I (Olfactory Nerve)

The olfactory nerve is unique, but not in ways that make it particularly interesting. The sensory neurons in the olfactory epithelium are outside the meninges and below the cribriform plate. They synapse in the bulb itself, and those secondary neurons project to the Anterior Olfactory Nucleus, and from there the input is transmitted to the frontal lobe as well as the uncus. It is this latter, temporal lobe connection that underlies the olfactory illusions sometimes experienced in epilepsy (so called “uncinate fits”).

II (Optic Nerve)

A discussion of the optic nerve begins with the retina. I will leave the detailed--the painfully detailed--physiology of the retina to another time, but there are some fun retina facts that you need to be able to regurgitate on command.

The layers of the retina:
This can be tricky because “inner” and “outer” are inexact terms. Just remember “choroid” and “vitreous” as the boundaries. The vitreous is of course the goo inside the globe, and the choroid is the layer closer to your brain. So from choroid to vitreous, the layers are
- Pigment Epithelium
- Rods/Cones
- Bipolar Cells
- Ganglion Cells
(This means that the receptors that actually receive visual input are at the bottom of the heap. This is called the “inverted retina”, and all vertebrates have this design.)

The Macula:
The central area (5mm diameter) of the retina, for acute vision.

The Fovea:
The central area of the macula (1.5mm diameter), almost entirely cones.

The Optic Nerve:
This is a blind spot. No receptors are here. Instead, fibers from all of the other receptors are gathered here to get on the optic nerve superhighway to the occipital cortex.
**The Optic Tract**

**Vision**
The fibers of the optic nerve shuffle at the chiasm, but in a very sensible way. The nasal fibers cross, and as a result the left optic tract contains all information about the right visual field, and the right optic tract contains all information about the left visual field.

In the process of crossing, however, the nasal fibers travel briefly forward into the contralateral optic nerve. This wrong turn towards the contralateral eye and subsequent U-turn is called **von Willebrand’s Knee**. Fibers then travel in the optic tract to synapse in the **Lateral Geniculate Nucleus**. From there, visual information travels more diffusely, in the optic radiations. Information about the inferior visual field travels in the superior (parietal) **optic radiations**. Information about the superior visual field travels in the inferior radiations (**Meyer’s Loop**). Both come together in the occipital cortex at the **calcarine fissure**. This pathway is worth memorizing, primarily so that you can make sense of the effect of lesions along its course (see figure above).

**Pupillary Light Reflex**
The light reflex seems very different when you compare it to the visual system. Don’t compare it to the visual system. Compare it to every other reflex in the body, and it makes perfect sense: An afferent nerve carries a stimulus to the neuraxis, and an efferent nerve carries the response to a muscle. The afferent nerve happens to be the **Optic Nerve**, which carries the stimulus to the **optic tract** but past the LGN (no synapse there) to the **Edinger-Westphal Nuclei** (the rostral third of the **Oculomotor Nucleus**) in the midbrain. The motor response travels in the **Oculomotor Nerve** (along the outside of the nerve) to the **pupillary sphincter**. Just like tapping a patellar tendon.

The difference of course is that both pupils constrict when one is stimulated. This is due to the fact that both Edinger-Westphal nuclei are stimulated simultaneously by afferents
from the optic tract. If the afferent portion of the reflex is compromised (at the optic nerve), then stimulation of the affected eye will not trigger constriction in either eye. This is dramatically demonstrated by the swinging flashlight test. When the good eye is stimulated, both eyes constrict (the efferent is fine bilaterally). When the flashlight is swung to the affected eye, it paradoxically dilates (in fact, both eyes do) due to the lack of afferent input into the Edinger-Westphal nucleus. This is the so called **Afferent Pupillary Defect**. Meditate on the name, and all will become clear.

**Oculomotor Nerve (III)**

**Nucleus**
Not counting the fibers going to the pupil, the **Oculomotor Nerve** innervates 5 muscles (*Inferior Rectus, Inferior Oblique, Medial Rectus, Superior Rectus, and Levator Palpebrae*). The nucleus, located in the dorsum of the midbrain, is therefore divided into clusters of cells devoted to their respective muscles.

The **oculomotor nerve** itself exits the midbrain at the level of the red nucleus in the **interpeduncular fossa**.

This proximity of cranial nerve fibers, cerebellar fibers, and pyramidal fibers, makes for potentially testable lacunar syndromes:

**Weber’s:** Ventromedial midbrain infarction causing ipsilateral IIId nerve palsy (involvement of the fascicles) and contralateral hemiplegia (involvement of the peduncle). Weber’s is ventral.
**Benedikt’s:** Dorsomedial midbrain infarction causing ipsilateral IIIrd nerve palsy (involvement of the fascicles) and contralateral tremor/dysmetria (involvement of the red nucleus). Benedikt is a traitor and so has a shaky hand.

