs
  -- Originate mainly in the pretectal nuclei

**Pre-ganglionic neurons**
- **Second-order neurons**
  -- Originate in the Edinger-Westphal nucleus
  -- Travels with CN3 until the cavernous sinus (CS)
  -- Exit CS with inferior division of CN3
  -- Synapse in ciliary ganglion

**Post-ganglionic neurons**
- **Third-order neurons**
  -- Originate in ciliary ganglion
  -- Travel with nerve to the muscle
**Parasympathetic pathway:**
- First-order neurons — *‘Top’ inputs*
  -- Originate mainly in the pretectal nuclei

**Pre-ganglionic neurons**
- Second-order neurons
  -- Originate in the Edinger-Westphal nucleus
  -- Travels with CN3 until the cavernous sinus (CS)
  -- Exit CS with inferior division of CN3
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**Post-ganglionic neurons**
- Third-order neurons
  -- Originate in ciliary ganglion
  -- Travel with nerve to the inferior oblique muscle

**Motility Disorders:** *Nontraumatic, Isolated, Unilateral CN3 Palsy*
Parasympathetic pathway:

First-order neurons
--Originate mainly in the pretectal nuclei

Second-order neurons
--Originate in the Edinger-Westphal nucleus
--Travels with CN3 until the cavernous sinus (CS)
--Exit CS with inferior division of CN3
--Synapse in ciliary ganglion

Post-ganglionic neurons
--Originate in ciliary ganglion
--Travel with nerve to the inferior oblique muscle
--At eye, jumps to nerves to reach the sphincter muscle

Pre-ganglionic neurons

Two words
Parasympathetic pathway:

**First-order neurons**
- ‘Top’ inputs
  - Originate mainly in the pretectal nuclei

**Second-order neurons**
- Originate in the Edinger-Westphal nucleus
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**Third-order neurons**
- Originate in ciliary ganglion
- Travel with nerve to the inferior oblique muscle
- At eye, jumps to posterior ciliary nerves to reach the sphincter muscle

Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy
Parasympathetic pathway:

First-order neurons  ‘Top’ inputs
--Originate mainly in the pretectal nuclei

Pre-ganglionic neurons

Note that the relative lengths of the pre- and post-ganglionic parasympathetic neurons are opposite of what they were for the sympathetics. Their pre-ganglionic fibers are relatively long, wending their way out to ganglia located near the end-organs they innervate. (Recall that sympathetic ganglia are all axial-CNS-adjacent.) From these far-flung ganglia, it is just a hop, skip and jump for the post-ganglionic neurons to reach their targets.

Post-ganglionic neurons

Third-order neurons
--Originate in ciliary ganglion
--Travel with nerve to the inferior oblique muscle
--At eye, jumps to posterior ciliary nerves to reach the sphincter muscle
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving  \textit{versus}  Pupil-sparing

OK, side-trip over. Now let’s use what we’ve learned to better understand the pathophysiology of CN3 palsies
Motility Disorders: *Nontraumatic, Isolated, Unilateral CN3 Palsy*

Why is pupil involvement the key issue regarding CN3 palsies?
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving versus Pupil-sparing

Why is pupil involvement the key issue regarding CN3 palsies?
Because of its implications regarding the underlying cause of the palsy
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving versus Pupil-sparing

Why is pupil involvement the key issue regarding CN3 palsies?
Because of its implications regarding the underlying cause of the palsy

Which potential cause of CN3 palsy in particular are we concerned about?
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Why is pupil involvement the key issue regarding CN3 palsies? Because of its implications regarding the underlying cause of the palsy.

Which potential cause of CN3 palsy in particular are we concerned about? Compression of the nerve by an aneurysm of the posterior communicating artery.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Why is pupil involvement the key issue regarding CN3 palsies?
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Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving  versus  Pupil-sparing

Why is pupil involvement the key issue regarding CN3 palsy?
Because of its implications regarding the underlying cause of the palsy

Which potential cause of CN3 palsy in particular are we concerned about?
Compression of the nerve by an aneurysm of the posterior communicating artery

(More specifically, the aneurysm usually is located at the junction of the PComm and internal-carotid arteries)
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy
Motility Disorders: **Nontraumatic, Isolated, Unilateral CN3 Palsy**

Why is pupil involvement the key issue regarding CN3 palsies?  
Because of its implications regarding the underlying cause of the palsy

Which potential cause of CN3 palsy in particular are we concerned about?  
Compression of the nerve by an aneurysm of the posterior communicating artery

Why should we be concerned about a PComm aneurysm?
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving versus Pupil-sparing

Why is pupil involvement the key issue regarding CN3 palsies? Because of its implications regarding the underlying cause of the palsy.

Which potential cause of CN3 palsy in particular are we concerned about? Compression of the nerve by an aneurysm of the posterior communicating artery.

Why should we be concerned about a PComm aneurysm? Because it is a potentially lethal condition, and its proper and timely dx may well save the pt’s life.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Why is pupil involvement the key issue regarding CN3 palsy?
Because of its implications regarding the underlying cause of the palsy

How is it that the status of the pupil implicates a compressive lesion as causing a CN3 palsy?

Why should we be concerned about a PComm aneurysm?
Because it is a potentially lethal condition, and its proper and timely dx may well save the pt's life
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving versus Pupil-sparing

Why is pupil involvement the key issue regarding CN3 palsies? Because of its implications regarding the underlying cause of the palsy.

How is it that the status of the pupil implicates a compressive lesion as causing a CN3 palsy? It has everything to do with the topography of the third nerve. Recall that the pre-ganglionic parasympathetics run in the superficial, outermost portion of the nerve.
Why is pupil involvement the key issue regarding CN3 palsies?
Because of its implications regarding the underlying cause of the palsy.

How is it that the status of the pupil implicates a compressive lesion as causing a CN3 palsy?
It has everything to do with the topography of the third nerve. Recall that the pre-ganglionic parasympathetics run in the superficial, outermost portion of the nerve. Given this, it stands to reason that a lesion compressing the nerve will bag these fibers, leaving the sympathetics unopposed to dilate the pupil on that side.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Getting down to clinical brass tacks: A pt presents with an apparent pupil-involving CN3 palsy. How should you approach this situation?
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Getting down to clinical brass tacks: A pt presents with an apparent pupil-involving CN3 palsy. How should you approach this situation?
Thusly: With two exceptions, a pupil-involving CN3 palsy is assumed to represent a Pcomm aneurysm until proven otherwise.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving

Pupil-sparing

Getting down to clinical brass tacks: A pt presents with an apparent pupil-involving CN3 palsy. How should you approach this situation? Thusly: With two exceptions, a pupil-involving CN3 palsy is assumed to represent a Pcomm aneurysm until proven otherwise.

What are the two exceptions?

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Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Getting down to clinical brass tacks: A pt presents with an apparent pupil-involving CN3 palsy. How should you approach this situation? Thusly: With two exceptions, a pupil-involving CN3 palsy is assumed to represent a Pcomm aneurysm until proven otherwise.

What are the two exceptions?
--If there is an appropriate trauma hx
--If the pupil finding is isolated, ie, if EOM function is intact (because the probability of an aneurysm in this scenario is essentially zero)
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Getting down to clinical brass tacks: A pt presents with an apparent pupil-involving CN3 palsy. How should you approach this situation? Thusly: With two exceptions, a pupil-involving CN3 palsy is assumed to represent a Pcomm aneurysm until proven otherwise.

What are the two exceptions?
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-- If the pupil finding is isolated, i.e., if EOM function is intact (because the probability of an aneurysm in this scenario is essentially zero)

What does appropriate mean in this context?
It means 1) the temporal relationship between the trauma and the onset of the palsy make sense, and 2) the trauma must have been severe enough to plausibly produce a CN3 palsy.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving

Pupil-sparing

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What are the two exceptions?
--If there is an appropriate trauma hx
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A patient presents with an enlarged pupil. Her motility is full to finger-following. Is it OK to send this patient home?

