Medical Neuroanatomy for the Boards and the Clinic

Finding the Lesion

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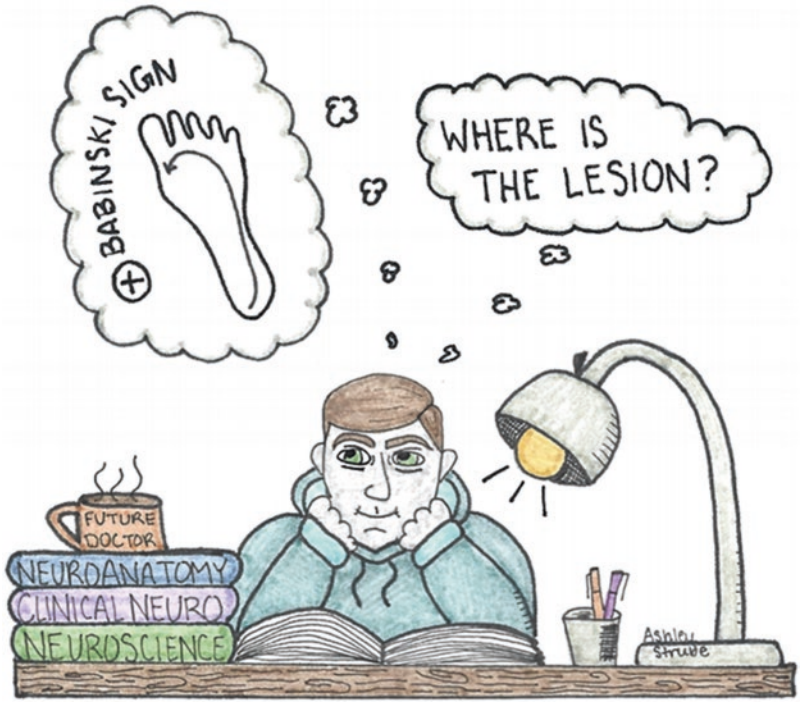
Introduction

This book is a systematic approach to learning neuroanatomy by studying various lesions to the nervous system and their subsequent signs and symptoms. If you are a medical student, this is not the time for simply memorizing a list of symptoms that go along with the name of a syndrome. Forget memorizing random isolated factoids with a series of flash cards. This is the point in your education when you need to understand the lesion scenarios. To do this you need to put everything together and develop a big picture view of the nervous system. When you can do this, then the details will make a lot more sense. With that said, everything that follows in the text is related to clinical scenarios. Think of it as lesions on hyperdrive.



It all comes down to understanding figures and diagrams. Chances are that if you do not understand a neuroanatomy case scenario it is because you do not have a picture in your mind of the tract. The text has numerous figures and

line drawings to explain the concepts. One reason for the line drawings rather than fancy illustrations is that you can easily practice reproducing the line drawings.

Where Is the Lesion?

A neurology patient, or a question on a board exam, is essentially a puzzle. You, the doctor, are presented with three or four symptoms and your job is to figure out, "Where is the one place in the nervous system that when lesioned will account for this patient's signs and symptoms?" For instance, just knowing that a patient has Babinski's sign on the left, does not tell you enough to say where the lesion is. All we know is that a UMN is damaged. The lesion could be in the right cerebral cortex, right internal capsule, right midbrain, right pons, right midbrain, or anywhere in the left spinal cord. Likewise, if a patient's right eye is deviated down and out, then it is likely that cranial nerve three is damaged. But the damage could be in the red nucleus, the cerebral peduncle, the cavernous sinus, or the superior orbital fissure. However, if you put these two facts together, the Babinski's on the left, and the third nerve palsy on the right, then you can predict that the lesion is in the right midbrain, close to the cerebral peduncle.

One of the hardest parts of neuroanatomy is relating a 2D cross-sectional image to the bigger 3D map of the nervous system. In a sense, you are memorizing the map of a large city with no street signs. If you are presented with a picture of one street intersection, with no signage, you need to know where you are, and all the streets coming and going into that intersection. Likewise, if you are given an image of the brain stem, you need to know where you are, and all the tracts coming and going through that image.

This book is not an exhaustive textbook for medical neuroanatomy and neurophysiology. This book presumes that you have at least a general idea of the layout of the nervous system. Do not try and use this book as your first introduction to the nervous system, although I do think it would be a good addition to your required books. Trust your professor and use whatever resources they recommend, and then add this book as a supplement. It can also be used as a reference to read right before a neurology-related rotation.

The book devotes a significant amount of time to the brainstem because it is the most complicated and important piece of anatomy. It is introduced early and then revisited several times as more information is added. While the book is mainly focused on neuroanatomy, in some regions it goes into neuropharmacology and neurophysiology, but this is mainly as these other fields relate to the anatomical connections. In several chapters, such as learning and memory, and the basal ganglia pathways, there are some explanations about more complex and theoretical ideas. These are complicated topics that I have simplified so that you become familiar with them for the boards, and for understanding the foundations of these topics. They are complex, debatable, and ever changing, and my explanations are only designed to get you into the ballpark. There is an enormous amount of written word devoted to them with plenty of material available for further reading.

The last section of the book contains a test on various brainstem structures. Make sure you don't just memorize the list, but that you understand each piece of the puzzle. There is also a list of 100 high-yield facts presented as a word association format. On the left side of the list is a keyword that should trigger some sort of quick response, which is found on the right. If you do not understand a topic in the list and its accompanying response, you can refer to the text for a more thorough explanation. After going through the book while you are studying for the boards, the list at the back would be good to continually trigger your memory circuits.

This book is not a clinical book, instead it is designed to give you the basic science portion of neuroscience so that you can better understand clinical scenarios. Every year, board exams become more clinically based, and neuroanatomy is a perfect topic for test writers to focus on basic science topics in a clinical format. But more importantly, hopefully the book will improve your powers of observation and your deductive reasoning skills when it comes to the neurological exam. A professor of mine used to state that the only diagnostic test better than your own reasoning skills is the pregnancy test, and that expensive tests should just be confirmation of what you have already deduced. This book does not mention high-tech expensive tests but instead relies on the meaning of various physical signs and symptoms to determine where the lesion is located.

I owe a huge debt of gratitude to all the students I have taught over the years. Medical students are inquisitive, sincere, have big hearts, and are a fun group to teach. I have heard hundreds of mnemonics over the years, typically from students between lectures. I don't remember most of the mnemonics, but a couple have stood out and I have used them here. Thanks to my former colleagues at the Western University of Health Sciences for allowing me to reproduce the brainstem pictures. And thanks to Dr. Wayne Krueger for the idea about the word association test. He made one for gross anatomy, and I have used his idea for neuroanatomy.

The list of references at the end of each chapter is more than just citations. They are authors who helped me understand the material and also taught me how to present it. I had several former students, Arial, Philip, and Taylor, all look at early drafts and provide criticisms from a student's perspective. And thanks to my kids, Phoebe, Noah, and Ingrid for putting up with me. Most of all to Susan, my wife, best friend, soul mate, and strongest supporter – I am indebted to you beyond measure.

Contents

About the Author

Jonathan Leo received his PhD from the University of Iowa where he studied the effect of alcohol on the developing brain. He has taught Medical Gross Anatomy and Medical Neuroanatomy at medical schools for 25 years. He has also served as the Director of a master's and PhD program in Anatomical Sciences. He has won numerous teaching awards. During this time, he has lectured as a board reviewer for 20 years and has lectured to medical students throughout the United States, Caribbean, Middle East, Europe, and China. He is a Professor of Anatomy at the Alabama College of Osteopathic Medicine in Dothan, Alabama.

1 The Three Long Tracts and Spinal Cord Lesions

When you see a patient, or an exam scenario, one of the first questions you will ask yourself is: is the lesion in the CNS or the PNS? If the signs and symptoms point to one or more of the three long tracts being compromised, then you will be thinking about the CNS. The three long tracts are the (1) corticospinal, (2) dorsal columns, and (3) spinothalamic. The corticospinal tract is a descending or motor pathway, and the dorsal columns and spinothalamic tracts are sensory pathways or ascending pathways. As they travel to or from the cerebral cortex, all three of these tracts decussate at some point in the CNS. What makes life complicated for students is that all three tracts decussate at different locations.

Before getting into the specifics, consider the big picture first: by the time we get to the cortex, everything is crossed, so a lesion in the cortex will lead to contralateral signs for all three tracts. But on the way to the cortex, because the tracts decussate at different locations, patients can present with mixed signs and symptoms. A patient with motor deficits on one side, and pain and temperature deficits on the contralateral side, most likely has a spinal cord lesion. A patient with an alternating pattern of motor deficits most likely has a lesion in the brainstem. For this first chapter, we will focus on the three long tracts in the spinal cord, then devote a significant amount of time to the brainstem, and then finish with the cortex. For thinking about how we function as human beings, obviously the cerebral cortex is the most complicated part of the CNS; however, the basic lesions of the cortex are fairly straightforward. For our purposes, when it comes to lesions, the brainstem is the most complicated region of the CNS.

Corticospinal Pathway

The major motor pathway is a two-neuron pathway consisting of upper motor neurons (UMNs) and lower motor neurons (LMNs) (Fig. 1.1). The UMN tract, also called the corticospinal tract, begins with cell bodies in the precentral gyrus and projects down through the corona radiata, the internal capsule, the cerebral peduncle, and then the caudal medulla, where about 90% of the fibers decussate at the pyramidal decussation. Once the fibers decussate, they enter the lateral funiculus of the spinal cord and continue down as the lateral corticospinal tract. The 10% of fibers that do not decussate travel down the cord as the anterior corticospinal tract. For the purposes of understanding the clinical scenarios, we are going to focus on the lateral corticospinal tract.

There are approximately one million fibers in the corticospinal tract as it moves down through the brainstem. As the tract descends in the spinal cord as the lateral corticospinal tract, at each level of the cord, fibers will peel off and project to the anterior horn cells, which are the beginning of the lower motor neurons (LMNs). The lower

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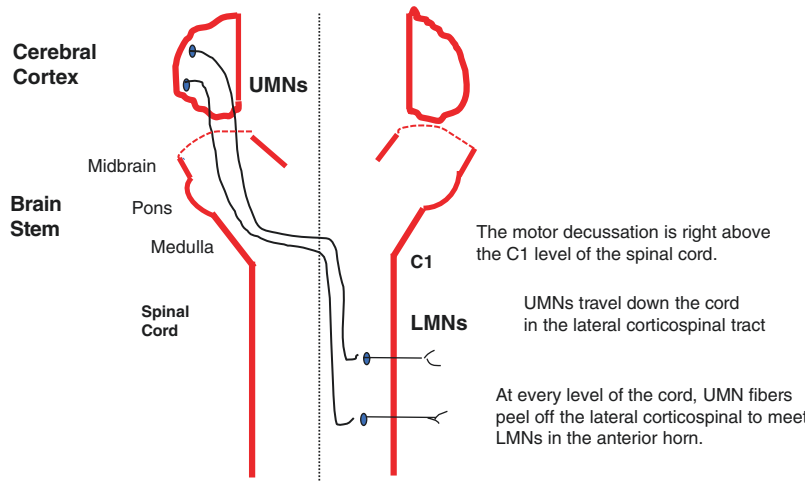

Fig. 1.1 Upper and lower motor neuron pathway showing synapses in the spinal cord. (Leo 2021)

motor neurons project out into the ventral roots, to eventually go on to form the motor component of the peripheral nerves.

Keep in mind that the pyramidal decussation is not a demarcation for the UMN and LMN neuron designation. Sometimes students make the mistake of thinking that the term "UMN" refers to the corticospinal tract above the pyramidal decussation, and the term "LMN" refers to tract below the pyramidal decussation. But this is not the case. Even below the decussation, you will find upper motor neurons. In fact, at every level of the spinal cord, you will find both UMNs and LMNs. Or another way to think of it is that if I told you that a patient had UMN signs on the right, that does not necessarily mean that there is a lesion in the left cortex. The lesion could be in the left cortex, but it could also be in the right spinal cord.

Damage to UMNs will lead to a different set of symptoms compared to damage to the LMNs. If the patient has UMN signs, then the lesion is in the CNS. If the patient has LMNs, then the lesion is most likely, but not necessarily, in the PNS. Lower motor neurons begin in the ventral horn, which is in the CNS, and leave on the ventral root to join a spinal nerve. The majority of a LMN is in the PNS, but a small part of it is in the CNS. A lesion to the ventral horn can result in LMN signs even though the lesion is in the CNS. Polio leads to lesions in the CNS, but it targets anterior horn cells resulting in LMN symptoms, such as hyporeflexia and decreased tone.

The hallmark sign of an UMN lesion is Babinski's sign. In a normal healthy individual, if the bottom of their foot is scratched, they will plantarflex their toes. In a patient with a lesion to the UMN pathway (or in a newborn), the toes will dorsiflex. In addition, UMN lesions will lead to spastic paralysis, hyperreflexia, increased muscle tone, and possibly priapism. It is more important for fine motor control of the hands and feet than the shoulders and hips. The farther out on a limb you go, the more important the corticospinal is for fine movement. An example would be someone with a lesion to UMNs in the internal capsule reaching up to grab an item from a shelf. With their shoulder muscles they can get their upper limb moving towards the shelf, but they cannot grab the item with their hand.

Cross Section of the Spinal Cord

When you take a cut through the spinal cord, you can see the dorsal side with the dorsal horns and the ventral side with the ventral horns (Fig. 1.2). If you stick your finger on the hot stove, the sensation travels on the spinal nerve toward the spinal cord. The sensation then travels on the dorsal root, with the dorsal root ganglion, and then enters the cord to synapsis in the dorsal horn. The ventral horn on the other hand is the location of the cell bodies for the LMNs or efferent fibers. These fibers travel on the ventral root to join the spinal nerve and then project to the muscle. If the

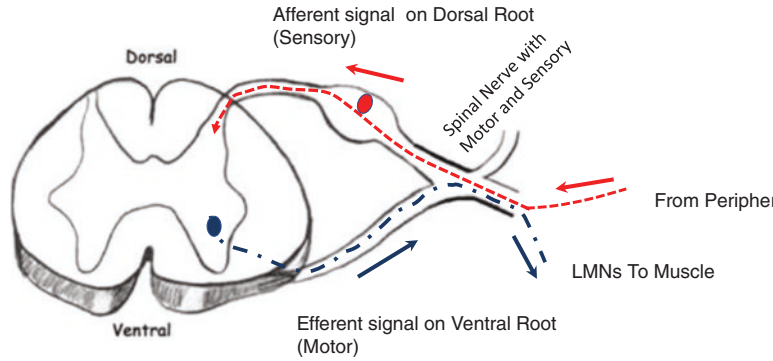

Fig. 1.2 Spinal cord cross section. On the dorsal side, primary afferents travel on dorsal roots to dorsal horn. Their cell bodies are in the dorsal root ganglion. On the ventral side the efferents which Are LMNs travel on ventral roots to the spinal and then to muscles. (Leo 2021)

Table 1.1 Upper and lower motor neuron deficits

Upper motor neuron deficit	Lower motor neuron deficit
Spastic paralysis	Flaccid paralysis
Hyperreflexia	Areflexia
Babinski's sign, clonus	No Babinski
Increased muscle tone	Decreased muscle tone
Muscle weakness	Fasciculations
Disuse atrophy of muscles	Atrophy
Decreased speed of voluntary movements	Fibrillations
Priapism	

ventral roots are cut, there will be a motor deficit; if the dorsal roots are cut, there will be a sensory deficit; and if the spinal nerve is cut, there will be a motor and sensory deficit.

Patients with LMN lesions will have complete flaccid paralysis of the muscles affected. They will also have absent or reduced reflexes and decreased muscle tone. They will also have fasciculations and fibrillations, which are small twitches of the muscle. Fasciculations are visible and have been described as looking like worms under the skin. Fibrillations occur in individual muscle fibers and are not visible (Table 1.1).

As an example of how to think about the loss of reflex with a LMN lesion, take the quadriceps. With a LMN injury, say to the femoral nerve innervating the quadriceps, there is no nervous system input to the muscles, in this case the quads, because the wire is cut. So, when you tap on the patellar tendon, there is no way that the muscle can move. With no electrical signal, there will be reduced tone to the muscles, and over time the muscles will atrophy. However, if you cut the UMN anywhere between the premotor cortex and the anterior horn, the LMN is still intact, and when you tap on the tendon, the afferent signal comes into the cord and synapses with LMN or efferent fiber, and the leg extends. In fact, when the reflex fires, it will be hyperactive. This sounds counterintuitive, but in a healthy individual when the tendon is tapped, one of the jobs of the cortex is to rein in, or check, the reflex. With an UMN deficit, this cortical inhibition is lost, and the reflex is hyperactive.

Here is another way to think of it. As an example, take a patient with a hemisection of the right cord at C5. The spinal cord below C5 is not completely atrophied. It still has a blood supply, is getting oxygen, and is still functioning tissue. But the patient has lost the ability of the cortex to send information down to L4 where the femoral nerve begins. If you give this patient a command to move their leg, they understand you, and they try to send the information from premotor cortex down to L4, but they cannot get the information past the cord lesion. Yet, if you tap on their patellar tendon, the afferents carry the information into the cord, a reflex loop is still intact, and the leg moves. The reflex loop does not need cortical influence.

Both UMN and LMN deficits can lead to muscle atrophy; however, with an UMN neuron injury, you will hear the term "disuse" atrophy. The difference is that with a LMN injury because there is no input to the muscle and it is devoid of any input, it will atrophy. With the UMN injury, the muscle still has an electrical signal coming into it; it has just lost the cortical input to make coordinated movements, which will lead to the patient not using the muscle. With these UMN patients, the goal of

Table 1.2 Grading muscle strength

Grade	Description
0/5	No muscle movement
1/5	Barely detectable movement
2/5	Movement with gravity eliminated
3/5	Movement against gravity
4/5	Movement against gravity and light resistance
5/5	Normal strength

Table 1.3 Grading reflexes

Grade	Description
4+	Very brisk response, hyperactive, with clonus
3+	Brisker than average
2+	Average, normal
1+	Diminished response
0	No response

physical and occupational therapy is to develop exercises so that the patient uses these muscles to minimize the potential "disuse atrophy."

It is important to understand the different symptoms between UMN and LMN lesions, such as hyperreflexia and hyporeflexia; however, you also need to be familiar with how these terms are reported or mentioned in test questions. Muscle strength is reported on a scale from zero to five, with five being "normal" and zero being no muscle contraction—or paralysis. A score of three is active movement against gravity without any resistance (Table 1.2).

Hemiparesis is a weakness or loss of strength on one side of the body. Hemiplegia is more severe and is typically a complete loss of strength—think paralysis—on one side of the body.

Deep Tendon Reflexes

Deep tendon reflexes are tested by short, sharp, "taps" on tendons. The main reflexes are the biceps (C5–C6), brachioradialis (C6), triceps (C7 and C8), patellar (L4), and Achilles (S1). The reflexes are graded on a scale of 1+ to 4+, with a 2+ being "normal." Hyperreflexia would be either a 3+, meaning a brisk response, or a 4+ being clonus. On the other hand, a 0 is an absent response, and +1 is a reduced reflex. The + sign simply denotes that it is the reflex test grade, not to be confused with the score on the strength grade. Hyperactive reflexes indicate an UMN lesion. Absent reflexes indicate a LMN injury (Table 1.3).

Rather than use the terms hyperreflexia and hyporeflexia, the question could say the patient's biceps reflex was 4+ or the quadriceps reflex was 1+.

Cerebral Peduncle, Basis Pontis, and Pyramid

It is important to pay attention to the location of these fibers within each level of the brainstem. In the midbrain the fibers are located in the middle one-third of the cerebral peduncle, in the pons they are in the basis pontis, and in the medulla they are in the pyramid (Fig. 1.3).

C5 Hemisection

Delving further into the example of a hemisection at C5, when the cord is cut at C5, then both UMNs and LMNs are cut—you have cut the corticospinal and the anterior horn. Think of a major highway with exit ramps. In this example there is an accident on the highway right at the point where the exit ramp leaves the road. The UMN pathway is the highway with its one million neurons coming down the cord. At each level of the cord, some, but not all, fibers will peel off at the exit ramps to innervate LMNs. With the lesion at C5, from the biceps point of view, you have cut a LMN, but from the quadriceps point of view, you have cut an UMN. Granted from the biceps point of view, you have really cut both a LMN and an UMN, but cutting the LMN will override any more subtle UMN issues. Think of your car and compare a dead battery to a blown engine. If your engine is destroyed, then whether the battery works or not is immaterial. If the LMNs are cut, it doesn't matter about the UMNs; there is simply no signal getting to the muscle.

With the lesion at C5, the biceps reflex will be absent or decreased (1+) while the quadriceps reflex will be increased (4+). In addition, the patient would have Babinski's sign. And all the motor signs would be on the ipsilateral side (Fig. 1.4).

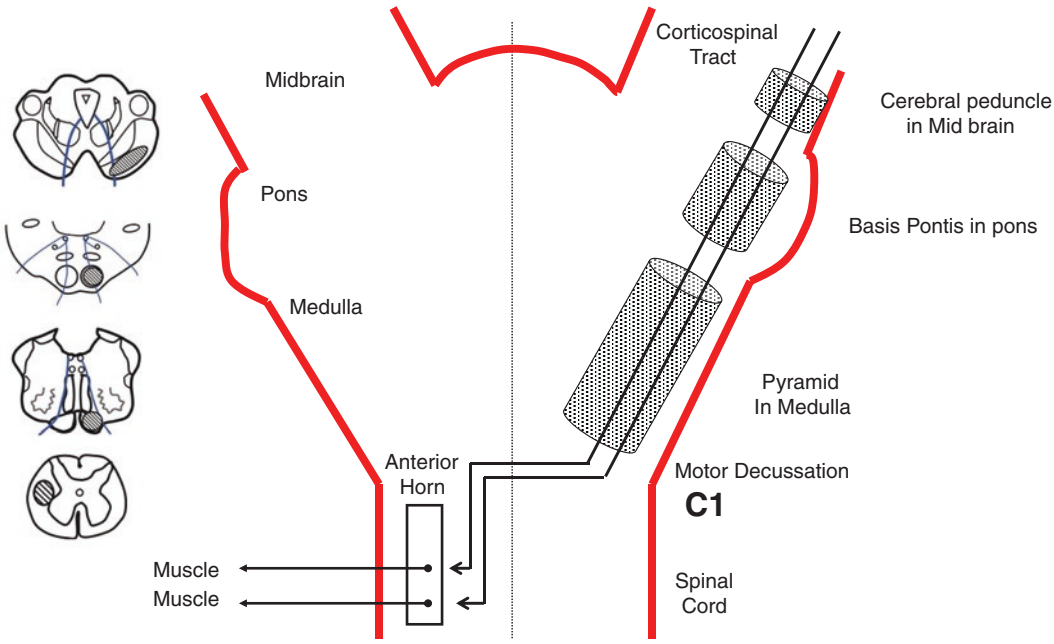

Fig. 1.3 Upper motor neurons descending through brain to spinal cord. (Leo 2021)

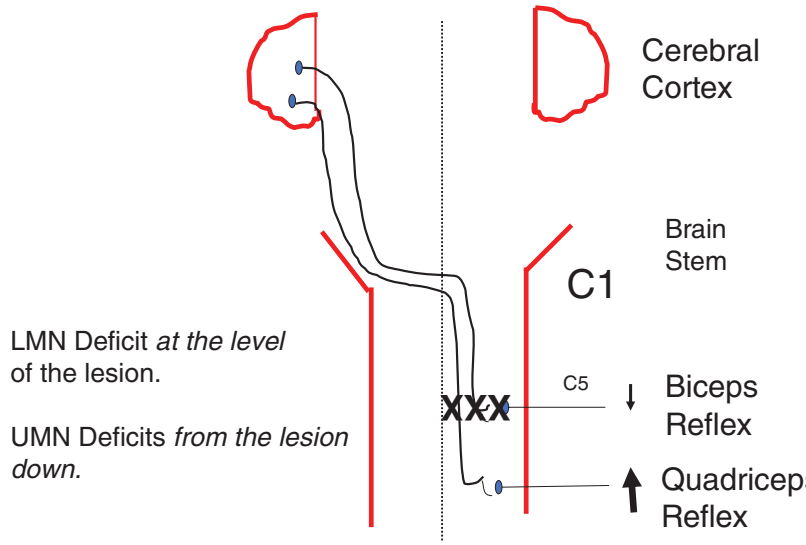

Fig. 1.4 Lesion at C5 level of the spinal cord. From the biceps point of view the LMN is cut. From the quadriceps point of view the UMN is cut. (Leo 2021)

Spinothalamic

The spinothalamic tract carries pain, temperature, and vague touch information from the periphery to the cerebral cortex (Fig. 1.5). We do not use the term UMN and LMN when referring to sensory tracts; instead we use the term primary, secondary, and tertiary neurons. The primary afferent begins somewhere in the periphery with a receptor. Take stepping on a tack with your big toe as an example. The pain sensation from the tack fires the primary afferents whose fibers project along the medial plantar nerve, into the sciatic nerve, and then onto the lumbosacral plexus. As the fiber approaches the cord, it has a cell body in the dorsal root ganglion (DRG) at the

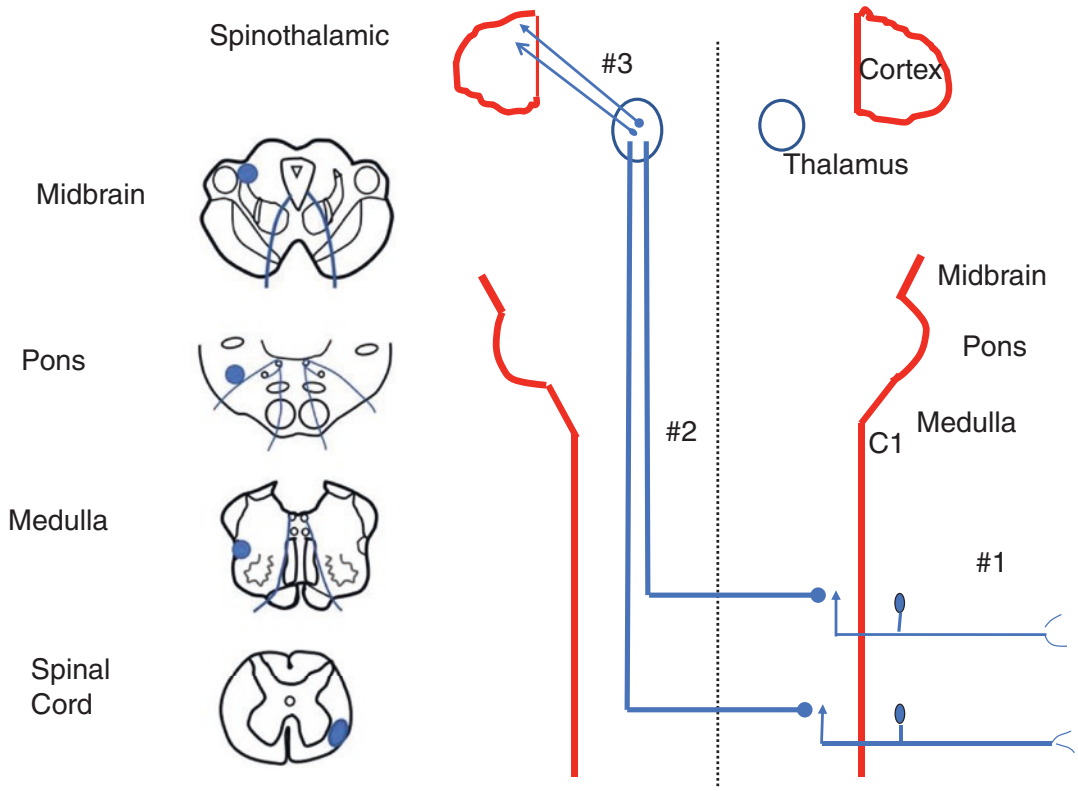

Fig. 1.5 Spinothalamic pathway showing the decussation in the spinal cord and pathway through the brainstem. (Leo 2021)

L4 level. The fiber, still the primary afferent, enters the cord and ascends for one or two segments before terminating in the dorsal horn, where it meets the secondary neuron. Figure 1.5 shows the primary afferent ascending in Lissauer's tract for one or two segments before synapsing. To simplify the remaining figures, the tract is shown entering and synapsing immediately.

The secondary neuron then sends a fiber which decussates in a structure called the anterior white commissure and ascends up the cord in the spinothalamic tract, which continues through the medulla, pons, and midbrain and eventually ends in the thalamus, specifically the ventral posterior lateral (VPL) nucleus of the thalamus. (See the Chap. 10 for more detail.) *Figure 1.5 shows the primary afferent ascending one or two segments before synapsing. For simplicity, the subsequent diagrams of spinothalamic just show it coming into the spinal cord and synapsing*.

From the VPL, the tertiary neuron, also called thalamocortical pathway, projects to the primary somatosensory cortex, also known as the postcentral gyrus. Note that the secondary fibers pass through the lateral side of the medulla, pons, and midbrain. Lesions to the spinothalamic tract will lead to hemianesthesia on the contralateral side of the body.

Paresthesia refers to "pins and needle" sensation and can result from CNS injuries or compression of peripheral nerves, such as the feeling in your fingers after bumping your medial epicondyle, or funny bone. Hypothesia is a reduced or total loss of pain sensations.

Dorsal Columns

The dorsal columns carry information about vibration, conscious proprioception, fine touch, and two-point discrimination (Fig. 1.6). Like the spino-

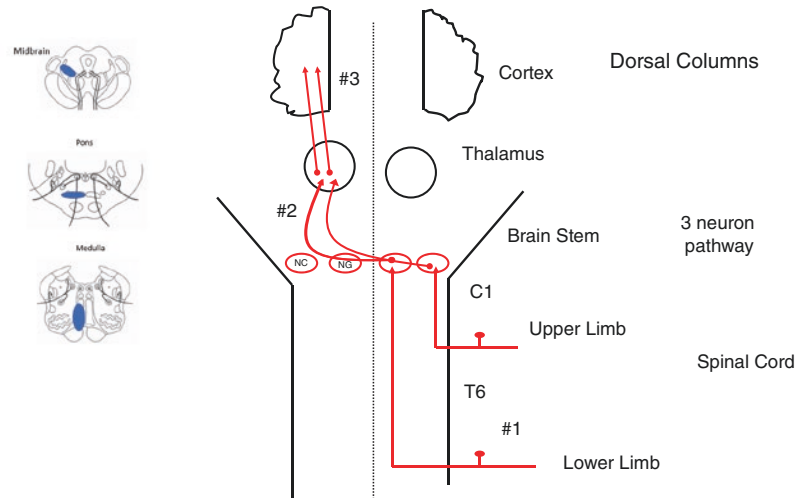

Fig. 1.6 Dorsal column pathway showing the decussation at the caudal medulla and pathway through the brainstem. (Leo 2021)

thalamic it is also a three-neuron pathway. An important landmark here is T6 of the cord. Fibers that carry information from the lower limb enter the cord below T6 and ascend in the fasciculus gracilis. Fibers from the upper limb enter the cord above T6 and ascend in the fasciculus cuneatus. These two pathways, fasciculus gracilis and fasciculus cuneatus, are together known as the dorsal columns. In the caudal medulla, the fibers from the fasciculus gracilis terminate in the nucleus gracilis, and fibers in the fasciculus cuneatus terminate in the nucleus cuneatus. Consider that a fiber carrying vibration information from the big toe would start in the big toe, ascend to the cord, enter the cord, ascend in fasciculus gracilis, and then terminate in nucleus gracilis in the caudal medulla near the base of the skull. In other words, this is a long neuron running almost the entire length of the body.

After the primary afferents synapse in the nucleus gracilis or cuneatus, the secondary afferents come out of the two nuclei (gracile and cuneate) as internal arcuate fibers, decussate to the opposite side, and form the medial lemniscus which sits on top of the pyramids (CST) in the medulla. The medial lemniscus fibers then ascend through the pons and medulla and eventually enter the VPL of the thalamus. As the medial lemniscus moves through the brainstem, it goes from a stick figure standing on the pyramid to a boomerang-shaped structure in the pons, to a hat-shaped structure in the midbrain.

One detail for these two important sensory tracts is that the spinothalamic tract carries "vague touch" information, while the dorsal column carries "fine touch" information. An example to illustrate the difference comes from having three coins in your pocket. If you have a quarter, a dime, and a nickel in your pocket, and you put your hand in your pocket, using your spinothalamic tract (vague touch), you can feel that there are three coins, but you can't differentiate one from the others. With your dorsal column pathway (fine touch), you can tell the difference between the quarter, the dime, and the nickel.

Damage to the dorsal column pathway can occur in the peripheral nerves, the spinal cord, the brainstem, the thalamus, or the cortex. With damage to the dorsal column pathway in the nerves, spinal cord, or thalamus, the patient is said to have *astereognosis*. With damage to the parietal cortex, the patient is said to have *agnosia*.

Summary of the Three Long Tracts

At this point, you should be able to take a blank piece of paper and draw out the schematic of these three tracts without even thinking about it (Fig. 1.7). Many patient scenarios will include these tracts, and many test questions on the board will include them. Do not expect a board question

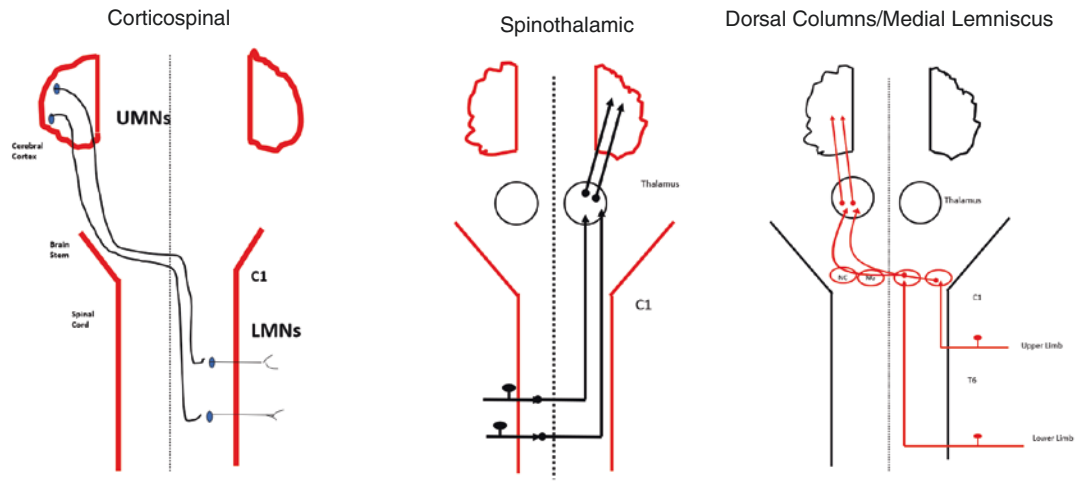

Fig. 1.7 The three long tracts. (Leo 2021)

to just ask you a specific, isolated factoid about one of these tracts. Instead expect to see these tracts woven together throughout numerous questions. When you are first wondering if the lesion is in the CNS or the PNS, look for the evidence of long tract signs. If a patient has UMN signs, or pain and temperature deficits, or proprioception and vibration deficit, then you suspect that the lesion is in the CNS, especially if large sections of the body are affected.

The Long Tracts in the Brainstem

Medulla

The brainstem is complicated; before going into the specifics, we need to look at the location of these three tracts in the medulla, pons, and midbrain. In the medulla the medial lemniscus stands vertically on the pyramids like a headless stick person holding their head. The feet rest on the pyramid and the shoulders are on top. The stick figure represents the orientation of the cervical, thoracic, lumbar, and sacral fibers that emerged from the nucleus gracilis and cuneatus as internal arcuate fibers and entered the medial lemniscus. The stick figure is holding its head, which represents the sensory fibers in the **ventral trigeminothalamic tract** (VTT) which is carrying information from the trigeminal system—or face.

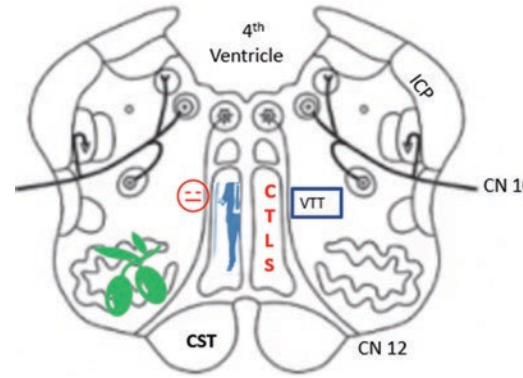

Fig. 1.8 The headless man represents the topography of the medial lemniscus with cervical fibers at the top, followed by thoracic, lumbar, and sacral in descending order. The face fibers are not in the medial lemniscus but are off to the side in the ventral trigeminothalamic tract (VTT). The man standing on the pyramid with the corticospinal tract (CST). The slippery olives are off to the left. (Leo 2021)

The shoulders of the stick figure, or top of the medial lemniscus in the orientation on the picture, lie approximately halfway between the pyramids and the floor of the fourth ventricle (Fig. 1.8).

Immediately above the medial lemniscus is the tectospinal tract, the medial longitudinal fasciculus, and hypoglossal (XII) nucleus. Lateral to the medial lemnisci are the inferior olivary nuclei. These olive-shaped nuclei are prominent structures and make excellent landmarks. As we move into the pons, the stick figure is about to slip on the olives (think of olives as being slippery) and fall. The corticospinal tract with the UMNs is in

the pyramid, which is superior to the decussation. Lesions to the pyramid will result in contralateral UMN signs.

Moving from Medulla into Pons

The pons is characterized by the bulbous pons which resembles a bulb on the ventral surface. The corticospinal tract is descending through the basis pontis. You can also see the "little headless person" (medial lemniscus) who has slipped off the "slippery olive" and now lies on its back with its foot lateral and shoulder medial. As we move up into the pons, the feet will rise toward the posterior surface. Within the pons are several cranial nerve nuclei as well as the scattered pontine nuclei which receive a projection from the cerebral cortex and then project to the cerebellum. On the dorsal side is the fourth ventricle.

In the middle of the pons, we start to see three sensory pathways line up together in a structure that looks something like a boomerang. The most medial pathway is the medial lemniscus, and then moving lateral is the spinal lemniscus (spinothalamic), and then the lateral lemniscus (auditory).

Midbrain

The midbrain is characterized by the two peduncles. It looks something like an upside-down mickey mouse, with the peduncles being Mickey's ears, and the red nucleus his eyes. The two peduncles project ventrally, and between them is the interpeduncular fossa with cranial nerve three coming through it. There are numerous lesions that can occur in this area.

The posterior portion of the midbrain is the tectum, with the superior and inferior colliculus. At the level of the inferior colliculus, we still have our boomerang. The "foot" of each medial lemniscus is now projecting superiorly. The medial lemniscus has migrated nearer to the lateral edge of the midbrain. Lateral to the "foot" of the medial lemniscus is the spinal lemniscus, and then the lateral lemniscus. The lateral lemniscus is terminating in the inferior colliculus. One way to differentiate the inferior from superior colliculus is that the inferior colliculus resembles a wine glass, with goblet being the nucleus and the stem being the lateral lemniscus.

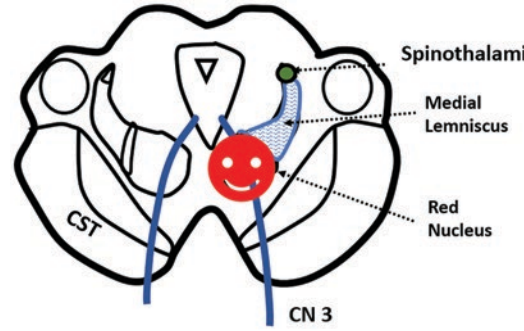

Fig. 1.9 The smiling face represents the red nucleus. The main part of the hat represents the medial lemniscus and the small bob on top of the hat is the spinothalamic. Corticospinal tract (CST) is in the middle one- third of the cerebral peduncle. (Leo 2021)

At the level of the superior colliculus, we have lost the lateral lemniscus since it terminated in the inferior colliculus. The most prominent structure here is the red nucleus. Here is an easy way to remember the structures here. Think of the red nucleus as a smiling face, and on the top of the face is a long stocking hat. The bulk of the hat represents the medial lemniscus, and the pom-pom on top of the hat is the spinothalamic (Fig. 1.9).

A Test on the Long Tracts

Before continuing, make sure you can do the following exercise. The purpose of this is to be able to relate a cross-sectional view with the longitudinal view. The numbers in the various spinal cord and brainstem sections represent lesions. For each lesion jot down whether the symptoms are ipsilateral or contralateral, what modality is affected, and where the cell body of origin is located for the fibers in that structure. The point of this exercise is to see the importance of having a visual image in your mind of the tracts. As we discuss the various lesions, these three tracts should be second nature (Fig. 1.10).

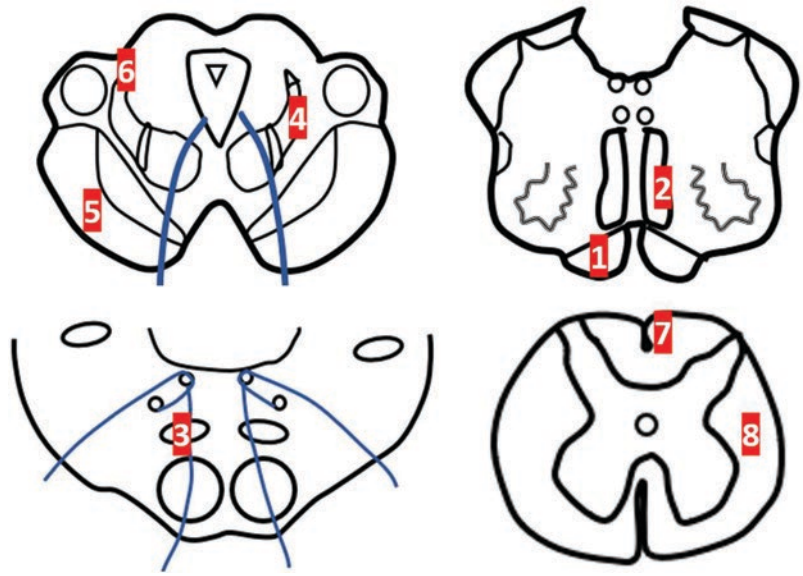

Fig. 1.10 Lesion test. Each number represents a lesion. What are the symptoms, are they contralateral or ipsilateral, and where is the cell body of origin (CBO) for each tract?

Key to Brainstem and Spinal Cord Lesions

1. Contralateral UMN signs, CBO—Precentral gyrus
2. Contralateral dorsal column signs, CBO—nucleus cuneatus and gracilis
3. Contralateral dorsal column signs, CBO—nucleus cuneatus and gracilis
4. Contralateral dorsal column signs, CBO—nucleus cuneatus and gracilis
5. Contralateral UMN signs, CBO—precentral gyrus
6. Contralateral loss of pain and temperature, CBO—dorsal horn
7. Ipsilateral dorsal column signs, CBO—DRG
8. Contralateral loss of pain and temperature, CBO—dorsal horn

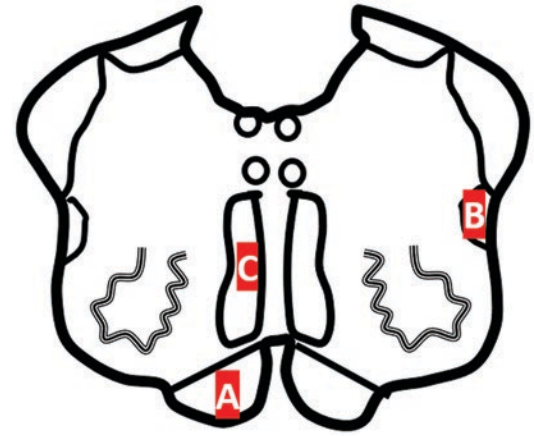

Fig. 1.11 Cross section through the medulla. At each lesion note the tract involved, what the symptoms are, and whether the symptoms are on the ipsilateral or contralateral side. (Leo 2021)

All of the questions above require putting several pieces of knowledge together. For instance, on the most superficial level, you need to know what you are looking at. Is it the medial lemniscus, corticospinal tract, etc.? And you also need to know what modality is running in each tract. But the harder part is looking at the section and the tract and knowing where you are in relation to the decussation. The question you need to ask yourself is: am I above or below the decussation?

If we take a section through the caudal medulla, we can walk through each tract. Looking at the pyramid (lesion A), we need to know that if we are in the pyramid, we have to be above the decussation, since when the fibers in the corticospinal tract reach the lowest level of the pyramid, they cross over to descend in the opposite cord. In addition, we should know that the cell bodies are in the precentral gyrus in the frontal lobe (Figs. 1.11 and 1.12).

If we look at the lesion in the spinothalamic tract (lesion B), then the symptoms will be on the contralateral side. Realize that these are the second-order neurons that originated in the dorsal horn.

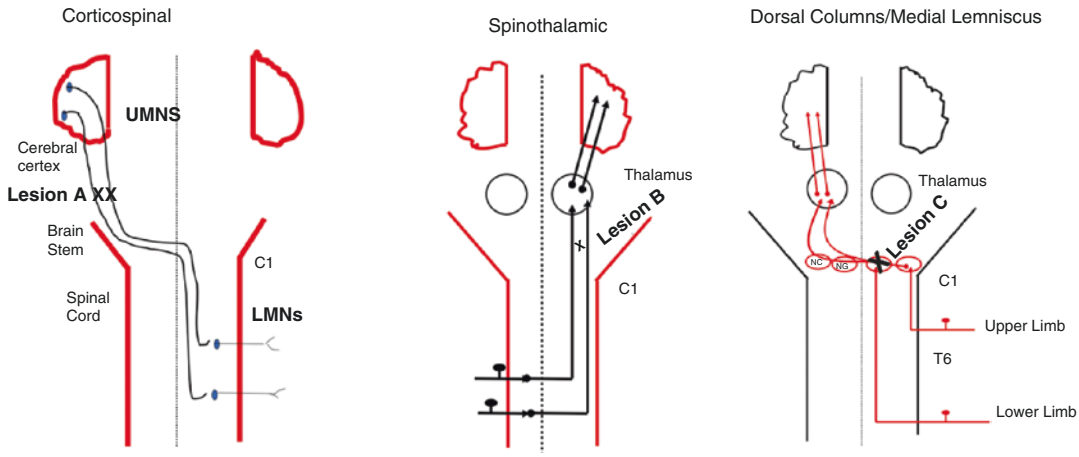

Fig. 1.12 The three long tracts and three lesions. (Leo 2021)

If we look at the nucleus gracilis (lesion C), we need to know that this is the termination of the first-order neurons that have their cell bodies in the dorsal root ganglion. If we have a small lesion to nucleus gracilis, then the symptoms will be on the ipsilateral lower limb. Remember gracilis carries lower limb information and cuneatus carries upper limb information (Fig. 1.11).

Brown-Sequard Syndrome

Big Picture The classic way to test your knowledge of the three long pathways is to present a patient scenario of Brown-Sequard syndrome—also referred to as a hemisection of the spinal cord. We have already talked about the motor deficits. In the patient scenario below, the patient has a lesion at C5 on the left. This will lead to left side spastic paralysis (ipsilateral side), right side loss of pain and temperature sensation (contralateral), and left side loss of the dorsal column modalities such as proprioception, vibratory sense, and conscious proprioception (ipsilateral). Note that the pain and temperature sensations are lost on one side, while the dorsal column sensations are lost on the opposite side—a disassociated sensory loss (Fig. 1.13).

The Details The main findings, of motor deficits on one side of the body and pain and temperature deficits on the opposite side, place the lesion in the

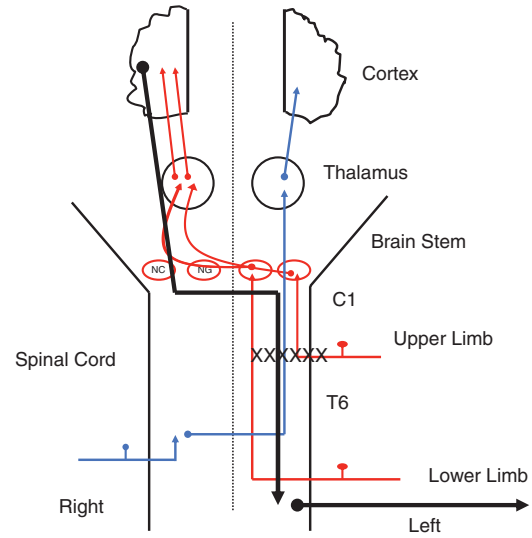

Fig. 1.13 Hemisection of spinal cord at C5 level. UMN signs are ipsilateral, Pain and temperature loss is contralateral, dorsal column symptoms are ipsilateral. (Leo 2021)

spinal cord, but there are more clinical details to look at so that we can be more specific about where exactly in the cord the lesion is located. Consider the motor findings first. If the lesion is at C5, because the anterior horn is damaged, you will have LMN signs at that level, so the biceps reflex would be decreased, or absent. But you have also cut the corticospinal tract at that level, so from the quadriceps point of view, you have cut an UMN, and its reflex will be increased. In fact, any reflex below C5 in this patient should be increased. At the

level of the lesion, you will have LMN signs, but from the lesion down, you will have UMN signs. In the real world, or on a test question, this is where you appreciate the value of the reflex hammer tests.

Brown-Sequard is an example of an incomplete lesion to the spinal cord. Many patients will recover motor function to some extent. Because their foot is inverted and extended, they will tend to scrape their foot along the ground. Their lower limb will tend to swing laterally at the hip joint. In the case of a bilateral injury to the CST, such as cerebral palsy, the gait is often described as "wooden soldier" gait because the lower limbs tend to be stiff and straight, and swing laterally when the patient walks.

Regarding the sensory loss, while the patient's major loss of pain and temperature sensation is on the contralateral side of the body starting one to two levels below the lesion, we can look at the loss in a little more detail. Because the primary afferent ascends one to two levels in Lissauer's tract before synapsing with the second-order neuro, the pain and sensation lose will start one to segments below the lesion on the contralateral side. In addition, because the ipsilateral dorsal horn is involved, there will an ipsilateral loss of pain and temperature sensation at the level of the lesion. In addition, there may be a paresthesia at the level of the lesion on the ipsilateral side because of the initial damage to the primary afferents.

And, last but not least, if the lesion is above T1, there will be an ipsilateral Horner's syndrome because of the loss of the descending fibers from the hypothalamus to the T1 lateral horn (the ciliospinal center of Budge).

Syringomyelia

Syringomyelia is another lesion where it is important to understand the neuroanatomy to explain the symptoms. Syringomyelia may be congenital or acquired, with the congenital form often going along with a Chiari type I malformation. The acquired form may arise following trauma or is present for unknown (idiopathic) reasons. Regardless of the cause, to understand the symptoms, you need to understand how the spinothalamic tract decussates. In contrast to the dorsal column pathway or the corticospinal tract that each decussates at one spot, the spinothalamic tract decussates at every level of the cord. Whether you are at C5, T5, or L5, you will find crossing fibers of the spinothalamic tract, referred to as the *anterior white commissure*.

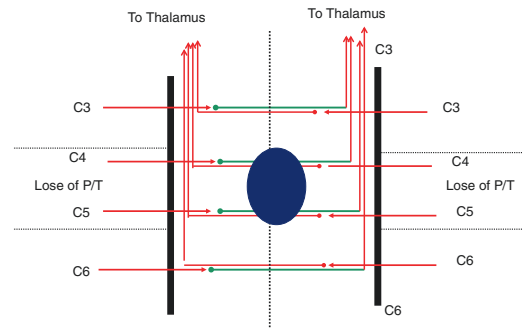

Fig. 1.14 Lesion at anterior white commisure. Bilateral loss of pain, temperature and vague touch at the level of the lesion. (Leo 2021)

The typical patient scenario will be a middle-aged woman who explains that she has lost pain sensation in both hands. There is no sensory deficit in the lower limbs. The lesion in this case is due to an expansion of the central canal which is in the center of the cord, and it usually happens in the cervical cord. The expansion will typically compress the anterior white commissure at several levels—say C5, C6, and C7 (Fig. 1.14).

It does not damage the actual spinothalamic tracts which are located out on the lateral side of the cord. If the lesion is the cervical area, you might hear the term a "cape-like loss" of pain and temperature which refers to the C5–C6 and maybe C7 dermatomes. These dermatomes start on your shoulders and come down to your hands. If it happens in the thoracic region, then you might hear the term a "belt-like loss" of pain and temperature referring to the fact that the dermatomes such as T3 or T4 resemble a belt.

