The extraocular muscles (EOMs) are innervated by cranial nerves 3, 4 and 6. (The reason they’re not in numerical order above will become clear shortly.)
The extraocular muscles (EOMs) are innervated by cranial nerves 3, 4 and 6. (The reason they’re not in numerical order above will become clear shortly.) CN3 innervates the superior, inferior and medial rectus muscles and the inferior oblique (as well as the levator palpebrae superioris, the main elevator of the upper lid). CN6 innervates the lateral rectus; CN4, the superior oblique.
<table>
<thead>
<tr>
<th>CN3</th>
<th>CN6</th>
<th>CN4</th>
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With respect to EOM issues, it is useful to divvy the system into four levels or pathways. (We will identify/introduce the four first, then discuss each in some detail.)
With respect to EOM issues, it is useful to divvy the system into four levels or pathways. (We will identify/introduce the four first, then discuss each in some detail.)

The first level is the **nuclear**. This level consists of the nuclei (i.e., the collection of cell bodies within the CNS) that give rise to the axons forming each nerve. Take note: *Every other level is defined in terms of its relationship to the nuclear level.*
The supranuclear pathways consists of inputs to the nuclei from centers in the cortex, cerebellum, vestibular system, etc.
Supranuclear

The *supranuclear pathways* consists of inputs to the nuclei from centers in the cortex, cerebellum, vestibular system, etc. These locations are ‘supra’ in that they carry signals to the nuclei.

Nuclear

Motility Disorders

CN3 Nucleus

CN6 Nucleus

CN4 Nucleus
The internuclear pathway consists of a set of axons projecting from the CN6 nucleus on one side to the CN3 nucleus on the other.
The internuclear pathway consists of a set of axons projecting from the CN6 nucleus on one side to the CN3 nucleus on the other. This pathway is called the medial longitudinal fasciculus (MLF).
The infranuclear pathway consists of everything below the nuclei: the axons as they run from the nuclei to the neuromuscular junction; the junction itself; and finally the EOMs themselves. (There are many subsections in this pathway; we will identify them shortly.)
This slide summarizes the basic organization of EOM control.

**Supranuclear**

**Nuclear**

**Internuclear**

**Infranuclear**

Extraocular muscle
This slide summarizes the basic organization of EOM control. When you encounter a pt with a motility issue, your first thought should be: Is this issue **nuclear**, **supranuclear**, **internuclear**, or **infranuclear** in origin?

**Supranuclear**

**Nuclear**

**Internuclear**

**Infranuclear**

Extraocular muscle
Next we will look at each level/pathway in more detail.
Let’s start with the infranuclear pathway.
Let’s start with the infranuclear pathway. There are a number of locations along this pathway at which a motility disorder might be induced; we will address them in anatomic order from central → peripheral.
The bundle of axons that leave a nucleus, but are still within the brainstem, is called a *fascicle*.
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The bundle of axons that leave a nucleus, but are still within the brainstem, is called a **fascicle**.

A **fascicular syndrome** is one in which an EOM issue is due to damage of a fascicle. Because the fascicles are located within the brainstem, it should come as no surprise that fascicular lesions do not present with *isolated* EOM abnormalities; rather, the ophthalmoparesis is accompanied by *nonocular* findings consistent with a CNS lesion. Thus, each fascicular syndrome consists of paresis of one or more EOMs along with a particular set of nonocular signs and symptoms. It is by this set of nonocular signs/symptoms that you will be expected to both **recognize** a fascicular syndrome as well as **identify the location** within the brainstem of the insult that caused it.
## Motility Disorders

### CN3 Fascicular Syndromes

<table>
<thead>
<tr>
<th>Syndrome</th>
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</tr>
<tr>
<td>Benedikt</td>
<td></td>
</tr>
<tr>
<td>Claude</td>
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</tr>
<tr>
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These are the **CN3 fascicular syndromes** covered in the BCSC.
## CN3 Fascicular Syndromes

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These are the **CN3 fascicular syndromes** covered in the BCSC, along with their nonocular signs/symptoms.
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# Motility Disorders

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These are the **CN3 fascicular syndromes** covered in the *BCSC*, along with their nonocular signs/symptoms, and their lesion locations. **Do not try to memorize the entire Table right now.** Rather, just look over the names until you are passingly familiar with them.
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These are the **CN3 fascicular syndromes** covered in the BCSC, along with their nonocular signs/symptoms, and their lesion locations. **Do not try to memorize the entire Table right now.** Rather, just look over the names until you are passingly familiar with them. You will be way ahead of the game at this juncture if you are simply able to identify the four CN3 fascicular syndromes.
**Motility Disorders**