No! In the setting of a possible CN3 palsy, finger-following is an inadequate test for ruling out EOM involvement. To truly rule out a partial/subtle external CN3 palsy, cover testing must be performed!

OK, OK, calm down. I did standard cover-testing, and everything seemed fine. Can I please let the pt go now?

No! Like finger-following, primary-gaze cover testing is inadequate for ruling out a CN3 palsy, which can be very subtle.

Sigh. OK then, how should cover testing be performed?

Cover testing should be performed while the pt is 'face turned' so as to place the eye in the fields of gaze in which a CN3 palsy would manifest; ie, in down-, up- and medial gaze. If a subtle palsy is present, putting the eye into the fields of action of the CN3-controlled EOMs will bring it out.

Only testing performed in this manner is considered adequate to rule out EOM involvement in a pupil-involving CN3 palsy!
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

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Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving

Pupil-sparing

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Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving

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Getting down to clinical brass tacks: A pt presents with an apparent pupil-involving CN3 palsy. How should you approach this situation?
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Sigh. OK then, how should cover testing be performed?

Pupil-sparing
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving

Getting down to clinical brass tacks: A pt presents with an apparent pupil-involving CN3 palsy. How should you approach this situation? Thusly: **With two exceptions**, a pupil-involving CN3 palsy is assumed to represent a Pcomm aneurysm until proven otherwise.

What are the two exceptions?

--If there is an appropriate trauma hx--

--If the pupil finding is isolated, ie, if EOM function is intact (because the probability of an aneurysm in this scenario is essentially zero)--

A patient presents with an enlarged pupil. Her motility is full to finger-following. Is it OK to send this patient home? **No!** In the setting of a possible CN3 palsy, finger-following is an inadequate test for ruling out EOM involvement. To truly rule out a partial/subtle external CN3 palsy, **cover testing must be performed!**

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Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving

Pupil-sparing

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What are the two exceptions?
--If there is an appropriate trauma hx
--If the pupil finding is isolated, ie, if EOM function is intact (because the probability of an aneurysm in this scenario is essentially zero)

What are the three likely causes of an isolated dilated pupil?
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Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving

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What are the two exceptions?
--If there is an appropriate trauma hx
--If the pupil finding is isolated, ie, if EOM function is intact (because the probability of an aneurysm in this scenario is essentially zero)

What are the three likely causes of an isolated dilated pupil?
--Pharmacologic dilation
--Adie’s tonic pupil
--Local iris damage (eg, posterior synechiae; post-surgical)
**Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy**

**Pupil-involving**

**Pupil-sparing**

Getting down to clinical brass tacks: A pt presents with an apparent pupil-involving CN3 palsy. How should you approach this situation? Thusly: With **two exceptions**, a pupil-involving CN3 palsy is assumed to represent a Pcomm aneurysm until proven otherwise.

**What are the two exceptions?**

--If there is an appropriate trauma hx

--If the pupil finding is isolated, ie, if EOM function is intact (because the probability of an aneurysm in this scenario is essentially zero)

**What are the three likely causes of an isolated dilated pupil?**

--Pharmacologic dilation

--Adie’s tonic pupil

--Local iris damage (eg, posterior synechiae; post-surgical)

(Adie’s tonic pupil is addressed at length in slide-set N4)
Getting down to clinical brass tacks: A pt presents with a pupil-involving CN3 palsy. How should you approach this situation? Thusly: With two exceptions, a pupil-involving CN3 palsy is assumed to represent a Pcomm aneurysm until proven otherwise

Further brass tacks: How should a pupil-involving CN3 palsy be handled?
Motility Disorders: *Nontraumatic, Isolated, Unilateral CN3 Palsy*

Getting down to clinical brass tacks: A pt presents with a pupil-involving CN3 palsy. How should you approach this situation?
Thusly: With two exceptions, a pupil-involving CN3 palsy is assumed to represent a Pcomm aneurysm until proven otherwise

Further brass tacks: How should a pupil-involving CN3 palsy be handled?
Emergent imaging of the CNS vasculature must be performed to rule out a Pcomm aneurysm
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving

Pupil-sparing

Getting down to clinical brass tacks: A pt presents with a pupil-involving CN3 palsy. How should you approach this situation?
Thusly: With two exceptions, a pupil-involving CN3 palsy is assumed to represent a Pcomm aneurysm until proven otherwise

Further brass tacks: How should a pupil-involving CN3 palsy be handled?
Emergent imaging of the CNS vasculature must be performed to rule out a Pcomm aneurysm.

What three imaging modalities are appropriate/available for detecting a Pcomm aneurysm?
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Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving

Getting down to clinical brass tacks: A pt presents with a pupil-involving CN3 palsy. How should you approach this situation? Thusly: With two exceptions, a pupil-involving CN3 palsy is assumed to represent a Pcomm aneurysm until proven otherwise

Further brass tacks: How should a pupil-involving CN3 palsy be handled? Emergent imaging of the CNS vasculature must be performed to rule out a Pcomm aneurysm.

What three imaging modalities are appropriate/available for detecting a Pcomm aneurysm?
--CT angiography (CTA)
--MR angiography (MRA)
--Catheter angiography

Pupil-sparing
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving

Pupil-sparing

Getting down to clinical brass tacks: A pt presents with a pupil-involving CN3 palsy. How should you approach this situation?
Thusly: With two exceptions, a pupil-involving CN3 palsy is assumed to represent a Pcomm aneurysm until proven otherwise.

Further brass tacks: How should a pupil-involving CN3 palsy be handled?
Emergent imaging of the CNS vasculature must be performed to rule out a Pcomm aneurysm.

What three imaging modalities are appropriate/available for detecting a Pcomm aneurysm?
--CT angiography (CTA)
--MR angiography (MRA)
--Catheter angiography

Which is best?
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving  Pupil-sparing

Getting down to clinical brass tacks: A pt presents with a pupil-involving CN3 palsy. How should you approach this situation?
Thusly: With two exceptions, a pupil-involving CN3 palsy is assumed to represent a Pcomm aneurysm until proven otherwise.

Further brass tacks: How should a pupil-involving CN3 palsy be handled?
Emergent imaging of the CNS vasculature must be performed to rule out a Pcomm aneurysm.

What three imaging modalities are appropriate/available for detecting a Pcomm aneurysm?
--CT angiography (CTA)
--MR angiography (MRA)
--Catheter angiography

Which is best?
Each has advantages and disadvantages; selection should be done in consultation with one’s local neuro-radiologist (although it should be said that the convenience and safety of CTA and MRA have rendered catheter angiography a distant third choice for diagnostic imaging)
Right posterior communicating artery aneurysm on CT angiogram
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving

Pupil-sparing

What does it mean to say a CN3 palsy is pupil-sparing?
Motility Disorders: *Nontraumatic, Isolated, Unilateral CN3 Palsy*

What does it mean to say a CN3 palsy is pupil-sparing?
Pretty much what it sounds like—EOM deficiencies consistent with a CN3 distribution are present, but there is no anisocoria, and pupil motor function is intact.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-sparing CN3 palsy
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

What does it mean to say a CN3 palsy is pupil-sparing?
Pretty much what it sounds like—EOM deficiencies consistent with a CN3 distribution are present, but there is no anisocoria, and pupil motor function is intact.

It was noted at the outset of the slide-set that most CN3 palsies are ischemic. What is the pathophysiology of this?