One caveat is that as the syrinx expands, it can impinge on the anterior horn cells which can lead to LMN signs in the muscles of the forearm and hands. It is unlikely that it would hit the corticospinal tract, so you would not expect the lower limbs to be affected.

Tabes Dorsalis

Tabes dorsalis is a slow degeneration of the dorsal columns resulting from untreated syphilis. Symptoms include unsteady gait, bladder control problems, progressive degeneration of the joints (Charcot joints), diminished deep tendon reflexes, loss of coordination, and episodes of intense PAIN—"lightning pain." Think of the "three Ps": *P*ain, *P*olyuria, and *P*aresthesia. Patients will present with a Romberg sign, a swaying with the eyes closed; Argyll Robertson pupil, a pupil that responds to accommodation but not light; and a tabetic gait or foot slap. Because the patient has lost proprioception, they lift their feet higher than normal when they walk, and the foot strikes the floor harder than normal which leads to a slapping noise.

Anterior Spinal Artery

The anterior spinal artery (ASA) arises from two small branches that come off the vertebral artery. These two small branches immediately unite to form the ASA, which travels down the anterior median fissure of the spinal cord to supply the anterior 2/3rds of the cord. As the artery travels down the cord, it receives contributions from the radicular arteries and the artery of Adamkiewicz. Lesions to this artery lead to bilateral loss of the spinothalamic and corticospinal pathways. The dorsal columns will be spared. The ASA can become occluded during surgery that affects the abdominal aorta. Aortic aneurysms, aortic dissections, and atherosclerosis of aorta can all lead to occlusion of ASA.

Subacute Combined Degeneration

Subacute combined degeneration results from a deficiency of vitamin B12 which leads to degeneration of the corticospinal tracts, dorsal columns, and dorsal spinocerebellar tracts. Patients will present with gait abnormalities, Romberg sign, muscle weakness, hyperreflexia, spasticity, and impairment of tactile sensation, proprioception, and vibration sense. Because of the loss of the dorsal columns, Lhermitte's sign may be present. Lhermitte's sign occurs when the patient flexes the neck—chin touching the chest—and they feel an electrical signal going up and down their spine.

Cervical Cord Syndrome

As the corticospinal tract travels down the spinal cord, the fibers destined for the upper limb are medial, and they peel off at various levels to travel to the anterior horn cells. Central cord syndrome is a lesion in the central part of the cord that damages these more medial fibers; thus, the patient has deficits in the upper limb, while the lower limb is spared. This is sometimes referred to as *sacral sparing*. Because it is typically the corticospinal tract that is affected, sensory information will often be spared, or at least will not be as severely affected as motor function.

Conus Medullaris Syndrome

Time for a thought experiment. Imagine you are in the anatomy lab and you remove the spinous process and lamina of the L1 vertebra. What level of the cord are you looking at? You are looking at the sacral cord—or the conus medullaris. Remember the spinal cord ends at the L1 vertebra. Conus medullaris syndrome usually comes from displaced L1 or L2 vertebra. Because the compression will be on both the peripheral nerves (cauda equina) emerging from the cord, and the cord itself, the patient will have a combination of UMN and LMN deficits in the lower limb. They will often have saddle anesthesia and deficits with the bladder and bowel.

Axonal Polyneuropathy

Axonal polyneuropathy results from damage to peripheral nerves. In patients, such as diabetics whose nerve fibers are compromised, it is the lon-

ger axons that first show pathology. This is why diabetics first see this pathology in the feet. As time progresses, the pathology moves up their lower limb. By the time the knee is affected, symptoms are typically starting to appear in the hands.

Guillain-Barre Syndrome

Guillain-Barre is an autoimmune in which the immune system attacks the peripheral nerves, usually following an acute bacterial or viral infection. The patient first reports symptoms in the lower limbs such as weakness and tingling. At first, symptoms can be mild and may dissipate; however, they can also become severe and quickly spread to affect the entire body.

Amyotrophic Lateral Sclerosis

ALS (Lou Gehrig's disease) starts as small punctate lesions that appear in the anterior horn cells and the corticospinal tracts. It is hard to diagnose in the early stages because the symptoms will be mild. The patient might have LMN signs on one limb, and UMN signs on another side of the body. An early sign are fasciculations. There are no sensory deficits, or higher cortical function deficits. As time goes on, and more lesions appear, the patient will eventually be wheelchair bound, and then become bedridden. Typical symptoms include constipation, difficulty breathing, drooling, and weight loss.

Spinal Shock

To illustrate spinal shock, take the example of a 28-year-old male in a motorcycle accident who suffered a hemisection on the right at C5. We are going to focus on the motor deficits. You are examining this patient 2 months after the injury, and you note an absent biceps reflex and increased patellar tendon reflex—classic motor deficits for this type of patient—LMN signs at the level of the lesion, and UMN signs from the lesion on down. However, when this patient was first brought into the emergency department, he did not have these signs. Instead, he was in spinal shock, and had complete LMN signs on the right side from the lesion down. At some point, within 24 hours to 1 week after the accident, he moved from spinal shock with no reflex activity to the more long-term presentation of LMN signs at the level of the lesion, and UMN signs from the lesion down. When he was brought into the emergency department, he had flaccid paralysis; 24 hours later he had spastic paralysis.

In the emergency department, when the patient is moving out of spinal shock, the first reflexes to return are the bulbocavernosus reflex and the anal wink. Both of which are functional tests for S 2, 3, and 4. In the real world, right after the accident, you might scratch the patient's foot every time you walk into the room to see if Babinski's is returning. In an exam scenario, you would most likely be given the results of two physical exams separated by several days.

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Corticobulbar Tract and Cranial Nerve Motor Nuclei

2

Corticobulbar

Just like the spinal cord, the cranial nerves have upper and lower motor neurons. Instead of calling it the corticospinal tract, we refer to the UMNs of cranial nerves as the corticobulbar tract. And the cranial nerve nuclei are analogous to the anterior horn cells, kind of.

In the spinal cord, the ventral horn is one continuous column of cells. It might not seem like that because you are used to seeing cross sections of the cord, and when you see a section at say C6 or T2 or L1 and you see the ventral horn, it looks like small punctate nucleus, but it is not. Again, it is one continuous column of cells running from C1 to S4. As you move into the brainstem, this column of cells breaks up into small discrete motor nuclei. Think of the brainstem like a ladder. At the bottom of the ladder is the medulla with the motor nuclei for the lower cranial nerves 9, 10, and 12 (CN 11 is in the cord). In the middle of the ladder is the pons with CNs 5, 6, and 7. At the top of the ladder is the midbrain with cranial nerves 3 and 4. With a patient scenario, you are wondering where on the ladder is the lesion. Is it at the top, middle, or bottom (Fig. 2.1)?

The cranial nerve nuclei and their nerves coming out are analogous to the LMNs emerging from the cord. These cranial nerve nuclei are given directions by the corticobulbar tract—equivalent to corticospinal. There are two differences compared to corticospinal though:

1. While the corticospinal tract decussates at the pyramidal decussation, the corticobulbar does not decussate at one spot, but instead decussates at the level of whichever nucleus the fibers are destined for. For example, the fibers going to the trigeminal motor nucleus will decussate at the level of the trigeminal nucleus in the pons, while the fibers destined for the hypoglossal nucleus will decussate at the level of the hypoglossal nucleus in the medulla, and the fibers destined for the abducens nucleus will decussate at the level of the abducens nucleus.
2. The ventral horn cells receive a contralateral input from the corticospinal tract. Some of the cranial nerves receive a contralateral input, but some receive a bilateral input.

In an earlier section, we looked at the location of the three tracts in the brainstem. We now want to look at the location of the corticospinal and corticobulbar tracts and their relationship to the cranial nerve nuclei. In the medulla the nucleus of the hypoglossal nerve is on the dorsal surface right near the fourth ventricle, but its LMN fibers project ventrally alongside the medial lemniscus and the corticospinal tract in the pyramid before exiting between the pyramid and inferior olive.

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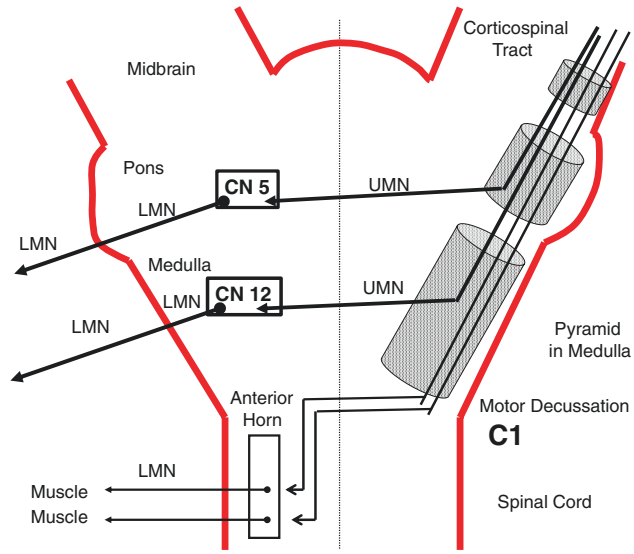

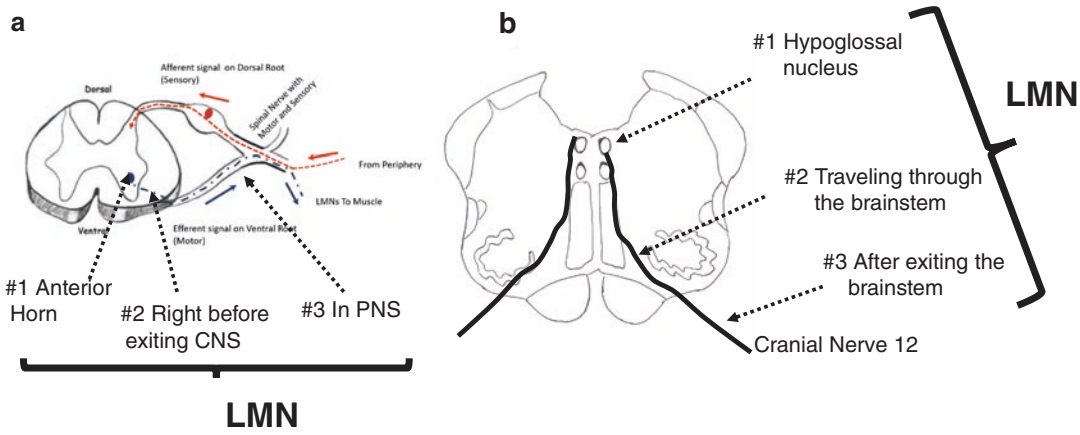

Fig. 2.2 Comparison of spinal LMNs and cranial nerve LMNs. Panel (**a**) Three parts to LMN going to a limb muscle. Anterior horn (part #1) sends fibers toward the spinal nerve (part #2) which in turn exit the CNS to enter the PNS (part #3). Panel (**b**) Three parts to LMNs of CN 12. Note that the nucleus of CN 12 (part #1) sends fibers out through the medulla (part #2), and the fibers then exit the medulla to travel onto (part #3) the tongue muscles—styloglossus, hypoglossus, and genioglossus. A lesion at any one of these parts would have an ipsilateral effect, with the tongue deviating toward the ipsilateral side. (Leo 2021)

Take CN 12 as just an example to focus on the LMNs of the cranial nerves (Fig. 2.2). There are really three sections of the LMN of CN 12: (1) there is the nucleus, with the cell body or the start of the LMN, (2) there are the fibers coming out of the nucleus that run through the medulla horizontally on their way to their exit point from the CNS, and (3) the fibers that have left the CNS and are now in the PNS. All three of these sections are part of the LMN. Every motor cranial nerve has the same basic organization. This organization is equivalent to the LMNs in the spinal cord which also have three parts: (1) the anterior horn, with the cell body or the start of the LMN, (2) the fibers coming out of the anterior horn cell traveling to the exit point from the cord, and (3) the fibers that have left the cord and are now in the PNS and on their way to the muscle. A lesion to any of these three parts of either the spinal nerve or the hypoglossal nerve will lead to LMN symptoms.

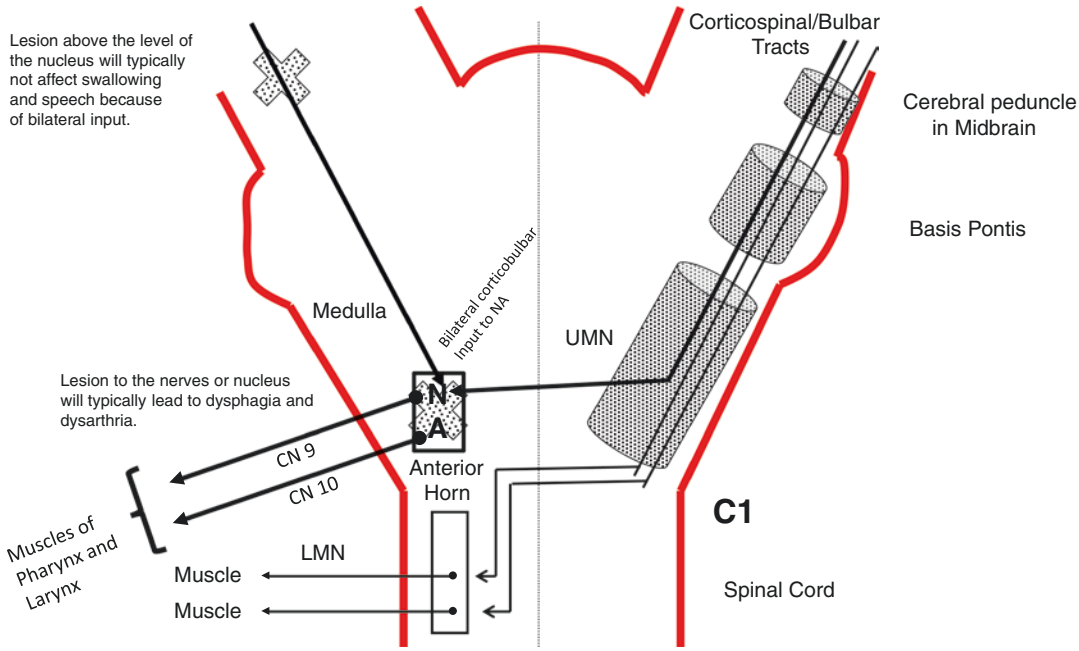

Fig. 2.3 Nucleus ambiguus (NA). Bilateral corticobulbar projections to NA. From NA, fibers of CN 9 and CN 10 project to the pharynx and larynx. (Leo 2021)

Nucleus Ambiguus

The nucleus ambiguus lives about halfway between the inferior olive and the inferior cerebellar peduncle (Fig. 2.3). You cannot see it—which is why it is called "ambiguous"—but even though it is invisible, you need to know where it is located. It is the motor nucleus for cranial nerves nine and ten. Coming out of it are fibers which go to both CN 9 and CN 10 to supply the pharynx, larynx, and palate. This is an example of how one cranial nerve nucleus can be involved with more than one nerve. A lesion to the nucleus ambiguus will lead to *dysphagia* (swallowing deficits) and *dysarthria* (speech deficits).

The nucleus ambiguus receives a bilateral corticobulbar input; thus, the muscles of the larynx and pharynx will typically be unaffected when there is a lesion in the cortex. For instance, if the right cortex is injured, the corticobulbar projection to the nucleus ambiguus could be destroyed; however, there is also a projection from the left side of the cerebral cortex to the nucleus, so it will still be functioning. The cortex lesion will not lead to dysarthria or dysphagia. If a structure has a bilateral input, it essentially has a backup, and if one input is damaged, the backup can cover for it.

As we move into the pons, the corticospinal tract lives in the basis pontis. In the middle of the pons are the medial lemniscus and spinothalamic tract (sometimes referred to as the spinal lemniscus). We can also see the motor nuclei of cranial nerves five, six, and seven and their LMN fibers running from nuclei to their exit points.

Facial Colliculus

An interesting relationship with clinical implications is the proximity of CNs 6 and 7 in the pons (Fig. 2.4). If you are standing in the fourth ventricle and look down at the floor, you will see a bump, known as the facial colliculus. This protuberance is made up of the LMN fibers of cranial nerve seven and the nucleus of cranial nerve six.

You can see in the cross section how the fibers of 7 run posteriorly to wrap around the nucleus of 6, turn ventrally, and then exit the pons. A lesion to the nucleus of 6 would also affect cranial nerve seven.

As you move into the midbrain, there are two nerves, cranial nerves three and four (Fig. 2.5), which are involved with the eye muscles. The motor nucleus of cranial nerve three projects ventrally and passes through the red nucleus and then passes close to the corticospinal tract located in the cerebral peduncle. Cranial nerve three exits between the two cerebral peduncles in a space appropriately titled the interpeduncular fossa. The corticobulbar input to cranial nerve nuclei is addressed in the next chapter.

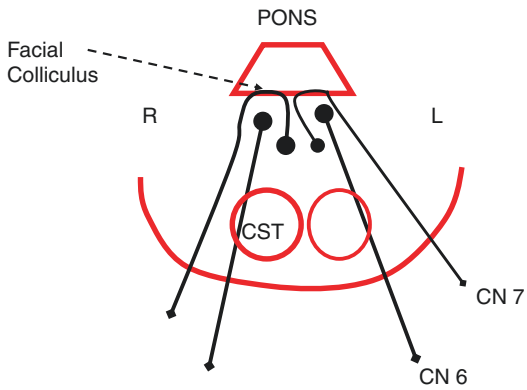

Fig. 2.4 Cross section through the pons. The facial colliculus is made up of the fibers of CN 7 passing around the nucleus of CN 6. (Leo 2021)

Cranial Nerve Five

The trigeminal ganglion sits in a depression on the floor of the middle cranial fossa referred to as Meckel's cave. Think of the ganglion as a three-fingered glove representing V1 (ophthalmic), V2 (maxillary), and V3 (mandibular). All three divisions have sensory fibers with cell bodies in the trigeminal ganglion, while V3 has a motor component to the muscles of mastication. A useful mnemonic to follow the three branches or fingers out of the skull is **SRO** or **S**tanding **R**oom **O**nly which refers to the fact that V1 goes through the **S**uperior orbital fissure, V2 through foramen **R**otundum, and V3 through foramen **O**vale.

The trigeminal nerve has four separate nuclei in the brainstem (Fig. 2.6). The pain and temperature fibers enter along V1, V2, and V3 and have their primary cell bodies in the trigeminal ganglion, which then enter the medulla and actually descend for a short distance in a tract called the spinal tract of V (equivalent to Lissauer's tract in

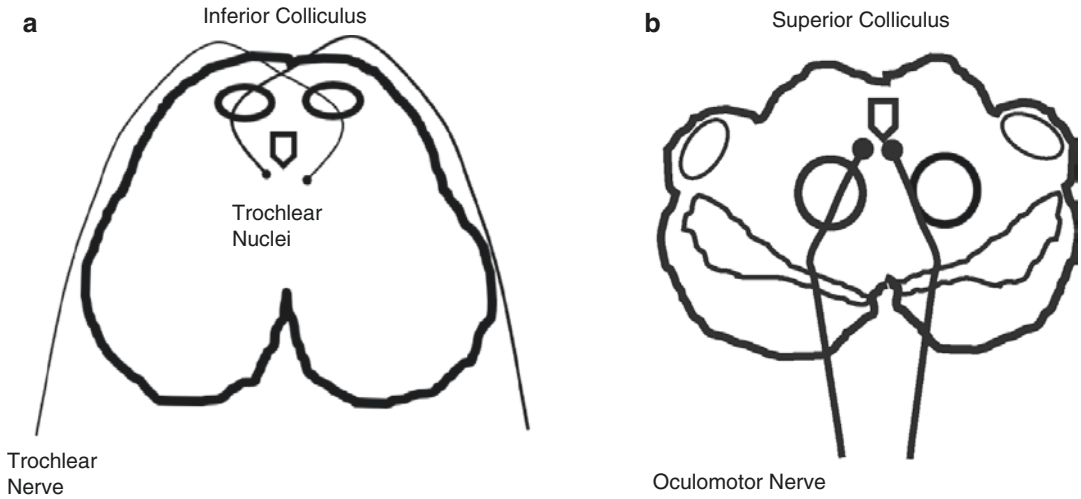

Fig. 2.5 Cross sections through the midbrain. Panel (**a**) is at the level of the inferior colliculus and CN 4. Note the LMN fibers coming out of the trochlear nuclei decussate before leaving the midbrain. Panel (**b**) is at the level of the superior colliculus and CN 3. Note CN 3 passes through the red nucleus. (Leo 2021)

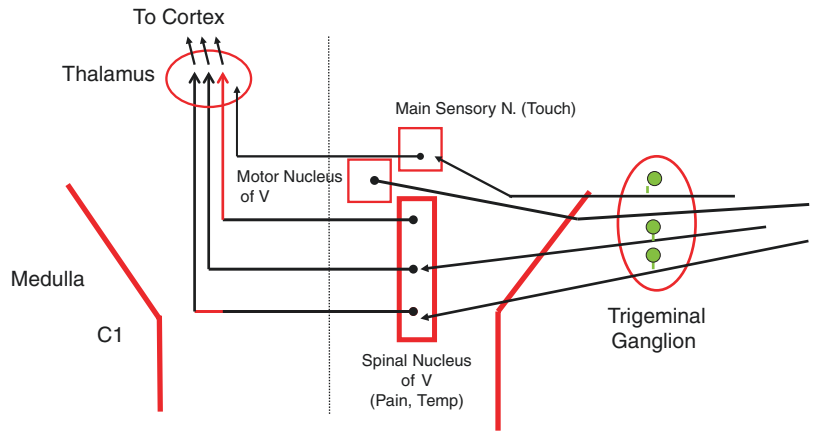

Fig. 2.6 Trigeminal nuclei. Primary afferents for pain and temperature have their cell bodies in the trigeminal ganglion and project to the spinal nucleus of V. Fibers carrying touch project to the main sensory. From these two nuclei, the fibers decussate and travel up to the VTT to the thalamus. Motor nucleus sends efferents to muscles of mastication. Mesencephalic nucleus is not shown. (Leo 2021)

the cord). These fibers terminate in the spinal nucleus of V (equivalent to the dorsal horn in the cord). The secondary afferents then project out of the nucleus, decussate, and enter the ventral trigeminothalamic tract (VTT) (equivalent to the spinothalamic tract) to ascend to the ventral posterior medial nucleus of the thalamus. Fibers carrying information about touch also have their cell bodies in the trigeminal ganglion, but when these fibers enter the cord, they terminate in the main sensory nucleus of V. From there the secondary afferents decussate and enter the VTT on their way to thalamus, and then go from the thalamus to the postcentral gyrus.

Proprioceptive fibers of CN 5 are somewhat unique, as their primary afferent cell bodies are not in the PNS but in the CNS. Looking at the picture, you can see that the primary afferents travel through the trigeminal ganglia but do not have a cell body in the ganglia. Their first cell body is in the mesencephalic nucleus which then sends a collateral to the motor nucleus, and is the circuit involved in the jaw-jerk reflex. The motor nucleus of the trigeminal nerve is just medial to the main sensory nucleus and sends fibers out through the trigeminal ganglion onto V3 (not onto V1 or V2).

For clinical scenarios, of particular interest is the close relationship of the spinal nucleus of V to the spinothalamic tract. In lateral brainstem injuries, both these structures can be lesioned. This will lead to an ipsilateral loss of pain and temperature sensation to the face, and contralateral loss of pain and temperature sensation to the body—from the neck down (Fig. 2.7).

Trigeminal neuralgia, or tic douloureux, refers to chronic excruciating pain emanating from the face due to disruption of cranial nerve five. Patients often first go to the dentist thinking they have an infected molar. Most cases are caused by compression of the superior cerebellar artery, which lies adjacent to the nerve as it exits the brainstem. It can also result from a latent herpes simplex virus residing in the trigeminal ganglion that during an outbreak leads to pain typically along V2 and V3 divisions. MS patients with a deterioration of the myelin sheath can also present with trigeminal neuralgia.

Vagus Nerve to the Head and Neck

Cranial nerve ten has motor, sensory, and parasympathetic fibers, and is the main nerve supply to the pharynx and larynx (Fig. 2.7). The first branch of the vagus is the **pharyngeal nerve** which goes to all the muscles of the pharynx and soft palate except for tensor veli palatini (CN 5) and stylopharyngeus (CN 9). With lesions to the pharyngeal nerve, the uvula will deviate away

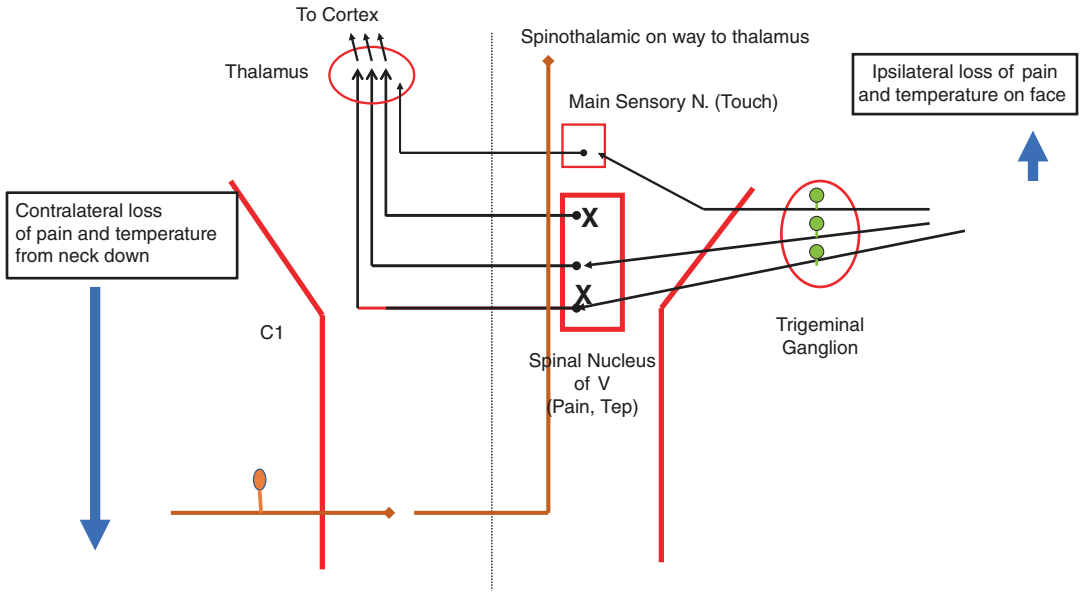

Fig. 2.7 Lateral medullary syndrome. Ipsilateral loss of pain and temperature to the face, and contralateral loss of pain and temperature to limbs. (Leo 2021)

from the side of the lesion when the patient is asked to say "Aaaahhhhh."

The next branch is the **superior laryngeal nerve** which splits into internal and external branches. The **internal branch** is responsible for sensation above the vocal cords. A fish bone or chicken bone caught in the throat can lodge in the piriform recess and lead to aggravation of the internal branch of the superior laryngeal nerve. The internal laryngeal nerve runs with the superior laryngeal artery (a branch of superior thyroid artery).

The **external branch** goes to the only external muscle of the larynx—the external cricothyroid. It runs with the superior thyroid artery for a moment and can be injured during thyroid surgery. A lesion to the external branch will lead to a soft, monotone voice, with a higher pitch than normal.

The **recurrent laryngeal** nerve comes off the vagus in the thorax and ascends in the neck to supply all the internal muscles of the larynx. One of the muscles it supplies is the posterior cricoarytenoid, which is responsible for opening the glottis. It crosses the inferior thyroid artery near the inferior pole of the thyroid gland. On the right side, it goes around the subclavian artery, and on the left, it goes around the aortic arch. A horse voice and difficulty with swallowing could be indicative of an aortic aneurysm (Fig. 2.8).

Injuries to the Recurrent Laryngeal Nerve

In a healthy individual, during inspiration the vocal cords will typically be abducted to open the glottis so that the individual can breathe. During phonation they will be adducted so that the vocal cords come close together and the air moving up from lungs can vibrate the cords. Clinical symptoms resulting from an injury to the recurrent laryngeal nerve will vary depending on the nature of the injury, but in general, with unilateral complete transections of the recurrent laryngeal nerve, typically the vocal cord will assume a median or paramedian position due to unopposed force from the cricothyroid muscle. It will remain in this median or paramedian position during respiration and phonation, so the glottis will be open during respiration.

If the injury is bilateral, then both vocal cords can assume the median or paramedian position,

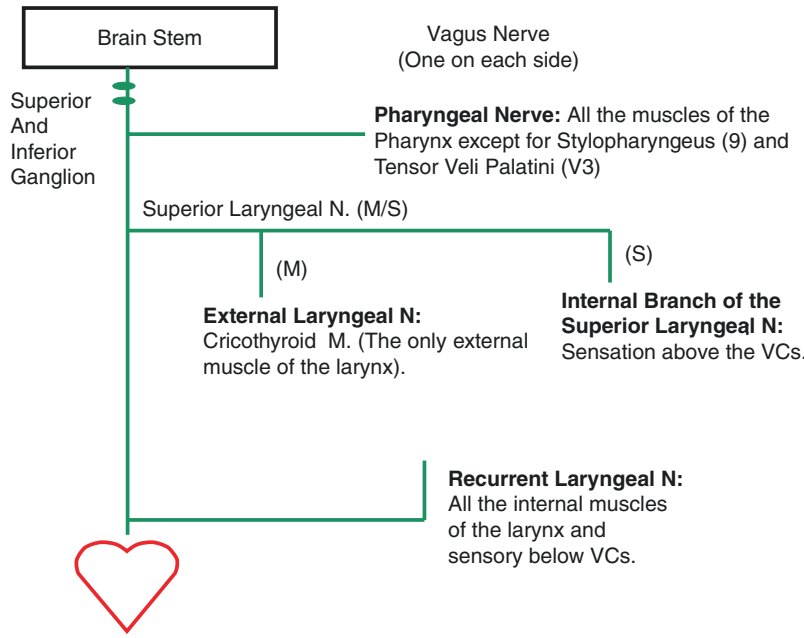

Fig. 2.8 Branches of the vagus nerve. (Leo 2021)

but in some cases, they will be adducted, and the glottis will remain closed, potentially leading to complete loss of the airway.

Cranial Nerve 11

The spinal accessory nucleus is located in the cervical spinal cord. Realize that this is nothing more than the anterior horn from C1 to C5 and is the origin of lower motor neurons that leave the nucleus and then ascend parallel to the cord and enter the skull through the foramen magnum. They then exit the skull through the jugular foramen and project to the sternocleidomastoid (SCM) and the trapezius muscles.

The corticobulbar fibers are somewhat unique to the accessory nerve. The portion of the accessory nucleus sending fibers to the trapezius receives a *contralateral* corticobulbar input, but the portion of the nucleus going to the sternocleidomastoid receives a *bilateral* corticobulbar input. Therefore, lesions in the cortex may lead to a loss of the trapezius but not sternocleidomastoid.

Cranial nerve 11 also has a cranial portion which is complicated. These fibers originate from nucleus ambiguus and come out of the brainstem with cranial nerve 10, but they quickly peel off from cranial nerve 10 and jump on cranial nerve 11 for just a moment. All this is happening within the skull. After briefly touching 11, this piece then quickly goes back to CN 10 and continues to run with CN 10 as the recurrent branch of CN 10. Remember from embryology that CN 10 comes from the 6th arch, except for the recurrent branch which comes from the 4th arch.

Cranial Nerve 12

The hypoglossal nucleus lies in the caudal medulla near the fourth ventricle. Fibers from the nucleus pass through the medulla between the pyramid and the inferior olive. Once they emerge from the skull through the hypoglossal canal, the nerve passes in the anterior triangle of the neck to innervate the hyoglossus, genioglossus, and styloglossus. The only tongue muscle not innervated by CN 12 is the palatoglossus which is innervated by CN 10. Lesions to CN 12 will lead to the tongue protruding toward the side of the lesion.

Jugular foramen syndrome results from a mass or trauma that compromises CNs 9, 10, and 11.

The patient will be dysarthric and dysphagic (CNs 9 and 10) and have a weakened gag reflex (CNs 9 and 10). And on attempted elevation of the chin, it will deviate to the ipsilateral (weak) side. The lesion will also compromise the ipsilateral otic ganglion (CN 9) and parotid gland secretion. If the mass is large enough, it would also compromise the superior cervical ganglion leading to a Horner's syndrome.

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Abducens Nerve Lesions

3

When you approach a patient with a deficit of the eye muscles, or see a board question, think of two parts to the typical scenario. The first part is when the patient is sitting in your office and you notice, or suspect, that something is amiss with the eyes. The second part of the exam is when you formally test the muscles by asking the patient to follow your finger as you move them through the test. We will first look at the actions of the eye muscles and their respective nerves. We will then look at how you would test the muscle and nerves. To do this we are going to look at two pictures to discuss the eye muscles.

Actions

The first picture shows the *actions* of the muscles (Fig. 3.1). This is the picture that you would see in a typical anatomy textbook. After all, anatomists like to talk about actions or function. Note that medial rectus and lateral rectus each only have one action. Lateral rectus pulls the eye laterally (abduction), and medial rectus pulls the eyes medially (adduction). However, the other four muscles each have three actions. Superior oblique pulls the eye down and out, while inferior oblique pulls the eye up and out. And superior rectus pulls the eye up and in, while inferior rectus pulls the down and in. Yet, we also need to pay attention to the oft-ignored intortion and extortion movements. Intortion is when the 12 o'clock position of your eye rotates toward your nose, and extortion is when it rotates away from the nose. Also, keep in mind, that because we want to focus both eyes on the same point at point at the same time (convergence) that when the healthy person fires, say the lateral rectus in one eye, that it will be the contralateral medial rectus that fires (Hering's law).

Don't confuse intortion and extortion with medial and lateral movements. Intortion and extortion involve the eyes rotating in the eye socket. While you are reading this, tilt your head to the left. If you did not have intortion and extortion, your world (the page) would tilt, but you know that the world stays level. This is because your left eye intorted and your right eye extorted. As your walk down the street and your head moves, this mechanism allows your eyes to compensate for head movements so that the world does not bob around and make you dizzy. When you look at the picture showing the actions of the muscles, you can see that there are two intorters (superior oblique and superior rectus), and two extorters (inferior oblique and inferior rectus).

The action picture for the eyes is important to understand because it explains what happens with the eyes when there is a nerve lesion.

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Cranial Nerve Six Lesion

The eye is a democracy. To look straight ahead, you need to have equal tension on medial and lateral rectus. If you have a deficit with the lateral rectus, then medial rectus will then take over and move the eye medially. The patient will have a medial strabismus. If they had a deficit with medial rectus, then lateral rectus takes over and they have a lateral strabismus.

Cranial Nerve Three Lesion

If you have a lesion to cranial nerve three, then you would lose all the muscles except lateral rectus and superior oblique which will lead to the eye projecting down and out—a lateral strabismus. Because cranial nerve three has parasympathetic fibers, the patient will also have ptosis (droopy eyelid) and mydriasis (dilated pupil).

Cranial Nerve Four Lesion

With a lesion to cranial nerve four, the patient loses the superior oblique, one of the two intorters. With weakened intortion, the right eye will now be extorted. With the right eye extorted, the patient now has two visual fields. To bring the world back to one visual field, the patient will have a head tilt away from the lesion side—in this case toward the left (Bielschowsky sign). This movement brings the right eye up to level, and since the muscles on the left are working, the left eye will intort. Keep in mind that you cannot look at a patient's eyeball and see intortion and extortion.

Testing

The next picture to look at it is the H test which shows how to test the eyes (Fig. 3.2). This is the picture that you would see in a typical clinical exam textbook. To test the MR and LR, you ask the person to look medially or laterally. However, if you want to test the right SO, first you ask the patient to look left, and then once the eye is pulled in, you ask the person to look down. The only way the adducted eye can look inferiorly is with SO. The first part of the test is when the patient looked medially which isolated the SO, so that the only way the patient can look down is with SO. The only way they look up is with IR. Ideally when you test the eye movements, you keep on the H lines, and do not take the diagonal shortcuts.

Keep in mind that when you test both eyes together, you cannot test the same muscle in each

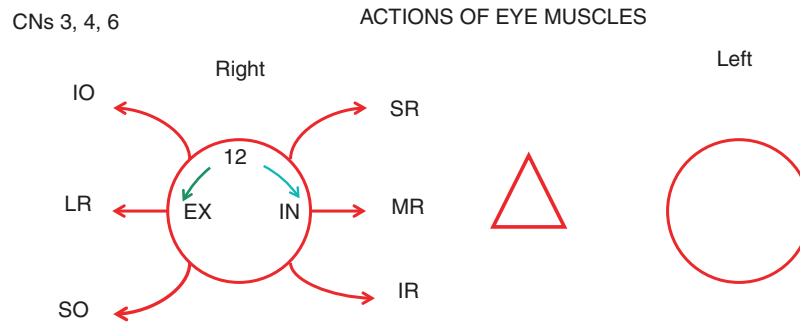

Fig. 3.1 Diagram showing the actions of each muscle. For instance, the superior oblique moves the eye down and out and intorts. And for instance, the inferior rectus moves the eye in and down and is an extorter. (Leo 2021)

Fig. 3.2 Testing of the eye muscles. Diagram of the H test. To test the superior oblique, the patient first looks in and then down. (Leo 2021)

eye at the same time. If you have the patient look to the left and down, then you are testing the right SO and the left IR.

Cortex Control from Frontal Eye Field

One of the more commonly tested mechanisms that is tested on board exams is lateral gaze. Before getting into the details, we will start with the big picture. Start off looking at something in your room, like a wall clock. If you move your head to the left, but want to stay focused on the clock, your eyes will slowly move to the right. However, if you keep moving to the left, eventually your eyes will quickly (fast phase) follow your head rotation. We can refer to these two movements as the slow phase and the fast phase. The slow phase is under control by your vestibular system, and you use this all the time when you are walking around. Without it you would be dizzy. With a head turn, the slow phase, which occurs first, is opposite the head turn.

Eventually, your eyes follow your head. This is the fast phase, and it's under control by your cortex. In contrast to the slow phase, you will notice that during the fast phase, your eyes do not take in everything in the visual world as they move. At one point your eyes are looking straight ahead, and the next moment you are looking off to the side, and during the movement your eyes did not see everything. In the following discussion, we are going to look at the fast phase. In the vestibular chapter, we will look at the slow phase.

Fast Phase of Nystagmus

The frontal eye fields are two bilateral structures that sit in the frontal lobe just anterior to the precentral gyrus. When one FEF fires, it drives the eyes toward the contralateral side. For instance, if the right frontal eye fires, the eye will move to the left. Tonic activity from both frontal eye fields keeps the eyes looking straight ahead. Therefore, if there is a lesion to the right frontal eye field, the eyes will drift right.

Let's look at the details of moving the eyes to the right. The signal starts in the left FEF and projects to the right paramedian pontine reticular formation (PPRF). The PPRF is small and sits right next to the abducens nucleus. Some textbook authors will show the PPRF in the schematic, while others will leave it out. For the purposes of clinical neuroanatomy, it doesn't really matter one way or the other. Both the PPRF and abducens nucleus are small structures and practically sit on top of each other. For our purposes, they are basically the same structure.

We are going to look at numerous lesions to this pathway, and we will look at how the eyes will appear at rest, and what the eyes will do

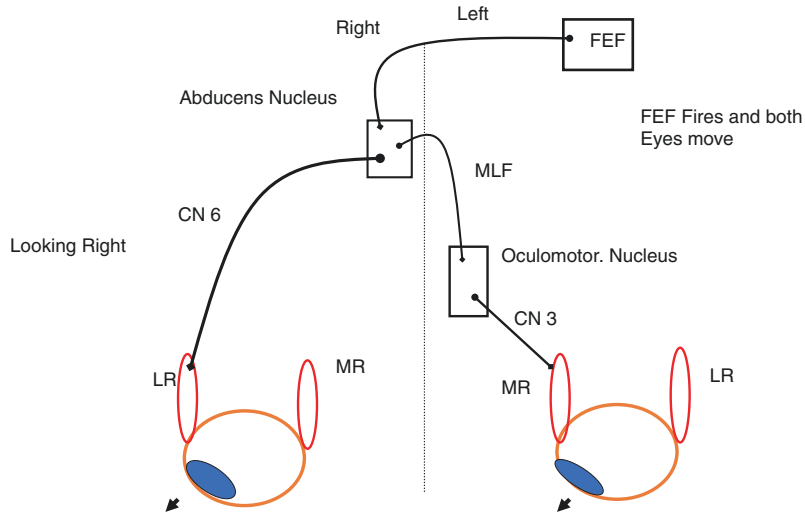

Fig. 3.3 Horizontal gaze pathway in a healthy individual

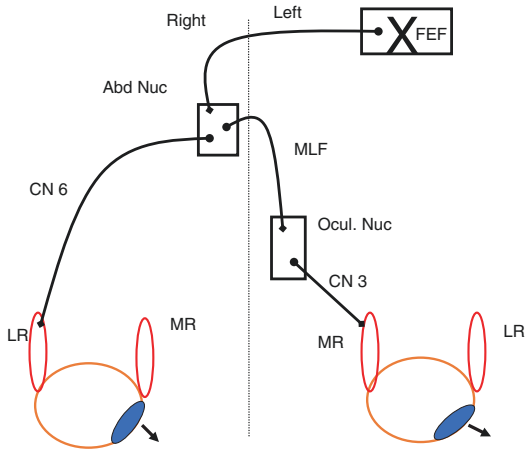

Fig. 3.4 Lesion #1 to the frontal eye field. Eyes at rest deviate toward the lesioned side. (Leo 2021)

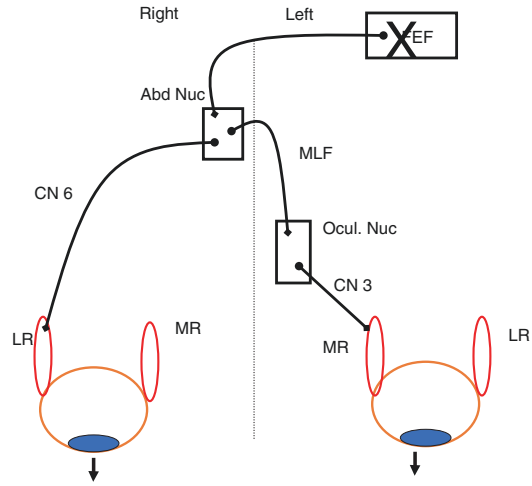

Fig. 3.5 Lesion #1 Frontal eye field lesion. Patient attempts to look right. The best that the eyes can do is midline. (Leo 2021)

when you test them. The key point is that lesions to the abducens nucleus affect both eyes.

We all know that the abducens nucleus projects to the ipsilateral lateral rectus nucleus, but it also projects via the medial longitudinal fasciculus (MLF) to the contralateral oculomotor nucleus and then to the medial rectus (Fig. 3.3). This system ensures that both eyes will move together to one side—lateral gaze. We need to discuss four different lesions to this system.

Lesion 1: Frontal Eye Field *Lateral Gaze Paralysis*. In a patient with a lesion to the left frontal eye field when you are talking to them, you will note that their eyes have a slow drift to the left at rest (Fig. 3.4). They can move their eyes to the midline but no further.

When you test their lateral gaze function, you will notice that their eyes have difficulty looking to the right (Fig. 3.5).

Lesion 2: Abducens Nerve *Ipsilateral Paralysis of Ocular Abduction*. In a patient with a lesion to the fibers of cranial nerve six, the patient will

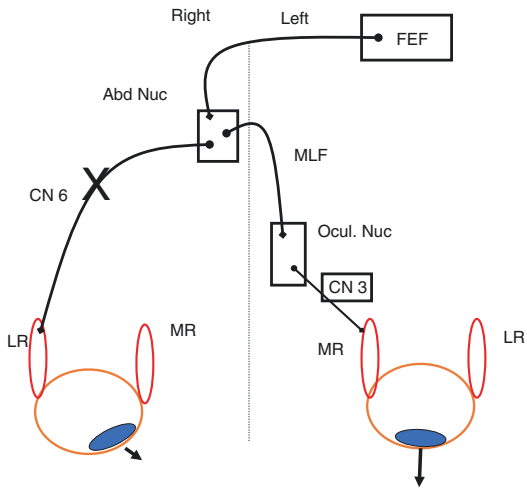

Fig. 3.6 Lesion #2 Abducens nerve lesion. At rest, medial strabismus of ipsilateral eye. (Leo 2021)

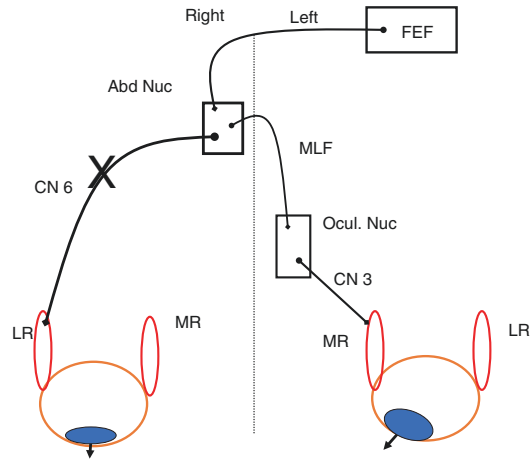

Fig. 3.7 Lesion #2 Abducens nerve lesion. On attempted lateral gaze, the best that the right eye can do is midline. (Leo 2021)

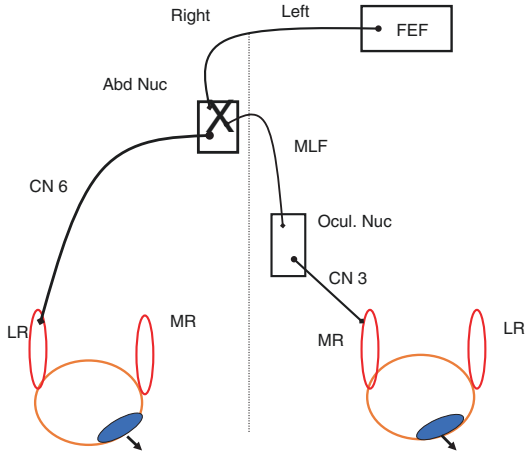

Fig. 3.8 Lesion #3 Abducens nucleus lesion. At rest, the eyes deviate to the left. (Leo 2021)

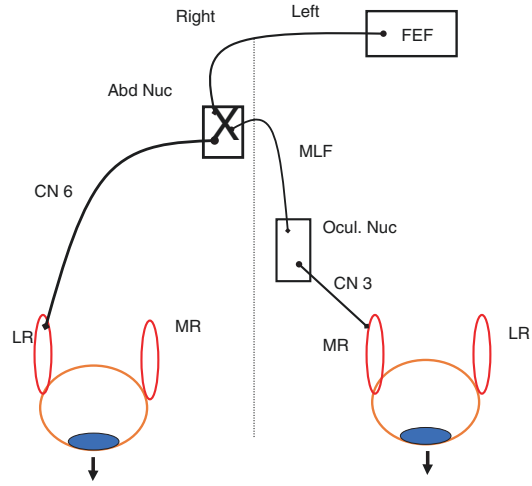

Fig. 3.9 Lesion #3 Abducens nucleus lesion. Attempt to look right and the best that the eyes can do is midline. (Leo 2021)

only have a deficit with one eye. At rest, this eye will be medially deviated (Fig. 3.6).

And when asked to look laterally, they have difficulty, paralysis of ipsilateral ocular abduction. Their left will function normally.

Lesion 3: Abducens Nucleus *Lateral Gaze Paralysis*. In a patient with a lesion to the abducens nucleus, both eyes will have a slow drift to the left at rest (Figs. 3.7 and 3.8).

When you ask them to look right, they will have difficulty with both eyes, known as *lateral gaze paralysis* (Fig. 3.9).

Lesion 4: Medial Longitudinal Fasciculus *Internuclear ophthalmoplegia.* In a patient with a lesion to the left MLF, the patient will not have any deficit when the eyes are at rest. Yet when asked to look to the right, their left eye will not be able to look right because medial rectus is not getting a

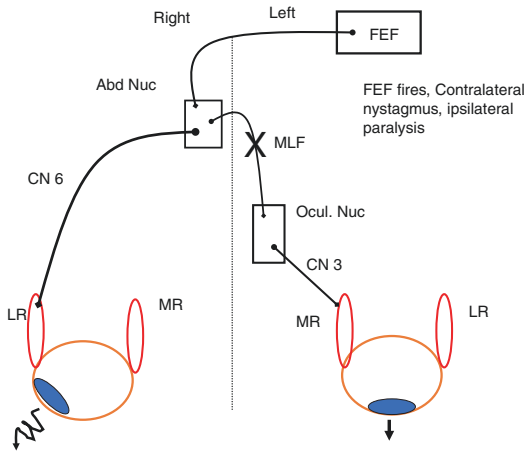

Fig. 3.10 Lesion #4 Medial longitudinal fasciculus lesion. Patient attempts to look right, and exhibits contralateral nystagmus and ipsilateral paralysis. (Leo 2021)

signal. And their right eye will flutter back and forth, which is known as effort nystagmus. They will not have nystagmus at rest. The nystagmus appears when they make an *effort* to look right. This patient with a lesion to the left MLF will not have any deficit looking to the left. Internuclear ophthalmoplegia is an early sign of MS. The lesion can be found on one side, like the example given, or it could be bilateral and affect both eyes (Fig. 3.10). If the lesion is present to both MLFs, when the patient looks right, the left eye will be frozen, with the right eye exhibiting nystagmus (as shown in the picture), but when asked to look right, deficits are reversed with the right eye being frozen and the left exhibiting nystagmus. In addition, at rest the eyes will be laterally deviated (exotropia), thus the name wall-eyed bilateral internuclear ophthalmoplegia (WEBINO) syndrome.

One and a Half Syndrome

In the one and a half syndrome, there is a lesion to the abducens nucleus and the MLF on the same side. If the lesion is on the right side, when the patient is asked to look to the right, the best that both eyes can do is the midline because of lesion to the nucleus (Fig. 3.11). And then when asked to look to the left, the

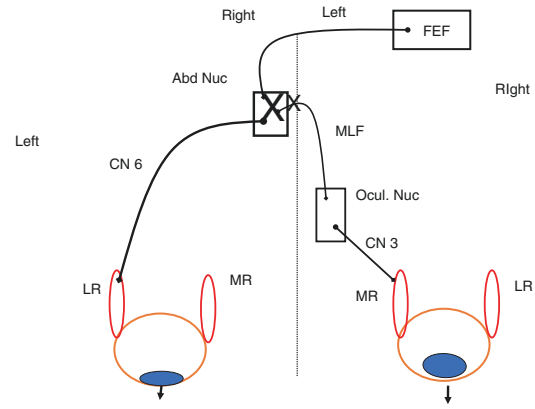

Fig. 3.11 One and a half syndrome. Patient looking right. Horizontal gaze paralysis. (Leo 2021)

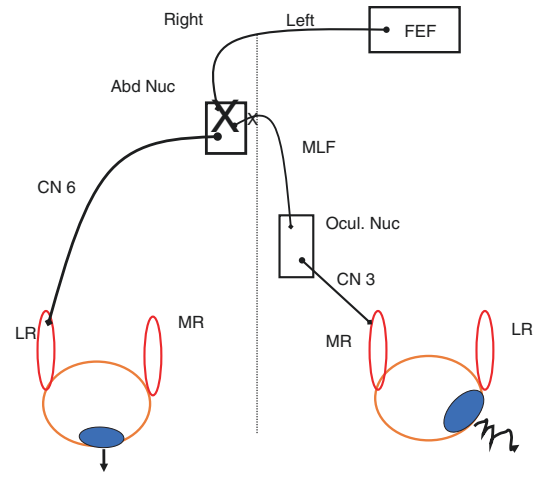

Fig. 3.12 One and a half syndrome. Looking left, paralysis of the right medial rectus. Nystagmus of the left eye. (Leo 2021)

right eye cannot do any better than the midline, and the left eye will have effort nystagmus, because of the lesion to the MLF (Fig. 3.12). *Remember lesions to the MLF will lead to contralateral effort nystagmus.*

Who Are the Neighbors?