**Claude’s:** Combination of Weber’s and Benedikt’s.

From there, the **Oculomotor Nerve** travels through the **Cavernous Sinus** (start keeping track of which nerves go through the cavernous sinus) and eventually the **Superior Orbital Fissure**. There the nerve splits into a superior and an inferior twig. The **Superior Division** innervates, sensibly, the **Superior Rectus** and **Levator**. The **Inferior Division** innervates the **Inferior Rectus, Inferior Oblique, Medial Rectus**, and the **Pupil**.

Recall that the fibers that constrict the pupil (the parasympathetics) are external to the fibers to the extraocular muscles. So external, that compressive lesions (e.g., AComm anuerysm) will compromise pupillary constriction before eye movement. Ischemic lesions (as seen in diabetes) will affect central fibers and so compromise movement before pupillary constriction (a “pupil sparing” IIIrd nerve lesion).

**Trochlear Nerve (IV)**

**Nucleus**
Located in the dorsal midbrain anterior to the aqueduct.

**Course**
Travels dorsally, decussating (the only cranial nerve that does so), and exits the **posterior midbrain** before travelling forward into the **Cavernous Sinus** (are you keeping track?), then through the **Superior Orbital Fissure** to the **Superior Oblique**.

**Lesion**
Lesions of the Trochlear Nerve (due to traumatic stretch most often, given its fragility and great length) cause diplopia. The superior oblique depresses and intorts the eye. A lesion therefore causes elevation and extortion. This is overcome by tilting the head away from the bad eye. Picture the good eye carrying the bad one on its back: “He’s not heavy; he’s my other eye.”

**Trigeminal Nerve (V)**

The trigeminal nerve can be divided up into its motor and sensory components:

**Motor**
The motor nucleus is at the level of the mid-pons and travels through the V3 division to innervate the muscles of mastication. V1 and V2 do not carry motor fibers. A favorite
question to ask is “Which of the following muscles is/is not innervated by the trigeminal nerve?” The choices are all muscles you chew and swallow with. Know the V3 muscles:

**Temporals, Masseter, Pterygoids (medial and lateral), Tensor Tympani, Tensor Veli Palatini, Mylohyoid, Anterior Belly of the Digastric.**

**Sensory**
There are three sensory nuclei:

1) **The Mesencephalic Nucleus** is located, as the name suggests, in the midbrain. It receives proprioceptive input from V3 and passes that along to the Thalamus.
2) **The Pontine Trigeminal Nucleus** (aka, the Principal Sensory Nucleus; aka, the Chief Sensory Nucleus) receives light touch sensation from all three divisions, including corneal stimulation which is noxious. It is located in the mid-pons.
3) **The Spinal Trigeminal Nucleus** is a long nucleus that extends from the mid-pons down to the top of the spinal cord. This is sensible, since it is just a continuation of the spinothalamic system that you recall from the spinal cord. This is the nucleus for pain and temperature sensation of the face.

Each nucleus sends fibers that cross the midline and then travel up to the VPM nucleus of the thalamus in the Ventral Trigeminothalamic Tract. The exception is the corneal reflex. Input from the cornea synapses in the Pontine Trigeminal Nucleus, and the output travels down VII bilaterally to squeeze the eyes shut.

Importantly, the Trigeminal Nerve also supplies nociception to the dura mater and associated blood vessels. V1, V2, and V3 all contribute.

**Course**
The Trigeminal Nerve emerges from the mid-pons and then splits into its three divisions.

1) **V1 (Ophthalmic)** travels through the **Cavernous Sinus** and then the **Superior Orbital Fissure** on the way to the scalp, eyes, frontal sinuses, and the lacrimal gland.
1) V2 (Maxillary) travels through the Cavernous Sinus and then the Foramen Rotundum on the way to the nose, cheeks, upper teeth, and the mucous glands of the nose and sinuses.

2) V3 (Mandibular) exits the Foramen Ovale (does not go through the Cavernous Sinus) on its way to supplying motor innervation to the muscles of mastication; receiving sensory input from the jaw, lower teeth, and anterior 2/3 of the tongue; as well as innervating the salivary glands.