The majority of nontraumatic isolated third nerve palsies are secondary to what pathologic event?
Microvascular injury; ie, ischemia

In which portion of the pathway does this sort of injury occur?
The subarachnoid (although it must be noted that it could occur along the cavernous sinus portion as well)

Microvascular injury; ie, ischemia
Motility Disorders: *Nontraumatic, Isolated, Unilateral CN3 Palsy*

Pupil-involving

Pupil-sparing

*What does it mean to say a CN3 palsy is pupil-sparing?*
Pretty much what it sounds like--EOM deficiencies consistent with a CN3 distribution are present, but there is no anisocoria, and pupil motor function is intact.

*It was noted at the outset of the slide-set that most CN3 palsies are ischemic. What is the pathophysiology of this?*
As with compressive lesions, it’s all about CN3 anatomy. Recall that CN3 is a large-diameter nerve. Because of its size, its inner fibers are too far from its surface to receive oxygen via passive diffusion. Thus, its inner fibers are nourished via vessels that perforate the nerve’s sheath and dive into its substance.

*The majority of nontraumatic isolated third nerve palsies are secondary to what pathologic event?*
Microvascular injury; ie, ischemia

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What is the name for blood vessels that service the inner aspect of a nerve?

The majority of nontraumatic isolated third nerve palsies are secondary to what pathologic event? Microvascular injury; ie, ischemia.

In which portion of the pathway does this sort of injury occur? The subarachnoid (although it must be noted that it could occur along the cavernous sinus portion as well).
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What is the name for blood vessels that service the inner aspect of a nerve?
Vasa nervora

The majority of nontraumatic isolated third nerve palsies are secondary to what pathologic event?
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How can the status of the pupil implicate ischemia as causing a CN3 palsy?

Yet again, look to the nerve’s topography for the explanation. Recall that the pre-ganglionic parasympathetics run in the superficial, outermost portion of the nerve. In this location, they are oxygenated not by perforating vasa nervora vessels, but rather via the innumerable pial vessels that surround the nerve. Given this, it stands to reason that an ischemic insult to the inner portion of the nerve will not bag the parasympathetic fibers, thereby leaving parasympathetic input to the pupil intact. Thus, the pupil will be of normal size and reactivity—no anisocoria, no ‘motor pupil.’

In which portion of the pathway does this sort of injury occur?

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Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

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If one of these vasa nervora vessels becomes occluded, the portion of CN3 supplied by it will suffer an ischemic injury, resulting in a palsy.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Does this mean a vascular CN3 palsy can’t involve the pupil?

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As with compressive lesions, it’s all about CN3 anatomy. Recall that CN3 is a large-diameter nerve. Because of its size, vessels that nourish CN3 must perforate the nerve’s sheath and dive into its substance. If one of these vasa nervora vessels becomes occluded, the portion of CN3 supplied by it will suffer an ischemic injury, resulting in a palsy.

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Does this mean a vascular CN3 palsy can’t involve the pupil?

No. Per the BCSC Neuro book, 20% of vascular thirds are pupil-involving.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Does this mean a vascular CN3 palsy can't involve the pupil? No. Per the BCSC Neuro book, [%.0f] of vascular thirds are pupil-involving.

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In which portion of the pathway does this sort of injury occur? The subarachnoid (although it must be noted that it could occur along the cavernous sinus portion as well).
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

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The majority of nontraumatic isolated third nerve palsies are secondary to what pathologic event? Microvascular injury; ie, ischemia.

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In a vascular, pupil-involving CN3 palsy, does the amount of anisocoria tend to be small, or large? It is almost always small (usually less than 1mm).

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Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

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It was noted at the outset of the slide-set that most CN3 palsies are ischemic. What is the pathophysiology of this?

- As with compressive lesions, it’s all about CN3 anatomy. Recall that CN3 is a large-diameter nerve. Because of its size, it is poorly vascularized compared to other cranial nerves. Postganglionic parasympathetics are nourished via vessels that perforate the nerve’s sheath and dive into its substance. If one of these vasa nervora vessels becomes occluded, the portion of CN3 supplied by it will suffer an ischemic injury, resulting in a palsy.

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Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving

Pupil-sparing

With regard to management, pupil-sparing nontraumatic isolated CN3 palsies are divided into two categories. What are they?
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving

- Pupil-sparing
  - Complete
  - Partial

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Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving

Pupil-sparing

Complete versus Partial

What is meant by referring to a pupil-sparing CN3 palsy as ‘complete’ vs ‘partial’?
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It refers to the status of the external muscles controlled by CN3. If they are all involved, the palsy is complete; if they are not, it is partial.

Why is the degree of involvement important?
What is meant by referring to a pupil-sparing CN3 palsy as ‘complete’ vs ‘partial’?
It refers to the status of the external muscles controlled by CN3. If they are all involved, the palsy is complete; if they are not, it is partial.

Why is the degree of involvement important?
Because of its clinical implications. A complete pupil-sparing CN3 palsy is virtually a lock to be vascular if the following pt-related conditions are met:

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Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

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Why is the degree of involvement important? Because of its clinical implications. A complete pupil-sparing CN3 palsy is virtually a lock to be vascular if the following pt-related conditions are met:
--The pt is a [bad word];
--the pt is over [worse word]; and
--the pt has no hx of [worse word].
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

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Why is the degree of involvement important?
Because of its clinical implications. A complete pupil-sparing CN3 palsy is virtually a lock to be vascular if the following pt-related conditions are met:
--The pt is a vasculopath;
--the pt is over 50; and
--the pt has no hx of cancer
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

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OK, so a vasculopathic, cancer-free, 50+ pt has a complete pupil-sparing CN3 palsy. Does this carry significant implications for management?
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OK, so a vasculopathic, cancer-free, 50+ pt has a complete pupil-sparing CN3 palsy. Does this carry significant implications for management?
It does, in that it means the pt need not undergo emergent imaging to r/o an aneurysm
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

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*Does this mean you can cut the pt loose, telling her to come back when she needs cataract surgery?*
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving

Pupil-sparing

Complete

Partial

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Does this mean you can cut the pt loose, telling her to come back when she needs cataract surgery?
No, such pts must be followed closely, and a general medical eval should be considered.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

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A complete pupil-sparing CN3 palsy is virtually a lock to be vascular if the following pt-related conditions are met:
- The pt is a vasculopath;
- the pt is over 50; and
- the pt has no hx of cancer.

What should this ‘general medical eval’ consist of?
- --
- --
- --

No! such pts must be followed closely, and a general medical eval should be considered to come back when she needs cataract surgery?
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

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- The pt is a vasculopath;
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What should this ‘general medical eval’ consist of?
- BP assessment
- Check blood glucose status (A1c, etc)
- Fasting lipid panel
- Consider checking inflammatory markers (eg, ESR)

No! such pts must be followed closely, and a general medical eval should be considered.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

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Does this mean you can cut the pt loose, telling her to come back when she needs cataract surgery? Not such pts must be followed closely, and a general medical eval should be considered.

While following the pt, what are you on the lookout for?
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- 
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Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

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Does this mean you can cut the pt loose, telling her to come back when she needs cataract surgery? No! Such pts must be followed closely, and a general medical eval should be considered.

While following the pt, what are you on the lookout for?
--The onset of pupil involvement; or
--The development of signs/symptoms involving other cranial nerves; or
--Failure of the palsy to resolve by amount of time
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

What is meant by referring to a pupil-sparing CN3 palsy as ‘complete’ vs ‘partial’?
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Does this mean you can cut the pt loose, telling her to come back when she needs cataract surgery?
No! Such pts must be followed closely, and a general medical eval should be considered.

While following the pt, what are you on the lookout for?
--The onset of pupil involvement; or
--The development of signs/symptoms involving other cranial nerves; or
--Failure of the palsy to resolve by 3 months
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving

Pupil-sparing

Complete versus Partial

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--The onset of pupil involvement; or
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--Failure of the palsy to resolve by 3 months

What should be done if any of these things come to pass?
Imaging should be pursued.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving

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--The development of signs/symptoms involving other cranial nerves; or
--Failure of the palsy to resolve by 3 months.

