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.
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 (ie, 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.
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.
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.

When you encounter a pt with a motility issue, your first thought should be: Is this deficit nuclear, supranuclear, internuclear, or infranuclear in origin?
When you encounter a pt with a motility issue, your first thought should be: *Is this issue nuclear, supranuclear, internuclear, or infranuclear in origin?*
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 $\rightarrow$ peripheral.
The bundle of axons that leave a nucleus, but are still within the brainstem, is called a **fascicle**.
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## Motility Disorders

### CN3 Fascicular Syndromes

<table>
<thead>
<tr>
<th>Syndrome</th>
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These are the **CN3 fascicular syndromes** covered in the *BCSC*
## Motility Disorders

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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. You will be way ahead of the game at this juncture if you are simply able to identify the four CN3 fascicular syndromes.
### CN6 Fascicular Syndromes

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<tr>
<td>Millard-Gubler</td>
<td>Ipsilateral CN7 and contralateral hemiplegia</td>
<td>Ventral pons</td>
</tr>
<tr>
<td>Foville</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.
Motility Disorders

- Supranuclear
- Infranuclear
- Nuclear
- Internuclear

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.
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...
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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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.
The nerves leave the subarachnoid space when they enter the cavernous sinus (CS).

Extraocular muscle
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 2ndry 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 conjunctival vessels, chemosis, and/or increased IOP.
Engorged conj vessels and chemosis 2ndry to CS pathology—take note!
After the CS, the next well-defined space is the orbit.
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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). 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). 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.
Orbital apex: All the nerves…
Orbital apex: All the nerves…including the ‘optic’ one
The NM junction is where the journey ends for the nerves.
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.’)
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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).
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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Motility Disorders

CN3 palsy

Pupil-involving versus Pupil-sparing

CN3 palsy
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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, leaving the sympathetics unopposed to dilate the pupil on that side.
CN3 topography—check out the arrowed part
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Now let’s look at the internuclear pathway.

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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This is an internuclear ophthalmoplegia (INO).
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This is an internuclear ophthalmoplegia (INO). 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!
Before discussing *supranuclear lesions*, we need to define the role of the efferent (ie, motor) component of the visual system. But before we do *that*, we have to define the role of the *afferent* system.

In primates, vision has two purposes: 1) to detect objects of interest (eg, things you may want to eat, or may want to eat you), and 2) to scrutinize objects of interest (ie, to determine definitely whether it’s an eat-er vs an eat-ee). It follows from this that the efferent visual system has two jobs: 1) Keep both foveas pointing at the current object of regard; and 2) rapidly redirect both foveas to a new object when one is detected in the periphery.
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Motility Disorders

Supranuclear

The supranuclear pathways consist of six systems in the primate CNS that deal with these fixation-related issues.

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## Motility Disorders

### Supranuclear

**Supranuclear**

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

1. The **ocular fixation system** is responsible for maintaining a high-quality image of a stationary object when the head is still.

### Internuclear

**Internuclear**

- Fascicular
- Subarachnoid
- Cavernous sinus
- Orbital
- Neuromuscular junction
- Extraocular muscle

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3) The *vergence system* is responsible for maintaining fixation on an object that is moving toward or away from the eyes, thus necessitating they converge or diverge. Many forms of vergence dysfunction can occur, including convergence insufficiency, divergence insufficiency, accommodative esotropia, and spasm of the near.

The supranuclear pathways consist of six systems in the primate CNS that deal with these fixation-related issues. Thus, lesions of a supranuclear pathway manifest as difficulties with either the maintenance or acquisition of bifixation.

**Internuclear**

**Infranuclear**

- Subarachnoid
- Cavernous sinus
- Orbital
- Neuromuscular junction
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**Supranuclear** six systems in the primate CNS that deal with these fixation-related issues

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Motility Disorders

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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).

Internuclear

Cavernous sinus

Orbital

Neuromuscular junction

Extraocular muscle

Infranuclear

Nuclear

Nucleus

MLF

Supranuclear

Fascicular

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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). The VOR is controlled by the vestibular labyrinth, ie, the semicircular canals and otoliths; the OKN system, by images sweeping across the retina.

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

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