(Nota Bene: V1 travels to the lacrimal gland, but it is the parasympathetic fibers of VII that travel through V1 to cause tearing. V2 travels to the mucous glands of the nose and sinuses, but it is the parasympathetic fibers of VII that travel through V2 to make your nose run. V3 travels to the submandibular salivary glands, but it is the parasympathetic fibers of VII that travel through V3 to make you drool. V3 travels to the anterior 2/3 of the tongue, but this sensory input is not received by trigeminal nuclei but rather by the Solitary Nucleus. The parasympathetic fibers of IX travel through V3 to the parotid gland.)

Lesions
Exceptionally rare in clinical practice (somewhat less rare on tests) as this nerve is almost never traumatized and its nuclei are not amenable to lacunation. Facial numbness is typically either intentional (anesthetic block) or caused centrally by thalamic infarction. Meditate on the Cavernous Sinus.

Abducens Nerve (VI)

Nucleus
Located at the floor of the fourth ventricle in the caudal pons. Some axons from this nucleus cross to the contralateral pons and travel in the MLF to the contralateral III nucleus to coordinate lateral gaze.
Course
The **Abducens Nerve** exits the ventral pons at the **Pontomedullary Junction**, then runs along the base of the **Clivus** before entering the **Cavernous Sinus** and the proceeding through the **Superior Orbital Fissure** to innervate the **Lateral Rectus**.

Lesions
The course of the nerve does much to suggest what lesions this flesh is heir to. **Brainstem** processes affecting the nucleus (MS, infarction), of course. Also processes involving the **basilar meninges** as it scoots along the clivus (Basilar meningitis, sarcoid, meningioma), **aneurysms** (PICA as it exits the brainstem, ICA in the Cavernous Sinus) and of course any pathology in the **Cavernous Sinus** itself (Tolosa-Hunt, aneurysm, carotid-cavernous fistula). The result of a peripheral lesion (i.e., outside of the nucleus) is an isolated lateral rectus palsy. Lesion of the VI nucleus does not allow activation of the contralateral III, so all lateral gaze to the lesioned side is compromised.

Facial Nerve (VII)
Nucleus (motor)
The nucleus of VII is located in the caudal pons at the level of the VI nucleus. In fact, the fascicles of VII travel dorsally and loop around the nucleus of VII before turning back to exit the ventral surface of the pons lateral to the abducens nerve. Lesions affecting the nucleus of VII therefore almost always affect VII by compromising the latter’s fascicles.

Course
The Facial Nerve is a jack of all trades. Three nuclei send fibers to the facial nerve, and the facial nerve distributes them through a web of ganglia and interconnected nerves. Consider the functions one at a time, and the anatomy makes more sense.

Motor
This is the most straightforward. The motor
nucleus of VII sends fibers via the root, through the Geniculate Ganglion (without synapse, of course). A twig branches off to the Stapedius (which acts to dampen loud noises). The main hunk of nerve continues through the Stylomastoid Foramen, sending branches first to the Stylohyoid and Posterior Belly of the Digastric. The remains of the nerve divide into the five branches that you know so well and innervate the muscles of facial expression.

**Tears, Snot, and Drool**
The nucleus for Tears, Snot, and Drool is the Superior Salivatory Nucleus, located just medial to the motor nucleus. It sends fibers to join with the motor fibers of VII and they all travel to the Geniculate Ganglion. Here they part ways. The fibers from the Superior Salivatory Nucleus that subserve Tears and Snot travel down the Greater Petrosal Nerve to the Pterygopalatine Ganglion (aka, the Sphenopalatine Ganglion) and from there via V1 to the lacrimal gland and via V2 to the nose and sinuses. The fibers that subserve Drool travel via the Chorda Tympani nerve to the Submandibular Ganglion to V3 on the way to the Submandibular and Sublingual Glands.

This all sounds complicated and involved, and in a sense it is, but meditation on the names and structures helps. Salivatory nucleus for Tears, Snot, and Drool? But of course. V1 as the route to the lacrimal gland? But of course. V2 as the route to the sinuses? But of course. Submandibular Ganglion on the way to the salivary glands? Via V3? Yes, yes, it all makes sense.

**Taste**
Taste from the anterior 2/3 of the tongue travels from the taste buds to the Corda Tympani (the same route taken by Drool nerves heading the other direction) to the Geniculate Ganglion and then to the Solitary Nucleus (dorsolateral to the motor nucleus).

**Skin Sensation**
VII also has a somatic sensory function. It has sensory fibers that serve the ear, auditory canal, and tympanic membrane. They travel back to the Geniculate Ganglion, and from there via V to the sensory nuclei of V (chief sensory nucleus and spinal nucleus).