What should be done if any of these things come to pass?

Imaging should be pursued.

What are you looking for on imaging if…

...anisocoria develops?

A Dat Pcomm aneurysm.

...other S/S develop?

A malignancy.

...the palsy fails to resolve by month 3?

Malignancy.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

What is meant by referring to a pupil-sparing CN3 palsy as ‘complete’ vs ‘partial’?
It refers to the status of the external muscles controlled by CN3. If they are all involved, the palsy is complete; if they are not, it is partial.

Why is the degree of involvement important?
Because of its clinical implications. A complete pupil-sparing CN3 palsy is virtually a lock to be vascular if the following pt-related conditions are met:
--The pt is a vasculopath;
--the pt is over 50 yrs old;
--the pt has no hx of cancer.

Does this mean you can cut the pt loose, telling her to come back when she needs cataract surgery?
No! such pts must be followed closely, and a general medical eval should be considered.

While following the pt, what are you on the lookout for?
--The onset of pupil involvement; or
--The development of signs/symptoms involving other cranial nerves; or
--Failure of the palsy to resolve by 3 months

What should be done if any of these things come to pass?
Imaging should be pursued.

What are you looking for on imaging if…
...anisocoria develops?
Dat Pcomm aneurysm.

...other S/S develop?
A malignancy.

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Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving vs Pupil-sparing

**Complete**

What is meant by referring to a pupil-sparing CN3 palsy as 'complete' vs 'partial'?

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Why is the degree of involvement important?

Because of its clinical implications. A complete pupil-sparing CN3 palsy is virtually a lock to be vascular if the following pt-related conditions are met:

- The pt is a vasculopathic;
- The pt is over 50;
- The pt has no hx of cancer.

OK, so a vasculopathic, cancer-free, 50+ pt has a complete pupil-sparing CN3 palsy. Does this carry significant implications for management?

It does, in that it means the pt need not undergo emergent imaging to rule out an aneurysm.

Does this mean you can cut the pt loose, telling her to come back when she needs cataract surgery?

No! Such pts must be followed closely, and a general medical eval should be considered.

While following the pt, what are you on the lookout for?

- The onset of pupil involvement;
- The development of signs/symptoms involving other cranial nerves;
- Failure of the palsy to resolve by 3 months.

What should be done if any of these things come to pass?

Imaging should be pursued.
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While following the pt, what are you on the lookout for?
--The onset of pupil involvement;
--The development of signs/symptoms involving other cranial nerves; or
--Failure of the palsy to resolve by 3 months.

What is meant by referring to a pupil-sparing CN3 palsy as ‘complete’ vs ‘partial’?

What should be done if any of these things come to pass?
Imaging should be pursued.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving

Pupil-sparing

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--The onset of pupil involvement;
--The development of signs/symptoms involving other cranial nerves; or
--Failure of the palsy to resolve by 3 months.

What should be done if any of these things come to pass?
Imaging should be pursued.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving

Pupil-sparing

Complete versus Partial

What is meant by referring to a pupil-sparing CN3 palsy as ‘complete’ vs ‘partial’?

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While following the pt, what are you on the lookout for?

--The onset of pupil involvement; or  
--The development of signs/symptoms involving other cranial nerves; or  
--Failure of the palsy to resolve by 3 months

What should be done if any of these things come to pass?

Imaging should be pursued

What are you looking for on imaging if…

...anisocoria develops? Dat Pcomm aneurysm

...other S/S develop? A malignancy

...the palsy fails to resolve by month 3?
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

What is meant by referring to a pupil-sparing CN3 palsy as 'complete' vs 'partial'?

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Does this mean you can cut the pt loose, telling her to come back when she needs cataract surgery?

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While following the pt, what are you on the lookout for?

-- The onset of pupil involvement; or
-- The development of signs/symptoms involving other cranial nerves; or
-- Failure of the palsy to resolve by 3 months.

What should be done if any of these things come to pass?

Imaging should be pursued.

What are you looking for on imaging if...

... anisocoria develops? A dural Pcomm aneurysm.
... other S/S develop? A malignancy.
... the palsy fails to resolve by month 3? Malignancy.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving

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While following the pt, what are you on the lookout for?

--The onset of pupil involvement; or
--The development of signs/symptoms involving other cranial nerves; or
--Failure of the palsy to resolve by 3 months

What should be done if any of these things come to pass?

Imaging should be pursued

At what location might one expect a malignancy to be found?

--
--

A malignancy

What are you looking for on imaging if...

--anisocoria develops?
--other S/S develop?
--the palsy fails to resolve by month 3?

Malignancy

At what location might one expect a malignancy to be found?

Dat Pcomm aneurysm

OK, so a vasculopathic, cancer-free, 50+ pt has a complete pupil-sparing CN3 palsy. Does this carry significant implications for management?

It does, in that it means the pt need not undergo emergent imaging to r/o an aneurysm.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving

Pupil-sparing

What is meant by referring to a pupil-sparing CN3 palsy as 'complete' vs 'partial'?

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Because of its clinical implications. A complete pupil-sparing CN3 palsy is virtually a lock to be vascular if the following pt-related conditions are met:

-- The pt is a vasculopath;
-- the pt is over 50; and
-- the pt has no hx of cancer

A malignancy is a remote possibility in such cases.

Does this mean you can cut the pt loose, telling her to come back when she needs cataract surgery?

Not! Such pts must be followed closely, and a general medical eval should be considered.

While following the pt, what are you on the lookout for?

-- The onset of pupil involvement; or
-- The development of signs/symptoms involving other cranial nerves; or
-- Failure of the palsy to resolve by 3 months

What should be done if any of these things come to pass?

Imaging should be pursued

At what location might one expect a malignancy to be found?

-- The skull base
-- The cavernous sinus

A malignancy

What is meant by referring to a pupil-sparing CN3 palsy as 'complete' vs 'partial'?

It refers to the status of the external muscles controlled by CN3. If they are all involved, the palsy is complete; if they are not, it is partial.

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What should be done if any of these things come to pass?

Imaging should be pursued
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Why is the degree of involvement important? Because of its clinical implications. A complete pupil-sparing CN3 palsy is virtually a lock to be vascular if the following pt-related conditions are met:

- The pt is a vasculopath;
- The pt is over 50;
- The pt has no hx of cancer

So a pt has a partial pupil-sparing CN3 palsy. What implications does this carry for etiology?
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving

Pupil-sparing

Complete versus Partial

What is meant by referring to a pupil-sparing CN3 palsy as ‘complete’ vs ‘partial’?
It refers to the status of the external muscles controlled by CN3. If they are all involved, the palsy is complete; if they are not, it is partial.

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Because of its clinical implications. A complete pupil-sparing CN3 palsy is virtually a lock to be vascular if the following pt-related conditions are met:
--- The pt is a vasculopath;
--- the pt is over 50; and
--- the pt has no hx of cancer

So a pt has a partial pupil-sparing CN3 palsy.

What implications does this carry for etiology?
It is much more concerning for a compressive lesion than is a complete pupil-sparing third
**Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy**

**Pupil-involving**

**Pupil-sparing**

- Complete
- Partial

**What is meant by referring to a pupil-sparing CN3 palsy as ‘complete’ vs ‘partial’?**

It refers to the status of the external muscles controlled by CN3. If they are all involved, the palsy is complete; if they are not, it is partial.

**Why is the degree of involvement important?**

Because of its clinical implications. **A complete pupil-sparing CN3 palsy is virtually a lock to be vascular** if the following pt-related conditions are met:

- The pt is a vasculopath;
- The pt is over 50; and
- The pt has no hx of cancer.

So a pt has a **partial** pupil-sparing CN3 palsy. **What implications does this carry for etiology?**

It is much more concerning for a compressive lesion than is a complete pupil-sparing third.