## CN6 Fascicular Syndromes

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<th>Syndrome</th>
<th>Ipsilateral 6th plus…</th>
<th>Lesion location</th>
</tr>
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<tr>
<td><strong>Millard-Gubler</strong></td>
<td>Ipsilateral CN7 and contralateral hemiplegia</td>
<td>Ventral pons</td>
</tr>
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<td><strong>Foville</strong></td>
<td>Ipsilateral CN7 and contralateral hemiplegia and facial hypoesthesia and loss of taste to anterior tongue</td>
<td>Tractus solitarius</td>
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Likewise, these are the **CN6 fascicular syndromes**. Again, just being able to identify the two of them is enough for now.
Finally, note that there are no CN4 fascicular syndromes covered in the BCSC.
Changing gears momentarily: Motility disorders 2ndry to **Nuclear-level** lesions are uncommon.
Changing gears momentarily: Motility disorders 2ndry to **Nuclear-level** lesions are uncommon. That said, and because the cranial-nerve nuclei are located within the brainstem, it shouldn’t come as a surprise that, like fascicular lesions, most motility disorders 2ndry to nuclear lesions present in concert with nonocular CNS findings.
Motility Disorders

Supranuclear

Infranuclear

Changing gears momentarily: Motility disorders 2ndry to Nuclear-level lesions are uncommon. That said, and because the cranial-nerve nuclei like fascicular lesions, most motility disorders 2ndry to Nuclear lesions present in concert with nonocular CNS findings.

Now back to our tour of the infranuclear pathway…

Nuclear

Internuclear

Supranuclear

Infranuclear

CN3 Nucleus

MLF

CN6 Nucleus

CN4 Nucleus

Extraocular muscle
The next portion commences once the axonal fibers exit the brainstem and enter the subarachnoid space. Now the fibers officially constitute a nerve.
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The next portion commences once the axonal fibers exit the brainstem and enter the subarachnoid space. Now the fibers officially constitute a nerve. One of the most common causes of CN palsies—ischemic damage, usually related to systemic vasculopathic conditions such as HTN and DM—usually occurs in the subarachnoid portion of the infranuclear pathway. Later in the slide-set, we will drill down on some important considerations regarding CN3 palsies secondary to insults in the subarachnoid portion of the infranuclear pathway.
Motility Disorders

Supranuclear

Nuclear

Internuclear

Fascicular

Subarachnoid

Cavernous sinus

Infranuclear

Extraocular muscle

The nerves leave the subarachnoid space when they enter the cavernous sinus (CS).
The nerves leave the subarachnoid space when they enter the cavernous sinus (CS). The CS are venous sinuses located just behind the orbits and lateral to the sella turcica/pituitary fossa.
There's one over here too

Cavernous sinuses
The nerves leave the subarachnoid space when they enter the cavernous sinus (CS). The CS are venous sinuses located just behind the orbits and lateral to the sella turcica/pituitary fossa. The hallmark of ophthalmoplegia secondary to a CS process is the involvement of multiple nerves simultaneously.
A number of critical structures are located within each CS. CN6 was alluded to a few slides ago--what are the others? Where within the CS is each located? -- The internal carotid artery: The cavern

-- CN6
-- CN3
-- CN4
-- V1
-- V2
-- Postganglionic sympathetics

Simultaneous deficits involving structures innervated by some (or all!) of these nerves is highly suggestive of CS pathology.
The nerves leave the subarachnoid space when they enter the cavernous sinus (CS). The CS are venous sinuses located just behind the orbits and lateral to the sella turcica/pituitary fossa. The hallmark of ophthalmoplegia secondary to a CS process is the involvement of multiple nerves simultaneously. Additionally, CS pathology can impede venous drainage of the eye, resulting in engorged conj vessels, chemosis, and/or increased IOP.
Engorged conj vessels and chemosis 2ndry to CS pathology—take note!
Supranuclear

Nuclear

Infranuclear

Motility Disorders

CN3
Nucleus

MLF

CN6
Nucleus

CN4
Nucleus

Fascicular

Subarachnoid

Cavernous sinus

Orbital

After the CS, the next well-defined space is the orbit.