Please marinate yourself in the message of these pages while studying the following figures, schematic and anatomical:
Lesion:
The facial nerve can of course be lacerated or compromised by inflammatory or neoplastic processes in the parotid gland. This does not interest examiners in the slightest. They are keen to know two things: First, can you tell the difference between a peripheral and a central cause of facial weakness? Of course you can. (Because the portion of the motor nucleus that subserves the muscles of the upper face is innervated bilaterally, it cannot be compromised by stroke, a unilateral central process). Second, can you tell from the symptoms of a Bell’s Palsy the level to which the inflammation extends? Note that the motor branch to the stapedius leaves the party after the Geniculate Ganglion but before the Chorda Tympani departs. The Chorda Tympani departs before the motor branches reach their target muscles. From this arrangement, could you predict the localization of a Bell’s Palsy that caused facial weakness and loss of taste without hyperacusis? This combination of anatomical form, physiological function, and clinical practicality is irresistible to examiners. Learn it.

Vestibulocochlear Nerve (VIII)

It makes sense to divide discussion of VIII along the lines of its two distinct functions.
Auditory
The end organ is of course the Cochlea. Sound waves in the air vibrate the Tympanic Membrane, which vibration is transmitted via a series of ossicles (Malleus-->Incus-->Stapes) to the Oval Window in the Cochlea. This cochlear fluid then jiggles and this vibrations is picked up by nerve endings of the Cochlear Nerve in the Scala Media compartment.

The Cochlear Nerve then travels via the Internal Auditory Meatus to the upper Medulla to synapse in the Ventral Cochlear Nucleus (low frequencies) and the Dorsal Cochlear Nucleus (high frequencies). This is the beginning of NCSLIMA. NCSLIMA is always always always the basis for at least one question.

Nerve
Cochlear nuclei
Superior olive
Lateral lemniscus
Inferior colliculus
Medial geniculate
Auditory cortex

The way this is asked is as a question about the peaks of the Brainstem Auditory Evoked Potential (or Response). There are five peaks. They correspond to the structures indicated by NCSLI. Note the bilaterality of the system. Unilateral lesions beyond the cochlear nucleus will not block auditory information from reaching auditory cortex.

Balance
The end organ for balance is the Vestibular Labyrinth, comprised of the Utricle/Saccule complex and the Semicircular Canals. The Utricle and Saccule detect head position relative to gravity (am I lying down or standing up?). The semicircular canals detect
head movement in any plane. The histology and physiology of these structures is complex and fascinating. I will not discuss it.

The vestibular nerve proceeds with the cochlear to the **rostral medulla** to synapse in the **Vestibular Nucleus**, really a complex of nuclei that relays vestibular input to a variety of interested parties.

Vestibular input is needed by the **brainstem** (III, IV, VI) for compensatory eye movements, by the **spinal cord** (vestibulospinal tract) for maintenance of posture, and by the **cerebellum** (vestibulocerebellar tract) for making suitable limb adjustments.

**Fun Fact:** **Decrebrate rigidity** is an example of CNS damage causing disinhibition of a reflex. In this case, **vestibulospinal tone** is disinhibited and so extensor posturing results.

**Glossopharyngeal Nerve (IX)**
The Glossopharyngeal Nerve has its fingers in quite a few pies, almost none of them as interesting to the clinician as they are to the examiner. Let us take them briefly, then, one by one.

**Motor**
The Glossopharyngeal Nerve does innervate a muscle of interest, the **Stylopharyngeus**. Its action is to elevate the pharynx during **gag**. The motor nucleus of IX responsible for this is the **Nucleus Ambiguus**, a column of motor neurons dorsal to the olive in the medulla.

**Taste**
Afferents from the **posterior 1/3 of the tongue** travel along IX back to the **Solitary Nucleus** (recall that this is the nucleus that receives taste information from the anterior 2/3 via VII).
**Sensation**
Sensory information from the **posterior 1/3 of the tongue** (not taste so much as temperature) travels back via IX to be deposited in the **Solitary Nucleus**. Sensory information from the skin behind the ear and the tympanic membrane itself is deposited in the **Spinal Nucleus of V**.

**BP and O₂**
**Baroreceptors in the Carotid Sinus and Chemoreceptors in the Carotid Body** send information about BP and O₂ levels, respectively, via IX. Both travel back to the **Solitary Nucleus**.

**Drool**
The **Inferior Salivatory Nucleus** sends parasympathetic fibers via **IX to V3** and from there to the **Parotid Gland**.

**Course**
IX exits the skull through the **jugular foramen** with the jugular vein, X, and XI (and very near to XII and the Carotid Artery). An isolated structural lesion of IX is therefore not seen.