**How should such pts be managed?**
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Pupil-involving

Pupil-sparing

Complete vs Partial

What is meant by referring to a pupil-sparing CN3 palsy as ‘complete’ vs ‘partial’?
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--The pt is a vasculopath;
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--the pt has no hx of cancer.

So a pt has a partial pupil-sparing CN3 palsy. What implications does this carry for etiology?
It is much more concerning for a compressive lesion than is a complete pupil-sparing third.

How should such pts be managed?
They should be imaged immediately.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

And finally, three related topics:
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

And finally, three related topics:

**Topic 1: CN3 palsies in kids.** *How should they be managed?*
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

And finally, three related topics:

**Topic 1: CN3 palsies in kids.** How should they be managed? If pupil-sparing, they can be followed; if pupil-involving, they must be imaged.
Motility Disorders: *Nontraumatic, Isolated, Unilateral CN3 Palsy*

And finally, three related topics:

**Topic 1: CN3 palsy in kids.** *How should they be managed?*
If pupil-sparing, they can be followed; **if pupil-involving, they must be imaged**

Are Pcomm aneurysms common in kids?
Motility Disorders: *Nontraumatic, Isolated, Unilateral CN3 Palsy*

And finally, three related topics:

**Topic 1: CN3 palsies in kids.** *How should they be managed?*
If pupil-sparing, they can be followed; **if pupil-involving, they must be imaged**

**Are Pcomm aneurysms common in kids?**
No, they are very rare
And finally, three related topics:

**Topic 1: CN3 palsies in kids.** How should they be managed?
If pupil-sparing, they can be followed; **if pupil-involving, they must be imaged**

*Are Pcomm aneurysms common in kids?*  
No, they are very rare

*What are common causes on CN3 palsy in kids?*
And finally, three related topics:

**Topic 1: CN3 palsies in kids. How should they be managed?**
If pupil-sparing, they can be followed; **if pupil-involving, they must be imaged**

*Are Pcomm aneurysms common in kids?*
No, they are very rare

*What are common causes on CN3 palsy in kids?*
Post-viral or -vaccinal syndromes
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

And finally, three related topics:

**Topic 1: CN3 palsies in kids.** How should they be managed? If pupil-sparing, they can be followed; if pupil-involving, they must be imaged.

**Topic 2: Pain.** Can etiology (ie, compressive vs ischemic) be differentiated on the basis of whether pain is present?
And finally, three related topics:

**Topic 1: CN3 palsies in kids.** *How should they be managed?* If pupil-sparing, they can be followed; if pupil-involving, they must be imaged.

**Topic 2: Pain.** *Can etiology (ie, compressive vs ischemic) be differentiated on the basis of whether pain is present?* No. While it is the case that most aneurysmal thirds are painful and most vascular are painless, exceptions are frequent enough that pain-status cannot reliably differentiate between them.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

And finally, three related topics:

**Topic 1: CN3 palsies in kids.** *How should they be managed?*
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**Topic 3: Aberrant regeneration.** *What the heck is it?*
And finally, three related topics:

**Topic 1: CN3 palsies in kids. How should they be managed?**
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**Topic 3: Aberrant regeneration.** *What the heck is it?*
A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

And finally, three related topics:

**Topic 1: CN3 palsy in kids.** *How should they be managed?* If pupil-sparing, they can be followed; if pupil-involving, they must be imaged.

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*What are the classic aberrant regeneration mis-connections?*
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

And finally, three related topics:

**Topic 1: CN3 palsies in kids.** *How should they be managed?*
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**Topic 3: Aberrant regeneration.** *What the heck is it?*
A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one.

**What are the classic aberrant regeneration mis-connections?**
--Attempted adduction
--Attempted globe adduction, elevation or depression
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

And finally, three related topics:

**Topic 1: CN3 palsies in kids.** *How should they be managed?* If pupil-sparing, they can be followed; if pupil-involving, they must be imaged.

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**Topic 3: Aberrant regeneration.** *What the heck is it?* A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one.

*What are the classic aberrant regeneration mis-connections?*

-- Attempted adduction ➔ eyelid retraction
-- Attempted globe adduction, elevation or depression ➔
And finally, three related topics:

**Topic 1: CN3 palsies in kids.** *How should they be managed?*
If pupil-sparing, they can be followed; if pupil-involving, they must be imaged.

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**Topic 3: Aberrant regeneration.** *What the heck is it?*
A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one.

*What are the classic aberrant regeneration mis-connections?*
--Attempted adduction $\rightarrow$ eyelid retraction $\leftarrow$ Attempted depression can do it as well
--Attempted globe adduction, elevation or depression $\rightarrow$
Aberrant regeneration of the right third nerve. A, In primary gaze, there is mild ptosis, pupillary mydriasis, and exotropia, all on the right.
Aberrant regeneration of the right third nerve. A, In primary gaze, there is mild ptosis, pupillary mydriasis, and exotropia, all on the right. B, With attempted downward gaze, the right eyelid retracts as fibers of the right third nerve supplying the inferior rectus now also innervate the levator muscle.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

And finally, three related topics:

**Topic 1: CN3 palsies in kids.** *How should they be managed?*
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*What are the classic aberrant regeneration mis-connections?*
--- Attempted adduction → eyelid retraction
--- Attempted globe adduction, elevation or depression → [miosis of the pupil]
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

And finally, three related topics:

**Topic 1: CN3 palsies in kids.** How should they be managed? If pupil-sparing, they can be followed; if pupil-involving, they must be imaged.

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*What are the classic aberrant regeneration mis-connections?*
- Attempted adduction → eyelid retraction
- Attempted globe adduction, elevation or depression → miosis of the pupil
This patient has a long-standing right 3rd nerve palsy causing anisocoria, partial ptosis OD, mild adduction deficit OD, and moderate elevation and depression deficits OD. In addition, there are signs of aberrant regeneration where there is miosis of the pupil and mild lid elevation on adduction OD.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

The phrase *eyelid retraction* should bring to mind several conditions…

*First, what is the most common cause of lid retraction?*

No. While it is the case that most aneurysmal thirds are painful and most vascular are painless, exceptions are frequent enough that pain-status cannot reliably differentiate between them.

**Topic 3: Aberrant regeneration.** *What the heck is it?*

A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one.

What are the classic aberrant regeneration mis-connections?

--Attempted adduction → *eyelid retraction*

--Attempted globe adduction, elevation → miosis of the pupil
The phrase *eyelid retraction* should bring to mind several conditions…

*First, what is the most common cause of lid retraction?*  
Thyroid eye dz (TED)

No. While it is the case that most aneurysmal thirds are painful and most vascular are painless, exceptions are frequent enough that pain-status cannot reliably differentiate between them.

**Topic 3: Aberrant regeneration. What the heck is it?**  
A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one.

What are the classic aberrant regeneration mis-connections?  
--Attempted adduction → eyelid retraction  
--Attempted globe adduction, elevation → miosis of the pupil
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

The phrase *eyelid retraction* should bring to mind several conditions…

*First, what is the most common cause of lid retraction?*  
Thyroid eye dz (TED). When you hear lid retraction, think TED first.

No. While it is the case that most aneurysmal thirds are painful and most vascular are painless, exceptions are frequent enough that pain-status cannot reliably differentiate between them.

**Topic 3: Aberrant regeneration.** *What the heck is it?*  
A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one.

What are the classic aberrant regeneration mis-connections?  
—Attempted adduction → *eyelid retraction*  
—Attempted globe adduction, elevation, depression → miosis of the pupil
TED: Lid retraction
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

The phrase *eyelid retraction* should bring to mind several conditions…

*First, what is the most common cause of lid retraction?* Thyroid eye dz (TED). *When you hear lid retraction, think TED first.*

*When TED pts move their eyes into downgaze, the upper lid will fail to follow the globe down. What is the name for this phenomenon?*

No. While it is the case that most aneurysmal thirds are painful and most vascular are painless, exceptions are frequent enough that pain-status cannot reliably differentiate between them.

