Eye Movements

Date: August 15, 2011 – 9:30 AM
Reading Assignment: Mason, Medical Neurobiology; Chapter 10 (pp 187-205) & Chapter 26 (pp 583-588).

Learning Objectives:

1. Know the muscles and the nerves responsible for opening and closing the eyelids.
2. Be able to compare the differences between pupillary and accommodation reflexes.
3. Know the muscles and the nerves responsible for the six cardinal directions of gaze.
4. Be familiar with the various types of eye movements.
5. Be able to identify nerve/muscle deficits based on abnormal eye movements.

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SMALL GROUP II
NEURO LOGY EXAM II
MOTOR SYSTEMS

Date: August 15, 2011 - 10:30 AM
Reading Assignment: Small Group Session. Neurological Examination of Sensation, Reflexes and Motor Function (Dr. Merchut)

Learning Objectives:

1. Explain how to test and grade muscle strength in patients.

2. Explain the anatomical correlates of different patterns of weakness, such as monoparesis, paraparesis, quadriparesis, hemiparesis, proximal weakness or distal weakness.

3. Define the concepts and significance of "spasticity," "rigidity," "fasciculation" and "fibrillation."

4. Contrast the findings of an upper motor neuron versus lower motor neuron lesion and the significance of each.

Demonstration of Motor Examination

Passive movement of limb to assess *muscle tone.*

Observation for *atrophy* or *fasciculations.*

Strength testing of individual muscles (define grading system of 0 to 5).

Case 1

A 10-year old boy falls out of a tree, landing on the side of his neck, which is very painful. He did not strike his head or lose consciousness. He can no longer move his right arm, and has no sensation there. In the hospital, you find that the right upper limb is flaccid and hypotonic, and that he can only shrug his right shoulder, while the other limbs are normal and strong. The right biceps, brachioradialis and triceps reflexes (MSRs) are 1+, while all others are 2+. There is no Babinski sign. Sensation to cotton, pin, temperature, vibration and position sense are virtually absent in the right upper limb only.

1. Is this an upper or lower motor neuron lesion?

2. What is the problem and its anatomical localization?

Case 2

A 41-year old neurologist goes roller-blading for the first time and falls down on the sidewalk, landing with his left knee bent under him. A large, swollen bruise develops at the lateral left knee. The next morning, he awakens to find that his left foot drops. Left dorsiflexion and toe extension is barely detectable at 1/5, while plantar flexion and other muscles are strong at 5/5. Touch and pinprick are nearly absent over the dorsum of the left foot, and along the lateral part of the left leg. Muscle stretch reflexes are all 2+. Peripheral pulses are normal, and there is no back tenderness or radicular pain.

1. What lesion has now become painfully evident to this ex-roller blader?

Case 3

You examine a 60-year old man who recently noticed weakness of his left limbs. He is a smoker who now has lung cancer. Although his right limbs are strong (5/5), he barely can lift his left upper and lower limbs up against gravity, and cannot offer any resistance to your efforts (3/5). When passively moving the left limbs, you initially feel more resistance, which then gives way as you continue to move them through an arc. Reflexes are 3+ in the left limbs, with left ankle clonus and a left Babinski sign. Sensory examination is entirely normal.

1. Is it an upper or lower motor neuron lesion?

2. What is the anatomical localization of this problem?

Case 4

An accomplished athlete, equestrian and actor is riding in a steeplechase competition. His horse falters in the midst of a jump, and he is thrown violently out of the saddle, landing on the back of his head. He cannot get off the ground, and has difficulty breathing. Mechanical ventilation is needed, and later in the hospital he is found to have a hypotonic, quadriplegia, with all muscle stretch reflexes absent, and no Babinski. Sensation to all modalities is absent below the clavicles; there is no sacral sparing. He appears to be awake, and moves his face and eyes on command, with normal pupillary, corneal and gag reflexes.

1. What is the anatomical localization of this problem?

2. Are upper motor neuron signs present? Why or why not?

3. Why is this man unable to breathe on his own?

Study Questions

1. What is an alpha motor neuron? …a gamma motor neuron?

2. Does a dorsal root lesion cause hyper- or hyporeflexia? Explain.

3. Functionally and anatomically, what distinguishes the spinal cord dorsal horn from the ventral horn?

4. Which descending pathways innervate (directly or indirectly) the alpha motor neuron?

5. What is the Brown-Sequard syndrome?

6. Explain how a spinal cord lesion can cause ipsilateral motor deficits and contralateral loss of pain.

7. What is the origin of the phrenic nerve?

8. Which cranial nerves control the gag reflex?

9. Describe the blood supply to the spinal cord.

Neurological Examination of Sensation, Reflexes and Motor Function (Dr. Merchut)

Sensation

1. Definitions and terminology

There are three types of **primary or basic sensation. Exteroceptive sensation** refers to external stimuli, typically light touch, pain, and temperature, detected by various receptors in the skin. **Proprioceptive sensation** refers to stimuli from muscles, tendons, ligaments and joints, in relation to position and movement of the body, limbs and digits, which is important for balance and coordination. **Interoceptive sensation** refers to internal stimuli affecting visceral organs, such as the perception of a distended bladder, or pain from an ulcerated stomach.

Cortical or combined sensation involves the simultaneous perception of several basic stimuli, further integrated and interpreted at the cortical level. For example, a small object could be recognized in the dark solely by its combined tactile characteristics of texture, shape, weight, temperature, and so on.

The special or unique sensations of vision, hearing, taste, and smell involve receptors and pathways that are anatomically localized to specific parts of the body. The clinical evaluation of these special sensations will be discussed elsewhere.

2. Clinical evaluation of patients

At this point, a few introductory comments about the neurological examination are needed. The bedside history and physical is concerned with **symptoms**, the subjective complaints of the patient, and **signs**, the objective abnormalities found on the physical examination. Signs and symptoms are then related to one, or perhaps a few, **lesions** or anatomical sites of abnormality in the nervous system. Initially, the signs and symptoms may appear as a confusing array, which cannot be attributed or related to a single anatomical area. After a closer look, armed with knowledge of neuroanatomy, a unique, single lesion, or "short list" of possible lesions, may become apparent. Try the approach of "Ockham's razor," attributed to Father William of Ockham, a Franciscan friar in the 14th-century, who wrote that "entities must not be multiplied beyond necessity." Some "classical" lesions or syndromes described in this course may be encountered infrequently in clinical practice, yet serve as worthy examples of how unusual groups of signs and symptoms can be related to just one lesion.

This neuroanatomical localization, along with other historical clues (severity and tempo of symptoms, relevant family history, occupational exposure, precipitating events such as trauma) suggests the **etiology**, or cause, of the patient's problem. A **differential diagnosis**, or list of possible diseases which may cause the patient's symptoms, can be narrowed down further by appropriate diagnostic testing. Recognition of a specific disease then allows for its specific treatment. With this practical goal in mind, the "intellectual process" or "mental game" of localization is not just an academic exercise, but a practical approach in clinical neurology. All experienced, skilled neurologists and neurosurgeons know that the history and physical is the most helpful and important part of this process.

3. Clinical evaluation of exteroceptive sensation

Patients may report a lack of sensation over part of the body, or may be unaware of the deficit. With various lesions of the sensory system, but particularly with peripheral nerve disorders, they may complain of **paresthesia or dysesthesia. Paresthesia** is an abnormal, spontaneous sensation, not provoked by stimuli, often described as tingling, or "pins and needles." **Dysesthesia** is an uncomfortable, at times painful, hypersensitivity to non-noxious stimuli and may be elicited when examining the patient.

The sensory examination consists of applying typical test stimuli to the patient's skin, while he or she, with eyes closed, tries to identify the type of stimulus correctly, and whether the stimulus is consistently decreased or absent over certain areas. **Light touch** may be tested with a wisp of cotton or light stroke of the finger. A blunted safety pin or broken cotton-swab stick may be used to test **pain (which is often referred to as "pin" or "pinprick" sensation)**. A cool metallic object (edge of the tuning fork) or tube of warm or cool water may be used to test **temperature** sensation. The examiner applies such test stimuli often at the distal lower limbs, alternating from left to right side, and moving proximally. The process is repeated for the upper limbs, and trunk or face.

Vibration sensation is assessed by applying a vibrating 128 hertz tuning fork to a bony structure such as the ankle or knuckle. The patient, with eyes closed, reports when the vibration is gone. Vibration sensation is abnormally decreased at the ankle or knuckle if the tuning fork is still perceived to vibrate more proximally at the patient's knee or elbow, or at the same bony site in the examiner. The latter comparison of patient to examiner is less valid if one person is much older, since vibration sensation normally declines with age.

4. Clinical evaluation of proprioception (proprioceptive sensation)

Proprioceptive sensation is also called **position sense** or joint sense. Testing is performed by raising or lowering the patient's finger or toe subtly a few degrees at one joint (perhaps easiest at the metacarpophalangeal or metatarsophalangeal joints). The patient, with eyes closed, identifies the movement as "up" or "down." If the patient detects only large excursions of the finger or toe, but consistently misses smaller movements, position sense is decreased there. If even large joint movements are not perceived, position sense is then absent. In that case, position sense may be preserved more proximally, which can be noted by testing more proximal joints such as the ankle or wrist.

5. Clinical evaluation of cortical or combined sensation

These sensory modalities involve object recognition (**gnosis**) as well as perception of objects or more complex stimuli. A lesion in the parietal sensory cortex or its connecting pathways produces a cortical sensory deficit in the contralateral body, while primary sensations may be relatively intact. **Stereognosis** refers to the tactile recognition of familiar or common objects, such as a penny or paper clip placed in the palm, with the patient's eyes closed. A deficit here may be referred to as astereognosis. **Graphesthesia**

involves the identification of numbers traced on the palm with the patient's eyes closed. A deficit of the latter is termed agraphesthesia or graphanesthesia. **Double simultaneous stimulation** refers to the ability to perceive two tactile stimuli applied simultaneously to the same bilateral parts of the body, such as both hands or both feet, again with the patient's eyes closed. When bilateral tactile stimuli are given, the consistent failure to detect a stimulus on one side is due to a contralateral parietal cortical lesion, and is described as **extinction on double simultaneous stimulation. Two-point discrimination** (also called **fine touch**) is the ability to detect the simultaneous application of two sharp points separated by a minimal distance on the skin. A deficit here consists of perceiving the two points as one point, or failing to feel it at all. The stimulus (special calipers, or an unfolded paper clip) should be perceived as two distinct points when only 3-4 mm apart at the fingertip, 20-30 mm apart at the dorsal hand and at greater distances of separation over the limbs and trunk. Although conveyed by the posterior columns, two-point discrimination is usually considered a cortical sensation.

6. Anatomical localization of sensory deficits

In disorders of peripheral nerves, initial involvement of the larger, more myelinated sensory fibers causes impairment of position sense and vibration, while initial involvement of the smaller, less myelinated or unmyelinated sensory fibers produces early impairment of temperature and pain (or pin) sensation. Eventually, if the peripheral neuropathy becomes extensive and severe, all fibers and all sensory modalities will be impaired.

If lesions exist in specific sensory pathways in the spinal cord or brainstem, certain sensory modalities may be lost while others are preserved. **Lesions of the posterior or dorsal columns** lead to deficits in position sense, vibration, and two-point discrimination. Although generally regarded as a primary or basic exteroceptive sensation, vibration sense is conveyed mainly via the posterior (dorsal) columns, and thus is clinically associated with the proprioceptive sensation of position sense. Isolated deficits of two-point discrimination have been associated with contralateral sensory (parietal) cortex lesions. **Lesions of the spinothalamic tract** create deficits in pain (pin) sensation and temperature. More than one spinal cord pathway conveys the sensation of light touch, so absence of light touch sensation occurs only in extensive lesions of the spinal cord or its dorsal roots (or in severe peripheral neuropathy or thalamic lesions).

It is not only the type of sensory loss that is important for localization of a lesion, but also where the deficit maps out on the patient's body. In the case of a **mononeuropathy,** sensation is decreased or lost in the territory of one peripheral nerve (Fig. 1). If there is a **polyneuropathy (peripheral neuropathy),** sensation is decreased or lost in several peripheral nerves, creating a **"stocking and glove"** distal pattern of deficit. **Dermatomal deficits** (Table 1) are sensory impairments in the territory of one or more dermatomes from one or multiple root lesions (Fig. 1). In the case of a single dermatomal lesion, a sensory deficit may not be clearly detected on examination because of the normal overlap of dermatomal sensory territories. The patient's own reported localization of sensory abnormality, paresthesia or dysesthesia is often more helpful in that situation. In **spinal cord lesions (myelopathies),** dissociation of sensation is characteristic (loss of one modality of sensation with preservation of another), although

this may also occur in brain stem lesions. **Intramedullary spinal cord lesions** occur **within** the spinal cord parenchyma, causing a **suspended** or vestlike sensory loss and **sacral** (dermatome) **sparing** of sensory deficit. **Extramedullary spinal cord lesions** compress the spinal cord from outside, creating an initial sensory loss in sacral segments, progressing up "to a level" because of lamination of the spinothalamic tract. A **hemisensory (hemibody)** deficit of basic sensations on the right or left side of the body including the face is caused by a contralateral **thalamic** lesion, or involvement of sensory pathways to the contralateral parietal lobe. Isolated or predominant deficits involving **cortical or combined sensation** typically occur on one side of the body, and are usually due to a lesion in the contralateral parietal sensory cortex.

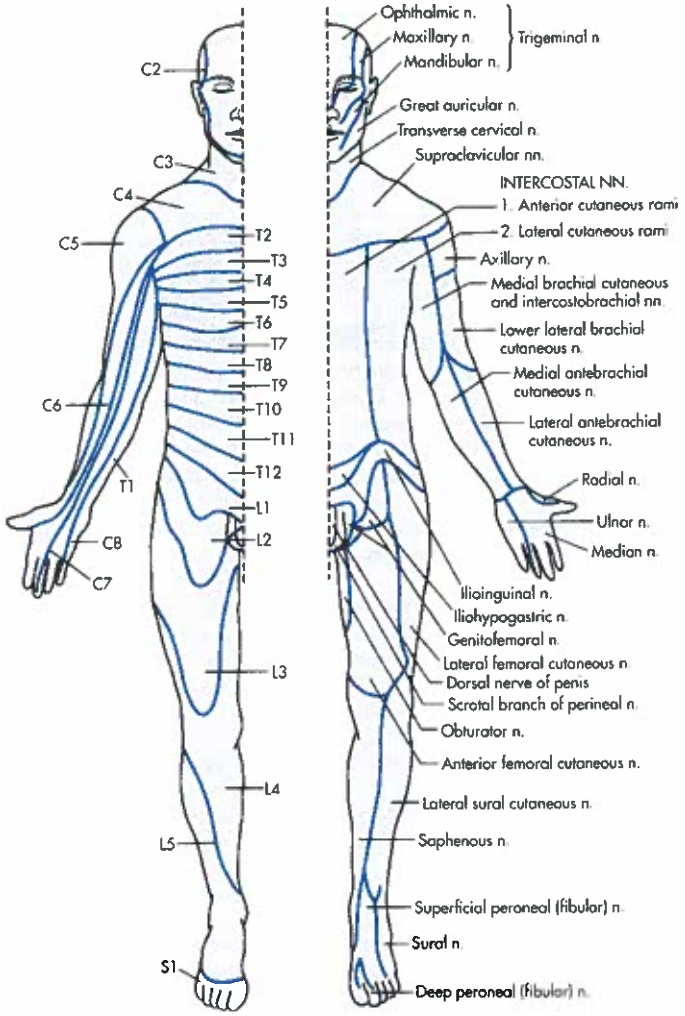

Fig. 1 Sensory territories for dermatomes and peripheral nerves (from Gilman S, Newman SW. Manter and Gatz's Essentials of Clinical Neuroanatomy and Neurophysiology. 9th ed. Philadelphia: FA Davis, 1996)

Table 1 Important Dermatomal Landmarks	
DERMATOME	BODY LANDMARK
C5	Lateral shoulder
C6	Thumb
C7	Index/middle fingers
C8,T1	Ring/little fingers
T4	Nipple
T10	Umbilicus
L3,4	Anterior thigh
L5	Dorsal foot
S1	Lateral foot/sole

Interoceptive sensation typically involves visceral pain, caused by an inflamed internal organ, as in appendicitis, or a sense of fullness or pressure, as from a distended bowel or bladder. It is poorly localized at times, in comparison to other modalities, except for the scenario of **referred pain. Referred pain** is perceived along a dermatome having sensory afferents from the same dorsal root level as the diseased internal organ. A heart attack may be heralded by pain along the inside of the left arm and forearm (C8, T1 dermatomes), while an infection below the right diaphragm may cause pain at the right shoulder (C3,4,5 dermatomes).

Reflexes

1. Definitions and terminology

A **reflex** is a quick, automatic, replicable motor response or muscle contraction provoked by a stimulus. In neurological disease, normal physiologic reflexes may be increased, decreased or lost, and abnormal pathologic reflexes may appear, especially with upper motor neuron lesions. Clinically important reflexes include **muscle stretch reflexes** (also called deep tendon reflexes, or commonly referred to just as "reflexes") and **superficial reflexes**.

2. Muscle stretch reflexes

Muscle stretch reflexes (MSRs) are elicited by the hammer tap of a selected tendon, which causes a brief or single contraction of its muscle. The commonly tested MSRs are listed in Table 2. The tendon tap causes passive stretching of its muscle and

neuromuscular spindles, which activates Ia sensory nerve fibers (**afferent reflex arc**), with subsequent depolarization of the alpha motor neurons (anterior horn cells) at that root level of the spinal cord. This depolarization of motor nerves leads to the contraction of muscle fibers and a visible muscle twitch (**efferent reflex arc**). Sometimes when a muscle stretch reflex cannot be elicited, it may be due to an anxious patient who is subconsciously tensing muscles. In that case, the examiner should perform a reinforcement maneuver to "distract" the patient and obtain the MSR. With the **Jendrassik maneuver,** the patient is asked to hook together his flexed fingers, attempting to pull them apart, while the examiner taps the tendons at the knee or ankle. Other reinforcement maneuvers may be used for obtaining upper limb reflexes, such as clenching the jaw. These maneuvers may actually lessen supraspinal inhibition of the reflex arc, rather than merely serving as a "mental distraction" for a tense, nervous patient.

Table 2 Muscle Stretch Reflexes	
Biceps	C5,6
Brachioradialis (radial)	C5,6
Triceps	C7,8
Finger flexors	C8,T1
Quadriceps (patellar, knee jerk)	L2,L3,L4
Achilles (ankle Jerk)	S1,2

MSRs are clinically graded on a scale of 0 to 4 (Table 3). An absent reflex despite reinforcement maneuvers is graded 0, while a reflex elicited only with reinforcement maneuvers is graded 1. An abnormally brisk reflex grade of 4 occurs when repetitive muscle contractions persist while the tendon is stretched. This is called **clonus,** and is best demonstrated at the Achilles' tendon (Fig. 2).

Table 3 Grading of reflexes (0-4)	
Grade	Response
0	Reflex absent despite reinforcement
1	Reflex present only with reinforcement
2	Average reflex
3	Very brisk reflex without clonus
4	Reflex followed by repetitive jerking movements (clonus)

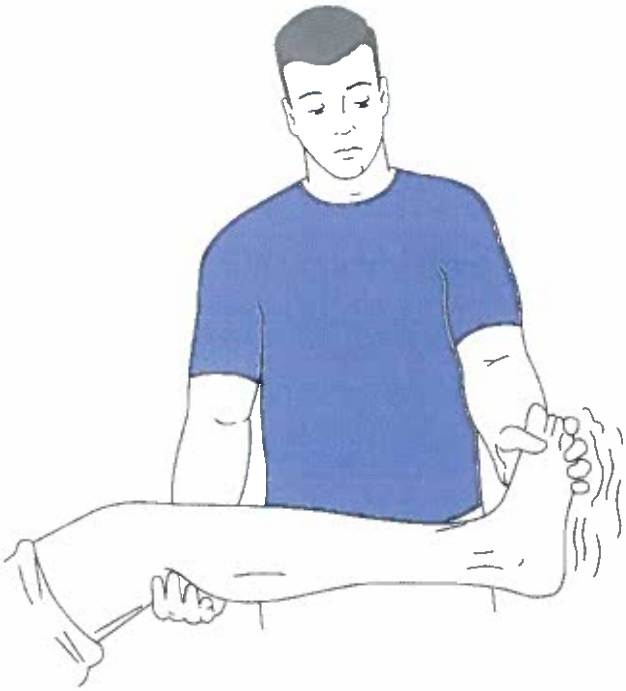

Fig. 2 Ankle clonus (repetitive jerks of plantar flexion as examiner maintains stretch on the Achilles' tendon)

3. Abnormalities of muscle stretch reflexes

Disorders disrupting the afferent or efferent reflex arcs may cause MSRs to be decreased (**hyporeflexia**) or absent (**areflexia**), which often occurs in polyneuropathy or radiculopathy. However, healthy older adults may have absent ankle reflexes merely due to aging. Abnormally increased MSRs (**hyperreflexia**) occur with upper motor neuron lesions, where the inhibitory effect on the local reflex circuit from descending supraspinal tracts is lessened. Besides the grading of individual reflexes, another significant abnormality is whether or not MSRs are symmetrical between the left and right sides. **Asymmetrical hyperreflexia** on one side of the body strongly suggests an upper motor neuron (corticospinal tract) lesion.

4. Superficial reflexes

Most **superficial reflexes** are cutaneous reflexes, provoked by tactile stimuli to a localized area of skin or mucous membrane. An exception is the pupillary light reflex, where stimulation involves shining light into the pupil of the eye. The **cranial nerve--mediated superficial reflexes** are characteristically **consensual**, with a bilateral response to a unilateral stimulus: touching one cornea produces a bilateral blink for the corneal reflex. The afferent and efferent reflex arcs consist of different cranial nerves (Table 4).

Table 4 Cranial Nerve Superficial Reflexes		
REFLEX	UNILATERAL STIMULUS (AFFERENT NERVE)	BILATERAL REFLEX (EFFERENT NERVE)
Pupillary	Shine light (CN II)	Pupils constrict (CN III)
Corneal	Touch cornea (CN V)	Eyes blink (CN VII)
Palpebral	Touch eyelid/lash (CN V)	Eyes blink (CN VII)
Gag (pharyngeal)	Touch pharynx (CN IX)	Gag (CN X)

Other cutaneous reflexes do not involve cranial nerves and may be diminished or absent from an interrupted reflex arc at the lower motor neuron level or from an upper motor neuron (corticospinal tract) lesion. The **abdominal reflex** consists of stroking the skin over each abdominal quadrant, whereby local muscle contraction causes retraction or deviation of the umbilicus toward the stimulus (reflex arcs at T7 through T12 and upper lumbar spinal cord segments). The abdominal reflex may be difficult to assess in obese patients or those with scars from abdominal surgery. The **cremasteric reflex** consists of stroking up the inner thigh, eliciting ipsilateral elevation of the testicle (reflex arcs at L1,2 spinal cord segments).

5. Pathological (abnormal) reflexes

The most important and reliable pathological reflex is the **Babinski sign,** which **indicates an upper motor neuron (corticospinal tract) lesion in the adult**. In infants, however, supraspinal tracts may take 1-2 years to normally myelinate, so the presence of a Babinski sign is not abnormal. The stimulus consists of stroking the lateral sole, from the heel to the ball of the foot (Fig. 3), causing slow dorsiflexion of the great toe (and less importantly fanning of the little toes). The Babinski sign notably is not a monosynaptic muscle stretch reflex. Other stimuli may also elicit "an upgoing toe," and these signs are named after those who first reported them. The Chaddock sign is elicited by stroking around the lateral ankle, then down the dorsolateral foot, and is a useful alternative to the Babinski sign in patients with ticklish feet.

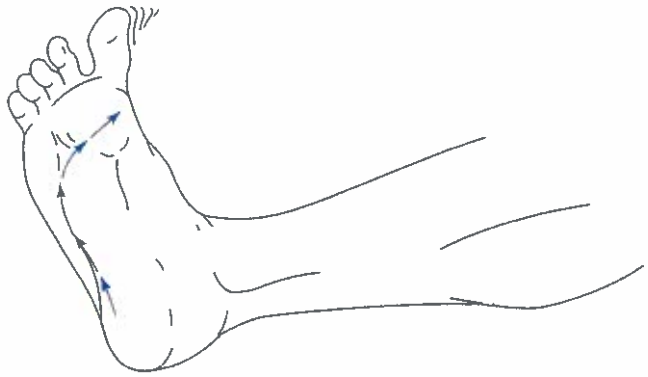

Fig. 3 The Babinski sign (stimulus applied in direction of the arrows)

There is no equivalent of the Babinski sign in the upper limbs. Digit flexor responses are the next best sign suggestive of an upper motor neuron lesion there. The examiner lifts or supports the patient's proximal middle finger, and then flicks its distal phalanx downwards (**Hoffman's sign**) or upwards (**Tromner's sign**), eliciting flexion of the fingers of that hand. This response, however, appears to involve the muscle stretch reflex of the finger flexors, which one would expect to be increased anyway in the presence of an upper motor neuron lesion.

6. Miscellaneous clinical signs

Meningeal signs are noted when the meninges are inflamed and irritated from infection or subarachnoid hemorrhage. Nuchal rigidity is the stiffness felt by the examiner when the patient's head is passively flexed in the anterior direction. **Kernig's sign** is present when the examiner feels resistance while attempting to fully extend the patient's knee with the hip in 90 degrees of flexion. **Brudzinski's sign** is present when the patient's hips and knees flex after the examiner passively flexes the neck.

Signs suggestive of nerve **root irritation or compression** include **Lasegue's sign,** the replication of radicular pain when the patient's hip is passively flexed with the knee in extension (straight leg raise maneuver).

Motor Function

1. Clinical evaluation of strength

Observation of the patient's gross body movements "in action" may reveal weakness, such as the dragging of a lower limb when walking across the room or standing up from a chair. The presence of a **pronator drift** suggests a subtle proximal upper limb weakness from a corticospinal tract lesion. The examiner would see slow pronation (palm turning towards the floor) and downward drift of an outstretched, supinated arm. Subtle weakness of the hand may be manifest more as impaired finger dexterity rather than gross weakness of certain muscles. The strength of individual

muscles can be graded on a scale of 0 to 5 (Table 5). As an example, a patient with a weak deltoid muscle may be able to abduct the arm only when lying supine in bed, since the arm is not abducted against gravity, but only moves in the horizontal plane of the bed: this would be graded as 2 out of 5. If the arm could be barely abducted against gravity, as when seated, but not offer much resistance to the examiner's effort, it would be graded as 3 out of 5.

Table 5 Grading of strength

GRADE	MUSCLE MOVEMENT
0	No movement
1	Flicker of movement
2	Movement only if gravity eliminated
3	Movement only against gravity
4	Movement against partial resistance
5	Movement against full resistance

2. Patterns of weakness

Focal weakness may occur in the territory of one peripheral nerve, or segmentally, such as the thigh or hand, where the weak muscles are innervated by more than one nerve or spinal root. The weakness of one limb may be partial **(monoparesis)** or complete **(monoplegia). Myelopathic** weakness, from a bilateral spinal cord lesion, may involve both lower limbs, from a lesion at the thoracic level. This lower limb weakness may be partial **(paraparesis)** or complete **(paraplegia).** All four limbs may be weak from a cervical spinal cord lesion, whether partial **(quadriparesis)** or complete **(quadriplegia).** Bilateral upper motor neuron lesions in the brain or brain stem could also cause paraparesis (or paraplegia) or quadriparesis (or quadriplegia). A **hemiparetic** (partial) or **hemiplegic** (complete) weakness of the upper and lower limbs on one side is typically due to an upper motor neuron lesion in the ipsilateral spinal cord or contralateral brain or brain stem. In a patient with muscle disease, the typical **myopathic** pattern of weakness involves the **proximal** limbs, namely at the shoulders and hips. In a patient with a peripheral neuropathy (polyneuropathy), the **neuropathic** pattern of weakness is **distal**, involving the feet, and later the hands.

3. Muscle tone

Muscle tone clinically is the resistance felt by the examiner when passively moving a patient's limb. Tone may be increased, **hypertonicity,** or decreased, **hypotonicity.** There are two types of hypertonicity: spasticity and rigidity. The increased tone in **spasticity** is unequal between agonist and antagonist muscles. This increased tone is especially increased in antigravity muscles (upper limb flexors, lower

limb extensors), which may allow patients the ability to stand and walk again. The perceived resistance varies as the limb is moved passively (**clasp-knife spasticity**). (Analogous to opening a clasp-knife or pocket-knife, there is more resistance when first pulling the blade out of the handle, and then the motion gets easier.). **Spasticity indicates an upper motor neuron lesion involving the pyramidal or corticospinal tract.** Loss or impairment of some descending motor pathways to the spinal cord presumably reduces some of the inhibition at the spinal cord level, leading to a relative overactivity of the gamma motor neurons. The gamma motor neurons tend to activate muscle spindles by shortening their intrafusal muscle fibers, making extrafusal muscle fibers very sensitive to stretch, thus creating the clinical signs of spasticity and hyperreflexia. However, clinical upper motor neuron lesions in patients vary from the precise upper motor neuron lesions seen in animal models.

Rigidity is the type of hypertonicity where the increased tone feels equal between agonist and antagonist muscles, so resistance feels constant as the limb is moved passively (**lead pipe rigidity**). (Analogous to bending a lead pipe, the resistance is constant throughout the task.). Rigidity is from a lesion in the **extrapyramidal** system. If tremor is present, passive limb movements produce a ratchety feeling (**cogwheel rigidity,** analogous to the jerky turning of a cogwheel inside a clock).

Hypotonicity is decreased muscle tone, usually from an afferent sensory or lower motor neuron lesion that interrupts the reflex arc of the muscle stretch reflex relevant to the tested limb. It has also been described in cerebellar disease, but may be difficult to observe clinically.

4. Muscle atrophy

Decreased bulk or wasting of a muscle indicates **muscle atrophy**, which is most prominent or severe in lower motor neuron lesions or myopathies (muscle disease). Milder degrees of atrophy occur in upper motor neuron lesions, or from disuse (actually "non use") of a limb, as in a patient confined to bed for other medical reasons.

Other signs of muscle denervation from a lower motor neuron lesion include fasciculations and fibrillations. A **fasciculation** is the grossly observable, spontaneous twitch of a group of muscle fibers innervated by a single lower motor neuron. More precisely, this is a spontaneous discharge of a **motor unit,** which consists of the lower motor neuron, its axon, and all the muscle fibers it controls. A **fibrillation** is the spontaneous twitch of an individual muscle fiber, which is visible only in the "naked" muscles of the tongue, not in limb muscles. Fibrillations always indicate denervation, while fasciculations occur with denervation as well as in benign conditions such as muscle fatigue. Generally, fasciculations are considered a serious sign of underlying neurological disease if other abnormal signs are present as well.

5. Upper versus lower motor neuron lesions

Upper or lower motor neuron lesions are the clinical syndromes which consist of distinct findings or signs pertaining to patterns and severity of weakness, changes in muscle tone or muscle stretch reflexes, and the presence or absence of fasciculations or pathological reflexes (Table 6). A precise, surgical lesion of the upper motor neurons or

corticospinal tract in an animal model may produce different deficits. Nonetheless, the presence of these findings in patients correlates very well with localization to an upper or lower motor neuron lesion, and is an **important concept for clinical neurology**. One scenario is an important exception to this clinical rule: **spinal or neurogenic shock**. In a sudden, severe spinal cord injury, typically from trauma, the expected upper motor neuron clinical signs are initially absent, only to gradually emerge days or weeks later. Thus, in spinal shock, paralysis is initially accompanied by diffuse hypotonia and areflexia. The latter findings may occasionally be seen also in acutely severe or extensive lesions of the brain or brainstem, as in a massive stroke.

Table 6 Clinical Signs of Motor Neuron Lesions

SIGN	UPPER MOTOR NEURON LESION	LOWER MOTOR NEURON LESION
Weakness	More diffuse	More focal
Atrophy	Mild, general	Severe, focal
Atrophy versus weakness	Severe weakness with relatively mild atrophy	Severe atrophy with milder weakness
Fasciculations	Never seen	May be present
Muscle tone	Increased (spasticity)*	Decreased
Muscle stretch reflexes	Increased*	Decreased to absent
Clonus	May be present*	Never present
Pathological reflexes (Babinski sign)	May be present*	Absent

*(except in spinal or neurogenic shock)

RETICULAR FORMATION

Date: August 16, 2011 – 9:30 AM
Reading Assignment: Reticular formation lecture notes – Gruener
Reticular formation presentation – Gruener
Medical Neurobiology by Mason – "425-453". "148-150". "625-630", "168b"

KEY CONCEPTS & LEARNING OBJECTIVES

1. After attending lecture and studying the assigned material you will be able to:
   a.) Outline the major organizational divisions and functions of the reticular formation.
   b.) Describe the ascending reticular activating system and how it relates to sleep-wake cycles
   c.) Describe the difference between sleep and coma and role of the ascending reticular activating system

2. After attending lecture and studying the assigned material you will be able to:
   a.) List the neurotransmitters released by the raphe and locus ceruleus neurons
   b.) Predict potential disorders that relate to their dysfunction or absence

3. After attending lecture and studying the assigned material you will be able to:
   a.) List the functional significance of opiate receptor locations within the central nervous system
   b.) Define the role of the reticular formation in pain modulation.

4. After attending lecture and studying the assigned material you will be able to:
   a.) Be able to draw the oculosympathetic pathway
   b.) Describe and explain the constellation of clinical findings referred to as the Horner's syndrome
   c.) Describe the pupillary findings and maneuvers that can identify the presence of a Horner's syndrome

5. After review of the clinical case presentations in the small groups you will be able to:
   a.) Suggest a site of dysfunction that will explain the signs and symptoms
   b.) Identify the expected site of an abnormality on an MRI scan of the brain
   c.) Start to develop three potential diagnoses (appropriate to the patients' clinical scenario, course and medical history) that would explain the etiology of their presentation.