The question that usually comes up at this point is: if you are looking at the patient's eyes, how do you tell the difference between a FEF lesion (#1 in previous example) and an abducens nerve

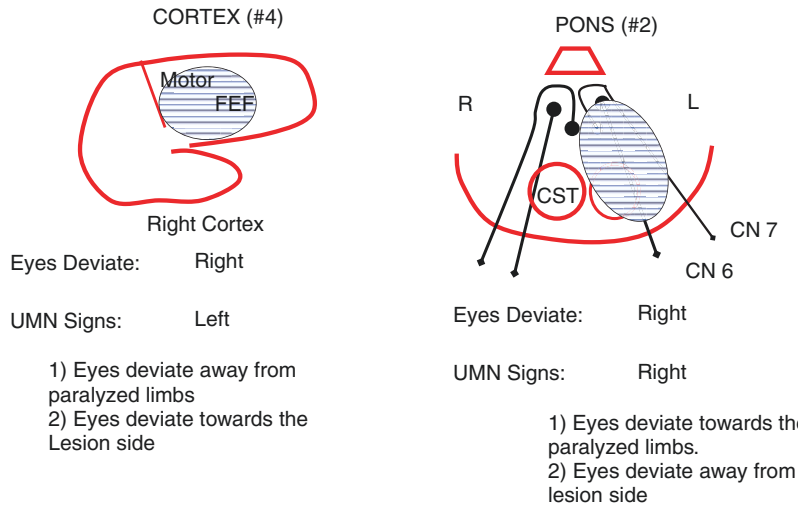

Fig. 3.13 Comparison of lesions to FEF and abducens nucleus and their surrounding structures. (Leo 2021)

lesion (#3 in previous example) since both these patients have the same eye movement deficit? All this brings up an important point; when you are first learning neuroanatomy, you naturally go through the tracts and cranial nerves one by one, such as one lecture on corticospinal tract, then one on cranial nerve seven, and one on cranial nerve six, and so on. But keep in mind that a patient does not present with just one tract or nerve that is affected. Patients present with multiple symptoms. Just like the board exams, you will not see a question on just cranial nerve seven, or just cranial nerve six, or just the corticospinal tract. You will be given patient scenarios that incorporate multiple systems. This is why when you learn about damage to a structure, you need to pay attention to its neighbors—since they can be compromised also. It is good to know your neighbors, especially in neuroanatomy.

The way to think about the typical neurology patient or a case study on the exam is that the patient will present with several different signs or symptoms. Your job is to figure out where can one lesion can account for all the symptoms. In the case of these two patients, consider that more than just the abducens nucleus or just the FEF will be compromised. Consider two different lesions (Fig. 3.13).

In the patient with a lesion to the right frontal eye field, at rest the eyes will slowly drift to the right. In addition, the precentral gyrus is damaged which will lead to UMN signs on the left. Thus, the eye deficit can be related to the UMN deficit by saying: "the patient's eyes drift away from the paralyzed side of the body." You will sometimes hear this referred to as "right-way eyes." (In addition, the patient will have a contralateral loss of lower facial muscles.)

In the patient with the lesion at the left abducens nucleus, the eyes will have a slow drift to the right (Foville's syndrome). Because the left corticospinal tract is damaged in the pons (above the decussation), they will have UMN signs on the right side of the body (contralateral) so the patient's eyes drift toward the paralyzed side of the body"—often referred to as "wrong-way eyes." (The patient will have an ipsilateral loss of both upper and lower muscles of the face on the left. See the chapter on the facial nerve for a more detailed explanation of the face deficits.)

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Vestibulocochlear Nerve Lesions

4

The vestibulocochlear nerve includes the auditory portion, which is responsible for hearing, and the vestibular portion, which is responsible for balance and eye movements. As mentioned in the previous chapter, when you focus on something in front of you, and then turn your head, your eyes slowly move opposite your head rotation. This is the slow phase of nystagmus, which is under control of the vestibular system.

Hair Cells, Potassium, and the Batteries

Both the auditory and the vestibular portions of the nerve utilize hair cells to detect either sound or balance. These hair cells have a unique mechanism of action which is the opposite of the other cells in the body. Whereas most cells maintain a higher concentration of Na^+ outside the cell, and a high concentration of K^+ inside the cell, the hair cells are opposite of this. K^+ is higher outside the hair cell, and Na^+ is higher inside the cell. There are K^+ channels on the cell membranes of the hair cell tips that when stimulated allow K^+ to come rushing into the cell which leads to a depolarization and release of transmitter. These hair cells do not have action potentials, but instead they have graded potentials. Thus, they are not "on" or "off," and they don't follow the "all-or-none" rule of action potentials, but instead, they have graded responses, becoming either more positive or more negative. The hair cell tips with their K^+ channels are the site where mechanical energy is transduced into electrical energy—the mechanotransducer.

In the auditory system, the base of each hair cells is on the basilar membrane, and the hair tips project into the scala media where they are bathed in endolymph with the high concentration of K^+. This high concentration of K^+ is maintained by the stria vascularis which is located on the outer edge of the scala media. The stria vascularis is equivalent to a battery, as it pumps positive ions into the endolymph or the ear. In the vestibular system, the K^+ gradient is maintained by the *dark cells*—also functioning like a battery.

Vestibulo-ocular Reflex

One job of the vestibular system is to move your eyes in response to either body or head movements—*the vestibulo-ocular reflex (sometimes referred to as oculovestibular reflex).* There are three semicircular canals on each side of the head. Each one senses a different movement of the head. We are going to focus on moving the head from side to side, which is detected by the lateral semicircular canal. As an analogy to the hair cells, think of an empty beaker. Take a feather, and with some epoxy attach the base of the feather to the beaker, and then fill the beaker with water. The base of the feather is stuck to the

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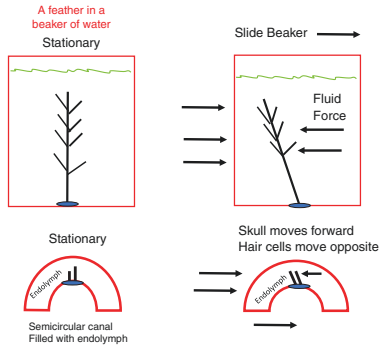

Fig. 4.1 The feather is equivalent to a hair cell, the beaker to the skull, and the water in beaker to the endolymph. When the beaker, or skull, slides in one direction, the fluid pushes the hair cell in the opposite direction. (Leo 2021)

beaker, but the feather itself is free to move in the water, whichever way the current flows. If the beaker is suddenly pushed to one side, say to the right as in the accompanying figure, the current will move left, and the hair cells will fall to the left. On each side of your head, you have a semicircular canal with hair cells surrounded by endolymph, or a beaker, with a feather, surrounded by water. When you turn your head, the semicircular canal on one side is pushed anterior, and on the other side is pushed posterior (Fig. 4.1).

Take a head turn to the left as an example. The semicircular canal on the left follows your head and is pushed posterior, and the hair cells fall anterior. This leads to a depolarization of the hair cell and a subsequent depolarization of the left vestibular nerve. Meanwhile on the right everything is reversed. The semicircular canal is pushed anteriorly with the hair cells falling posteriorly, hyperpolarizing the right vestibular nerve.

Continuing with the head turn to the left, the left vestibular nerve fires, and projects into the brainstem to fire the left medial rectus and the right lateral rectus so that both eyes move to the right. This slow phase is strictly under control of the brainstem (Fig. 4.2). Just like tapping on the quadriceps tendon tests the integrity of the spinal cord reflex, you can put either cold or warm water in the ear to test the integrity of the brainstem pathway in the picture (Bárány test).

Cold or warm water in the ear canal sets up a convection current which moves the hair cells, essentially tricking the person into thinking that their head turned. The direction of the convection current depends on the temperature of the water. The cold water in the right ear will cause the eyes to slowly deviate to the right and then quickly go left. The eyes will go back and forth alternating between slow and fast. Warm water will also lead to a slow and fast phase but in the opposite directions. Warm water in the right ear leads to slow deviation to the left and fast deviation to the right (Fig. 4.2). When you hear the term terminology of say a "fast beating nystagmus to the left," realize that the person would also be expected to have a slow gaze to the right.

If you apply cold or warm water and observe a slow phase of eye movements, this tells you that the brainstem pathways are intact. Just like tapping on the knee tells you that the spinal cord reflex pathways are intact. If you see a fast phase after the slow phase, this tells you that the cortex is intact. In a healthy patient, you would observe this slow phase followed by a fast phase after applying either cold or warm water (Fig. 4.3 Panel a).

This test can come into play with a comatose patient. Coma can result from diffuse neuronal dysfunction or a bilateral structural lesion leading to a disruption of the reticular activating system. In the case of lesions, they can be divided into supratentorial (cerebral cortex or diencephalon) or infratentorial (brainstem). Imagine you have two patients in the hospital, and both are in a coma: one patient has a bilateral cortical deficit, and the other has a bilateral brainstem deficit. In the patient with the cortex deficit, cold or warm water placed in the ear will typically lead to a slow phase (the brainstem pathways are intact), but there will be no corresponding fast phase (patient #1 in accompanying image). In the patient with the bilateral brainstem deficit, if you put warm or cold water in either ear, there will be no slow phase (the brainstem pathways are disrupted). In this brainstem patient, since there is no initial slow phase, there will be no subsequent fast phase (Table 4.1).

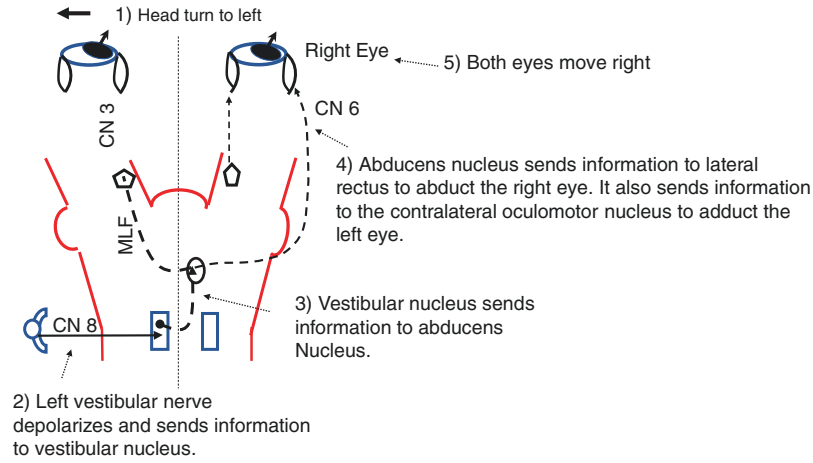

Fig. 4.2 Vestibulo-ocular reflex—slow phase. With a head turn to the left, the right vestibular nerve is depolarized leading to both eyes turning to the right. Note that there is no cortical involvement in this pathway. This is the slow phase. It can be tested by adding cold or warm water in the ear. (Leo 2021)

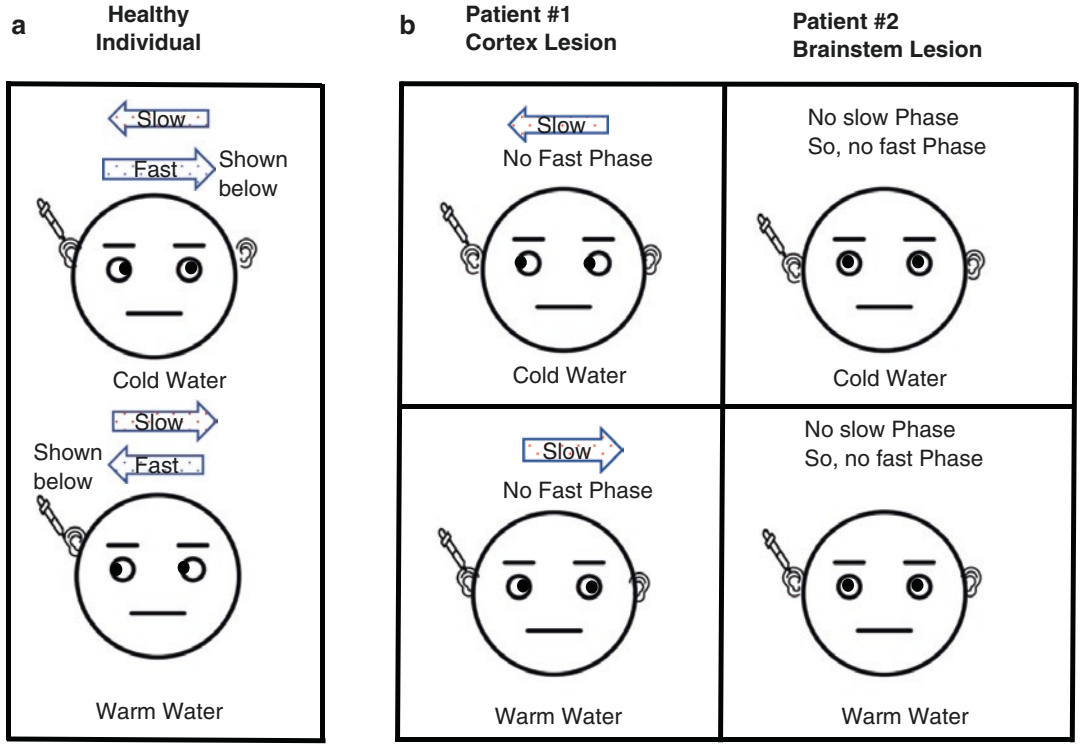

Fig. 4.3 Panel (**a**). In a healthy individual when you add cold water to the right ear there is a slow phase to the right followed by a fast phase to the left (Eyes in the picture show fast phase movement). Warm water leads to the opposite motions. Panel (**b**). With a cortex lesion with cold or warm water there is a slow phase but no corresponding fast phase (normally cortex does fast phase). With a brainstem injury there is no slow phase, and without the initial slow phase there is no corresponding fast phase. (Leo 2021)

In *postrotatory nystagmus* the eye movements are opposite the normal movements. If you spin someone around in a swivel chair (approximately ten turns), and then stop the chair and have them attempt to look straight ahead, you will notice their eyes going back and forth. The lay person will notice the eyes are fluttering, but there is more to it. If you look closely, you will see a slow

phase in the direction of the original turn and a fast phase away from the head turn—in other words the eye movements are opposite what you would notice if the person just turned their head. This is because when you spin in the chair enough times, the fluid in your semicircular canals will catch up with your head, just like if you spin a beaker around the fluid will start spinning with the beaker, and then when you stop the head turn, or the beaker spinning, the fluid keeps going and turns the hair cells opposite the normal head turn.

Table 4.1 Vestibulo-ocular response and comatose patient

	Slow phase	Fast phase	Lesion
Coma patient #1 Add cold or warm H_2O	Present	No fast phase	Cortex
Coma patient #2 Add cold or warm H_2O	No slow phase	NA	Brainstem

Oculocephalic Reflex

The *doll's eye reflex* or oculocephalic reflex is another way to test for a comatose patient. If the brainstem is intact when you turn the patient's head to either side, the eyes should turn away from the head rotation. If the eyes follow the head rotation, this indicates that the brainstem pathways are disrupted (Fig. 4.4).

There are four vestibular nuclei in the brainstem: lateral, medial, inferior, and superior. The medial and superior vestibular nuclei send fibers that ascend via the medial longitudinal fasciculus (MLF) to the cranial nerve nuclei involved in eye movements. Lesions to these vestibular nuclei will lead to a fast phase of nystagmus to the contralateral side. Let's walk through the reasoning of this. Take your left vestibular system. The left vestibular nerve is responsible for the slow phase to the right—the fast phase will

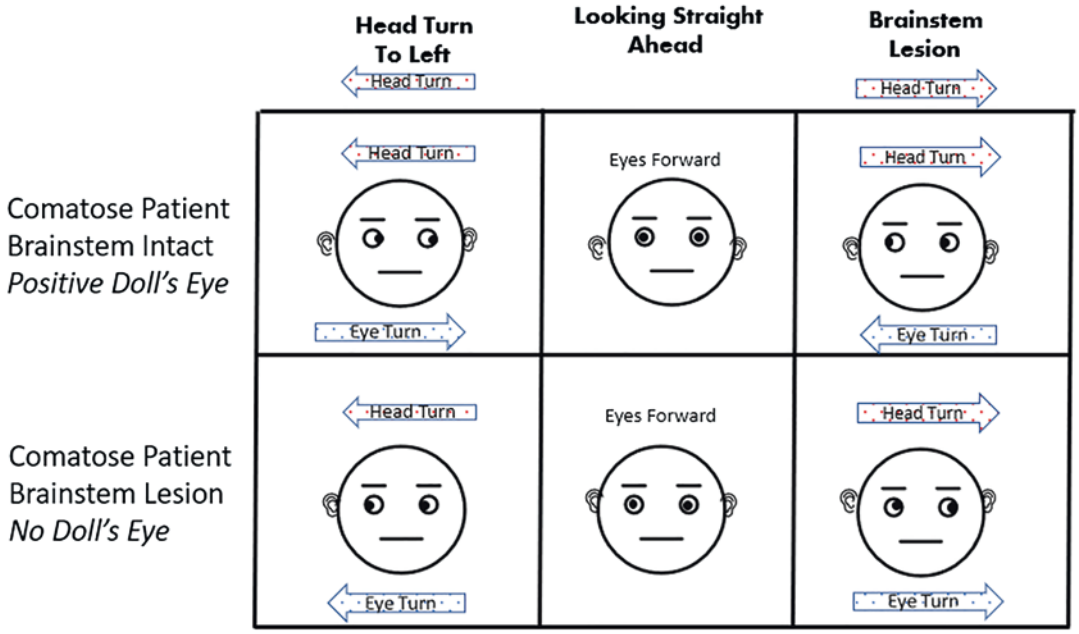

Fig. 4.4 Doll's eye. Panel (**a**). You start off with the patient looking straight, and then turn the head to the right and left. Because the brainstem is intact the eyes will turn opposite the head rotation – Positive Doll's eye. In panel (**b**) the patient has a brainstem injury, and when you turn the head in either direction the eyes follow the head. (Leo 2021)

be to the left. If the left system is damaged, then the right overtakes it, slowly driving the eye to the left and quickly to the right. Remember lesions to the medial or superior vestibular nucleus lead to a fast-beating nystagmus to the contralateral side.

The *utricle and saccule* are also part of the vestibular apparatus. Their sensory epithelium is referred to as the macula, which also has hair cells. The macula of the saccule is in vertical position and sense vertical acceleration. The macula of the utricle is oriented horizontally and senses horizontal acceleration. The hair cells are covered by a gelatinous cap which in turn is covered by the otolithic membrane which has calcium crystals or canaliths embedded in it. The weight of the canaliths on the otolithic membrane puts pressure on the hair cells. Just like the semicircular canals, head movements result in shearing forces which bend the hair cells in the utricle and saccule.

Running somewhat down the middle, or axis, of the macula is the striola. When the head tilts, the hair cells on one side will tilt toward the striola and depolarize while the hair cells on the other side will tilt away and hyperpolarize.

Benign paroxysmal positional vertigo (BPPV) is a common cause of vertigo—the feeling of spinning while not moving. It results from the canaliths, which normally lie in the utricle, coming loose and becoming misplaced. In some cases, they can be moved back into place with appropriate head movements, referred to as a *canalith repositioning procedure*, also known as the Epley maneuver.

The hair cells in the vestibular system are extremely sensitive; thus, any perturbations in the amount of fluid in the semicircular canals are problematic. *Meniere's disease* is thought to be caused by excessive fluid in the semicircular canals which leads to unwanted movement of the hair cells which leads to dizziness.

Lateral Vestibular Nucleus and Lateral Vestibulospinal Tract

The lateral vestibulospinal tract projects from the lateral vestibular nucleus to the ipsilateral antigravity muscles. If you are in a standing position and get pushed on the right shoulder, then the extensor muscles on your left will contract to maintain your upright stance. If you lesion the left nucleus or tract, you will have ipsilateral ataxia. When these patients walk, they will tend to deviate or sway toward the lesioned side.

Decorticate and Decerebrate Rigidity

Coma is the result of a bilateral lesion to either the brainstem or the cerebral cortex. In both cases, the lower limbs will be similar—the feet will be planterflexed. It is the upper limb position that will be different. There are three tracts that come into play with both scenarios: (1) corticospinal, (2) rubrospinal, and (3) lateral vestibulospinal. In decorticate rigidity, the lesion is above the red nucleus, so both the rubrospinal and lateral vestibulospinal tracts are intact. The rubrospinal tract projects to the flexors of the upper limb, so there will flexion at the elbows. In addition, the lateral vestibulospinal tract going to the extensors of the lower limb is intact, so there will be extension of the patient's leg and foot.

Decerebrate rigidity is a lesion below the red nucleus, so the rubrospinal is now cut, which leads to extension of the upper limbs. Just like decorticate, the lateral vestibulospinal tract is intact so the lower limbs are extended.

One way to remember this, is that in decorticate rigidity, with your upper limbs flexed, you are basically making an "O" with your upper limbs, and since your hands are point up, the lesion is up high—above the red nucleus, and in the cortex (Fig. 4.5).

Auditory

The basilar membrane runs down the middle of the cochlea from base to apex and is responsible for our ability to differentiate various tones. The key feature of the basilar membrane is that it is not a uniform structure, so that different regions of the membrane will vibrate in response to different tones. At its base, the membrane is narrower, thicker, and stiffer so that it responds to

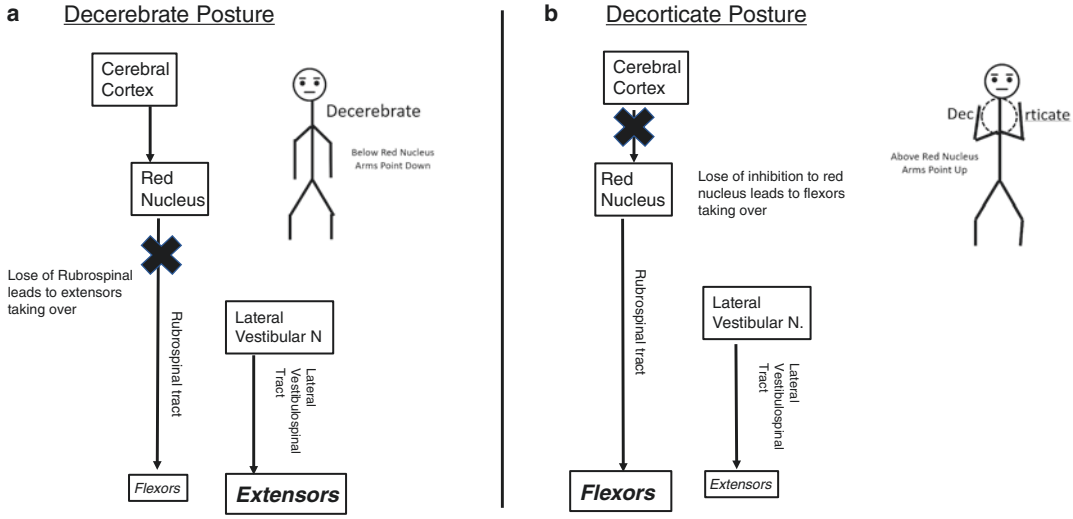

Fig. 4.5 Decerebrate and Decorticate Pathways. Panel (**a**). In decerebrate posture there is a lesion below the red nucleus so lateral vestibular tract predominates leading to extensor activity. Panel (**b**). In decorticate posture there is a lesion above the red nucleus. The uninhibited rubrospinal tract to flexors leads flexion of the upper limbs. The decorticate patient has their arms pointed up, making an "O" with their upper limbs. (Leo 2021)

high frequencies; at the apex, the membrane is wider, thinner, and more pliable so that it responds to low frequencies. In other words, different parts of the membrane are tuned to different tones. In some other species, birds, for example, the ability to detect tones is based on their hair cells being tuned to different tones.

There are two types of hair cells located on the basilar membrane—the inner hair cells and the outer hair cells. Both have afferent fibers leaving the cells projecting into the CNS, and efferent fibers projecting to the hair cells. The inner hair cells are lined up in just one row, on the inner part of the organ of Corti. Ninety-five percent of the afferent fibers in the auditory nerve come from the inner hair cells. Most of the efferent fibers in the auditory nerve project to the outer hair cells, which are lined up in three rows. The outer hair cells are somewhat unique in that they are able to change shape. They can go from short and squat to tall and thin. As they become taller, the hair cells reach up closer to the tectorial membrane.

Overlying the top of the inner hair cells is the tectorial membrane, which runs parallel to the basilar membrane. When the basilar membrane vibrates, there is a shearing force on the hair cells which leads to either a depolarization or hyperpolarization depending on whether there is upward or downward force on the hair cells. The shearing force transduces the mechanical change into an electrical change. This is sensed by the inner hair cells which lead to depolarization of the afferent fibers, and the sensation of hearing. However, the inner hair cells lead to miniscule movements of the basilar membrane and by themselves cannot account for the sensitivity of human hearing. This is where the outer hair cells, sometimes called *the cochlear amplifier*, come into play.

The outer hair cells also reach up and touch the tectorial membrane and with their ability to change shape can amplify the movement of the basilar membrane over 100 times. The motor protein in the outer hair cells that changes shape in response to the efferent input is *prestin*. Aspirin (salicylate) interferes with the outer hair cell motility.

If you are at a cocktail party, your ability to tune out the background noise and hear the person next to you is also thought to be due to the outer hair cells and their ability to change shape and hyperpolarize. As we age, the outer hair cells lose their ability to respond, and hearing is reduced causing a deficit in conversational hearing. Older individuals often have a hard time hearing softer voices. They do not have a deficit hearing loud sounds.

Weber's and Rinne's Tests

In a patient with hearing loss, you want to determine if there is a conduction deficit or a sensorineuronal deficit. The conducting portion involves the external and middle ear (malleus, incus, and stapes), while the sensorineuronal portion involves the vibrations of the basilar membrane and the subsequent action potentials in the cochlear nerve. If you tap on your mastoid process, the sound you hear is coming through the bone.

In **Weber's test**, the clinician holds a tuning fork to the center of the forehead. With no deficit the sound will be heard on both sides equally, there is no localization to one side or the other. If there is a conduction deficit, then the sound will localize to the side with the deficit. You can demonstrate this on yourself by putting your finger on your right tragus and humming. You have just given yourself a conduction deficit, and the sound will localize to the right ear. The reasoning for why the sound localizes to the ear with the deficit is controversial and people debate the mechanism, but mechanism aside the sound will localize to the ear with the conduction deficit, say wax in the ear for instance (Table 4.2).

However, Weber's is not definitive, because sound localizing to the right could also be due to a sensorineuronal loss on the left.

This is where **Rinne's test** comes in. In Rinne's test the clinician starts by holding a vibrating tuning fork just outside the ear and asks the patient to signal when they cannot hear the vibrations. The clinician then touches the fork to the mastoid process. In a healthy person, air conduction *should last longer than bone conduction (typically twice as long). This is referred to as a positive Rinne's test.* If bone conduction is stronger, then this suggests that there is a conduction deficit on that side—a negative Rinne's test. However, this is where it gets confusing; with Rinne's test, if there is a sensorineuronal deficit, both air conduction and bone conduction will be decreased, with the net result being that air conduction is still superior to bone conduction. Note that this is the same scenario as the healthy nerve. The reason for air conduction still being greater than bone conduction with a sensorineuronal deficit is that both are reduced on the damaged side. This is the shortcoming of the test and is why for more accurate determination you would want to conduct audiometry testing.

Table 4.2 Tuning fork interpretation

Test	Normal	Conductive deafness	Sensorineuronal deafness
Rinne	AC > BC	BC > AC	AC > BC
Weber	Not lateralized	Lateralized to the weaker ear	Lateralized to the functioning ear

Examples of a Conduction Deficit

In otosclerosis, the stapes develops a bony outgrowth which inhibits the proper movement of the oval window leading to a reduction in movement of the perilymph and basilar membrane.

Cholesteatoma is an uncontrolled growth of the squamous epithelium in the middle ear which engulfs and eventually destroys the ossicles. Both otosclerosis and cholesteatoma lead to conduction deficits.

Audiometry and Audiograms

An audiogram is a representation of an individual's hearing ability. On the x-axis, running from top to bottom, we see loudness measured in decibels going from 0 to 120 db. Running on the x-axis from left to right is pitch going from low to high sounds measured in Hertz—think of a piano keyboard with the high notes on the right and low notes on the left. For each frequency, there is a point representing the decibels the person can hear. Hearing will be represented as two lines, one for each ear. The person can hear *everything below the line.* The picture below shows air conduction only. Bone conduction is not shown. The left ear is represented as either an "X" or blue line, while the right ear is either an "O" or a red line. Normal hearing falls into the 0–20 decibels for each frequency. Mild hearing loss will be between 20 and 40 decibels. Profound hearing loss will be between 90 and 120 decibels (Fig. 4.6).

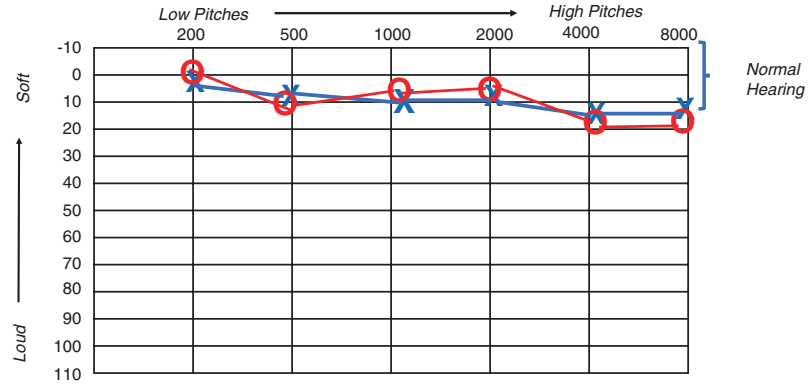

Fig. 4.6 Audiogram showing just air conduction in a healthy individual. Note that this person can hear everything below the line. Red O's are right ear. Blue X's are left ear. Note this is not a real audiogram but is just an example for showing concepts. (Leo 2021)

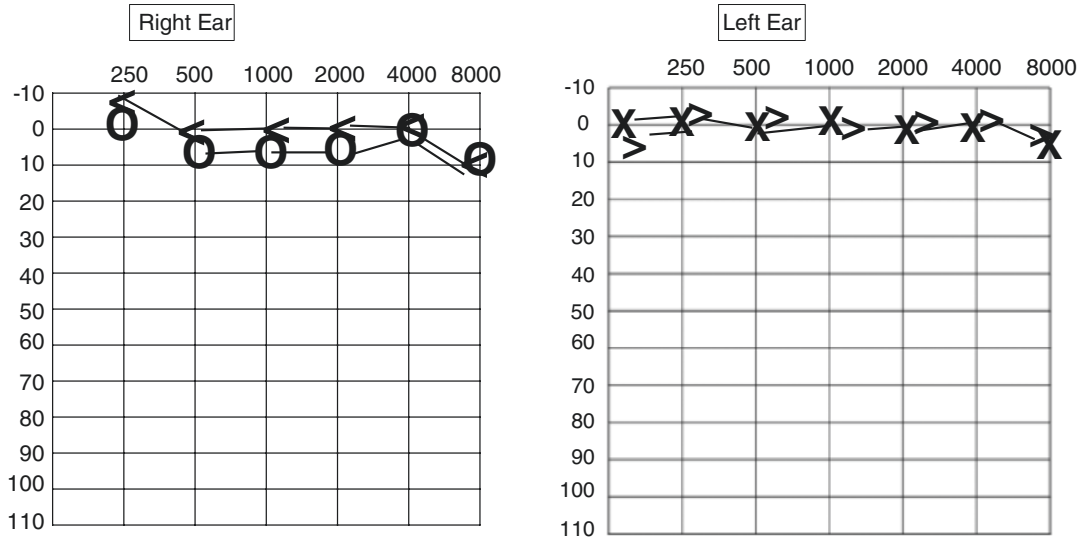

Fig. 4.7 Audiogram showing no hearing deficit in either ear. Bone conduction and air conduction are similar for both ears. O and X represent air conduction. < and > represent bone conduction. Note this is not a real audiogram but is just an example for showing concepts. (Leo 2021)

The next figure (Fig. 4.7) separates out each ear into its own audiogram and shows bone conduction as either an < or > symbol (greater than or less than). When you look at an audiogram of a healthy individual, you see that both bone conduction and air conduction will be roughly at the same location.

With a conduction deficit, air conduction will be reduced, but bone conduction will be normal, so the gap between the two will be greater. In the picture below, note the separation between air conduction and bone conduction on the right ear (Fig. 4.8).

With a sensorineuronal deficit, both air and bone conduction will be reduced on the audiogram, meaning that there is no gap between the air conduction line and the bone conduction line. In Fig. 4.9 note that both air and bone conduction are reduced in equal amounts on the left.

Auditory-Central Portion

The auditory portion of cranial nerve eight comes into the pons and projects to both the ventral and dorsal cochlear nuclei (Fig. 4.10). From the

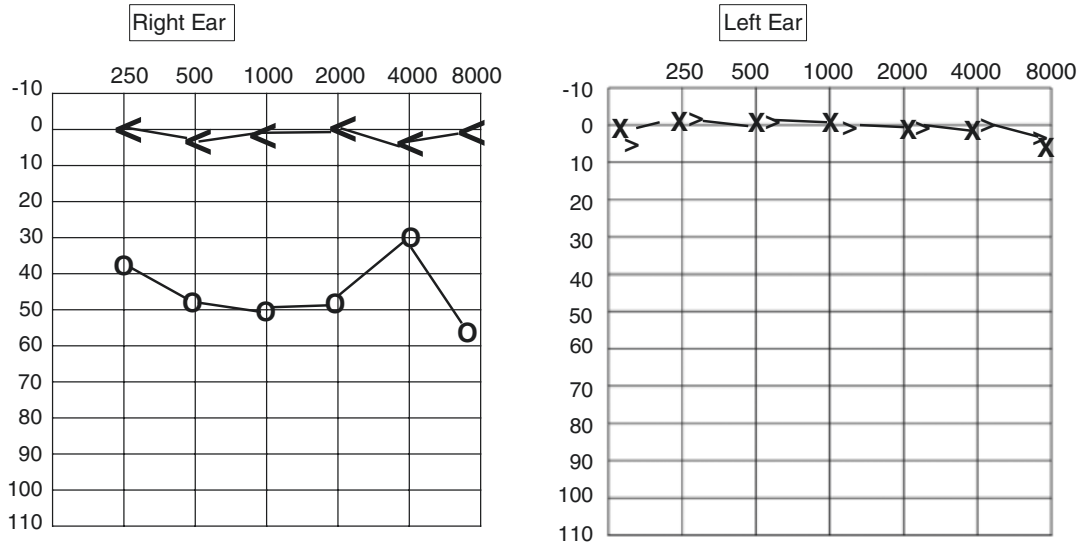

Fig. 4.8 Audiogram. In the right ear, bone conduction is greater than air conduction indicating a conductive hearing loss. There is no deficit in the left ear. Note this is not a real audiogram but is just an example for showing concepts. (Leo 2021)

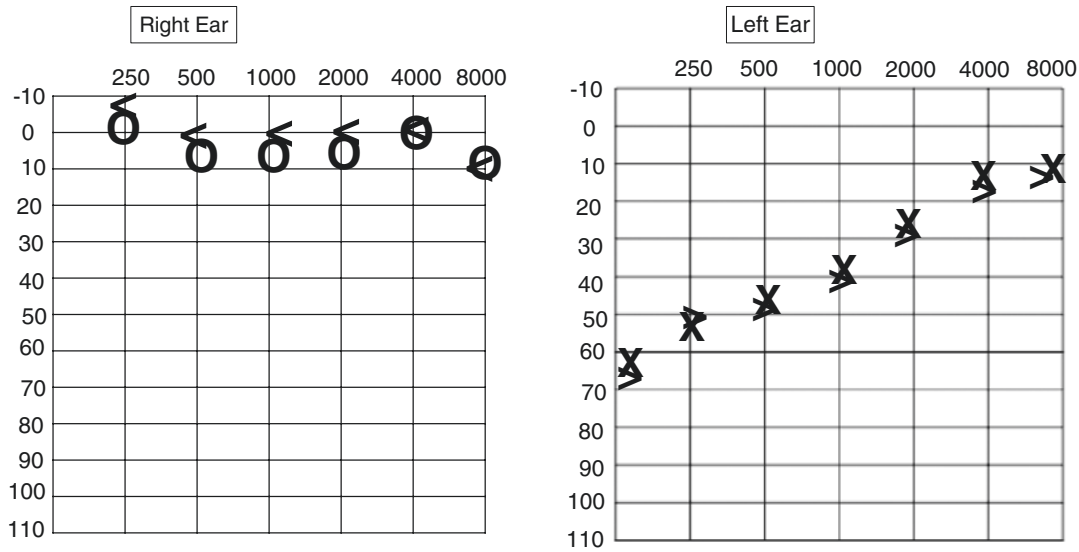

Fig. 4.9 Audiogram. Hearing in the right ear is normal for both bone and air conduction. In the left ear both bone and air conduction are diminished indicating a sensorineuronal deficit. Note this is not a real audiogram but is just an example for showing concepts. (Leo 2021)

cochlear nuclei, approximately 75% of the information projects to the contralateral side through the trapezoid body, while 25% ascends on the ipsilateral side. On both sides the information ascends in the lateral lemniscus to the inferior colliculus, and then to the medial geniculate body, which then projects to the auditory cortex. The auditory cortex, also known as Heschl's gyrus, sits atop the superior temporal gyrus. Because of the bilateral auditory projections, there are two ways to look at lesions here. One is that a lesion along this pathway will lead to bilateral effects—a bilateral diminution of hearing with the loss greatest on the contralateral side of the body—and, two, lesions here will only have minor deficits because the other side is essentially a backup.

Lesions along this pathway will lead to patients complaining that while they can hear, they have difficulty localizing where the sound is emanating from.

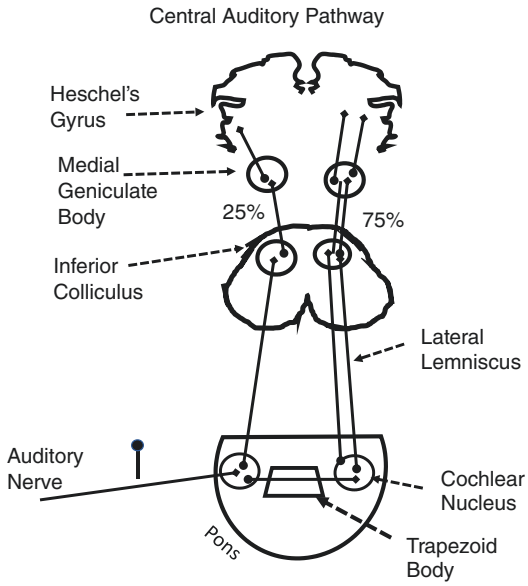

Fig. 4.10 Central Auditory Pathways. The information from the auditory nerve enters the CNS and 75% decussates to contralateral side and ascends, while 25% ascends on ipsilateral side. (Leo, 2021)

Lesions to the cochlear nerve or the cochlear nucleus will lead to complete 100% deafness from the ipsilateral ear.

An *acoustic neuroma* is a benign schwannoma of the eight cranial nerve typically between where the nerve exits the brainstem and where it enters the internal acoustic meatus. The clinical symptoms will usually start off with an auditory deficit followed by a vestibular deficit. As the tumor expands, it can also encroach on other cranial nerves such as the trigeminal and facial nerves. An important aspect to keep in mind is that when you are looking at the signs and symptoms of acoustic neuroma, it might be tempting to conclude that the lesion is in the CNS. But this lesion is in the PNS. The acoustic neuroma patient can have many symptoms, but if you look closely, you see that the deficits do not implicate the long tracts.

The *labyrinthian artery* is a branch of the basilar artery and perfuses the vestibulocochlear nerve. The facial nerve, the vestibulocochlear nerve, and the labyrinthian artery all travel together through the internal acoustic meatus. A sudden presentation of deafness and vertigo could be the result of a compromised labyrinthian artery.

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Visual Field Lesions

5

It is important not to confuse, on the one hand, how we refer to the retina and, on the other hand, how we refer to the visual fields. The nasal retina sees the temporal visual field; and vice versa, the temporal retina sees the nasal visual fields. If you are looking at the retina through the ophthalmoscope and observe pathology on the temporal retina, realize that the patient will have a nasal field defect.

Information from each nasal retina travels back along the optic nerve and decussates at the optic chiasm. Information from each temporal retina travels back along the optic nerve, but at the chiasm it does not cross over, and instead stays on the same side. From the optic tracts, the information goes to the lateral geniculate bodies where it synapses. From the LGB, the information then travels on the optic radiations to the occipital cortex. The fact that the nasal retina fibers decussate while the temporal retina fibers stay ipsilateral allows the right and left visual fields to stay separate and go to one side of the brain. The right visual field thus makes it to the left brain, while the left visual world makes it to the right brain.

It is common during your first course on neuroanatomy to discuss the various lesions by looking at shaded pictures of the visual field. The shaded area shows what the patient *cannot* see during visual field testing. But keep in mind that you need to test each eye individually so the other eye should be closed during the test. This is because of the overlap of the nasal fields, and that we see objects in the nasal fields with both eyes (Fig. 5.1).

Lesion #1 *Anopia*. This is a complete lesion to the optic nerve. This could be due to an occlusion of the ophthalmic artery which is the sole blood supply of the retina. This lesion would lead to complete blindness in this eye.

Lesion #2 *Bitemporal hemianopia*. This is a lesion to the optic chiasm most likely due to a pituitary tumor which damages the fibers from the nasal retinas of both eyes which see the temporal visual fields.

Lesion #3 *Nasal hemianopia*. This is a lesion to just the corner of the optic chiasm which could be due to an aneurysm of the internal carotid artery. This would block the information coming from the temporal retina which is nasal visual field of just one eye.

Lesion #4 *Left homonymous hemianopia*. This is a lesion to the right optic tract which will lead to a loss in the right nasal visual field and the left temporal visual field.

Lesion #5 *Left homonymous hemianopia.* This a lesion to the optic radiations which would lead to the same deficit as the lesion to the optic tract. However, there is a difference in the patient presentation. The patient with the lesion to the optic radiations will have an intact pupillary light reflex, while the patient with the optic tract lesion will have a disrupted light reflex.

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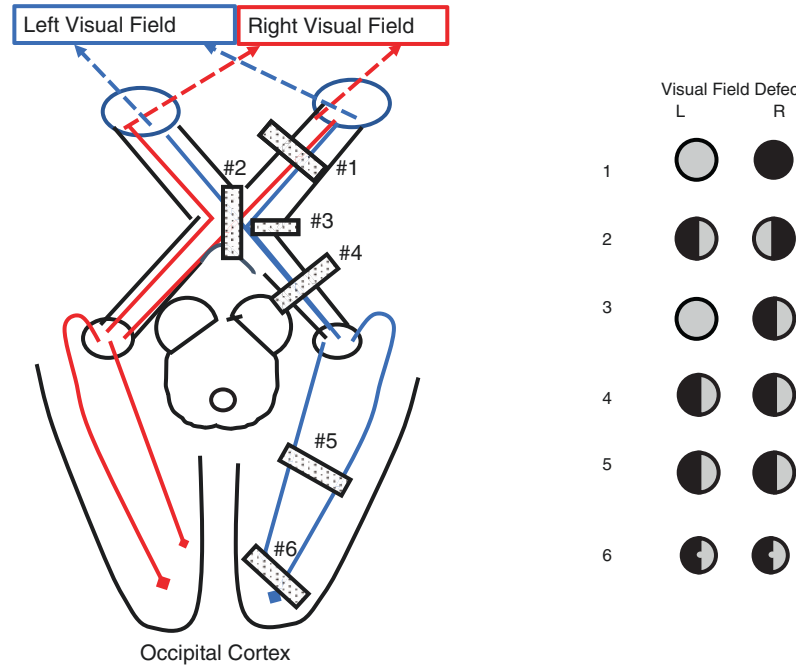


Fig. 5.1 Lesions and visual field deficits. (Leo 2021)

Lesion #6 *Left homonymous hemianopia with macular sparing*. This is a lesion to the occipital pole which will lead to contralateral homonymous hemianopsia; however, this patient will have macular sparing.

Some Advanced Visual Field Defects

Pie in the Sky and Pie on the Floor

Fibers leaving the lateral geniculate nucleus head for the occipital lobe, but there is a slightly different path for fibers from the superior retina versus inferior retina (Fig. 5.2). The fibers from the superior retina head straight back to the cuneate gyrus of the occipital lobe, while fibers from the inferior retina take a detour into the temporal lobe, forming a loop before heading to the lingual gyrus of the occipital lobe. The detour of these fibers is called *Meyer's loop*.

Lesions in the temporal lobe will often damage Meyer's loop resulting in a patient with "pie in the sky" or a superior quadrantanopia. This is because the fibers in Meyer's loop come from the inferior temporal retinas, which take in information from the superior fields of both eyes.

Lesions in the parietal lobe may lead to "pie on the floor" which is basically the opposite of the temporal lobe lesion. The patients will lose the fibers from the superior retinas, which take in information from the inferior fields.

Optic Chiasm Details

When you look at a midsagittal section of the optic chiasm, you will see that the fibers from the superior retina are located superiorly in the chiasm, while the fibers from the inferior retina are located inferiorly. But again, note that the fibers from the superior retina take in information from the inferior field, while the inferior fibers take in information from the superior field. In its initial stages, a craniopharyngioma will compress the superior surface of the chiasm which will lead to an inferior field defect. As the craniopharyngioma expands, it will eventually encompass the entire temporal field (Fig. 5.3).

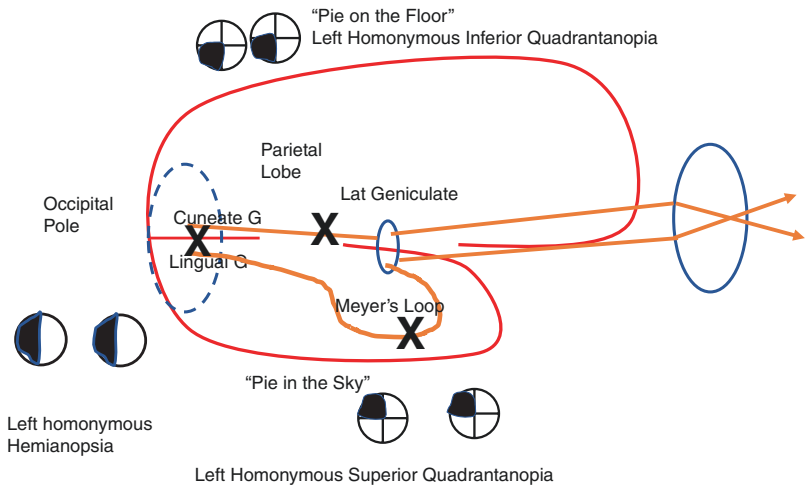


Fig. 5.2 Meyer's loop and "pie in the sky". (Leo 2021)

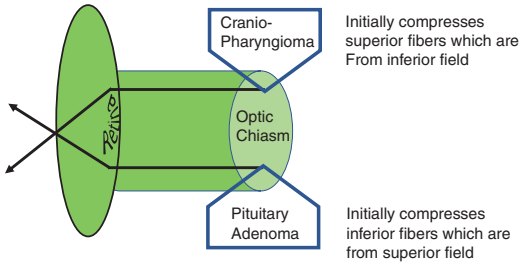


Fig. 5.3 Lesions to the optic chiasm. Craniopharyngioma compresses the superior chiasm which leads to inferior field defects. Pituitary adenomas compress the inferior chiasm which is superior field. (Leo 2021)

The opposite of this is a pituitary adenoma which is located inferior to the optic chiasm, and it will first impinge on the fibers from the inferior retina which is superior field.

Prechiasmal Versus Retrochiasmal Lesions

Lesions to the retina or optic nerve can lead to visual acuity deficits and loss of color vision in the ipsilateral eye, and an ipsilateral RAPD. With lesions past the optic chiasm, there will be no deficit in visual acuity or the ability to see colors (achromatopsia). Take the optic tract for instance. The optic tract receives information from both eyes, and thus both foveas. Therefore, a lesion to the optic tract will not completely block the information from either eye, as information from both foveas are represented in both optic tracts. A lesion to the optic tract will also lead to a contralateral RAPD, and contralateral bow-tie atrophy of the optic disc. These topics are discussed in more detail with the retina.

Cortical Blindness

Lesions to the occipital cortex can lead to cortical blindness, either unilateral or bilateral. In these patients, because cranial nerves two and three are intact, the light reflexes and eye movements are not affected. It can be permanent or temporary, and can result from a compromised posterior cerebral artery, preeclampsia, carbon monoxide poisoning, or the side effects of cyclosporine.

Swinging Flashlight Test

The swinging flashlight test involves starting with a patient in a semi-darkened room and then moving the penlight back and forth from one eye to the other. In a healthy individual, the light will cause each eye to constrict. As the examiner goes back and forth from one eye to the other, both eyes will constrict.

This procedure tests the integrity of cranial nerves two and three and the brainstem circuits

involved in constriction. When a light is shown to one eye, the information travels on the optic nerve, to the optic tract, and then prior to the LGB, the fibers peel off from the optic tract to project to the pretectal nucleus. The pretectal nucleus is located near the superior colliculus and posterior commissure. The two pretectal nuclei talk to each other via the posterior commissure which allows the pretectal nucleus fibers to send information bilaterally to both Edinger-Westphal nuclei and then from there to the constrictor pupillae muscles to constrict both eyes. The response of the eye that the light is shown to is referred to as the *direct response*, while the response in the opposite eye, which also constricts, is referred to as the *consensual response*.

Relative Afferent Pupillary Defect (RAPD) Also Called Marcus Gunn Pupil

A patient with a lesion to the retina or the optic nerve will have a relative afferent pupillary defect (RAPD) (Fig. 5.4). In a patient with a deficit in the optic nerve, for example, during the swinging flashlight test when you shine your penlight into the lesioned eye, it dilates. This is often referred to as a paradoxical dilation because you would expect the eye to constrict when you shine the light in the eye. The reasoning for this is shown in the picture below. The patient has a lesion to the right optic nerve. When the light is shown in the left eye, the pretectal nucleus is receiving 100% of the information from that eye. The fibers from the pretectal nucleus project to both eyes and lead to constriction. When the light moves to the right eye, which in this example has 50% of its fibers compromised, then the pretectal nucleus senses less light than a moment ago, so both eyes dilate—in other words when the light moves from the healthy eye to the pathological eye, the brain thinks the world got darker, so the eyes dilate.

Argyll Robertson Pupil

In a patient with an Argyll Robertson pupil, the pupil responds to accommodation but not the light reflex (Fig. 5.5).

The reasoning for this is as follows (Fig. 5.6). The light reflex does not use the occipital cortex. As mentioned above, instead these fibers peel off the tract to enter the pretectal nucleus. However, the pathway for accommodation does use the occipital lobe. When you test the accommodation reflex by moving your finger toward the person's nose, the signal is traveling down the optic tract and optic radiations and going to the occipital cortex. The patient consciously sees your finger moving toward their nose with their occipital cortex. From the cortex the pathway then projects to the Edinger-Westphal nucleus bypassing the pretectal region and posterior commissure. The lesion involved in Argyll Robertson pupil is at the

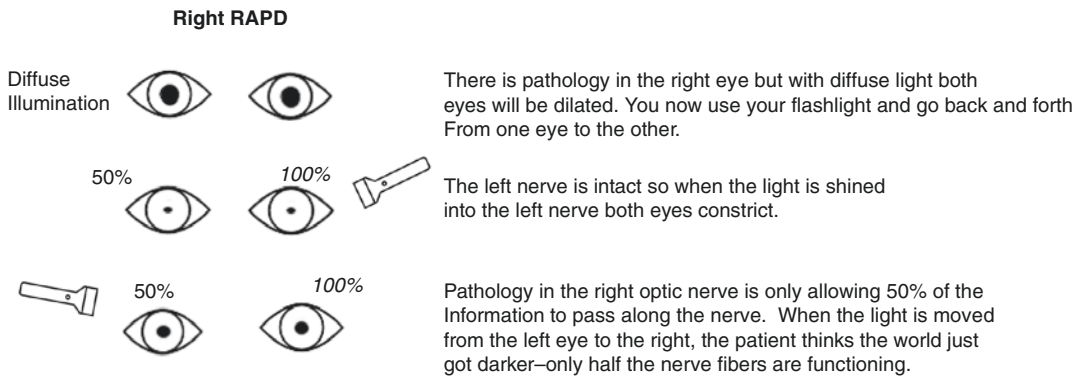


Fig. 5.4 Relative afferent pupillary defect (RAPD). There is a defect in right optic nerve affecting 50% of the fibers. Light in the left eye leads to constriction. Light in the right eye leads to a bilateral dilation. (Leo 2021)

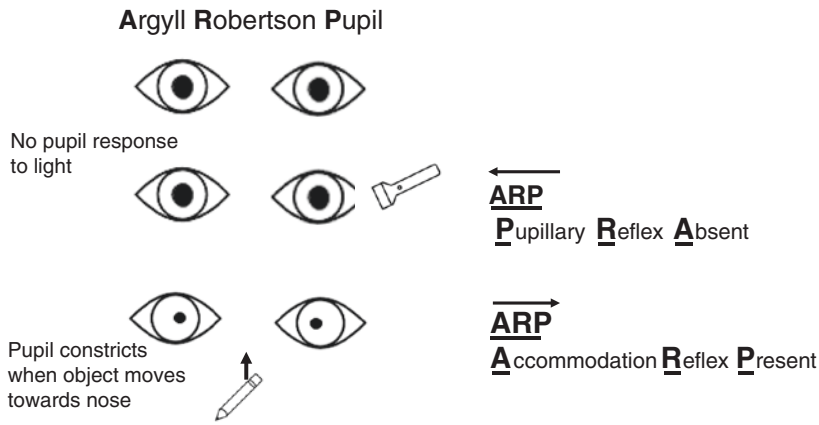


Fig. 5.5 Argyll Robertson pupil. When light is shined in eye, there is no pupillary response. When object moves towards the nose there is pupillary constriction (both eyes also move medially, and lenses thicken). (Leo 2021)

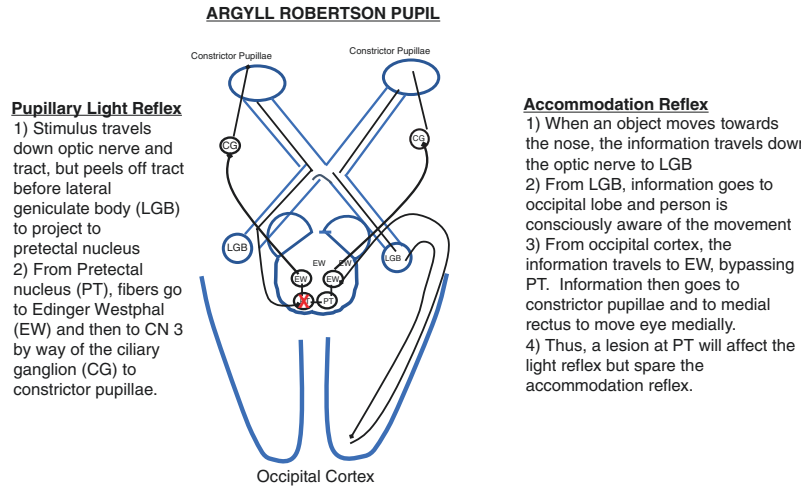


Fig. 5.6 Comparison of the light and the accommodation flexes. (Leo 2021)

posterior commissure which disrupts the light reflex pathway but not the accommodation pathway. Argyll Robertson is often the result of untreated or late-stage syphilis.