*Topic 3: Aberrant regeneration. What the heck is it?* A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one.

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—Attempted adduction → eyelid retraction
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Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

The phrase *eyelid retraction* should bring to mind several conditions…

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Thyroid eye dz (TED). *When you hear lid retraction, think TED first.*

*When TED pts move their eyes into downgaze, the upper lid will fail to follow the globe down. What is the name for this phenomenon?*
Lid lag

No. While it is the case that most aneurysmal thirds are painful and most vascular are painless, exceptions are frequent enough that pain-status cannot reliably differentiate between them.

*Topic 3: Aberrant regeneration. What the heck is it?*
A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one

What are the classic aberrant regeneration mis-connections?
—Attempted adduction → *eyelid retraction*
—Attempted globe adduction, elevation, depression → miosis of the pupil
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

Unilateral. Note how the normal right upper lid has ‘followed’ the globe into downgaze

TED: Lid lag
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

The phrase *eyelid retraction* should bring to mind several conditions…

*First, what is the most common cause of lid retraction?*
Thyroid eye dz (TED). When you hear lid retraction, think TED first.

*When TED pts move their eyes into downgaze, the upper lid will fail to follow the globe down. What is the name for this phenomenon?*
Lid lag

*What is the eponymous name for lid lag 2ndry to TED?*

No. While it is the case that most aneurysmal thirds are painful and most vascular are painless, exceptions are frequent enough that pain-status cannot reliably differentiate between them.

**Topic 3: Aberrant regeneration. What the heck is it?**
A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one

*What are the classic aberrant regeneration mis-connections?*
   — Attempted adduction ➔ eyelid retraction
   — Attempted globe adduction, elevation, depression ➔ miosis of the pupil
The phrase *eyelid retraction* should bring to mind several conditions…

*First, what is the most common cause of lid retraction?*  
Thyroid eye dz (TED). *When you hear lid retraction, think TED first.*

*When TED pts move their eyes into downgaze, the upper lid will fail to follow the globe down. What is the name for this phenomenon?*  
Lid lag

*What is the eponymous name for lid lag 2ndry to TED?*  
von Graefe’s sign

No. While it is the case that most aneurysmal thirds are painful and most vascular are painless, exceptions are frequent enough that pain-status cannot reliably differentiate between them.

**Topic 3: Aberrant regeneration.** *What the heck is it?*  
A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one.

What are the classic aberrant regeneration mis-connections?  
→ Attempted adduction → eyelid retraction  
→ Attempted globe adduction, elevation → miosis of the pupil
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

The phrase *eyelid retraction* should bring to mind several conditions...

First, what is the most common cause of lid retraction? Thyroid eye dz (TED). When you hear lid retraction, think TED first.

When TED patients move their eyes into downgaze, the upper lid will fail to follow the globe down. What is this phenomenon called? Lid lag. What is the eponymous name for lid lag secondary to TED? von Graefe's sign.

what well-known brainstem syndrome is associated with lid retraction? Parinaud syndrome. What is the eponymous name for lid retraction in Parinaud syndrome? Collier's sign. Parinaud's has four cardinal findings. What are the other three? Lid retraction, light-near dissociation, impaired upgaze, convergence-retraction nystagmus.

Topic 3: Aberrant regeneration. *What the heck is it?* A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one.

What are the classic aberrant regeneration/mis-connections? Attempted adduction → eyelid retraction. Attempted globe adduction, elevation, depression → miosis of the pupil.
**Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy**

The phrase *eyelid retraction* should bring to mind several conditions…

*First, what is the most common cause of lid retraction?*  
Thyroid eye dz (TED). When you hear lid retraction, think TED first.

*What is the name for this phenomenon?*  
*Lid lag*

*What is the eponymous name for lid lag 2ndry to TED?*  
*von Graefe’s sign*  

*What well-known brainstem syndrome is associated with lid retraction?*  
Parinaud syndrome

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Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

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First, what is the most common cause of lid retraction?
Thyroid eye dz (TED). When you hear lid retraction, think TED first.

When TED, what happens when the eyes go down?
The upper lid fails to follow the globe down.

What is this phenomenon called?
Lid lag

What is the eponymous name for lid lag 2ndary to TED?
von Graefe's sign

What is the name for the phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one?
Aberrant regeneration

What well-known brainstem syndrome is associated with lid retraction?
Parinaud syndrome

What is the eponymous name for lid retraction in Parinaud syndrome?
Collier's sign

Parinaud's has four cardinal findings. What are the other three?
--Lid retraction--Light-near dissociation--Impaired upgaze--Convergence-retraction nystagmus

What are the classic aberrant regeneration mis-connections?

--Attempted adduction → eyelid retraction
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What is the eponymous name for lid retraction in Parinaud syndrome? Collier’s sign

Parinaud’s has four cardinal findings. What are the other three? --Lid retraction --Light-near dissociation --Impaired upgaze --Convergence-retraction nystagmus

What are the classic aberrant regeneration mis-connections? --Attempted adduction → eyelid retraction --Attempted globe adduction, elevation → miosis of the pupil

Topic 3: Aberrant regeneration. What the heck is it? A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one
Parinaud syndrome. The combination of lid retraction + impaired upgaze gives rise to a characteristic appearance known as *setting sun sign*
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

The phrase *eyelid retraction* should bring to mind several conditions...

First, what is the most common cause of *lid retraction*? Thyroid eye dz (TED). When you hear lid retraction, think TED first.

What well-known brainstem syndrome is associated with *lid retraction*? Parinaud syndrome. Its cardinal findings include:
- Lid retraction
- Light-near dissociation
- Impaired upgaze
- Convergence-retraction nystagmus

There is a form of *ptosis* that is associated with *lid lag*—which one? Congenital myogenic ptosis. In downgaze, their appearance will suggest lid retraction.

In a nutshell, what is the pathogenesis of congenital myogenic ptosis? The levator fails to develop properly, with some or all of its muscle fibers replaced by fibrofatty tissue.

OK, I can see how a lack of functioning levator leads to ptosis, but why do these pts have lid lag? Because the fibrofatty tissue can neither contract (causing ptosis) nor relax (causing lid lag).

Topic 3: Aberrant regeneration. *What the heck is it?* A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one.

What are the classic aberrant regeneration mis-connections?
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Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

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What well-known brainstem syndrome is associated with lid retraction?  
Parinaud syndrome

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What are the classic aberrant regeneration mis-connections?  
—Attempted adduction → eyelid retraction
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What are the classic aberrant regeneration mis-connections?

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Parinaud syndrome

Collier's sign

Lid lag

von Graefe's sign

Light-near dissociation

Impaired upgaze

Convergence-retraction nystagmus

Parinaud's has four cardinal findings. What are the other three?

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Because the fibrofatty tissue can neither contract (causing ptosis) nor relax (causing lid lag)

Topic 3: Aberrant regeneration. What the heck is it?
A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one

What are the classic aberrant regeneration mis-connections?
—Attempted adduction  →  eyelid retraction
—Attempted globe adduction, elevation, or depression  →  miosis of the pupil
**Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy**

The phrase **eyelid retraction** should bring to mind several conditions...

First, what is the most common cause of lid retraction?

**Thyroid eye dz**

More info: Slide-set O5

What well-known brainstem syndrome is associated with lid retraction?

**Parinaud syndrome**

More info: Slide-set N16

There is a form of ptosis that is associated with lid lag—which one?

**Congenital myogenic ptosis**

More info: Slide-set O2

In a nutshell, what is the pathogenesis of congenital myogenic ptosis?

The levator fails to develop properly, with some or all of its muscle fibers replaced by fibrofatty tissue.

OK, I can see how a lack of functioning levator leads to ptosis, but why do these pts have lid lag?