RETICULAR FORMATION

Overview of the Reticular Formation (RF)

- The term **reticular formation** refers to the network within the brainstem, although it continues rostrally into the thalamus and hypothalamus and caudally into the propriospinal network of the spinal cord.
- A "coordinating system" (like the Limbic system) with "connections" to sensory, somatic motor and visceral motor systems
- Unique cytoarchitecture: dendrites are often long and relatively straight (often arborize within a transverse plane), axons are long as well and extend for considerable distances; cell bodies can be quite large. This structure allows the convergence of somatosensory input onto these neurons and divergence of their efferent outputs.
    - The "connectivity" of their cytoarchitecture allows stimulation of one body area to have an excitatory effect while stimulation of another body site could result in inhibition of those same neurons.
- Organization can be subdivided into three neuronal cell "columns" (medial to lateral) as well as on the basis of their neurotransmitter release

  Neuronal columns (many nuclei and names, but these are some of the major ones):
    - The median ("midline") reticular formation
        - Essentially a column of serotonergic neurons (series of raphe nuclei)
    - The paramedian reticular formation (contains the largest cells) – **"efferent" zone**
        - Locations: Medulla – ***Ventral reticular nucleus*** and ***Gigantocellular reticular nucleus,*** Pontine – ***Caudal pontine nucleus*** and the ***PPRF;*** Midbrain – ***Mesencephalic***
    - The lateral (or parvocellular, small-celled) reticular formation – **"afferent" zone**
        - Extends from the medulla to the pons
        - Receives collaterals from all sensory pathways including special senses
        - Projects to the paramedian zone

  Neurotransmitter release:
    - *Aminergic neurons of the reticular formation*
        - *Serotonergic – brainstem midline; reaches "all" CNS gray matter*
        - *Dopaminergic –* ***ventral tegmental nuclei*** (midbrain)
        - *Noradrenergic – most are located in the* ***locus ceruleus*** (pons)
        - *(Epinephrine-secreting – relatively scarce, exist in the medulla)*
    - *Cholinergic neurons are found in the* ***pedunculopontine nucleus***

- The functions of the reticular formation include:
    - Pattern generator
        - Eye movements; horizontal (PPRF) and vertical (riMLF)
        - Rhythmical chewing movements (pons)
        - Posture and locomotion (midbrain and pons)
        - Swallowing, vomiting, coughing and sneezing (medulla)
        - Micturition (pons)
    - Respiratory control (medulla)
    - Cardiovascular control (medulla)
    - Sleeping and wakefulness control

    - Sensory modulation or "gate" control
        - The term "gating" refers to "modulation" of synaptic transmission from one set of neurons to the next.
- **Ascending Reticular Activating System** (ARAS) is a physiological concept based on these neurons having an arousal effect on neurons within the cerebral cortex (An important contributor are the cholinergic neurons of the RF; close to the locus ceruleus in the pons)

Neuroanatomical "Roadmaps and sites" within the Reticular Formation

Afferents mainly to the medial portion of the RF (esp. the Gigantocellular, Caudal and PPRF)

- Spinoreticular
    - Collateral fibers of the spinothalamic tract, widespread bilateral distribution, but without somatotopy
- Trigeminal, vestibular, auditory and visceral
    - Project to the parvocellular zone (vestibular fibers also to the PPRF)
- Cerebelloreticular
    - Project to the paramedian reticular nuclei; primarily originate from the fastigial nucleus
- Tectoreticular
    - From the superior colliculus' deeper layers
- Corticoreticular
    - Originate in motor and premotor cortex and targeted towards the cells of origin of the reticulospinal tracts (provides a mechanism of cortical feedback)

Efferents originate mainly from the Gigantocellular, Caudal and PPRF nuclei

- Projections to the spinal cord
    - Via the **pontine** and **medullary reticulospinal tracts**
    - Descend bilaterally, no somatotopy, terminate primarily in the intermediate gray of the spinal cord and can be excitatory or inhibitory
    - Effects axial muscles of posture and locomotion (may influence the central transmission of sensory pathways)
- Projections to the brainstem
    - Via the **reticulobulbar fibers** (many brainstem reticular formation fibers travel within the **central tegmental tract**)
    - Has indirect connections to cranial nerve motor and sensory nuclei, direct to dorsal column nuclei and to parasympathetic nuclei

Autonomic Centers (Brainstem areas involved with specific autonomic functions)

- Respiratory control centers (expiratory, inspiratory, apneustic and pneumotaxic)
- Cardiovascular control centers (vasomotor pressor/depressor, cardioacceleratory and inhibitory)
    - Afferents arise from baroreceptors (carotid sinus and aortic arch), chemoreceptors (carotid sinus, lateral reticular formation chemosensitive area in the medulla) and stretch receptors (lung and respiratory muscles)
    - Efferents arise from reticular formation neurons within the pons and medulla

Other important anatomical and functional areas

- **Serotonergic and Noradrenergic Systems**
  - **General Description**
    - Wide distribution, large number of receptors and signal transduction elements leads to the complexity of their pattern of expression
    - Role in integrative behavioral and neuroendocrine functions, sleep-arousal mechanism, modulates the action of other neurotransmitters, pain suppression (via input to the periaqueductal gray)
  - **Aminergic neurons in the reticular formation**
    - **Raphe Nuclei –** origin of serotonergic projections to widespread areas of cerebral cortex, cerebellum, brainstem and spinal cord. Afferents from the cerebral cortex, hippocampus, hypothalamus and periaqueductal gray
    - **Locus Ceruleus –** origin of noradrenergic (noradrenaline, norepinephrine) projections to all areas of the central nervous system (via the central tegmental tract, median forebrain bundle, dorsal longitudinal fasciculus and superior cerebellar peduncle). Afferents from other reticular nuclei, periaqueductal gray, hypothalamus, amygdala and prefrontal cortex
- **Periaqueductal Gray (PAG)**
  - Envelops the cerebral aqueduct in the midbrain and has widespread afferent inputs and efferent connections to the cerebral cortex
  - PAG has an excitatory projection to the ***magnus raphe nucleus (MRN)*** in the medulla. MAG projects (within Lissauer's tract) onto neurons within the substantia gelatinosa. Activation of the MRN (many of its projections release serotonin) excites inhibitory interneurons in the substantia gelatinosa and induces both pre- and postsynaptic inhibition of the projection neurons of the lateral spinothalamic and spinoreticular tracts that results in analgesia
  - The projection from PAG to the MRN is normally under inhibition by internuncial neurons within PAG; those internuncial neurons have opioid receptors on their cell membrane surface. When the opioid receptors on these internuncial neurons are activated, the internuncial neurons are inhibited and the inhibition of those neurons within PAG is then decreased

Some clinical correlates:

- **Horner's syndrome**
  - Clinically consists of ptosis (due to weakness of Müller's muscle), ipsilateral miosis, apparent enophthalmos, anhidrosis of the ipsilateral face and dilatation lag (affected pupil dilates slower than the unaffected pupil).
  - Indicates an interruption of the **oculosympathetic pathway**
    - **First order neuron** originates in the hypothalamus and projects ipsilaterally down the brainstem into the spinal cord where it synapses with the next neuron (second order neuron) within the intermediolateral gray matter of the spinal cord at the C8-T2 level
    - This, **second order neuron** (preganglionic) within the spinal cord, exits in the T1 (C8-T2) ventral root and via the white rami communicantes (closely related to the pleura of the lung apex) enters the sympathetic paravertebral chain and ascends up to the superior cervical ganglia where they will then synapse onto the next neuron (third order neuron)
    - **Third order neuron** (postganglionic) arises from the superior cervical ganglion and forms a plexus around the carotid artery. Those fibers that will innervate sweat glands (and piloerection) will accompany the branches of the external carotid artery. The remainder accompany the internal carotid artery into the carotid canal and then into the cavernous sinus. Within the sinus a large component of these sympathetic fibers join the ophthalmic (V1) division of the trigeminal nerve, but join the sixth (abducens) nerve temporarily before doing so. The ophthalmic nerve will enter the orbit and most of these sympathetic fibers will cross over to the long nasociliary nerves that innervate the intrinsic muscles of the eye (sympathetic fibers also travel with all of the ocular motor nerves as well as the ophthalmic artery, but the portion accompanying the ophthalmic division is the largest)
- **Ascending Reticular Activating System (ARAS)** is a physiological concept. However, via ascending projections from the reticular formation it plays a role in our level of alertness, sleep-wake rhythms and alerting reactions. The cerebral cortex can also affect our level of alertness via projections to the reticular formation, as can real or imaginary mental imagery. Finally, the cerebral cortex can inhibit other sensory input to allow us to focus our attention

Reticular Formation

August 16, 2011

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Reticular Formation

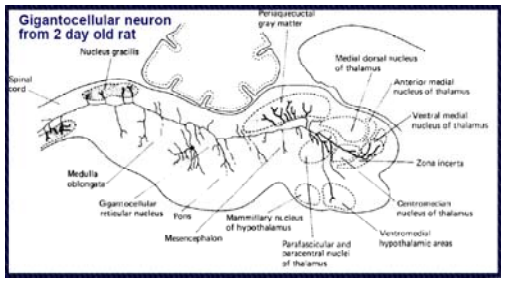
August 16, 2011

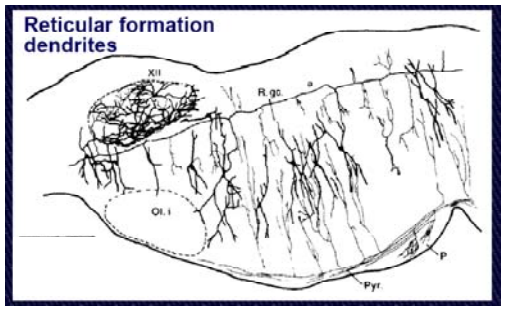
Objectives

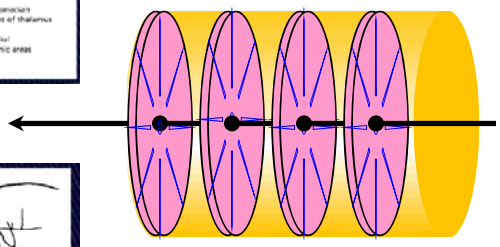
- ✓ **Outline the major divisions of the RF**
- ✓ **Describe the ARAS & difference between sleep & coma**
- ✓ **List the neurotransmitters of the raphe and locus ceruleus and predict the effects of their dysfunction**
- ✓ **List the functional significance & location of opiate receptors**
- ✓ **Be able to draw and describe the outcome of lesions of the oculosympathetic pathway (Horner's syndrome**

General Overview

- ***Reticular formation*** - network of neurons within the brainstem
- "Coordinating system" with connections to sensory and motor (somatic and visceral) systems
- Unique cytoarchitecture (allows ***convergence*** of somatosensory information and ***divergence*** of efferent outputs)
- Range of functions:
  - Pattern generator (eye, chewing, swallowing, coughing sneezing, locomotor)
  - Centers for respiratory/cardiovascular/micturition control
  - Sleeping and Wakefulness
  - Nociception



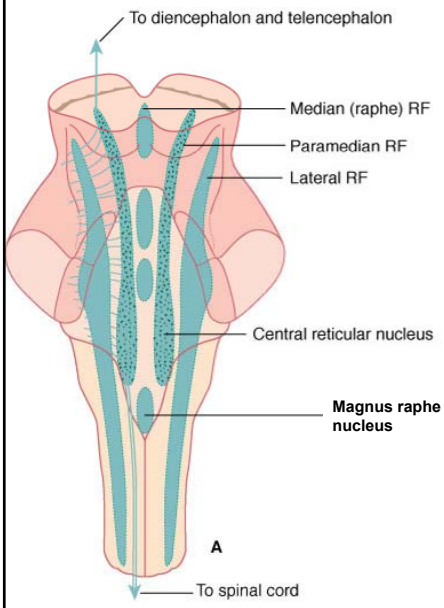




Kandell ER, JH Schwartz. Principles of Neural Science; Elsevier, 1995

Brodal A. Neurological Anatomy, 3rd Ed.; Oxford University Press, 1981

Reticular Formation Nuclei



Midline Zone

Aminergic neurons

Medial Zone ("Effector" zone)

Medulla

Ventral reticular n.

Gigantocellular reticular n.

Pontine

Caudal pontine reticular n.

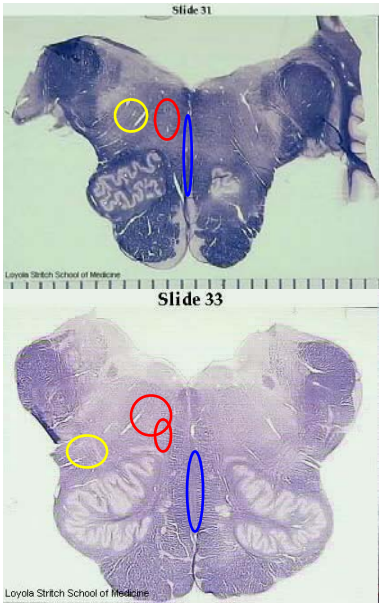
Oral pontine reticular n.

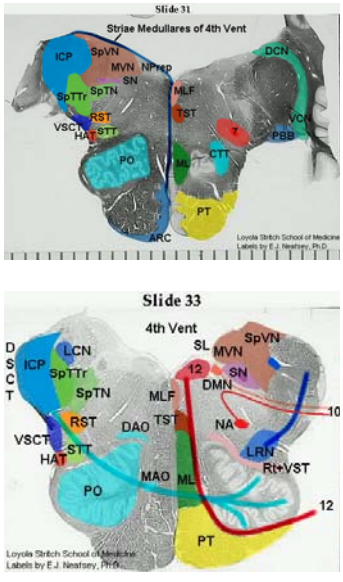
Mesencephalic reticular n.

Lateral Zone ("Sensory" zone)

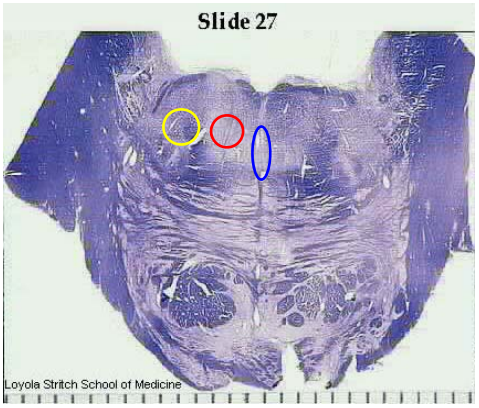
Fitzgerald MJT, Gruener G, Mtui E. Clinical Neuroanatomy and related Neuroscience, 5th Ed., W. B. Saunders 2007

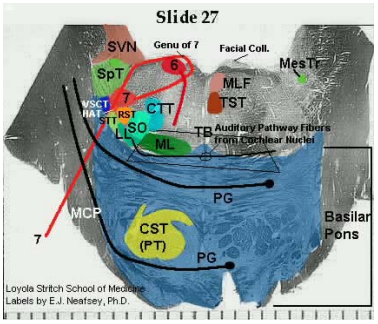
Medullary



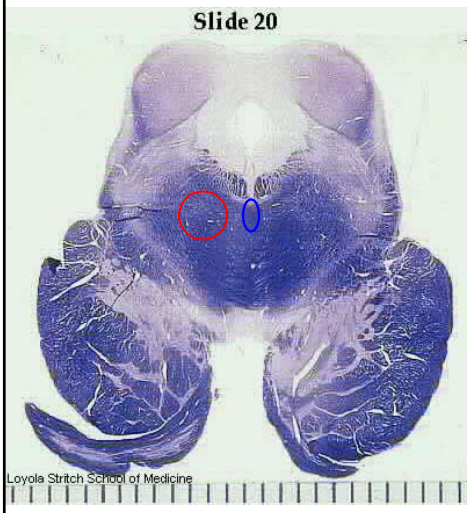


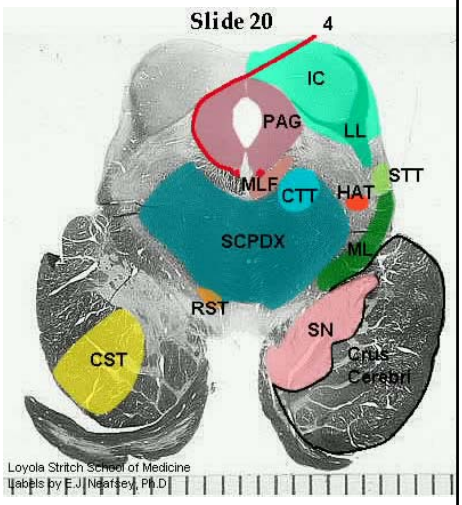
Caudal Pontine





Mesencephalic





Reticular Formation Afferents

- **Afferents**

  (Primarily project <u>to the</u> gigantocellularis, caudal and oral pontine nuclei – the medial or paramedian group)

  – Spinoreticular – receives collaterals from spinothalamic tract, widespread bilateral distribution, no somatotopy

  – Cranial nerves (trigeminal, vestibular, auditory and CN IX & X) – project to the **lateral parvocellular area**

  – Cerebelloreticular – primarily from the fastigial nucleus

  – Tectoreticular – superior colliculi origin

  – Corticoreticular – Motor and premotor cortex onto neurons of origin of the reticulospinal tract (medial group)

Reticular Formation Efferents

- **Efferents**

  (Arise <u>from the</u> gigantocellularis, caudal and oral pontine nuclei – the medial group)

  ➢ <u>Spinal cord termination</u> – ***Pontine and Medullary spinoreticular tracts***

  – Descend bilaterally in ventral lateral funiculi, no somatotopy, terminate in intermediate gray of spinal cord, inhibitory or excitatory

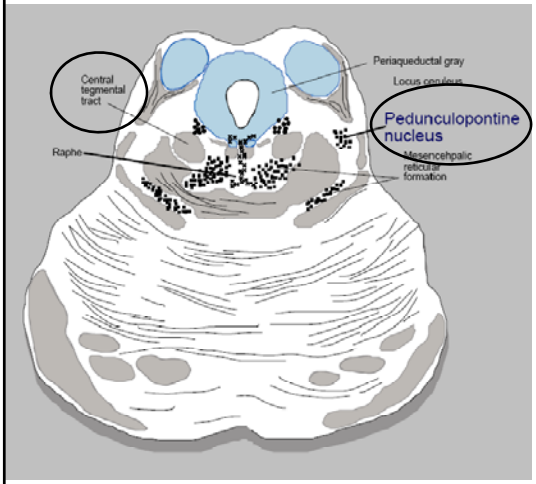
  – Effect on axial muscles of posture and locomotion

  ➢ <u>Brain stem termination</u> – ***Reticulobulbar tract*** and ***Central tegmental tract***

  – Indirect to cranial nerve motor and sensory nuclei, direct to dorsal column and parasympathetic nuclei

  – Intralaminar nuclei of thalamus, basal forebrain nuclei, hypothalamus, amygdala, medial septal nuclei

Pedunculopontine Nuclei



Locomotor Pattern Generators

- **Spinal Generators**
- **Mesencephalic locomotor area**
  - ***Pedunculopontine nucleus***

Sends fibers down the central tegmental tract to the **oral and caudal pontine nuclei** (extensor motor neurons) and **medullary magnocellular neurons** (flexor motor neurons); cholinergic neurons

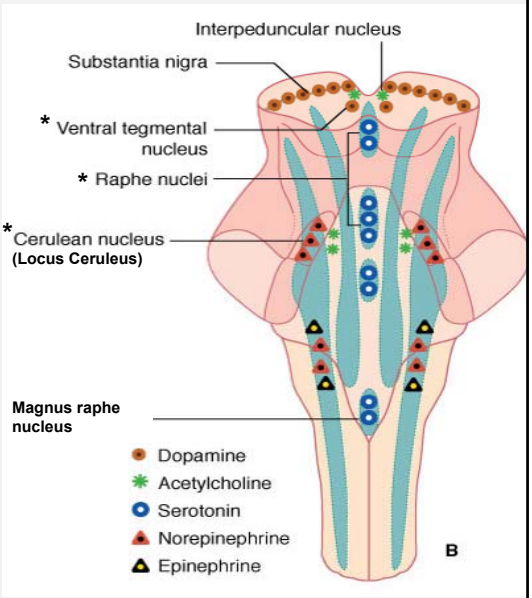
- **Motor areas of cerebral cortex and corpus striatum**

Castro, Merchut, Neafsey, Wurster; Neuroscience: An Outline Approach, 2002

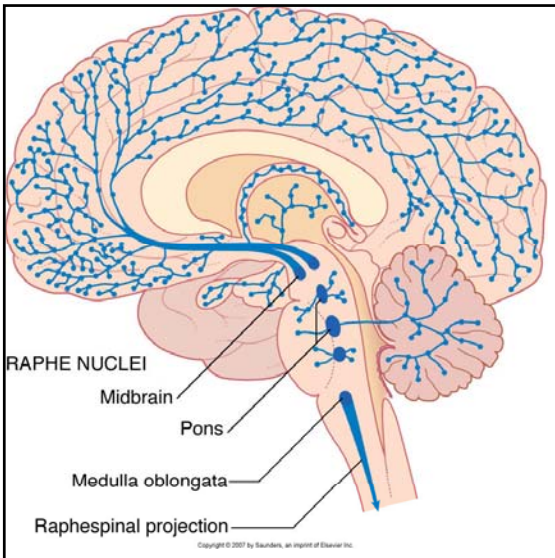
Reticular Formation

Function of the serotonergic and adrenergic systems:

- Integrative behavioral and neuroendocrine functions
- Sleep-arousal mechanisms
- Modulate actions of other transmitters
- Brain growth and development
- Pain suppression



Fitzgerald MJT, Gruener G, Mtui E. Clinical Neuroanatomy and related Neuroscience, 5th Ed., W. B. Saunders 2007



Serotonergic Projections

Largest Territorial distribution of any CNS neurons

Midbrain – projects to cerebral cortex

Pons – ramifies in brainstem and cerebellum

Medulla – Projects to the spinal cord

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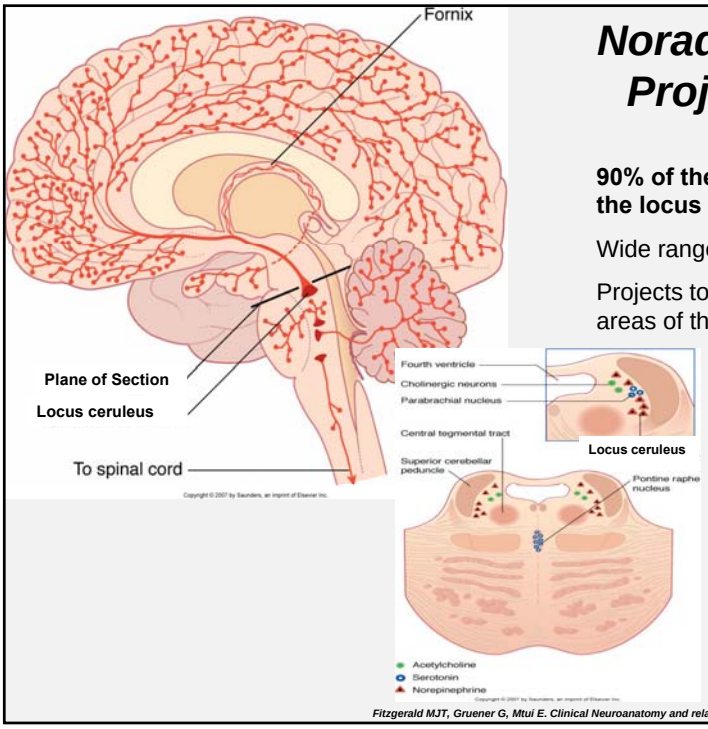


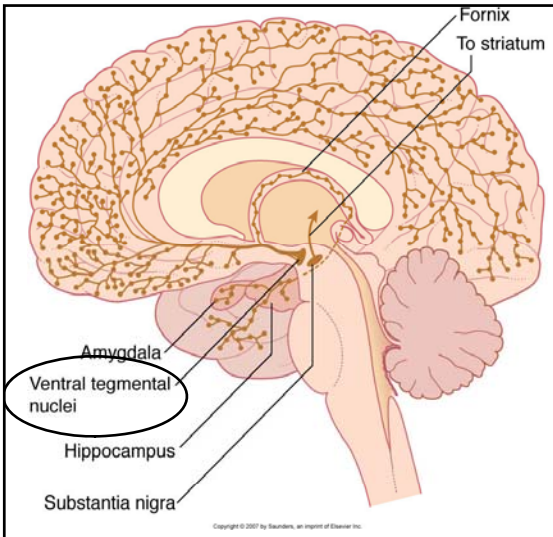
Noradrenergic Projections

90% of these neurons are in the locus ceruleus

Wide range of afferents

Projects to essentially all areas of the CNS

Fitzgerald MJT, Gruener G, Mtui E. Clinical Neuroanatomy and related Neuroscience, 5th Ed., W. B. Saunders 2007



Dopaminergic Projections

Ventral tegmental nuclei (and **substantia nigra**)

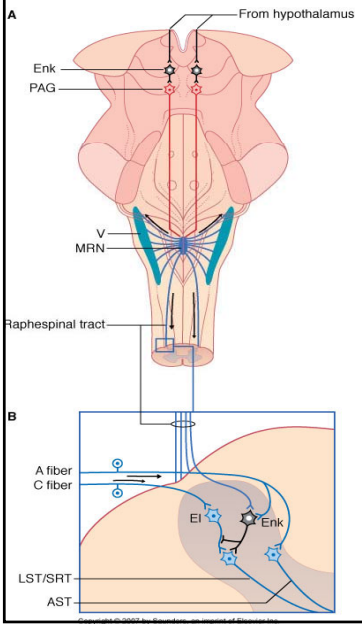
Ventral tegmental nuclei – project via

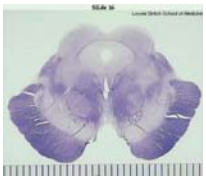
mesocortical fibers to the frontal lobe and

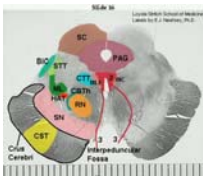
mesolimbic fibers to the nucleus accumbens

Fitzgerald MJT, Gruener G, Mtui E. Clinical Neuroanatomy and related Neuroscience, 5th Ed., W. B. Saunders 2007

Periaqueductal Gray (PAG)







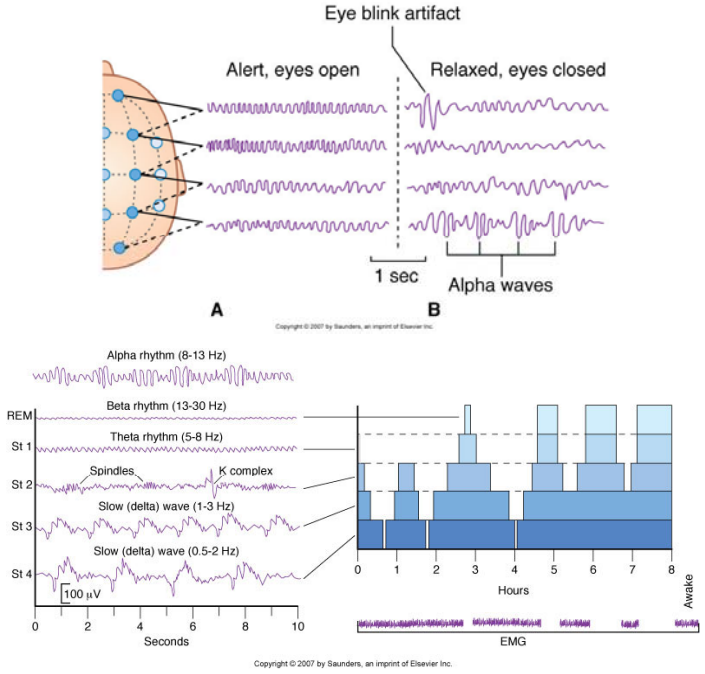
Magnus Raphe Nucleus projects to the cord via the ***Raphespinal fibers*** and descend bilaterally within Lissauer's tract, terminating in the substantia gelatinosa. These fibers liberate **serotonin,** exciting inhibitory internuncials and inhibiting nociceptive projection cells

PAG has an excitatory projection to the MRN, but normally inhibited by internuncial neurons. These internuncials are themselves inhibited by **opioid peptides** and **β-endorphins**

Fitzgerald MJT, Gruener G, Mtui E. Clinical Neuroanatomy and related Neuroscience, 5th Ed., W. B. Saunders 2007

Ascending Reticular Activating System

- Refers to the role of the reticular formation in activation of the cerebral cortex, but there are other "candidates"
  - ***Cholinergic neurons close to the locus ceruleus***
  - Hypothalamus – **tuberomammillary body**
  - Basal forebrain – **nucleus basalis of Meynert**
- ARAS plays a role in our level of alertness, sleep-wake rhythms and alerting (***startle***) reactions
- The cerebral cortex projects to the RF and can influence alertness (as can visual, auditory as well as mental imagery) and inhibits other sensory input which allows focusing your attention



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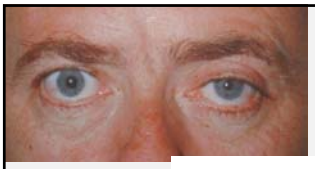
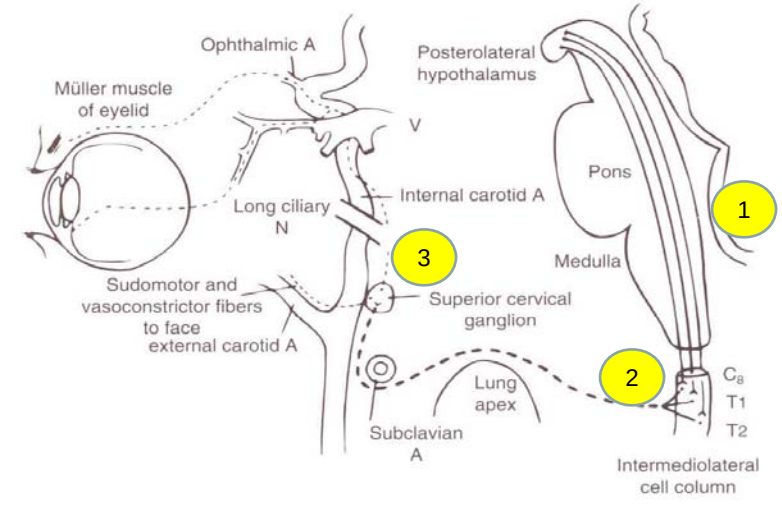


Sympathetic innervation of the eye



Brazis PW, Masdeu JC, Biller J. Localization in clinical Neurology, 5th ed. 2007
http://www.gesundheit.de/roche/index.html?c=http://www.gesundheit.de/roche/ro15000/r16517.008.html

Video case presentation

Pupillary response in an individual with Horner's syndrome

Continuum October 2003

CEREBELLUM

Date: August 16, 2011 – 10:30 AM; August 17, 2011 – 9:30 AM
Reading Assignment: Cerebellum lecture notes - Gruener
Cerebellum presentation – Gruener
Medical Neurobiology by Mason – 217-222, "243-254", 537-558

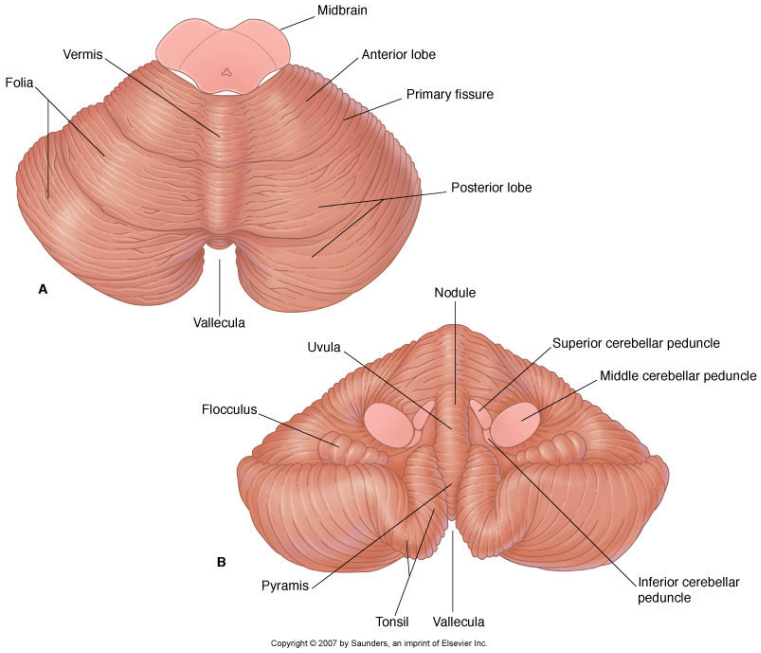
KEY CONCEPTS & LEARNING OBJECTIVES

1. After attending lecture and studying the assigned material you will be able to:
   a.) Outline the major organizational divisions of the cerebellum (transverse and longitudinal)
   b.) Describe the somatotopic maps of the cerebellum
   c.) Identify the cerebellar peduncles and deep nuclei
   d.) List the inputs and outputs of the cerebellum
2. After attending lecture and studying the assigned material you will be able to:
   a.) Describe the functional components of the cerebellar cortex
   b.) Define the origins of the mossy and climbing fibers
3. After attending lecture and studying the assigned material you will be able to:
   a.) List the afferent and efferent contributions to each cerebellar peduncle
   b.) Recall the four major motor decussations ("Extra credit")
4. After attending lecture and studying the assigned material you will be able to:
   a.) Describe the functional components of the cerebellum
   b.) Be able to predict and describe the clinical manifestations of focal lesions
5. After review of the clinical case presentations in the small groups you will be able to:
   a.) Suggest a site of dysfunction that will explain the signs and symptoms
   b.) Identify the expected site of abnormality on an MRI scan of the brain
   c.) Start to develop three potential diagnoses (appropriate to the patients' clinical scenario, course and medical history) that would explain the etiology of their presentation.

CEREBELLUM

Overview of the Cerebellum

Gross Anatomy



Transverse Divisions are formed by transverse fissures

- ***Primary fissure***: divides the cerebellum into an ***anterior*** and a ***posterior lobe.*** A ***horizontal fissure*** then divides the posterior lobe as well.
- ***Posterior lateral fissure***: separates the flocculonodular lobe from the body of the cerebellum

Longitudinal Divisions are the result of functional connections

- Vermis
- Hemisphere
  - Paravermal
  - Lateral

Three peduncles convey the inputs and outputs of each half of the cerebellum

- ***Superior cerebellar peduncle*** (***brachium conjunctivum***)
- ***Middle cerebellar peduncle*** (***brachium pontis***)
- ***Inferior cerebellar peduncle*** (***restiform body***, ***juxtarestiform body***)

Deep nuclei are embedded in cerebellar white matter of each hemisphere (medial to lateral named as..)