Extraocular muscle
After the CS, the next well-defined space is the orbit. But, superior orbital fissure (SOF) is also good, if not better (the Neuro book breaks out the fissure as a separate structure in the pathway).
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After the CS, the next well-defined space is the orbit. But, *superior orbital fissure* (SOF) is also good, if not better (the *Neuro* book breaks out the fissure as a separate structure in the pathway). Likewise, orbital apex is also legit as a 'locale' on the infranuclear pathway.

Frequently, CS and SOF lesions are clinically indistinguishable, because both can present with involvement of any subset of nerves that pass through both.
After the CS, the next well-defined space is the orbit. But, *superior orbital fissure* (SOF) is also good, if not better (the *Neuro* book breaks out the fissure as a separate structure in the pathway). Likewise, orbital apex is also legit as a ‘locale’ on the infranuclear pathway.

Frequently, CS and SOF lesions are clinically indistinguishable, because both can present with involvement of any subset of nerves that pass through both. However, lesions of the orbital apex are easily recognized differentiated from CS and SOF lesions, because apical lesions involve the *optic nerve* as well.
Motility Disorders

Orbital apex: All the nerves…
Orbital apex: All the nerves…including the ‘optic’ one
Motility Disorders

Supranuclear

Nuclear

Internuclear

CN3 Nucleus

MLF

CN6 Nucleus

CN4 Nucleus

Fascicular

Subarachnoid

Cavernous sinus

Orbital

Neuromuscular junction

Extraocular muscle

Infranuclear

The NM junction is where the journey ends for the nerves.
Motility Disorders

Supranuclear

Nuclear

Internuclear

CN3 Nucleus

MLF

CN6 Nucleus

CN4 Nucleus

Fascicular

Subarachnoid

Cavernous sinus

Orbital

Neuromuscular junction

Extraocular muscle

The NM junction is where the journey ends for the nerves. The “prototypical” disease of the NM junction is *myasthenia gravis*. 
And finally…There is pathology localized to the EOMs themselves.
And finally... There is pathology localized to the EOMs themselves. This includes conditions such as thyroid eye dz, orbital myositis, and myopathy (eg, CPEO.)
One commonly encountered motility issue is the *nontraumatic, isolated unilateral CN3 palsy*. (*Isolated* means ‘absent nonocular of other signs or symptoms.’)
One commonly encountered motility issue is the nontraumatic, isolated unilateral CN3 palsy. (Isolated means ‘absent nonocular of other signs or symptoms.’) The majority of nontraumatic, isolated CN3 palsies are secondary to an insult to the subarachnoid portion of the infranuclear pathway.
One commonly encountered motility issue is the nontraumatic, isolated unilateral CN3 palsy. (Isolated means ‘absent nonocular of other signs or symptoms.’) The majority of nontraumatic, isolated CN3 palsies are secondary to an insult to the subarachnoid portion of the infranuclear pathway. Two such insults are of particular note: an ischemic event, and a compressive event. These are noteworthy because of how common they are (ischemic), and of how potentially dire the consequences are (compressive).
A nontraumatic, isolated unilateral CN3 palsy will present with unilateral ophthalmoparesis involving some or all of the EOMs innervated by CN3: the *superior*, *inferior* and *medial rectus* muscles; the *inferior oblique*; and the *levator* muscle of the lid.
CN3 palsy. Note the classic ‘down and out’ eye position. Note also the presence of ‘thumb sign’ (ie, that the lid had to be manually elevated to see the eye in the first place).
Motility Disorders

**CN3 palsy**

A nontraumatic, isolated unilateral CN3 palsy will present with unilateral ophthalmoparesis involving some or all of the EOMs innervated by CN3: the superior, inferior and medial rectus muscles; the inferior oblique; and the levator muscle of the lid. Of particular note, the pupil might be affected as well. This is because CN3 carries preganglionic parasympathetic fibers to the pupil, and if these are bagged, that pupil will be larger (because of the dilatory inputs from the unopposed sympathetics) than the fellow eye’s.
Did you notice the dilated pupil?
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This last point must be emphasized, because clinical status of the pupil plays a pivotal role in the management of CN3 palsies.
Motility Disorders

CN3 palsy

Pupil-involving  versus  Pupil-sparing

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Motility Disorders

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CN3 palsy
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Motility Disorders

**CN3 palsy**

Pupil-involving  **versus**  Pupil-sparing

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How can the status of the pupil implicate an aneurysm as causing a CN3 palsy? It has to do with the topography of the third nerve. The pre-ganglionic parasympathetics run in the superficial, outermost portion of the nerve. Given this, a lesion compressing the nerve will bag these fibers, leaving the sympathetics unopposed to dilate the pupil on that side.
CN3 topography—check out the arrowed part
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How can the status of the pupil implicate an aneurysm as causing a CN3 palsy? It has to do with the topography of the third nerve. 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.
Now let’s look at the **internuclear pathway**.