Adie's Pupil

Adie's pupil is a tonic dilated pupil that is the result of damage to the ciliary ganglion or the postganglionic fibers on the short ciliary nerves traveling to the constrictor pupillae muscle (think the opposite of Horner's). The etiology is unclear, but it is thought to be either an autoimmune disease or the result of an infection. It is more common in women than men. It is typically seen in one eye; however, it can progress to the other eye. While initially the eye is affected, Adie's often goes along with excessive sweating and the absence of the knee-jerk reflex.

Pilocarpine is a cholinergic agonist that if strong enough will lead to constriction of the pupil. A dilute solution of pilocarpine (0.1%) is normally not strong enough to constrict the pupil—except in the patient with Adie's pupil. The reason for this is that in the Adie's pupil, over time there is a compensatory upregulation of muscarinic cholinergic receptors in the constrictor pupillae. With this increased number of receptors, when the affected eye is presented with the dilute solution, it is now able to constrict. In the patient's normal eye, there will be no response to the dilute solution of pilocarpine. This is referred to as *denervation supersensitivity*.

The Retina

At first glance there are several facets of the neuronal organization of the retina that seem counterintuitive. The neuronal portion of the retina has a receptor layer (rods and cones), a relay (bipolar cells), and finally an output layer (ganglion cells). If a human engineer designed the eye, they would most likely have the receptor, the relay, and the output all in a straight line, with the receptor layer directly facing the light source, but evolution has led to a different design (Fig. 5.7). The receptor layer of rods and cones is in the deepest layer, the bipolar cells are in the middle, and the ganglion cells are the most superficial layer. Thus, the light coming in through the lens passes the first two layers before hitting the rods and cones—this organization is referred to as the inverted retina. At first glance it seems odd, but this allows the retinal pigmented epithelial (RPE) layer to be situated behind the rods and cones to catch the back spatter of light but not block the incoming light rays. The pigmented layer supplies a steady source of nutrients such as vitamin A to the neuronal layer, and it also absorbs the waste products generated by the constant runover of the rods and cones. If the retina did not have this inverted arrangement, and the RPE layer was the first layer, then it would be like putting window blinds up between the light source and the sensors.

The impulse starts with graded potentials, not action potentials, in the rods and cones, which then stimulate the bipolar cells, which in turn trigger action potentials in the ganglion cells of the retina. Thus, the light rays and action potentials are going in opposite directions with light coming into the retina, and nerve stimuli going out.

The cones which are responsible for visual acuity are located in the fovea, which is the center of the macula. The rods are located on the periphery and sense low levels of light. If you are outside on a clear night, you can sometimes see a star when you look off to the side, but not when you look directly at it. This is because when you look directly at the light, you are lining up your cones which are not sensitive to low light. Whereas when you look off to the side, you are able to sense the low light with your rods.

The fovea is also the thinnest part of the retina. At the fovea, the nerve fiber layers are pushed off to the side, resembling something like a crater, with the cones in the central part of the fovea

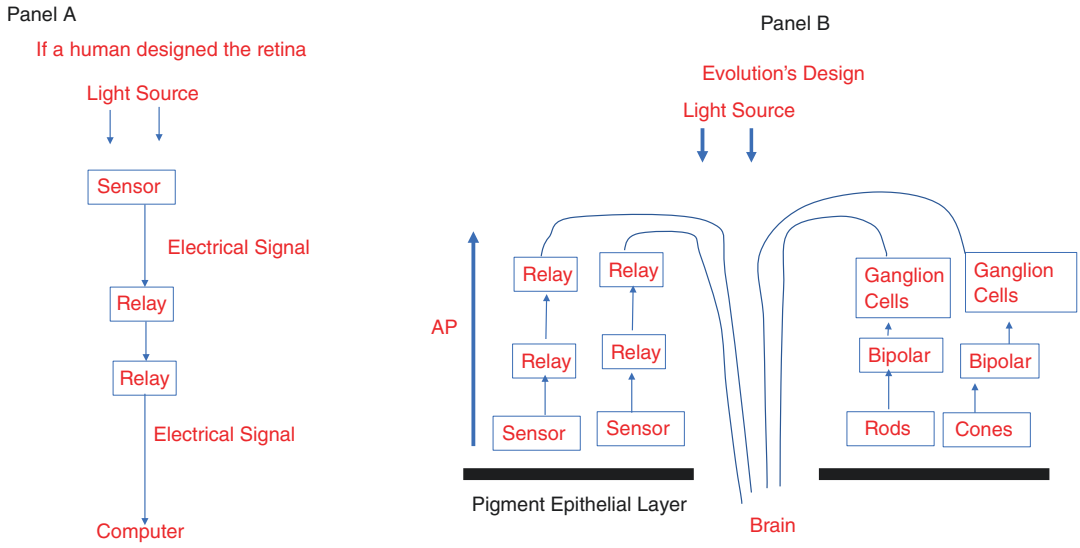


Fig. 5.7 Panel (**a**) is how a human engineer would probably design the retina with the primary sensors in the front of the retina. Panel (**b**) is evolution's design with primary sensors at the back of the retina. (Leo 2021)

referred to as the fovea pit. The cones in this area are not covered by the other nerve fiber layers. As the fibers are pushed off to the side, they are referred to as the fovea slope. At the top of the fovea slope is the fovea rim (the top of the crater) which are the pushed aside fibers.

Another counterintuitive aspect of the retina concerns when the rods and cones are depolarized or hyperpolarized. At first glance, it would make sense that when you "see" something that this results in a depolarization event, like when you touch something, there is a depolarization event. However, this is not the case. When you are in the dark, the graded potentials in the rods and cones are depolarized, and they release glutamate. Conversely, when the lights are turned on and you "see" something, the rods and cones are hyperpolarized, and less glutamate is released. The bipolar cells are subdivided into "on" and "off" subgroups, which in turn either depolarize or hyperpolarize in response to a depolarized rod or cone.

Retinal Fiber Organization

The fibers coming out of the ganglion cells all head toward the optic nerve (optic disc) and in turn project to the lateral geniculate body. Normally the optic disc is indented slightly. If we look closely at the optic nerve head, there are four quadrants—four pieces of the pie—and this is clinically significant. Fibers from the temporal retina project to the superior and inferior quadrants. Fibers from the macula project from the fovea toward the lateral quadrant. We call these fibers the *papillomacular bundle*. Fibers from the nasal retina head toward the medial quadrant. This has important clinical implications. Keep in mind that temporal fibers are responsible for the nasal field and vice versa.

Papilledema refers to swelling of the optic nerve. At the optic disc, all the fibers coming from the ganglion cells converge on the optic disc to form the optic nerve and travel toward the lateral geniculate nucleus. Normally the optic disc is indented slightly. Increased intracranial pressure from either a tumor, infection, abscess, bleeding, meningitis, or encephalitis will lead to pressure on the optic nerve leading to a swollen, or choked, look, to the optic disc. Some patients report hearing a "swooshing" sound or machinery-like sound when lying down. It is thought that this results from compression of the dural venous sinuses and subsequent disruption in flow. One test to confirm papilledema is a lumbar puncture to determine CSF pressure.

Bow-Tie Atrophy

Wallerian degeneration occurs when a nerve is lesioned and the distal portion of the nerve degenerates. Lesions of the optic nerve, chiasm, or tract will lead to Wallerian degeneration of the ganglion cell fibers which can be followed back to the optic disc. Following a lesion to the optic tract, there will be a pattern of nerve cell degeneration at the disc that leads to a specific pattern of loss that looks like a bow tie, which can be visible on fundoscopic exam.

Let's walk through the logic of "bow-tie atrophy." A lesion to the middle of the chiasm damages fibers going to the nasal half of the eye, while the temporal retinal fibers are unaffected. This will lead to atrophy of the fibers coming into the medial and lateral quadrants of each optic disc; it will spare the superior and inferior quadrants (Fig. 5.8).

Lesions to the optic tract will also lead to bow-tie atrophy but only on the contralateral side. The logic is as follows: (1) a lesion to the right optic tract will damage fibers coming from the left nasal retina, whose fibers in turn are going to the lateral and medial quadrants of the optic nerve.

Optic Tract Pathology

Lesions to either the optic tract or the optic radiations can lead to a contralateral homonymous hemianopsia. To determine if the lesion is in the nerve or the tract, we have to look at other signs. Besides the visual field defect, optic tract lesions will also lead to a contralateral RAPD and a contralateral bow-tie atrophy.

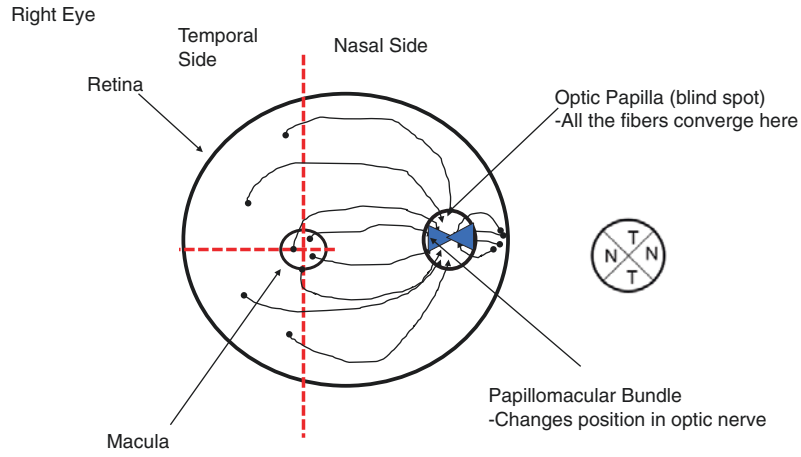


Fig. 5.8 Representation of nerve fibers travelling to optic tract. Temporal fibers come into superior and inferior quadrants, papillomacular fibers to the lateral quadrant, nasal fibers to medial quadrant. (Leo 2021)

The contralateral RAPD occurs because at the chiasm, it is not a 50/50 crossover of fibers. When the optic nerves meet at the chiasm, 60% of the fibers will cross and 40% will stay on ipsilateral side. Thus, in either one of the optic tracts, more of the fibers are from the contralateral eye, so a lesion at the tract leads to a greater loss on the contralateral side, which leads to the contralateral RAPD. A lesion to the optic radiations will not have any effect on the pupillary light reflex.

Central Scotoma

In some conditions, such as multiple sclerosis, hypertension, methanol poisoning, nutritional deficiencies, etc., patients will lose just one small piece in the central part of the visual field—a central scotoma. These patients would have a bilateral central scotoma. If the central scotoma is only on one side, you would suspect a more localized issue such as a vascular insult.

The reason for the scotoma is that the central part of the visual field is the fovea in the macula. The fibers coming out of the macula are the most metabolically active in the retina and are the most susceptible to insult. In addition, these fibers converge on the lateral quadrant of the optic disc, and then move into the optic nerve and head toward the chiasm. As the fibers move along the optic nerve, they assume a position in the center of the optic nerve.

Retinal Detachment

As the light enters the eye and moves toward the rods and cones, the pigmented epithelial layer catches the back spatter of light. But this layer also nourishes and maintains the rods and cones by providing nutrients and removing waste products. For instance, the RPE supplies a constant source of vitamin A, a precursor of rhodopsin, to the rods and cones. This pigmented epithelial layer has a layer of cilia that projects to the rods and cones so that these substances can be shuttled back and forth across the membrane. As we age, the cilia can tear, and the rods and cones will pull away from this layer—retinal detachment. The patient often reports that their vision resembles a room with the shaded being pulled down.

Surrounding the retina is the **choroid**, a spongelike structure which has the highest blood flow in the body. The retina is one of the most metabolically active parts of the body; thus, it produces a significant amount of heat. The choroid is essentially a heat exchanger and allows the heat from the retina to dissipate into the bloodstream. As we all know, staring into the sun can burn the retina, but interestingly it is more likely to do this in a cadaver, because of the loss of the heat exchanger. Choroidal detachment is when the choroid becomes detached from the retina either from a buildup of blood or serous fluid. Serous fluid detachments can occur in cancer patients, as a side effect from certain medica-

tions, or following eye surgery. The patient reports an uncomfortable feeling but not severe pain. Hemorrhagic detachment on the other hand is extremely painful. It can also occur following eye surgery particularly in patients taking blood thinners.

Blood Supply to the Retina

The blood supply to the retina comes from two sources, both of which are branches of the ophthalmic artery, which in turn is a branch of the internal carotid. The first branch is the central artery of the retina which pierces the optic nerve, travels down the nerve, and emerges onto the retina at the optic disc. From here the artery branches out into superior and inferior divisions, and then temporal and nasal divisions, all of which perfuse the inner half of the retina. The second source of blood to the retina comes from a set of 3–5 posterior ciliary arteries which travel on the periphery of the nerve and perfuse the outer half of the choroid and outer half of the retina. You can think of this second set as really arteries to the choroid which in turn supply blood to the outer half of the retina.

Occlusion to the central artery of the retina will lead to a *cherry red spot* on a fundoscopic exam. It is often caused by an embolus in a hypertensive patient breaking loose from the heart or carotid artery. It is essentially a stroke in the eye. In the early stages, on a fundoscopic exam, you might see segmentation or "box-caring" (the segmentation of the blood looks like train cars) of the blood in the branches of the central artery. Most of the retina will have a pale look to it since it has lost its blood supply to the inner portion. However, at the fovea there is a red spot because the nerve fiber layer is so thin here that you can see the underlying blood supply from the posterior ciliary arteries (choroidal arteries). Diabetic retinopathy refers to the fact that in diabetics, the blood vessels of the eye become distorted and then multiply which can lead to leakage of fluid into the retina.

Optic neuritis is an inflammation of the optic nerve. It can be either to the intrabulbar part of the nerve, *papillitis*, or proximal to the bulb, *retrobulbar neuritis*. The most common cause of optic neuritis is multiple sclerosis. MS leads to inflammation and damage to the myelin sheath of the optic nerve.

Both open-angle and closed-angle glaucoma result from increased pressure in the anterior chamber of the eye. Aqueous humor is produced by the ciliary body in the posterior chamber of the eye and then percolates around the iris to the anterior chamber where it drains via both the trabecular meshwork into the canal of Schlemm and the uveoscleral drainage system. In open-angle glaucoma, there is no change in the angle between the iris and the cornea—it stays open—but the trabecular meshwork is blocked. This leads to a slow buildup of pressure. It is painless and the visual field loss is slow, so by the time the patient presents with noticeable symptoms, the disease process is significant. There is no cure, which makes early detection important. Once a diagnosis is made, preventive measures to slow the progress can be implemented. Initial treatment usually involves hypotensive drops to reduce the pressure. A trabeculotomy can be performed to open up the trabecular meshwork by creating a new opening between the anterior chamber and the subconjunctival space.

Closed-angle glaucoma is a sudden painful presentation that typically results in a visit to the emergency room. In closed-angle glaucoma, there is a change to the shape of the iris such that it sags and closes off the angle so that both the canal of Schlemm and the uveoscleral opening are blocked. Without treatment, the retina is at risk, and permanent vision loss is a possibility. The most common treatment for closed-angle glaucoma is a trabeculectomy which involves removing a piece of the trabecular mesh.

Goldmann Visual Fields

When you first took neuroanatomy, you most likely worked through visual field defects with the type of pictures that I used in the examples above. In those pictures the visual field defects

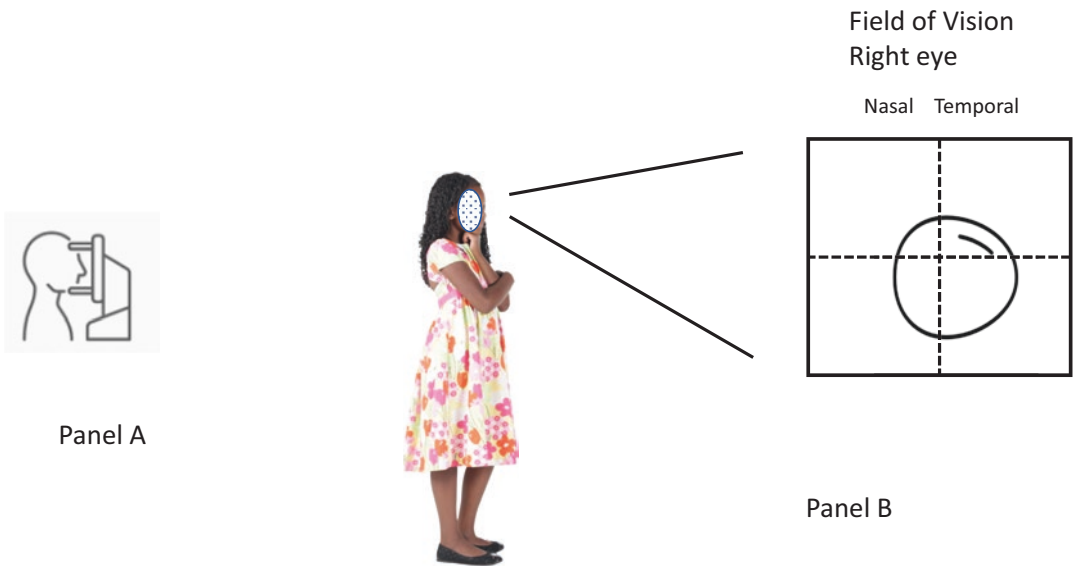


Fig. 5.9 Panel (**a**) shows the patient being tested in the perimetry bowl. Panel (**b**) depicts the visual field of the standing woman. Note that inferior field covers more area than the superior field. And the temporal field covers more area than the nasal field (Leo 2021)

are represented by the shaded portion. Goldmann visual field defects represent the visual fields from a different point of view. Rather than show what the patient can't see, they show what the patient can see. A Goldmann field is generated by perimetry bowl testing, which involves the patient's chin resting on brace and looking forward into a bowl-shaped structure.

With their head stationary, they are then shown various small lights in the periphery of the bowl. When they see a light, they respond by clicking a button. This generates a line (isopter) representing the perimeter of the patient's visual field. As we get older, our visual field gets smaller. When you look at a picture of the Goldmann field, such as the one below, note that it is from the patient's point of view (Fig. 5.9).

In the fundoscopic view, on the other hand, you are looking into the patient's eye, toward their brain. A couple of things stand out when looking at a normal Goldmann field: (1) our inferior fields cover more territory than our superior visual fields, (2) our temporal fields encompass more territory than our nasal fields, and (3) the physiological blind spot is located temporally. Remember the nasal retina sees the temporal field. The picture below (Fig. 5.10) shows the Goldmann fields of both eyes.

Again, you want to be able to differentiate from the view of the fundoscopic exam (Fig. 5.11) when you are looking inward toward the patient's eye, versus the Goldmann field depiction which is from the patient's point of view looking outward (Fig. 5.12).

Be prepared on a board exam for either of the pictures shown below. They both represent a pituitary tumor and a subsequent bitemporal hemianopia. The picture on the right has the visual field deficits blacked out showing what the patient *cannot see*. The picture on the left shows what the patient *can see* as depicted by a Goldmann field test, and the picture on the right shows the visual field defects, what the patient cannot see.

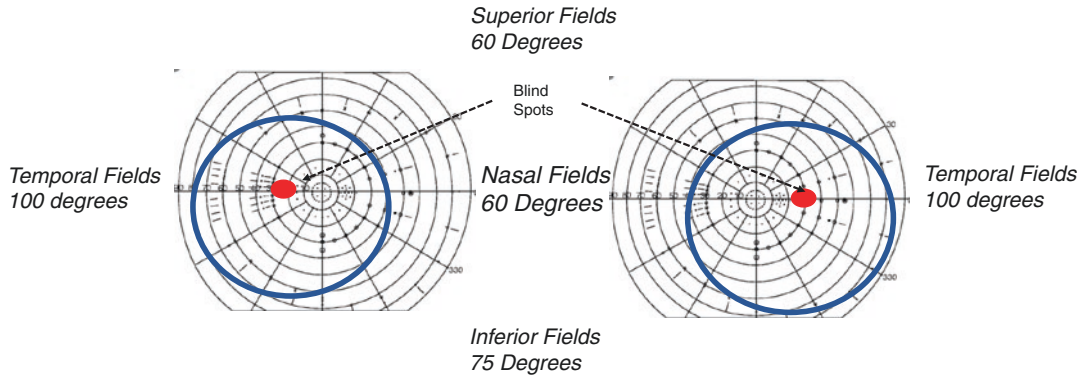
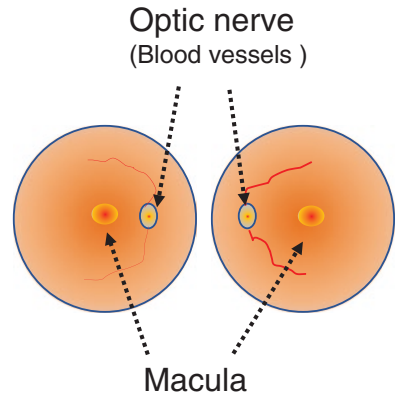


Fig. 5.10 Goldmann Visual fields of healthy individual for each eye. Note this is not drawn exactly to scale and is strictly for teaching purposes. The optic discs are in the nasal half of each retina, which equates to physiological blind spots in the temporal fields.

Fig. 5.11 Fundoscopic exam. Note the optic nerve is located medially which translates into the blind spot being in the temporal field



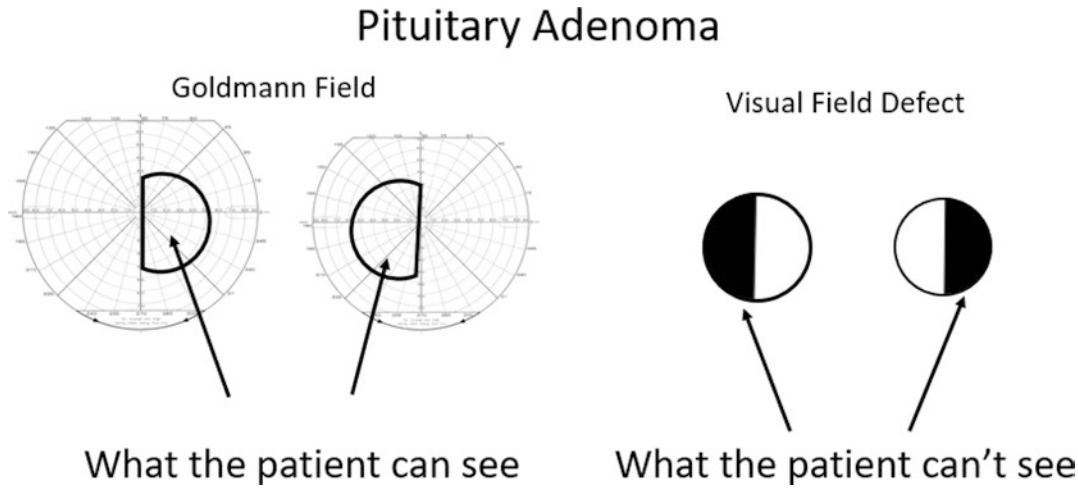


Fig. 5.12 Comparison of Goldmann Field representation and visual field defect representation in the same patient. (Leo 2021)

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Autonomics and Lesions

6

The first thing is to clarify the difference between autonomic ganglia and sensory ganglia (Fig. 6.1).

Looking at the picture, we have divided the CNS from the PNS with the pia mater. All the efferent motor neurons have their cell bodies of origin in the CNS. If we are talking about the cord, then the fibers come from the ventral horn. If we are talking about the brainstem, then the fibers come from cranial nerve nuclei. Somatosensory fibers on the other hand have their cell bodies in the periphery, either in the DRG or their respective cranial nerve nuclei such as trigeminal or geniculate. These ganglia have a cell body *but no synapse*.

The Parasympathetics to the Head

When we discuss the parasympathetics, we need to differentiate preganglionic from postganglionic. The preganglionic fibers going out on cranial nerves come out of nuclei in the brainstem and travel on to synapse at peripherally located autonomic ganglia which will have a *cell body and a synapse*. These parasympathetic preganglionic fibers are cholinergic and synapse on nicotinic cholinergic receptors on the postganglionic cells. The postganglionic fibers which are also cholinergic will then travel to the target, whether it's a gland or smooth muscle, and synapse on a muscarinic receptor.

You need to remember this list forever: cranial nerves three, seven, nine, and ten. These are the four cranial nerves with parasympathetic fibers (Fig. 6.2). Note that cranial nerve five is not on our list of nerves that have parasympathetics; however, while no parasympathetics originate on cranial nerve five, three of the nerves with parasympathetics, three, seven, and nine, all take advantage of cranial nerve five and hitch a ride on cranial nerve five to get to their targets. A helpful mnemonic for remembering the parasympathetics is SLUDD, which stands for **s**alvation, **l**acrimation, **u**rination, **d**igestion, and **d**efecation. For the head it is the **s**alvation and **l**acrimation portion of the mnemonic that is important. Acetylcholine released from the presynaptic neurons binds to nicotinic receptors on the postganglionic neurons. The postganglionic neurons in turn bind to muscarinic receptors on either a gland or smooth muscle. Acetylcholine is then broken down by acetylcholinesterase. Direct-acting cholinergic agonists mimic the effect of acetylcholine. Indirect-acting agonists inhibit the acetylcholinesterase, thus producing cholinergic effects.

Drug effects of cholinergic agents can lead to cholinergic toxicity. Another useful mnemonic and a variation on SLUDD is SLUDGE, standing for **s**alvation, **l**acrimation, **u**rinary incontinence, **d**iarrhea, **g**astrointestinal upset, and **e**mesis. In terms of the head, the picture below shows the salvation and lacrimation effects of parasympathetics.

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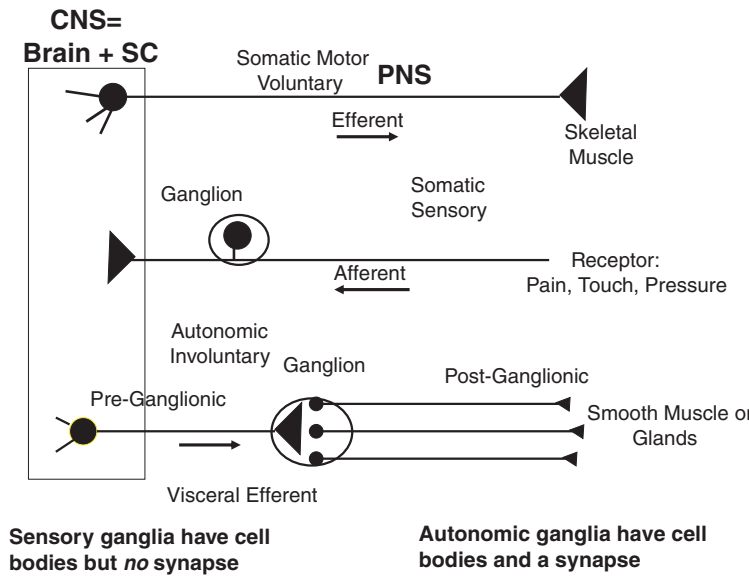


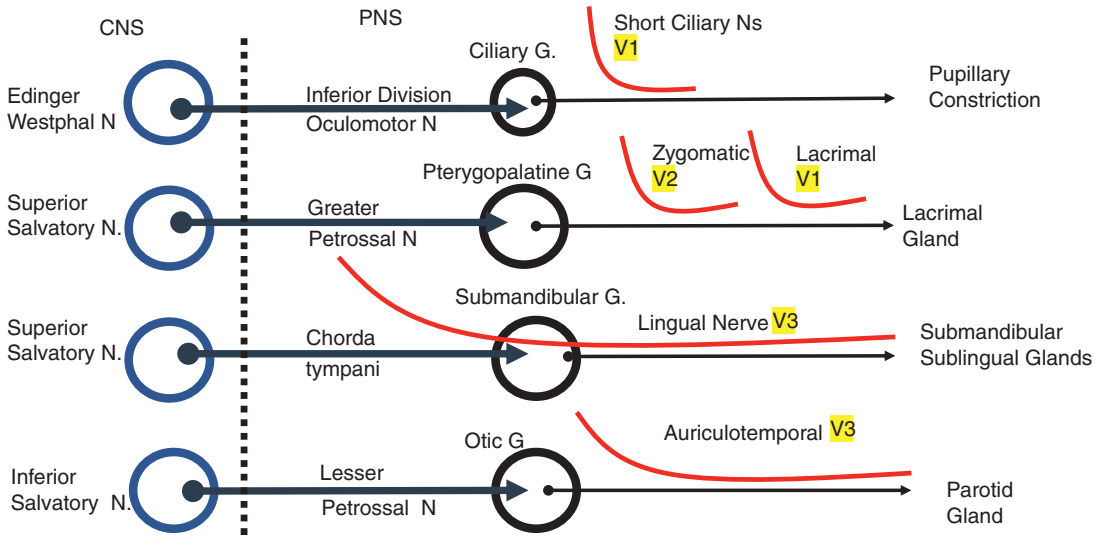


Fig. 6.2 Cranial nerve parasympathetic pathways. Fibers from CNs 3, 7, and 9 hitch a ride on CN 5. (Leo 2021)

Cranial Nerve Three

Cranial nerve three's parasympathetic fibers come out of the Edinger-Westphal nucleus in the midbrain, travel through the midbrain, and then exit the brainstem at the interpeduncular fossa to eventually reach the orbit. In the orbit the parasympathetics travel on the inferior division of the oculomotor on their way to the ciliary ganglion. After synapsing at the ciliary ganglion, the fibers travel on the short ciliary nerves to the eye.

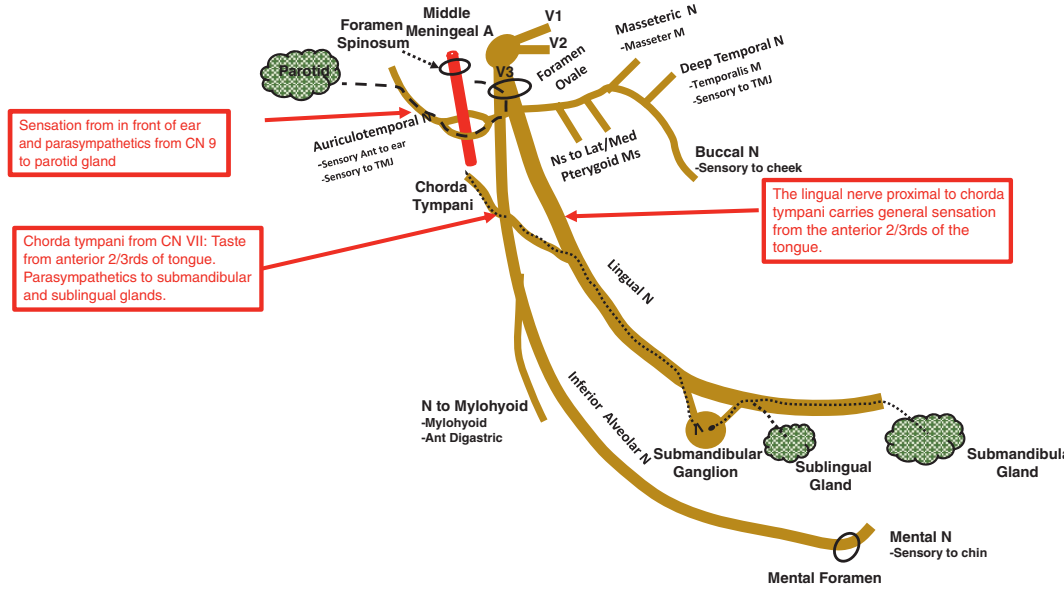


Fig. 6.3 Chorda tympani. Preganglionic fibers (dashed line) from cranial nerve seven part of the chorda tympani and jump on the lingual nerve which is a branch of V3. In the floor of the mouth, the preganglionic fibers peel off to synapse in the submandibular ganglion. Postganglionics then travel to the submandibular and sublingual glands. Note the auriculotemporal nerve splitting to go around the middle meningeal artery. (Leo 2021)

Cranial Nerve Seven

Cranial nerve seven has two parasympathetic branches. The first is the greater petrosal nerve that projects to the pterygopalatine ganglion in the pterygopalatine fossa. The postganglionics then jump onto the zygomatic temporal branch of the infraorbital nerve, which is a branch of V2, and then jump again onto the lacrimal nerve which is a branch of V1 to make their way to the lacrimal gland. The other group of parasympathetics of CN 7 leave in the chorda tympani, travel through the middle ear between the incus and malleus, exit the skull through the petrotympanic fissure where they enter the infratemporal fossa to join the lingual nerve, and project to the submandibular ganglion. The postganglionics then project to the submandibular and sublingual glands. Keep in mind that the lingual nerve is a branch of V3 and carries temperature, pain, and touch sensations back along the trigeminal nerve (Fig. 6.3).

Cranial Nerve Nine

Cranial nerve nine's preganglionic fibers originate in the inferior salivatory nucleus, contribute to the tympanic plexus, then emerge as the lesser petrosal nerve and travel along the base of the skull, exit the skull through the foramen ovale, and project to the otic ganglion (Fig. 6.4). From the otic ganglion, the postganglionic fibers jump on the auriculotemporal nerve, a branch of V3, and hitch a ride to the parotid gland.

Crocodile Tears

All these parasympathetic fibers are delicate fine fibers that can be easily torn in traumatic injuries, such as a car accident. They will eventually regrow; however, during this process they can get confused and become incorrectly wired, leading to alterations in the appropriate para-

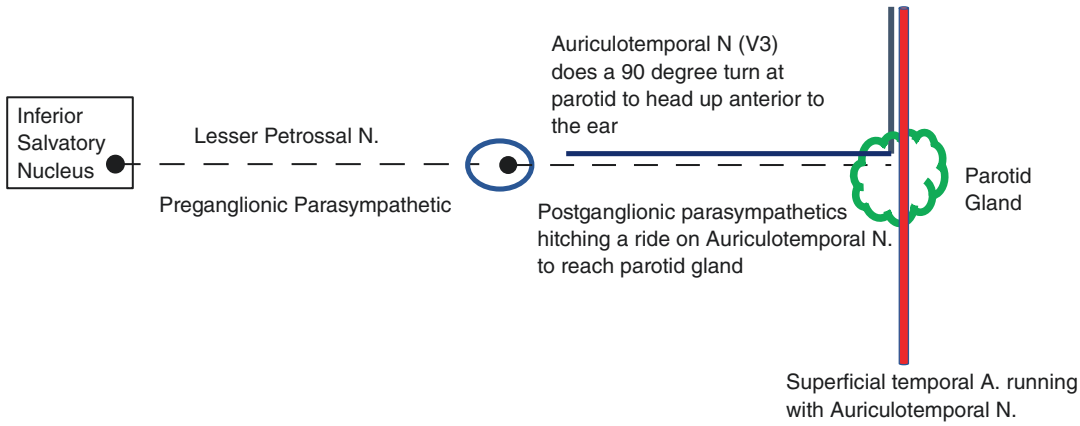


Fig. 6.4 Cranial nerve nine Parasympathetic. Lesser petrosal N. with preganglionics travel to otic ganglion, and then the postganglionics travel on the auriculotemporal n. to the parotid gland. (Leo 2021)

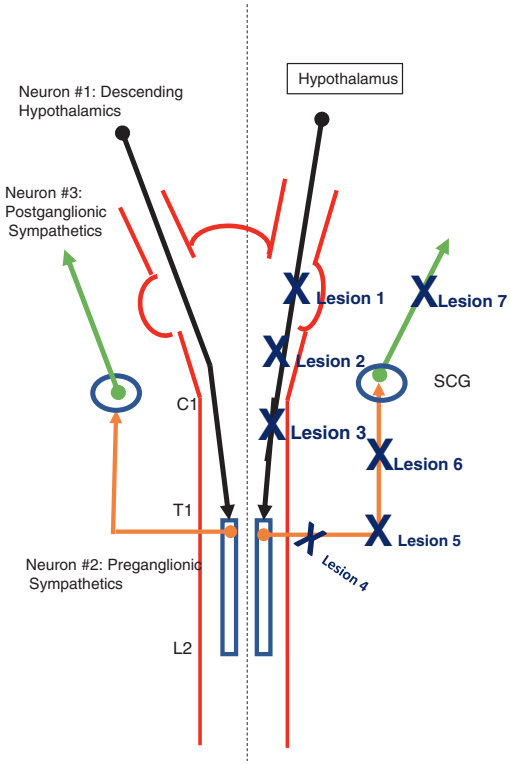
sympathetic responses. For instance, when the patient is waiting in line at the drive-thru for their cheeseburger, instead of salivating they will cry.

Sympathetics to the Face

The sympathetic projection to the face is a three-neuron pathway. When you finished gross anatomy, you probably thought of it as just a two-neuron pathway because at that point you probably just talked about pre- and postganglionic fibers, with the preganglionic fibers coming out of the lateral horn from T1. However, when you took neuroanatomy, you learned about the descending sympathetic fibers coming down from the hypothalamus projecting to the preganglionics originating at T1 (Fig. 6.5).

The first neuron comes from the hypothalamus and projects down to T1 of the lateral horn via the dorsolateral fasciculus (DLF). From the lateral horn at T1, the cholinergic preganglionics (neuron #2) jump onto the sympathetic chain and travel up to the superior cervical ganglion (SCG). After synapsing in the ganglion, the postganglionics (neuron #3), which use norepinephrine, run on blood vessels and nerves to travel to the face and importantly the eye where they are responsible for dilating the eye. These postganglionic neurons synapse on adrenergic receptors. An exception is the postganglionic sympathetics to the sweat glands which are cholinergic. Damage to the sympathetics anywhere along this pathway will lead to Horner's syndrome which consists of a constricted pupil, a slight droopy eye, and a red face. Tumors of the lung, lower brachial plexus injuries, aneurysms of the carotid artery, etc. can lead to Horner's syndrome.

There are seven lesions depicted in the picture of the sympathetic pathway above, all of which will result in Horner's syndrome. As the first-order neurons descend from the hypothalamus through the brainstem, they are located on the lateral side, so they are typically compromised in lateral pontine syndrome (Lesion 1) and lateral medullary syndrome (Lesion 2), as they descend down the cord, realize that a hemisection of the cord about T1 will result in Horner's syndrome (Lesion 3), as the preganglionics emerge through the roots at T1, they can be injured in a lower brachial plexus injury (Lesion 4), as the preganglionics travel near the root of the lung, they can be injured by a lung tumor (Lesion 5), as they travel up to the SCG on the carotid artery, they can be compromised by an aneurysm of the carotid artery (Lesion 6), and as they travel through the cavernous sinus (Lesion 7), they can also be injured.



Lesion 1: Lateral Pontine Syndrome
Lesion 2: Lateral Medullary Syndrome
Lesion 3: Hemisection of spinal cord
Lesion 4: Lower Brachial Plexus Injury
Lesion 5: Pancoast Tumor
Lesion 6: Internal Carotid Aneurysm
Lesion 7: Cavernous Sinus Infection

Fig. 6.5 Sympathetic pathway and Horner's syndrome. The descending fibers from the hypothalamus project to the lateral horn at T1 in the spinal cord. Preganglionics then project to the superior cervical ganglion. Postganglionics then project to targets in the face and particularly the eye. (Leo 2021)

Coma, the Autonomics, and the Eyes

For a patient in a coma, depending on where the lesion is, the pupils will assume a characteristic shape. The picture below is a perfect example of the importance of *understanding* the scenarios rather than just memorizing the plain facts. If you look at the picture, it can seem daunting to just memorize what the pupil does when certain regions are lesioned. It makes sense to walk through this logically (Fig. 6.6).

The thin dashed (red) line represents the descending sympathetics projecting from the hypothalamus down to T1. The thick (blue) horizontal line represents the preganglionic parasympathetic fibers projecting from the Edinger-Westphal nucleus to the eye. The lesions compromise either the sympathetics, the parasympathetics, or both. Location is everything.

Lesion #1 is to the hypothalamus which will damage the sympathetics. With the parasympathetics taking over, the pupil will be constricted.

Lesion # 2 is to the tectum which will damage the parasympathetics. With the sympathetics taking over, the pupil will be dilated.

Lesion #3 is to tegmentum of the midbrain which will damage both sympathetics and parasympathetics leading to the eye in the mid-position.

Lesion #4 is to either the lateral pons, lateral medulla, or spinal cord above T1 which will damage the descending sympathetics causing Horner's syndrome.

Lesion #5 is an uncal herniation which damages the preganglionic parasympathetic fibers on CN 3 which will lead to an ipsilateral dilated (blown) pupil.

Lesion #6 is the result of drug-induced pinpoint pupils.

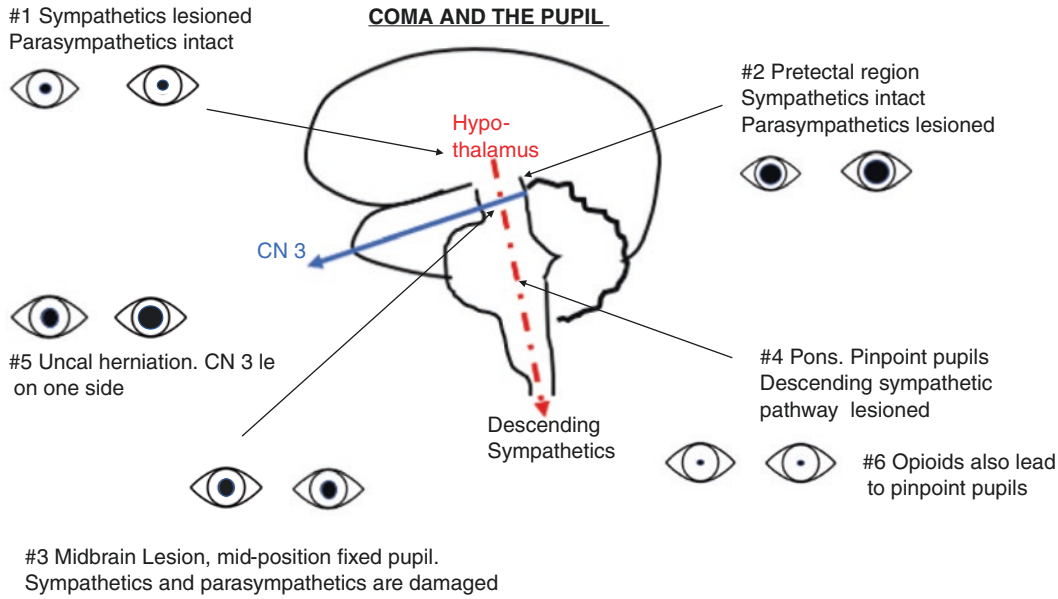


Fig. 6.6 Dashed vertical line represents the sympathetics. Solid horizontal line represents the parasympathetics

Reynaud's Disease

In Reynaud's disease the sympathetic nervous system to the arteries of the upper limbs is overactive leading to cyanosis and pain in the fingers. In severe cases a stellate ganglion sympathectomy may be performed to relieve the symptoms; however, a potential complication of the surgery is that because of normal human variation, some patients may develop Horner's syndrome.

Overview of Autonomics to the GI Tract

The parasympathetics are responsible for peristalsis and opening the various sphincters of the GI tract. When looking at the SLU**DD** mnemonic, think of the DD part—**d**igestion and **d**efecation.

Go back in time to when you took gross anatomy, and you were dissecting the region around the celiac trunk and found a nerve plexus. This is the celiac plexus, and in this plexus, we have a celiac ganglion. Is this a parasympathetic or a sympathetic ganglion?

To answer this, we need to start with a simple picture of the gut tube divided into foregut, midgut, and hindgut. In the picture, one side of the tube shows the parasympathetics, and one side shows the sympathetics.

On the parasympathetic side, we have the vagus nerve sending preganglionic fibers to the foregut and midgut and the pelvic splanchnics sending preganglionics into the hindgut. These preganglionics synapse with terminal ganglia, invisible to the naked eye, which are located in the walls of the GI tract.

On the sympathetic side, we see the thoracic splanchnic nerves coming into the celiac and superior mesenteric ganglia, which are located at the origins of their respective arteries from the aorta. You can see these ganglia with the naked eye when you are dissecting. The postganglionics then travel on the branches of the celiac trunk and superior mesenteric artery to the foregut and midgut. The lumbar splanchnics coming from L1 and L2 project to the inferior mesenteric ganglia and synapse, and then the postganglionics jump onto branches of the inferior mesenteric artery to the hindgut structures. Keep in mind that thoracic and lumbar splanchnic nerves are preganglionic *sympathetic*

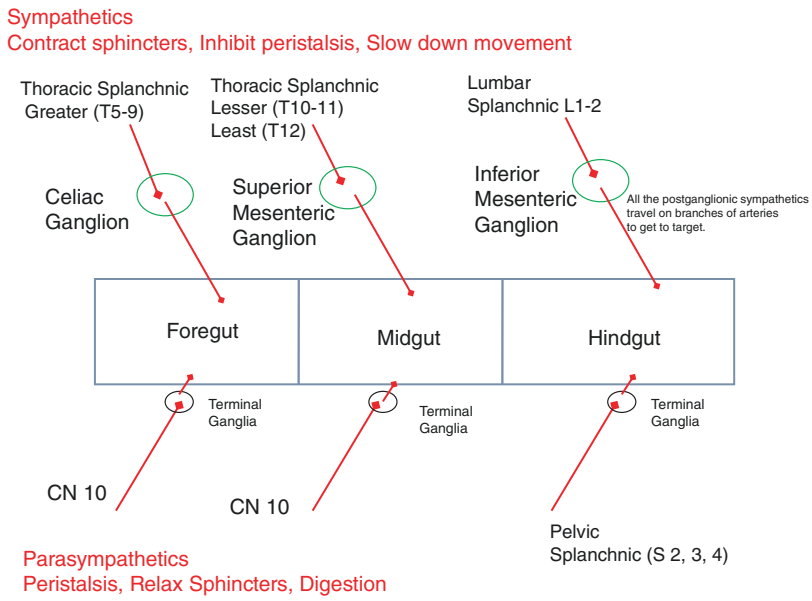


Fig. 6.7 Overview of autonomic projections to the GI tract

fibers, while the pelvic splanchnic nerves are preganglionic *parasympathetic* fibers (Fig. 6.7).

Going into greater detail, there are three thoracic splanchnic (sympathetic) nerves:

Greater splanchnic nerves from T5 to T9 projecting to the celiac ganglion

Lesser splanchnic nerves from T10 to T11 projecting to the superior mesenteric ganglion

Least splanchnic nerve from T12 projecting to the aorticorenal ganglion (often considered a subdivision of the superior mesenteric ganglion)

The pain fibers from the GI tract follow back along the sympathetic fibers and are responsible for visceral pain sensations. Pain from the foregut travels along the greater splanchnic nerves and is referred to the epigastric region; from the midgut along the lesser splanchnic and is referred to the umbilical area; and from the hindgut along the least splanchnic nerves and is referred to the hypogastric region.

Hirschsprung's disease results from a failure of neural crest to migrate into the hindgut. With no pelvic splanchnic nerves or peristalsis in the hindgut, the descending colon and sigmoid colon become constricted resulting in fecal material backing up in the descending colon.

Bladder and Bowel Control

Bladder and bowel control operates on the same basic mechanisms. The names of the various sphincters change whether you are talking about the bowel or bladder, but the nerve control of the two is similar. We will look at bowel control first. The bowel has internal and external anal sphincters. The internal anal sphincter is a smooth muscle under control of the autonomic system via the pelvic splanchnic nerves coming from S 2, 3, and 4. The external anal sphincter is a skeletal muscle under control of the somatic nervous system via the inferior rectal nerve, a branch of the pudendal nerve (Fig. 6.8).

The diagram shows the three different states of bowel control (Fig. 6.8). In the first panel, the anal canal is empty. The pudendal nerve and external anal sphincter are relaxed, while the internal anal sphincter is tonically active. In the middle panel, material has moved into the anal canal. This activates the sensory afferent nerves, which travel back to the cord at S2, 3, and 4 and make a connection to the efferent pelvic splanchnic nerves to relax the internal anal sphincter. This is strictly a reflex loop with no conscious or

cortical input at this point. If the individual in this instance is a 6-month-old infant, then the fecal material will come out. The 6 month old's corticospinal tract is not developed enough to send a signal from the cortex down to the cord, and onward to the pudendal nerve, so the infant is strictly operating on the reflex arc.

In an adult though, when something moves into the canal and the internal anal sphincter relaxes, the adult can then voluntarily fire their pudendal nerve and contract the external anal sphincter. The adult will then look for the bathroom, sit down, relax, pick up a magazine or a board review book, and relax their external anal sphincter to void. This entire process is sometimes referred to as the urge to purge.

When it comes to the bladder, instead of the internal and external anal sphincter, there are the internal and external urethral sphincters, plus the detrusor muscle. During the filling stage, the internal urethral sphincter is contracted, and the detrusor is relaxed. During voiding the detrusor contracts, and the internal and external urethral sphincters relax. With this in mind, we have two lesions to discuss.

Upper Motor Neuron: Spastic Bladder and Bowel

In this first scenario (Fig. 6.9), there is a lesion in the cervical or thoracic cord which will lead to blockage of the corticospinal pathway. The sacral regions are still functioning; they are just cut off from cortical control. This person's reflex is still intact; they just have no voluntary control so they will have spontaneous voiding. The bladder fills up, sensory fibers tell the sacral cord that the bladder is full, the reflex loop is active, and the efferent fibers relax the external anal sphincter. The reflex loop is operating on its own and has no cortical involvement.