- ***Fastigial***
- ***Globose*** (sometimes called the posterior interposed nucleus)
- ***Emboliform*** (sometimes called the anterior interposed nucleus)
- ***Dentate***

Common organizational principles

- Input reaches the cerebellum cortex as ***mossy*** and ***climbing fibers***
- Purkinje cells in the cerebellar cortex project to the deep cerebellar nuclei (and also collaterals to the granule cells)
- Each side of the cerebellum affects the ipsilateral half of the body

Cerebellum receives numerous inputs (approximations)

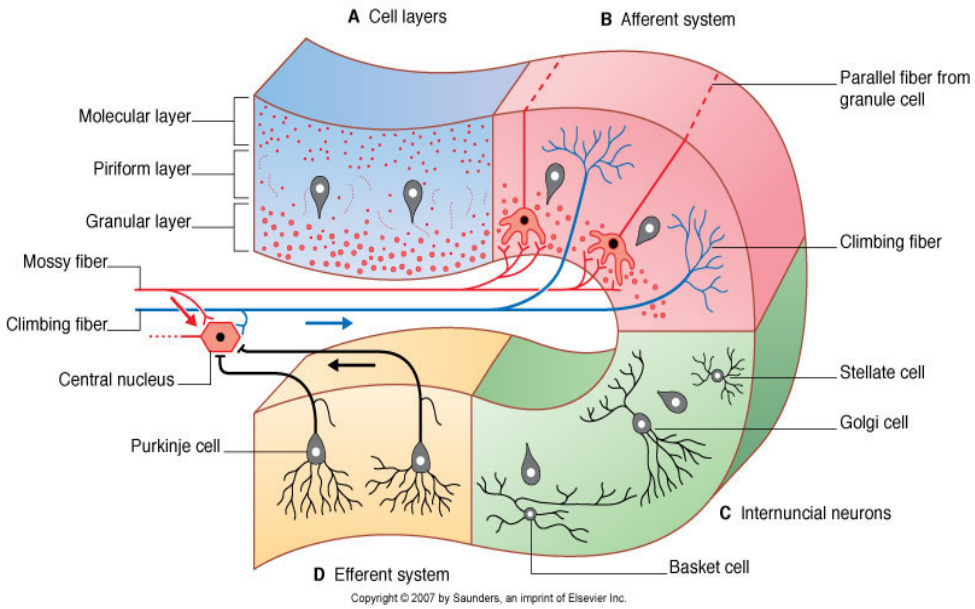
- Vestibular inputs project to the flocculus and the vermis
- Spinal cord inputs project to the vermis and medial hemisphere
- Cerebral cortex projects to the pontine nuclei and then widespread to the cerebellum
- Inferior olivary nucleus has a widespread projection to the cerebellum (as the climbing fibers)
- Visual and auditory information also reach the cerebellum via the pontine nuclei

Longitudinal zone have specific outputs (approximations)

- Vermis projects to the fastigial nucleus (equilibrium and coordination of eye movements)
- Medial and lateral hemisphere project to the interposed and dentate nucleus (medial hemisphere - regulation and coordination of motor tone; lateral hemisphere - planning and coordination of movements)

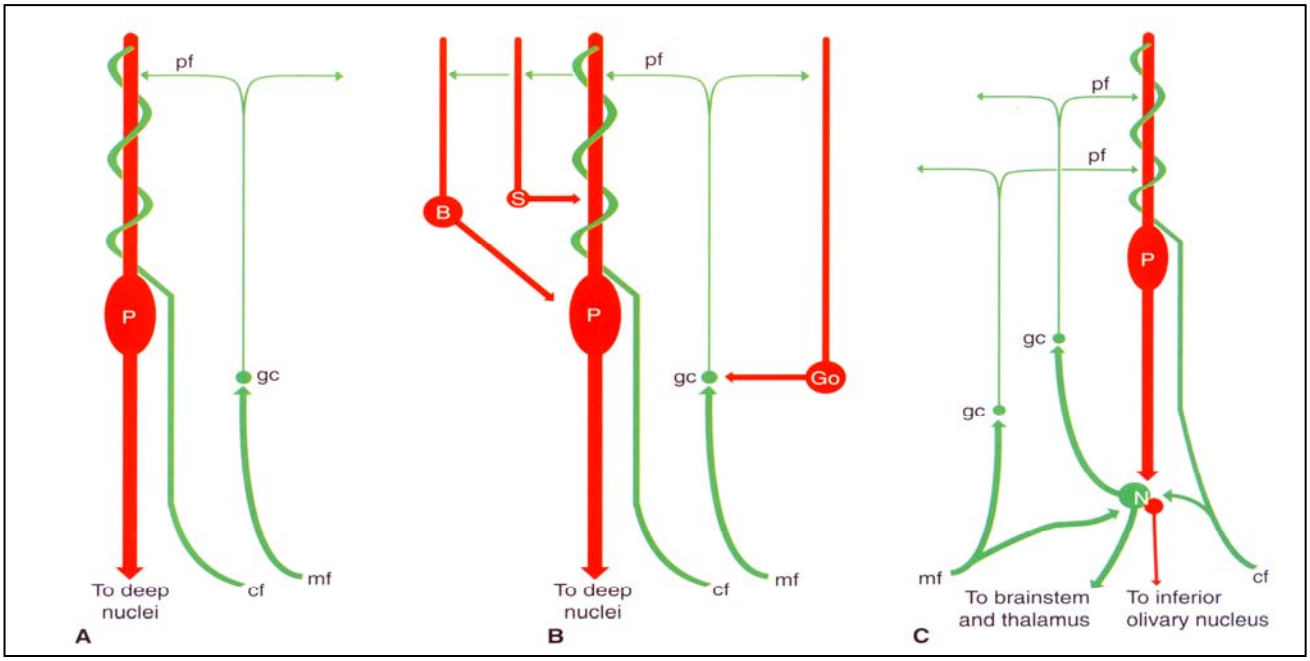
Histology

- Three –layered
  - ***Molecular layer***
  - ***"Purkinje" cell layer***
  - ***Granular layer***



  - *Molecular layer* – consists mainly of axons and dendrites of cerebellar neurons
  - *Purkinje cell layer* – single layer of neurons; only neurons whose axons leave the cerebellar cortex to synapse on the deep cerebellar nuclei, **inhibiting** those nuclei
  - *Granular layer* – consists of small granular cells that send their axons into the molecular layer where they bifurcate into unmyelinated ***parallel fibers,*** which extend along the long axis of the folium. Each parallel fiber passes through and synapses on the dendritic tress of Purkinje cells (up to 500), all are **excitatory** synapses.

- ***Climbing fibers*** originate from the contralateral inferior olivary nucleus; a single climbing fiber ends on each Purkinje cells dendritic tree (making thousands of synapses) as well as sending collaterals onto the deep cerebellar nuclei, all of those are **excitatory**.
- ***Mossy fibers*** represent all of the other afferents to the cerebellar cortex, ending on the dendrites of granule cells (mossy fiber → granule cell → parallel fiber → Purkinje cell, up to 250) and also deep cerebellar nuclei, all **excitatory**
- ***Basket cells*** (axons synapse on the Purkinje cell body) and S***tellate cells*** (axons synapse on the Purkinje cell dendrites), are inhibitory interneurons within the molecular cell layer where their dendrites are activated by the parallel fibers, but their output on the Purkinje cells are **inhibitory**.
- ***Golgi cells*** are within the granular cell layer, but their dendrites are within the molecular cell layer and activated by parallel fibers. Their axons synapse upon the granular cells and are **inhibitor**y



Neuroanatomical "Roadmaps"

Connections to the differing cerebellar zones

***Vestibulocerebellum* –** flocculonodular lobe and part of the uvular which receive vestibular information

***Spinocerebellum* –** most of the vermis and medial hemisphere (except the nodulus and uvula) which receive spinal inputs

Neocerebellum (or ***pontocerebellum***) – lateral hemisphere receives projections from the cerebral cortex via the pontine nuclei

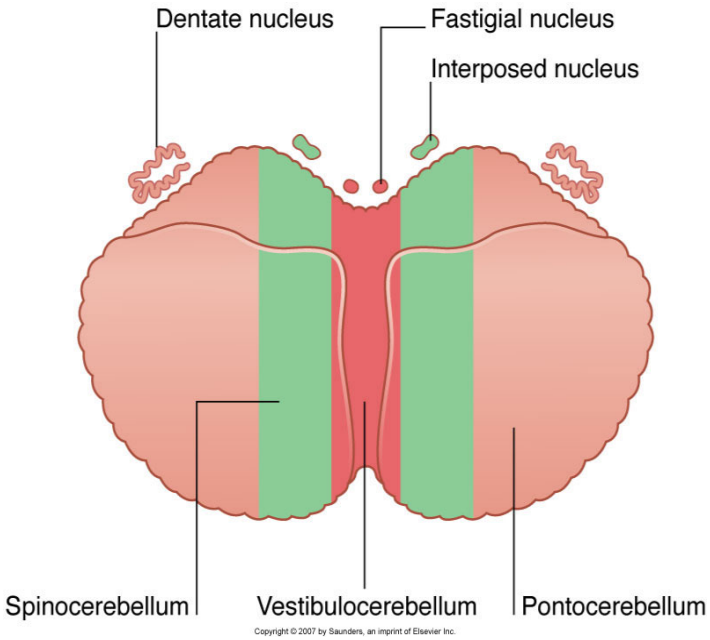
Primary Afferents to the Cerebellum

Tract	Origin	Termination	Peduncle
Vestibulocerebellar	Vestibular ganglia	Nodulus and uvula - Ipsilateral	Inferior
Vestibulocerebellar	Vestibular nuclei	Flocculus, nodulus and vermis - Bilateral	Inferior
Anterior spinocerebellar	Ascends in contralateral spinal cord (T12-L5)	Vermis and intermediate zone - Ipsilateral	Superior
Posterior spinocerebellar	Clarke's nucleus (T1-L2/3)	Vermis and intermediate zone - Ipsilateral	Inferior
Cuneocerebellar	Lateral cuneate nucleus (medulla)	Vermis and intermediate zone - Ipsilateral	Inferior
Rostral spinocerebellar	*Ipsilateral spinal cord (cervical)*	*Vermis and intermediate zone? - Ipsilateral*	*Inferior Superior*
Reticulocerebellar	Lateral, paramedian, reticular tegmental nuclei	Vermis and intermediate zone - Ipsilateral	Inferior (Middle - reticular tegmental nucleus)
Trigeminocerebellar	Spinal and main sensory nucleus of V	Vermis and intermediate zone - Ipsilateral	Inferior
Olivocerebellar	Inferior olivary, accessory olivary nuclei	All areas - Contralateral	Inferior
Pontocerebellar	Pontine nuclei	Anterior and posterior lobes – Contralateral Vermis – Ipsilateral	Middle

Primary Efferents from the Cerebellum

- Entire output of the cerebellum occurs through axons of Purkinje cells
- Axons of the Purkinje cells predominantly project to the deep cerebellar nuclei
  - Vermis projects to the fastigial nucleus
  - Medial hemisphere projects to the interposed nucleus
  - Lateral hemisphere projects to the dentate nucleus
  - Some axons from Purkinje cells in the flocculonodular lobe and vermis will enter the juxtarestiform body and end on the vestibular nuclei
    - Cerebellar "access" to neurons of the spinal cord (via vestibulospinal tracts)
- Most neurons of the deep cerebellar nuclei use glutamate as their neurotransmitter and make excitatory synapses on neurons they contact
  - All the neurons of the deep cerebellar nuclei project back to the cerebellar cortex

- **Fastigial nucleus** *(Fastigiobulbar tracts)*
  - Projects to the vestibular nuclei of both sides
  - Projects to contralateral reticular formation
  - Ipsilateral projection enters juxtarestiform body on same side
  - Contralateral projection crosses midline in the cerebellum (loops over the superior cerebellar peduncle through the ***uncinate or hook fasciculus***) and then enters the juxtarestiform body on the contralateral side



- **Interposed nucleus**
  - Major output enters the superior cerebellar peduncle, decussating in the midbrain
    - Some fibers turn caudally as the ***Descending limb of the superior cerebellar peduncle*** (inhibitory fibers to the inferior olivary nucleus or reticular formation)
  - Some of these ascending/decussating fibers will end in the red nucleus (magnocellular part); this part of the red nucleus gives rise to the rubrospinal tract (small nucleus and tract in man)
  - Majority of decussating fibers pass through/around the red nucleus, join the thalamic fasciculus and end in the VL/VA complex of the thalamus; information is relayed to the limb areas of the motor cortex.

- **Dentate nucleus** *(Dentatorubrothalamic tract)*
  - Major output enters the superior cerebellar peduncle, decussating in the midbrain
    - Some fibers turn caudally as the ***Descending limb of the superior cerebellar peduncle*** (inhibitory fibers to the inferior olivary nucleus or reticular formation)
  - Some of these ascending/decussating fibers will end in the red nucleus (parvocellular part); this part of the red nucleus gives rise to a projection to the inferior olivary nucleus (within the central tegmental tract). **Dentate nucleus → Parvocellular Red nucleus → Inferior olivary nucleus → Cerebellar cortex → Dentate nucleus loop** (may be involved in motor learning of the cerebellum)
  - Majority of decussating fibers pass through/around the red nucleus, join the thalamic fasciculus and end in the VL/VA complex of the thalamus; information is relayed to the motor and premotor cortex

Functions of the longitudinal zones

- Flocculus and vermis – maintenance of equilibrium and coordinating slow eye movements
- Vermis – regulation of posture and stereotyped movements programmed in the brainstem and spinal cord (walking)
- Medial hemispheres – Adjusting limb movements
- Lateral hemispheres – Participates in the planning and programming of voluntary movements (learned and skilled)

Some clinical correlates:

- Injury to the flocculus
  - Dysfunction of slow eye movements, tendency to have a general loss of "equilibrium"
- Injury to the midline
  - Anterior lobe or superior cerebellar vermal syndrome – Broad based staggering gait, incoordination of leg movements
- Injury to the lateral hemisphere
  - Ipsilateral dysfunction of limb movements (dysmetria, intention "tremor", dysdiadochokinesia), hypotonia, hyporeflexia and "pendular" reflexes.

Cerebellum – Part 1

August 16, 2011

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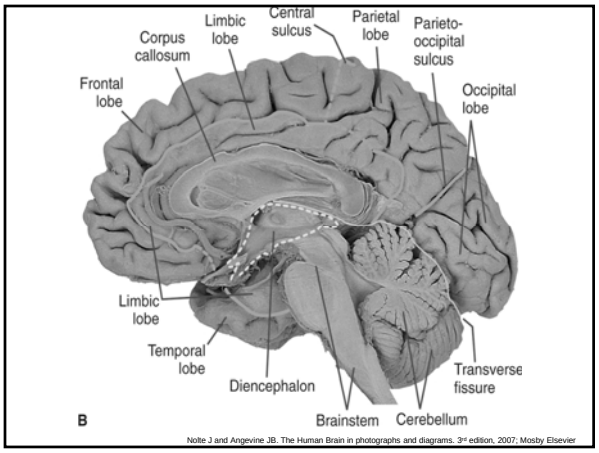
Cerebellum – Part 1

August 16, 2011

Objectives

- ✓ Describe the gross anatomy of the cerebellum
  - Transverse divisions
  - Longitudinal divisions
- ✓ Describe the functional connections
  - Distribution of inputs and outputs
- ✓ Identify the layers and make-up of the cerebellar cortex
- ✓ Define the origins of the mossy fibers and climbing fibers
- ✓ Identify the cerebellar peduncles, nuclei and afferent and efferent contributions



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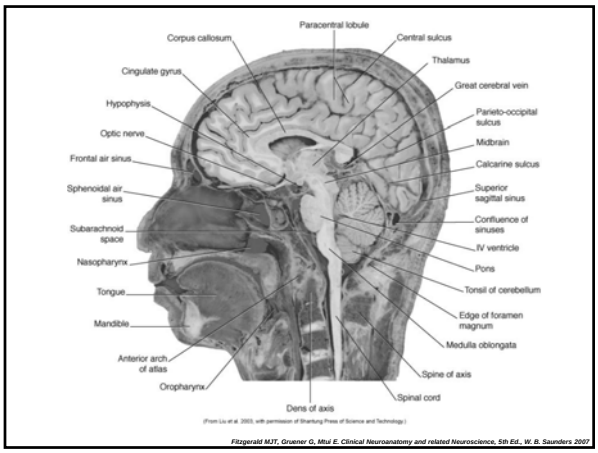

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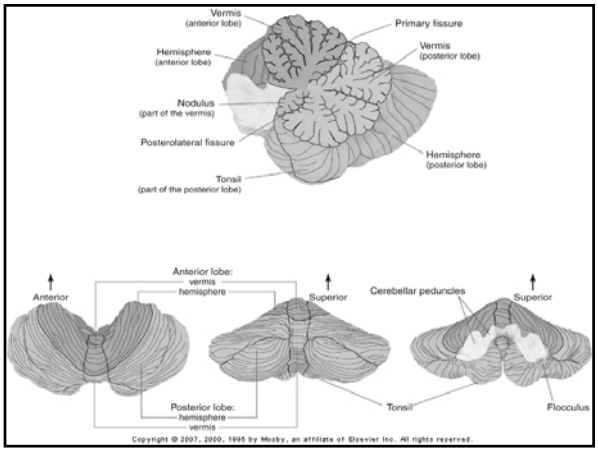

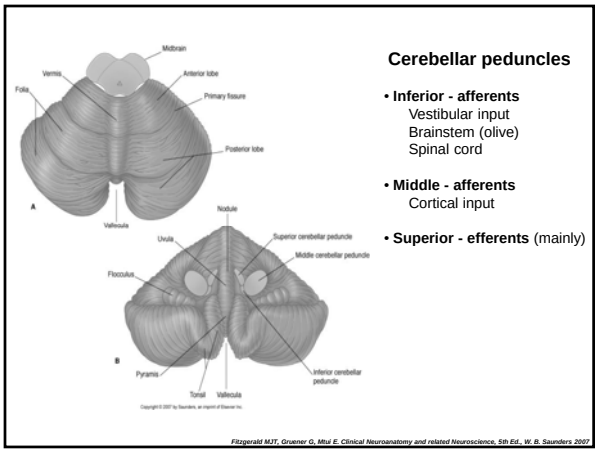

Cerebellar peduncles

- **Inferior - afferents**
  Vestibular input
  Brainstem (olive)
  Spinal cord
- **Middle - afferents**
  Cortical input
- **Superior - efferents** (mainly)

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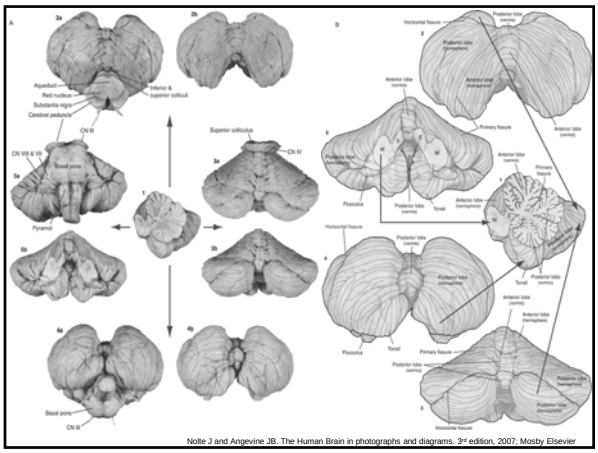

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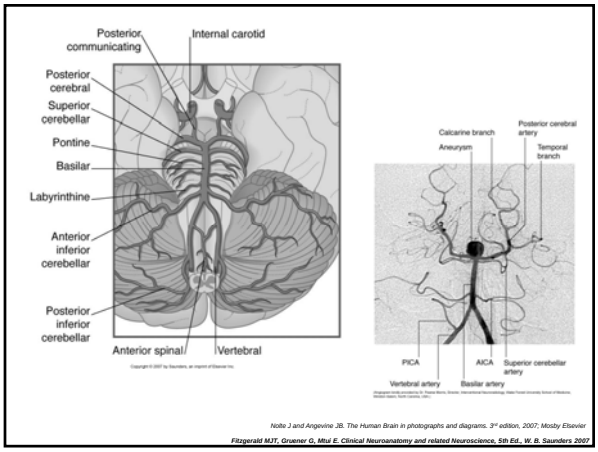

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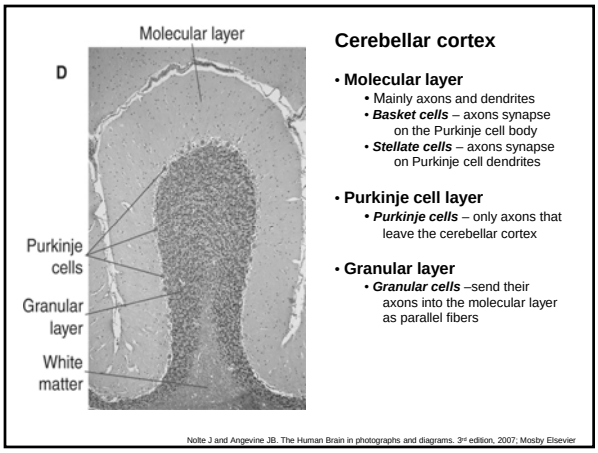

Cerebellar cortex

- **Molecular layer**
  - Mainly axons and dendrites
  - ***Basket cells*** – axons synapse on the Purkinje cell body
  - ***Stellate cells*** – axons synapse on Purkinje cell dendrites
- **Purkinje cell layer**
  - ***Purkinje cells*** – only axons that leave the cerebellar cortex
- **Granular layer**
  - ***Granular cells*** –send their axons into the molecular layer as parallel fibers

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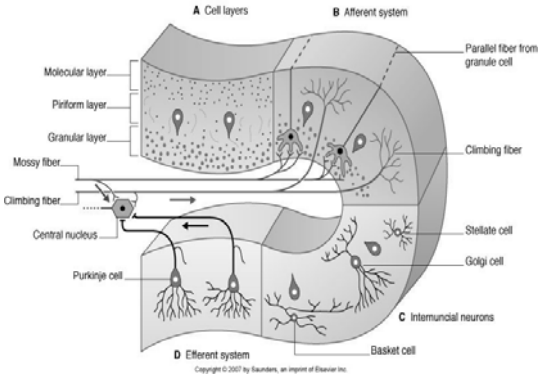

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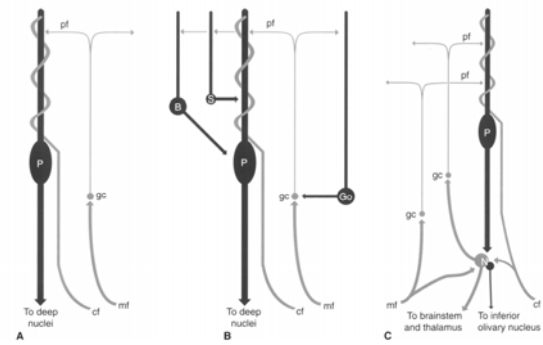

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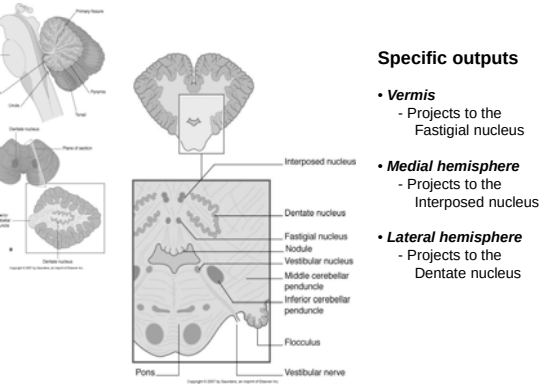

Specific outputs

- ***Vermis***
  - Projects to the Fastigial nucleus
- ***Medial hemisphere***
  - Projects to the Interposed nucleus
- ***Lateral hemisphere***
  - Projects to the Dentate nucleus

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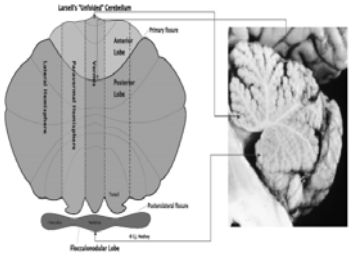

Functional Connections

- **Flocculonodular**
  Equilibrium and eye movements
- **Vermis**
  Equilibrium and eye movements
- **Medial hemisphere**
  Regulation and coordination of motor tone
- **Lateral hemisphere**
  Planning and coordination of movements

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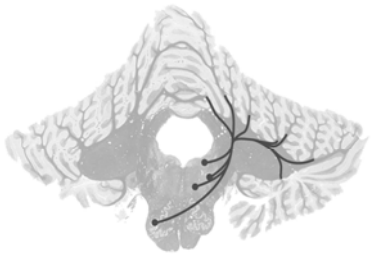
Inferior Cerebellar Peduncle



Major input route:

Inferior olivary nucleus
Vestibular nuclei
Trigeminal nuclei
Reticular formation
Spinal cord

Cerebellar efferents

Vestibular nuclei

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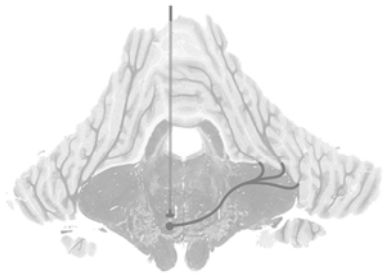
Middle Cerebellar Peduncle



Major input route:

Cerebral cortex

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Superior Cerebellar Peduncle

Input route:

Anterior Spinocerebellar tract

Cerebellar efferents

Originate from the deep cerebellar nuclei

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Cerebellum – Part 2

August 17, 2011

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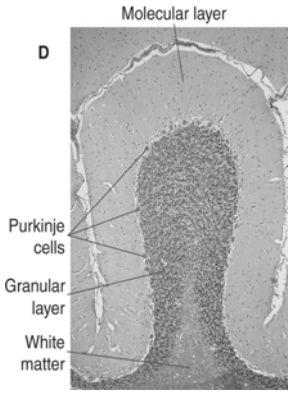
Cerebellum – Part 2

August 17, 2011

Objectives

- ✓ Describe the origins and projections of the mossy and climbing fibers
- ✓ Describe the scheme of mossy fiber activity
- ✓ Define the anatomical contributions of the cerebellar peduncles
- ✓ Recognize the somatotopic maps of the cerebellum
- ✓ "Extra credit" – Describe the four motor decussations of the brainstem



Cerebellar cortex

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- **Purkinje cell layer**
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  - ***Granular cells*** –send their axons into the molecular layer as parallel fibers

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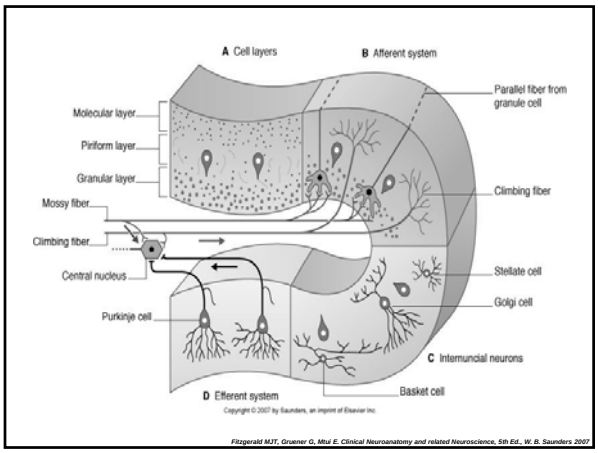

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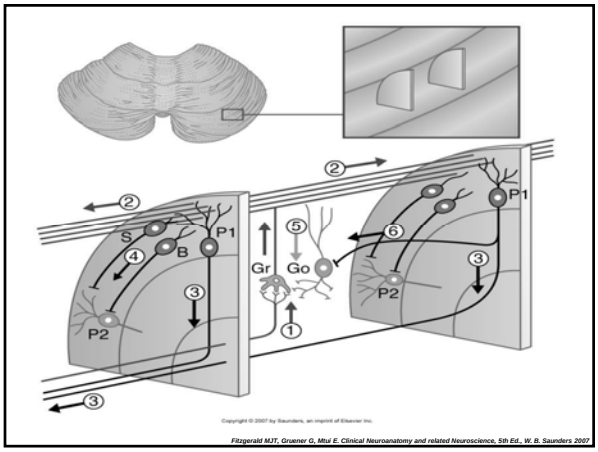

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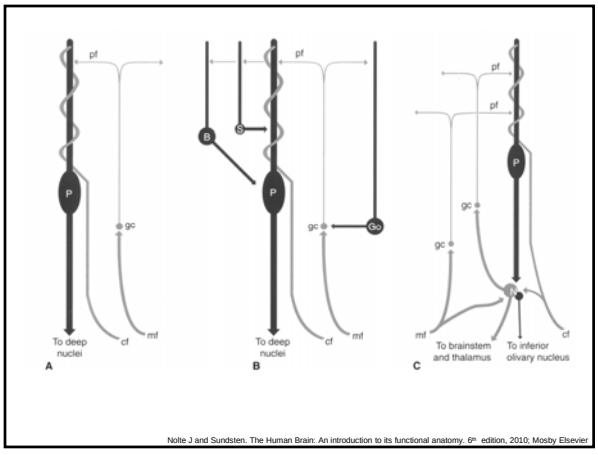

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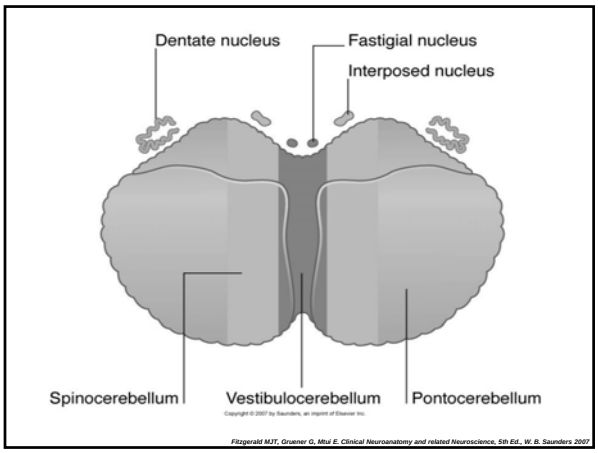

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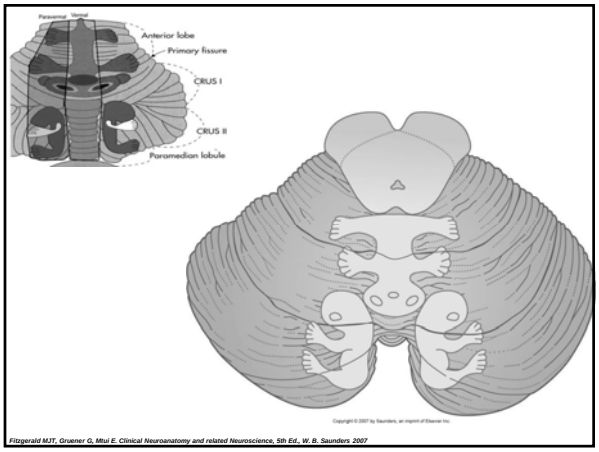

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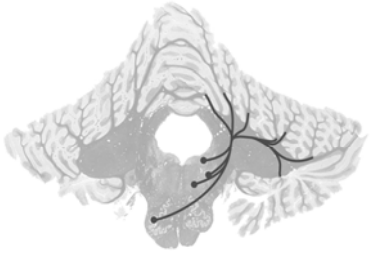
Inferior Cerebellar Peduncle



Major input route:

Inferior olivary nucleus
Vestibular nuclei
Trigeminal nuclei
Reticular formation
Spinal cord

Cerebellar efferents

Vestibular nuclei

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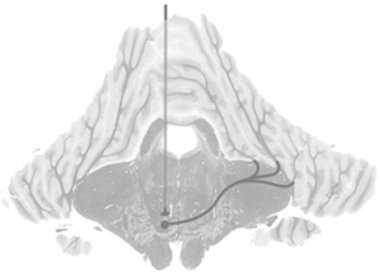
Middle Cerebellar Peduncle



Major input route:

Cerebral cortex

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Superior Cerebellar Peduncle

Input route:

Anterior Spinocerebellar tract

Cerebellar efferents

Originate from the deep cerebellar nuclei

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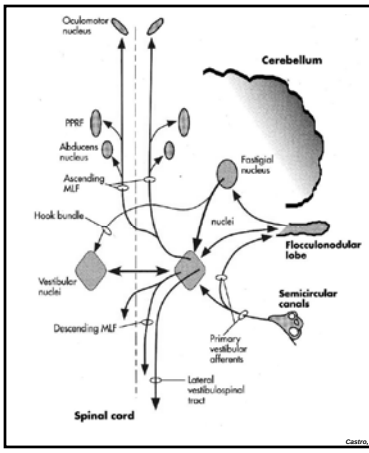
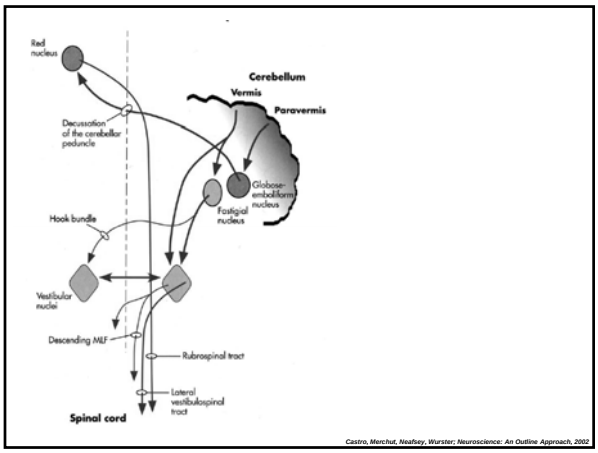


Castro, Merchut, Neafsey, Wurster; Neuroscience: An Outline Approach, 2002



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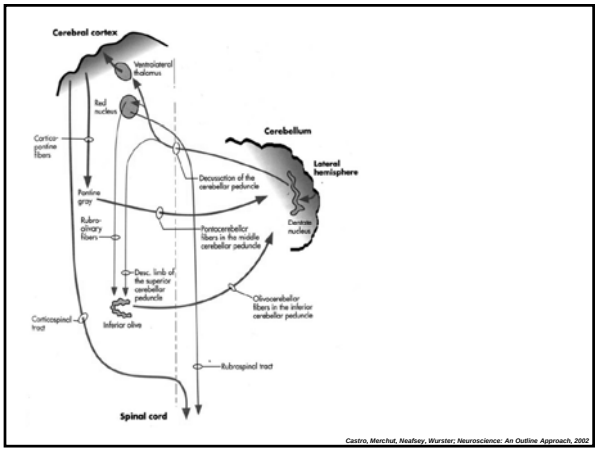

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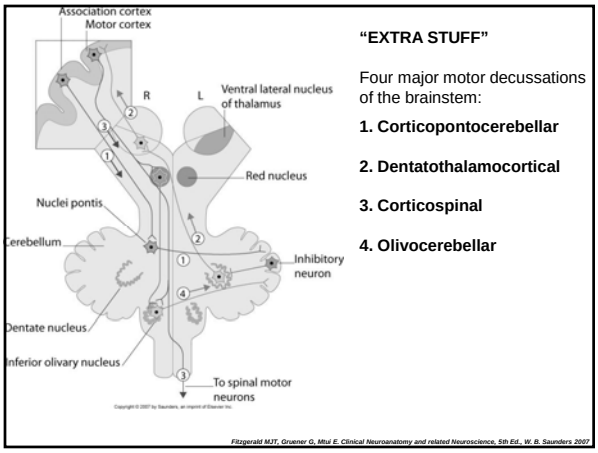

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"EXTRA STUFF"

Four major motor decussations of the brainstem:

1. Corticopontocerebellar

2. Dentatothalamocortical

3. Corticospinal

4. Olivocerebellar

Lab 3. Pons & Midbrain

Lesion Lessons

Lesion 4.1 Anne T. Pasta

(Slice of Brain © 1993 Univs. of Utah and Washington; E.C. Alvord, Jr., Univ. of Washington)

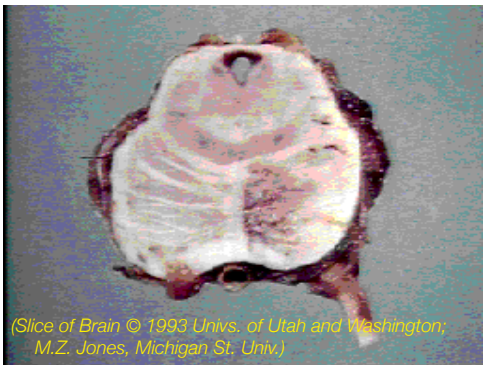
Web note

i) Location

ii) Signs/symptoms

iii) Cause:

Lesion 4.2 Colin S. Terase



(Slice of Brain © 1993 Univs. of Utah and Washington; M.Z. Jones, Michigan St. Univ.)