Because the fibrofatty tissue can neither contract (causing ptosis) nor relax (causing lid lag).

These are some of the conditions that must be considered when faced with a case of lid retraction.

$
\text{Topic 3: Aberrant regeneration}
\quad \text{What the heck is it?}
\quad \text{A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one.}$

What are the classic aberrant regeneration mis-connections?

$\rightarrow$ Attempted adduction $\rightarrow$ eyelid retraction

$\rightarrow$ Attempted globe adduction, elevation, depression $\rightarrow$ miosis of the pupil
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

And finally, three related topics:

**Topic 1: CN3 palsies in kids.** How should they be managed? If pupil-sparing, they can be followed; if pupil-involving, they must be imaged.

**Topic 2: Pain.** Can etiology (ie, compressive vs ischemic) be differentiated on the basis of whether pain is present? No. While it is the case that most aneurysmal thirds are painful and most vascular are painless, exceptions are frequent enough that pain-status cannot reliably differentiate between them.

**Topic 3: Aberrant regeneration.** What the heck is it? A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one.

*Of the three main causes of isolated unilateral CN3 palsy (ie, traumatic, compressive and ischemic), which is/are capable of resulting in aberrant regeneration?*
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

And finally, three related topics:

**Topic 1: CN3 palsies in kids.** How should they be managed? If pupil-sparing, they can be followed; if pupil-involving, they must be imaged.

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**Topic 3: Aberrant regeneration.** What the heck is it? A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one.

*Of the three main causes of isolated unilateral CN3 palsy (ie, traumatic, compressive and ischemic), which is/are capable of resulting in aberrant regeneration? Both and can; on the other hand, never does.*
And finally, three related topics:

**Topic 1: CN3 palsies in kids.** *How should they be managed?* If pupil-sparing, they can be followed; if pupil-involving, they must be imaged.

**Topic 2: Pain.** *Can etiology (ie, compressive vs ischemic) be differentiated on the basis of whether pain is present?* No. While it is the case that most aneurysmal thirds are painful and most vascular are painless, exceptions are frequent enough that pain-status cannot reliably differentiate between them.

**Topic 3: Aberrant regeneration.** *What the heck is it?* A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one.

*Of the three main causes of isolated unilateral CN3 palsy (ie, traumatic, compressive and ischemic), which is/are capable of resulting in aberrant regeneration?* Both traumatic and compressive can; on the other hand, ischemic **never** does.
And finally, three related topics:

**Topic 1: CN3 palsies in kids.** How should they be managed? If pupil-sparing, they can be followed; if pupil-involving, they must be imaged.

**Topic 2: Pain.** Can etiology (ie, compressive vs ischemic) be differentiated on the basis of whether pain is present? No. While it is the case that most aneurysmal thirds are painful and most vascular are painless, exceptions are frequent enough that pain-status cannot reliably differentiate between them.

*So if you encounter aberrant regeneration, what should you inquire about?*

Both traumatic and compressive can... ischemic never does.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

And finally, three related topics:

**Topic 1: CN3 palsies in kids.** How should they be managed? If pupil-sparing, they can be followed; if pupil-involving, they must be imaged.

**Topic 2: Pain.** Can etiology (ie, compressive vs ischemic) be differentiated on the basis of whether pain is present? No. While it is the case that most aneurysmal thirds are painful and most vascular are painless, exceptions are frequent enough that pain-status cannot reliably differentiate between them.

**Topic 3: Aberrant regeneration.** What the heck is it? A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one.

Of the three main causes of isolated unilateral CN3 palsy (ie, traumatic, compressive and ischemic), which is/are capable of resulting in aberrant regeneration? Both traumatic and compressive can. Ischemic never does.

So if you encounter aberrant regeneration, what should you inquire about? Whether the pt has a hx of head trauma significant enough to produce a traumatic CN3 palsy.
And finally, three related topics:

**Topic 1: CN3 palsies in kids.** *How should they be managed?*  
If pupil-sparing, they can be followed; if pupil-involving, they must be imaged.

**Topic 2: Pain.** *Can etiology (ie, compressive vs ischemic) be differentiated on the basis of whether pain is present?*  
No. While it is the case that most aneurysmal thirds are painful and most vascular are painless, exceptions are frequent enough that pain-status cannot reliably differentiate between them.

*So if you encounter aberrant regeneration, what should you inquire about?*  
Whether the pt has a hx of head trauma significant enough to produce a traumatic CN3 palsy.

*And what should you do if the pt denies such a history?*  
Assume there’s a compressive etiology, and pursue imaging.

Both traumatic and compressive can result in aberrant regeneration, but ischemic never does.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

And finally, three related topics:

**Topic 1: CN3 palsies in kids.** *How should they be managed?*
If pupil-sparing, they can be followed; if pupil-involving, they must be imaged.

**Topic 2: Pain.** *Can etiology (ie, compressive vs ischemic) be differentiated on the basis of whether pain is present?*
No. While it is the case that most aneurysmal thirds are painful and most vascular are painless, exceptions are frequent enough that pain-status cannot reliably differentiate between them.

*So if you encounter aberrant regeneration, what should you inquire about?*
Whether the pt has a hx of head trauma significant enough to produce a traumatic CN3 palsy.

*And what should you do if the pt denies such a history?*
Assume there’s a compressive etiology, and pursue imaging.

Both traumatic and compressive can cause aberrant regeneration; ischemic never does.
Motility Disorders: *Nontraumatic, Isolated, Unilateral CN3 Palsy*

And finally, three related topics:

*In this context, to what does the term primary aberrant regeneration refer?*

**Primary Topic 3: Aberrant regeneration.** *What the heck is it?*
A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one...
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

And finally, three related topics:

1. **Topic 1: CN3 palsies in kids.** How should they be managed? If pupil-sparing, they can be followed; if pupil-involving, they must be imaged.

2. **Topic 2: Pain.** Can etiology (ie, compressive vs ischemic) be differentiated on the basis of whether pain is present? No. While it is the case that most aneurysmal thirds are painful and most vascular are painless, exceptions are frequent enough that pain-status cannot reliably differentiate between them.

3. **Topic 3: Aberrant regeneration.** What the heck is it? A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one.

**In this context, to what does the term primary aberrant regeneration refer?** It refers to the presence of aberrant-regeneration-type EOM movements absent a clear history of a precipitating CN3 palsy.

**Primary**

**Topic 3: Aberrant regeneration.** What the heck is it? A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

And finally, three related topics:

In this context, to what does the term primary aberrant regeneration refer? It refers to the presence of aberrant-regeneration-type EOM movements absent a clear history of a precipitating CN3 palsy.

What etiology is suggested by this presentation?

Primary Aberrant regeneration. What the heck is it?
A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

And finally, three related topics:

In this context, to what does the term primary aberrant regeneration refer? It refers to the presence of aberrant-regeneration-type EOM movements absent a clear history of a precipitating CN3 palsy.

What etiology is suggested by this presentation? A slowly-expanding compressive lesion in the parasellar region.

Primary aberrant regeneration. What the heck is it? A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

And finally, three related topics:

Topic 1: CN3 palsies in kids. How should they be managed? If pupil-sparing, they can be followed; if pupil-involving, they must be imaged.

Topic 2: Pain. Can etiology (ie, compressive vs ischemic) be differentiated on the basis of whether pain is present? No. While it is the case that most aneurysmal thirds are painful and most vascular are painless, exceptions are frequent enough that pain-status cannot reliably differentiate between them.

Topic 3: Aberrant regeneration. What the heck is it? A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one.

Primary aberrant regeneration. What the heck is it? A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one.

How should one manage a pt with primary aberrant regeneration? It refers to the presence of aberrant-regeneration-type EOM movements absent a clear history of a precipitating CN3 palsy. What etiology is suggested by this presentation? A slowly-expanding compressive lesion in the parasellar region. A slowly-expanding compressive lesion in the parasellar region.