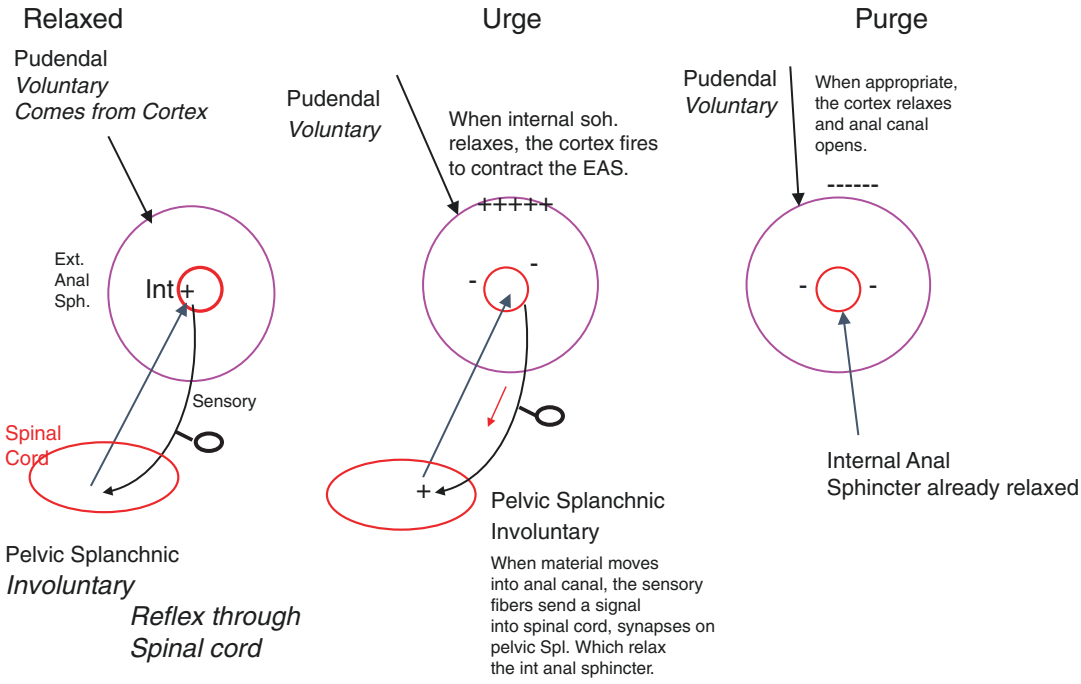


Fig. 6.8 Autonomic and somatic nerve control of rectum. (Leo 2020)

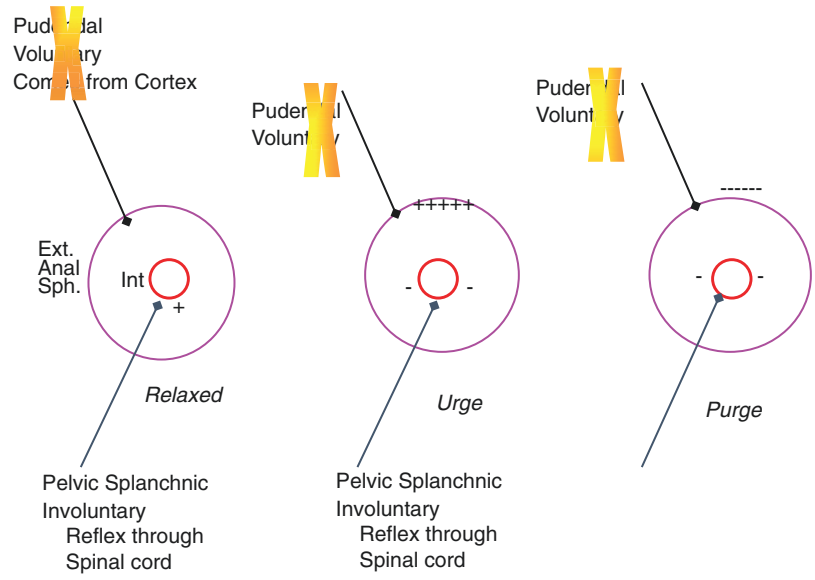


Fig. 6.9 With a lesion to the cord above S2, 3, 4 then the reflex arc is still present and internal anal sphincter will relax. Because the patient has no control over pudendal nerve the bowel is only operating at the reflex level. "Upper Motor Neuron Deficit" "Spastic Bowel (Bladder)." (Leo 2020)

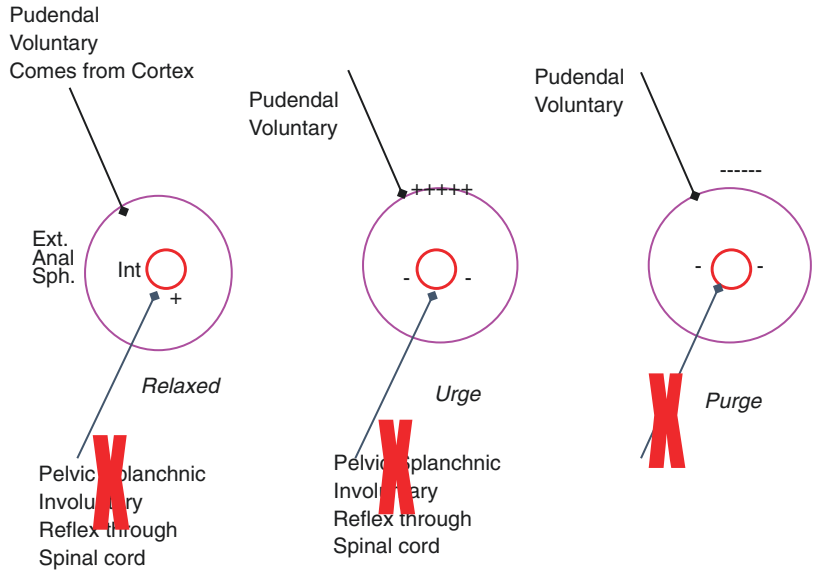


Fig. 6.10 Bowel control and LMN injury. With trauma to the pelvis that damages the conus medullaris (S 2, 3, 4) there is nor reflex arc or cortical control. The internal anal sphincter remains tonically active, and person cannot void. Fecal contents will build up until they eventually dribble out. "Lower Motor Neuron Deficit" "Flaccid Bowel (Bladder)". (Leo 2021)

Lower Motor Neuron: Flaccid Bladder and Bowel

In this second scenario (see Fig. 6.10), there is trauma to the sacral region, and the lower motor neurons are lost. In this case, the internal anal sphincter remains tonically active, and the individual does not have the ability to relax the muscle, and the patient's anal canal will fill up with material, and there will be a slow seepage of contents out of the anal canal and bladder.

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Facial Nerve Lesions

7

We are going to first talk about the peripheral pathway of the facial nerve as it leaves the brainstem (LMNs). Then, we will focus on the corticobulbar input to the facial motor nucleus (UMNs).

Cranial nerve seven is a mixed nerve with motor, sensory, and parasympathetic fibers. Keep in mind that each modality in the nerve has a different nucleus in the brainstem:

1. Motor fibers project out of the CNS from the *facial motor nucleus*.
2. Taste fibers (sensory) travel back to the *nucleus solitarius* in the medulla and pons.
3. Sensory fibers for touch travel back to the *spinal nucleus of V* also in the medulla and pons.
4. Secretomotor fibers project from the *superior salivatory nucleus* in the pons to peripherally located ganglia, and from there to the lacrimal, submandibular, and sublingual glands.

When cranial nerve seven emerges from the brainstem, realize that the four types of fibers mentioned above are present. Almost immediately, cranial nerve seven jumps into the internal acoustic meatus, an opening in the petrous portion of the temporal bone. The nerve then meanders through a corridor in the skull called the facial canal and eventually exits onto the face through the stylomastoid foramen. Once it comes out of the stylomastoid foramen, it courses through the parotid gland dividing into five branches that supply the muscles of facial expression, **T**emporal, **Z**ygomatic, **B**uccal, **M**arginal Mandibular, and **C**ervical, **T**o **Z**anzibar **B**y **M**otor **C**ar.

But let's back up to the nerve in the facial canal because this is where it gets interesting, and complicated. For clinical medicine it is important to understand the pathway of CN 7 in the facial canal. In the canal there are three branches, and they all have different components in them (Fig. 7.1).

Keep in mind when you look at these nerves, you don't "see" all these individual components standing out, you simply see the nerves themselves, but as a clinician or a test taker, you should be able to "visualize" the different components within each nerve so that you can answer clinical scenarios. In other words, the lingual nerve, either before or after the chorda tympani joins it, looks the same, but you need to know that there are different fibers in the lingual nerve either before or after the chorda tympani (Fig. 7.2).

1. The *greater petrosal nerve* is the first branch in the canal, and it consists of preganglionic parasympathetic fibers (abbreviated as GPN in picture) which travel on the floor of the skull to eventually cross the foramen lacerum, where it meets up with the deep petrosal nerve (sympathetic fibers) to form the nerve of the pterygoid canal. The preganglionic parasym-

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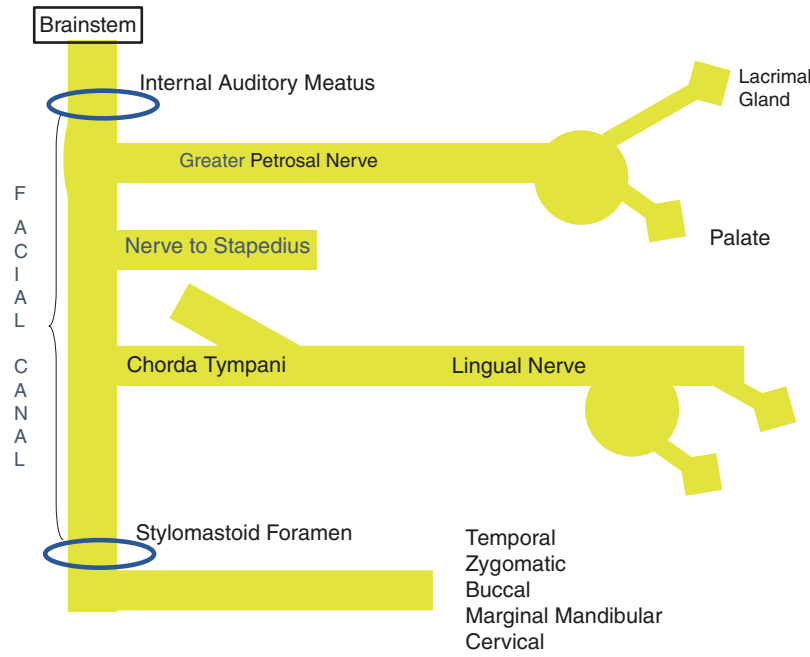

Fig. 7.1 Facial nerve branches

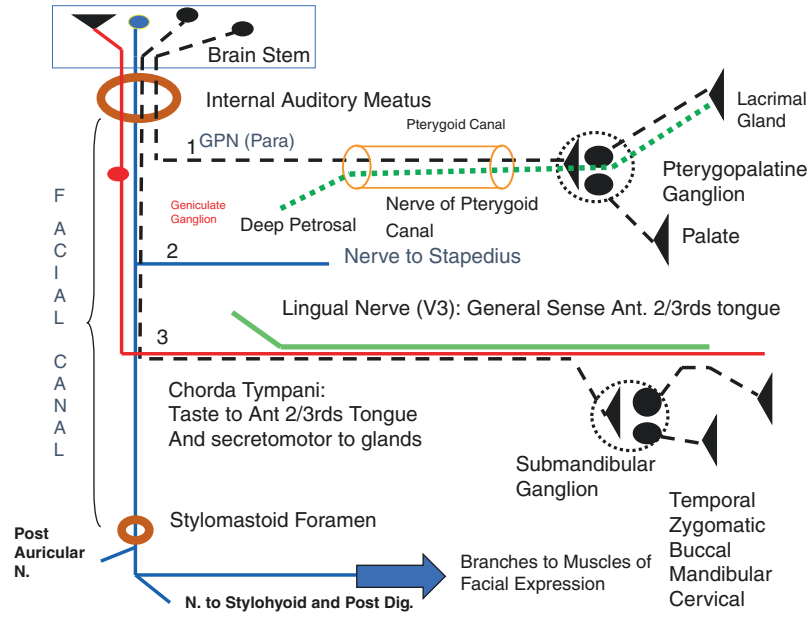

Fig. 7.2 Facial nerve pathway. White rami – pre-ganglionic sympathetics from T1–L2 ("on ramp"). Gray rami – post-ganglionic sympathetics throughout entire spinal column ("off ramp"). (Modified from Goldberg 1991; Leo 2021)

pathetic fibers run through the pterygoid canal to gain access to the pterygopalatine fossa where they synapse in the pterygopalatine ganglion. After synapsing in the ganglion, the postganglionics travel up to the lacrimal gland via branches of V2 (zygomatic) and V1 (lacrimal nerve).

2. The *nerve to stapedius* is the second branch in the canal, and it travels to the stapedius and is involved in sound dampening. Damage to the nerve will lead to hyperacusis. Lesions here will result in the patient complaining about loud noises. Do not confuse this with a deficit to cranial nerve eight.

3. The *chorda tympani* is the third branch, and it travels through the middle ear, exits through the petrotympanic fissure, enters the infratemporal fossa, and joins the lingual nerve. The chorda tympani contains two types of fibers. It has preganglionic parasympathetic fibers destined for the submandibular ganglion, which in turn sends postganglionic fibers to the submandibular and sublingual glands. The chorda tympani also conveys taste information from the anterior two-thirds of the tongue. In the infratemporal fossa, it joins the lingual nerve, a branch of V2 carrying information about general sensation from the anterior two-thirds of the tongue.

There are several common lesions to consider with the facial nerve (Fig. 7.3):

Lesion A: With a parotid tumor or surgical complications of the parotid gland, the facial nerve can be compromised. In this scenario, the patient will lose the muscles of facial expression on one side of the face, but since the nerve in the facial canal is intact, there will no deficit in hearing, taste, or glandular sections of lacrimal and glands of the mouth.

Lesion B represents classic *Bell's palsy*. In Bell's palsy, an infection of cranial nerve seven is thought to lead to inflammation and subsequent compression of the nerve in the canal. In this scenario, the patient will lose the muscles of facial expression; taste from the anterior 2/3rds of the tongue; secretions from the lacrimal gland leading to a dry eye; and the submandibular and sublingual glands. Plus, because of loss of the stapedius, they will complain that loud noises are aggravating (hyperacusis). Loss of the submandibular and sublingual will not be obvious because the patient still receives secretions from the contralateral glands.

While Bell's palsy typically involves all the branches in the facial canal, it is possible for a tumor or other mass to only damage some of the branches. For instance, if there was a lesion to the facial nerve between the nerve to stapedius and the chord tympani, then the stapedius and lacrimal gland would be spared in this patient.

Lesion C is an acoustic neuroma. Because of the proximity of cranial nerves seven and eight as they enter the internal acoustic meatus, an acoustic neuroma which originates on cranial nerve eight can also damage cranial nerve seven. This is

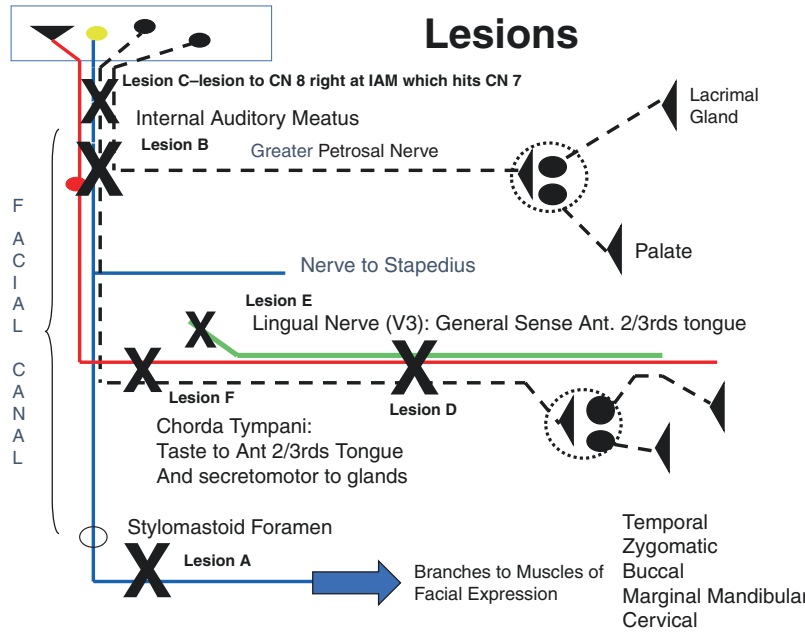

Fig. 7.3 Facial nerve lesions

somewhat rare but worth noting. The patient would have all the signs of the Bell's palsy patient, plus a hearing and balance deficit.

Lesion D: Another common injury involves the lingual nerve. The dentist needs to be careful of the lingual nerve when removing a wisdom tooth. If the lingual nerve is severed, then the patient will lose taste to the anterior two-thirds of the tongue; the secretomotor fibers to the submandibular and sublingual glands; and general sense from the anterior two-thirds of the tongue. Remember the chorda tympani joins the lingual nerve, and the lingual nerve is a branch of V3 carrying general sense information from the tongue.

Lesion E is to the lingual nerve before the chorda tympani joins it, so taste and the glands would be spared, but the patient would lose general sensation from the anterior two-thirds of the tongue.

Lesion F is to the chorda tympani before it joins the lingual nerve, so only taste and the glands would be affected.

Corticobulbar Projections to Cranial Nerve Seven

The facial motor nucleus is located in the pons, and it can be divided into half. The upper part of the nucleus supplies the upper part of the face, and the lower part of the nucleus supplies the lower part of the face. The cortex control of the nucleus arises in the face area of the precentral gyrus which projects down as the corticobulbar pathway. Of clinical importance is the fact that the upper part of the nucleus receives a bilateral cortical input, while the lower part of the nucleus only receives a contralateral input (Fig. 7.4).

A lesion to the cortex will result in a loss of the contralateral lower facial muscles. Since the upper part of the facial nucleus receives information from the other side, it will still function. Granted the muscles might be weaker but the patient will still be able to close their eye and smile on that side. If the lesion is to the nucleus in the brainstem, then the patient will lose both the upper and lower facial muscles on the ipsilateral side.

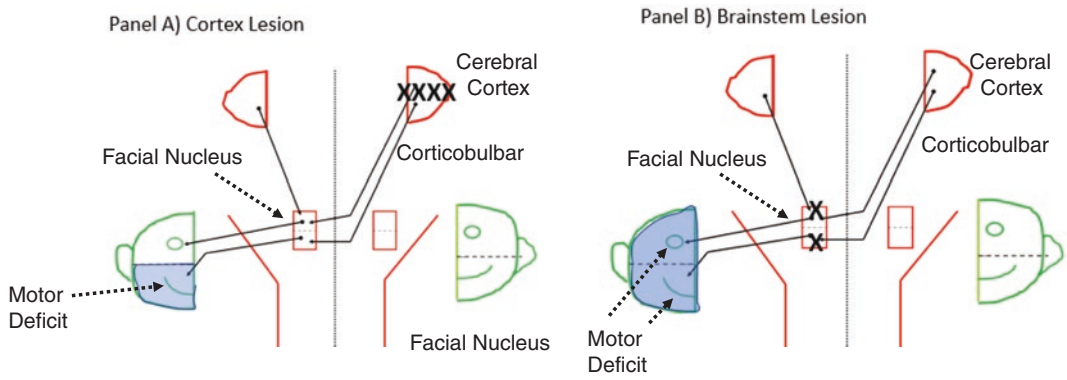

Fig. 7.4 Corticobulbar input to facial motor nucleus. The upper part of the nucleus receives a bilateral input. The lower part of the nucleus receives a contralateral input. (Leo 2021)

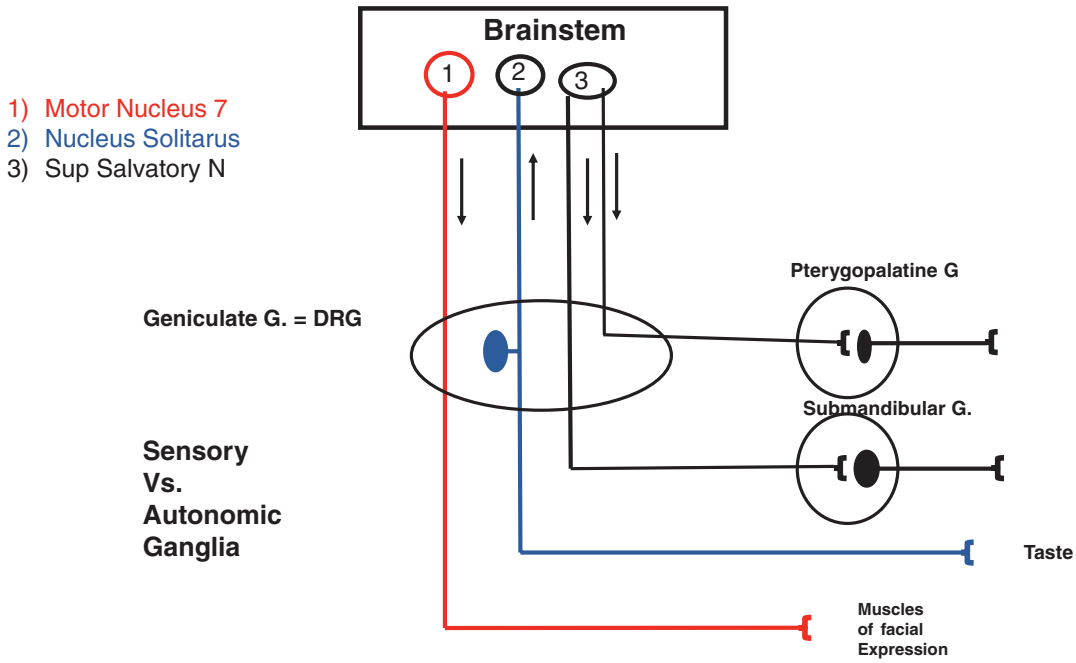

Fig. 7.5 Comparison of autonomic and sensory ganglion of facial nerve

Cranial Nerve Seven and Cell Bodies

Because cranial nerve seven has motor, sensory, and parasympathetic fibers, it is also a good time to revisit cell bodies. When you look at the *motor* fibers of 7, they have their cell bodies in the motor nucleus of 7 which is inside the pons—these are functionally equivalent to the motor nerves to the limbs coming out of the anterior horn cells. The *sensory* fibers for general sense, which come from a small area by the external ear, have their cell bodies in the geniculate ganglion (cell bodies, no synapse) inside the facial canal. These fibers are functionally equivalent to the sensory fibers from limbs that have their cell bodies in the dorsal root ganglion. The taste fibers also have their primary cell body in the geniculate ganglion. These fibers enter the pons and project to the nucleus solitarius. The parasympathetic fibers come from the superior salivatory nucleus and project to either the submandibular or sublingual ganglion (synapse and cell body). From the ganglion, the postganglionic fibers travel to the glands—lacrimal, submandibular, and sublingual (Fig. 7.5).

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Cerebellar Lesions

8

The cerebellum sits between the cerebral cortex and the spinal cord and is referred to as the "comparator" because it compares one stream of information descending from the cortex and another stream of information ascending from the spinal cord. The cerebral cortex is sending commands—the plan of action—down to your muscles via the corticospinal and corticobulbar pathways, and the cerebellum is listening in, or getting a sample of those commands. Meanwhile as your limb is moving, there is information about proprioception coming into the spinal cord and traveling up to the cerebellum. The cerebellum then compares what you *plan to do* with your limbs, with *what is really happening* with your limbs, and then adjusts or fine-tunes the movement by projecting back to the thalamus and cerebral cortex. Lesions to the cerebellum do not result in paralysis, or loss of strength, but result in an intention tremor.

Lobes, Zones, and Divisions

There are three ways that scientists have divided up the cerebellum. The first is on an anatomic basis by lobes. If you take a midsagittal cut through the cerebellum, you notice two prominent fissures: (1) the primary fissure, which gives us the large *anterior* and *posterior lobes*, and (2) the posterolateral fissure, which gives us the small *flocculonodular lobe*. We can also talk about zones, which moving medial to lateral gives us the *vermis*, *intermediate zone*, *and lateral hemispheres*. Or we can talk about functional divisions, which are based on connections, giving us the *cerebrocerebellum*, *spinocerebellum*, and *vestibulocerebellum*. The central inferior part of the vermis is referred to as the tonsil, which in the presence of increased intracranial pressure can herniate through the foramen magnum.

Corticospinal and Corticopontocerebellar

Take the circuits involved in picking up a piece of paper on the street in front of you, but to complicate this movement, there is a slight breeze in the air, which causes the paper to move as you are reaching for it. On Fig. 8.1 you can see the corticospinal tract projecting down from the left cerebral cortex to the right cord to tell the hand to move toward the paper. As the signal travels through the pons on its way to the spinal cord, it sends a sample of the information to the pontine nuclei, which in turn sends its information into the contralateral cerebellum via the middle cerebellar peduncle. It is via this corticopontocerebellar pathway that the cerebellum listens into your plan to move your arm and pick up the paper. Note that this is an **afferent** pathway into the cerebellum (Fig. 8.1).

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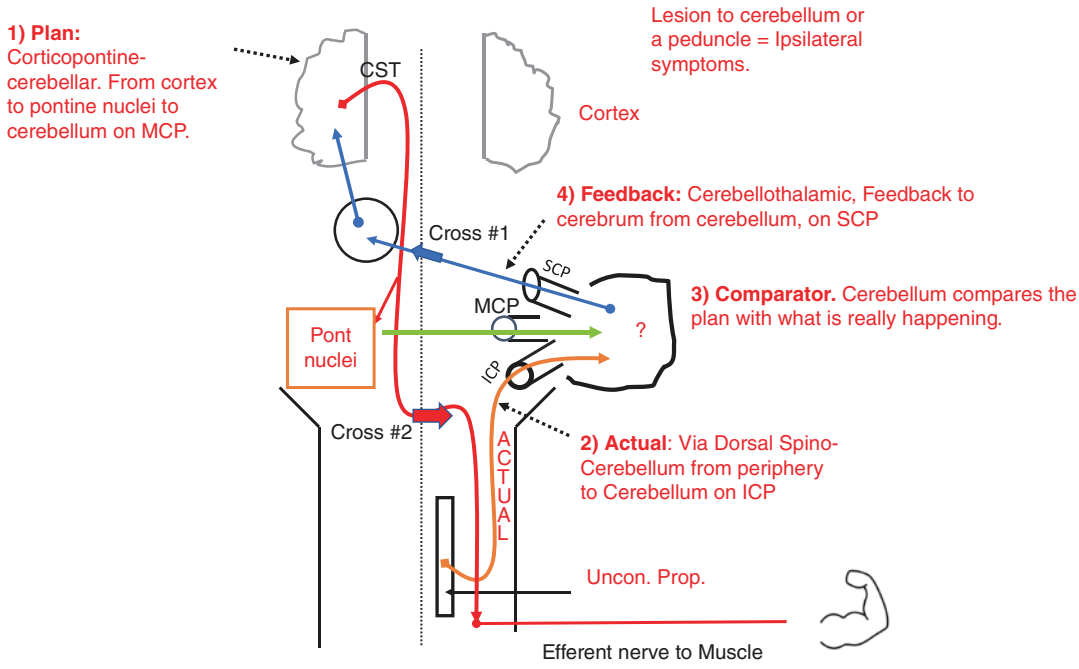

Fig. 8.1 Cerebellar inputs and outputs. It is a double-crossed pathway. Decussation #1 is the dentatothalamic. Decussation #2 is the corticospinal tract. (Leo 2021)

Dorsal Spinocerebellar and Cuneocerebellar

As your right arm is moving toward the piece of paper, there is all sort of proprioceptive information about the relationship of your arm to the paper coming into your cerebellum, especially important since the wind is moving the paper and your initial plan will need to be modified in midcourse. The proprioceptive information comes into the spinal cord and synapses in the dorsal nucleus of Clark which runs from T1 to L2. After synapsing, the fibers jump onto the dorsal spinocerebellar tract. The equivalent nucleus and tract for the neck are the lateral cuneate nucleus and the cuneocerebellar tract, which also travel through the inferior cerebellar peduncle. The dorsal spinocerebellar and cuneocerebellar are both **afferent** pathways into the cerebellum carrying information about what is actually happening with your limb (Fig. 8.2).

There is also a ventral spinocerebellar pathway projecting from the spinal cord to the cerebellum, which crosses twice. When it enters the spinal cord, it crosses immediately to the contralateral side, it travels up the spinal cord, and then in the brainstem, it crosses back to the original side before entering the cerebellum. When you think about the lesions to the spinal cord and nervous system, it is not that important.

Dentatothalamic

The right cerebellum receives information about the plan via the middle cerebellar peduncle, while the proprioceptive information is entering through the inferior peduncle. To fine-tune the movement, so that you can pick up the paper, the right cerebellum sends its information out of the cerebellum on the superior cerebellar peduncle via the dentatothalamic pathway to the contralateral thalamus, which in turn goes to the left cerebral cortex. And originating in the left cerebral cortex is the corticospinal tract sending information to the right forearm (remember, corticospinal decussates).

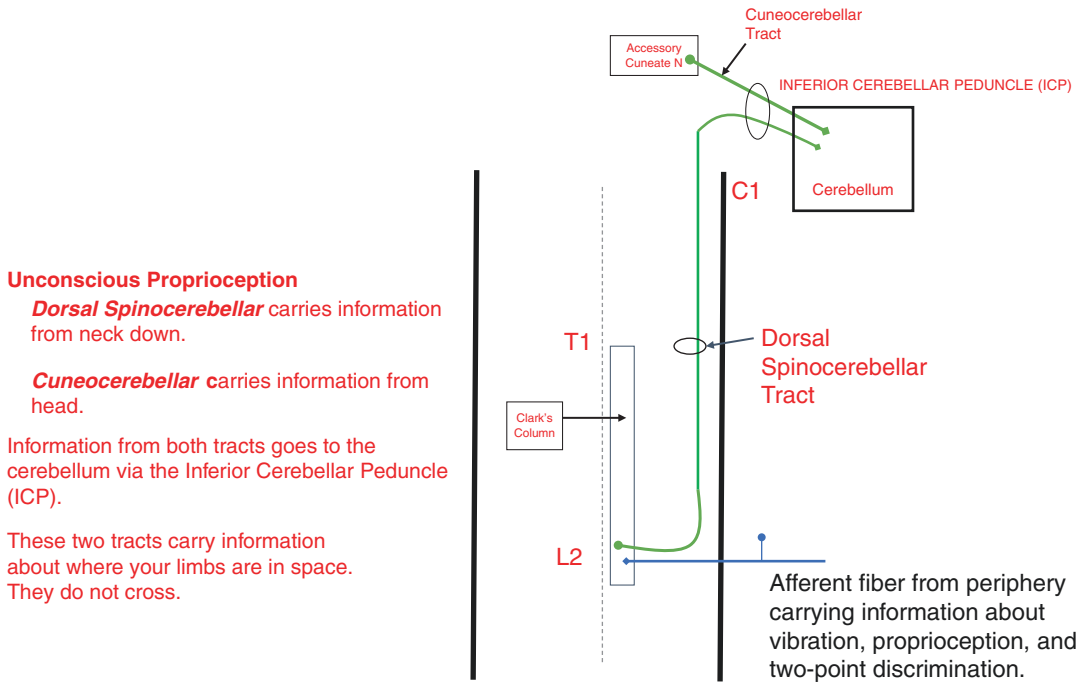

Fig. 8.2 Dorsal spinocerebellar and cuneocerebellar pathways. (Leo 2021)

This circuit explains why if you have a lesion to the cerebellum or one its peduncles, the signs and symptoms will be on the ipsilateral side. This is because the circuit has two crossing points. Take a lesion to the right cerebellum. The output from the right cerebellum decussates (crossing #1) to project to the left thalamus, which in turn goes to the left cerebral cortex, but the left cerebral cortex sends information down the corticospinal tract which decussates in the pyramidal decussation (cross #2) to go to the right cord, and then to the right upper limb. Thus, a lesion to the right cerebellum will disrupt movements on the right side of the body.

Cerebellar patients will have an "intention tremor" which refers to the fact that in most cases if a cerebellar patient is sitting in your office, you will likely not see a tremor at rest. The tremor will not appear until the patient intends to move. For instance, if the patient is asked to touch their nose, they will have a tremor, and importantly the tremor will get worse as their finger approaches the target.

A common lesion that leads to cerebellar signs is lateral medullary syndrome which damages the dorsal spinocerebellar tracts, leading to ipsilateral ataxia. These are addressed in more detail in the Chap. 13.

Internal Cerebellar Circuitry

In the previous section, we looked at the tracts coming into and out of the cerebellum with the idea that the cerebellum compares the plan with the actual movement and then fine-tunes the ongoing movement. On the picture of the schematic, you will see a question mark located in the cerebellum. We are now going to zoom in with a microscope and look at some of the internal circuitry.

Just like the cerebral cortex, the exterior of the cerebellum consists of gray matter; however, unlike the cerebrum with its six layers, the cerebellum has three layers. Deep to the gray matter is the white matter, with four nuclei embedded in

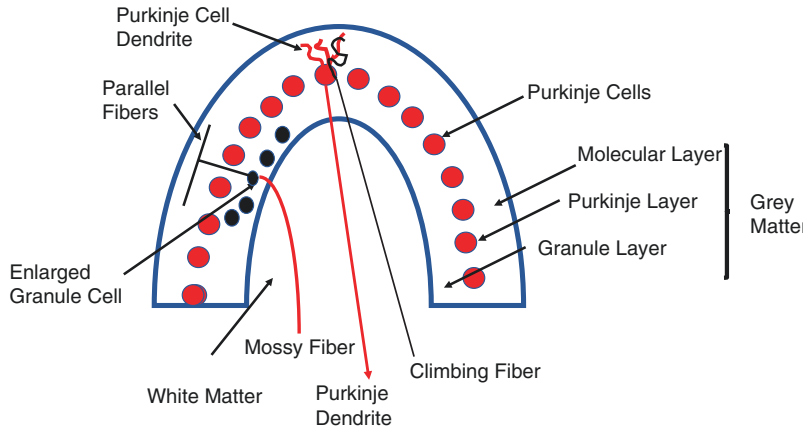

Fig. 8.3 The three layers of the cerebellar gray matter. (Leo 2021)

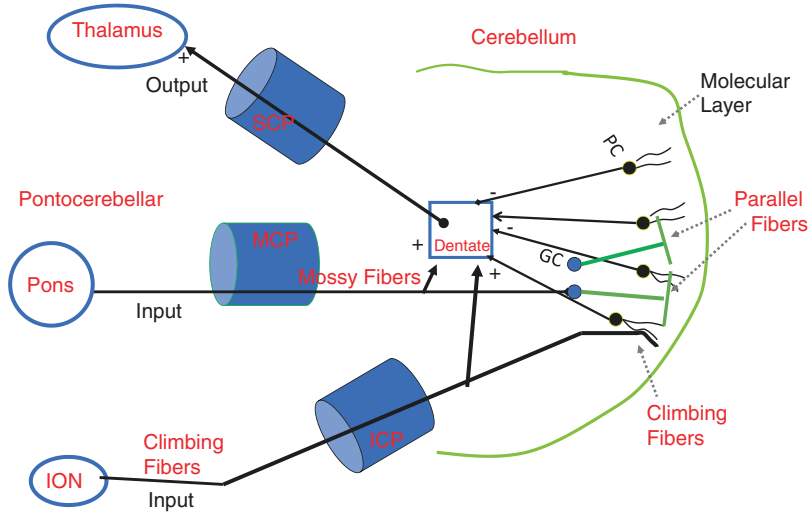

Fig. 8.4 The three cerebellar peduncles. Climbing fibers from inferior olive (IO), parallel fibers from granule cells, Mossy fibers from all extrinsic nuclei IO. PC Purkinje cell, GC granule cell. (Leo 2021)

the white matter on each side. From outside to inside, the layers of the gray matter are (1) molecular, (2) Purkinje, and (3) granule (Fig. 8.3).

The Purkinje layer gets its name from the flask-shaped Purkinje cells which are lined up in rows of monolayers. Their dendrites project out into the molecular layer, and their axons project down through the granule cell layer to synapse on the deep cerebellar nuclei, which are embedded in white matter.

The granule cells are much more numerous than the Purkinje cells and cover a wider area. The granule cells have axons that project up into the molecular layer and bifurcate to form a T, referred to as parallel fibers. The parallel fibers travel across the molecular layer synapsing on rows of Purkinje cells (and basket and stellate cells).

The molecular layer is made up of the dendrites of Purkinje cells, climbing fibers, parallel fibers, and basket and stellate cells. The basket and stellate cells are involved in lateral inhibition.

Cerebellar Inputs

There are numerous inputs to the cerebellum, but they can be subdivided into two classes: (1) climbing fibers and (2) mossy fibers (Fig. 8.4).

The **climbing fibers** only come from the inferior olivary nucleus (ION). As they enter the cerebellum, they send a collateral to the deep cerebellar nuclei and then continue onto the Purkinje cell dendrites where they resemble a

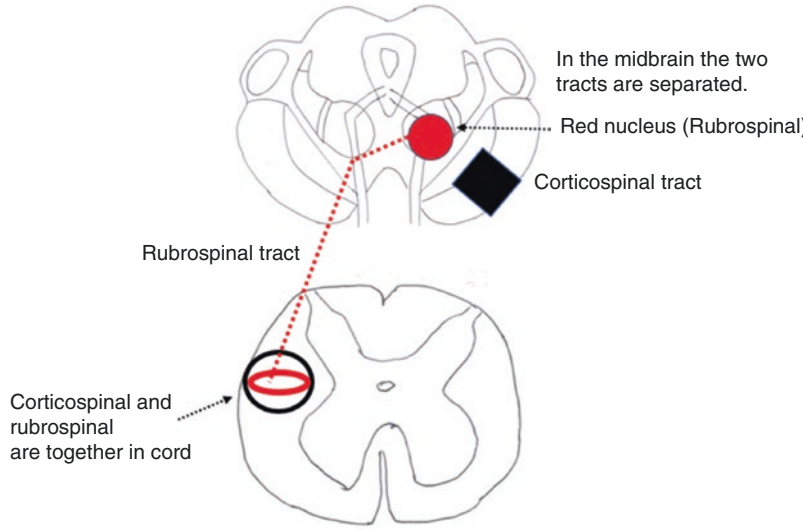

Fig. 8.5 Rubrospinal tract. The rubrospinal tract originates in the red nucleus. In the midbrain the nucleus is separate from the corticospinal tract. In the spinal tract, the two tracts sit right on top of each other. Webster's syndrome affects CST, Benedikt's affects rubrospinal, and Brown-Sequard affects both tracts. (Leo 2021)

vine wrapping itself around a trellis—thus the name "climbing fiber." There is a one-to-one connection between climbing fibers and Purkinje cells. They are excitatory and are thought to be involved with error correction.

Every other input to the cerebellum is characterized as a **mossy fiber**. The mossy fibers send a collateral to the deep cerebellar nuclei and then continue onto the granule cells which in turn project into the molecular layer as parallel fibers. In contrast to the one-to-one relationship of climbing fibers and Purkinje cells, each parallel fiber synapses on thousands of Purkinje cells.

Red Nucleus

The red nucleus receives a projection from the cerebellum and projects to the contralateral flexors of the upper limb via the rubrospinal tract. For the purposes of human clinical neuroanatomy, lesions to the rubrospinal tract in the spinal cord are not often discussed because the rubrospinal tract sits practically on top of the corticospinal tract, so that a lesion to the rubrospinal tract would also lead to a lesion of the corticospinal tract. And the patient would exhibit UMN signs. The rubrospinal tract is also discussed in the section of decerebrate and decorticate rigidity.

In the midbrain, the red nucleus, which is the start of the rubrospinal tract, is separated from the corticospinal tract, so that a lesion to the red nucleus will not necessarily damage the corticospinal tract. Lesions of the red nucleus will lead to a contralateral tremor (Fig. 8.5).

Deep Cerebellar Nuclei

The four deep nuclei are the **fastigial**, **globose**, **emboliform**, and **dentate**. Each of these nuclei receives an excitatory input from either the climbing or mossy fibers, and an inhibitory input from the Purkinje cells. Like a computer, the deep nuclei are monitoring and responding to the differential barrages of excitatory and inhibitory inputs. These nuclei in turn then send an excitatory projection onto the thalamus.

Basket Cells, Stellate Cells, and Lateral Inhibition

Lateral inhibition is a way to increase contrast in the nervous system by firing one group of neurons while simultaneously inhibiting the neighboring neurons. In the cerebellar cortex, Purkinje cells are lined up in rows, with parallel fibers from the granule cells running down each row. A single parallel fiber can synapse with hundreds of thousands of Purkinje cells. When a parallel fiber depolarizes, it "turns on" a row of Purkinje cells.

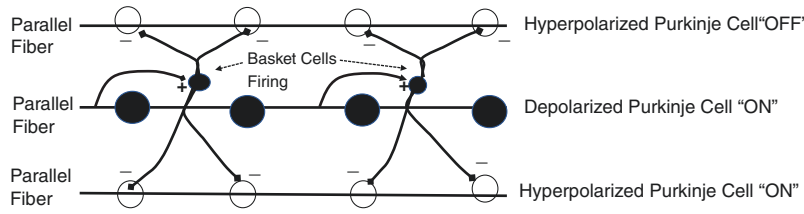

Fig. 8.6 Lateral inhibition in the cerebellum. (Leo 2021)

At the same time, the collaterals from the parallel fibers will contact basket and stellate cells which are inhibitory to the neighboring rows of Purkinje cells, and will inhibit or "turn off" the neighbors. Various other regions of the nervous system such as visual and auditory regions also use lateral inhibition to increase the contrast of their incoming signals (Fig. 8.6).

Deep Cerebellar Nuclei

The deep nuclei do not project directly to the lower motor neurons, but instead, exert their influence by projecting to areas of the extrapyramidal and pyramidal systems.

The **fastigial nucleus** projects to vestibular and reticular nuclei which give off vestibulospinal and reticulospinal tracts. The **dentate nucleus** sends some fibers to the red nucleus, while the **globose and emboliform** projects its efferent fibers mainly to the red nucleus. The red nucleus gives rise to the rubrospinal tract. The rest of the ascending deep nuclei fibers join the red nuclei fibers and go to the thalamus and precentral gyrus. In this manner, the cerebellum can affect corticospinal output.

The somatotopic organization of the cerebellum is not as precise as in the cortical areas, and we can only make rough generalization about it. The trunk afferents project to the vermis and paravermal cortex, and their efferents are primarily concerned with posture, muscle tone, and stabilization of the proximal limb musculature. The lateral hemispheres reciprocally interact with cerebral cortex for fine control of distal muscles.

Clinical Symptoms of Cerebellar Lesions

Lesions to the cerebellum will result in the various signs and symptoms:

Ataxia: a disturbance in posture and gait. Lesions of the midline region of the cerebellum cause difficulty in maintaining an upright stance. The gait is staggering like that seen in drunkenness.

Dysmetria: the inability to stop a movement at the intended target. For example, in the cerebellar patient, if you ask the patient to touch their nose, they have a tremor. Notably, the tremor becomes more severe the closer the finger gets to the target.

Dysdiadochokinesia: the inability to perform alternating rapid movements such as pronation-supination of the hands.

Hypotonia: decreased muscle tone.

Intention tremor: is often present during purposeful movements. It is not present at rest.

Nystagmus: is present with cerebellar lesions due to disruption of the vestibular fibers or vestibular nuclei.

Central pontine myelinolysis occurs in patients with hyponatremia who have had their low sodium levels treated too quickly which leads to a pathological response resulting in demyelination of the corticospinal and corticobulbar tracts in the pons. The patients present with quadriparesis, cranial nerve deficits, and emotional lability.

Olivopontocerebellar atrophy is characterized by degeneration in the cerebellum, pons, and inferior olive resulting in deficits with balance,

coordination, posture, voluntary movements, and bladder control. Symptoms usually begin in the lower limbs and progress to the upper limbs and then onto the cranial nerves. The initial symptom is usually a broad-based gait.

Medulloblastomas arise from neuroectoderm, are found in the cerebellum close to the fourth ventricle, and are one of the most common tumors in children. Increased intracranial pressure can lead to blockage of the fourth ventricle. Patients present with a wide-based gait, and truncal ataxia (drunken sailor gait) affecting the midline muscles such as shoulder and hip.

Dandy-Walker syndrome is a congenital malformation of the fourth ventricle and the cerebellum. The vermis of the cerebellum is either absent or smaller than normal. Most patients will present with hydrocephalus due to blockage of the foramen of Magendie.

Progressive supranuclear palsy (PSP) is due to degeneration of the substantia nigra, midbrain, and the dentate nucleus of the cerebellum. PSP patients and Parkinson's patients have similar motor deficits. However, PSP patients tend to stand upright with the head bent backward and tend to fall backward (axial rigidity), which contrasts to Parkinson's patients who tend to lean forward and fall forward. The PSP patients will have eye movement deficits and subsequent trouble shifting their gaze, which leads to blurred vision. They also have deficits with opening their eyes and tend to blink excessively. PSP patients tend to have a wide-eyed stare, furrowing of the forehead, and a permanent frown. Sagittal MRIs of a PSP patient can show a *hummingbird sign*, which is due to the degeneration of the brainstem.

Chiari malformations refer to brain tissue herniating into the spinal canal. There are two types of Chiari malformations. In a *type I Chiari malformation*, there is a downward displacement of the cerebellar tonsils on the brainstem at the foramen magnum. It is often not diagnosed until adolescence or adulthood, and the patient may be asymptomatic. It may go along with syringomyelia. *Type II* is usually diagnosed in young children, and there is a herniation of the cerebellum and the brainstem through the foramen magnum. These patients are also often diagnosed with a myelomeningocele. The most common treatment of Chiari malformations is decompression of the posterior cranial fossa.

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Basal Ganglia Lesions

9

To move your hand, your corticospinal tract fires—like the stepping on the car's gas pedal. However, when your hand is at rest and not moving, besides not pressing on the gas pedal, think of a parking brake which is in the "on" position and keeping your hand at rest. The basal ganglia is the parking brake. When it comes time to move your hand, milliseconds before the movement, you need to turn the brake "off." The following schematics focus on how we turn the brake on or off. Lesions in the basal ganglia can disrupt the break and can lead to tremors.

The picture above (Fig. 9.1) is a simplistic picture showing the two main categories of basal ganglia diseases. Think of "movement" existing on a spectrum, with so-called normal movement in the midline. At the far-right end are hyperkinetic disorders, such as Huntington's chorea. These patients have too much movement. At the other end, to the left, are hypokinetic disorders such as Parkinson's. These patients have a paucity of movement, either bradykinesia (slower movements) or akinesia (fewer movements).

Before getting into the specifics, we need to look at the big picture by starting with the symptoms and working backward from the symptoms, to the cerebrum, to the thalamus, and finally to the basal ganglia (the brake). Take a Huntington's patient who has a tremor at rest; they are hyperkinetic and have too much movement, meaning that the cortex is overactive, and since the cortex is controlled by the thalamus, the thalamus is also overactive, which means that the brake, or the basal ganglia, is underactive—it is "off."

On the other end of the spectrum, take the Parkinson's patient with not enough movement, who is stuck, or frozen. It makes sense that their cortex is underactive, which in turn means that their thalamus is underactive, which then means that their brake—the basal ganglia—is stuck in the "on" position and cannot be relaxed. There are three neurotransmitters that play a role in normal and pathological functioning of the basal ganglia: *glutamate, gaba, and dopamine*.

We can divide the basal ganglia circuit up into inputs and outputs. The input nuclei are the caudate and putamen (together they are referred to as the striatum), which receive information from the cerebral cortex. The output nuclei which are really "the brake" are the internal globus pallidus and substantia nigra pars reticularis.

The major excitatory transmitter in this schematic is glutamate, and the major inhibitory transmitter is gaba. Between the input nuclei and the output nuclei are several internal loops, which is where the basal ganglia becomes complicated. The input nuclei talk to the output nuclei via two pathways: the direct and indirect pathways.

The terms direct and indirect pathways refer to the information coming out of the striatum (caudate and putamen) and projecting to "the brake"—the internal globus pallidus and the substantia nigra pars reticularis. The information coming out of striatum either goes "directly" to

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the brake, or "indirectly" via the external globus pallidus, to subthalamic nucleus, and then to the brake. If we look at the brake, we can see that the two pathways coming into it give us an "off" switch and an "on" switch (Fig. 9.2).

Before proceeding, we need to digress for a moment and think about disinhibition, because there are several sites of disinhibition in these circuits. If we look at the image below, we can see that an excitatory input to a target, whether a gland or another neuron, will increase the activity in the target, while an inhibitory neuron will decrease the activity—this is all very obvious. If we now add an excitatory coming to an inhibitory, then activity in the first neuron will also decrease the target activity. But with an inhibitory neuron projecting to another inhibitory neuron, it is not quite as obvious. When we increase the activity in the preganglionic inhibitory neuron, then we increase the inhibition on the postganglionic neuron, but this is an inhibitory neuron, so we actually increase the activity in the target (Fig. 9.3).

Start with the schematic of the basal ganglia when your hand is at rest. If we look at the brake, we clearly want that to be in the "on" position. Coming into the brake is an "on" switch from the indirect pathway, glutamate release from the subthalamic nucleus, and an "off" switch from the direct side, a gabaergic projection from the caudate. In the case of the hand at rest, we want the "on" switch from the subthalamic to be active. Glutamate coming from the subthalamic will increase the activity of the internal globus pallidus/substantia nigra reticularis, which in turn is inhibitory (gaba) to the thalamus which reigns in the cortex, and corticospinal tract remains at rest.

When it comes time to move, the pathways flip-flop, and the indirect side will prevail over the direct which will inhibit the brake and allow for movement.

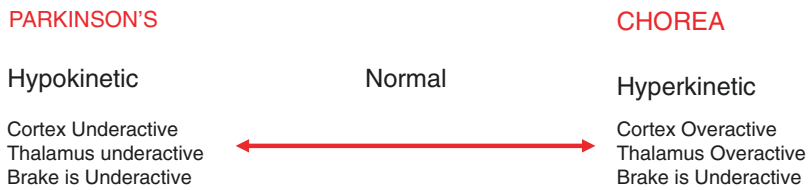

Fig. 9.1 Contrast of activity in structures of a Parkinson's (hypokinetic) patient to a Huntington's chorea patient (hyperkinetic). The "brake" is the globus pallidus internal section and the substantia nigra pars reticulata. In Parkinson's patient the brake is overactive or "on." In a Huntington's chorea patient, the brake is underactive or "off"

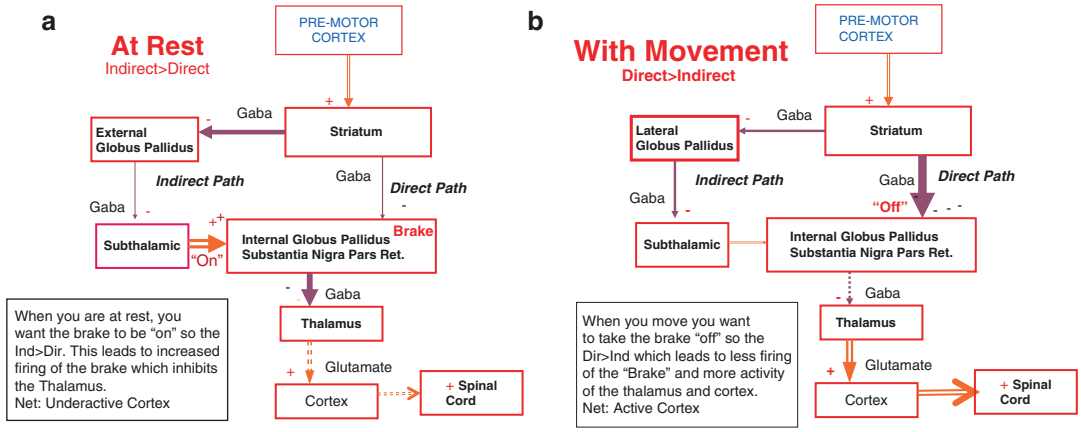

Fig. 9.2 Basal ganglia schematic. Panel A shows the activity in the structures while the person is active. Panel B shows the activity in the structures during movement. (Leo 2021)

Hemiballismus

The simplest lesion to discuss here is hemiballismus which is a wild flinging motion of the limbs due to a lesion—typically a stroke—of the subthalamic nucleus. If you take the subthalamic nucleus out of the equation, then the brake is "off," and the direct side is overactive, and there is too much movement (Fig. 9.4).

Huntington's Chorea

In Huntington's there is a degeneration of the caudate nucleus that leads to a reduced output to the external globus pallidus. Thus, like hemiballismus, without the indirect pathway, the direct pathway takes over, and there is too much movement—a hyperkinetic disorder (Fig. 9.4).

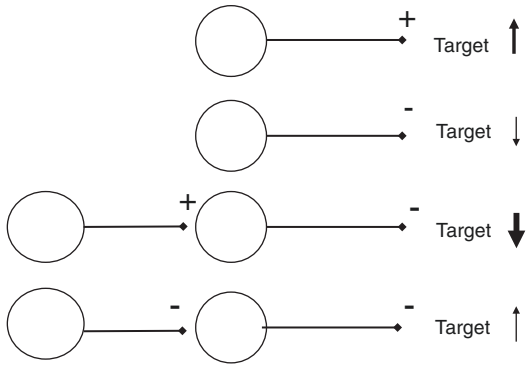

Fig. 9.3 Disinhibition. An excitatory neuron will increase activity in a target; an inhibitory neuron will decrease activity. A, excitatory coming into an inhibitory will decrease target activity. An inhibitory projecting results in an increase (disinhibition) in target activity. (Leo 2021)

Parkinson's Disease

To discuss Parkinson's disease, we need to introduce one other actor to the schematic—the substantia nigra pars compacta (SNpc). The SNpc has a dopaminergic projection to the striatum. Dopamine has two receptors—D1 and D2. The D2 receptors are located on the projections of indirect pathway and are inhibitory. The D1 receptors are on the projections of the direct pathway and are excitatory (Fig. 9.5).