Web note

i) Location

ii) Signs/symptoms

iii) Cause:

Pontine Level of the Facial Genu

Locate and note the following:

Basilar pons

– massive ventral structure provides the most obvious change from previous medullary levels.

- *pontine gray* - large nuclear groups in the *basilar pons*.
  – origin of the *middle cerebellar peduncle*
- *pontocerebellar* axons - originate from *pontine gray* neurons and cross to form the *middle cerebellar peduncle*.
- *corticopontine* axons- huge projection that terminates in the basilar *pontine gray*.
- *corticospinal tract* axons
  – large bundles of axons surrounded by the basilar *pontine gray.*
  – course caudally to form the *pyramids* in the medulla.

Question classic

Is the middle cerebellar peduncle composed of climbing or mossy fibers?

Pontine tegmentum

- *medial lemniscus* - has now assumed a "horizontal" position and forms part of the border between the basilar pons and *pontine tegmentum*.
- *central tegmental tract* - located just dorsally to the medial lemniscus.
  – descends from the midbrain to the *inferior olive*.
- *superior olivary nucleus* - pale staining area lateral to the *central tegmental tract*.
  – gives rise to the efferent *olivocochlear* projection to the inner ear.
- *lateral lemniscus* - lateral to the *medial lemniscus*.
  – composed of secondary auditory projections from the *cochlear nuclei*.
- *trapezoid body* (area enclosed in trapezoid) - crossing pathway arising from the *cochlear nuclei* and passing beneath and through the *medial lemniscus*.
  – as they course lateral to the *medial lemniscus*, these axons turn rostrally to form the *lateral lemniscus* which ascends to the *inferior colliculus*.
  – some secondary auditory fibers synapse in the *superior olive*.
- *facial nerve* - SVE axons from the *facial motor nucleus* can be seen making their internal loop or genu over the *abducens nucleus* just below the floor of the *fourth ventricle*.
- *spinal trigeminal tract* and *nucleus* - located lateral to the *facial nerve* axons.
- *CN VI axons* - can be seen exiting the ventromedial aspect of the *abducens nucleus*.

Question classic

What sensory modalities are carried by the medial and lateral lemnisci?

Question classic

What muscle is innervated by the CN VI?

Label these structures on Figure 1.

• *facial colliculus*	• *pontine gray*	• *spinal nuc. and tract of V*
• *abducens nucleus*	• *corticospinal tract*	• *mesencephalic tract of V*
• *abducens nerve*	• *pontocerebellar fibers*	• *vent. spinocerebellar tract*
• *facial nerve*	• *middle cerebellar peduncle*	• *central tegmental tract*
• *ascending MLF*	• *spinothalamic tract*	• *trapezoid body*
• *tectospinal tract*	• *lateral lemniscus*	• *superior olive*
• *medial lemniscus*	• *facial nucleus*	• *fourth ventricle*

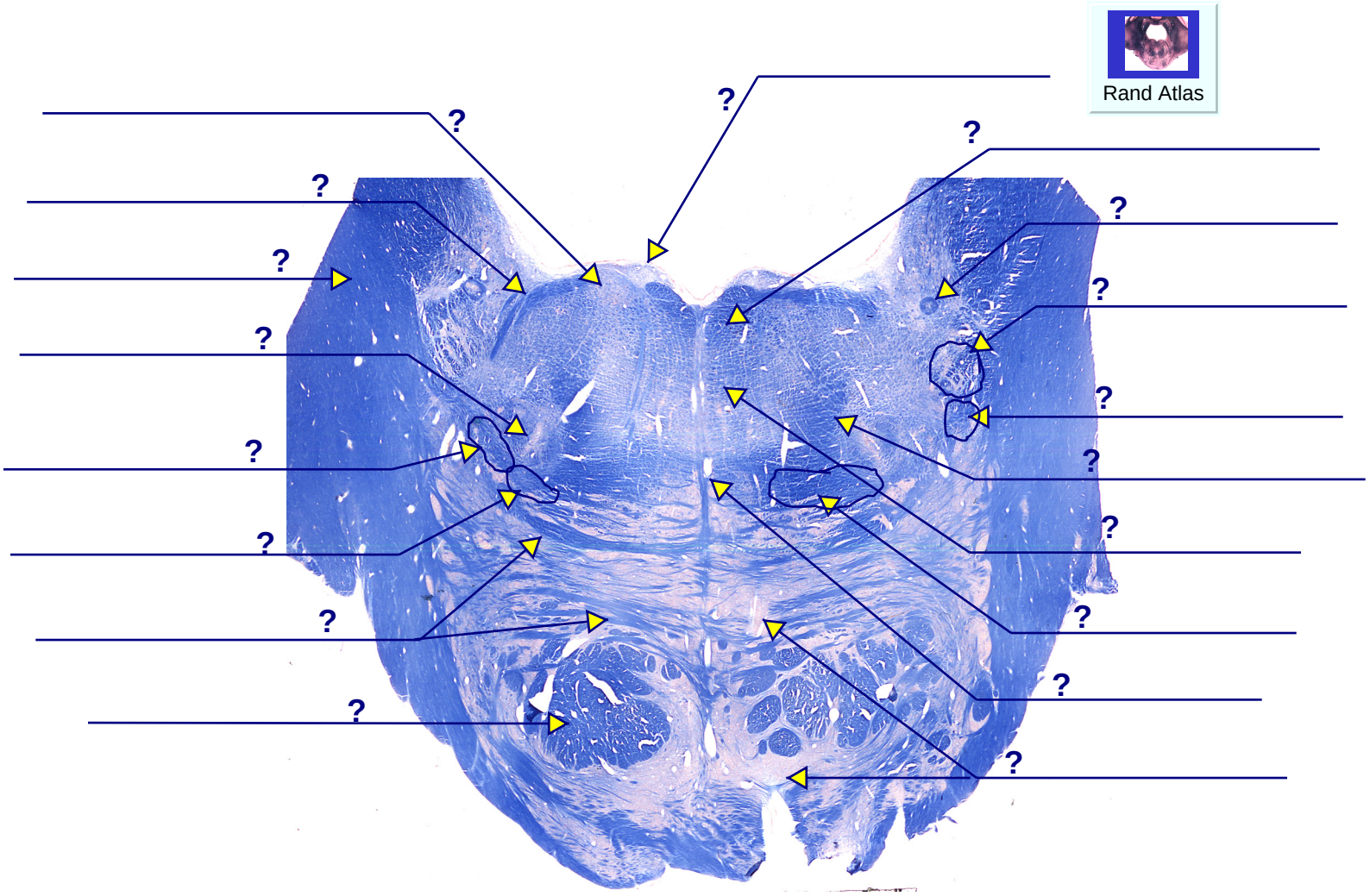


Fig 1. Pontine level of the facial nerve.

Case Break

Double Vision

A 70 year old hypertensive man, Willie Maykitt, awakens one morning with double vision and weakness of his right arm and leg. On examination there is full lateral gaze to the right, but neither eye can move to the left past the midline. Vertical gaze is normal. The right upper and lower limbs are spastic, moderately weak, and hyperreflexic compared to the left.

1. Where is the lesion?

2. What centers or tracts are involved?

3. Which is the most likely cause and why: ischemic infarct, hemorrhage, or tumor?

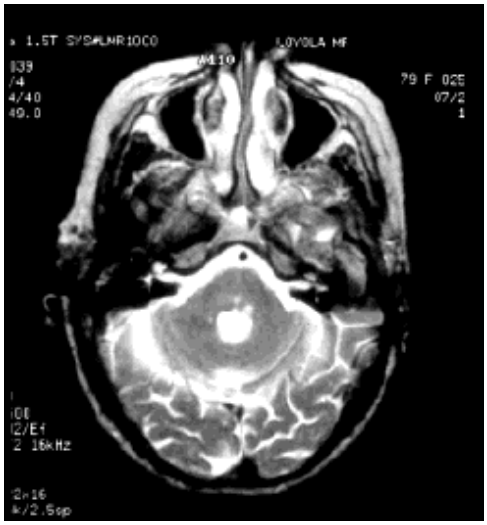
He makes a full recovery over the next 6 months, but then double vision suddenly returns. You now notice that the left eye cannot adduct past the midline, while there is nystagmus in the fully abducting right eye. All other eye movements are full.

4. Where is this lesion?

5. Where is it in relation to his previous lesion?

6. What arterial territory is involved?

Inter-Course Q's



On this axial MRI identify the pons, fourth ventricle, cerebellum, middle cerebellar peduncles, and cerebral cortex. Also identify the basilar artery. Finally, locate the small infarct in the PPRF.

Pontine Level of the Trigeminal Motor Nucleus

Locate and note the following:

- *superior cerebellar peduncles* - prominent pathway leaving the cerebellum in the roof of the fourth ventricle.
- *middle cerebellar peduncles* - huge pathway entering the cerebellum laterally.
- *motor trigeminal nucleus* - an SVE nucleus innervating the branchial arch derived muscles of mastication.

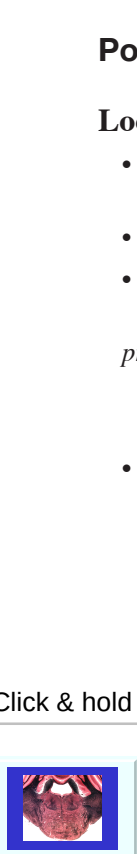
principal sensory trigeminal nucleus - found lateral to the *motor trigeminal nucleus*.

– observe the relation of the *trigeminal nerve root* to the *principal trigeminal nucleus* and *trigeminal motor nucleus* as best seen on the higher power view.

- *ventral spinocerebellar tract* - courses over the external surface of the *superior cerebellar peduncle* enter the cerebellum (as best seen the left side of this figure).

Label these structures on Figure 2.		
• *sup. cerebellar peduncle*	• *ascending MLF*	• *ventral spinocerebellar tr.*
• *middle cerebellar peduncle*	• *motor nucleus of V*	• *central tegmental tract*
• *corticospinal tract*	• *principal sensory nuc. of V*	• *lateral lemniscus*
• *medial lemniscus*	• *mesencephalic tract of V*	• *spinothalamic tract*
• *fourth ventricle*		

Click & hold



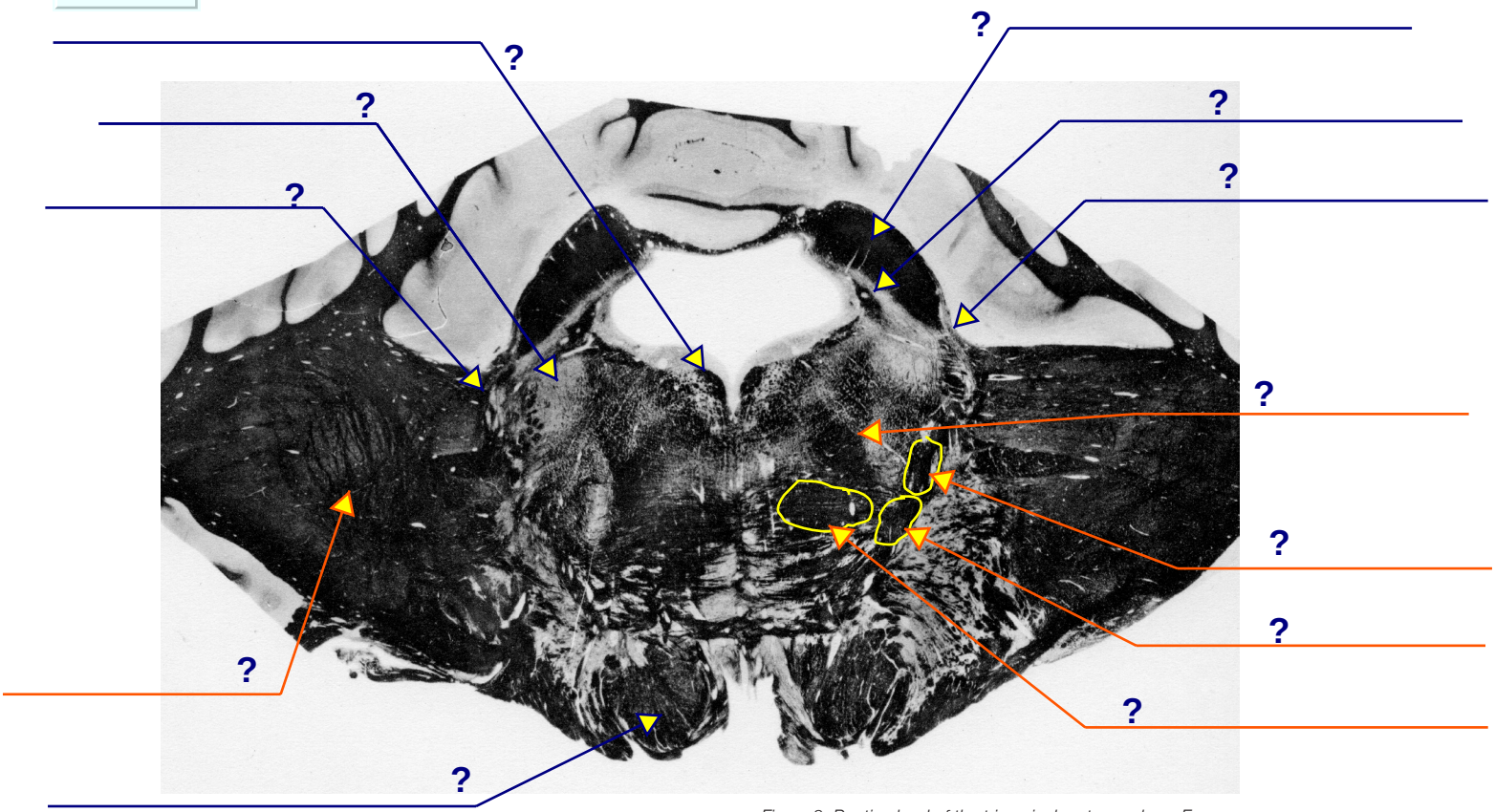


Figure 2. Pontine level of the trigeminal motor nucleus. From Jelgersma Tabular 95-862, 1931.

Case Break

Cheek Pain

A patient, Penny Pinscher, sees you after suffering 3 months of paroxysmal, lightning-like pain in the right cheek, which recurs dozens of times daily, often triggered off by touching the face. The neurological examination is normal.

1. What is this clinical syndrome called?

2. If this is a young woman who has recovered from previous episodes of paraparesis and left optic neuritis (temporary blindness), where could the lesion be and what is the cause?

3. What would you consider more likely if her right cheek becomes permanently numb to pin or cotton sensation, or she becomes deaf in the right ear?

Locate the following on this section:

- *CN IV* - exits dorsally (white arrow)
- *locus ceruleus* - pigmented region just lateral to the *cerebral aqueduct*
- *superior cerebellar peduncle* - near the dorsolateral surface
- *basilar pons* - prominent ventrally

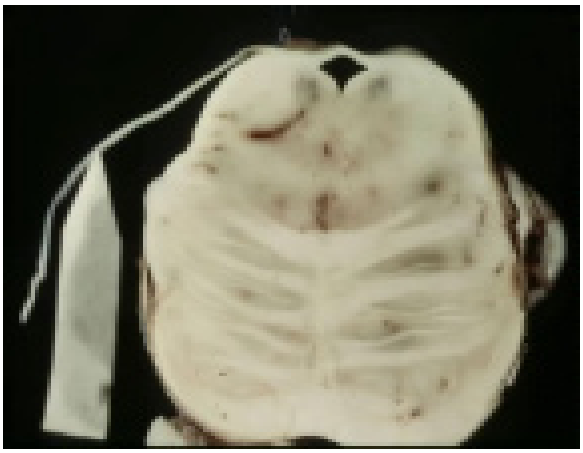


Figure 3. Gross brain stem section through the level of the pons.

Level of the Isthmus and Trochlear Nerve

Locate and note the following:

- *trochlear nerve* - decussates dorsally above the *aqueduct*
- *superior cerebellar peduncles* – prominent in the dorsolateral brain stem tegmentum.
- *periaqueductal gray (PAG)* – surrounding the cerebral aqueduct
- *lateral lemniscus* – courses superficial to the *superior cerebellar peduncle* enroute to the *inferior colliculus*.
- *mesencephalic trigeminal tract* – found lateral to the PAG and medial to the *superior cerebellar peduncle*.
- *locus ceruleus* - cluster of darkly staining, pigmented cells in the lateral region of the PAG.

  – have extremely widespread noradrenergic (NA) projections.
- *raphe nuclei* – cluster of darkly stained neurons along the midline within the PAG and ventral to the MLF.

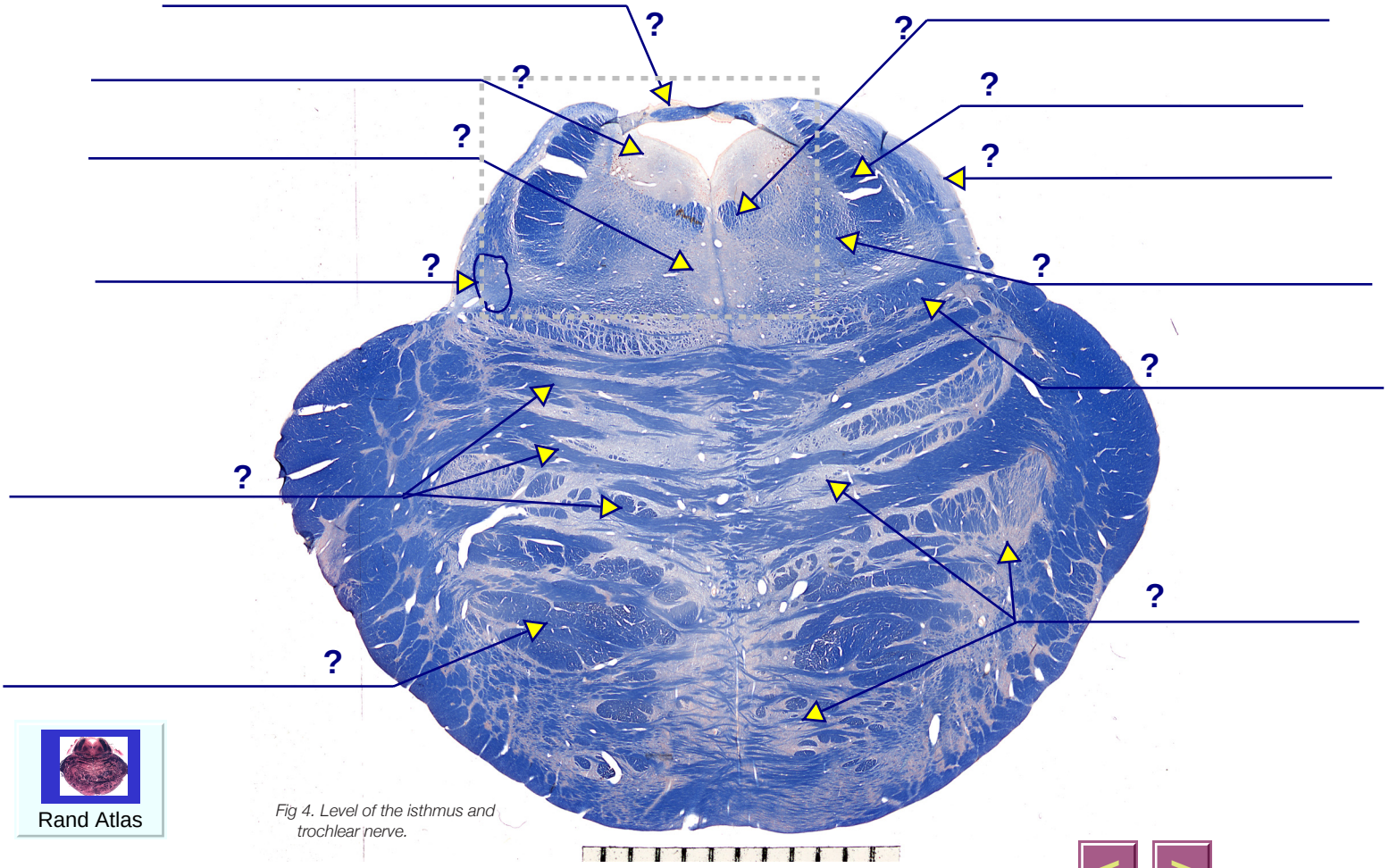
  – have widespread serotonergic projections.

Label these structures on Figure 4.

- *trochlear nerve*
- *periaqueductal gray*
- *sup. cerebellar peduncle*
- *lateral lemniscus*
- *medial lemniscus*
- *spinothalamic tract*
- *central tegmental tract*
- *pontine gray*
- *corticospinal tract*
- *corticopontine axons*
- *pontocerebellar fibers*
- *ascending MLF*
- *midline raphe nuclei*

Structures surrounding the PAG are best seen at a higher magnification.

Hi power view



Rand Atlas

Fig 4. Level of the isthmus and trochlear nerve.

Midbrain Level of the Inferior Colliculus

Locate and note the following:

- *crus cerebri* - massive structure at the ventral aspect of the midbrain.
  - – contains the *corticospinal*, *corticobulbar*, and *corticopontine tracts*
- *substantia nigra* - a black pigmented region located just above the *crus cerebri*.
- *decussation of the superior cerebellar peduncles* - large structure virtually obliterating the midline in the tegmentum.
- *lateral lemniscus* - fans out dorsally as it terminates in the *inferior colliculus* ("golf ball on tee").
- *inferior colliculus* - a major element of the auditory system.
- *trochlear nucleus* - very small nucleus just dorsal to the *MLF*

Question classic

Transmitter associated with the substantia nigra?

Label these structures on Figure 5.

- *trochlear nucleus*
- *periaqueductal gray*
- *sup. cerebellar peduncle decussation*
- *lateral lemniscus*
- *medial lemniscus*
- *spinothalamic tract*
- *central tegmental tract*
- *pontine gray*
- *crus cerebri*
- *substantia nigra*
- *ascending MLF*

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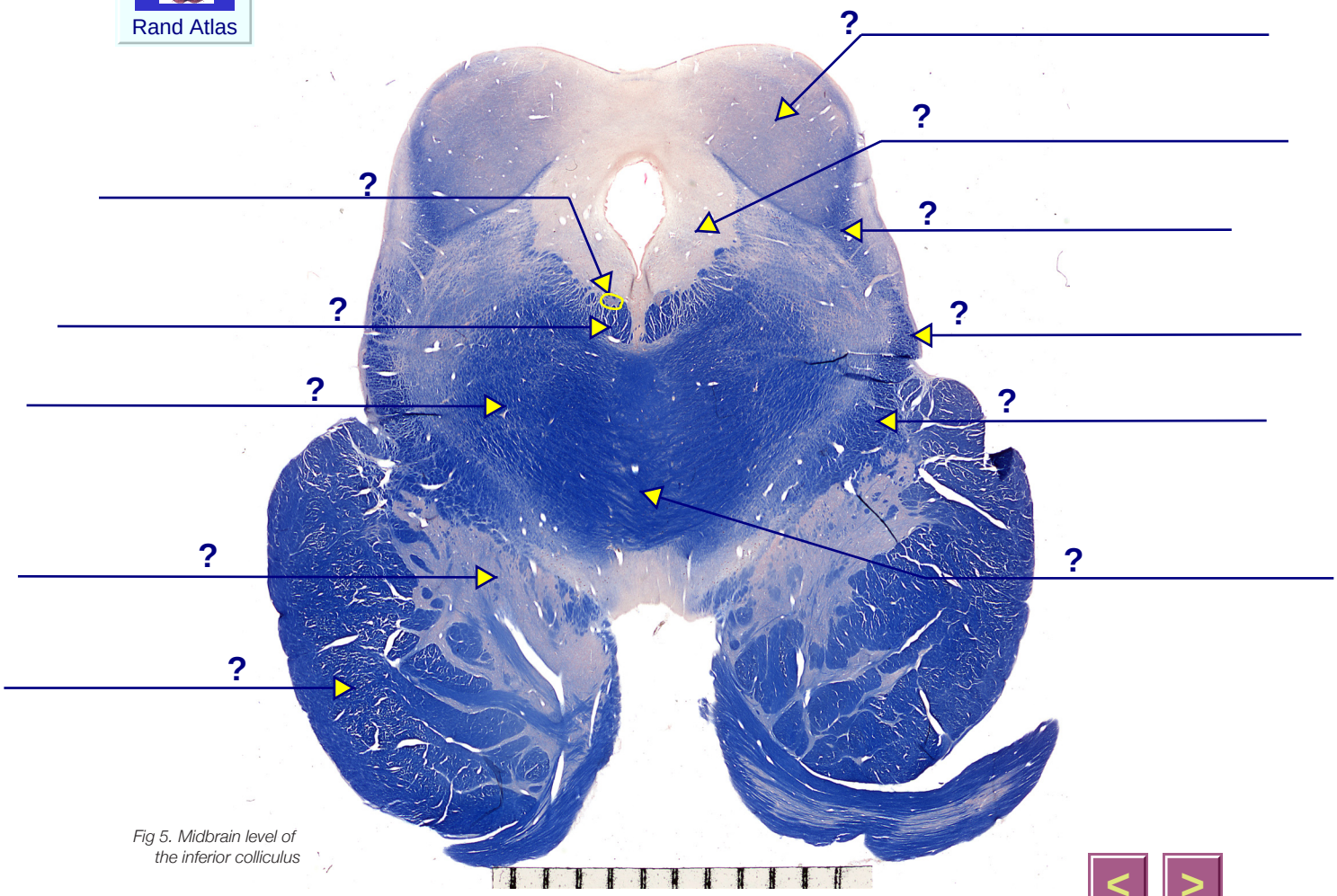

Fig 5. Midbrain level of the inferior colliculus

Midbrain Level of Superior Colliculus

Locate and note the following:

- *superior colliculus* – extremely important nucleus in controlling eye-head movements in orienting to a variety of stimuli.
- *tectospinal tract* – colliculus efferent (located on many previous sections).
- *brachium of the inferior colliculus* – located on the surface of the brainstem ventrolateral to the *superior colliculus*.
  - an auditory pathway projecting from the *inferior colliculus* (located just caudally) to the *medial geniculate body* of the thalamus (located rostrally).
- *crus cerebri* – massive structure at the ventral aspect of the midbrain.
  - contains the *corticospinal*, *corticobulbar*, and *corticopontine tracts*
- *substantia nigra* – a black pigmented region located just above the *crus cerebri*.
  - component of the basal ganglia that provides dopaminergic innervation the *caudate* and *putamen*.
  - degenerates in *Parkinson's disease*.
- *oculomotor nucleus* – located medial to the MLF.
- *interpeduncular fossa* – ventral space, midline space containing the exiting rootlets of CN III.

The crus cerebri contains the...

- *frontopontine projections medially*
- *corticospinal and corticobulbar projections in the middle*
- *parieto-temporo-occipital pontine projections laterally*

Label these structures on Figure 6.

- *oculomotor nucleus*
- *Edinger-Wesphal nucleus*
- *sup. cerebellar peduncle*
- *brachium of the inf. collic.*
- *medial lemniscus*
- *spinothalamic tract*
- *central tegmental tract*
- *cerebral aqueduct*
- *crus cerebri*
- *substantia nigra*
- *ascending MLF*

Rand Atlas

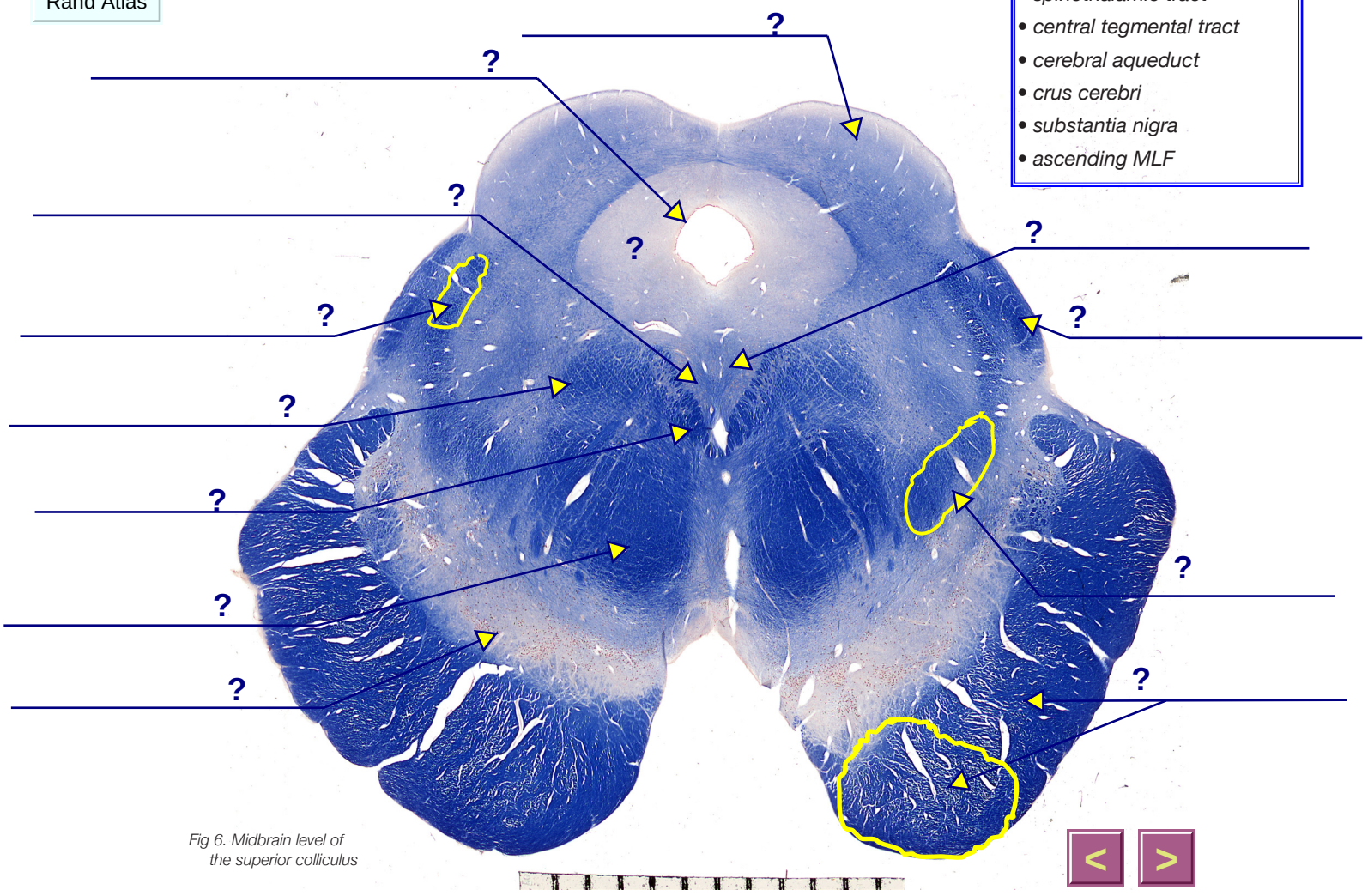

Fig 6. Midbrain level of the superior colliculus

Midbrain Level of the Red Nucleus

Locate and note the following:

- *red nucleus* – located the middle of the tegmentum above the *substantia nigra*.
  - – is the source of the *rubrospinal tract* and is major termination region for the *superior cerebellar peduncle* (although many SCP fibers continue on to the *thalamus* as *cerebello-thalamic projections).*
- *interstitial nucleus of Cajal* – an accessory *oculomotor nucleus* located within the MLF.
  - – is involved in control of vertical eye movements.

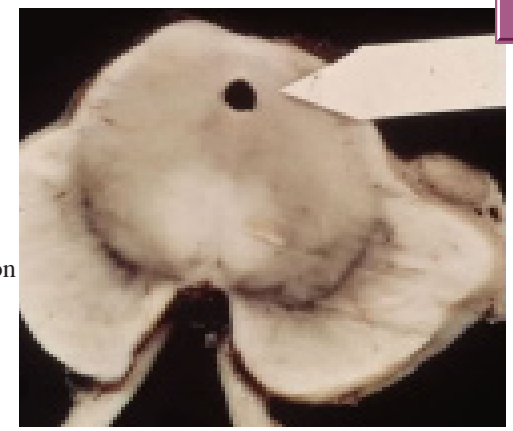

Fig 7. Gross section through the midbrain. Note the following:
- *CN III - exits in the interpeduncular fossa*
- *cerebral aqueduct*
- *decussation of the superiorcerebellar peduncles - in the middle of the tegmentum*
- *substantia nigra - on each side just above the crus cerebri.*

Label these structures on Figure 8.

• superior colliculus	• periaqueductal gray
• cerebral aqueduct	• oculomotor nucleus
• medial lemniscus	• oculomotor nerve
• red nucleus	• brachium of the inf.coll.
• interstitial nuc of Cajal	• substantia nigra
• crus cerebri	• spinothalamic tract
• cerebello-thalamic tr.	• CN III axons

Important clinical correlation

A portion of the oculomotor nucleus straddles the midline; this is known as the Edinger-Westphal nucleus, and it gives rise to parasympathetic fibers that travel in the oculomotor nerve to the ciliary ganglion.

These fibers are an essential element of the circuit of the pupillary light reflex (light in one eye causes both pupils to constrict).