**Lesion**
**Glossopharyngeal Neuralgia.** Excruciatingly painful in the posterior 1/3 of the tongue and the ear. An elegant marriage of anatomic localization and symptomatology.
**Vagus Nerve (X)**
The Vagus Nerve subserves many functions with seemingly no common thread. Diagrams only compound this impression of complexity. I have included two, one schematic (above) and one anatomical (at right). Their contemplation does not bring clarity but rather prompts the thought, “Will I ever be happy again?” Courage, dear reader. We will tackle the functions one by one.

**Motor**
The motor fibers of X arise in the **Nucleus Ambigus** (just as the motor fibers of IX do). They proceed through the **Jugular Foramen** to innervate the muscles of the **pharynx and larynx**. (Everything you need to talk or swallow except for Stylopharyngeus, which is innervated by IX and the Tensor Veli Palatini, which is innervated by V.) Especially important is the **Recurrent Laryngeal Nerve**, which innervates the intrinsic muscles of the Larynx after wrapping around vessels (subclavian on the right, aortic arch on the left) to U-turn back to the vocal cords.

**Parasympathetic Connections**
This is where the Vagus Nerve shines. It has important connections to the **heart, lungs, and gut**. They originate in the **Dorsal Nucleus of X**, which lies in the medulla at the floor of the Fourth Ventricle. From there fibers travel with X through the Jugular Foramen and then to the appropriate ganglia. Being parasympathetic, these fibers do not synapse on any smooth muscles, but rather on postganglionic neurons, which go on to do the dirty work. (Fun Fact: Once upon a time the Vagus Nerve was routinely sectioned as part of the treatment of ulcers.)

**Somatic Sensation**
Sensory information from the **External Tympanic Membrane and the skin of the Ear** (how many nerves does the skin of the Ear need?) travel through X before being shunted off to the **sensory nuclei of V**, where it belongs. Sensation from the Palate also follows this route, and is the afferent limb of the gag reflex.
**Visceral Sensation**

“Sensation” may not be the best word here. “Information” is likely better. **Information from the gut, lungs, and aorta travels back to the brainstem via X to the Solitary Nucleus.** The connection in the aorta is analogous to the connections of IX in the Carotid Artery. Baroreceptors in the Aortic Arch register pressure. Chemoreceptors in the Aortic Bodies register O₂ concentrations. This information is largely used to trigger reflex regulation of visceral processes. Some information reaches cortex in the form of fullness, tummy aches, and the like.

**Lesions**

Isolated lesions in the brainstem and at the skull base do not occur. When they occur in conjunction with other cranial neuropathies, the vagus deficits are dysarthria and dysphagia, with particular difficulty in palatal elevation. More interesting to the examiner is the possibility of a lesion of the Recurrent Laryngeal Nerve, which travels past the aortic arch (aneurysm), carina (lung tumor), and past a plexus of lymph nodes (lymphoma, spread of lung cancer). The nerve is commonly damaged in carotid endarterectomy.

**The Accessory Nerve (XI)**

The Accessory Nerve is this family’s red-headed stepchild. It is pure motor, and its nucleus isn’t even in the brainstem. Its nuclei consist of the lateral aspect of the ventral gray in C1 through C5. The rootlets emerge from the lateral cord and then sneak back through the foramen magnum so that they can come together and pretend to be a cranial nerve by leaving through the jugular foramen. From there it proceeds to innervate the ipsilateral sternocleidomastoid and trapezius. The function of this nerve is too obvious to explain. Frankly, it makes me want to turn my head and shrug.

**The Hypoglossal Nerve (XII)**

The Hypoglossal Nerve moves the tongue, but also has an afferent function, transmitting proprioceptive information about the tongue to the Chief Sensory Nucleus of V (so you don’t bite it, I guess).

**Nucleus and Course**

The Nucleus of XII lies in the dorsal medulla, and the fibers exit between the pyramids and the inferior olive. From there the nerve passes through the Hypoglossal Canal on its way to innervate the intrinsic tongue muscles as well as the extrinsics Genioglossus, Styloglossus, and Hyoglossus.

**Lesions**

The tongue, like limb muscles, receives crossed innervation from cortex. Bilaterality of innervation is variable. It is therefore possible to have tongue weakness from a hemispheric stroke. A left sided stroke can therefore cause right sided tongue paresis. Lesions of the XII nucleus and nerve will of course cause ipsilateral deficits. The tongue deviates toward the weak side due to the uneven pulling power of the hemiparetic
genioglossus. Picture yourself pulling out a drawer with one weak arm and one strong one. The drawer will turn towards the weak side, no?