This results in the indirect pathway being more active than the direct pathway so that the brake is stuck in the "on" position. This leads to patient being somewhat frozen with a blank facial expression. The terminology can be confusing here. You will often here statements such as "dopamine drives movement" or that "dopamine increases the direct pathway." The wording here is complicated and needs an important clarification. While dopamine increases activity of the direct pathway, the direct pathway is inhibitory, so when the activity in the direct path is increased, we are really increasing the inhibition. Or put another way, dopamine drives movement, but it does this by leading to more inhibition coming out of the direct pathway (Fig. 9.6).

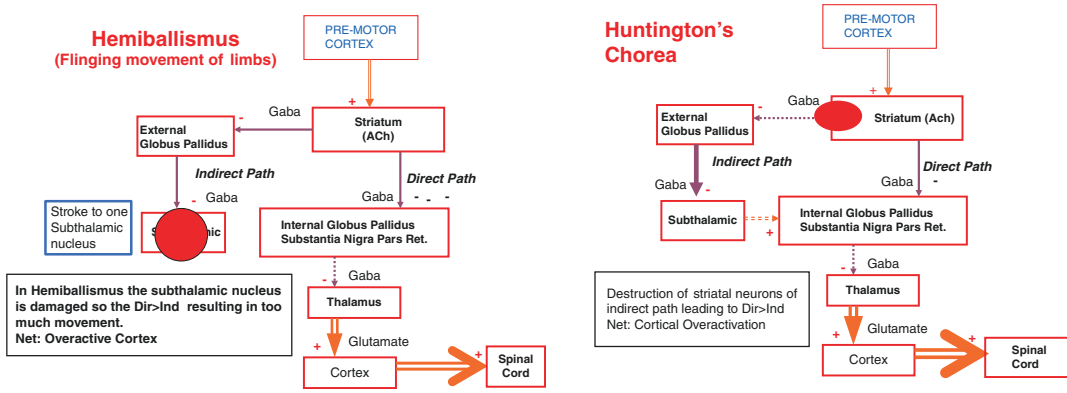

Fig. 9.4 Basal ganglia activity in hyperkinetic disorders. Panel A shows the activity in various structures in a patient with hemiballismus following a stroke to the subthalamic nucleus. Panel B shows the activity in structures of a patient diagnosed with Huntington's chorea. (Leo 2021)

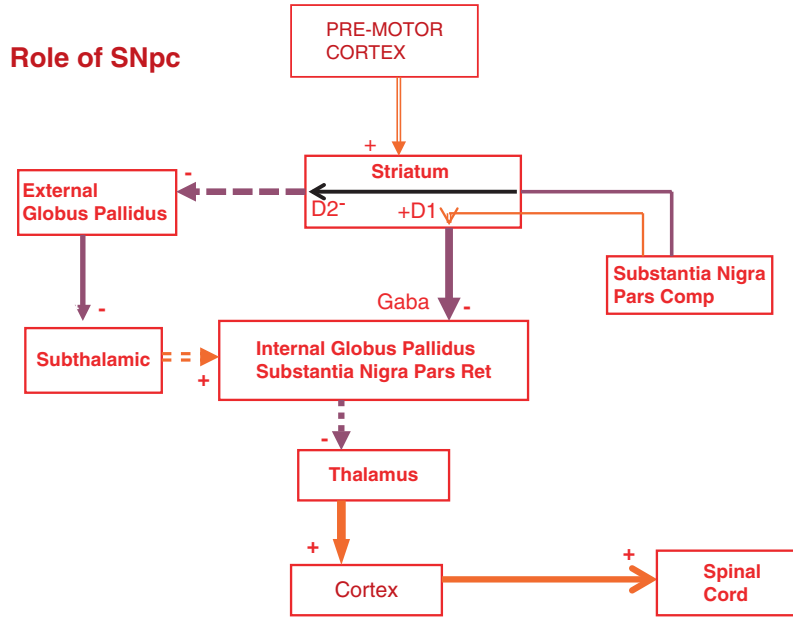

Fig. 9.5 Role of substantia nigra pars compacta in movement. Cells of the striatum have two types of dopamine receptors: D1 and D2. The D1 receptors are excitatory, while the D2 are inhibitory

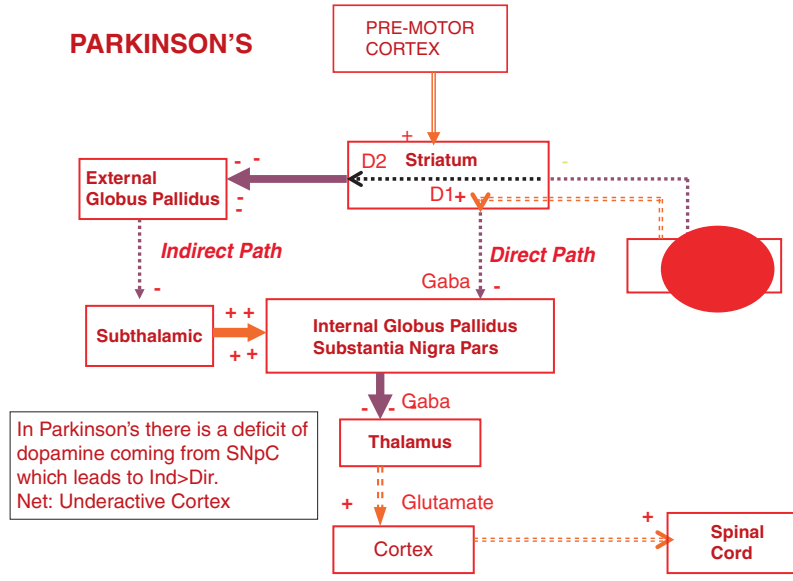

Fig. 9.6 Parkinson's symptoms result from loss of dopamine in substantia nigra pars compacta. (Leo 2021)

Acetylcholine and Parkinson's

Besides dopamine, when we talk about Parkinson's, we need to look at acetylcholine. Within the caudate there are cholinergic interneurons that along with the dopaminergic cells synapse with the projection neurons coming out of the caudate. These cholinergics are excitatory so they have the opposite effects of dopamine. If dopamine is depleted, then the cholinergics in the system will exacerbate the Parkinson's symptoms. Thus, in addition to trying to increase dopamine levels, another line of pharmacotherapy is to block acetylcholine (Fig. 9.7).

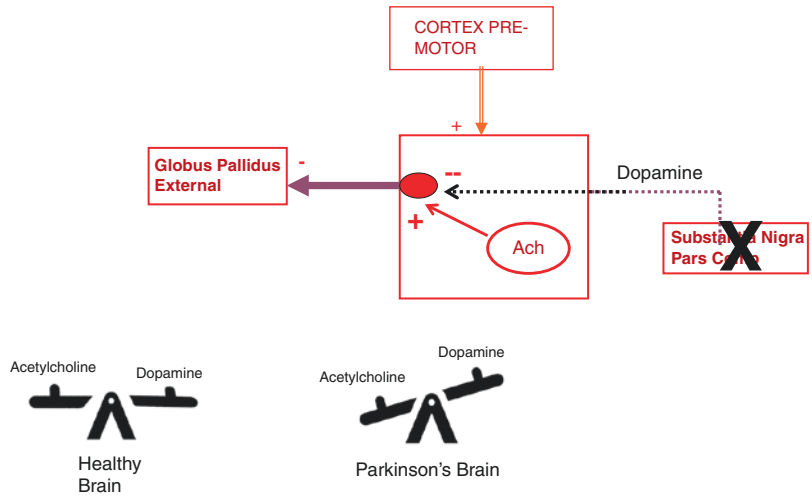

Fig. 9.7 Relationship of acetylcholine and dopamine in caudate. In Parkinson's patient there is a deficit in dopamine coming from SNpC leading to an imbalance with acetylcholine. (Leo 2021)

Glabellar Reflex

Parkinson's patients may have a positive glabellar reflex (Myerson's sign). When their glabella is tapped, they continue to blink their eyes. Healthy individuals will blink their eyes several times and then stop, while the Parkinson's patient will keep blinking for a much longer time.

Wilson's Disease

Wilson's disease, also known as hepatolenticular degeneration, is due to a genetic defect that leads to a pathological buildup of copper in the body. It usually presents in the mid-twenties to thirties. In the liver the copper buildup leads to cirrhosis; in the eye it leads to a buildup on the inner surface of the cornea and results in Kayser-Fleischer rings; and in the brain excess copper produces lesions in the putamen and globous pallidus. Wilson's patients have a characteristic wing-beating tremor, rigidity, and mental deterioration.

Various Basal Ganglia Pathology

Methanol poisoning attacks the putamen, optic nerves, and retina. Carbon monoxide poisoning is thought to damage the globus pallidus (although this is controversial). A stroke to one caudate nucleus will lead to chorea symptoms on the contralateral side of the body. Tourette's syndrome which is characterized as excessive speech and wild flinging movements of the limbs is thought to be related to a hyperkinetic disorder with pathology in the indirect pathway—the brake is off.

Parkinson's Medications

This book is not a pharmacology text, but because the drugs for Parkinson's tie into this subject, it seems appropriate to at least mention them. The goal of these medications is to either increase dopamine or decrease acetylcholine. A good mnemonic for these is *CARROT SALAD*.

COMT inhibitor (entacapone, tolcapone) COMT is one of the enzymes that breaks down dopamine, so naturally blocking it would lead to more dopamine present in the synapse.

Selegiline inhibits monoamine oxidase-B (MAO-B)

Anticholinergics (trihexyphenidyl) The anticholinergics block the cholinergic activity.

L-Dopa (carbidopa) inhibits the peripheral breakdown of L-Dopa so that more L-Dopa can cross the blood-brain barrier to enter the CNS.

Dopamine agonists (bromocriptine) increase dopaminergic activity.

Medial Pallidotomies and Deep Brain Stimulation

Imagine you are an enterprising neurosurgeon and pondering where to use ablation surgery to restore movement in a Parkinson's patient. If you turn to the schematic for the direct and indirect pathways, you would say to yourself: in a Parkinson's patient, the bake is overactive, so we should remove the brake which is the medial globus pallidus. It is the theory behind the direct and indirect pathways that gave rise to the use of *medial pallidotomies*. It is also the thinking that gives rise to deep brain stimulation for movement disorders. The stimulating electrodes are usually placed in either the medial globus pallidus or the subthalamic nucleus. One issue to point out is that while it is referred to as "stimulation," it is unclear if it is leading to more activity in the target, or if it is disrupting the target so that its firing is reduced.

Gaba, Barbiturates, and Benzodiazepines

Glutamate is synthesized to gaba by glutamate decarboxylase. Both the barbiturates and benzodiazepines stimulate the gaba receptor. In 1864, Adolf von Baeyer synthesized barbital which at first showed little promise, but after several tweaks, most notably by adding an amphetamine and renaming it as phenobarbital, it became a success. It subsequently went on to be prescribed for conditions such as insomnia, anxiety, neurosis, psychosis, and epilepsy. Its use peaked in the 1930s and 1940s, but by the 1970s, it was also increasingly being used as a recreational drug. Their side effects are magnified when mixed with alcohol. Because of their side effects and their abuse potential, they are used infrequently. Marilyn Monroe died from an overdose of barbiturates. In 1997, the Heaven's Gate Cult committed mass suicide in California by drinking a mixture of phenobarbital and alcohol.

As the barbiturates fell out of favor, they were replaced by benzodiazepines such as diazepam (Valium) and alprazolam (Xanax) which are prescribed for various conditions such as panic disorder, anxiety disorders, and insomnia. Valium was synthesized in 1963, and by the 1970s, it was one of the most prescribed medications in the country. Ten years later, it became clear that they also had serious side effects and were widely abused. As the benzodiazepines fell out of favor, new classes of medications with fewer side effects, such as D2 blockers (chlorpromazine), the tricyclics, and eventually the SSRIs, become available. The serious abuse problems and increasing evidence that large numbers of people became addicted to the barbiturates and benzodiazepines all led to congressional committees, lawsuits, investigative reports, and changes to medical education. Fast forward to the current time period, we are repeating history with the opioid epidemic, and the subsequent congressional committees, investigative reports, and subsequent changes to medical education.

The table above (9.1) shows the changes in various structures in Huntington's and Parkinson's patients. Words of warning: Do not panic at the sight of this table. There are certain facts in neuroanatomy that you should remember for the rest

Table 9.1 Summary of changes to basal ganglia structures in Parkinson's and Huntington's patients

	Parkinson's	Huntington's
Clinical presentation	Hypokinetic (overstabilization)	Hyperkinetic (tremor)
Cortex	Underactive	Overactive
Thalamus	Underactive	Overactive
GPI and SNpr (brake)	Overactive, more inhibition	Underactive, less inhibition
Subthalamic (turns brake on	Overactive	Underactive
GP external	Underactive	Overactive, more inhibition
Caudate/putamen	Decreased activity	Deficit (weakened projection to GP external
SNpc	Dopamine deficit	

of your career, such as the meaning of Babinski's sign. If I tap you on the shoulder 20 years from now and ask you the meaning of Babinski's sign, then you should be able to rattle it off without thinking about it. This summary table of the basal ganglia table is not like that. No one expects you 30 years from now to remember what exactly happens to the internal section of globus pallidus in Huntington's patients. Rather, I would look at the direct and indirect pathway with the table in front of you and compare what happens in these two patients. Make sure everything makes sense.

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Thalamus

10

Organization

The thalamus is an almond-shaped structure sitting atop the brainstem and nestled in at the center of the cerebrum. It is often referred to as the doorway to the cortex as everything, except olfaction, traveling up to the cortex goes through the thalamus. Think of the thalamus as acting like a flashlight which allows you to focus on important things while ignoring non-important things. Imagine sitting in a coffee shop reading this book, and there are all sorts of sensory inputs coming into your thalamus competing for the book's attention. There is the sound of people ordering, maybe there is a cold breeze that comes and goes as someone opens the door, there is the smell of the coffee and other odors in the air, and there are all types of interesting people coming and going in your visual fields. All this information is flooding your thalamus, but, presumably, you want to pay attention to what you are reading. Your thalamus, like a flashlight, focuses on the page in front of you and tries to ignore all the other sensory inputs. If someone comes rushing into the front door yelling, then your thalamus, or flashlight, is going to change its focus and shift to the person in the door.

Circuits

To diagram the thalamus, in the accompanying figure, we are going to pull out the thalamus and enlarge it. Running down the middle of the thalamus is a white matter bundle called the internal medullary lamina. It forms a Y shape at the anterior portion. Tucked in at the Y is the anterior nucleus of the thalamus which is involved with the limbic system. Along the medial side is the **dorsomedial (DM) nucleus**; on the lateral side, we have several nuclei. Going from anterior to posterior, we have **ventral anterior (VA)**, **ventral lateral (VL)**, **ventral posterior** divided into **ventral posterior medial (VPM)** and **ventral posterior lateral (VPL)**, and **pulvinar (PUV)**. Hanging off the back of the PUV are two knobs, the **lateral geniculate body (LGB)** and the **medial geniculate body (MGB)**.

Each of these nuclei has an input, coming from another region of the nervous system, and a corresponding projection to a region of the cerebral cortex (Fig. 10.1). Starting with the ventral tier, the first nucleus is the ventral anterior (VA). The VA receives information from the basal ganglia, and projects to the premotor cortex. Right behind the VA is the ventral lateral (VL) which receives information from the cere-

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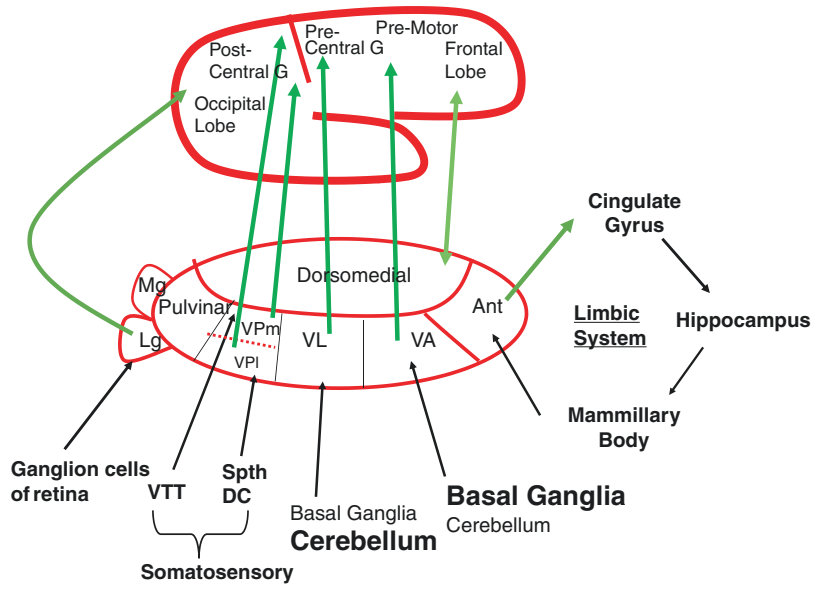

Fig. 10.1 Overview of the thalamus and its inputs and outputs. (Leo 2021)

bellum and projects to the primary motor cortex—the precentral gyrus. It makes sense for the basal ganglia to project to premotor cortex, when you consider that the basal ganglia are involved with taking the brake "off" several milliseconds before you move. Likewise, it makes sense that the cerebellum projects to the precentral gyrus since it is involved with ongoing movement. The VA and VL are often referred to as the motor thalamus.

Next in line are the VPM and VPL which receive the somatosensory information from the face and limbs. The spinothalamic and dorsal column/medial lemniscus pathways project to the VPL, while the ventral trigeminothalamic tract (VTT), coming from the trigeminal system, projects to the VPM. The VPL and VPM in turn project to the limb and face areas of the primary sensory cortex—precentral gyrus.

At the front of the thalamus is the anterior nucleus which is part of the Papez circuit and is discussed in the chapter on the limbic system.

The pulvinar is essentially a catchall for receiving information from various association areas. Not to downplay its function but it does not play a prominent role when it comes to understanding the various lesions. The lateral geniculate body (LGB) receives information from the retina, or more specifically the ganglion cells of the retina, and in turn projects to the occipital cortex. The medial geniculate body (MGB) receives information from the lateral lemniscus and is discussed with the auditory pathways.

The dorsal medial nucleus is the largest thalamic nucleus, and it talks to the frontal and limbic lobes. It is also discussed more in those two chapters.

The last nucleus to mention is the thin reticular nucleus, which surrounds the lateral side of the thalamus and resembles an eggshell. If the thalamus is the doorway to the cortex, the reticular nucleus is the security guard, controlling what information gets to go onto the cortex. Because the nucleus is long, thin, and surrounds the thalamus, it is hard to study. Especially when you consider that it's virtually impossible to find a patient with a lesion to the thalamic reticular nucleus that spares the surrounding structures.

Thalamic Pain Syndrome

The most important clinical scenario with the thalamus involves a lesion to the VPL and VPM. Both these nuclei receive blood from the

thalamogeniculate arteries (some books will mention the thalamoperforate arteries). A stroke in this region will lead to *thalamic pain syndrome*, also called *Dejerine-Roussy syndrome*. The initial symptom will be a loss of somatosensory sensation to the contralateral side of the body. However, after several days the symptoms will turn to intractable, excruciating pain emanating from THE contralateral side of the body. Pain relievers will typically not relieve the patient's symptoms.

Internal Capsule and Lacunar Infarcts

Sitting just medial to the thalamus is the internal capsule. The ascending and descending fibers to and from the cerebral cortex travel through the internal capsule which on horizontal section is V-shaped. The most important parts are the genu and posterior limb. The genu carries corticobulbar fibers destined for the cranial nerve nuclei, while the posterior limb carries corticospinal fibers (Fig. 10.2).

The easiest way to talk about it is to draw a stick figure with the head at the genu and the upper and lower limbs coming back into the posterior limb. Nestled in, medial to the posterior limb, is the thalamus. At the back of the thalamus are the medial and lateral geniculate bodies. The medial geniculate has fibers that head to the temporal lobe by going deep to the internal capsule—sublenticular. The lateral geniculate body has fibers that go behind (posterior) to the internal capsule—retrolenticular.

The internal capsule is especially susceptible to lacunar infarcts. The small vessels perfusing this region come off much wider arteries. In a hypertensive patient, these small arteries are under enormous pressure—imagine turning on a garden hose and winding down the sprayer to a pinhole with the water coming out a high pressure. Strokes in this area will lead to small areas of pathology—resembling a small lake—right around the compromised vessel.

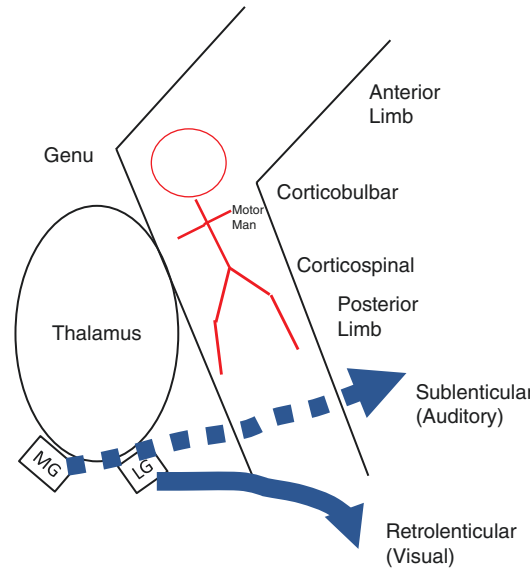

Fig. 10.2 Internal capsule and its relationship to the thalamus. Note that the corticobulbar fibers are in the genu, while the corticospinal fibers (motor man) are in the posterior limb. (Leo 2021)

Lateral Striate Arteries

There are several potential lesions in the area of the internal capsule and thalamus which can lead to various syndromes (Table 10.1). Lesions limited to the posterior limb can lead to "pure motor deficits" which are characterized by only motor symptoms, usually due to small infarcts in hypertensive individuals of the lateral striate arteries. The initial stroke might only lead to symptoms in one part of the body, say the upper limbs. But over time it is quite possible that pathology of more of these small arteries become involved with more parts of the body affected.

A lesion in the internal capsule will damage the UMNs, but it will also spare tracts in the spinal cord that are more involved with involuntary movements—such as reticulospinal and vestibular spinal. These patients with "capsular degeneration" will have some rudimentary movements. With their shoulder muscles, they can maneuver their upper limbs toward a kitchen shelf, but

Table 10.1 Lacunar infarcts: subtypes

Syndrome	Artery	Symptoms
Pure motor hemiparesis Posterior limb IC	Lateral striate A.	Hemiparesis of upper and lower limbs and face
Pure sensory syndrome VPL and VPM of thalamus	Thalamogeniculate A.	Sensory loss on the face, arm leg
Sensory-motor stroke Both IC and thalamus	Anterior choroidal A	Sensory and motor deficits on contralateral side

because their hands are more severely affected, they will have difficulty grabbing an item on the shelf. The same is true for their lower limbs. The UMN patient will be able to walk by swinging their lower limbs at the hip, but movement at the knees and especially their ankles will be weaker. When they walk, they will swing their lower limbs at the hip with their limb swinging laterally.

Thalamogeniculate Arteries

In a patient with a pure sensory deficit, such as thalamic pain syndrome, one possible location is in the thalamus, which would typically be due to deficits of the thalamogeniculate arteries.

Anterior Choroidal Arteries

Although it is rare, and the symptoms can vary from one patient to another, strokes to the anterior choroidal artery can compromise blood flow to the cerebral peduncle and the optic tract. Thus, the patient can have contralateral hemiplegia, and contralateral homonymous hemianopia. In some scenarios the thalamus can also be involved in which case the patients would have contralateral sensory deficits.

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Limbic Circuit and Lesions

11

Limbic Circuit

The limbic circuit, or Papez circuit, is a loop involving several subcortical structures that are involved in memory and emotions. Information from the hippocampus projects via the fornix to the mammillary bodies, then to the anterior nucleus of the thalamus via the mammillothalamic tract, which in turn projects to the cingulate gyrus, and then back to the hippocampus (Fig. 11.1).

Hippocampus

The most important structure is the hippocampus, which resembles a seahorse, and is located just caudal to the amygdala and forms the floor of the inferior horn of the lateral ventricle. It is thought that the hippocampus is neither the site nor the location of memories, but is involved with making memory circuits. The hippocampus includes the dentate gyrus and the cornu ammonis (CA) fields (CA1–CA3). The CA1 region or *Sommer's sector* appears to be the most sensitive region of the hippocampus to anoxia and other insults.

One of the more famous patients in neurology is Henry Molaison, usually referred to as HM. HM had intractable temporal lobe epilepsy, and in 1953, when he was 27 years old, his surgeon William Scoville removed both HMs medial temporal lobes. After the surgery HM had profound anterograde amnesia and could never make new memories. He did not have retrograde amnesia and could remember memories of his life before the surgery. For instance, he knew that Richard Nixon was the president at the time of his surgery, but he could never learn who the current president was. Much of what we know about memory came from HM, and his psychologist Brenda Milner who extensively documented his condition. HM lived until he was 82 years old.

In Alzheimer's disease plaques and tangles first appear in the hippocampus. In the early stages of the disease, the patients have difficulty with anterograde memory—they cannot make new memories. Memories from their past tend to be intact. For instance, a 70-year-old patient cannot tell you what they had for breakfast earlier in the day, but they can tell you who was in their first grade class.

Both late-stage Parkinson's and Alzheimer's patients share some characteristics. Both can have memory problems and motor deficits. One way to think about their progression is that Alzheimer's is a descending disease. It starts in the cerebral cortex with subtle memory deficits. As the disease progresses, the pathology moves into other structures, and the patient can start to exhibit motor deficits. Parkinson's on the other hand is an ascending disease meaning that it starts in the midbrain with subtle motor deficits. As the disease pro-

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gresses, the pathology is evident in higher brain centers, and the patient exhibits memory and cognitive deficits.

Fornix

The fornix is the outflow tract of the hippocampus. It starts as the fimbria which is a white band of myelinated fibers forming a band of fibers called the **crus**. The two crura are situated on the roof of the lateral ventricles (posteriorly) and come together as the body of the fornix which sit side by side over the thalamus. The body of the fornix descends and separates into the **columns of the fornix,** located caudal to the anterior commissure. They then curve back through the hypothalamus to their major destination, the mammillary bodies.

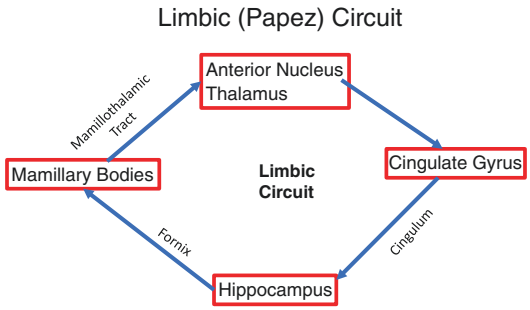

Fig. 11.1 Overview of the limbic circuit

Wernicke-Korsakoff's

Wernicke-Korsakoff's results from a thiamine (vitamin B1) deficiency that leads to degeneration of the mammillary bodies, the mammillothalamic tract, and the anterior and dorsomedial nucleus of the thalamus. Think of this as a two-step disease. Wernicke's is the first part and consists of a triad of symptoms: ophthalmoplegia, ataxia, and confusion. If Wernicke's is left untreated, it will often move into the next stage. Korsakoff's patients exhibit anterograde and retrograde amnesia, and tend to confabulate or make up stories. To remember it, think of a coat rack (Fig. 11.2).

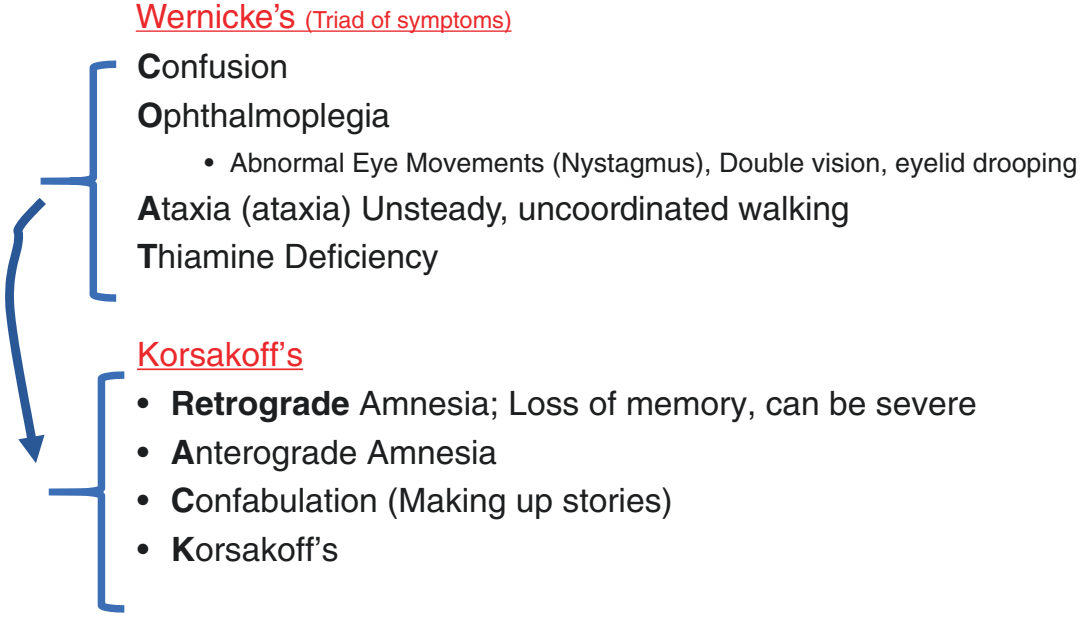

Fig. 11.2 Wernicke-Korsakoff's. In the typical scenario, the patient starts off with Wernicke's, which is potentially treatable. Left untreated, patient moves to Korsakoff's

Kluver-Bucy Syndrome

Kluver-Bucy syndrome, which exists mostly in textbooks, or board exams, results from a bilateral lesion to the medial temporal lobe. It is extremely rare in humans. The patients will exhibit hypersexuality with no preference for gender, they will be placid and show little fear response, and they tend to put objects into their mouth—hyperorality.

Amygdala

The amygdala is a major player in how we respond to emotions, mainly fear. Imagine walking down a path and you almost step on a snake. Your fear response will kick in; you will probably step back, maybe scream, and possibly run in the other direction. Several seconds later you might logically conclude that it was only a garter snake which poses no threat. You owe your immediate fear response to your amygdala, which sent information directly to your cerebral cortex, bypassing your thalamus. But then, several seconds later, your cortex decided that the threat was not that threatening, and you relaxed. The amygdala is one of the major structures thought to be involved in PTSD. An overactive amygdala is also thought to be responsible for many of the behaviors in patients with anxiety disorders. The term "amygdala hijack" refers to how in certain stressful situations the amygdala takes over. Imagine driving through town, you get cut off, and you make an unwanted gesture to the driver. However, a minute or two later, you immediately regret your response—maybe it was your grandmother who cut you off. Your amygdala was responsible for the sudden, impulsive outburst, while the delayed, more contemplative response came from your prefrontal cortex.

The amygdala is a solid mass of gray matter—think of a soccer ball—and lies in the temporal lobe, deep to the uncus and just rostral to the hippocampus, which some have said looks like a cat's paw. To identify these two structures on a coronal section, think of a foot (hippocampus) kicking a soccer ball (the amygdala). In coronal sections you might get a brain slice through just the amygdala (the ball), or a cut through just the hippocampus (the foot), or possibly a cut through both. If the cut happens to be through both, it will likely be through the point where the foot is kicking the ball, with the posterior edge of the amygdala, and anterior part of the hippocampus in the same slice. Fibers from part of the amygdala project via the stria terminalis to the anterior hypothalamus, preoptic area, and the hypothalamus. The stria terminalis lies medial to the caudate nucleus.

Hippocampus, Amygdala, and Orbitofrontal Cortex and Memories

When you see a picture of an apple, there are all kinds of memories that can be evoked. On a somewhat superficial level, you remember how the shiny skin of the apple feels, you remember what it smells like, and you remember the slightly crunchy feeling of biting into it. But the apple might also elicit more emotional memories: like your grandmother, and her apple pies; or fall days, drinking cider; or your childhood, eating applejack cereal; or, if you have the right brand, you might even think about your cell phone or your computer. It is thought that the sensory information about "the apple" came into your prefrontal cortex, and then projected to the hippocampus which packaged all these memories into circuits and sent the circuits back to the frontal lobe and other regions for storage. The amygdala comes into play for the emotional part of the memories and seems to be especially important in warning us about dangers in the environment (Fig. 11.3).

Proustian Moment

One of the more famous insights into memory and its close relationship to olfaction came from Marcel Proust, who in 1907 observed that certain odors trigger autobiographical memories. He noticed that a certain kind of desert (Madeline

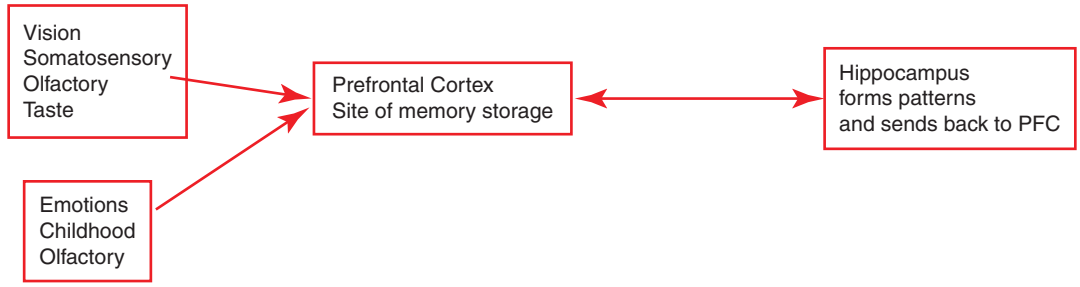

Fig. 11.3 Simplified overview of structures involved with memory. (Leo 2021)

cakes) triggered memories about his aunt. For a modern reference to the Proustian moment, see the 2019 movie *Ratatouille*, in which the snobby restaurant critic, who is used to upscale French cooking, is given the simple dish of Ratatouille, the French version of a simple stew. At first, he is aghast at the idea of such a simple dish, but the first taste releases a flood of happy childhood memories and he is won over.

Mesolimbic Pathway

The mesolimbic pathway includes several nuclei, but the most important one is the ventral tegmental area (VTA) located in the midbrain and its dopaminergic projection to the nucleus accumbens in the basal forebrain. This is the hypothesized "reward pathway" and is thought to be essential to monitoring pleasurable activities. In a sense, during a normal day, we are doing our best to accommodate this pathway. We start off with our coffee, which increases dopamine; we then drive to work with the music on, which increases dopamine; maybe we have a midmorning chocolate bar snack, which increases dopamine; maybe we have a beer later that night, which increases dopamine; and the list goes on. Life is all about dopamine, but too much dopamine can be problematic.

Dopaminergic Medications and Schizophrenia

Drugs or medications, such as cocaine and amphetamine, which increase dopamine levels are thought to act on the mesolimbic pathway and can lead to psychosis. Both amphetamine and cocaine block the reuptake of dopamine, while amphetamine also promotes the release of dopamine. On the other hand, drugs that block dopamine receptors in the mesolimbic system decrease psychotic symptoms,

The *dopamine hypothesis of schizophrenia* is the idea that schizophrenia results from excessive dopaminergic activity. This is the opposite of Parkinson's patients who have too little dopamine. However, it is not just the dopamine *levels* that are important; it is *where* in the brain the dopamine is altered. The dopamine depletion in Parkinson's is found in the substantia nigra or the nigrostriatal pathway, while the hypothesized excess of dopamine in schizophrenia is in the mesolimbic pathway (Fig. 11.4).

The first generation of antipsychotics, such as chlorpromazine (Thorazine), blocked D2 dopaminergic receptors and reduced psychotic symptoms in patients diagnosed with schizophrenia. Their efficacy was thought to be due to acting on the mesolimbic pathway, while the motor side effects were thought to be due to its action on the nigrostriatal pathway. Thus, the dilemma of the medication: The increased dopamine, is responsible for both the efficacy and the side effects.

When talking about the motor side effects of the antipsychotics, there are two important terms. *Tardive dyskinesia* refers to involuntary repetitive movements such as eye blinking and facial grimaces. *Akathisia* refers to an unpleasant sensation of restless that makes it hard to sit still. The patient reports the need to pace back and forth.

How do you block dopamine where it is in excess while increasing it where it is in short supply? One theory is that this is accomplished

by the second-generation antipsychotics, also referred to as the *atypicals,* such as Risperdal and Seroquel, which act on both D2 and 5-HT2A receptors. To explain the mechanism of these drugs, we need to look at the dorsal raphe serotonergic projection to the striatum and substantia nigra. Along the way to the striatum, the dorsal raphe sends collaterals to the substantia nigra. This projection acts on the 5-HT2A receptors which are inhibitory to the substantia nigra; thus, the dorsal raphe is acting like a brake on the substantia nigra's projection to the striatum. One of the actions of the second-generation antipsychotics is to block this receptor, so it will take the brake off this pathway and increase dopamine coming out of the nigrostriatal pathway. Granted, this seems somewhat counterintuitive, because at the same time the medication also blocks dopamine at the substantia nigra terminals.

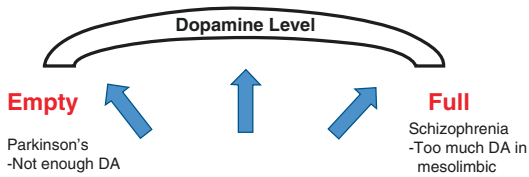

Fig. 11.4 Simplified overview of dopamine. Parkinson's patients have lost dopamine levels in the substantia nigra. Dopamine theory of schizophrenia attributes condition to an excess of dopamine in the mesolimbic pathway. (Leo 2021)

How can a medication which increases dopamine at one receptor and decreases dopamine at another receptor have a net change? After all, it seems that the two actions would balance each other out, with no net impact on dopamine levels. However, what is thought to happen, or hypothesized, is that in different regions of the brain, there are different ratios of these two receptors, allowing the drug to have different effects in different regions based on these ratios—it can increase dopamine in one region while decreasing it in another (Fig. 11.5).

In summary, the first-generation antipsychotics act on the D2 receptor, which leads to decreased dopamine in the mesolimbic pathway, responsible for the medication's efficacy, but also leads to decreased dopaminergic activity in the nigrostriatal pathway, responsible for the medication's side effects. The second-generation medications, or least one hypothesis of their mechanism of action, act to decrease the activity in the mesolimbic pathway, leading to its efficacy, while also increasing the activity in nigrostriatal pathway by acting on D2 and 5-HT2A

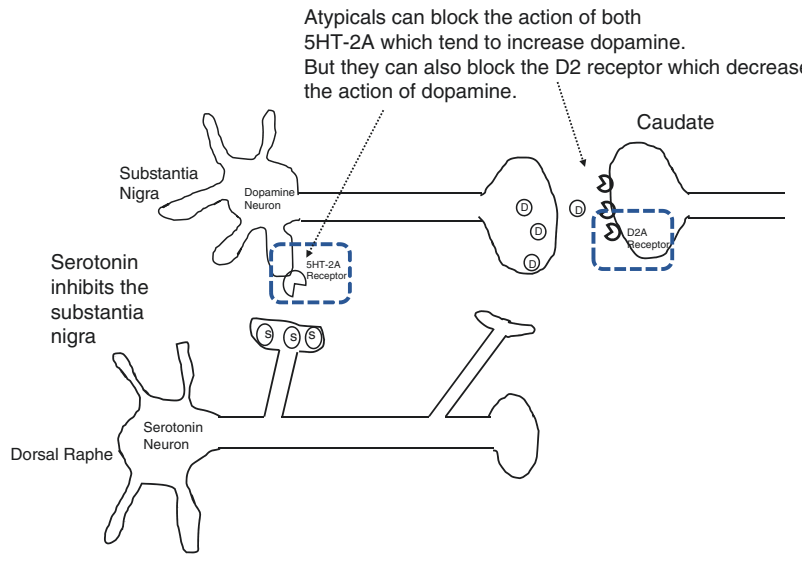

Fig. 11.5 Overview of dorsal raphe connection to substantia nigra. Serotonin released from the dorsal raphe inhibits the release of dopamine from the substantia nigra. Atypicals can block the action of serotonin. The overall action of dopamine would depend on the ratio of the two receptors. (Leo 2021)

receptors, and thus minimizing the side effects. Keep in mind this is an overly simplistic notion but provides the basis for understanding the ideas behind how the neuroanatomy, neurophysiology, neuropathology, and neuropharmacology work together.

Chemical Neuroanatomy of the Brainstem

There are several nuclei in the brainstem with widespread projections to cortical and subcortical regions. For memorizing the clinical neuroanatomy, the projections are the simple part, because they simply go to large portions of the cerebral cortex and many of the subcortical structures—in short, they go all over the place. The more complicated aspect is the function of their neurotransmitters, and how these various nuclei are implicated in various behaviors and psychological conditions. The explanations below are all overly simplified (Fig. 11.6).

The **locus coeruleus** is in the pons near the floor of the fourth ventricle and is the main site of *norepinephrine*. It is thought to be involved in arousal, alertness attention, and the stress response. Attention Deficit Hyperactivity Disorder (ADHD) is thought to be due to alterations in the locus coeruleus. The synthesis of norepinephrine starts with tyrosine, which is converted to dopa by tyrosine hydroxylase. Dopa is then converted to dopamine by dopadecarboxylase. In sympathetic neurons, dopamine is then converted into norepinephrine by dopamine B-hydroxylase. In the adrenal medulla, norepinephrine will be converted into epinephrine. All three, dopamine, epinephrine, and norepinephrine, can be broken down by catechol-O-methyltransferase (COMT) and monoamine oxidase (MAO) or taken back up in the nerve terminal by their respective reuptake transporter.

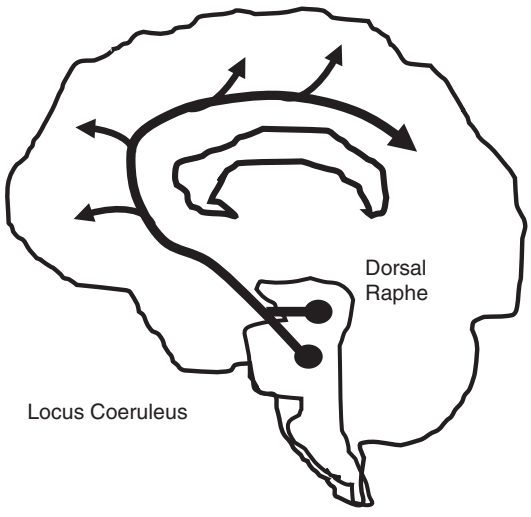

Fig. 11.6 Overview of dorsal raphe and locus coeruleus locations and projections. (Leo 2021)

COMT is located principally in postsynaptic terminals. There are two forms of MAO both which are located in the outer membrane of mitochondria of nerve terminals and glia. MAO-A is in noradrenergic and dopaminergic terminals, and MAO-B is located in serotonergic terminals.

The **dorsal raphe** is a subdivision of the reticular formation and uses *serotonin*; thus, it is thought to be involved in clinical depression. The synthesis of serotonin starts with tryptophan which is metabolized to 5-hydroxytryptophan by tryptophan hydroxylase (rate-limiting step), and then to serotonin by 5-hydroxytryptophan decarboxylase. Serotonin is then taken back up in the presynaptic cell by the serotonin reuptake transporter (SERT). In the presynaptic cells, serotonin is transported into vesicles by the vesicular monoamine transporter (VMAT) and stored until needed.

The dorsal raphe has also been implicated in the descending pain pathway. It has an excitatory serotonergic projection to enkephalin interneurons in the dorsal horn. These enkephalin interneurons are in turn inhibitory to the primary afferents.

The **periaqueductal gray (PAG)** surrounds the cerebral aqueduct and is also involved in the descending control of pain. Intuitively, it makes sense to think of pain as a signal coming in from the periphery to higher centers, but there are also descending pathways involved in the pain response. These pathways can either heighten or lessen pain perception.

The PAG sends a descending projection down to the rostral ventral medulla (RVM)

which in turn projects down to the dorsal horn of the spinal cord. Its descending pathway uses endogenous opioids to inhibit the incoming pain pathways. The endogenous opiates such as enkephalins, B-endorphins, and dynorphins are found in high concentrations in the structures involved in the descending control of pain.

The reticular activating system (RAS) projects to the cortex, thalamus, and hypothalamus. It is a mix of cholinergic and adrenergic neurons and is involved in maintaining alertness. Bilateral lesions result in coma.

The **area postrema** is in the medulla near the vagal trigone at the base of the fourth ventricle. The endothelial cells in this area lack tight junctions, which enables it to monitor the bloodstream. It is involved in the vomiting response.

The **pedunculopontine nucleus,** along with the nucleus basalis of Meynert, is a source of cholinergic projections to higher cortical areas and is thought to be involved in both Alzheimer's and Parkinson's patients.

Reuptake Transporters

When it comes to medications, the three neurotransmitters dopamine, serotonin, and norepinephrine are intimately related, largely due to their reuptake transporters. Each transmitter has a specific transporter: norepinephrine, NERT; dopamine, DAT; or serotonin, SERT. There is considerable overlap between reuptake and conditions. Wellbutrin (bupropion) inhibits the NERT and DAT and is used as an antidepressant but is also prescribed for smoking cessation; reboxetine inhibits NERT and is also used as an antidepressant; duloxetine (Cymbalta) is another antidepressant that blocks NERT but is also prescribed for urinary incontinence; venlafaxine (Effexor) is an antidepressant but also prescribed for ADHD and inhibits NERT and SERT; and the SSRIs such as Prozac, Paxil, Zoloft, and Celexa are antidepressants and block SERT; and last but not least is Strattera which blocks NERT is prescribed for ADHD—it was not effective in clinical trials for depression (Table 11.1). The take-home point is that there are no strict lines of demarcation between conditions and mechanism, but instead there is significant overlap between conditions and medications.

Table 11.1 Summary of medications acting on reuptake transporters

Medication	Reuptake transporter	Conditions
Imipramine (Tofranil)	NERT, SERT	Antidepressant
Wellbutrin (bupropion)	NERT, DAT	Antidepressant Smoking cessation
Reboxetine (Edronax)	NERT	Antidepressant
Duloxetine (Cymbalta)	NERT, SERT	Antidepressant Urinary incontinence
Venlafaxine (Effexor)	NERT, SERT	Antidepressant ADHD
Prozac, Paxil, Zoloft	SERT	Antidepressant
Atomoxetine (Strattera)	NERT	ADHD

Chemical Imbalance Theory of Depression

The chemical imbalance theory of depression postulates that depression is due to low levels of catecholamines. It was first formulated in 1965 based on the observations that changes in behavior resulted from the administration of various drugs that altered catecholamine levels. It was noted that drugs that decreased catecholamines had a sedating effect, while drugs that increased catecholamines had an energizing effect. Observations on the three drugs below formed the keystone of the theory:

1. Iproniazid was first used to treat TB patients, but it was also noted that it had a calming effect. At the time, the mechanism was not known, but it was eventually discovered that iproniazid blocked MAO.

2. Imipramine, the first tricyclic, was first used as an antihistamine when it was discovered that it had an energizing effect and that it blocked the norepinephrine reuptake transporter leading to increased levels of catecholamines.
3. Reserpine was first given for hypertension, and it was observed that it had a sedating effect on rabbits. The sedating effect came from increasing serotonin levels by binding to VMAT and blocking the reuptake of serotonin into the vesicles.

The theory was eventually refined to the idea that the most important catecholamine was serotonin. *Serotonin syndrome* results from overactivation of the serotonin receptors leading to tremors, hyperreflexia, rigidity, tachycardia, and hypertension.

Psychedelics and the Serotonin 5-HT2A Receptor

The psychedelics or hallucinogens are powerful mood-altering drugs that act to increase serotonin levels in the brain by agonist activity at the 5-HT2A receptor which is located on the postsynaptic cell at serotonergic synapses. The 5-HT2A receptor is found in several regions of the brain, but the main action of the psychedelics is thought to be the pyramidal cells located in layer V of the prefrontal cortex. The psychedelics are commonly used as recreational drugs, while their legitimate use for medical conditions is debated.

LSD (lysergic acid diethylamide) became famous in the 1950s as one of the first hallucinogenic drugs. It was originally investigated by the CIA, US Army, and medical organizations but currently is not an active area of investigation by the National Institutes of Health (NIH).

Psilocybin is a recreational hallucinogen found in certain mushrooms that increase serotonin levels. It has been tested for medical use in depression and anxiety, but it is not approved at this time.

MDMA (3,4-methylenedioxymethamphetamine, ecstasy, molly) acts to increase levels of serotonin, dopamine, and norepinephrine, giving it the effect of both psychostimulants and hallucinogens. The dopamine increase is thought to be responsible for increased energy, the norepinephrine for increased heart rate and blood pressure, and serotonin for the increased sexual arousal and emotional closeness. It is currently licensed for limited use in psychotherapy. Among psychopharmacologists, there is debate about whether MDMA should be classified as a psychedelic or not.

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How the Brain Works: LTP, NMDA, and NO

12

Long-Term Potentiation and Learning, or How the Brain Works

In 1949, before we had any high-tech technology, molecular biology (Watson and Crick presented the double-helix model of DNA in 1953), or knowledge of the workings of the brain, Hebb proposed that learning takes place in the synapse. He proposed that when associations are made in our mind, it is because neurons fired together, which resulted in strengthened synapses. For example, when a dog hears a bell, there is no obvious reaction in the dog, but when you sound a bell, and give the dog food, there will be a reaction. Eventually, the dog will learn that bell and food go together, so that when the bell is rung, the dog will react.

When Hebb proposed the idea of strengthening synapses as the key to learning, he did not know what those changes could be, but he and others postulated that there could be (1) presynaptic changes, possibly more glutamate released from presynaptic cell; (2) postsynaptic changes, possibly more receptors moved to the postsynaptic membrane; or (3) extrasynaptic changes, maybe alterations in the ability of cells such as astrocytes to reuptake neurotransmitter from the synaptic cleft. He also pointed out that for presynaptic changes to occur, the postsynaptic cell would have to be able to send a signal back to the presynaptic cell. He referred to this proposed molecule as a **retrograde messenger**. At the time, scientists did not know what that retrograde messenger might be, but they knew that whatever it was, it had to act extremely fast (Fig. 12.1).

In the 1970s an experimental model of isolated rabbit hippocampal slices in a petri dish was developed as a model for learning and memory. Figure 12.2 shows three neurons involved in the model—two presynaptic neurons and one postsynaptic neuron. In each of the two presynaptic cells (imagine one being the bell and one being the food), they placed stimulating electrodes, and in the single postganglionic cell, they placed a recording electrode. Over several hours they fired one of the stimulating electrodes (neuron #1, the bell) and established a baseline of activity in the postsynaptic cell. They then fired neurons #1 and #2 (bell and food) together and increased the activity in the recording electrode. They then waited several hours and fired neuron #1 and observed that there was increased activity in the recoding electrode. In other words, by pairing the two neurons together,

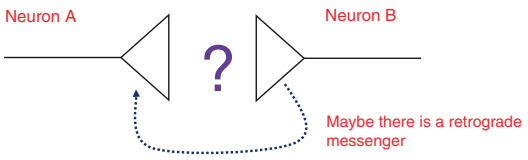

Fig. 12.1 Hebb's theory. Hebb proposed that when two neurons fire together, something happens at the synapse. To strengthen the synapse so that neuron A's efficiency is increased. This theory suggests that there is some sort of retrograde messenger

J. Leo, *Medical Neuroanatomy for the Boards and the Clinic*,
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they had increased the strength of the synapse. At this point it was still not clear how the synapse was strengthened.

NMDA and AMPA Receptors

In the 1980s, an unusual aspect of glutamate and its receptors was discovered that is thought to play a role in LTP. There are two types of glutamate receptor: NMDA and non-NMDA (or AMPA receptor). The AMPA receptor is ligand gated meaning that glutamate binds to it, the channel opens, and Na^+ enters the cell. The NMDA receptor is ligand and voltage gated meaning that it needs the combination of a ligand binding, plus a large enough voltage change to open the channel. At rest, Mg^{2+} blocks the channel. The voltage change moves the Mg^{2+} out of the channel. When the NMDA receptor opens, it allows Ca^{2+} to enter the cell.