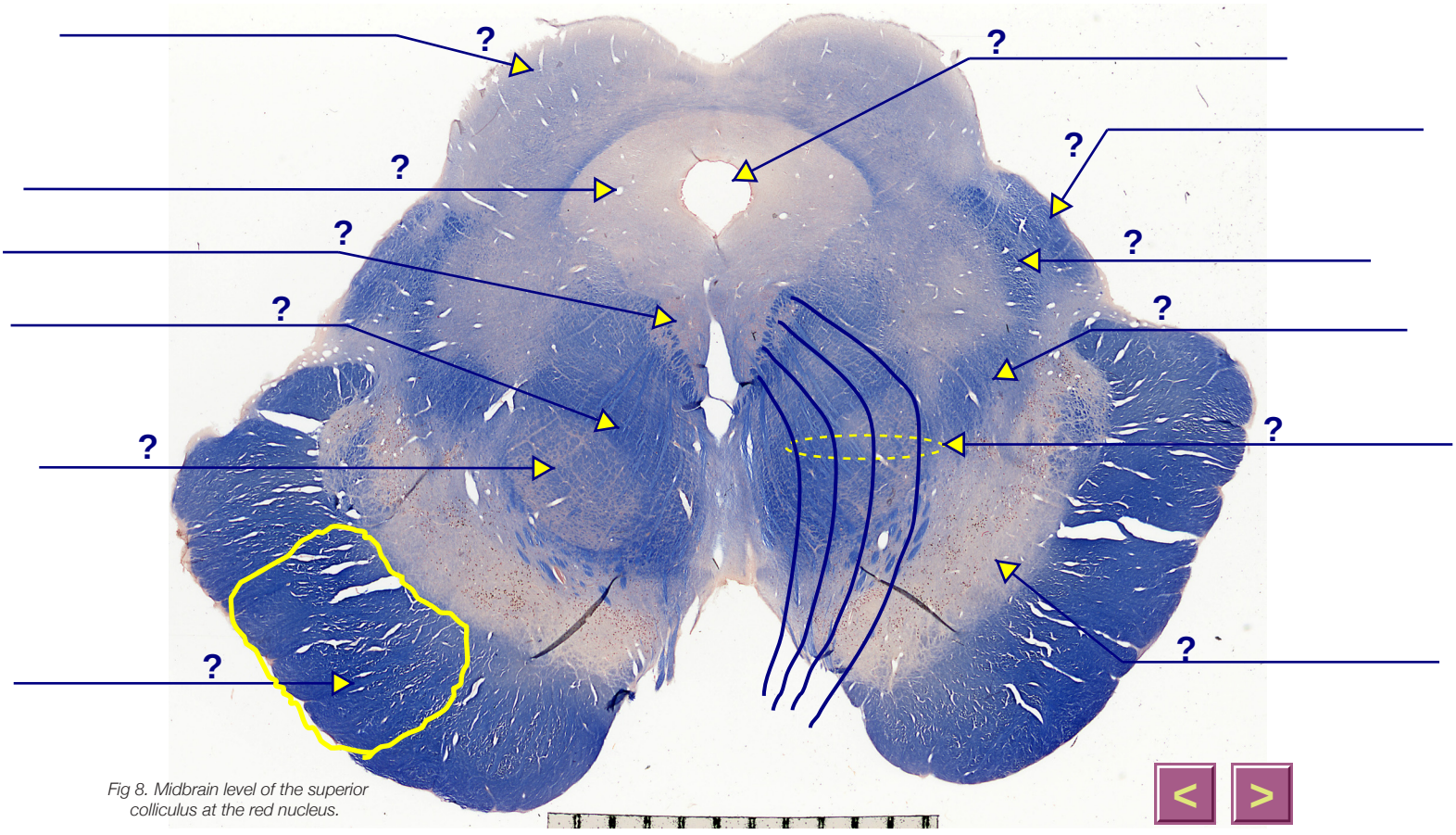

Fig 8. Midbrain level of the superior colliculus at the red nucleus.

Midbrain-Diencephalon Transition

Locate and note the following:

- *pulvinar* - large thalamic nucleus in the posterior thalamus
- *medial geniculate* nucleus – relays auditory information to the primary auditory cortex
- *brachium of the inferior colliculus* - terminates in the *medial geniculate*, the final relay station in the auditory pathway.
- *lateral geniculate nucleus* – relays visual information to the primary visual cortex.
- *brachium of the superior colliculus* - arches over the *medial geniculate body* enroute to the *lateral geniculate*.
- *optic radiations* - efferents from the *lateral geniculate* to the visual cortex in the occipital lobe.
- *pineal body* - located dorsal to the superior colliculus in the midline.

  – secretes the hormone *melatonin*.

Question classic

What is the main input to the inferior colliculus?

Label these structures on Figure 8.

• *superior colliculus*	• *corpus callosum*
• *pulvinar*	• *oculomotor nucleus*
• *medial lemniscus*	• *oculomotor nerve*
• *pineal gland*	• *brachium of the inf.coll.*
• *central tegmental tract*	• *brachium of the sup. coll.*
• *medial geniculate*	• *spinothalamic tract*
• *lateral geniculate*	• *optic radiations*
• *MLF*	• *decus. of the sup cbllr ped.*
• *pons*	• *PAG*


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Other structures on this slide will be studied in Lab 6.

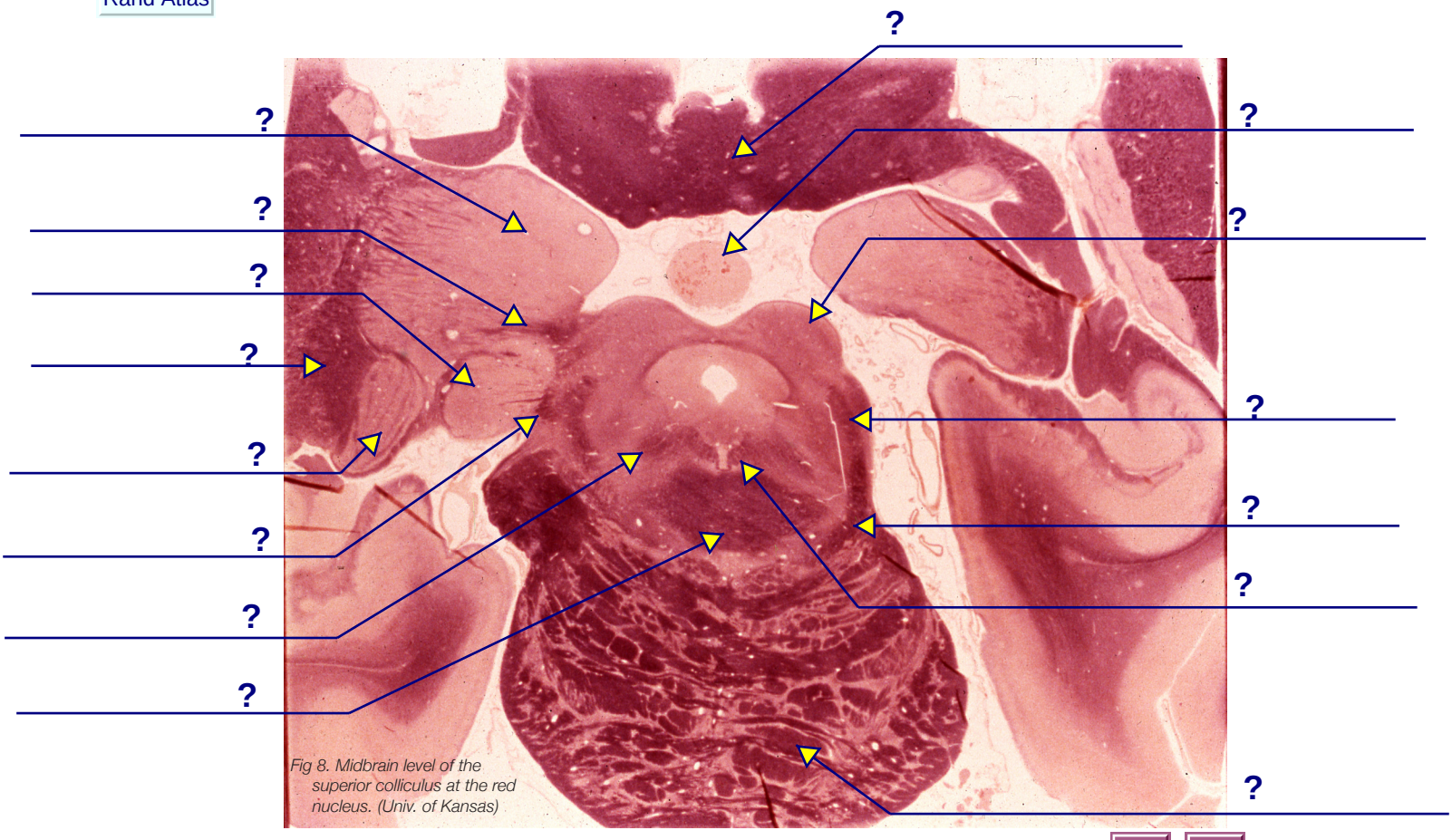


Fig 8. Midbrain level of the superior colliculus at the red nucleus. (Univ. of Kansas)

C. Review Questions

1. What is the major input to the basilar pontine gray?

2. What is the relationship of the middle cerebellar peduncle to the pontine gray?

3. Which cranial nerve courses immediately deep to the facial colliculus?

4. Which cranial nerve nucleus is found deep to the facial colliculus?

5. What is the tectum?

6. Which functional components are associated with the facial nerve? ...the trigeminal nucleus?

7. Where does the lateral lemniscus terminate?

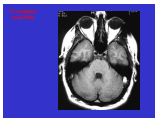
8. What is the origin and termination of the central tegmental tract?

9. Describe the localization of cortical fibers in the crus cerebri.

10. What is peculiar about the course of the trochlear nerve?

Label these structures on Figure 9.

• *medial rectus muscle*	• *sphenoid sinus*
• *lateral rectus muscle*	• *internal carotid artery*
• *basilar artery*	• *temporal lobe*
• *basilar pons*	• *middle cerebellar peduncle*
• *fourth ventricle*	• *cerebellar hemisphere*



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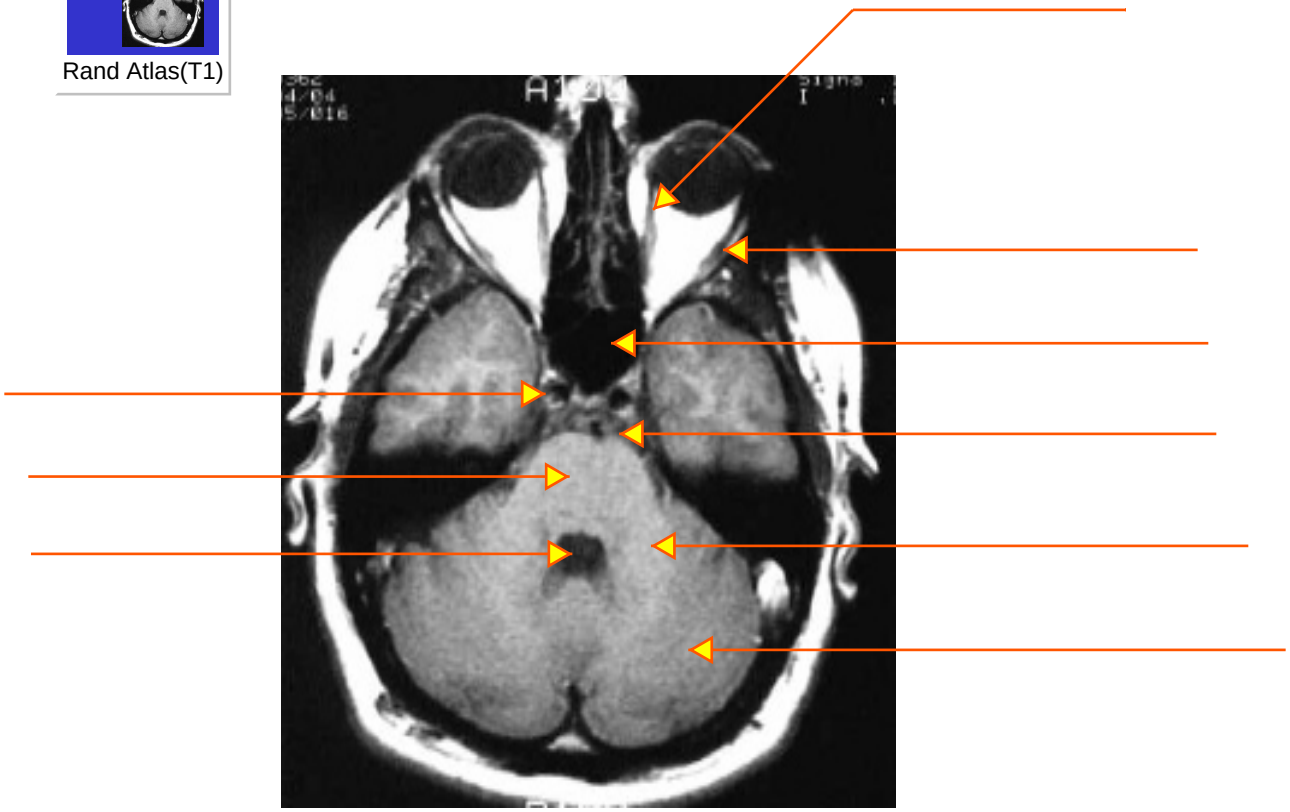
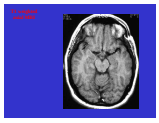


Fig 9. T1 Axial MRI. (From Rand Swenson Darthmouth Medical School)

Label these structures on Figure 10.

• *optic chiasm*	• *optic tract*
• *pituitary stalk (infundibulum)*	• *middle cerebral artery*
• *mammilary body*	• *amygdala*
• *red nucleus*	• *superior colliculus*
• *cerebellar vermis*	• *midbrain*
• *orbital cortex*	• *occipital cortex*



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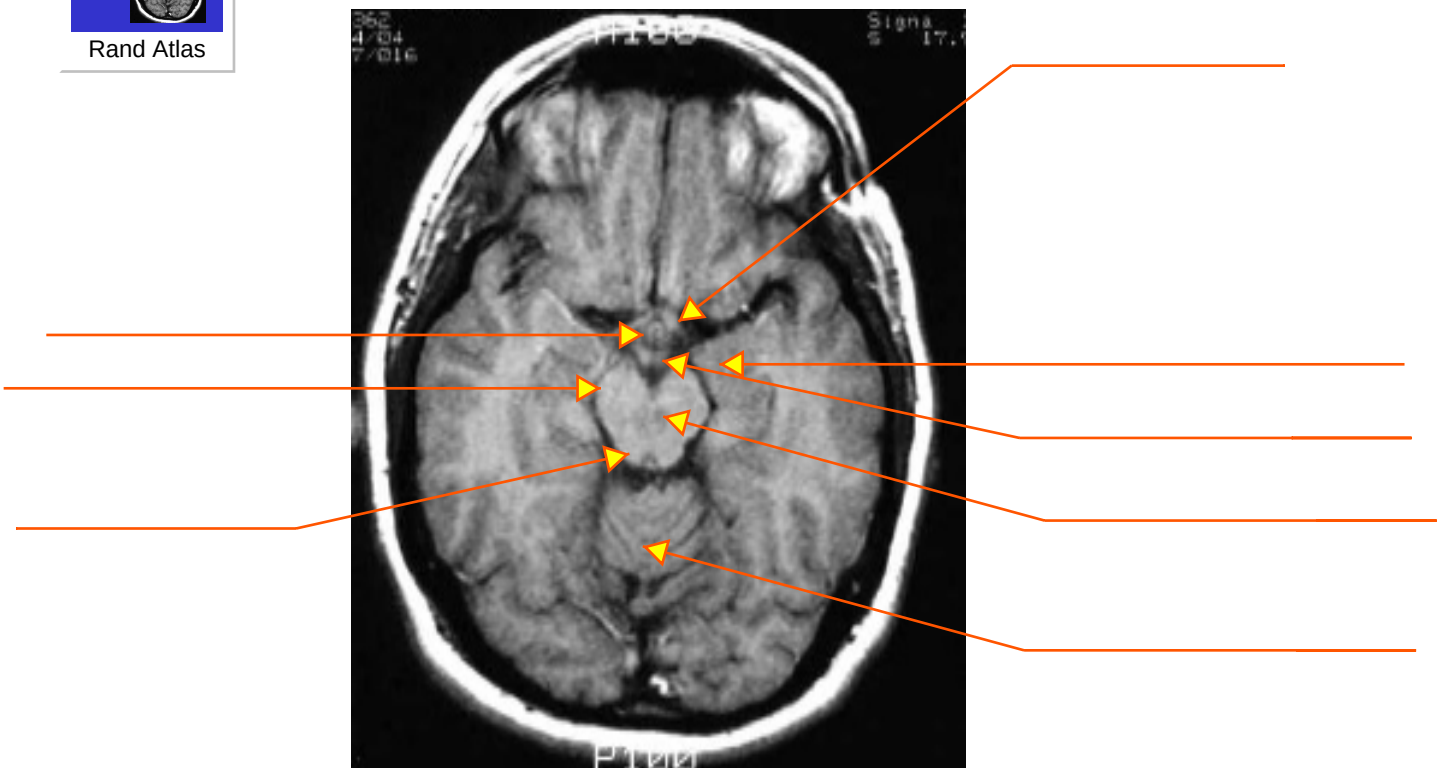

Fig 10. T1 Axial MRI. (From Rand Swenson Darthmouth Medical School)

Patient Puzzle

Patient 4.1. Case of seeing double

Patient: Mr. Al Fresco Age: 26 Occupation: Skydiving instructor

Signs and Symptoms:

- Mr. Fresco complains of double vision.
- His vision is normal when only using one or the other eye.
- He says he can walk fine and notices no other symptoms.

Diagnosis:

1. How can you explain the facial motor signs seen in the movie?

Al Fresco movie

2. What did the pupillary light reflexes indicate?

3. Do you think Mr. Fresco has a cortical lesion? A brain stem lesion?

4. Do you think Mr. Fresco could reflexly move his eyes to the right in response to an unexpected bright flash?

Related questions:

1. What are the direct and consensual light reflexes?

2. Can you diagram the neuroanatomy controlling horizontal, conjugate eye deviation?

3. How can you distinguish a lesion to the facial nerve from a lesion of corticobulbar projections to the facial nucleus?

4. Where is the internal genu of Cranial Nerve VII?

5. What functional components are associated with cranial nerves II, III, IV, VI and VII?

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CLINICAL CORRELATION: CRANIAL NERVES

Date: August 18, 2011 - 9:30 AM
Reading Assignment: refer to posted handout in LUMEN calendar

KEY CONCEPTS AND LEARNING OBJECTIVES

1. Describe the typical clinical deficits found with lesions of the oculomotor, trochlear, and abducens nerves (CN III, IV and VI).

2. Define the concepts and significance of "diplopia," "nystagmus," and "internuclear ophthalmoplegia (MLF syndrome)."

3. Explain the normal reactions of the pupil (light reflex, near reflex) and why it acts abnormally in the relative afferent pupillary defect (RAPD).

4. Explain the clinical signs of Horner's syndrome and how it can be caused by neck trauma, an apical lung tumor, or a lateral medullary infarction.

5. Explain the syndrome of trigeminal neuralgia and how it may be treated.

6. Contrast the clinical features of an upper motor neuron versus lower motor neuron cause of facial paralysis.

7. List other signs and symptoms which may accompany facial paralysis in lesions of the facial nerve or its nucleus.

8. Recognize that lesions of vagal nerve branches may cause ipsilateral sagging of the palatal arch or vocal cord paralysis.

9. Contrast the clinical features of an upper motor neuron versus lower motor neuron cause of unilateral tongue weakness.

10. Recognize that a crossed brain stem syndrome consists of cranial nerve involvement on one side and a clinical sensory or motor deficit on the opposite side of the body.

11. List the signs and symptoms of the medial midbrain (Weber) syndrome and the lateral medullary (Wallenberg) syndrome.

Cranial Nerves, Brain Stem Reflexes, and Brain Stem Disorders (Dr. Merchut)

Cranial Nerves and Brain Stem Reflexes

1. Olfactory Nerve (CN I)

Olfaction is usually not tested during a neurological examination unless the patient has mentioned a problem with the sense of smell. Testing is done by bringing an aromatic substance, such as an alcohol pad or packet of coffee grounds, to one nostril at a time, with the patient identifying the odor with eyes closed. Impaired smell most commonly occurs from the mucosal swelling and inflammation during sinusitis or an **upper respiratory infection**. A permanent loss of smell may occur after severe **head trauma**, where the olfactory nerve branches are sheared or torn where they pass through the bony cribriform plate. Another persistent loss of smell may be caused by a **tumor near the olfactory lobe** at the skull base, such as a meningioma.

2. Optic Nerve (CN II)

(CN II will be discussed in the section Visual, Auditory, and Vestibular Systems.)

3. Oculomotor (CN III), Trochlear (CN IV), and Abducens (CN VI) Nerves

Cranial nerves III, IV and VI innervate the extraocular muscles, which are tested by the patient tracking or following a target (examiner's finger or pen) up and down and side to side. Diagonal tracking may also be tested: looking up and rightward, looking down and rightward, looking up and leftward, and looking down and leftward. Observe and note the directions in which eye movements are limited or impaired---it may be difficult at first to localize the problem specifically to one of these cranial nerves, since some extraocular muscles have multiple actions because of their diagonally oriented insertion on the eyeball.

In this discussion of eye movements, the initial position of the eyeball is in primary gaze or "looking straight ahead." Since the superior and inferior oblique muscles insert more posteriorly on the eyeball, their contraction also abducts the eyeball: the superior oblique depresses and abducts the eye, while the inferior oblique elevates and abducts the eye (see Fig.1). Since the superior and inferior recti insert more anteriorly on the eyeball, their contraction also adducts the eyeball: the superior rectus elevates and adducts the eye, while the inferior rectus depresses and adducts the eye. (Here is the final part of the "picture," although at the risk of greater confusion: Muscles inserted on the top of the eyeball (superior rectus and superior oblique) will also rotate the eye medially or inward (intorsion), while muscles inserted on the bottom of the eyeball (inferior rectus and inferior oblique) will also rotate the eye laterally or outward (extorsion).) In contrast, two muscles have simple lateral actions on the eyeball: abduction by the lateral rectus and adduction by the medial rectus.

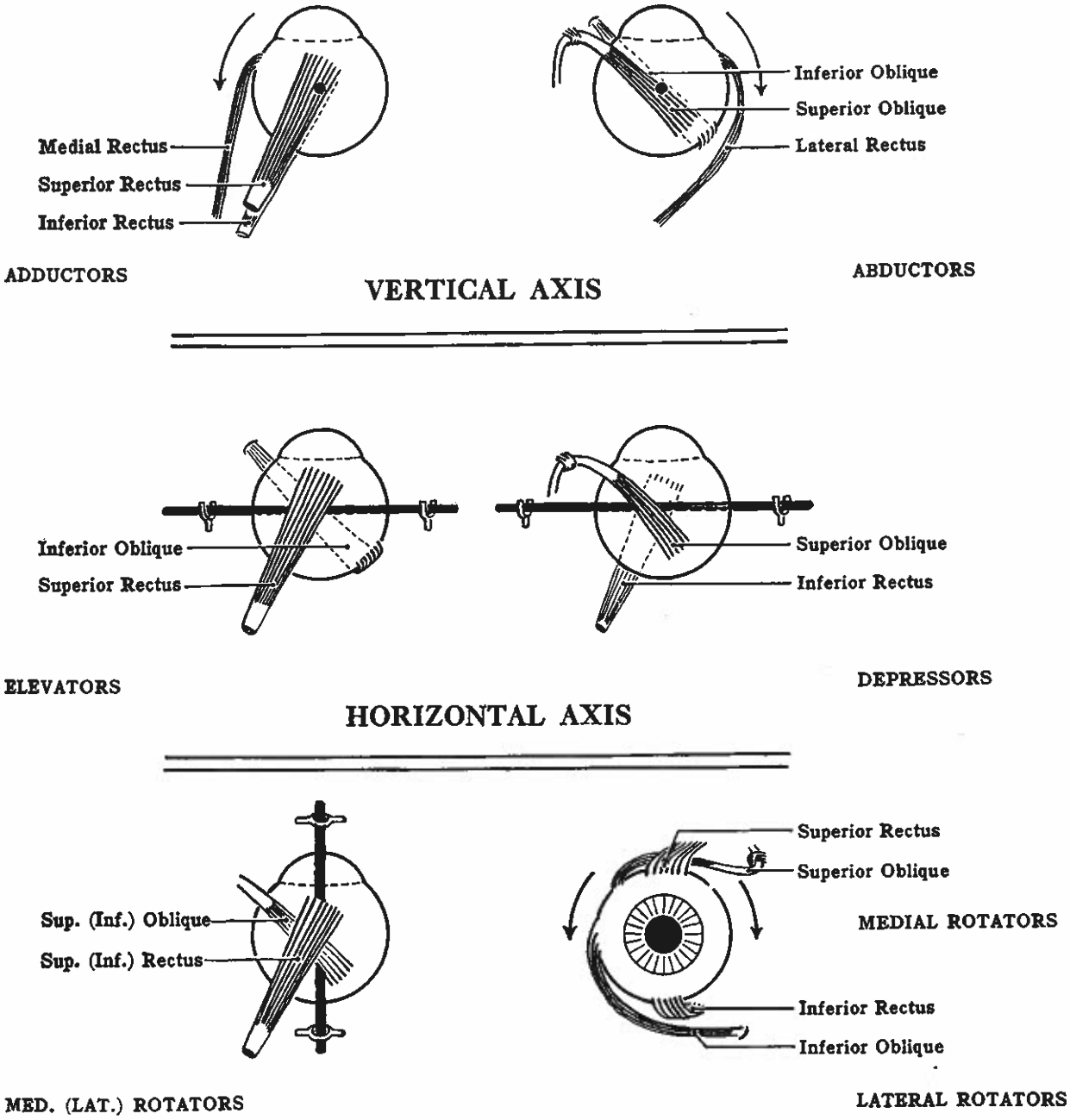


Fig. 1 Actions of the six extraocular muscles.
The right eyeball is shown above (from Grant's Atlas of Anatomy, 6th ed., 1972).

Given the complex movements of the extraocular muscles that elevate or depress the eyeball, how can you best determine which muscle is malfunctioning? If elevation of the eye appears incomplete, the superior rectus or inferior oblique (or both) may be weak. When the patient turns this eye inward (adduction), weakness of elevation from this

starting position is mainly due to the inferior oblique, since the adducted eyeball is aligned parallel to this muscle. When the patient turns this eye outward (abduction), weakness of elevation from this starting position is mainly due to the superior rectus. On the other hand, if depression of the eye appears incomplete, the superior oblique or inferior rectus (or both) may be weak. Thus, when the patient turns this eye outward (abduction), weakness of depression from this starting position is mainly due to the inferior rectus. When the patient turns this eye inward (adduction), weakness of depression from this starting position is mainly due to the superior oblique. Examining in this manner is referred to as testing the "cardinal directions of gaze," where eye depression or elevation is isolated to a single extraocular muscle, since the eye begins moving from a starting position of abduction or adduction, not from primary "straight ahead" gaze.

Starting position	Action tested by examiner	Corresponding single muscle tested
Out (abducted)	Eye elevation	Superior rectus
Out (abducted)	Eye depression	Inferior rectus
In (adducted)	Eye elevation	Inferior oblique
In (adducted)	Eye depression	Superior oblique
Out	Eye abduction	Lateral rectus
In	Eye adduction	Medial rectus

Table 1. Cardinal Directions of Gaze: positions in which only a single extraocular muscle is tested in isolation.

Clinically, the deficit from a complete **oculomotor nerve (CN III) lesion** is usually striking (see Fig. 2). Paralysis of the levator palpebrae superioris muscle may cause such complete **ptosis** that the ipsilateral drooping eyelid entirely covers the eye. If the eyelid is passively pulled up, the involved eye tends to be somewhat abducted or outwardly deviated because of the unopposed action of the lateral rectus muscle. Indeed, the patient is **only able to abduct the eye** since the abducens nerve is spared. The **pupil of the involved eye is large and unreactive to light,** directly or consensually, since the parasympathetic innervation of the pupil is impaired. The trochlear (CN IV) nerve is the only cranial nerve which exits the brain stem dorsally, and decussates to innervate the contralateral superior oblique muscle. A trochlear nerve (CN IV) lesion produces a subtle deficit that is difficult to detect clinically. Impairment of downward gaze (depression of the eyeball) is best noted when the involved eye is in the adducted position. An **abducens nerve (CN VI) lesion** affects only the ipsilateral lateral rectus muscle, impairing abduction of the affected eyeball.

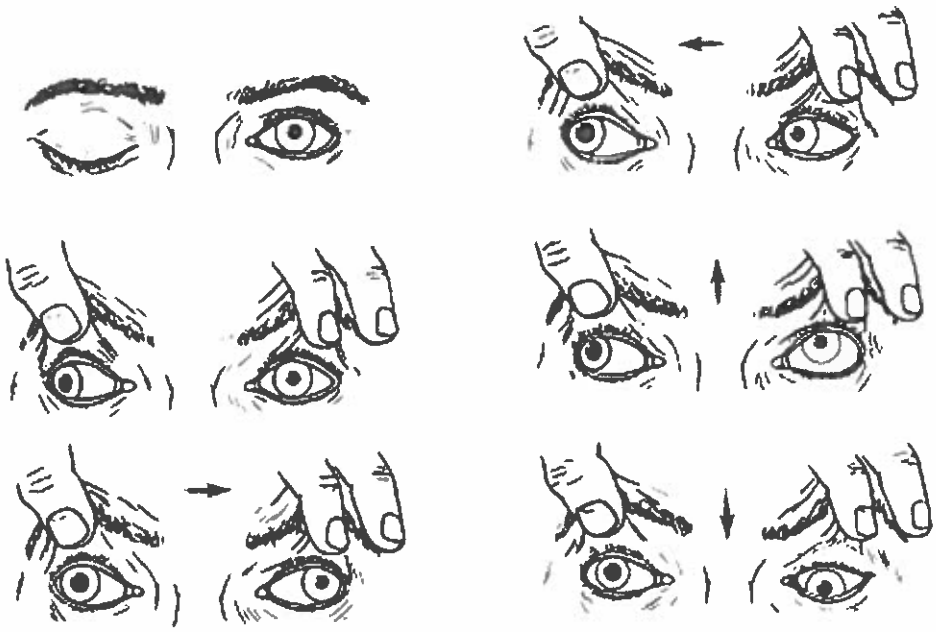


Fig. 2 Complete lesion of right CN III. The patient is asked to look in the directions of the arrows (from Rodnitzky RL. Van Allen's pictorial manual of neurologic tests. 3rd ed. Chicago:Year Book Medical, 1988)

4. Eye movement disorders

Normal binocular vision depends on analogous or equivalent areas of the retina of each eye perceiving the same visual stimulus. If the eyeballs are not perfectly aligned in primary position ("looking straight ahead") or when conjugately moving to other positions, a visual image may appear blurred or doubled (binocular diplopia). **Binocular diplopia** is the more common type of diplopia and **resolves if the patient covers either eye**. It can be caused by lesions of cranial nerves III, IV or VI, or their related extraocular muscles (or neuromuscular junctions therein). In the case of a severe or complete oculomotor nerve lesion, however, diplopia would be eliminated by the ptosis covering the involved eye. There are also connecting pathways within the brain stem which coordinate the actions of these extraocular muscles, plus connections with the vestibular and cerebellar systems allowing for smooth, reflexive eye movements as well. Thus, lesions involving these brain stem or cerebellar connections could also cause diplopia. **Monocular diplopia** is relatively rare and **occurs when looking with one eye alone**. It may occur from a problem in the "optical system" of an eye, such as a dislocated lens or detached retina, or may be related to a psychiatric disorder, but not from neurological disease, strictly speaking.

Patients complaining of diplopia may also be noted to have **nystagmus**, which refers to repetitive, oscillatory, jerky eye movements. Nystagmus can be physiological or normally induced, as when suddenly stopping someone rotating in a swivel chair.

Pathological or abnormal nystagmus occurs with lesions of the vestibular system, brain stem, or cerebellum which upset the normal control or balance of conjugate eye movements. Such lesions typically produce asymmetrical nystagmus, more prominent with certain eye movements or positions, while nystagmus caused by drug toxicity usually is symmetrical and present with virtually all eye movements or positions. For example, a vestibular lesion produces horizontal nystagmus, with a slow component or eyeball jerk toward the side of the lesion, and a fast component in the other direction.

Internuclear ophthalmoplegia (INO) refers to the paralysis of extraocular muscles ("ophthalmoplegia") from a lesion between the nuclei ("internuclear") involved with lateral gaze (oculomotor and abducens nuclei). Such a lesion interrupts the **ascending medial longitudinal fasciculus (MLF),** and therefore this disorder is also called the **MLF syndrome.** To have coordinated horizontal gaze rightward, for example, the right paramedian pontine reticular formation (PPRF) must activate both the right abducens nucleus in the pons and the left oculomotor nucleus in the midbrain, so that the right lateral rectus and left medial rectus muscles move the eyes to the right. The ascending MLF leaves the right PPRF, decussates early and rises to join the left oculomotor nucleus. A lesion along the main left-sided course of the MLF here, en route from pons to midbrain, produces paralysis of adduction of the left eye, with nystagmus of the abducting right eye (see Fig. 3). Since the left oculomotor nucleus never gets the "MLF signal," the left eye cannot adduct and right lateral gaze is impaired. However, the left medial rectus still functions, since both eyes adduct or converge when looking closely at an object (the near reflex, described below). **The most common causes of MLF lesions are multiple sclerosis in younger patients and ischemic infarction in older patients**.

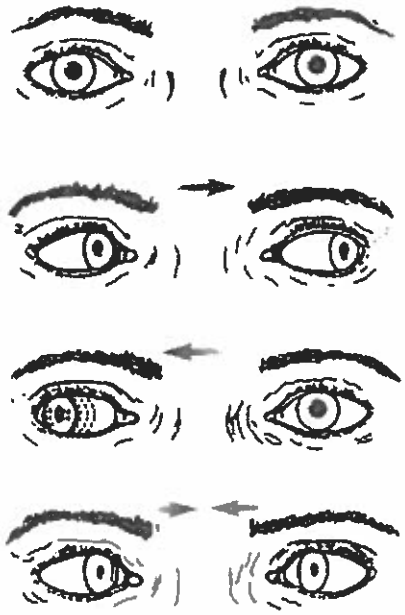


Fig. 3 Left MLF syndrome with attempted gaze in the direction of the arrows (from Rodnitzky RL. Van Allen's pictorial manual of neurologic tests. 3rd ed. Chicago:Year Book Medical, 1988)

5. Disorders of the pupil

Abnormalities of the pupil are discussed here since they are often encountered with lesions of the cranial nerves or pathways associated with eye movements. The normal **pupillary light reflex** is elicited by shining light into one eye, causing not only its pupil to constrict (direct response) but also that of the other eye (consensual response). This reflex pathway involves retinal ganglion cells projecting bilaterally to the pretectal area (rostral to the superior colliculus), which then projects to the Edinger-Westphal nucleus of CN III. For example, a left optic nerve lesion impairs the afferent part of this consensual reflex, so neither pupil constricts when light is shined into the left eye, yet both pupils constrict when light is shined into the right eye. A right CN III lesion interrupts the efferent part of this consensual reflex, so the enlarged right pupil never constricts when light is shined in either eye, yet the left pupil constricts with light shined in either eye.

A **relative afferent pupillary defect (RAPD)** may occur from a partial optic nerve or retinal lesion. Both pupils may initially constrict to light, but after moving the light source from the normal to the abnormal eye ("swinging flashlight test"), pupillary dilatation occurs because of relatively reduced afferent input at the affected eye. If one were to observe both eyes simultaneously, the light stimulus produces direct and consensual pupillary constriction, but to a lesser degree when the affected eye is stimulated.