As mentioned previously, the MLF runs from the CN6 nucleus on one side to the CN3 nucleus on the other. More specifically, the MLF runs to the medial rectus (MR) subnucleus on that side. The MLF facilitates coordinated lateral gaze of both eyes by causing the contralateral MR to fire simultaneously with the ipsilateral lateral rectus (LR), thus ensuring both eyes turn into lateral gaze together.
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So if the depicted CN6 nucleus is on a pt’s left side, the depicted MLF runs to her right MR subnucleus.
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If the MLF is bagged, the impulse intended to result in the firing of the contralateral MR is affected...
Now let’s look at the internuclear pathway. As mentioned previously, the MLF runs from the CN6 nucleus on one side to the CN3 nucleus on the other. More specifically, the MLF runs to the medial rectus (MR) subnucleus on the side contralateral to gaze. Thus, if the MLF is bagged, the impulse intended to result in the firing of the contralateral MR is affected…but the impulse to the ipsilateral LR gets through unscathed. Sending impulses (via the MLF) to her right MR subnucleus, which in turn causes the right MR to contract simultaneously—and both eyes shift into left gaze in coordinated fashion.
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This is an internuclear ophthalmoplegia (INO)
Now let's look at the internuclear pathway. As mentioned previously, the MLF runs from the CN6 nucleus on one side to the CN3 nucleus on the other. More specifically, the MLF runs to the medial rectus (MR) subnucleus on that side. The MLF facilitates coordinated lateral gaze of both eyes by causing the contralateral MR to fire simultaneously with the ipsilateral lateral rectus (LR), thus ensuring both eyes turn into lateral gaze together.

So if the depicted CN6 nucleus is on a patient's left side, the depicted MLF runs to her right MR subnucleus. When the patient endeavors to look to her left, the left CN6 nucleus causes the left LR to contract while also sending impulses (via the MLF) to her right MR subnucleus, which in turn causes the right MR to contract simultaneously—and both eyes shift into left gaze in coordinated fashion.

If the MLF is bagged, the impulse intended to result in the firing of the contralateral MR is affected...but the impulse to the ipsilateral LR gets through unscathed. Thus, attempted lateral gaze results in normal abduction of the ipsilateral eye, but impaired adduction of the contralateral eye.

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The causative event for an INO is a function of pt age:
-- In a teen/young adult, it is usually demyelinating dz (ie, MS)
-- In an older adult, it is usually 2ndry to a CVA

Always consider pseudo-INO 2ndry to myasthenia gravis (MG)—MG can mimic any motility disorder that does not involve the pupil!
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**Supranuclear**

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**Subarachnoid**

Cavernous sinus

**Infranuclear**

Orbital

Neuromuscular junction

**Extraocular muscle**

**Internuclear**

Six systems in the primate CNS that deal with these fixation-related issues.
1) The **ocular fixation system**

2) The **smooth-pursuit system**

3) The **vergence system**

4) The **vestibulo-ocular reflex (VOR) system** and the 5) **optokinetic nystagmus (OKN) system** are responsible for holding an image steady during head rotations—either brief and rapid (VOR) or slower and sustained (OKN).
Supranuclear

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Infranuclear

Cavernous sinus

Orbital

Neuromuscular junction

Extraocular muscle
**Motility Disorders**

**Supranuclear**

six systems in the primate CNS that deal with these fixation-related issues

1) The *ocular fixation system*

2) The *smooth-pursuit system*

3) The *vergence system*

4) The *vestibulo-ocular reflex (VOR) system* and the 5) *optokinetic nystagmus (OKN) system*

6) The *saccadic system* is responsible for rapidly shifting fixation from the current object of interest to a new one located in the visual periphery.

**Infranuclear**

- Cavernous sinus
- Orbital
- Neuromuscular junction
- Extraocular muscle
That’s it! Go through this slide-set a couple of times (at least) until you feel like you have a handle on it. When you’re ready, do slide-set N18, which covers this material in a Q&A format (and more detail).