In the petri dish example above when neuron #1 fires, just the AMPA receptor opens. Because there is an insufficient voltage change, the NMDA receptor does not open. When neurons #1 and #2 fire, the voltage change is sufficient to also open the NMDA receptor.

If we look close at the postsynaptic cell membrane, we can see that when just the bell fires, then neuron #1 is firing while neuron #2 is quiet (Fig. 12.3). This leads to glutamate binding to only half the AMPA receptors. With only half the AMPA receptors occupied, there is not enough voltage change to open the NMDA receptor.

When the neuron #1 and neuron #2 fire, then all the AMPA receptors are occupied, there is a voltage change in membrane, and the Mg^{2+} blocker is moved out which allows calcium to enter the cell. This increase in intracellular calcium can lead to multiple effects in the postsynaptic cell. After many experiments it was determined that a critical step is the activation of nitric oxide synthase (NOS) which produces nitric oxide (NO). Nitric oxide is a gas and can diffuse back very quickly to the presynaptic cell making it the perfect candidate for the long-postulated and sought-after retrograde messenger (Fig. 12.4).

Endothelial-Derived Relaxing Factor = NO

The following explanation is somewhat of a historical note, but it also ties in neuroscience with cardiology. Before scientists used the name nitric oxide, it had another name: **endothelial-derived relaxing factor (EDRF)**. The name EDRF comes from the fact that in preparations of capillaries in a petri dish, if acetylcholine was added to the preparation, it would lead to vasodilation, with an

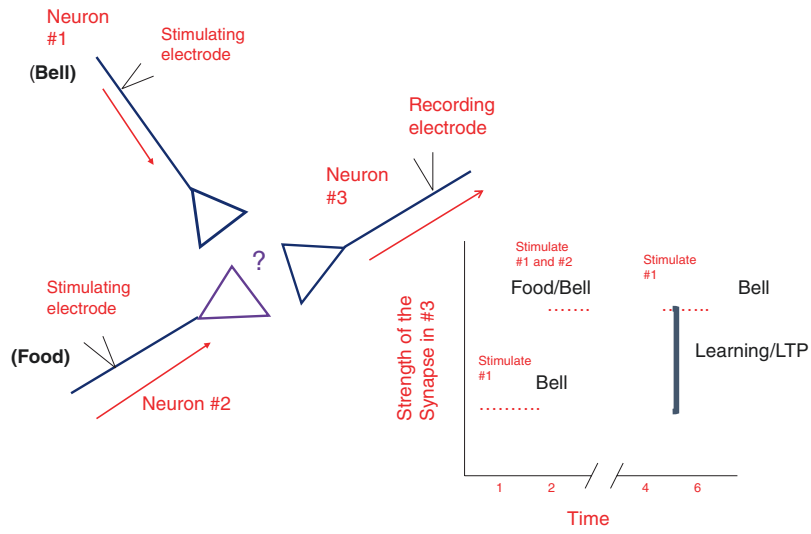

Fig. 12.2 Simplified version of LTP with an analogy to Pavlov's dogs. Neurons #1 and #2 have stimulating electrodes, while recordings are made in neuron #3. See text for details. (Leo 2021)

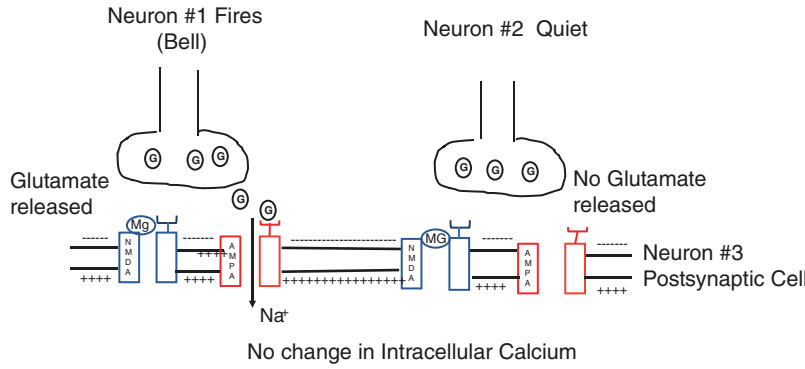

Fig. 12.3 Low-level stimulus—the bell. When only neuron #1 fires, there is not enough voltage change to move Mg^{2+} out of the NMDA channel on the postsynaptic cell. The open AMPA receptor allows Na^{+} to enter the cell but Ca^{++} is blocked. (Leo 2021)

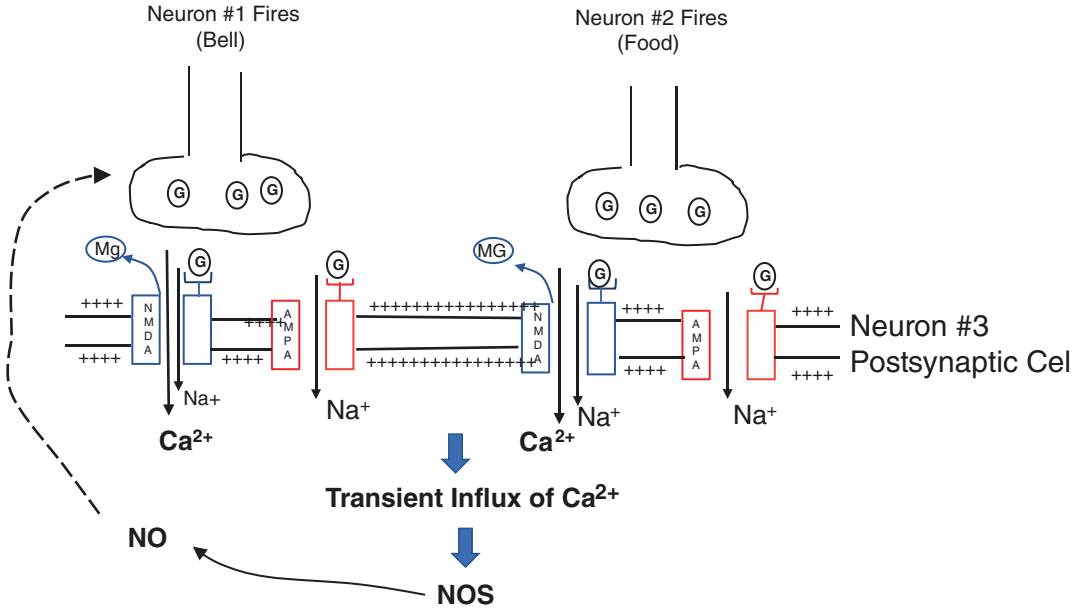

Fig. 12.4 More stimulus—bell and food. When neurons #1 and #2 fire together, the voltage change moves Mg^{+} out of the NMDA channel on the postsynaptic cell. This along with glutamate binding to the NMDA receptors allows Ca^{2+} to move through the channel, increasing intracellular Ca^{2+} concentration, which can bind to NOS to produce NO which acts as retrograde messenger. (Leo 2021)

important caveat—endothelial cells also had to be present. If the endothelial cells were removed, then acetylcholine lost its ability to vasodilate. In other words, scientists knew there was something—but they didn't know what—that was derived from endothelial cells that led to vasodilation, thus the name EDRF. It was eventually shown that this hypothesized EDRF was indeed NO. Robert Furchgott and Louis Ignarro won the Nobel Prize for this, a finding which eventually led to the development of Viagra. Viagra acts on the NO pathway to lead to vasodilation.

Nitric Oxide: The Good, the Bad, and the Ugly

The flip side to the beneficial side of nitric oxide in learning and development is that cell death which goes by many names is all based on the fact that too much NO can lead to cell death. When it comes to neuronal damage, you will hear the terms glutamate toxicity, calcium toxicity, excitotoxicity, and free radical-induced damage. They all relate to the idea that too much NO leads to cell death. Immediately after a stroke, there is

a pocket of initial neuronal damage, but over time there is a wave of cell death that spreads out from this initial damage. As cells die, they release their contents and flood the microenvironment with glutamate. This excess glutamate then overloads the neighboring cells which leads to calcium flooding the cell, activation of NOS, and in turn overproduction of NO, and a spreading wave of cell death. This is one reason that patients in the ER who have just had a stroke are given Mg^{2+} to block the NMDA receptor. Pharmaceutical companies are naturally trying to develop treatments to block this wave of cell death following a stroke. NMDA receptor channel blockers for stroke patients are an active area of research but so far have failed to yield positive studies.

Because disruption of the NMDA/NO pathway has been implicated in so many pathologies, there are several medications already in use. For instance, memantine, a NMDA receptor blocker, is given to Alzheimer's patients to balance glutamate levels. Ketamine is an NMDA agonist and is used as sedative, or off-label antidepressant, or in some cases as a hallucinogenic drug.

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Brainstem Lesions

13

Now that we have talked in depth about cranial nerves and several other pathways, we are going to go back to the brainstem to look at some details. For the brainstem lesions, you want to make sure you understand (1) why the patient exhibits various signs and symptoms, (2) which artery is affected, and (3) the specific circuits for each compromised tract. In addition, for any given structure, you want to pay attention to its neighbors. Not every syndrome is a textbook scenario. Tumors for instance can start off small and then expand over time and compress neighboring structures. At this point in your studies, you are much better off understanding the concepts than just memorizing lists of symptoms that go along with syndromes.

Alternating Hemiplegia

If you see a patient with alternating motor deficits, such as hemiplegia on one side and a cranial nerve motor deficit on the opposite side, then you think about the brainstem as a possible site for the lesion. To explain this, we need to relate the UMNs in the corticospinal and corticobulbar tracts to the LMNs of cranial nerves. As the corticobulbar and corticospinal tracts descend through the brainstem, they cross the LMNs coming out of the various nuclei.

Think of the cranial nerve nuclei and their LMNs as being stacked up on a ladder. At the bottom of the ladder, the medulla, is the LMN of CN 12. In the middle of the ladder, the pons, is the LMNs of CN 6 and CN 7. And on top of the ladder, the midbrain, is the LMN of CN 3. Also running down the brainstem is the corticospinal tract sending information to the spinal cord, and this tract runs right next to the LMNs of these cranial nerves. In the picture below, you can see the UMN fibers of the corticobulbar tract crossing the LMNs of CNs 3, 6, and 12 (Fig. 13.1).

Inferior Alternating Hemiplegia

Let's start with a lesion in the medullary pyramid. A lesion to the pyramid will result in contralateral UMN signs to the limbs since the lesion is above the motor decussation. But running immediately lateral to the pyramid are the LMNs of the hypoglossal nerve that came out of the hypoglossal nucleus. And the same lesion will lead to an ipsilateral loss of cranial nerve twelve. Consider the patient's presentation and your thought process. If you saw a patient with a dense hemiplegia to the limbs on one side, you would be tempted to think of the cervical cord as a potential site of the lesion, but if you see a tongue deficit on the opposite of the hemiplegia, then you immediately think of the brainstem. How high up on the ladder are you? You are at the level of the nerve that is on the opposite side of the hemiplegia. In this case, it is at the level of 12. The isolated CN deficit tells you the level of the lesion.

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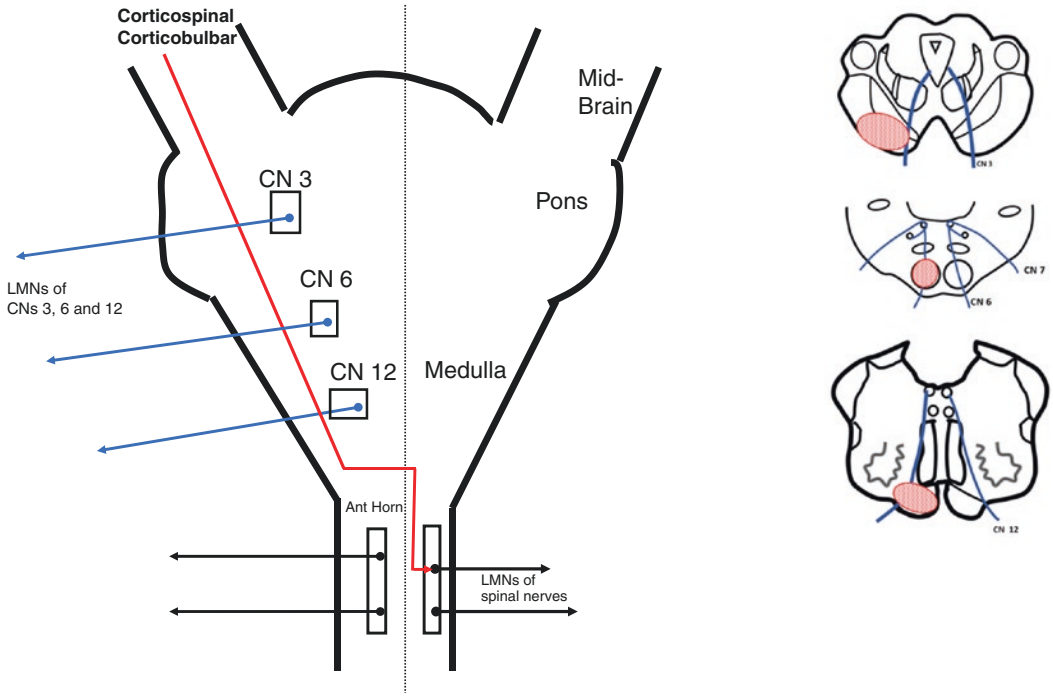


Fig. 13.1 Relationship of corticobulbar pathway to LMNs of cranial nerves 3, 6, and 12. (Leo 2021)

The term *inferior alternating hemiplegia* aptly explains the syndrome of a cranial nerve 12 deficit on one side and UMN signs from the neck down on the contralateral side. It is *inferior* because it is in the medulla. The most common scenario for this lesion would be an occlusion of the anterior spinal artery which leads to medial medullary syndrome. In addition to the inferior alternating hemiplegia, the occlusion usually compromises the medial lemniscus which would lead to a contralateral loss of dorsal columns (vibration, proprioception, two-point discrimination) (Fig. 13.2).

Middle Alternating Hemiplegia

We are moving the lesion up the ladder to the pons. In this case, the lesion will compromise the LMNs of CN 6 and the corticospinal and corticobulbar tracts. This leads to an ipsilateral medial strabismus, and contralateral upper motor neuron signs to the limbs. Again, if you see a patient with a hemiplegia on one side, and just one, or maybe two, cranial nerve defects on the contralateral side, then you think alternating hemiplegia, and the lesion will be at the level of the cranial nerve deficit, which in this case is CN 6, which is in the caudal pons, thus the term middle alternating hemiplegia (Fig. 13.3).

Superior Alternating Hemiplegia

We are now moving the lesion up the ladder to the midbrain where it damages the corticospinal and corticobulbar tracts and the LMNs of cranial nerve three. The patient will have an ipsilateral lateral strabismus and contralateral UMN signs—hemiplegia—from the neck down. This is usually the result of a stroke in branches of the posterior cerebral artery as it wraps around the cerebral peduncle (Fig. 13.4).

All three alternating hemiplegic patients, superior, middle, and inferior, have the same signs

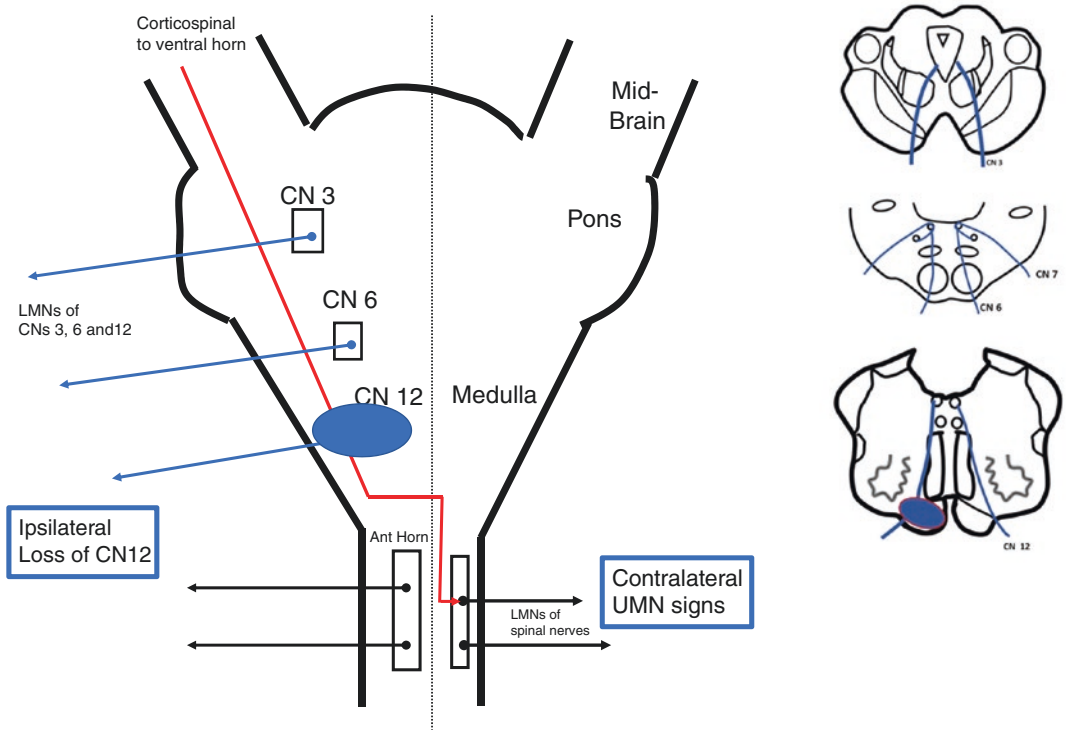


Fig. 13.2 Inferior alternating hemiplegia. Lesion affects corticobulbar tract and LMNs of cranial nerve 12. (Leo 2021)

from the neck down, but one has a third nerve palsy (superior), one has sixth nerve palsy (middle), and one has a twelfth nerve palsy (inferior).

Rule of Fours

In a 1995 paper, Peter Gates presented a simple way for the non-neurologist to think about brainstem lesions. His "rule of fours" points out that in the brainstem, there are four Midline structures beginning with the letter "M," and there are four structures on the Side beginning with "S," four Ms and four Ss. In addition, there are 4 cranial nerves in the medulla, 9, 10, 11, and 12; 4 cranial nerves in the pons, 5, 6, 7, and 8; and 4 in the midbrain and above, 1, 2, 3, and 4 (Fig. 13.5).

The four Ms on the medial side are the Motor pathway (corticospinal and corticobulbar tracts), the Medial lemniscus, the MLF, and the Motor cranial nerves—either 12, 6, or 3—depending where you are. The motor cranial nerves on the medial side are CN 12 in the medulla, 6 in the lower pons, and 3 in the midbrain. Sound familiar? This relates to an inferior alternating hemiplegia in the medulla, middle alternating hemiplegia in the pons, and superior alternating hemiplegia in the midbrain. On the lateral side are the four Ss—the Spinothalamic, the Spinal nucleus of V, the **S**ympathetics (descending sympathetics), and the **S**pinocerebellar (dorsal spinocerebellar pathway traveling in the inferior cerebellar peduncle).

Lateral pontine and lateral medullary syndromes both damage the four Ss. Both syndromes include an ipsilateral loss of pain and temperature sensation to the face because the spinal nucleus of V is damaged, a contralateral loss of pain and temperature to the limbs because the spinothalamic is damaged, Horner's syndrome because the descending hypothalamics are affected, and balance problems because the dorsal spinocerebellar is damaged. The difference between the two is that lateral medullary affects

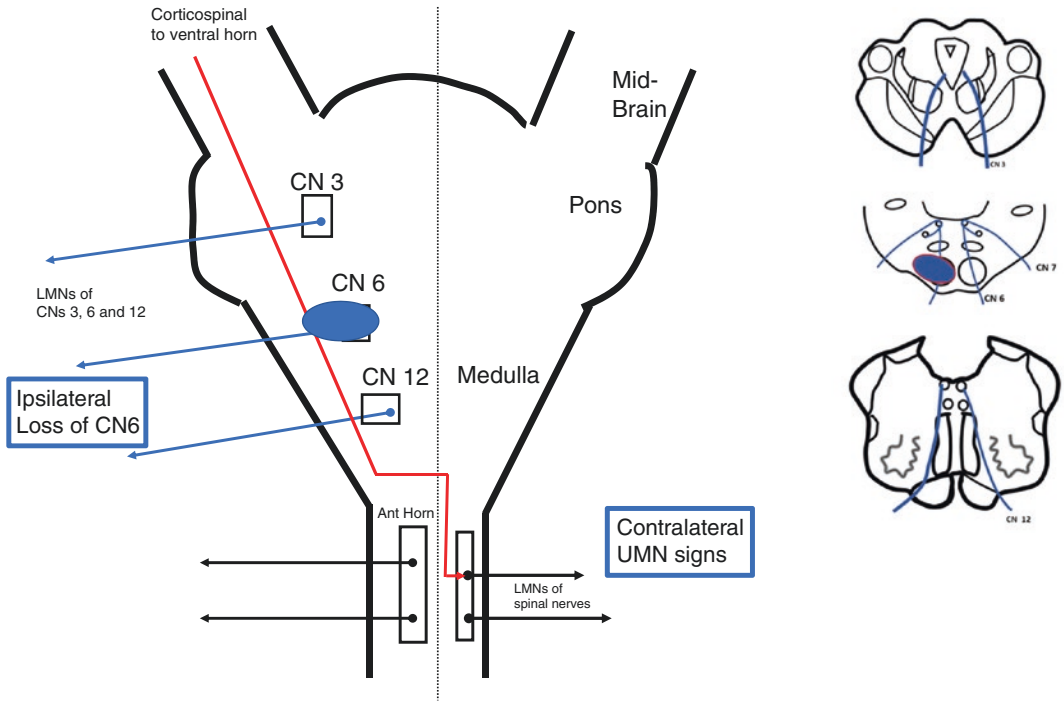


Fig. 13.3 Middle alternating hemiplegia. Lesion in the pons affects the corticobulbar tract and the LMNs of cranial nerve six. (Leo 2021)

cranial nerves lower on the ladder, CNs 9 and 10, while lateral pontine affects CNs higher up on ladder, CNs 5, 7, and 8.

Medial syndromes, such as medial medullary, medial pontine, and medial midbrain, damage the corticospinal and corticobulbar tracts and various cranial nerves, giving us either and inferior, middle, or superior alternating hemiplegia, depending on where the lesion is.

Lateral Medullary Syndrome

In lateral medullary syndrome, there is a stroke to the lateral side of the medulla usually due to an occlusion of either the vertebral artery or posterior inferior cerebellar artery. A hallmark of this lesion is an ipsilateral loss of pain and temperature to the face, and a contralateral loss of pain and temperature to the limbs. The loss of ipsilateral pain and temperature sensation results from damage to the spinal nucleus and tract of V. Running right next to the spinal nucleus of V is the spinothalamic tract, and lesions to the spinothalamic tract result in a contralateral loss of pain and temperature to the limbs (Fig. 13.6).

There are other aspects to the syndrome. The inferior cerebellar peduncle is damaged so there is ipsilateral ataxia. Because we are low down on the ladder, the lower cranial nerve structures such as nucleus ambiguus going to cranial nerves nine and ten will be affected. Oftentimes cranial nerve eight is also affected, so there will be a fast-beating nystagmus to the contralateral side. In addition, the patient will have an ipsilateral Horner's syndrome due to lesioning of the descending hypothalamic fibers traveling down to the lateral horn at T1.

It is important to pay attention to what is not affected in this scenario. Note that the lesion spares the pyramids, the medial lemniscus, and the nucleus and fibers of cranial nerve 12.

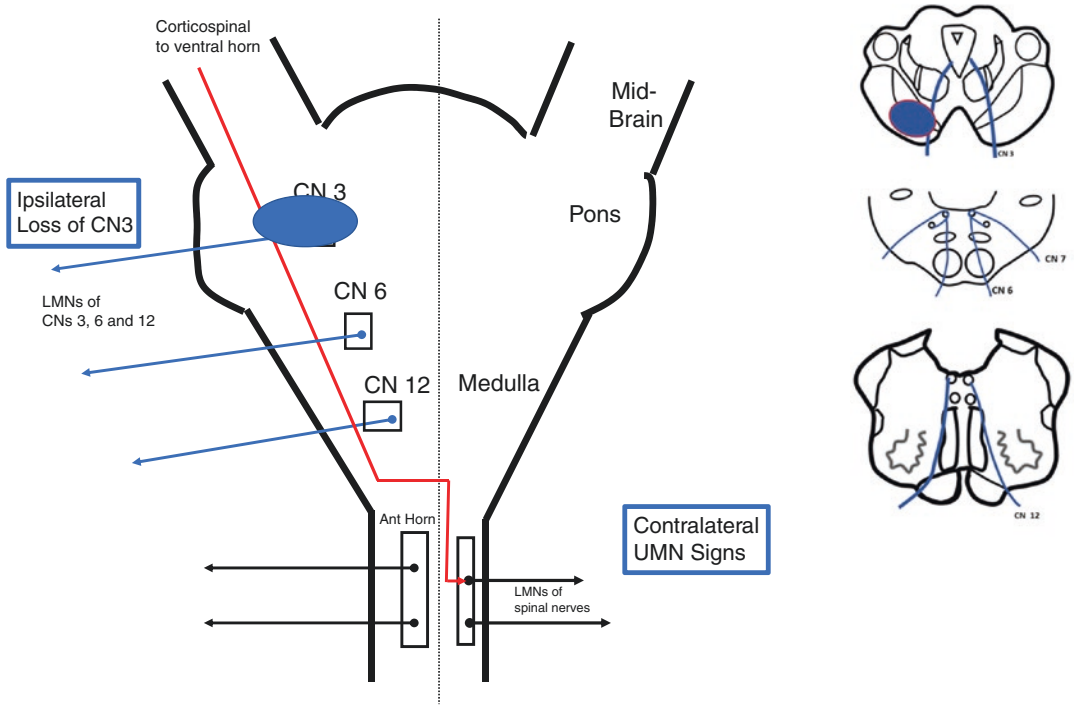
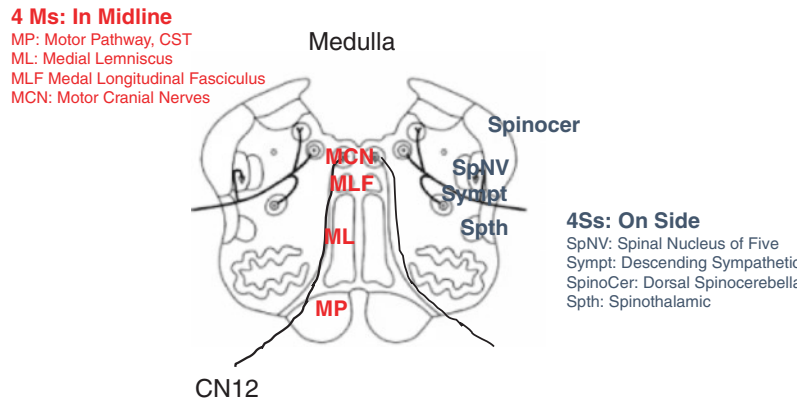


Fig. 13.4 Superior alternating hemiplegia. Lesion affects the corticobulbar tract and LMNs of cranial nerve three. (Leo 2021)

Fig. 13.5 Rule of fours



Medial Medullary Syndrome

Medial medullary syndrome is the result of an occlusion to either the vertebral or the anterior spinal artery. The patient will have a contralateral loss of motor function from the neck down and an ipsilateral loss of cranial nerve 12. In addition, they will likely have a contralateral loss of the dorsal columns/medial lemniscus modalities. The other name for this is inferior alternating hemiplegia. These patients will not have Horner's syndrome, since the descending hypothalamics located in the dorsal longitudinal fasciculus (DLF) are located laterally in the brainstem (Fig. 13.7).

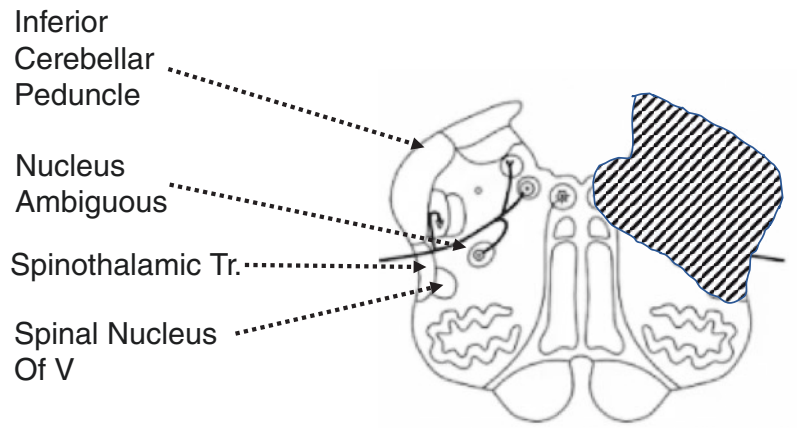


Fig. 13.6 Lateral medullary syndrome. Due to occlusion of posterior inferior cerebellar artery, or vertebral artery. (Leo 2021)

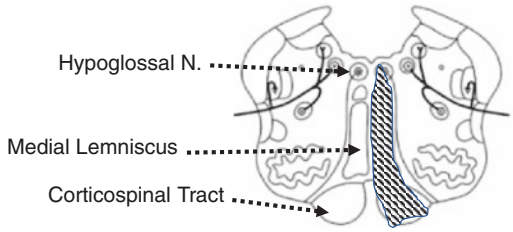


Fig. 13.7 Medial medullary syndrome. Due to occlusion of vertebral A. or anterior spinal artery. (Leo 2021)

Lateral Pontine Syndrome

This is similar to lateral medullary syndrome, just a bit higher up on the ladder, and is due to an occlusion of the anterior inferior cerebellar artery. Like lateral medullary syndrome, the patient will have an ipsilateral loss of pain and temperature to the face due to damage to the spinal nucleus of V, and contralateral loss of pain and temperature to the body due to damage to the spinothalamic pathway. But since the lesion is in the pons, in the middle of the ladder, the middle cranial nerves, such as CNs 5, 7, and 8, will be affected. Horner's syndrome will also typically be present.

Medial Pontine Syndrome

In medial pontine syndrome, there is a deficit to the corticospinal and corticobulbar tracts traveling through the pons which will lead to a contralateral UMN deficit. Running through these tracts are LMN fibers from cranial nerve six. Damage to these fibers will lead to an ipsilateral CN 6 palsy (one eye is affected). However, if the lesion is large enough, it could also damage the nucleus of CN 6 which would lead to a paralysis of ipsilateral horizontal gaze (both eyes are affected). In addition, again if the lesion is large enough, it could compromise CN 7 which would lead to an ipsilateral CN 7 deficit. The problematic arteries in medial pontine syndrome are perforating branches of the basilar artery (Fig. 13.8).

There are several different variations of medial pontine syndrome depending on which structures are lesioned. They are named after the original authors of these conditions such as Foville's, Raymond-Cestan's, and Millard-Gubler. It is not important to be preoccupied with the specifics of each original description, as subsequent authors have expanded on the initial descriptions. In other words, at this point in your career, unless you are going to be a neurologist, there is no point to memorize a list of symptoms to go with each syndrome. Instead, make sure if you see a set of signs and symptoms that you can think through the case and determine where the lesion is located and what structures have been compromised.

Medial Midbrain Syndrome

Running laterally or horizontally, across the cerebral peduncle, is the posterior cerebral artery on its way to the occipital lobe. As it passes by the

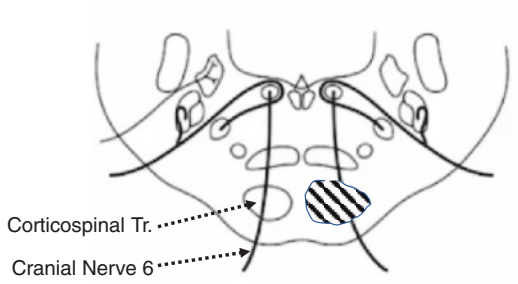


Fig. 13.8 Medial pontine syndrome. Usually caused by occlusion of perforating branches of the basilar artery. (Leo 2021)

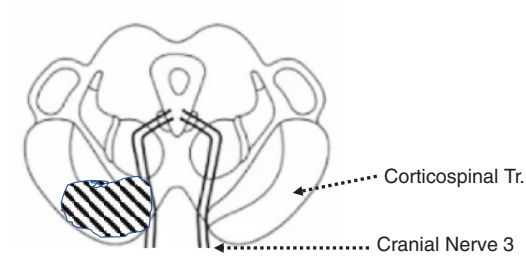


Fig. 13.9 Medial midbrain syndrome. Due to occlusion of posterior cerebral artery. (Leo 2021)

peduncle, it sends branches into the medial midbrain perfusing the peduncle with its corticospinal and corticobulbar tracts along with the accompanying oculomotor nerve. Damage here will lead to contralateral upper motor neuron deficits from the lesion down, and an ipsilateral CN 3 palsy. The CN 3 palsy will lead to the eye going down and out (lateral strabismus). Because the preganglionic fibers coming from Edinger-Westphal on their way to the ciliary ganglion are also affected, the patient will have a dilated pupil and droopy eyelid (Fig. 13.9).

What happens to this patient's face? You really don't need information about the face to determine where the lesion is in this patient, but in case it is mentioned, you should understand the logic of the facial deficits. We need to focus on the corticobulbar fibers that are damaged at the peduncle. Because the lesion is at the level of CN 3, we know that we are at the top of the ladder. Meanwhile, CN 7 is lower down on the ladder, and sits at the level of the pons. Thus, the lesion at the level of CN 3 hits corticobulbar fibers that have not crossed over yet to CN 7. At the level of the lesion, the corticobulbar fibers are still traveling down, through the lesion, and will eventually cross over below the lesion—at the level of 7. And the nucleus of CN 7 is divided into half, with the upper part getting a bilateral input, and the lower part getting a contralateral input. Thus, in medial Midbrain syndrome, the contralateral lower face is affected.

Benedikt's Syndrome

Benedikt's syndrome involves a lesion to the red nucleus and its surrounding structures. Coming out of the red nucleus is the rubrospinal tract which projects to the contralateral LMNs. It is related to the cerebellum, so a lesion here will result in a contralateral tremor. Running through the red nucleus are the fibers of CN 3, so a lesion here will also result in an ipsilateral CN 3 palsy. If the lesion is large enough, it can compromise the medial lemniscus, sitting next to the red nucleus, leading to contralateral dorsal column symptoms. And the lesion could potentially compromise the spinothalamic tract leading to a contralateral deficit with pain and temperature.

Locked-In Syndrome

The basilar artery travels along the center of the pons and terminates by bifurcating into the posterior cerebral arteries—like a T. Along the way the basilar sends branches into the pons. A lesion to the top of the basilar artery can lead to locked-in-syndrome, which is a loss of all motor function except for limited eye movements. Higher cortical functions are all intact. In 1995, Jean-Dominique Bauby, a 43-year-old magazine editor, was driving to work and had a stroke of his basilar artery. He lost all motor function except for his ability to blink. He subsequently wrote the book, *The Diving Bell and the Butterfly* by blinking out the letters. At night he would plan what he wanted to say, and then in the day he would dictate the text. His stenographer would slide their finger along the posted alphabet in his room, and

Bauby would blink when the finger was on the letter he wanted. They would then move onto the next letter. The diving bell was his body, which was like a dead weight; and the butterfly was his mind, which was intact and able to fly around his memory banks. The day after his book was published, a heroic work, he died.

Cranial Nerve Three and Seven Common Lesions

Cranial nerve three palsies are common to see in a clinical encounter or on a board exam. However, just knowing that there is a lesion to CN 3 does not answer the question: where is the lesion? A lesion to cranial nerve three could be at multiple sites along its pathway; thus, we need to look at what other symptoms the patient would have (Figs. 13.7 and 13.10).

Lesion #1 is to CN 3 as it travels through the red nucleus which would result in Benedikt's syndrome. The patient will have an ipsilateral CN 3 deficit and a contralateral tremor.

Lesion #2 is to the cerebral peduncle right near the corticospinal and corticobulbar pathways which would result in contralateral UMN signs. The artery involved is typically the posterior cerebral.

Lesion #3 is an uncal herniation. The typical scenario is someone hit on the head. Take a baseball player who was hit by a ball to the left skull and brought to the ED with a subdural hematoma. The pressure from the hematoma can lead to the left medial temporal lobe, particularly the uncus, herniating out of the skull at the tentorium cerebelli. The left uncal herniation will compress the left oculomotor nerve resulting in a dilated pupil, often referred to as a *blown pupil*, and the eye deviating down and out.

As the uncus herniates out on the left, it can push the brainstem toward the right. On the right side, the tentorium known as Kernohan's notch will compress the right cerebral peduncle with the corticospinal tract. Compression on the right

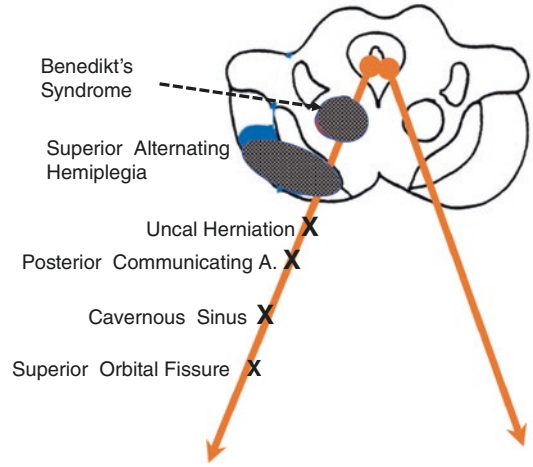


Fig. 13.10 Six lesions to cranial nerve three. (Leo 2021)

corticospinal tract will lead to left side UMN signs. Thus, the eye deficit will be on the same side as the UMN signs. The left UMN sign is sometimes referred to as a false localizing sign, as it is opposite the typical alternating hemiplegia. In addition, the left uncus can also put pressure on the left posterior cerebral artery which will lead to a right homonymous hemianopia.

Lesion #4 is due to an aneurysm of the posterior cerebral artery which compresses the third nerve and can result in a blown pupil. In the early stages of the aneurysm, the parasympathetic fibers of the nerve located peripherally will be compressed first leading to a pupillary dilation. As the aneurysm expands, the motor fibers will also be compressed which will lead to the lateral strabismus (Figs. 13.8 and 13.11).

Lesion #5 occurs to the cranial nerve three as it travels through the cavernous sinus. An infection on the face can travel back along the deep facial veins and eventually enter the cavernous sinus. Traveling through the sinus are all the nerves associated with the eye: 3, 4, 6, V1, and also V2. Thus, the patient will have ophthalmoplegia. However, due the to the fact that CN 6 is located deeper in the sinus, while the other nerves are on the lateral wall, the initial eye deficit will be a CN 6 palsy

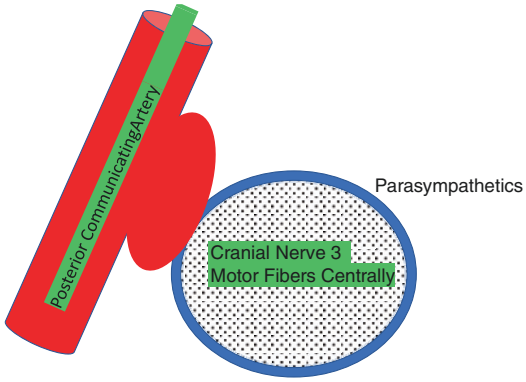


Fig. 13.11 Cranial nerve organization of fibers. The parasympathetic fibers involved with the pupil are located on the periphery of the nerve. The motor fibers are located centrally. An aneurysm of the posterior communicating artery will compress the parasympathetic fibers first. (Leo 2021)

with a medial strabismus. Eventually, as the lesion enlarges, and all the eye muscles are affected, the patient will have full on ophthalmoplegia.

Lesion #6 is to the superior orbital fissure. The superior orbital fissure can be subdivided into two parts by the tendinous origin of the eye muscles. One part is in the SOF but outside the tendinous insertion. The second part is with both the tendinous insertion and the SOF. A saying for the nerves traveling through the SOF is LFT 36N. The LFT part stands for **l**acrimal, **f**rontal and **t**rochlea, all of which travel in the SOF, but outside the tendinous insertion. The 36N stands for CN 3, CN 6 and the nasociliary nerve (a branch of V1) which all travel through the SOF but also within the tendinous insertion. A lesion in the fissure will lead to ophthalmoplegia. Note the optic nerve does not travel through the SOF, so visual acuity is not affected.

Parinaud's Syndrome

Another lesion or syndrome in this area is Parinaud's which results from pressure on the tectum and cranial nerves three and four. Parinaud's patients will have a paralysis of upward gaze which is sometimes referred to as "setting sun sign." The eyes are deviated inferior (downward) as if they are about to dip below the horizon. Because of the pressure on the tectum, the patients will often have hydrocephalus.

Trochlear Nucleus

We discussed cranial nerve four with eye movements, but one thing to note with cranial nerve four is that it is the LMN that decussates before leaving the CNS. Let's think about it from the lesion point of view. We know that if we lesion the right trochlear nerve, the head will tilt to the left—the right nerve goes to the right superior oblique which is an intorter. If we lose that right intorter, the eye will be extorted, so to compensate, we lean away from the damaged side which is to the left. However, if we lesion the right nucleus, keep in mind this is going to the left nerve, so the left eye is extorted, and we will lean to the right. The short version: with an abducens nerve lesion, the patient leans to opposite side, but with a nucleus lesion, the patient leans to the same side (Fig. 13.12).

Arteries to the Brainstem

The two vertebral arteries travel up through the foramen transversarium of C6-C1 and enter the skull through the foramen magnum and unit to form the single basilar artery. Right before joining they give off the right and left posterior inferior cerebellar arteries (PICA) that supply the cerebellum and brainstem and are one of potential arteries to be involved with lateral medullary syndrome. Coming off the basilar close to its origin is the anterior inferior cerebellar artery (AICA) which is involved with lateral pontine

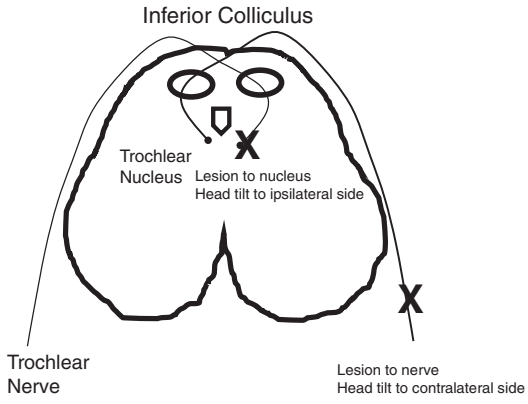
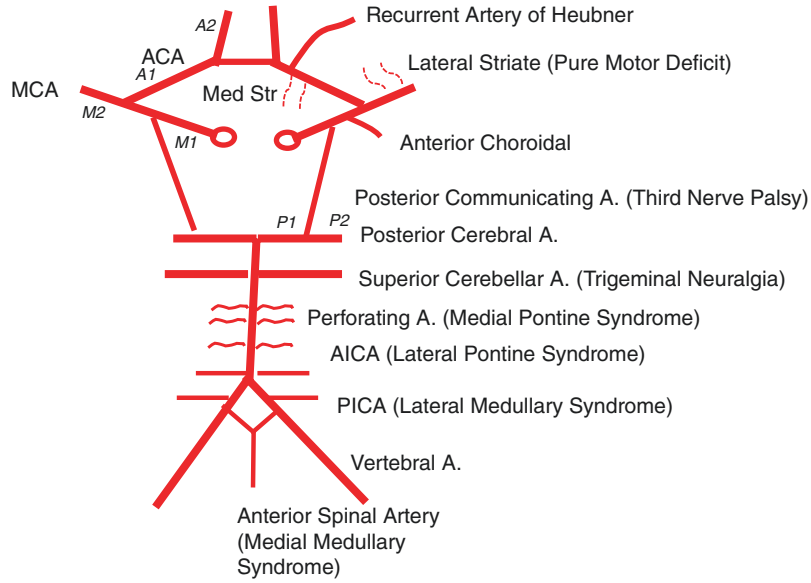


Fig. 13.12 Decussation of cranial nerve four LMNs. This is the only time where a LMN decussates before leaving the CNS. The right trochlear nucleus goes to the left superior oblique. A lesion to trochlear nerve will lead to a head tilt to opposite side. A lesion to the nucleus will lead to an ipsilateral head tilt. (Leo 2021)

syndrome. Perforating branches of the basilar artery penetrating the pons are involved with medial pontine syndrome.

Close to the termination of the basilar artery are the right and left superior cerebellar arteries (SCA), followed by the posterior cerebral arteries (PCA). The posterior cerebral arteries wrap around the cerebral peduncle and send branches into the midbrain. These branches of posterior cerebral arteries are involved with medial midbrain syndrome. The posterior cerebral arteries also give off the posterior communicating arteries that join the circle of Willis. The superior cerebellar arteries are thought to be involved with trigeminal neuralgia compression of the artery on the nerve affects V1 and V2. All the branches mentioned above were discussed in more detail with the various brainstem lesions (Figs. 13.9 and 13.13).

Fig. 13.13 Various arteries and syndromes



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Cerebral Cortex Lesions

14

With lesions to the cerebral cortex, or cerebrum, think of the As: aphasia, agnosia, apraxia, anopsia, asomatognosia, alexia, and agraphia. Patients with lesions to the brainstem on the other hand often exhibit one or more of the four "D"s. Dysphagia is a swallowing deficit, and dysarthria is a deficit with speaking. Both of these are found in patients with lesions to nucleus ambiguus. Diplopia or blurred vision is found in patients with deficits to CN 3, 4, or 6. Dysmetria or past pointing is found in patients with cerebellar involvement. Lateral brainstem injuries often lead to cerebellar symptoms because of involvement of the cerebellar peduncles.

There are two major dividing lines in the cerebral cortex. The first is the central sulcus which divides the frontal lobe from parietal lobe. The second is the lateral fissure which demarcates the temporal lobe.

The frontal lobe includes the prefrontal cortex with the orbitofrontal cortex. One of the more famous patients in neurology is Phineas Gage. Phineas was working on a railroad when an explosion sent a steel rod through the left side of the skull damaging his prefrontal cortex. He essentially had one of the first lobotomies. Although he lost vision in his left eye, he could still see with his right eye, he could still hear, and his other senses were intact. However, Phineas was just not the same person. He lost his inhibitions and was prone to saying whatever came to his mind. His condition provided some of the first insights into the role of the frontal lobe. As mentioned in the chapter on the limbic system, the orbitofrontal cortex on the inferior surface of the frontal lobe receives a sample of information from all the different senses coming into our nervous system. It is thought that the orbitofrontal cortex integrates this information and, along with the hippocampus and amygdala, is involved in decision-making.

The central sulcus is bounded anteriorly by the precentral gyrus, also known as the primary motor cortex, and posteriorly by the postcentral gyrus, also known as the primary sensory cortex. Both these gyri are organized topographically with the superior portion being the lower limb, and the inferior portion being the face and upper limb. Think of an upside-down stick figure on each gyrus. If you look at the medial side of the cortex, each gyrus can also be seen. The piece of cortex with the central sulcus in the middle on this medial view is named the paracentral lobule—it represents primary motor and primary sensory for the contralateral lower limb. Lesions here will naturally affect the lower limb on opposite side (Fig. 14.1).

Broca's Aphasia

For most of us, language is located on the left side of the cortex. Broca's area lives on the inferior frontal gyrus and is responsible for the

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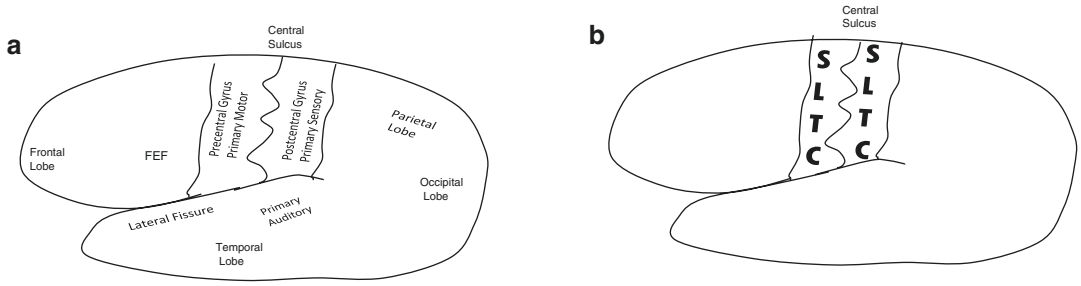


Fig. 14.1 Cerebral cortex. Panel A shows the precentral gyrus also known as primary motor cortex anterior to the central sulcus. Posterior to the central sulcus is the postcentral sulcus also known as primary sensory cortex. Panel B shows the topographical layout of pre- and postcentral gyri. C, T, >, and S = cervical, thoracic, lumbar, and sacral. (Leo 2021)

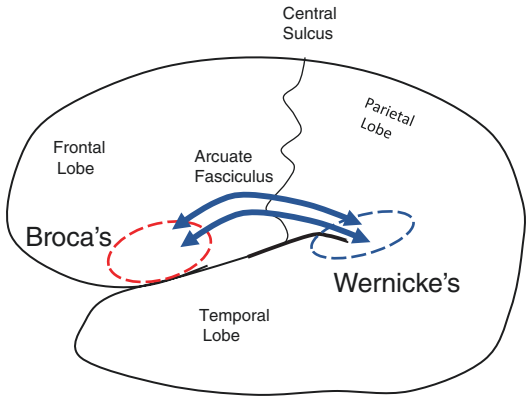


Fig. 14.2 Language regions. Broca's area is located on the frontal gyrus. Wernicke's is located in the temporal lobe. The two regions communicate with each other through the arcuate fasciculus. (Leo 2021)

speaking or motor component of language (Fig. 14.2). In other words, it takes all the various parts of a sentence, verb, subject, objects, and prepositions, and puts them all together to make a coherent sentence. Lesions here will result in "broken speech" meaning that the patient can speak, and the words come out, but there are not put together in sentences. If you ask the patient what they have been doing today, they understand the question, and they want to give you a long explanation of their day, but instead they just get random words out. Their speech is considered non-fluent, or "broken."

Wernicke's Aphasia

Wernicke's area is located in the left temporal lobe and is responsible for comprehending speech—it is the part of your brain that you are using right now as you read this page. Lesions here will result in "word salad." Think of a tossed salad with all the components present but just tossed into the bowl with little organization. Patients with Wernicke's can speak but the words are jumbled and mixed up. If you ask the Wernicke's patient to tell you about their day, they keep on talking, but their words are all jumbled. They are "fluent" but they don't make sense.

Conduction Aphasia

In a healthy individual, during a normal conversation, Wernicke's and Broca's talk to each other via the *arcuate fasciculus*. Lesions of the arcuate fasciculus lead to a conduction aphasia. These patients sound like a Wernicke's patient—they are both fluent and do not make sense. However, in contrast to the Wernicke's patient, the conduction aphasic understands you. If two aphasiac patients are sitting in your office and one has Wernicke's and one has conductive aphasia, they will both sound very similar. They are both fluent but make little sense, so how do you tell them apart? If you give them a command to follow, the conductive patient will understand you and fol-

low through with the directions, but the Wernicke's patient does not follow through. The conduction aphasiac understood you, but the Wernicke's patient did not.

Frontal lobe patients will often shuffle their feet and take short steps—*Marche à petit pas* (*sometimes referred to as a magnetic gait*). This closely resembles Parkinson's patients who also have a short shuffling gait; however, a Parkinson's patient will tend to lean forward, while the frontal lobe patient stands upright. Frontal lobe patients exhibit frontal release signs such as the grasp, Moro, and rooting reflexes. These are reflexes common in infants that may return in frontal lobe patients.

Cortical Blood Supply

The internal carotid artery enters the skull through the carotid canal and crosses the foramen lacerum and then enters the cavernous sinus where it does a 180^0 turn to form the genu of the internal carotid artery. At this bend, the internal carotid gives off the ophthalmic artery, which in turn gives off the central artery of the retina. After the bend, as the internal carotid approaches the ventral surface of the brain, it splits into the middle and anterior cerebral artery.

The blood supply to the cerebral cortex comes from the middle cerebral, anterior cerebral, and posterior cerebral arteries. If you imagine placing your hand on your brain, you are covering the territory of the middle cerebral artery (Fig. 14.3). It gets the lateral surface of the cortex except for the edges. The superior edge is perfused by the anterior cerebral, while the inferior edge and the occipital pole are perfused by the posterior cerebral.