The **near reflex** occurs when viewing a nearby object and normally consists of pupillary constriction, lens accommodation ("thickening"), and convergence of the eyes. In certain disorders, there is selective disruption of the pupillary light reflex pathway at the superior colliculus or pretectal area, but connections for the near reflex are preserved. This creates **dissociation of light and near reflexes (light-near dissociation)** such that the pupils only constrict during the near reflex, but not to a light stimulus. Classic causes of light-near dissociation include the dorsal midbrain syndrome and the Argyll Robertson pupils in neurosyphilis. The dorsal midbrain (Parinaud's) syndrome classically refers to a pineal tumor compressing the dorsal midbrain but may also occur from an ischemic infarction there. As the midbrain centers for vertical gaze may be also involved in this syndrome, impairment of upward gaze may accompany light-near dissociation of the pupils.

Horner's syndrome occurs from a lesion disrupting the oculosympathetic pathway, causing **miosis** (a smaller, constricted pupil which dilates poorly in darkness), **anhidrosis** (decreased sweating in the ipsilateral face since sweat glands have sympathetic innervation), and mild **ptosis** (paralysis of the superior tarsal muscle). The oculosympathetic pathway is relatively long and consists of three neurons in series. First-order neurons descending down the brain stem may be involved by a lateral medullary infarction (Wallenberg syndrome). Second-order neurons originating from the intermediolateral cell column in the spinal cord at C8 to T2 levels may be affected by a tumor as they course through the apex of the lung. Third-order neurons arising from the superior cervical sympathetic ganglion ascend up the internal carotid artery where they may be affected by neck trauma. It should be noted that the ptosis in Horner's syndrome is subtle and mild in comparison to the more obvious ptosis from an oculomotor (CN III) nerve lesion.

6. Trigeminal Nerve (CN V)

The trigeminal nerve has sensory and motor functions. Sensation over the face and anterior scalp is conveyed to the brain stem by three divisions or branches: **V-1 (ophthalmic), V-2 (maxillary), and V-3 (mandibular).** These branches may be compressed by tumors particularly where they pass through bony foramina in the skull base, or may be affected by infection or inflammation there. A V-1 sensory deficit over the forehead (see Fig. 4) should also involve the anterior scalp, while a V-3 sensory deficit should not involve the corner of the jaw or the neck. Thus, sensory deficits not confined to the trigeminal nerve territory may be due to lesions in the contralateral thalamus or parietal lobe, or may be associated with psychiatric disorders. Trigeminal branch sensory deficits may accompany other cranial nerve lesions. A V-1 territory sensory impairment plus ipsilateral involvement of cranial nerves III, IV and VI may occur from a lesion at the superior orbital fissure or nearby cavernous sinus.

Trigeminal neuralgia is a painful syndrome of irritation or inflammation of one of the trigeminal nerve sensory branches which "short circuits" or "misfires." Patients experience episodic, lightning-like jabs or "electrical shocks" of pain usually in the territory of V-2 or V-3, several times daily, provoked by talking, chewing or touching the face. No sensory or other cranial nerve deficits are found on neurological examination however. A multiple sclerosis lesion at the trigeminal nerve entry region into the pons is often the cause in younger patients. In older patients, a trigeminal nerve branch is often compressed by a tortuous or kinked blood vessel (often the superior cerebellar artery), which can be surgically repositioned or padded. Other treatments include oral anticonvulsants such as carbamazepine, gabapentin or others to relieve the nerve "misfiring" or procedures to destroy the nerve branch involved.

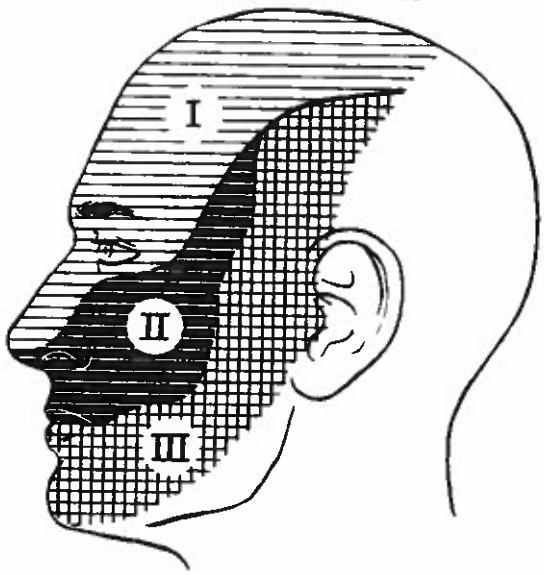


Fig. 4 Trigeminal nerve sensory territories: V-1 (V-I) Ophthalmic, V-2 (V-II) Maxillary, and V-3 (V-III) Mandibular (from Rodnitzky RL. Van Allen's pictorial manual of neurologic tests. 3rd ed. Chicago:Year Book Medical, 1988)

The trigeminal nerve also innervates the muscles of chewing or mastication---the masseter and temporalis muscles. A lower motor neuron lesion of the trigeminal motor nerve is rare and produces atrophy and weakness in these ipsilateral muscles, with the jaw deviating toward the side of the lesion. Both ipsilateral and contralateral upper motor neurons in the motor cortex control the trigeminal motor nerve on one side, so an upper motor neuron lesion on one side does not produce any jaw deviation or severe weakness. Bilateral upper motor neuron lesions here, however, may cause **hyper-reflexia of the jaw jerk**, since it is a muscle stretch reflex (tested by gently tapping on the chin with the mouth slightly opened and relaxed).

7. Facial Nerve (CN VII)

Each facial nerve, originating from its facial nucleus in the pons, innervates the ipsilateral facial muscles, from uppermost frontalis to lowermost platysma. **A lower motor neuron facial paralysis involves the nucleus or nerve of CN VII and causes a relatively severe paralysis of the entire ipsilateral half of the face.** This would be the isolated finding with a lesion at or near the stylomastoid foramen (see lesion 1 in Fig. 5). Other signs and symptoms accompany facial nerve lesions within the temporal bone. Ipsilateral facial paralysis plus **impaired taste over the anterior 2/3 of the tongue indicates that the chorda tympani branch of the facial nerve is also involved** (lesion 2A in Fig. 5), while a slightly more proximal lesion (lesion 2B in Fig. 5) also involves the facial nerve branch to the stapedius muscle. The stapedius muscle acts to dampen middle ear ossicle movements in the presence of loud sounds, so an unpleasant sensitivity to sound (**hyperacusis**) is a symptom of stapedius muscle denervation. A lesion at the internal auditory meatus or **cerebellopontine angle** would create all the deficits as in lesion 2B plus hearing impairment and tinnitus, an unpleasant, persistent ringing or buzzing sound or pitch, from involvement of the adjacent CN VIII. This lesion (lesion 3 in Fig. 5) is often from an acoustic neuroma, a tumor arising from CN VIII. A lesion at or near the facial nucleus in the pons (lesion 4 in Fig. 5), such as a small ischemic infarction, would most likely also create ipsilateral weakness of lateral gaze, from involvement of the adjacent PPRF and CN VI.

In addition to tumors or trauma causing lesions of CN VII in its course outside the pons, a very common syndrome is **Bell's palsy** or idiopathic facial nerve paralysis. The patient may awaken to suddenly notice severe paralysis of one side of the face, sometimes with ipsilateral hyperacusis and impaired taste. A short course of oral corticosteroid medication hastens recovery from the presumed facial nerve inflammation where it travels through the temporal (petrous) bone. Herpes simplex or other viruses may cause this inflammation, so anti-viral medication may also be part of the treatment. In general, most patients with Bell's palsy recover fully after a few weeks.

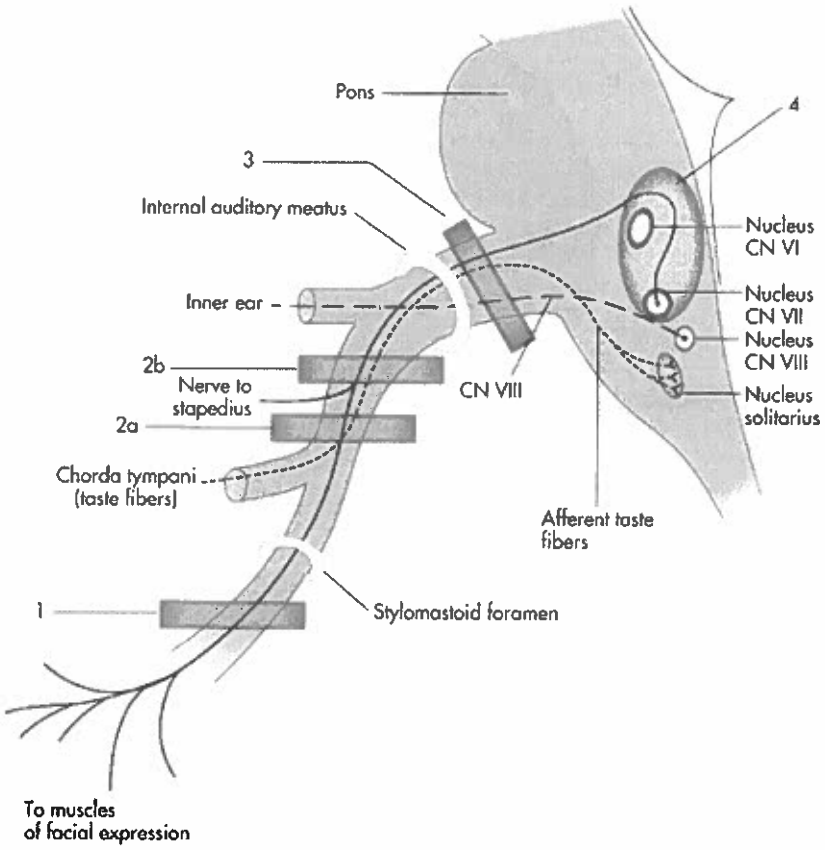


Fig. 5 Nuclear and infranuclear lesions of the facial nerve.

Facial paralysis may also occur with lesions of the upper motor neurons that control the facial (CN VII) nucleus. The part of the CN VII nucleus which innervates the upper face or forehead is controlled by upper motor neurons (corticobulbar tract fibers) originating both ipsilaterally and contralaterally, while the rest of the CN VII nucleus is controlled only by contralateral upper motor neurons (see Fig. 6). Thus, **facial paralysis from an upper motor neuron lesion causes a relatively milder paralysis of only the lower part of the contralateral face, sparing the forehead.**

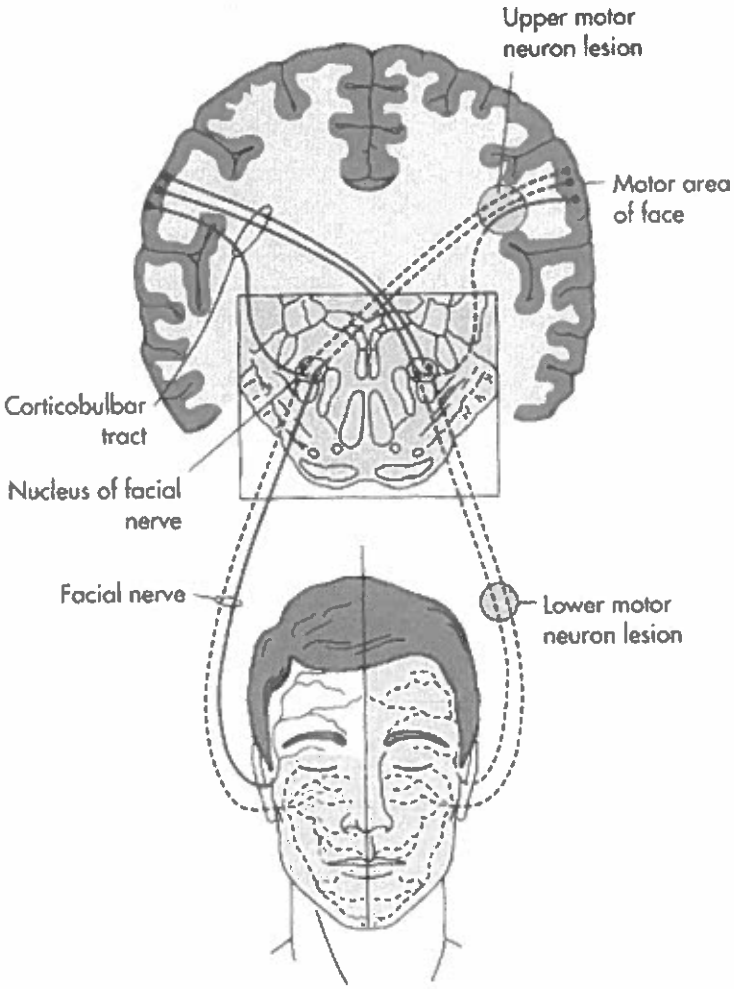


Fig. 6 Upper versus lower motor neuron facial paralysis. The shaded areas of the face show the distribution of the facial muscles paralyzed after a supranuclear lesion of the corticobulbar tract (upper motor neuron lesion) and after a lesion of the facial nerve or its nucleus (lower motor neuron lesion) (from Gilman S, Winans SS. Manter and Gatz's essentials of clinical neuroanatomy and neurophysiology. 6th ed. Philadelphia: FA Davis, 1982)

8. Vestibulocochlear Nerve (CN VIII)

(CN VIII will be discussed in the section Visual, Auditory, and Vestibular Systems.)

9. Glossopharyngeal (CN IX) and Vagus (CN X) Nerves

Cranial nerves IX and X have similar or shared functions, but taste, visceral afferent, and visceral efferent functions cannot be tested clinically. Both nerves innervate

pharyngeal and laryngeal muscles, so glossopharyngeal or vagus nerve lesions can cause impairments of speech or swallowing, but it is often difficult to test each nerve separately. A decreased or absent **gag reflex** when touching one side of the pharynx suggests a glossopharyngeal nerve lesion on that side. The gag reflex is difficult to evaluate, however, since some patients virtually never gag, while others are very sensitive to pharyngeal stimulation and hate being tested. Elevation of the palatal arch is readily observed when asking the patient to say "ah" (see Fig. 7) and reflects vagal nerve function. A **lower motor neuron lesion of vagal nerve** branches innervating the palate causes **ipsilateral drooping or sagging of the palatal arch** with the uvula pointing toward the other (normal) side. A **lower motor neuron lesion of vagal nerve** branches innervating the larynx causes **hoarseness** from ipsilateral paralysis of vocal cord muscles.

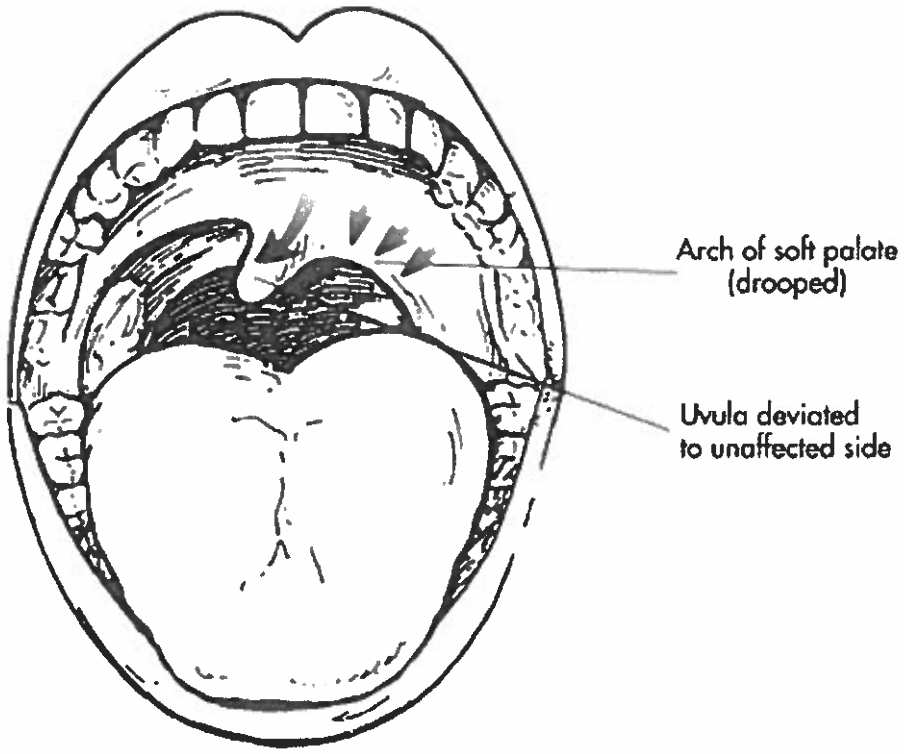


Fig. 7 A lesion of the left vagal nerve branches innervating the soft palate.

10. Spinal Accessory Nerve (CN XI)

A lower motor neuron lesion of CN XI weakens the ipsilateral sternocleidomastoid and trapezius muscles, which it innervates. Decreased elevation or shrugging of the shoulder is observed along with weakness in turning the head to the opposite side.

11. Hypoglossal Nerve (CN XII)

The hypoglossal nerve innervates the muscles of the tongue on each side. Most important for clinical testing is the genioglossus muscle, which protrudes each side of the tongue forward. A **lower motor neuron lesion of CN XII on one side causes the protruded tongue to deviate or turn toward the affected or weak side**, since the contralateral genioglossus muscle normally pushes its half of the tongue forward. Over time, the affected half of the tongue would **atrophy and fasciculations and fibrillations** would be observed there. In a few patients, the upper motor neurons (corticobulbar tract fibers) controlling the CN XII nucleus only arise contralaterally. In that case, an ischemic infarction of the left frontal lobe would impair the right hypoglossal nucleus, weakening protrusion of the right half of the tongue such that the **protruded tongue may deviate or turn toward the side opposite its upper motor neuron lesion**. In most patients, however, ipsilateral and contralateral upper motor neurons control each hypoglossal nucleus, so a frontal lobe lesion on one side would not cause weakness or deviation of the tongue.

Brain Stem Disorders

1. Types of cranial nerve lesions

One or more cranial nerves may be impaired by various kinds of pathology in their anatomical vicinity, such as tumors or fractures of the skull base, or infection or inflammation of the meninges. Polyneuropathies affecting multiple nerves in the limbs and trunk, caused by diabetes or the Guillain-Barre syndrome, may also involve cranial nerves. All these lesions involve one or more cranial nerves outside the brain stem.

Lesions within the brain stem itself often are from ischemic infarction, hemorrhage, tumor or multiple sclerosis. It would be unusual for one of these disorders to just involve a cranial nerve or two inside the brain stem. Most often anatomically adjacent fiber tracts are also involved.

2. Brain stem syndromes

Crossed brain stem syndromes consist of **cranial nerve involvement on one side and** an adjacent fiber tract lesion, creating **a clinical sensory or motor deficit on the opposite side of the body**. These clinical findings help localize the problem to a particular area or level of the brain stem. For example, a right pontine lesion involves the right facial nucleus and the right corticospinal tract, creating a lower motor neuron paralysis of the entire right half of the face plus an upper motor neuron paralysis of the left upper and lower limbs (left hemiparesis). Another example is a lesion in the left lateral medulla which involves the left descending spinal tract of CN V and the left spinothalamic tract, which consists of afferents from the right side of the spinal cord that have already decussated within the cord itself. The unusual clinical features include deficits of pain (pinprick) and temperature over the left face and right limbs and body. Two well-known crossed brain stem syndromes are discussed below.

The **medial midbrain syndrome (Weber syndrome)** may be due to an ischemic infarction from an occluded branch of the posterior cerebral artery. CN III and the nearby cerebral peduncle (corticospinal and corticobulbar tracts) are involved, creating an **ipsilateral oculomotor nerve lesion and upper motor neuron weakness of the contralateral face and limbs**.

The **lateral medullary syndrome (Wallenberg syndrome)** may be due to an ischemic infarction from an occluded vertebral artery or its PICA (posterior inferior cerebellar artery) branch. The features making it a "crossed brain stem syndrome" are **pain (pinprick) and temperature impairment in the ipsilateral face and contralateral limbs and body**, as explained above. Other symptoms may include hoarseness, vertigo, nausea and vomiting, and clumsiness. In addition to the sensory deficits mentioned, other signs may include nystagmus (vestibular nuclei), ipsilateral limb dysmetria (inferior cerebellar peduncle), ipsilateral Horner's syndrome (descending sympathetic tract), and ipsilateral palatal and vocal cord paralysis (nucleus ambiguus). It should be noted that in this syndrome position sense and strength are preserved.

CLINICAL NEUROANATOMY: TOUR OF THE POSTERIOR FOSSA

Date: August 18, 2011 – 11:00 AM
Reading Assignment:

KEY CONCEPTS & LEARNING OBJECTIVES

1) Define elements of the patient history that localize symptoms to structures in the posterior fossa.

2) Define some of the pathological mechanisms that are associated with specific posterior fossa clinical syndromes.

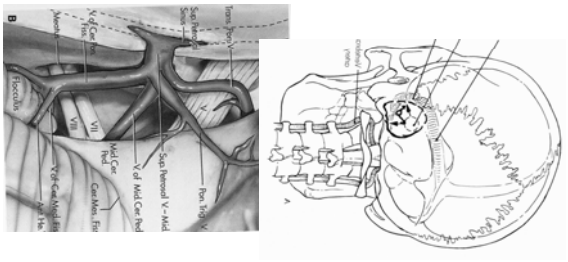
3) Review previously discussed neuroanatomy (ie., info from lectures on the pons) in the context of a clinical scenario.

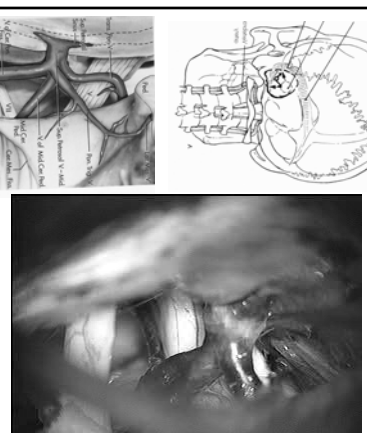
4) Introduction to the analysis of neuroimaging studies such as brain MRI.

5) Introduce surgical techniques and the concept of neurosurgical micro-anatomy used in the thearapeutic intervention for the above.

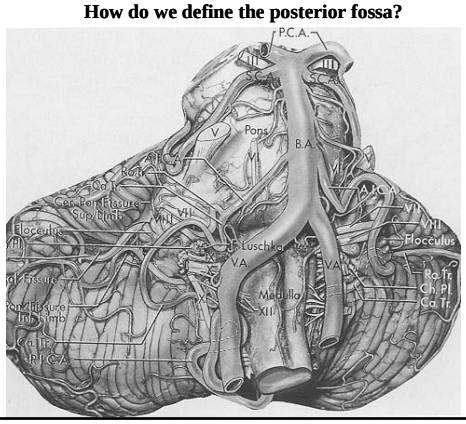
A Tour of the Posterior Fossa

Douglas E. Anderson, MD
Dept. of Neurological Surgery
Loyola University Medical Center

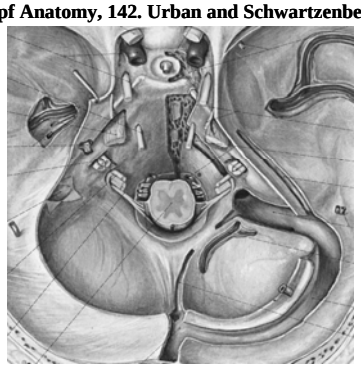




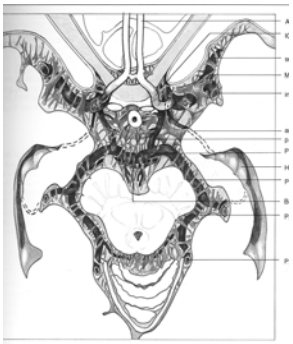
How do we define the posterior fossa?



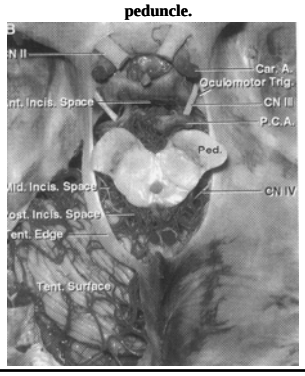
The anatomic boundaries of the posterior fossa, viewed through the removed tentorium, mesencephalon, pons and cerebellum. (Pernkopf Anatomy, 142. Urban and Schwartzenberg, 1964)



Cerebrospinal fluid cisterns at the skull base



Superior anatomic boundaries of the posterior fossa: superior view of the tentorial incisura after removing the cerebrum. The tentorial edges sweep along the the lateral margin of the cerebral peduncle.



A "clinical-anatomic" Tour of the Posterior Fossa

- What are the main goals of the lecture?
  - While we study neuroscience by anatomic category, (ie., the medulla), pathological processes affect multiple systems simultaneously, so that an introduction to anatomical principles in which osteology, vascular anatomy, cisternal and ventricular anatomy, and neuroanatomy are considered simultaneously is essential to clinical diagnosis and treatment.
  - Clinical syndromes consist of a variable constellation of symptoms and signs. We'll look at a few (especially increased ICP) of the bewildering array of syndromes associated with posterior fossa pathology.
  - Recognition of the importance of the "art of listening" to the patient during the elicitation of the clinical history.

A "clinical-functional anatomic" Tour of the Posterior Fossa

- Perspective:
  - The posterior fossa includes some of the most complex and crucial anatomy in the human body.
  - CSF flow is dependent on the Foramina Magendie and Luschka.
  - The majority of the cranial nerves arise here, and if and when malfunction or disease occurs, one can be faced with severely painful, disabling, disfiguring syndromes.
  - Arteries are almost all "terminal" with little collateral circulation whereas venous circulation is redundant.
  - Brain stem neuroanatomically dense, cerebellum seems to be highly redundant except for the major deep nuclei (esp dentate)
  - Lesions of the PF present unique challenges in diagnosis and treatment due to the dense anatomic arena.

Clinical syndromes of the posterior fossa

"The art of the practice of medicine is to be learned only by experience."

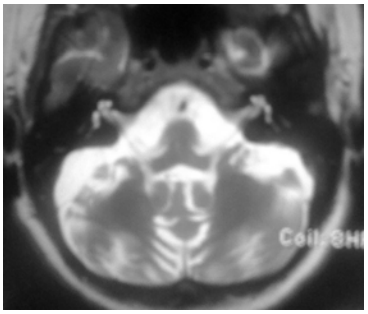
-Sir William Osler

- narrative clinical history/stories
- neurological examination findings
  - Inductive neuroanatomical correlation
- "data review" – neuroimaging and other laboratory data
- The "assessment" or differential diagnosis
- "the plan" - therapeutic strategies
  - Surveillance
  - Medical rx
  - microneurosurgical technique
  - Stereotactic radiosurgery
- Outcome analysis – "patient assessed outcome"

Categories of Neuropathology

- Congenital (spina bifida),(see also metabolic)
- Neoplastic – primary (intrinsic or extrinsic) or metastatic.
- Vascular – occlusive or hemorrhagic
- Metabolic (EtOH)/Genetic (Enzyme defect)
- Traumatic – (distinctly idiosyncratic)
- Infectious – meningitis or abscess
- Degenerative – (Parkinson's, Alzheimer's Diseases)
- Inflammatory/Immunological – MS,
- Paroxysmal disorders
- "Disorders of the mind"

T2 weighted axial MRI of a 20 year old woman 10 years post MVA with "brain stem" and cerebellar injury: ataxia on the right, decreased movement on the left, diplopia and visual disturbance, and hearing loss.



Common Complaints associated with posterior fossa syndromes:

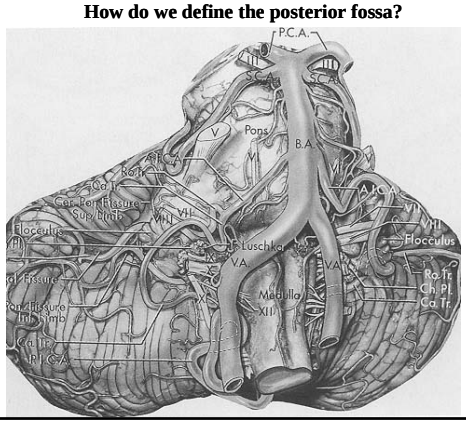
- **Headache – neck pain, head tilt**
- **Nausea – vomiting**
- **Visual disturbance**
- **Facial Pain/ hypesthsesia/ parasthesia (also extremities and trunk)**
- **Dizziness/ imbalance/vertigo**
- **Hearing loss**
- **Dysphagia**
- **Ataxia**
- **Tremor**

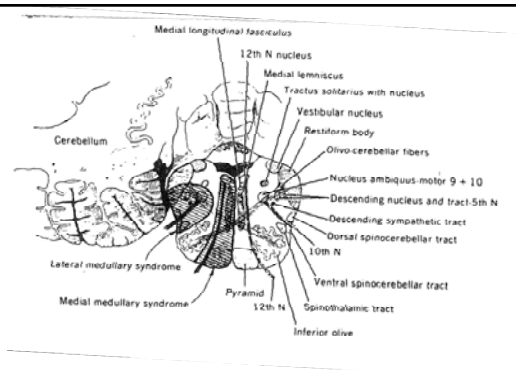
- **Associated historical clues &/or neurological signs:**
  - HA – onset (prodrome, chronology, and tempo), duration, amplitude, and course, frequency, focality, sleep interruption and associated complaints.
  - Dizziness – associated gait abnormality, associated EOM dysfx, associated hearing loss.
  - Hearing loss – associated facial numbness, balance abn.
  - N&V – assoc. HA and /or papilledema.
  - Loss of consciousness

Sample board question: A 65 year old man has loss of pain and temperature sensation on the right side of the face and from the neck down on the left. Examination shows partial paralysis of the soft palate larynx, and pharynx, and ataxia all on the right. The most likely cause of these findings is thrombosis to which of the following arteries?

- A. Basilar
- B. Right posterior inferior cerebellar
- C. left posterior inferior cerebellar
- D. Right superior cerebellar
- E. Left superior cerebellar

How do we define the posterior fossa?



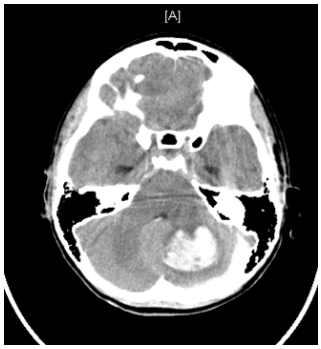


But lateral medullary syndrome can be caused by vertebral, PICA, or the lateral medullary arteries, depending on individual variation.
Illustration from Adams and Victor, Neurology.

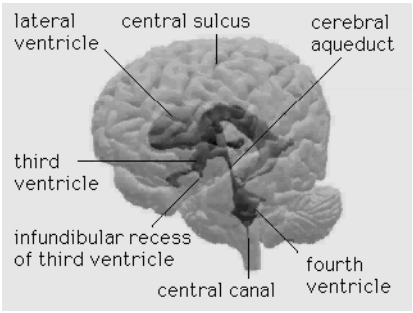
First example - A 13 year old girl with HA, nausea and LOC.

- HX - Onset – sudden (chronology- @ 3AM, 5-10 mins then defervescence and tempo – severe onset with gradual subsidence), frequency- recurrent HA in 1 hr, duration -, amplitude and course – worst HA of her life with LOC, focality – posterior neck and spread, sleep interruption (always a “red flag”) and associated complaints N and V.
- EXAM – comatose, fixed mid-position pupils, no gag, question of “extensor and flexor posturing” in the ambulance. She was intubated on arrival to ER.

A 13 year old girl with HA, nausea and LOC

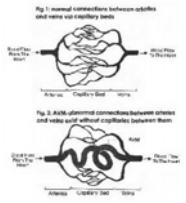


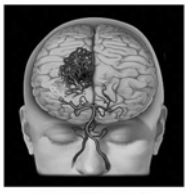
Ventricular obstruction due to acute cerebellar hemorrhage



Arteriovenous Malformations (AVMs)

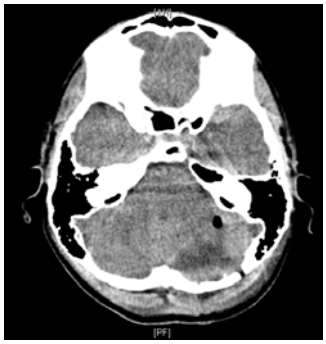
- AVMs are abnormal, direct connections between arteries and veins.
- They have a higher tendency to rupture (compared to normal vasculature).
- Sx: Many people with AVMs experience few symptoms, however symptoms can include dizziness, pain, and neurologic deficits (due to rupture or mass effect), among many other possible symptoms.
- Tx:
  - Conservative Tx: involves the management of symptoms
  - Interventional Tx: Microsurgical excision, stereotactic radiosurgery, or embolization



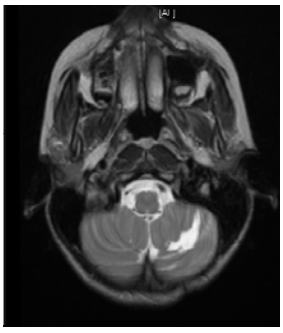


Arteriovenous Malformation (AVM)

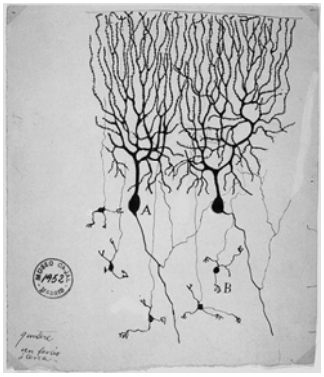
Immediate post-operative CT axial cut at the level of the middle cerebellar peduncle



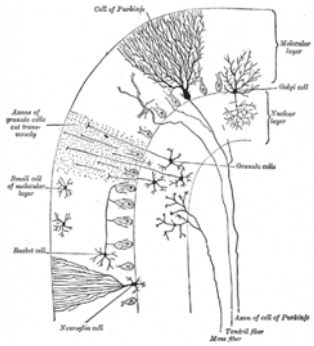
13 year old girl – s/p resection of cerebellar hematoma secondary to cerebellar AVM - 6 months postop



Santiago Ramon y Cajal's drawing: Purkingie cell of a pigeon - 1899



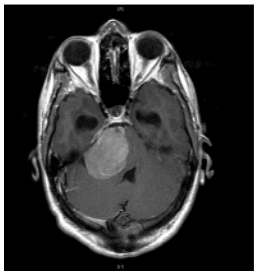
Transverse section- cerebellar folium

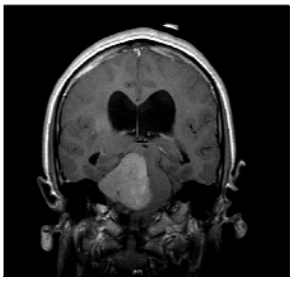


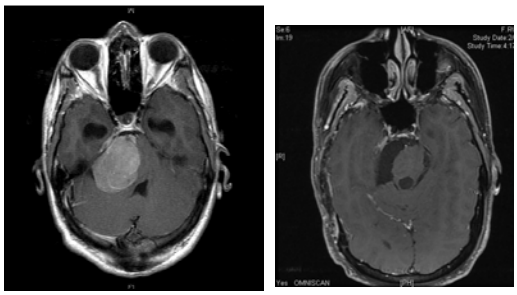
Interspersed between Purkinje cells in the cerebellum are *granule cells*: so called because of their tiny appearance as little particles (granules) when first discovered. They turned out to be complete nerve cells. There are as many as *40 billion* granule cells in the cerebellum. Shepherd (1974) wrote, "It is commonly stated that the human brain contains 10 billion nerve cells, as evidence of its fantastic complexity; clearly those statements do not take into account the granule cells of the cerebellum!"