Primary aberrant regeneration. What the heck is it? A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one.

In this context, to what does the term primary aberrant regeneration refer? It refers to the presence of aberrant-regeneration-type EOM movements absent a clear history of a precipitating CN3 palsy.

What etiology is suggested by this presentation? A slowly-expanding compressive lesion in the parasellar region. A slowly-expanding compressive lesion in the parasellar region.

How should one manage a pt with primary aberrant regeneration? Via imaging with special attention to the parasellar region (looking for a meningioma) and cavernous sinus (looking for an aneurysm of the internal carotid).
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

And finally, three related topics:

In this context, to what does the term primary aberrant regeneration refer?
It refers to the presence of aberrant-regeneration-type EOM movements absent a clear history of a precipitating CN3 palsy.

What etiology is suggested by this presentation?
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How should one manage a pt with primary aberrant regeneration?
Via imaging with special attention to the parasellar region (looking for a meningioma) and cavernous sinus (looking for an aneurysm of the internal carotid).

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A phenomenon in which healing nerve fibers form incorrect connections, resulting in impulses intended for one muscle stimulating a different one.
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

And finally, three related topics:

**Topic 1:** CN3 palsies in kids. How should they be managed? If pupil-sparing, they can be followed; if pupil-involving, they must be imaged.

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Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

And finally, three related topics:

**Topic 1: CN3 palsies in kids.** *How should they be managed?*
If pupil-sparing, they can be followed; if pupil-involving, they must be imaged.

**Topic 2: Pain.** *Can etiology (ie, compressive vs ischemic) be differentiated on the basis of whether pain is present?*
No. While it is the case that most aneurysmal thirds are painful and most vascular are painless, exceptions are frequent enough that pain-status cannot reliably differentiate between them.

**Topic 3: Aberrant regeneration of the...?**
*Finally—the Neuro book addresses in some depth the aberrant regeneration of another cranial nerve—which one?*
And finally, three related topics:

**Topic 1: CN3 palsies in kids.** *How should they be managed?* If pupil-sparing, they can be followed; if pupil-involving, they must be imaged.

**Topic 2: Pain.** *Can etiology (ie, compressive vs ischemic) be differentiated on the basis of whether pain is present?* No. While it is the case that most aneurysmal thirds are painful and most vascular are painless, exceptions are frequent enough that pain-status cannot reliably differentiate between them.

**Topic 3: Aberrant regeneration of the...facial nerve**

*Finally—the Neuro book addresses in some depth the aberrant regeneration of another cranial nerve—which one?* CN7
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

And finally, three related topics:

**Topic 1: CN3 palsies in kids.** *How should they be managed?*
If pupil-sparing, they can be followed; if pupil-involving, they must be imaged.

**Topic 2: Pain.** *Can etiology (ie, compressive vs ischemic) be differentiated on the basis of whether pain is present?*
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**Topic 3: Aberrant regeneration of the...facial nerve**

*Finally—the Neuro book addresses in some depth the aberrant regeneration of another cranial nerve—which one?*  
CN7

*What is the classic prior event that results in aberrant regeneration of CN7?*
Motility Disorders: Nontraumatic, Isolated, Unilateral CN3 Palsy

And finally, three related topics:

Topic 1: CN3 palsy in kids. How should they be managed? If pupil-sparing, they can be followed; if pupil-involving, they must be imaged.

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Topic 3: Aberrant regeneration of the...facial nerve

Finally—the Neuro book addresses in some depth the aberrant regeneration of another cranial nerve—which one? CN7

What is the classic prior event that results in aberrant regeneration of CN7? Bell’s palsy
And finally, three related topics:

**Topic 1: CN3 palsies in kids.** *How should they be managed?* If pupil-sparing, they can be followed; if pupil-involving, they must be imaged.

**Topic 2: Pain.** *Can etiology (ie, compressive vs ischemic) be differentiated on the basis of whether pain is present?* No. While it is the case that most aneurysmal thirds are painful and most vascular are painless, exceptions are frequent enough that pain-status cannot reliably differentiate between them.

**Topic 3: Aberrant regeneration of the...facial nerve**

*Finally—the Neuro book addresses in some depth the aberrant regeneration of CN7. What are the classic ophthalmic manifestations of aberrant regeneration of CN7?*

Bell’s palsy
And finally, three related topics:

**Topic 1: CN3 palsies in kids.** *How should they be managed?*
If pupil-sparing, they can be followed; if pupil-involving, they must be imaged.

**Topic 2: Pain.** *Can etiology (ie, compressive vs ischemic) be differentiated on the basis of whether pain is present?*
No. While it is the case that most aneurysmal thirds are painful and most vascular are painless, exceptions are frequent enough that pain-status cannot reliably differentiate between them.

**Topic 3: Aberrant regeneration** of the... facial nerve

*Finally—the Neuro book addresses in some depth the aberrant regeneration of another cranial nerve—which one?*

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**What are the classic ophthalmic manifestations of aberrant regeneration of CN7?**
--Blinking causes... *[one of two things, or both]*
--Movements of the lower face cause...

**What is the classic prior event that results in aberrant regeneration of CN7?**
Bell’s palsy
And finally, three related topics:

**Topic 1: CN3 palsies in kids.** How should they be managed? If pupil-sparing, they can be followed; if pupil-involving, they must be imaged.

**Topic 2: Pain.** Can etiology (ie, compressive vs ischemic) be differentiated on the basis of whether pain is present? No. While it is the case that most aneurysmal thirds are painful and most vascular are painless, exceptions are frequent enough that pain-status cannot reliably differentiate between them.

**Topic 3: Aberrant regeneration of the...facial nerve**

Finally—the Neuro book addresses in some depth the aberrant regeneration of... CNs, CN7?

What are the classic ophthalmic manifestations of aberrant regeneration of CN7?
--Blinking causes... twitching at the corner of the mouth, or chin dimpling
--Movements of the lower face cause...

What is the classic prior event that results in aberrant regeneration of CN7? Bell’s palsy
Aberrant regeneration of CN7 after Bell’s palsy: narrowing of the palpebral aperture on the affected side during cheek puffing.
And finally, three related topics:

**Topic 1: CN3 palsies in kids.** *How should they be managed?*
If pupil-sparing, they can be followed; if pupil-involving, they must be imaged

**Topic 2: Pain.** *Can etiology (ie, compressive vs ischemic) be differentiated on the basis of whether pain is present?*
No. While it is the case that most aneurysmal thirds are painful and most vascular are painless, exceptions are frequent enough that pain-status cannot reliably differentiate between them.

**Topic 3: Aberrant regeneration**

*Finally—the Neuro book addresses in some depth the aberrant regeneration of another cranial nerve—which one?*

*What is the classic prior event that results in aberrant regeneration of CN7?*
Bell’s palsy

*What are the classic ophthalmic manifestations of aberrant regeneration of CN7?*
--Blinking causes…twitching at the corner of the mouth, or chin dimpling
--Movements of the lower face cause…?
And finally, three related topics:

**Topic 1: CN3 palsies in kids.** *How should they be managed?* If pupil-sparing, they can be followed; if pupil-involving, they must be imaged.

**Topic 2: Pain.** *Can etiology (ie, compressive vs ischemic) be differentiated on the basis of whether pain is present?* No. While it is the case that most aneurysmal thirds are painful and most vascular are painless, exceptions are frequent enough that pain-status cannot reliably differentiate between them.

**Topic 3: Aberrant regeneration of the...facial nerve**

*Finally—the Neuro book addresses in some depth the aberrant regeneration of CNs, but this is very complex...*

- What are the classic ophthalmic manifestations of aberrant regeneration of CN7? Bell’s palsy
  - Blinking causes... **twitching at the corner of the mouth, or chin dimpling**
  - Movements of the lower face cause... **involuntary lid closure**