The first branches of the middle cerebral are the lateral striate arteries which travel deep into the cerebrum and perfuse the internal capsule. Strokes in these arteries can lead to a "pure motor deficit"—see the section on the internal capsule. The middle cerebral heads toward the lateral side of the cortex as the M1 branch; as it approaches the lateral fissure, it splits into the M2 branches. One, which is called the superior branch, continues superiorly up to the frontal lobe, and an inferior branch going to the temporal lobe. The superior branch supplies Broca's area and the face and upper limb territory of the precentral gyrus, so a stroke here will lead Broca's aphasia, plus contralateral motor deficits to the upper limb and face. Keep in mind that the patient will not have Babinski's sign because the lower limb region of the precentral gyrus is typically not affected.

A lesion to the inferior division of the middle cerebral artery could lead to Wernicke's aphasia.

From the origin of the *anterior cerebral artery* to the anterior communicating artery is the A1 segment. Coming off this A1 segment are the first branches of the which are the small medial striate

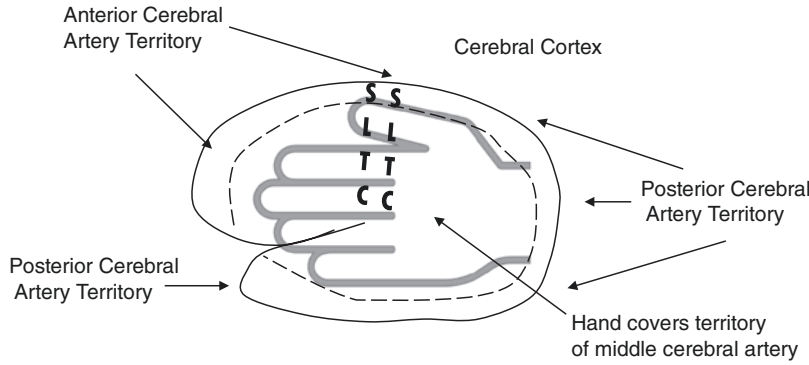


Fig. 14.3 Arteries to the cerebral cortex. Imagine placing your hand on the head, which is covering your brain. Your hand is overlying the territory of middle cerebral artery. The edges of the brain—surrounding your hand—are territories of two other arteries, the posterior and anterior cerebral arteries. (Leo 2021)

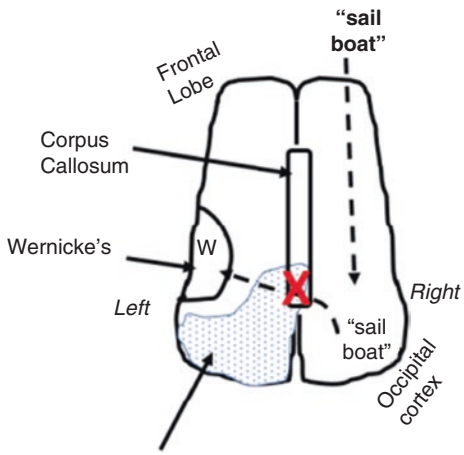
arteries perfusing parts of the internal capsule. The A2 segment then continues on and splits into the pericallosal and callosomarginal arteries. The callosomarginal travels superior to the cingulate gyrus, while the pericallosal artery travels between the corpus callosum and the cingulate gyrus. The callosomarginal artery sends branches to the medial surface of the cerebral cortex, including the paracentral lobule. The paracentral lobule is a small region on the medial surface of the cortex that includes the ends of the precentral and postcentral gyri, which is the territory for motor and sensory supply to the contralateral lower limb. Lesions of the callosomarginal, or the anterior cerebral artery itself, can lead to a motor and sensory deficit to the contralateral lower limb. Along with the motor and sensory deficits, the patient could present with incontinence because the nerves to the pelvic region can be affected.

The *posterior cerebral arteries* arise from the basilar artery then travel along each cerebral peduncle toward the occipital cortex. From its origin to the posterior communicating artery is the P1 segment. The thalamogeniculate artery arises from P1 and perfuses the VPM and VPL of the thalamus.

Alexia Without Agraphia

To understand how a stroke can lead to a patient who can write but not read, we need to talk about several cortical areas and their connections. When we read something, we are seeing the words with our occipital cortex, but we need to do more than just "see" the words—just "seeing" the words or symbols is not enough. To make sense of these words, we need to send the information from both the right and left occipital lobes to Wernicke's area on the left. The left occipital lobe has a short, straight projection to Wernicke's on the left that does not have to go through the corpus callosum. But the right occipital cortex needs to send its information across the corpus callosum through the splenium of the corpus callosum to go from right to left. Wernicke's then turns these symbols into meaningful language.

The posterior cerebral artery eventually goes to the occipital cortex and the splenium of the corpus callosum. A lesion to the splenium results in a patient who can write but cannot read—alexia without agraphia (Fig. 14.4). When the patient is shown a written sentence, they can "see" the words with their right occipital lobe because the information travels along their optic



1) The patient has a stroke to the posterior cerebral artery. which damages the occipital cortex and splenium of corpus callosum
2) The patient is told to write the word "sailboat" which they can do.
3) Several minutes later they cannot read the word.
4) The word "sailboat" makes it to the right occipital cortex but not to the left cortex because it is damaged.
5) To understand the letters making up the word " sailboat" the information needs to cross in the splenium to project to Wernicke's but the splenium is lesioned which blocks the information flow from right to left

Fig. 14.4 Alexia without agraphia. (Leo 2021)

nerves, tracts, and radiations to the right occipital cortex. They cannot see the letters with the left cortex since it has been compromised. For the patient to understand these "words" that made their way back to their right cortex, they need to send the information from the right cortex across to Wernicke's area, but since the splenium is damaged, they cannot do this. Thus, while they can see the words with the right occipital cortex, they cannot understand the words since the information cannot get from the right occipital cortex to Wernicke's area on the left.

If the damage is on the right side, they would not have this deficit. They would see the words with the left cortex, and it is a direct connection from left occipital cortex to left Wernicke's area—the information does not need to go through the splenium. Not to overcomplicate it, but if we are talking about an individual with language on their right side, then the scenarios would be reversed—if the stroke was on the right side, they would have alexia without agraphia, and if it was on the left, they would not have this deficit.

Parietal Lobe

The parietal lobe is considered an association cortex. It receives information from various regions of the cerebral cortex and then integrates this information. Lesions to the right parietal lobe result in patients with left side neglect. If you ask them to draw a clock, they will typically accurately draw just the right side of the clock but not the left side. Or if you give them a plate of food, they will eat everything on the right side and then ask for more. You simply turn the plate, and they continue eating.

The right parietal lobe is also the site of our ability to sense tone, rhythm, intonation, and the deeper meaning of language—referred to as prosody. The easiest way to think of this is the communication between a mother and a toddler. When a toddler hears their mother state their name, the child can tell if the mother is happy, sad, mad, proud, worried, etc. There is more to just stating the name; there is meaning in the tone. Likewise, the mother can sense the nuances of meaning when the child says "mom." Lesions to the parietal lobe can lead to prosodic deficits.

Man in a Barrel

Where the anterior and middle cerebral arteries meet is a watershed zone, and watershed zones are problematic for those with low pressure or hypotensive moments (Fig. 14.5). A lesion here where middle cerebral artery and anterior cerebral artery meet will result in a syndrome which is sometimes referred to as "man in a barrel." You need to understand the topography of the precentral and postcentral gyrus to understand these symptoms. Imagine standing with a barrel around your midsection. In these patients, their face is intact, their lower limb is intact, and their hands can be intact. Their deficit is in their midsection.

Fig. 14.5 Man in a barrel. The barrel represents the area compromised in hypotensive patients. (Leo 2021)

Gerstmann's Syndrome

Gerstmann's syndrome results from lesions, usually strokes, to the angular gyrus of the nondominant parietal lobe (usually on the right). There are four classic symptoms: acalculia, cannot do simple math; finger agnosia, do not know their own fingers; agraphia,-cannot write; and right-left disorientation. The syndrome can also be present in young children as the result of a developmental disorder.

Temporal Lobe

The medial temporal lobe houses the amygdala and hippocampus. Lesions in this area are discussed with the limbic system. A lesion in the temporal lobe is exemplified by the case of the composer George Gershwin who died from a glioblastoma in his temporal lobe. Prior to his death, he reported that several times while he was playing the piano, he just forgot the music—like a short circuit—and that prior to these events, he reported smelling a "pungent odor" like burning rubber, an uncinate fit. Evidently the tumor was aggravating his hippocampus which led to memory issues, and his amygdala, which caused him to complain of noxious odors. It does not appear in Gershwin's medical file, but similar patients often present with a superior homonymous quadrantanopia.

Cingulate Gyrus

One hypothesis of the neuropathology of *obsessive-compulsive disorder* (OCD) is that there is a perturbation in the anterior portion of the cingulate gyrus and its connection with the orbitofrontal cortex.

Wet, Wacky, and Wobbly: Normal Pressure Hydrocephalus

Normal pressure hydrocephalus (NPH) can occur in an elderly patient whose has an enlarged lateral ventricles. The enlarged ventricles fills with fluid and puts pressure on the cerebral cortex which can lead to incontinence, confusion, and ataxia, also known as *wet*, *wacky*, *and wobbly*. A shunt from the lateral ventricle to the peritoneum is likely to relieve the symptoms. To test whether the shunt will work or not, a spinal tap, basically a temporary shunt, can be performed. The spinal tap should relieve some of the pressure on the cortex. If the patient improves, then they are a good candidate for a permanent shunt. NPH is thought to be caused by decreased absorption of CSF from the arachnoid granulations.

The **nucleus basalis of Meynert** sits in the basal forebrain and has cholinergic fibers projecting to the prefrontal cortex, thalamus, and hypothalamus. It is involved in the later stages of Alzheimer's and Parkinson's dementia. Aricept (Donepezil) is an acetylcholinesterase blocker that is given to Alzheimer's patients to restore cholinergic levels.

Apraxia

Patients with apraxia have a motor deficit, even though the motor pathway is intact. My analogy is to a computer program that is working perfectly, but the password is wrong, and you cannot access the program. There are several types of apraxia, but let's start with a patient who has damage on the anterior portion of the corpus callosum (possible the anterior cerebral artery) who has *transcortical apraxia*. This patient cannot follow a command to move their left hand, but they can move their right hand. When you ask this person to move their left hand, they hear you and understand what you are asking, because Wernicke's region is intact. Furthermore, they want to follow your command to move their left hand, but to do this they need to send the information from Wernicke's to the right precentral gyrus. However, the information from Wernicke's cannot cross to the right side of the brain because the corpus callosum is damaged.

They can successfully move their right hand because the information from Wernicke's goes straight to the left precentral gyrus without having to go through the corpus callosum. You also

might notice that, while they cannot move the left hand following a command, during the exam they might reach up and scratch their head with their left hand. This is because scratching their head is not based on the connection from Wernicke's to the motor cortex. It is just a simple reflex-like activity. Again, there is no deficit with the precentral gyrus, or the corticospinal pathway, or the peripheral nerves, or the muscles—the entire program is intact. The deficit is with gaining access to the program—Wernicke's cannot get the password over to the precentral gyrus to turn it on.

Childhood apraxia of speech (CAS) or verbal apraxia is a developmental disorder where the child understands you and wants to communicate but has difficulty making a sentence. In contrast to dysarthria, which typically involves difficulty speaking because of a nerve or muscle deficit, CAS is thought to be caused by a cortical issue. Speech is affected but not intelligence.

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15 Fibers, Reflexes, and Radiculopathies

Fiber Classification

Nerve fiber classification is very confusing because of the different classification systems, the overlap between categories, and variations in species. All of which leaves the student pondering how much of this relates to clinical medicine and wondering how much they need to know. The most important characteristic is speed or *conduction velocity*, which is based on fiber diameter and whether the fiber is myelinated or not. The thicker the fiber, the faster the conduction velocity. And myelin-enclosed fibers have much faster conduction velocity. And if we think about what information we want to get to our CNS as fast as possible, it is proprioceptive information. As we move our muscles, we need the feedback quickly to make adjustments. Pain on the other hand is obviously important, but we don't need to transmit it to our cortex as fast as the proprioceptive information.

Nerve fibers are categorized into three main groups: A, B, and C. Group A fibers are large diameter and myelinated, both of which give them the highest conduction velocity. Group B fibers are myelinated but have a small diameter. Because of this small diameter, they have low conduction velocity. Basically, they are the preganglionic fibers of the autonomic nervous system. Group C fibers are unmyelinated, with a small diameter giving them the lowest conduction velocity. They carry pain information (mechanical, thermal, and pain).

Group A fibers can be further subdivided into A alpha, A beta, A gamma, and A delta.

A alpha fibers are the alpha motor neurons that innervate extrafusal muscle fibers and are responsible for muscle contraction. They have a high conduction velocity.

A gamma fibers innervate intrafusal muscle spindles of nuclear bag and nuclear chain fibers. These are the thickest, fastest fibers carrying information from Golgi tendon organs and muscle spindles. Note that they can be even further subdivided into:

- *1a* coming from muscle spindles monitoring the length of the tendon
- *1b* from Golgi tendons monitoring tensions of the tendon

A beta fibers carry sensory information from muscle spindle endings.

A delta fibers carry information about pain perception. A delta fibers are small, myelinated fibers carrying pain information (mechanical and thermal). If you step on a tack, you immediately feel a sharp pain via your myelinated A delta fibers. This will be followed in a moment by a more diffuse, dull pain, which is being transmitted on nonmyelinated C fibers.

J. Leo, *Medical Neuroanatomy for the Boards and the Clinic*,
https://doi.org/10.1007/978-3-030-88835-0_15

Deep Tendon Reflexes

When you tap on a certain tendon, you are testing the reflex circuit between the muscle spindles, the spinal cord, and the muscle. If you see hyperreflexia or hyporeflexia, then this suggests pathology. Muscle spindles are the intrafusal fibers within the muscle belly that respond to stretch. For muscle **S**pindles think **S**tretch. As an example, take the Achilles' tendon reflex. When you tap at the heel, the muscle spindles, either nuclear bag or nuclear chain fibers, sense the elongation and send afferent signals traveling on 1a afferent fibers to the dorsal roots. At the L1 level, the fibers enter the cord, travel through the dorsal horn, and then detour to the ventral horn to make a direct projection onto the large alpha motor neurons that will project out the ventral roots, onto the sciatic nerve, to eventually send information to and stimulate the plantar flexors, *extrafusal fibers*, of the foot.

In addition to this alpha motor neuron activity, the small unmyelinated gamma motor neurons will send information to the *intrafusal* muscle fibers. Note that this reflex is a monosynaptic pathway consisting of two neurons, one sensory or afferent fiber, and one motor or efferent fiber, and just one synapse in the gray matter of the spinal cord.

Concurrent with the muscle activity in plantar flexors, at the same time the antagonist muscles in the anterior leg will be inhibited via a polysynaptic pathway. In this case, the afferent information comes into the cord, and goes to an inhibitory interneuron, which then inhibits the dorsiflexors of the leg. The inhibition of the antagonist muscle group is referred to as reciprocal inhibition.

Golgi Tendon Organs

Golgi tendon organs are located in the tendons, and they measure tension. When stimulated, they lead to relaxation of the muscle to prevent excessive strain on the muscle fibers—the inverse myotatic reflex. Golgi tendon organs are small capsules embedded with free nerve endings that sense tension. Once a Golgi tendon organ is stimulated, it sends signals into the spinal cord on a 1b fiber, when then contacts an interneuron which in turn projects to the alpha motor neuron to an interneuron, which leads to relaxation of the muscle under strain. For Golgi **T**endon organs, think **T**ension.

The clasp-knife reflex is a sign of UMN pathology. During the neurological exam, it occurs when the examiner attempts to flex a joint. There is an initial resistance against the movement, which suddenly gives way, the muscles relax, and the limb moves freely—like when you close a pocketknife, and you push the blade a bit to get it started, but then all of sudden, the knife snaps shut. This sudden closing is due to the action of the Golgi tendon organ sensing the tension and leading to relaxation of the muscles.

In summary, in a typical mixed nerve, there are three types of motor fibers coming into a muscle:

1. Alpha motor neurons to extrafusal fibers
2. Gamma motor neurons to intrafusal fibers
3. Unmyelinated C fibers, which are postganglionic autonomic efferents

And there are three types of sensory fibers leaving the muscle:

1. 1a fibers originating from nuclear bag and nuclear chain fibers in the muscle spindles
2. 1b fibers originating in the Golgi tendon organs
3. Various fibers from the tissue surrounding the muscle

Hypotonia, which is either a diminished or absent muscle tone, occurs when a peripheral nerve (LMN) is cut. *Hypertonia*, which is increased muscle tone, occurs when the corticospinal tract (UMN) is cut.

Superficial Reflexes

In contrast to the hyperactive DTRs, in patients with UMN injuries, the superficial reflexes, such as abdominal, cremaster, and corneal, will typi-

cally be absent. The abdominal reflexes are stimulated by stroking gently on the abdomen from lateral to medial and looking for contraction of the abdominal muscles. The umbilicus should move toward the side of the scratching. However, the clinical utility of these reflexes is debatable. The *presence* of the reflexes is a good sign, but their *absence* does not necessarily indicate a lesion. The reflexes are absent in a fair number of healthy individuals, the elderly, patients who have had surgery, and parous women. The mechanism of these abdominal reflexes is also up for debate.

Dermatome, Peripheral Nerve, and Myotome Maps

A myotome is a group of muscles innervated by one spinal nerve level. A word of warning is in order about the tables below, especially the myotome table (Table 15.1). If you look in three different books, you might see subtle differences in these tables among the three books. This is most likely due to normal human variation that leads to slight differences in the various studies. Do not panic however, because the information on a specific movement in any one patient or on a board exam is only one finding among many others, and it will not be the sole piece of information that you need to determine where the lesion is located.

When it comes to sensory loss, you want to keep two maps in your mind—the dermatome map and the peripheral nerve map. Most anatomy textbooks will show the two maps side by side. With a spinal cord patient, you want to think about the dermatome map. With a lesion to a peripheral nerve such as either the radial or femoral nerve, you need to think about the peripheral nerve map. With a CNS lesion, you want to focus on the dermatome map. I will leave the PNS lesions and the peripheral nerve map to the gross anatomists, with one exception: the radiculopathies. With a radiculopathy which is in the PNS, right next to the cord, and before the nerve fibers join the brachial or lumbar plexuses, you want to think about dermatomes (Table 15.2).

Table 15.1 Myotomes

Spinal level	Movement
C5	Shoulder abduction
C6	Elbow flexion
C7	Elbow extension
C8	Wrist flexion
T1	Finger abduction
L2	Hip flexion
L5	Dorsiflexion
S1	Plantar flexion

Table 15.2 Dermatome map

Spinal level	Region
C6	Thumb
C7	Middle fingers
C8	Fifth digit
T1	Armpit
T4	Nipple
T10	Umbilicus
L1	Inguinal
L2, 3	Anteromedial thigh
L4	Medial leg, foot
L5	Anterior leg, dorsum of the foot
S1	Lateral foot
S2, 3, 4	Gluteal region

Radiculopathies

Radiculopathies (damage to the roots) are often the result of herniated discs. The discs themselves have an outer thick, strong nucleus fibrous, and an inner core of the softer nucleus pulposus, which is the remnant of the embryological notochord. The anterior portion of the disc is held in place by the anterior longitudinal ligament, and posteriorly by the posterior longitudinal ligament. The weak point in this region is the lateral portion of the posterior longitudinal ligament. If this ligament gives way, the nucleus pulposus will herniate in a posterior lateral direction and compress the nerve exiting one level down.

To understand the symptoms of a radiculopathy, before getting into the specifics, make sure you understand the big picture difference between cutting a nerve or a root. When you cut a peripheral nerve, the muscle innervated by that nerve will be completely (100%) paralyzed. For instance, if you cut the femoral nerve, then the

quadriceps muscle group is completely paralyzed. However, if you cut a root, the muscle group will just be weak. This is because peripheral nerves receive contributions from several different spinal levels. For instance, the femoral nerve to the quadriceps gets contributions from L2, L3, and L4, so if just one of these roots is damaged, say L2, the muscles innervated by the femoral nerve will just be weak, because L3 and L4 are still intact.

In the lumber area, the spinal cord ends at the L1 vertebra. The nerves coming out at the lower cord then travel down as the cauda equina to exit through their appropriate intervertebral foramen. Looking at the vertebra from the posterior view, imagine we have cut the pedicle of each vertebra with a bone saw. We can see the pedicles are at the top of each vertebra. The intervertebral canal is between the pedicles of each vertebra. If we focus on the L4 and L5 vertebra, we see a disc between the two, and exiting at the top of the foramen is the L4 nerve. If this disc herniates, then it will not hit L4, which is exiting about the disc, but will hit the L5 nerve as it passes by the disc to exit one level down. In other words, a disc herniation between L4 and L5 will hit the nerve exiting one level down, which is L5 (Fig. 15.1).

If we move to the cervical area, everything changes (Fig. 15.1). The first thing to note is that numbering of the nerves is different. The C1 nerve comes out above the C1 vertebra, and C2 nerve exits above C2, and so forth for the other cervical nerves. These nerves do not have to travel down the vertebral canal, but instead exit straight out of their respective foramen. If the disc between C3 and C4 is displaced, then the C4 nerve will be damaged, but this is the nerve that is exiting at this level.

The most common disc herniations are in the lower limb region to either L4, L5, or S1. With a disc injury, you want to think of three tests. The first is the reflex test, the second is the muscle test (the myotome), and three is the sensory loss related to dermatome. Not every level has a good reflex test (Table 15.3).

Spondylolysis is a stress fracture in the pars interarticularis, at the collar in the scotty dog picture. The most common site is L5. *Spondylolisthesis* is when one vertebra slides for-

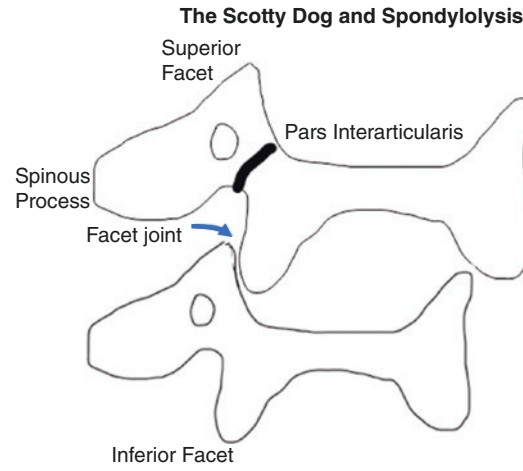

Fig. 15.2 Scotty dog and spondylolysis. The dog's collar is the pars interarticularis which is the site of spondylolysis. The facet joint is between the superior articular facet (the dog's head) and the inferior articular process (the dog's front foot) of vertebra above it

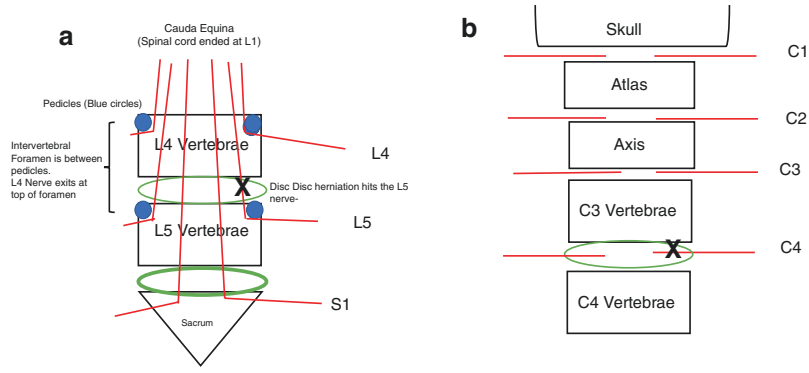

Fig. 15.1 Panel A is a disc herniation between L4 and L5 that hits the L5 nerve which exits one level inferior. Panel B shows the cervical nerves exiting above their various vertebral bodies. A disc herniation between C3 and C5 hits the nerve exiting at that level—in this case. (Leo 2021)

Table 15.3 Radiculopathies and major symptoms

	L4	L5	S1
Reflex test	Patellar tendon	No good reflex	Achilles reflex
Muscle test	Quadriceps	Dorsiflexing toes	Plantar flex ankle
Sensory loss	Lateral thigh, medial leg, and medial foot	Lateral leg, dorsum of the foot	Posterior thigh, lateral leg, and lateral foot

ward over the vertebra below it (*listhesis* = *to slip*). *Ankylosing spondylitis* refers to fused vertebra. The patient will have a hunched forward position. A hangman's fracture is a bilateral fracture at the pars interarticularis of C2.

On a radiograph an easy way to picture a spondylolysis is to think of a picture of a scotty dog. The fracture of the pars interarticularis occurs at the dog's collar (Fig. 15.2).

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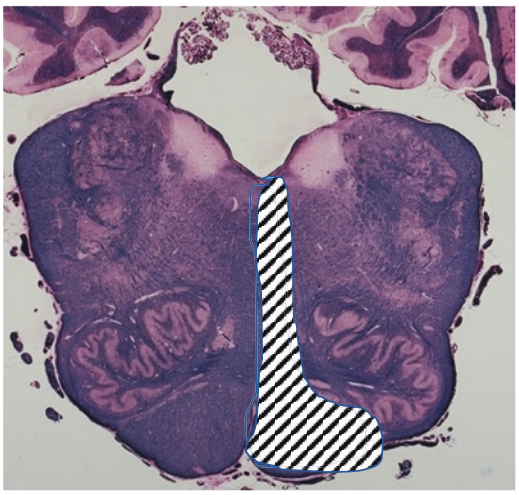
Summary of Blood Vessels and Lesion Test

16

Each picture below represents a lesion scenario. For each patient, list the symptoms, the tract involved, and the cell body of origin for the compromised fibers. If it is a vascular incident, list the artery involved.

Lesion #1



Syndrome:
Artery:

Symptom	Tract	Cell body of Origin

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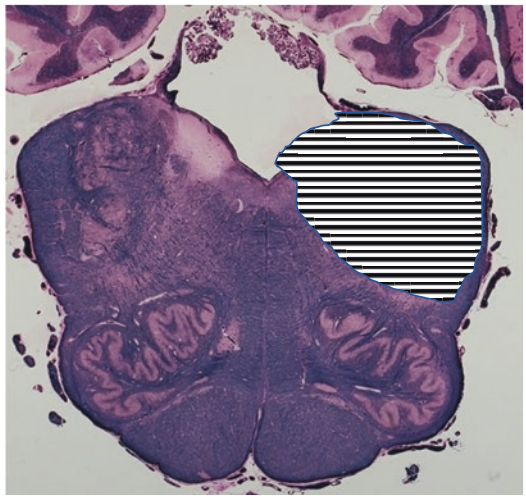
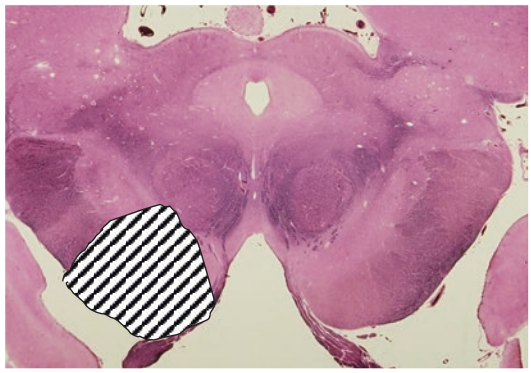
Lesion #2



Syndrome:
Artery:

Symptom	Tract or Nucleus Compromised	Cell body of Origin (for tracts)

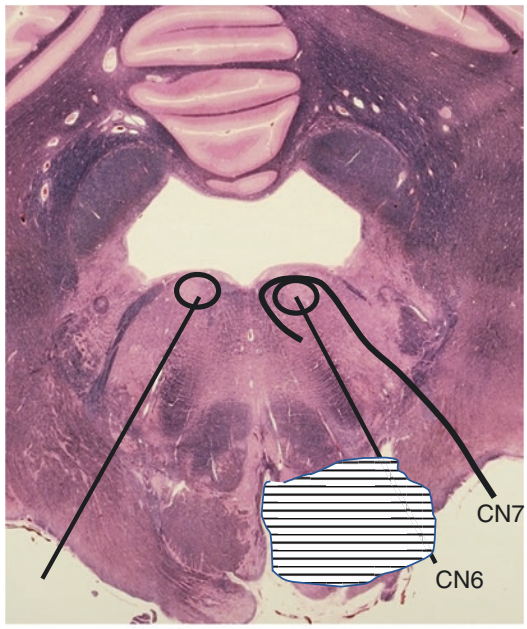
Lesion #3



Syndrome:
Artery:

Symptom	Tract	Cell body of Origin

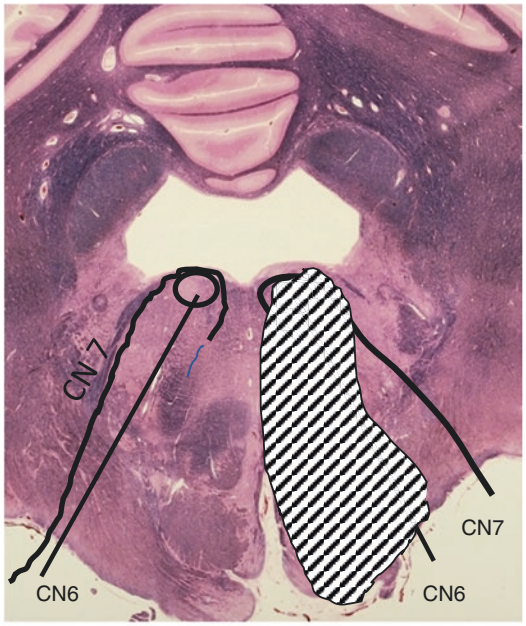
Lesion #4A



Syndrome:
Artery:

Symptom	Tract	Cell body of Origin

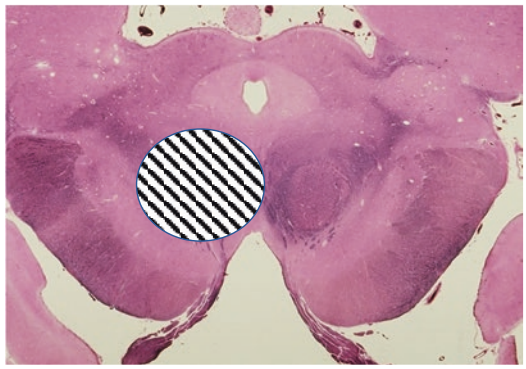
Lesion #4B (Hint: there is a subtle difference between 4A and 4B.)



Syndrome:
Artery:

Symptom	Tract	Cell body of origin

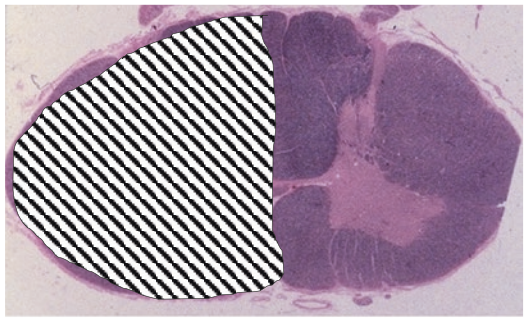
Lesion #5



Syndrome:
Artery:

Symptom	Tract or Nucleus	Cell body of Origin

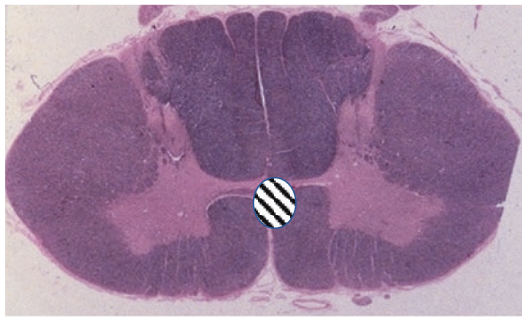
Lesion #6



Syndrome:

Symptom	Tract	Cell body of Origin

Lesion #7

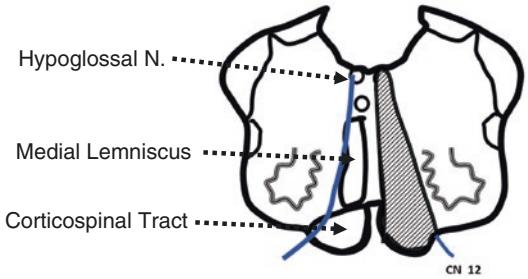


Syndrome:

Symptom	Tract	Cell body of Origin

Answers to Lesion Test

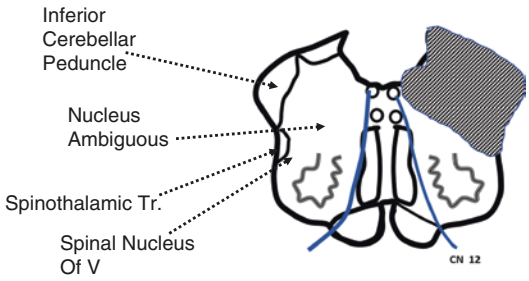
Lesion #1 Key



Syndrome: Medial medullary syndrome
Artery: Vertebral artery, anterior spinal artery

Symptom	Tract	Cell body of origin
Contralateral UMN sign	Corticospinal	Precentral gyrus (Fig. 1.3)
Contralateral dorsal column signs	Medial lemniscus	Nucleus cuneatus and gracilis (Fig. 1.5)
Ipsilateral CN 12 deficit	CN 12	Hypoglossal nucleus (Fig. 2.1)

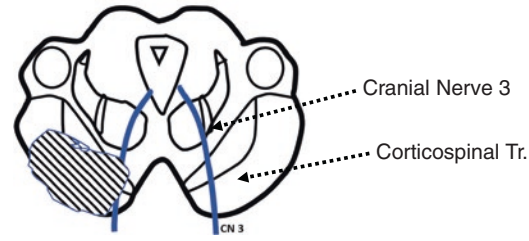
Lesion #2 Key



Syndrome: Lateral medullary syndrome
Artery: Posterior inferior cerebellar

Symptom	Tract or nucleus compromised	Cell body of origin (for tracts)
Ipsilateral loss of pain and temp to the face	Spinal nucleus of V and spinal tract of V	Trigeminal ganglion (Fig. 2.6)
Contralateral loss of pain and temp to limbs	Spinothalamic tract	Dorsal horn (Fig. 1.4)
Dysphagia, dysarthria	Nucleus ambiguus CNs 9 and 10	Nucleus ambiguus (Fig. 2.1)
Ipsilateral ataxia	Inferior cerebellar peduncle	Dorsal nucleus of Clark (Fig. 1.5)
Horner's syndrome	Descending spinothalamics	Hypothalamus (Fig. 6.5)
Fast-beating nystagmus to contralateral side	Vestibular nucleus	

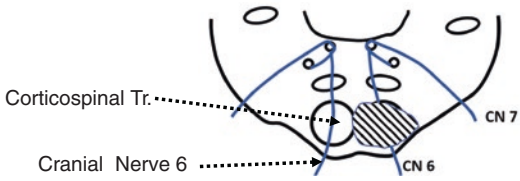
Lesion #3 Key



Syndrome: Medial midbrain syndrome
Artery: Posterior cerebral

Symptom	Tract	Cell body of origin
Contralateral UMN	Corticospinal	Precentral gyrus (Fig. 1.3)
Ipsilateral CN 3 deficit	CN 3	Oculomotor nucleus (Fig. 13.7)
Ptosis, dilated pupil	CNS	Edinger-Westphal nucleus (Fig. 13.7)
Contralateral lower face weakness	Corticobulbar	Precentral gyrus (Fig. 7.4)

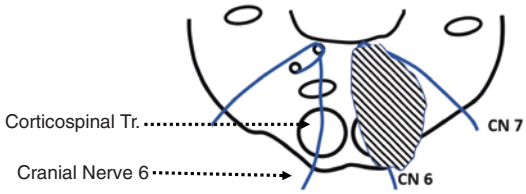
Lesion #4A Key



Syndrome: Medial pontine
Artery: Paramedian branches of basilar

Symptom	Tract	Cell body of origin
Contralateral UMN signs	Corticospinal	Precentral gyrus (Fig. 1.3)
Ipsilateral medial strabismus	CN 6	Abducens nucleus (Fig. 3.6)

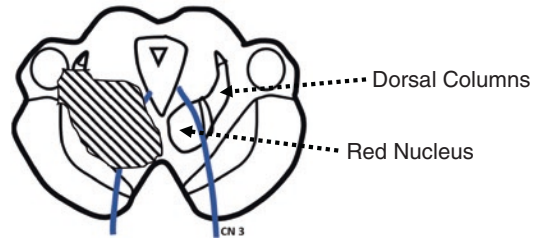
Lesion #4B Key



Symptom	Tract	Cell body of origin
Contralateral UMN signs	Corticospinal	Precentral gyrus (Fig. 1.3)
Ipsilateral loss of facial expression	CN 7	Facial motor nucleus (Fig. 7.4)
Lateral gaze paralysis	Abducens nucleus	Abducens nucleus (Fig. 3.6)

Note that 4A and 4B are almost identical, except that patient A has a lesion to the abducens nerve so only the ipsilateral eye is affected—paralysis of ipsilateral ocular abduction. While patient B has a lesion to the abducens nucleus, so both eyes are affected—lateral gaze paralysis.

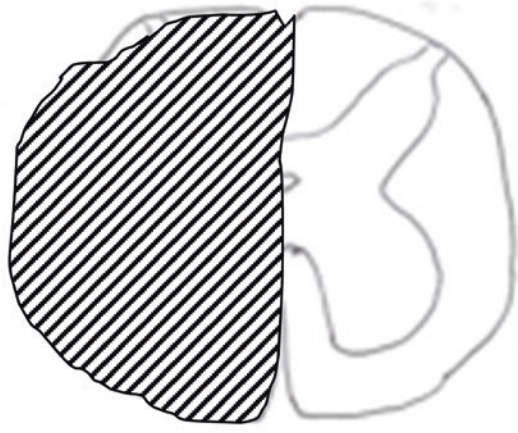
Lesion #5 Key



Syndrome: Benedikt's syndrome
Artery: Perforating branches of posterior cerebral

Symptom	Tract or nucleus	Cell body of origin
Contralateral tremor	Red nucleus	Red nucleus (Fig. 8.5)
Ipsilateral CN 3 palsy	CN 3	Oculomotor nucleus (Fig. 13.7)
Ptosis, dilated pupil	CN 3	Edinger-Westphal nucleus (Fig. 13.7)

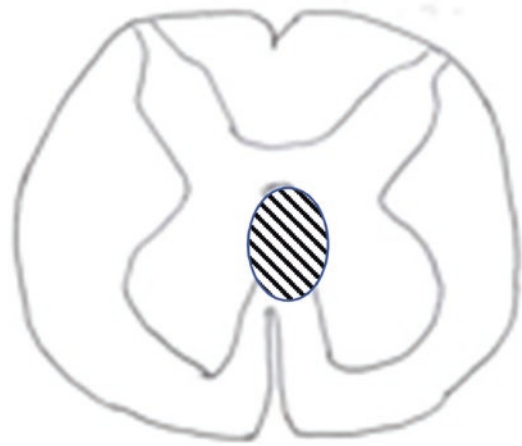
Lesion #6 Key



Syndrome: Hemisection of cord at C5

Symptom	Tract	Cell body of origin
LMN signs at C5	Anterior horn	Anterior horn (fig)
UMN sings in the lower limb	Corticospinal	Precentral gyrus (fig)
Contralateral loss of pain and temperature in from C5 down	Spinothalamic	Dorsal horn (fig)
Ipsilateral loss of pain and temperature at C5	Lissauer's tract	DRG (fig)
Horner's syndrome	Descending hypothalamics	Hypothalamus (fig)
Ipsilateral dorsal column signs	Fasciculus gracilis and cuneatus	DRG (fig)

Lesion #7 Key



Syndrome: Syringomyelia

Symptom	Tract	Cell body of origin
Contralateral loss of pain and temperature to upper limbs	Anterior white commissure	Dorsal horns, bilateral (Fig. 1.13)

This is just a summary of arteries and syndromes. See text for more details. There are potential variations in all these syndromes from one patient to another (Table 16.1).

Table 16.1 Summary of major arteries and syndromes

Artery	Syndrome
Anterior spinal	Medial medullary syndrome (also from vertebral artery)
Posterior inferior cerebellar	Lateral medullary syndrome
Anterior inferior cerebellar	Lateral pontine syndrome
Basilar	Locked-in syndrome
Perforating branches of basilar	Medial pontine syndrome
Posterior cerebral and brainstem	Medial midbrain
Posterior cerebral and occipital lobe	Various visual field deficits
Posterior cerebral and temporal lobe	Pie in the sky, memory issues
Anterior communicating artery	Possible hypothalamus and visual field deficits
Anterior cerebral	Alexia without agraphia
Lateral striate	Typically, pure motor deficits
Posterior communicating	Third nerve palsy
Superior cerebellar	Trigeminal neuralgia
Anterior cerebral	Apraxia, bladder and bowel deficits, loss of motor and sensory to contralateral lower limb
Middle cerebral artery, superior Division	Broca's aphasia, UMN to contralateral face and upper limb
Middle cerebral artery, inferior Division	Hearing deficit, Wernicke's aphasia Possible Gerstmann's syndrome
Anterior choroidal	Contralateral hemiplegia and homonymous hemianopsia
Thalamogeniculate arteries	Thalamic pain syndrome
Central artery of the retina	Cherry red spot due to lack of perfusion to inner retinal layers
Labyrinthine artery	Hearing and balance deficits

100 High-Yield Neuroanatomy Buzz words

17

In the left-hand column below, you will find 100 words that should trigger a response. With a blank sheet of paper, cover up the answers on the right, and test yourself by seeing what the words on the left trigger. These are 100 high-yield facts that you should be familiar with before a clinical rotation or a board exam. Each buzzword is explained in the book.

1	Syringomyelia	1	Bilateral loss of pain and temperature at the level of lesion. Possible LMN deficit in upper limbs. Cavitation of central canal
2	Hemisection of the spinal cord	2	Contralateral loss of pain from lesion down, ipsilateral UMN signs from lesion down, ipsilateral loss of DCs from lesion down. Belt-like loss of P/T at the level of lesion. Horner's if above C7
3	Tabes dorsalis	3	Three "Ps" pain, paresthesia, and polyuria. Most likely. Romberg sign. Argyll Robertson pupil
4	Anterior spinal artery occlusion in the cord	4	Bilateral paresis and bilateral loss of pain to the lower limbs. Most common site of pathology is artery of Adamkiewicz. Usually occurs at T9-12 level. Side effect of aortic surgery or spine surgery
5	Posterior spinal artery occlusion	5	Damages dorsal columns on one side. Ipsilateral deficit of conscious proprioception
6	L4 radiculopathy	6	Sensory loss on medial foot and leg; patellar tendon weak, quadriceps weakness
7	L5 radiculopathy	7	Sensory loss on dorsum of the foot, no good reflex test, dorsiflexion of toes
8	S1 radiculopathy	8	Sensory loss on lateral foot, Achilles tendon reflex, plantar flexion
9	Dentate nucleus projection	9	VL, VA of thalamus and red nucleus
10	Gerstmann's syndrome	10	Acalculia, finger agnosia, agraphia, R/L disorientation, posterior lobule of parietal lobe, particularly the angular and supramarginal gyri
11	Three layers of the cerebellum	11	Molecular, Purkinje, granule
12	Pinpoint pupils	12	Pontine lesion, or opioids
13	Vestibular nuclei lesions	13	Fast nystagmus to contralateral side, ataxia ipsilateral (falling toward ipsi side)
14	Medial Midbrain Syndrome	14	Ipsilateral CN deficit, contra UMN to the body, contralateral lower face. Posterior cerebral artery

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15	Medial medullary syndrome	15	Ipsilateral CN 12 deficit, contralateral UMN signs on the body. Contralateral DC signs. No Horner's syndrome. Anterior spinal or vertebral artery
16	Benedikt's syndrome	16	Contralateral tremor, ipsilateral CN 3 deficit, maybe contralateral dorsal column signs
17	Dorsal midbrain syndrome	17	Paralysis of upward gaze. Hydrocephalus. Parinaud syndrome. "Setting sun sign"
18	Lateral medullary syndrome	18	Ipsilateral loss of pain and temperature on the face, contralateral loss of pain and temperature on the body, ataxia, dysphagia, dysarthria, nystagmus to contralateral side. Horner's. Most likely PICA or vertebral artery
19	Uncal herniation	19	Compresses CN 3. Ipsilateral CN deficit, contralateral homonymous hemianopia, and ipsilateral UMN signs (most likely, but could be contralateral UMN signs. Books will vary on UMN side). Cerebral peduncle is compressed at Kernohan's notch
20	Posterior communicating artery aneurysm	20	Compresses CN 3. Dilated pupil, possibly ophthalmoplegia
21	Meyer's loop	21	"Pie in the sky," superior quadrantanopia
22	Pie on the floor	22	Parietal lobe. Inferior quadrantanopia
23	Alexia without agraphia	23	Splenium of corpus callosum. Lesion to occipital artery on dominant side that damages left occipital lobe and splenium Typically *left* posterior cerebral
24	Lingual gyrus lesion	24	Contralateral superior quadrantanopia with macular sparing
25	Cuneate gyrus lesion	25	Contralateral inferior quadrantanopia with macular sparing
26	RAPD	26	Paradoxical dilation of the pupil. Due to lesion of optic nerve or retina
27	Adie's pupil	27	Parasympathetic deficit. Dilated pupil
28	Craniopharyngioma and visual defect	28	Bitemporal visual field defect. Starts in inferior field
29	Adenoma and visual defect	29	Bitemporal visual field defect. Starts in superior field
30	Cherry red spot	30	Occluded central artery of the retina
31	Lesion to nondominant parietal lobe	31	Contralateral neglect, think clockface picture
32	Tumor in pterygopalatine fossa, what is CN nerve?	32	V2 and its branches
33	Medial pontine lesion	33	Paralysis of lateral gaze to ipsilateral side (CN 6 nucleus), ipsilateral facial palsy (CN 7 fibers), contralateral hemiparesis (corticobulbar tract). At rest eyes will drift toward the paralyzed side of body—"wrong-way eyes." Paramedian branch of basilar artery
34	Decorticate rigidity	34	Bilateral lesion above red nucleus. Upper limbs flexed at the elbow
35	Decerebrate rigidity	35	Bilateral lesion below red nucleus, but above vestibular nucleus. Upper limbs extended at the elbow
36	Cold water in the right ear. Which way is slow deviation?	36	Right
37	Spinning chair test and postrotatory movement. Which direction is slow deviation at stop after spinning?	37	In direction of spinning
38	Argyll Robertson pupil	38	Pupil reacts to accommodation but not light. Neurosyphilis patients

39	Thalamic pain syndrome	39	Contralateral loss of pain followed by excreting pain emanating from contralateral side of body— – thalamogeniculate arteries
40	Basal ganglia. Direct and indirect pathways are from which nucleus?	40	Caudate and putamen
41	Hemiballismus	41	Subthalamic nucleus
42	Dopamine drives movement by driving the direct or indirect pathway?	42	Direct, although the direct pathway is inhibitory. Dopamine increases output of direct pathway so inhibition is increased
43	**Wernicke's** symptoms	43	Ataxia, ophthalmoplegia, confusion (triad)
44	**Korsakoff's symptoms**	44	Confabulation, hallucinations
45	Wernicke-Korsakoff's site of pathology	45	Mammillary bodies, medio-dorsal nucleus of thalamus
46	Kluver-Bucy	46	Medial temporal lobe, placidity, loss of fear hypersexuality, hyperorality
47	Amygdala	47	Responsible for response to fear
48	Nucleus basalis of Meynert	48	Degeneration of cholinergics, Alzheimer's
49	Cell bodies of fibers in optic tract	49	Ganglion cells of the retina
50	Locked-in syndrome	50	Lesion to basilar artery. Patient loses all motor control except for some eye movements
51	Lesion at stylomastoid foramen	51	Loss of muscles of facial expression
52	Lesion in facial canal	52	Loss of muscles of facial expression plus a dry eye, hyperacusis, and loss of some glands to the palate and mouth
53	Lesion to inferior cerebellar peduncle	53	Ipsilateral ataxia
54	Lesion at the genu of internal capsule	54	Loss of contralateral corticobulbar input to CNs. Loss of contralateral lower face
55	Anoxia, most sensitive part of the hippocampus	55	CA1—Sommer's sector
56	Wilson's disease	56	Genetic, hepatolenticular degeneration. Copper builds up in putamen and globus pallidus
57	Carbon monoxide poisoning	57	Globus pallidus
58	Methanol poisoning	58	Putamen
59	Superior division of MCA occlusion	59	Broca's aphasia, contralateral UMNs to the face and arm. Lower limb spared
60	Inferior division of MCA occlusion	60	Wernicke's aphasia. Possible contralateral homonymous hemianopia
61	Normal pressure hydrocephalus	61	Wet, wacky, wobbly
62	Facial colliculus	62	Facial nucleus and fibers of CN 6. Significant because they are so close
63	Which thalamic nucleus is in limbic circuit?	63	Anterior
64	Thalamic pain syndrome, artery?	64	Contralateral pain, thalamogeniculate A's.
65	NMDA receptor	65	Ligand and voltage gated. Involved in LTP
66	Scotty dog's collar	66	Pars interarticularis
67	Asking the patient to adduct the eye and then look inferior tests the	67	Superior oblique
68	Expected response of a comatose patient with an intact brainstem to cold water in the left ear?	68	Slow eye nystagmus is absent
69	Lesion to the left MLF. What happens on attempted gaze to the left, and to the right?	69	Normal gaze to the left. On gaze to the right, inability to adduct the left eye, nystagmus in the right eye. Think contralateral nystagmus

70	Expected response of a comatose patient with an intact cortex to warm water in the right ear	70	No eye movements
71	Bilateral bow-tie atrophy	71	Optic chiasm
72	Orbitofrontal lobe	72	Decision-making
73	Phineas Gage	73	Railroad accident. First frontal lobotomy
74	Alexia without agraphia	74	Posterior cerebral artery on dominant side
75	Clockface picture	75	Parietal lobe on nondominant side
76	CN 9 parasympathetics travel on?	76	Auriculotemporal nerve a branch of V3
77	Area postrema	77	Vomiting
78	Jet lag	78	Suprachiasmatic nucleus, melatonin receptors
79	Ventral tegmental area (VTA)	79	Motivation, reward, behavior. Behaviors associated with drug use. High concentration of dopamine receptors
80	Obsessive-compulsive disorder	80	Cingulate gyrus
81	Locus coeruleus	81	Principal site for norepinephrine, thought to be involved with ADHD
82	Dorsal raphe	82	Principal site for serotonin, thought to be involved in clinical depression
83	Periaqueductal gray	83	High concentration of opioid receptors. Involved in descending control of pain
84	Disc herniation between L4 and L5. Root exiting at that level or level below? And what root?	84	Nerve exiting one level below. L5 root
85	Disc herniation between C5 and C6. Root exiting at that level or one level below? And which root?	85	Root exiting at that level. C6 root
86	Disc herniation. Which ligament gives way?	86	Posterior longitudinal ligament. On lateral edge
87	Right CN 4 nerve palsy. Which way head tilt?	87	Left
88	Cavernous sinus. Which CNs travel through it? And symptoms of compression?	88	All nerves associated with eye: CNs 3, 4, 6. Plus V1 and V2. So ophthalmoplegia and V1 and V2 territory. Not V3
89	Horner's syndrome found in medial or lateral brainstem strokes?	89	Lateral
90	Trigeminal neuralgia, artery?	90	Superior cerebellar artery
91	Anterior choroidal artery	91	Contralateral hemiparesis, contralateral homonymous hemianopia
92	Watershed Infarct in cerebral cortex	92	Between MCA and PCA. Effects upper-limb territory, spares lower limb and face territory "man in a barrel"
93	Guillain-Barre	93	Autoimmune, often follows respiratory or intestinal infection. Begins in lower limbs and ascends: weakness, ataxia, paresthesia, eventual paralysis
94	LTP, what, where?	94	Long-term potentiation, hippocampus, learning and memory
95	Damage to medial temporal lobe following a CVA	95	CA1 of hippocampus
96	Wallerian degeneration, direction	96	Anterograde
97	Coma due to loss of?	97	Reticular activating system (RAS)
98	Central cord syndrome	98	Motor deficits more than sensory. Upper limb. Lower limbs spared usually
99	Conus medullaris syndrome	99	Combination UMN +LMN signs to lower limb
100	Optic tract lesion	100	Contralateral homonymous hemianopia, contralateral RAPD, contralateral bow-tie atrophy

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