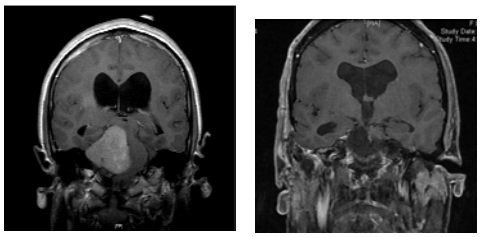
Second Example: 53 year old man presents to ER

- CC: imbalance, gradual unsteadiness of gait. Floater (visual obscuration) Insensitivity of the right eye to an inadvertent mild trauma.
- HPI: 2-3 weeks, HA, blurred vision.
- PMH: scoliosis, congenital heart defect.
- Exam: CNs II, III, V, VII, VIII, IX, X

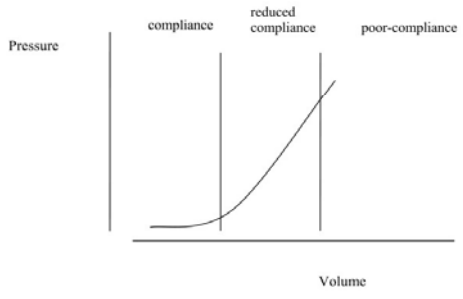




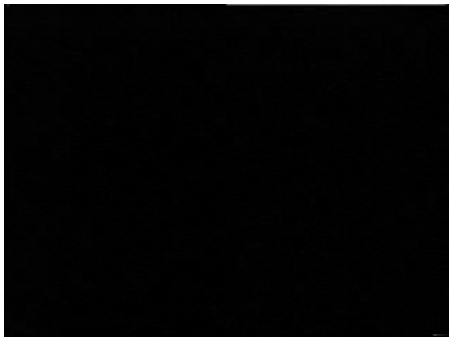




Intracranial Pressure-volume compliance curve



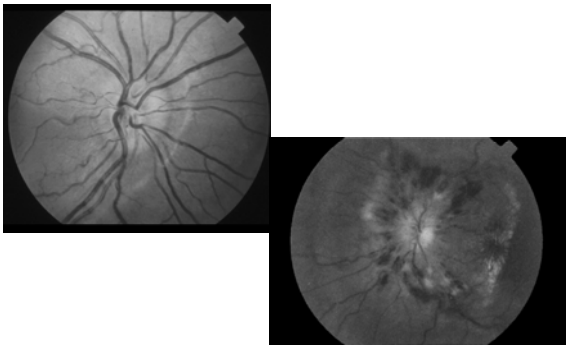
Third Example: 11 yr. old girl with denovo headache, visual disturbance.



11 yr. old girl with denovo headache, visual disturbance.

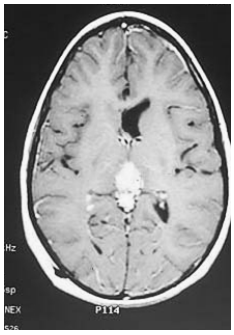
- Clinical History
  - Headache, neck pain, nausea, vomiting, head tilt, visual disturbance.
- Examination
  - Nl MS, papilledema, CN's otherwise nl. MST nl., Sensory exam nl., Cerebellar exam nl.
- Assessment
  - Increased intracranial pressure
  - Intracranial tumor vs. hydrocephalus

Funduscopic examination-
left normal, right florid papilledema with retinal hemorrhage



11 yr. old girl with denovo headache, visual disturbance.

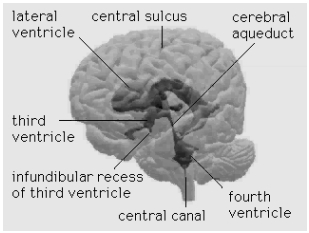
- Imaging Studies
- MRI scan with contrast showing pineal region lesion.
- Required emergency shunting of the CSF trapped in the lateral ventricles.



11 yr. old girl with denovo headache, visual disturbance.

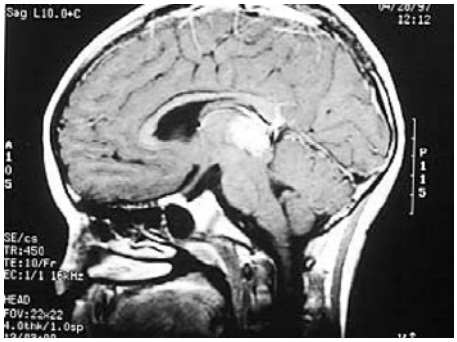
Ventricular anatomy:

Lateral venticles
foramen of Monroe III ventricle
aqueduct / Iter of Sylvius
IV Ventricle
Foramina of Luschka and Magendie

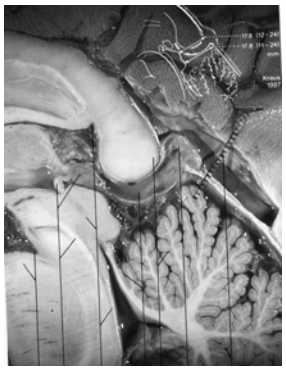


University of Washington, Digital Anatomist, 1994

11 yr. old girl with denovo headache, visual disturbance.



Structures at the tentorial incisura



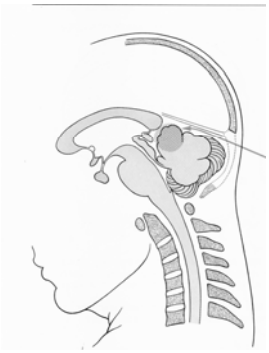
- Pons and caudal recess of IP fossa.
- (Epithal) Commisure, pineal.
- Fornix, central grey, rhomboid fossa.
- Vein of Galen, lingula.
- Splenium of CC, central lobe.
- Arachnoidal tissue.
- Straight sinus.

- Johannes Lang, Clinical Anatomy of the Posterior Fossa and its Foramina, Thieme 1991.

11 yr. old girl with denovo headache, visual disturbance.

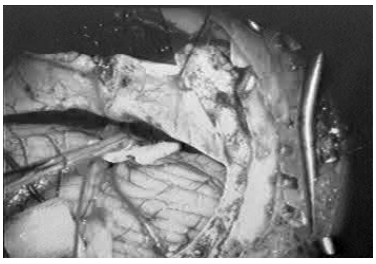
Surgery performed via an infratentorial – supracerebellar approach.

High speed drill with 6mm cutting burr, then 5-6 mm diamond burr, to "blue line" the bone (especially in children) supplemented with Kerrison rongeurs, for the initial craniotomy.

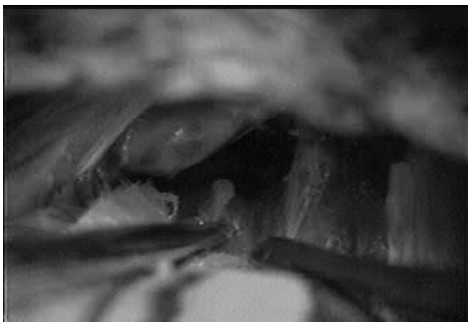


11 yr. old girl with denovo headache, visual disturbance.

Surgery performed via an infratentorial – supracerebellar approach.



11 yr. old girl with denovo headache, visual disturbance.



Summary-

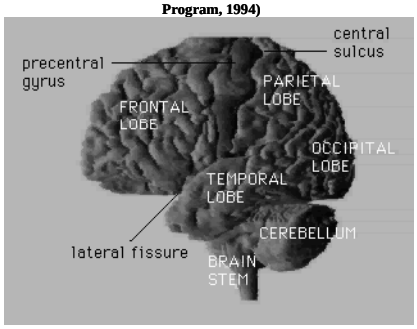
Stephanie is now a junior in college having recovered from surgery and completed chemotherapy for embryonal cell carcinoma with no evidence of recurrence thus far.

3 yr. old girl with progressive hemiparesis, facial weakness and EOM dysfx.

- Clinical History
  - Grandmother brought child to ER with acute onset of left limp in March 1998. Problem deemed inoperable.
  - Continued deterioration; unable to walk in June 1998.
- Examination
  - MS lethargic, CN's reveal EOMs abn with VII paresis. MST reveals left dense hemiparesis, Sensory exam nl., Cerebellar exam nl.
- Assessment
  - Right brain stem pathology.

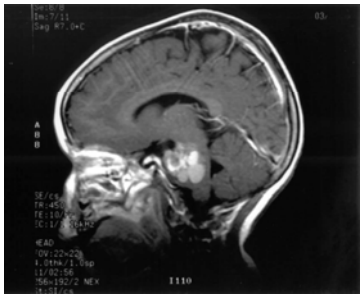
3 yr. old girl with progressive hemiparesis, facial weakness and EOM findings.

(Interactive Brain Atlas. University of Washington, Digital Anatomist Program, 1994)

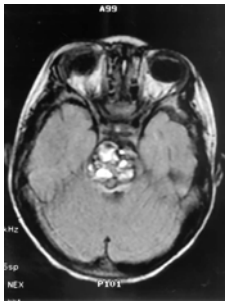


3 yr. old girl with progressive hemiparesis.

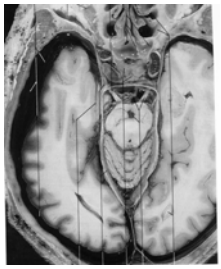
- Imaging Studies
- MRI Sagittal with contrast.



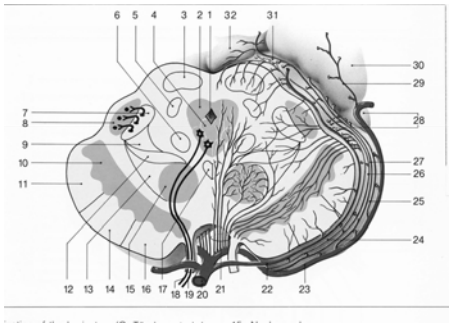
3 yr. old girl with progressive hemiparesis.

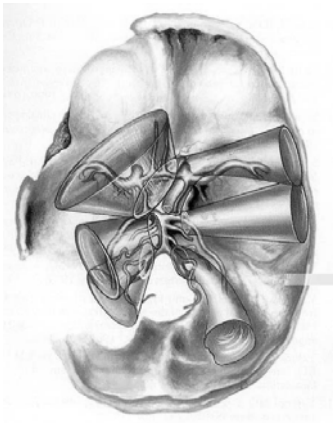


Surgery contemplated via a cranio-orbital-zygomatic approach.

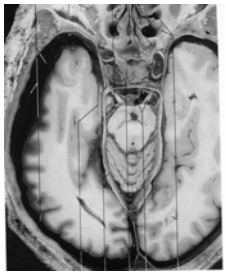


3 yr. old girl with progressive hemiparesis.

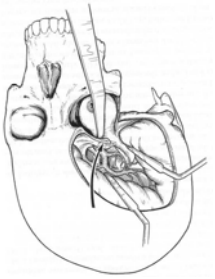




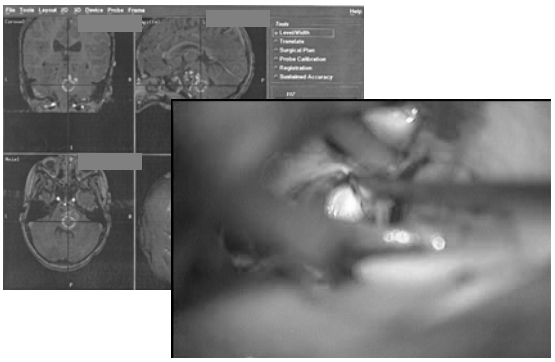
3 yr. old girl with progressive hemiparesis.



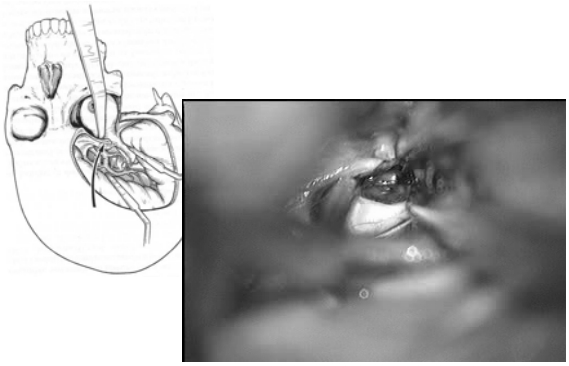
Surgery performed via a cranio-orbital-zygomatic approach.



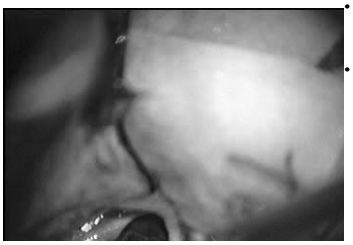
3 year old girl with progressive hemiparesis.



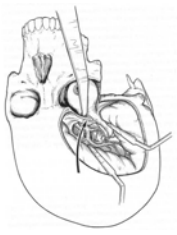
3 year old girl with progressive hemiparesis.



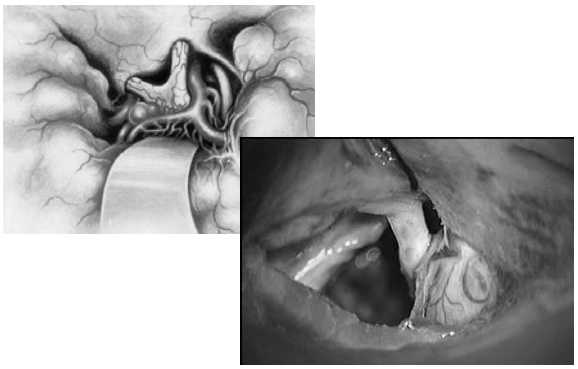
3 year old girl with progressive hemiparesis.



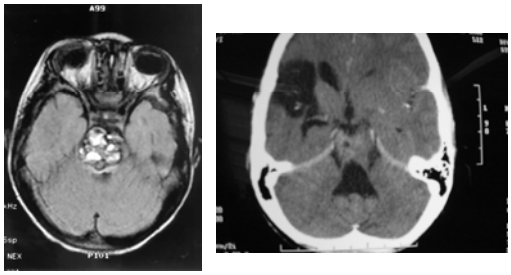
- **After 13 hrs. of surgery body of angioma is removed en bloc.**
- **III anatomically intact.**



3 year old girl with progressive hemiparesis.



Pre and 1 yr. post op MRI and CT scan with contrast.

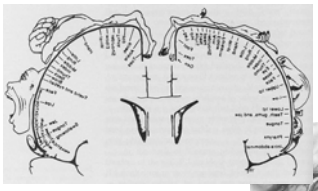


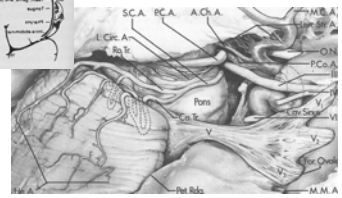
Fifth example – 53 year old man with progressive, intermittent, intractable (R) facial pain.

- Clinical History-
  - One year history of progressive excruciating intermittent right facial pain unresponsive to dental work and meds.
- Examination- normal
- Assessment
  - Trigeminal neuralgia or tic douloureux
    - Differential diagnosis includes: Dental pain, Herpetic neuralgia, tumor of Vth CN, Vascular HA, atypical facial pain.

53 year old man with progressive, intermittent, intractable (R) facial pain.

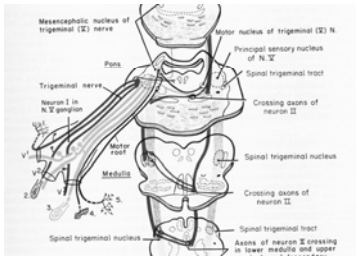
- Clinical Anatomy





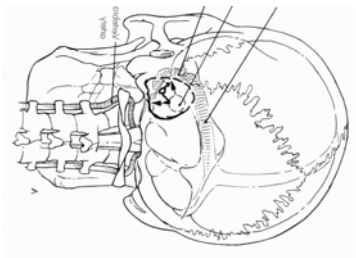
53 year old man with progressive, intermittent, intractable (R) facial pain.

- Clinical Anatomy



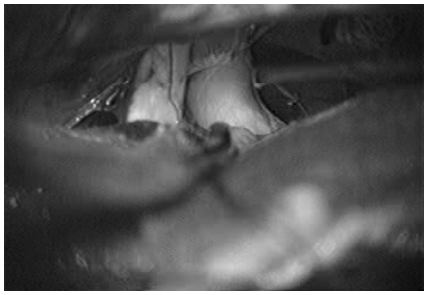
53 year old man with progressive, intermittent, intractable (R) facial pain.

Surgery performed (after failure of medical management) via a right retrosigmoid - suboccipital craniotomy.



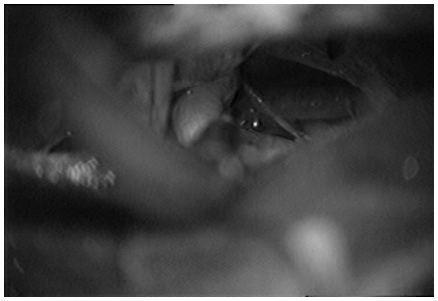
53 year old man with progressive, intermittent, intractable (R) facial pain.

Surgery performed via a retrosigmoid - suboccipital craniotomy



53 year old man with progressive, intermittent, intractable (R) facial pain.

Surgery performed via a retrosigmoid - suboccipital craniotomy



Summary

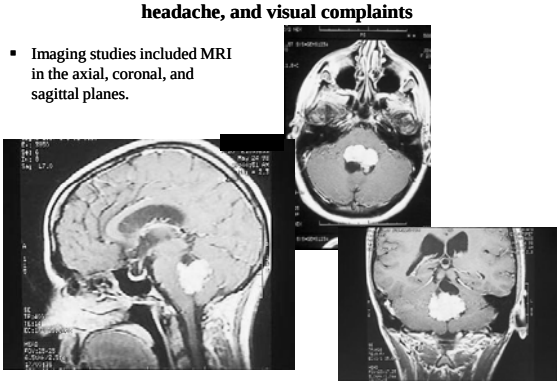
- 53 year old man with progressive, intermittent, intractable (R) facial pain.
- Vascular cross compression at the brain stem root entry zone caused focal irritation/demyelination of the Vth CN and resultant increased activity in the descending nucleus of V: clinically, tic douloureux or trigeminal neuralgia.
- Pain has been completely relieved since surgery and patient has tapered off all medicines.

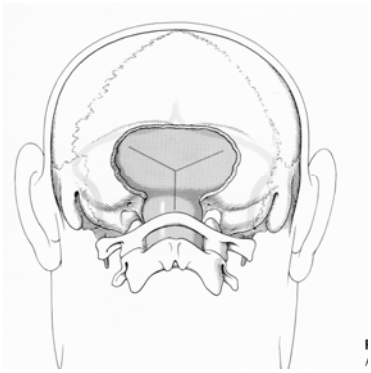
Sixth Example – 19 year old woman with intermittent hearing loss, progressive headache, and visual complaints

- Clinical History
  - Headache-like pressure sensation with crescendo then dissipation.
  - Auditory obscurations.
- Examination
  - Nl MS, mild papilledema, CN's otherwise nl. MST nl., Sensory exam nl., Cerebellar exam nl.
- Assessment
  - Increased intracranial pressure
  - Intracranial tumor vs. hydrocephalus

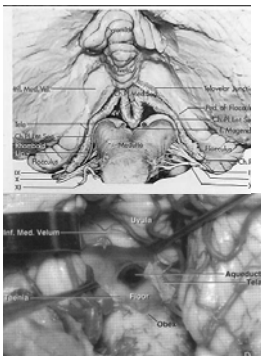
19 year old woman with intermittent hearing loss, progressive headache, and visual complaints

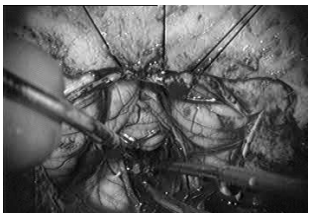
- Imaging studies included MRI in the axial, coronal, and sagittal planes.



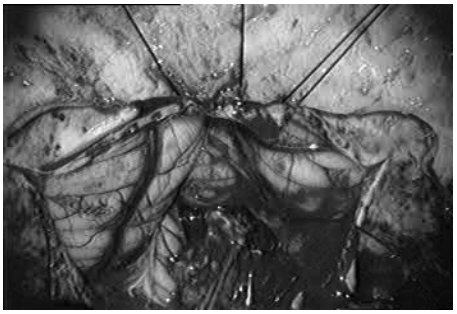


19 year old woman with intermittent hearing loss, progressive headache, and visual complaints.





19 year old woman with intermittent hearing loss, progressive headache, and visual complaints



19 year old woman with intermittent hearing loss, progressive headache, and visual complaints

- **Summary –**
  - Patient has returned to college and has no residual symptoms.
  - One year postop MRI reveals no recurrence.

Sample Exam Question

All of the structures except which of the following can be found passing through the foramen magnum.

A. Vertebral arteries
B. Spinal root of the accessory nerve
C. Spinal cord
D. Descending vagal nerve efferents.

While the knowledge necessary to answer the above is important, it is the clinical pattern recognition associated with pathology at the foramen magnum that derives from this neuroanatomy "data base", that is the ultimate goal of such knowledge.

SMALL GROUP III
BRAIN STEM AND SPINAL CORD

Date: August 19, 2011 - 8:30 AM
Reading Assignment:
refer to posted handout in LUMEN -
http://www.meddean.luc.edu/lumen/restricted/calendar_restricted/Neuro1112/SGs/SG3Readings.pdf

- Cranial Nerves, Brain Stem Reflexes, and Brain Stem Disorders (Dr. Merchut)
- Spinal Cord Disorders (Dr. Merchut)

Learning Objectives:

CRANIAL NERVES:

1. Describe the typical clinical deficits found with lesions of the oculomotor, trochlear, and abducens nerves (CN III, IV and VI).

2. Define the concepts and significance of "diplopia," "nystagmus," and "internuclear ophthalmoplegia (MLF syndrome)."

3. Explain the normal reactions of the pupil (light reflex, near reflex) and why it acts abnormally in the relative afferent pupillary defect (RAPD).

4. Explain the clinical signs of Horner's syndrome and how it can be caused by neck trauma, an apical lung tumor, or a lateral medullary infarction.

5. Explain the syndrome of trigeminal neuralgia and how it may be treated.

6. Contrast the clinical features of an upper motor neuron versus lower motor neuron cause of facial paralysis.

7. List other signs and symptoms which may accompany facial paralysis in lesions of the facial nerve or its nucleus.

8. Recognize that lesions of vagal nerve branches may cause ipsilateral sagging of the palatal arch or vocal cord paralysis.

9. Contrast the clinical features of an upper motor neuron versus lower motor neuron cause of unilateral tongue weakness.

10. Recognize that a crossed brain stem syndrome consists of cranial nerve involvement on one side and a clinical sensory or motor deficit on the opposite side of the body.

11. List the signs and symptoms of the medial midbrain (Weber) syndrome and the lateral medullary (Wallenberg) syndrome.

SPINAL CORD DISORDERS

List the clinical signs found with upper motor neuron (UMN) lesions versus lower motor neuron (LMN) lesions, and then use these findings to localize lesions to cervical, thoracic, or lumbar levels of the spinal cord.

2. Recognize that any expected UMN signs from acute, severe spinal cord trauma may be temporarily absent due to spinal or neurogenic shock, where only LMN signs are present.

3. For a radiculopathy, be able to predict which root level is involved based on the dermatomal distribution of radicular pain and pattern of muscle weakness and reflex loss.

4. Recognize that an extramedullary spinal cord lesion is usually associated with radicular pain and sensory impairment of pain and temperature up to the level of the lesion without sacral sparing.

5. Recognize that an intramedullary spinal cord lesion is usually associated with diffuse or no pain, with a suspended impairment of pain and temperature sensation with sacral sparing.

6. List the signs and symptoms of the following spinal cord syndromes, based on the involvement or sparing of spinal roots, lower motor neurons, upper motor neurons, posterior (dorsal) column pathways, or the spinothalamic tract:
   ---spinal cord transection or transverse myelopathy (myelitis)
   ---spinal cord hemisection (Brown-Sequard syndrome)
   ---syringomyelia or syrinx
   ---anterior spinal artery syndrome
   ---posterolateral syndrome or subacute combined degeneration
   ---amyotrophic lateral sclerosis
   ---tabes dorsalis

7. List the common causes of the following spinal cord syndromes:
   ---spinal cord transection or transverse myelopathy (myelitis) from trauma, extramedullary tumors, spinal stenosis, viral infections, multiple sclerosis
   ---spinal cord hemisection (Brown-Sequard syndrome) from trauma, extramedullary tumors, degenerative spine disease including herniated intervertebral discs
   ---syringomyelia or syrinx from prior trauma, intramedullary tumors
   ---anterior spinal artery syndrome from aortic atherosclerosis or aortic surgery

---posterolateral syndrome or subacute combined degeneration from vitamin B12 deficiency
---amyotrophic lateral sclerosis (motor neuron disease of unknown cause)
---tabes dorsalis from syphilis

Case 1

A 79-year old woman with uncontrolled hypertension is taken to the ER one summer afternoon because of the acute onset of nausea, vomiting, dizziness and blurred vision. She has a history of diabetes mellitus and depression.

While being examined in the ER, a physician notices that her left face becomes droopy, and her speech slurred. When you arrive to see her, she is alert, oriented and cooperative. She complains of double vision only when looking toward her left. You note incomplete abduction of her left eye, but other eye movements are full, and the pupils are equal and reactive to light. Her visual fields and optic discs appear normal. The upper and lower parts of the left face are weak. Other cranial nerves appear intact. (The left upper limb and distal right lower limb are weak, but these are the chronic residuals of previous trauma, according to the patient.) Reflexes in the right upper and lower limbs are increased (2-3+) compared to the left side (1-2+). There is no Babinski sign. The sensory examination is unremarkable.

1. Where is the lesion causing her diplopia?

2. Where is the lesion causing her left facial weakness?

3. What region of the brain or brainstem could include the lesions of (A) and (B) above, plus harbor another nearby lesion causing the right hyper-reflexia?

SHOW THE SCHEMATIC CROSS-SECTION OF THE PONS HERE

4. What is the likeliest pathology occurring at this region?

5. What diagnostic testing should be done?

6 . What do think happened to the patient?

Case 2

A 77-year-old woman notices hot and cold sensations in her lower limbs, especially on the left, over the past three months. On occasion she has some left inguinal pain, but no back or limb pain. At times her right knee would "give out" and she would stagger when walking. These symptoms have been gradually getting worse. She has a history of myocardial infarction, with permanent pacemaker for arrhythmia.

On examination, she is alert and oriented, with normal visual fields and cranial nerves. There is mild (4/5) weakness of right hip flexion (iliopsoas) and knee flexion (hamstrings) but the other muscles are strong. Upper limb reflexes are equal and 2+, but the knee reflexes are 3+ on the right, 1+ on the left. Both ankle reflexes are absent. There is a right Babinski sign. Pinprick (pain) and temperature sensation are decreased on the left side from the top of the scapula (posteriorly) and just below the nipple (anteriorly) on down. There is no sacral sparing. Proprioception seems to be decreased at the right toes.

1. Where could a lesion in the central nervous system cause the weakness in her right lower limb with its associated signs?

2. Where could a lesion cause her sensory deficit to pinprick (pain) and temperature?

3. Where could a lesion cause her deficit to proprioception?

4. Could any single region of the central nervous system contain all of the lesions discussed in (1), (2) and (3)?

5. What is the likeliest pathology occurring here?

6. What diagnostic testing is indicated here? (Note that she has a pacemaker.)

7 . What do you think happened to the patient?

Case 3

A 63-year old man is employed as an equipment transporter and truck driver at a local school. Along with a coworker, he rolls up a large gym mat, carrying it over his shoulder down a stairway. Suddenly, he feels a sharp, painful sensation of heat from his neck to the interscapular area accompanied by shoulder achiness. Although the pain spontaneously disappears, he still feels some "pushing down pressure" at times in the neck and shoulders. Although his strength remains intact, ever since this incident he does not readily feel lacerations or the temperature of the shower water over his arms. His past history includes hypertension, elevated cholesterol, heart disease requiring coronary bypass surgery, and peripheral vascular disease requiring stenting of the aorta and right lower limb. He has a 90-pack year smoking history.

On examination, cotton, pinprick and temperature sensation were absent or reduced over both upper limbs, over the torso anteriorly, from the jaw line to just between the nipples and umbilicus, and over the torso posteriorly, from the occiput to just below the inferior angle of both scapulae. Sensation over the top of the scalp, face and lower body was normal. Vibration and proprioception were normal throughout. Triceps, knee and ankle reflexes were 2+ and equal, but reflexes were 0 to 1+ at the biceps and brachioradialis. Strength, gait, cerebellar testing, visual fields and cranial nerves were all normal.

1. Where could a lesion cause his sensory deficit to pinprick (pain) and temperature?

2. Is sacral sparing present? If so, why?

3. Why is sensation to vibration and proprioception unaffected?

4. Why are the biceps and brachioradialis reflexes absent or reduced, yet there is no clinical weakness present?

5. What is the likeliest pathology here?

6. What diagnostic testing would be most helpful to confirm your clinical diagnosis?

Case 4

A 52-year-old man reports three weeks of lower back pain, unrelated to any specific activity or incident. This pain radiates into his right buttock and posterior thigh and calf. He has no past medical history, and participates routinely in sports.

On examination, you note a few fasciculations in his right calf and dorsal foot. There is mild (4/5) weakness of right foot dorsiflexion and toe extension, with other muscles strong. Knee and ankle reflexes are equal at 2+ and there is no Babinski sign. Sensation to pinprick is decreased over the right dorsal foot. With the patient lying supine, his pain is reproduced when you grab his ankle and passively lift his right leg off the examination table.

A) Why does passive hip flexion of his extended right lower limb reproduce his pain?

B) What possible lesions could cause his weakness and sensory impairment?

C) What do you think happened to this patient?

Study Questions

1. What is the PPRF and its relation to conjugate deviation of the eyes?

2. Is the facial paralysis in the patient in Case 1 an upper or lower motor neuron problem?

3. What does a positive Babinski sign often represent?

4. What constitutes a motor unit?

5. Which pathway relays pain and temperature sensation from the body? ...from the head?

6. How does a dermatomal sensory loss pattern typically differ from a peripheral nerve cutaneous sensory loss?

7. What do hyperactive versus hypoactive tendon reflexes indicate?

8. What are the distinguishing anatomical features between thoracic and low cervical spinal cord levels?

9. Which cranial nerve(s) relays cutaneous sensation from the face? What about the back of the head?

10. Which dermatome corresponds to the level of the nipples?…the umbilicus?

11. How does a lesion in the area of the central canal affect spinothalamic projections?

12. What are muscle fasciculations? …muscle fibrillations?

13. What are gamma motor neurons and their relationship to the muscle stretch reflex?

14. What are the alar and basal plates in the developing nervous system?

Cranial Nerves, Brain Stem Reflexes, and Brain Stem Disorders (Dr. Merchut)

Cranial Nerves and Brain Stem Reflexes

1. Olfactory Nerve (CN I)

Olfaction is usually not tested during a neurological examination unless the patient has mentioned a problem with the sense of smell. Testing is done by bringing an aromatic substance, such as an alcohol pad or packet of coffee grounds, to one nostril at a time, with the patient identifying the odor with eyes closed. Impaired smell most commonly occurs from the mucosal swelling and inflammation during sinusitis or an **upper respiratory infection**. A permanent loss of smell may occur after severe **head trauma**, where the olfactory nerve branches are sheared or torn where they pass through the bony cribriform plate. Another persistent loss of smell may be caused by a **tumor near the olfactory lobe** at the skull base, such as a meningioma.

2. Optic Nerve (CN II)

(CN II will be discussed in the section Visual, Auditory, and Vestibular Systems.)

3. Oculomotor (CN III), Trochlear (CN IV), and Abducens (CN VI) Nerves

Cranial nerves III, IV and VI innervate the extraocular muscles, which are tested by the patient tracking or following a target (examiner's finger or pen) up and down and side to side. Diagonal tracking may also be tested: looking up and rightward, looking down and rightward, looking up and leftward, and looking down and leftward. Observe and note the directions in which eye movements are limited or impaired---it may be difficult at first to localize the problem specifically to one of these cranial nerves, since some extraocular muscles have multiple actions because of their diagonally oriented insertion on the eyeball.

In this discussion of eye movements, the initial position of the eyeball is in primary gaze or "looking straight ahead." Since the superior and inferior oblique muscles insert more posteriorly on the eyeball, their contraction also abducts the eyeball: the superior oblique depresses and abducts the eye, while the inferior oblique elevates and abducts the eye (see Fig.1). Since the superior and inferior recti insert more anteriorly on the eyeball, their contraction also adducts the eyeball: the superior rectus elevates and adducts the eye, while the inferior rectus depresses and adducts the eye. (Here is the final part of the "picture," although at the risk of greater confusion: Muscles inserted on the top of the eyeball (superior rectus and superior oblique) will also rotate the eye medially or inward (intorsion), while muscles inserted on the bottom of the eyeball (inferior rectus and inferior oblique) will also rotate the eye laterally or outward (extorsion).) In contrast, two muscles have simple lateral actions on the eyeball: abduction by the lateral rectus and adduction by the medial rectus.

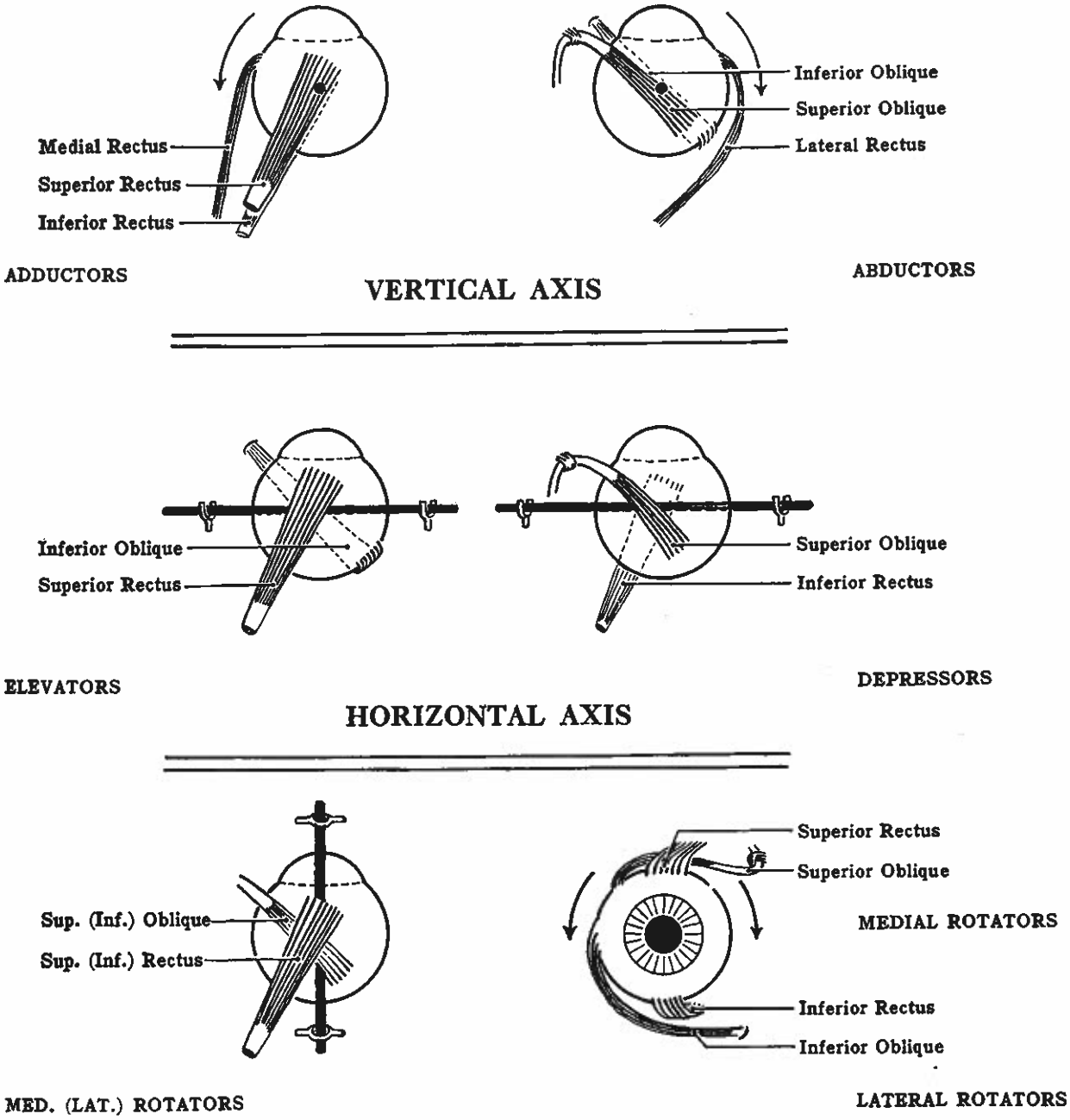


Fig. 1 Actions of the six extraocular muscles.
The right eyeball is shown above (from Grant's Atlas of Anatomy, 6th ed., 1972).

Given the complex movements of the extraocular muscles that elevate or depress the eyeball, how can you best determine which muscle is malfunctioning? If elevation of the eye appears incomplete, the superior rectus or inferior oblique (or both) may be weak. When the patient turns this eye inward (adduction), weakness of elevation from this

starting position is mainly due to the inferior oblique, since the adducted eyeball is aligned parallel to this muscle. When the patient turns this eye outward (abduction), weakness of elevation from this starting position is mainly due to the superior rectus. On the other hand, if depression of the eye appears incomplete, the superior oblique or inferior rectus (or both) may be weak. Thus, when the patient turns this eye outward (abduction), weakness of depression from this starting position is mainly due to the inferior rectus. When the patient turns this eye inward (adduction), weakness of depression from this starting position is mainly due to the superior oblique. Examining in this manner is referred to as testing the "cardinal directions of gaze," where eye depression or elevation is isolated to a single extraocular muscle, since the eye begins moving from a starting position of abduction or adduction, not from primary "straight ahead" gaze.

Starting position	Action tested by examiner	Corresponding single muscle tested
Out (abducted)	Eye elevation	Superior rectus
Out (abducted)	Eye depression	Inferior rectus
In (adducted)	Eye elevation	Inferior oblique
In (adducted)	Eye depression	Superior oblique
Out	Eye abduction	Lateral rectus
In	Eye adduction	Medial rectus

Table 1. Cardinal Directions of Gaze: positions in which only a single extraocular muscle is tested in isolation.

Clinically, the deficit from a complete **oculomotor nerve (CN III) lesion** is usually striking (see Fig. 2). Paralysis of the levator palpebrae superioris muscle may cause such complete **ptosis** that the ipsilateral drooping eyelid entirely covers the eye. If the eyelid is passively pulled up, the involved eye tends to be somewhat abducted or outwardly deviated because of the unopposed action of the lateral rectus muscle. Indeed, the patient is **only able to abduct the eye** since the abducens nerve is spared. The **pupil of the involved eye is large and unreactive to light,** directly or consensually, since the parasympathetic innervation of the pupil is impaired. The trochlear (CN IV) nerve is the only cranial nerve which exits the brain stem dorsally, and decussates to innervate the contralateral superior oblique muscle. A trochlear nerve (CN IV) lesion produces a subtle deficit that is difficult to detect clinically. Impairment of downward gaze (depression of the eyeball) is best noted when the involved eye is in the adducted position. An **abducens nerve (CN VI) lesion** affects only the ipsilateral lateral rectus muscle, impairing abduction of the affected eyeball.

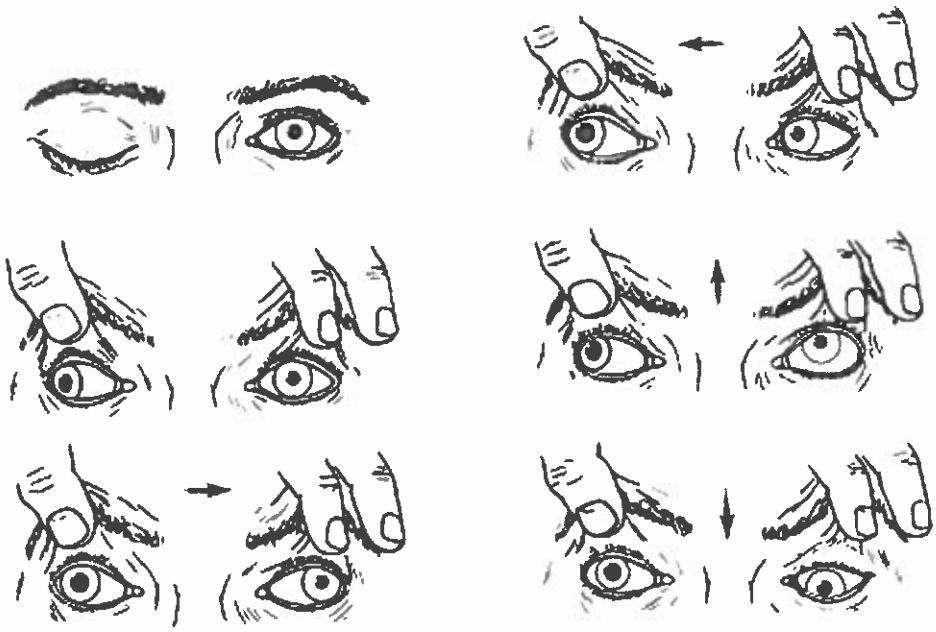


Fig. 2 Complete lesion of right CN III. The patient is asked to look in the directions of the arrows (from Rodnitzky RL. Van Allen's pictorial manual of neurologic tests. 3rd ed. Chicago:Year Book Medical, 1988)

4. Eye movement disorders

Normal binocular vision depends on analogous or equivalent areas of the retina of each eye perceiving the same visual stimulus. If the eyeballs are not perfectly aligned in primary position ("looking straight ahead") or when conjugately moving to other positions, a visual image may appear blurred or doubled (binocular diplopia). **Binocular diplopia** is the more common type of diplopia and **resolves if the patient covers either eye**. It can be caused by lesions of cranial nerves III, IV or VI, or their related extraocular muscles (or neuromuscular junctions therein). In the case of a severe or complete oculomotor nerve lesion, however, diplopia would be eliminated by the ptosis covering the involved eye. There are also connecting pathways within the brain stem which coordinate the actions of these extraocular muscles, plus connections with the vestibular and cerebellar systems allowing for smooth, reflexive eye movements as well. Thus, lesions involving these brain stem or cerebellar connections could also cause diplopia. **Monocular diplopia** is relatively rare and **occurs when looking with one eye alone**. It may occur from a problem in the "optical system" of an eye, such as a dislocated lens or detached retina, or may be related to a psychiatric disorder, but not from neurological disease, strictly speaking.

Patients complaining of diplopia may also be noted to have **nystagmus**, which refers to repetitive, oscillatory, jerky eye movements. Nystagmus can be physiological or normally induced, as when suddenly stopping someone rotating in a swivel chair.

Pathological or abnormal nystagmus occurs with lesions of the vestibular system, brain stem, or cerebellum which upset the normal control or balance of conjugate eye movements. Such lesions typically produce asymmetrical nystagmus, more prominent with certain eye movements or positions, while nystagmus caused by drug toxicity usually is symmetrical and present with virtually all eye movements or positions. For example, a vestibular lesion produces horizontal nystagmus, with a slow component or eyeball jerk toward the side of the lesion, and a fast component in the other direction.

Internuclear ophthalmoplegia (INO) refers to the paralysis of extraocular muscles ("ophthalmoplegia") from a lesion between the nuclei ("internuclear") involved with lateral gaze (oculomotor and abducens nuclei). Such a lesion interrupts the **ascending medial longitudinal fasciculus (MLF),** and therefore this disorder is also called the **MLF syndrome.** To have coordinated horizontal gaze rightward, for example, the right paramedian pontine reticular formation (PPRF) must activate both the right abducens nucleus in the pons and the left oculomotor nucleus in the midbrain, so that the right lateral rectus and left medial rectus muscles move the eyes to the right. The ascending MLF leaves the right PPRF, decussates early and rises to join the left oculomotor nucleus. A lesion along the main left-sided course of the MLF here, en route from pons to midbrain, produces paralysis of adduction of the left eye, with nystagmus of the abducting right eye (see Fig. 3). Since the left oculomotor nucleus never gets the "MLF signal," the left eye cannot adduct and right lateral gaze is impaired. However, the left medial rectus still functions, since both eyes adduct or converge when looking closely at an object (the near reflex, described below). **The most common causes of MLF lesions are multiple sclerosis in younger patients and ischemic infarction in older patients**.

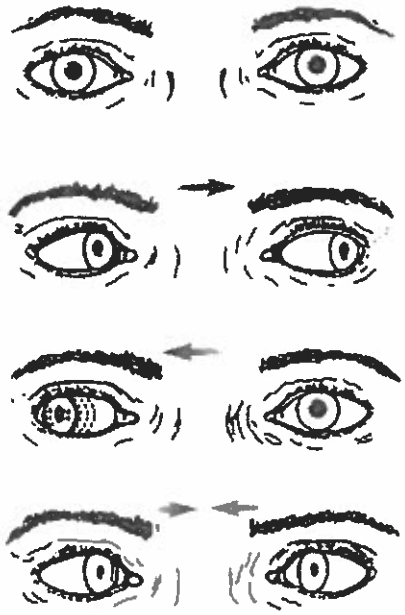


Fig. 3 Left MLF syndrome with attempted gaze in the direction of the arrows (from Rodnitzky RL. Van Allen's pictorial manual of neurologic tests. 3rd ed. Chicago:Year Book Medical, 1988)

5. Disorders of the pupil

Abnormalities of the pupil are discussed here since they are often encountered with lesions of the cranial nerves or pathways associated with eye movements. The normal **pupillary light reflex** is elicited by shining light into one eye, causing not only its pupil to constrict (direct response) but also that of the other eye (consensual response). This reflex pathway involves retinal ganglion cells projecting bilaterally to the pretectal area (rostral to the superior colliculus), which then projects to the Edinger-Westphal nucleus of CN III. For example, a left optic nerve lesion impairs the afferent part of this consensual reflex, so neither pupil constricts when light is shined into the left eye, yet both pupils constrict when light is shined into the right eye. A right CN III lesion interrupts the efferent part of this consensual reflex, so the enlarged right pupil never constricts when light is shined in either eye, yet the left pupil constricts with light shined in either eye.

A **relative afferent pupillary defect (RAPD)** may occur from a partial optic nerve or retinal lesion. Both pupils may initially constrict to light, but after moving the light source from the normal to the abnormal eye ("swinging flashlight test"), pupillary dilatation occurs because of relatively reduced afferent input at the affected eye. If one were to observe both eyes simultaneously, the light stimulus produces direct and consensual pupillary constriction, but to a lesser degree when the affected eye is stimulated.

The **near reflex** occurs when viewing a nearby object and normally consists of pupillary constriction, lens accommodation ("thickening"), and convergence of the eyes. In certain disorders, there is selective disruption of the pupillary light reflex pathway at the superior colliculus or pretectal area, but connections for the near reflex are preserved. This creates **dissociation of light and near reflexes (light-near dissociation)** such that the pupils only constrict during the near reflex, but not to a light stimulus. Classic causes of light-near dissociation include the dorsal midbrain syndrome and the Argyll Robertson pupils in neurosyphilis. The dorsal midbrain (Parinaud's) syndrome classically refers to a pineal tumor compressing the dorsal midbrain but may also occur from an ischemic infarction there. As the midbrain centers for vertical gaze may be also involved in this syndrome, impairment of upward gaze may accompany light-near dissociation of the pupils.

Horner's syndrome occurs from a lesion disrupting the oculosympathetic pathway, causing **miosis** (a smaller, constricted pupil which dilates poorly in darkness), **anhidrosis** (decreased sweating in the ipsilateral face since sweat glands have sympathetic innervation), and mild **ptosis** (paralysis of the superior tarsal muscle). The oculosympathetic pathway is relatively long and consists of three neurons in series. First-order neurons descending down the brain stem may be involved by a lateral medullary infarction (Wallenberg syndrome). Second-order neurons originating from the intermediolateral cell column in the spinal cord at C8 to T2 levels may be affected by a tumor as they course through the apex of the lung. Third-order neurons arising from the superior cervical sympathetic ganglion ascend up the internal carotid artery where they may be affected by neck trauma. It should be noted that the ptosis in Horner's syndrome is subtle and mild in comparison to the more obvious ptosis from an oculomotor (CN III) nerve lesion.

6. Trigeminal Nerve (CN V)

The trigeminal nerve has sensory and motor functions. Sensation over the face and anterior scalp is conveyed to the brain stem by three divisions or branches: **V-1 (ophthalmic), V-2 (maxillary), and V-3 (mandibular).** These branches may be compressed by tumors particularly where they pass through bony foramina in the skull base, or may be affected by infection or inflammation there. A V-1 sensory deficit over the forehead (see Fig. 4) should also involve the anterior scalp, while a V-3 sensory deficit should not involve the corner of the jaw or the neck. Thus, sensory deficits not confined to the trigeminal nerve territory may be due to lesions in the contralateral thalamus or parietal lobe, or may be associated with psychiatric disorders. Trigeminal branch sensory deficits may accompany other cranial nerve lesions. A V-1 territory sensory impairment plus ipsilateral involvement of cranial nerves III, IV and VI may occur from a lesion at the superior orbital fissure or nearby cavernous sinus.

Trigeminal neuralgia is a painful syndrome of irritation or inflammation of one of the trigeminal nerve sensory branches which "short circuits" or "misfires." Patients experience episodic, lightning-like jabs or "electrical shocks" of pain usually in the territory of V-2 or V-3, several times daily, provoked by talking, chewing or touching the face. No sensory or other cranial nerve deficits are found on neurological examination however. A multiple sclerosis lesion at the trigeminal nerve entry region into the pons is often the cause in younger patients. In older patients, a trigeminal nerve branch is often compressed by a tortuous or kinked blood vessel (often the superior cerebellar artery), which can be surgically repositioned or padded. Other treatments include oral anticonvulsants such as carbamazepine, gabapentin or others to relieve the nerve "misfiring" or procedures to destroy the nerve branch involved.

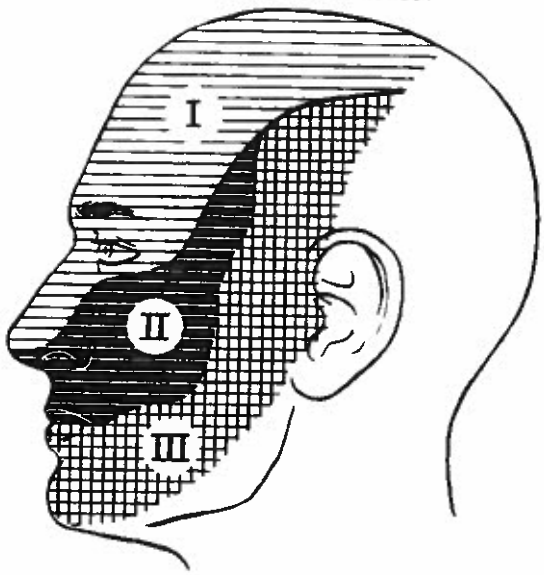


Fig. 4 Trigeminal nerve sensory territories: V-1 (V-I) Ophthalmic, V-2 (V-II) Maxillary, and V-3 (V-III) Mandibular (from Rodnitzky RL. Van Allen's pictorial manual of neurologic tests. 3rd ed. Chicago:Year Book Medical, 1988)

The trigeminal nerve also innervates the muscles of chewing or mastication---the masseter and temporalis muscles. A lower motor neuron lesion of the trigeminal motor nerve is rare and produces atrophy and weakness in these ipsilateral muscles, with the jaw deviating toward the side of the lesion. Both ipsilateral and contralateral upper motor neurons in the motor cortex control the trigeminal motor nerve on one side, so an upper motor neuron lesion on one side does not produce any jaw deviation or severe weakness. Bilateral upper motor neuron lesions here, however, may cause **hyper-reflexia of the jaw jerk**, since it is a muscle stretch reflex (tested by gently tapping on the chin with the mouth slightly opened and relaxed).

7. Facial Nerve (CN VII)

Each facial nerve, originating from its facial nucleus in the pons, innervates the ipsilateral facial muscles, from uppermost frontalis to lowermost platysma. **A lower motor neuron facial paralysis involves the nucleus or nerve of CN VII and causes a relatively severe paralysis of the entire ipsilateral half of the face.** This would be the isolated finding with a lesion at or near the stylomastoid foramen (see lesion 1 in Fig. 5). Other signs and symptoms accompany facial nerve lesions within the temporal bone. Ipsilateral facial paralysis plus **impaired taste over the anterior 2/3 of the tongue indicates that the chorda tympani branch of the facial nerve is also involved** (lesion 2A in Fig. 5), while a slightly more proximal lesion (lesion 2B in Fig. 5) also involves the facial nerve branch to the stapedius muscle. The stapedius muscle acts to dampen middle ear ossicle movements in the presence of loud sounds, so an unpleasant sensitivity to sound (**hyperacusis**) is a symptom of stapedius muscle denervation. A lesion at the internal auditory meatus or **cerebellopontine angle** would create all the deficits as in lesion 2B plus hearing impairment and tinnitus, an unpleasant, persistent ringing or buzzing sound or pitch, from involvement of the adjacent CN VIII. This lesion (lesion 3 in Fig. 5) is often from an acoustic neuroma, a tumor arising from CN VIII. A lesion at or near the facial nucleus in the pons (lesion 4 in Fig. 5), such as a small ischemic infarction, would most likely also create ipsilateral weakness of lateral gaze, from involvement of the adjacent PPRF and CN VI.

In addition to tumors or trauma causing lesions of CN VII in its course outside the pons, a very common syndrome is **Bell's palsy** or idiopathic facial nerve paralysis. The patient may awaken to suddenly notice severe paralysis of one side of the face, sometimes with ipsilateral hyperacusis and impaired taste. A short course of oral corticosteroid medication hastens recovery from the presumed facial nerve inflammation where it travels through the temporal (petrous) bone. Herpes simplex or other viruses may cause this inflammation, so anti-viral medication may also be part of the treatment. In general, most patients with Bell's palsy recover fully after a few weeks.

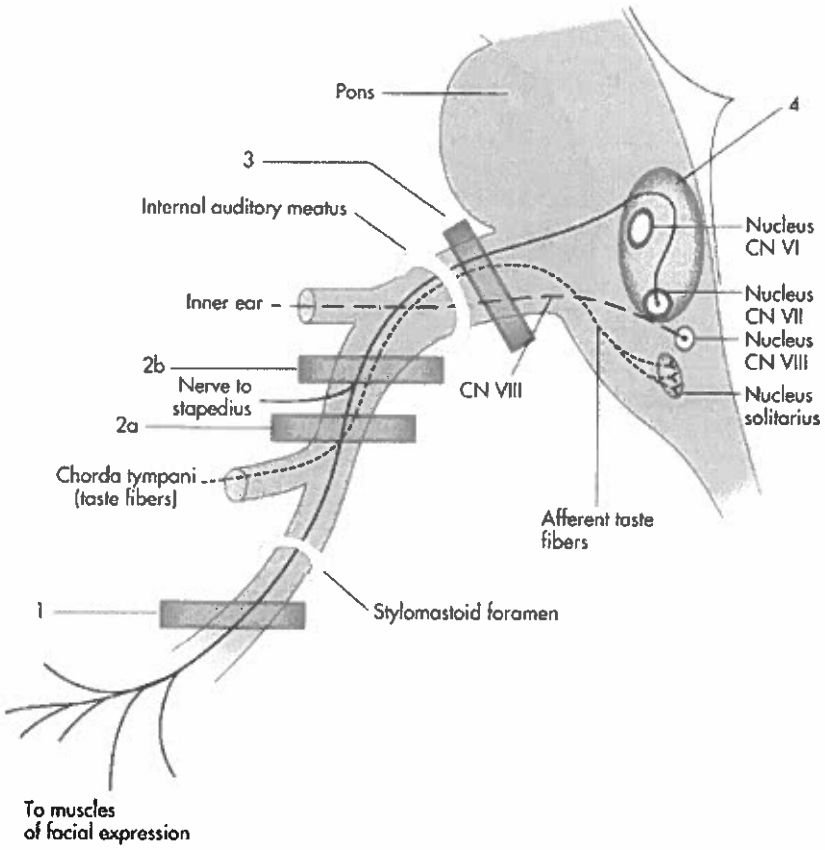


Fig. 5 Nuclear and infranuclear lesions of the facial nerve.

Facial paralysis may also occur with lesions of the upper motor neurons that control the facial (CN VII) nucleus. The part of the CN VII nucleus which innervates the upper face or forehead is controlled by upper motor neurons (corticobulbar tract fibers) originating both ipsilaterally and contralaterally, while the rest of the CN VII nucleus is controlled only by contralateral upper motor neurons (see Fig. 6). Thus, **facial paralysis from an upper motor neuron lesion causes a relatively milder paralysis of only the lower part of the contralateral face, sparing the forehead.**

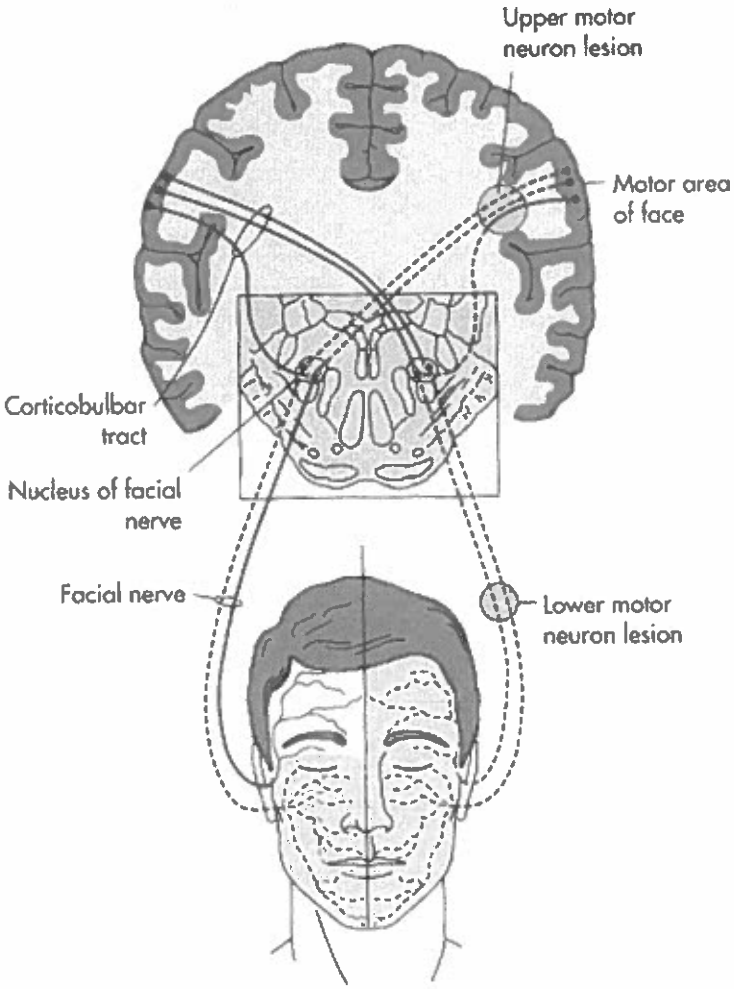


Fig. 6 Upper versus lower motor neuron facial paralysis. The shaded areas of the face show the distribution of the facial muscles paralyzed after a supranuclear lesion of the corticobulbar tract (upper motor neuron lesion) and after a lesion of the facial nerve or its nucleus (lower motor neuron lesion) (from Gilman S, Winans SS. Manter and Gatz's essentials of clinical neuroanatomy and neurophysiology. 6th ed. Philadelphia: FA Davis, 1982)

8. Vestibulocochlear Nerve (CN VIII)

(CN VIII will be discussed in the section Visual, Auditory, and Vestibular Systems.)

9. Glossopharyngeal (CN IX) and Vagus (CN X) Nerves

Cranial nerves IX and X have similar or shared functions, but taste, visceral afferent, and visceral efferent functions cannot be tested clinically. Both nerves innervate

pharyngeal and laryngeal muscles, so glossopharyngeal or vagus nerve lesions can cause impairments of speech or swallowing, but it is often difficult to test each nerve separately. A decreased or absent **gag reflex** when touching one side of the pharynx suggests a glossopharyngeal nerve lesion on that side. The gag reflex is difficult to evaluate, however, since some patients virtually never gag, while others are very sensitive to pharyngeal stimulation and hate being tested. Elevation of the palatal arch is readily observed when asking the patient to say "ah" (see Fig. 7) and reflects vagal nerve function. A **lower motor neuron lesion of vagal nerve** branches innervating the palate causes **ipsilateral drooping or sagging of the palatal arch** with the uvula pointing toward the other (normal) side. A **lower motor neuron lesion of vagal nerve** branches innervating the larynx causes **hoarseness** from ipsilateral paralysis of vocal cord muscles.

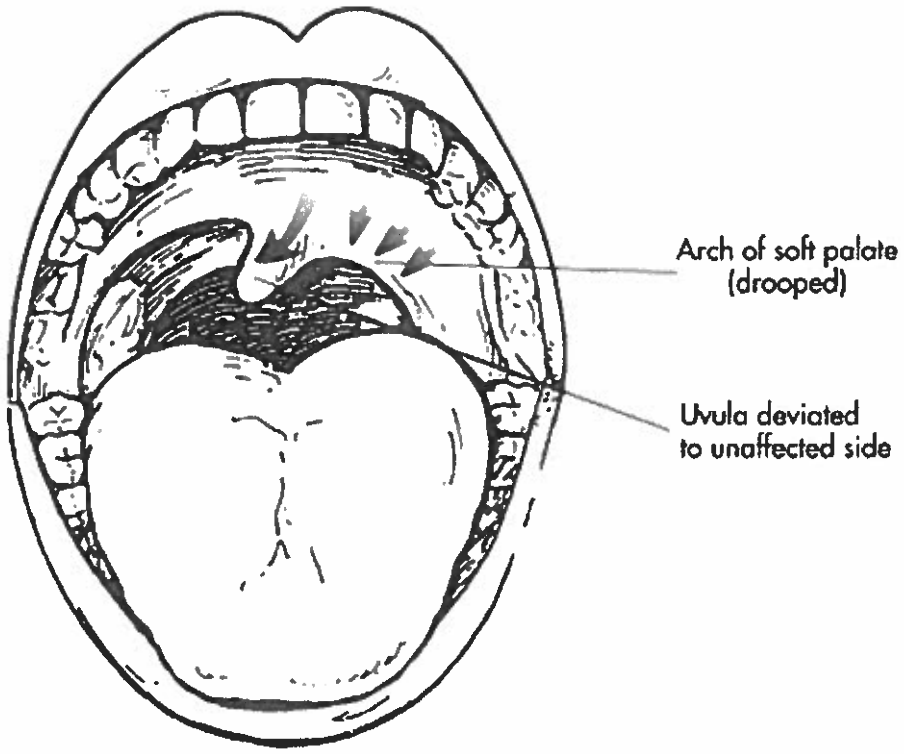


Fig. 7 A lesion of the left vagal nerve branches innervating the soft palate.

10. Spinal Accessory Nerve (CN XI)

A lower motor neuron lesion of CN XI weakens the ipsilateral sternocleidomastoid and trapezius muscles, which it innervates. Decreased elevation or shrugging of the shoulder is observed along with weakness in turning the head to the opposite side.

11. Hypoglossal Nerve (CN XII)

The hypoglossal nerve innervates the muscles of the tongue on each side. Most important for clinical testing is the genioglossus muscle, which protrudes each side of the tongue forward. A **lower motor neuron lesion of CN XII on one side causes the protruded tongue to deviate or turn toward the affected or weak side**, since the contralateral genioglossus muscle normally pushes its half of the tongue forward. Over time, the affected half of the tongue would **atrophy and fasciculations and fibrillations** would be observed there. In a few patients, the upper motor neurons (corticobulbar tract fibers) controlling the CN XII nucleus only arise contralaterally. In that case, an ischemic infarction of the left frontal lobe would impair the right hypoglossal nucleus, weakening protrusion of the right half of the tongue such that the **protruded tongue may deviate or turn toward the side opposite its upper motor neuron lesion**. In most patients, however, ipsilateral and contralateral upper motor neurons control each hypoglossal nucleus, so a frontal lobe lesion on one side would not cause weakness or deviation of the tongue.

Brain Stem Disorders

1. Types of cranial nerve lesions

One or more cranial nerves may be impaired by various kinds of pathology in their anatomical vicinity, such as tumors or fractures of the skull base, or infection or inflammation of the meninges. Polyneuropathies affecting multiple nerves in the limbs and trunk, caused by diabetes or the Guillain-Barre syndrome, may also involve cranial nerves. All these lesions involve one or more cranial nerves outside the brain stem.

Lesions within the brain stem itself often are from ischemic infarction, hemorrhage, tumor or multiple sclerosis. It would be unusual for one of these disorders to just involve a cranial nerve or two inside the brain stem. Most often anatomically adjacent fiber tracts are also involved.

2. Brain stem syndromes

Crossed brain stem syndromes consist of **cranial nerve involvement on one side and** an adjacent fiber tract lesion, creating **a clinical sensory or motor deficit on the opposite side of the body**. These clinical findings help localize the problem to a particular area or level of the brain stem. For example, a right pontine lesion involves the right facial nucleus and the right corticospinal tract, creating a lower motor neuron paralysis of the entire right half of the face plus an upper motor neuron paralysis of the left upper and lower limbs (left hemiparesis). Another example is a lesion in the left lateral medulla which involves the left descending spinal tract of CN V and the left spinothalamic tract, which consists of afferents from the right side of the spinal cord that have already decussated within the cord itself. The unusual clinical features include deficits of pain (pinprick) and temperature over the left face and right limbs and body. Two well-known crossed brain stem syndromes are discussed below.

The **medial midbrain syndrome (Weber syndrome)** may be due to an ischemic infarction from an occluded branch of the posterior cerebral artery. CN III and the nearby cerebral peduncle (corticospinal and corticobulbar tracts) are involved, creating an **ipsilateral oculomotor nerve lesion and upper motor neuron weakness of the contralateral face and limbs**.

The **lateral medullary syndrome (Wallenberg syndrome)** may be due to an ischemic infarction from an occluded vertebral artery or its PICA (posterior inferior cerebellar artery) branch. The features making it a "crossed brain stem syndrome" are **pain (pinprick) and temperature impairment in the ipsilateral face and contralateral limbs and body**, as explained above. Other symptoms may include hoarseness, vertigo, nausea and vomiting, and clumsiness. In addition to the sensory deficits mentioned, other signs may include nystagmus (vestibular nuclei), ipsilateral limb dysmetria (inferior cerebellar peduncle), ipsilateral Horner's syndrome (descending sympathetic tract), and ipsilateral palatal and vocal cord paralysis (nucleus ambiguus). It should be noted that in this syndrome position sense and strength are preserved.

Spinal Cord Disorders (Dr. Merchut)

Clinical signs and symptoms in spinal cord lesions

1. Motor signs and symptoms

Lower motor neuron (LMN) signs (Table 1) are found in a limb if some of its muscles are innervated by anterior horn cells (lower motor neurons) affected at the level of the spinal cord lesion. Although weakness may be readily apparent, it may take several days to weeks for atrophy to evolve. As an example, a bilateral spinal cord lesion at the C5 level would injure the anterior horn cells or ventral motor roots there, producing LMN signs in the biceps brachii and deltoid muscles, but not in muscles innervated by other anterior horn cells at other levels. Commonly tested limb muscles related to different levels of the spinal cord are listed in Table 2. It is clinically difficult or impossible to test muscles of the thorax or abdominal wall, so thoracic spinal cord lesions are primarily detected by the upper motor neuron signs produced, as well as other findings.

Upper motor neuron (UMN) signs (see Table 1) are found in a limb if a more rostral spinal cord lesion affects the corticospinal tract (upper motor neurons) descending to the anterior horn cells which innervate the muscles in that limb. As an example, a bilateral spinal cord lesion at C5 disrupts the corticospinal tracts at that level, and creates UMN signs in both lower limbs, as well as in the distal upper limbs, since those affected muscles are not innervated by the C5 anterior horn cells or ventral motor roots. In another case where UMN signs are found only in the right lower limb, the corticospinal tract may be affected by an ispilateral (right sided) spinal cord lesion at a cervical or thoracic level, or from a contralateral (left sided) brainstem or brain lesion. Other signs or symptoms may help determine the lesion more precisely.

Table 1 Clinical Signs of Motor Neuron Lesions

SIGN	UPPER MOTOR NEURON LESION	LOWER MOTOR NEURON LESION
Weakness	More diffuse	More focal
Atrophy	Mild, general	Severe, focal
Atrophy versus weakness	Severe weakness with relatively mild atrophy	Severe atrophy with milder weakness
Fasciculations	Never seen	May be present
Muscle tone	Increased (spasticity)*	Decreased
Muscle stretch reflexes	Increased*	Decreased to absent
Clonus	May be present*	Never present
Pathological reflexes (Babinski sign)	May be present*	Absent

*(except in spinal or neurogenic shock)

Table 2 Motor Innervation of Selected Muscles	
ROOT	MUSCLE
C5,C6	Deltoid, biceps
C7,C8	Triceps
C8,T1	Interossei, flexor digitorum (finger flexors)
L2,3,4	Iliopsoas (hip flexor), quadriceps
L4,5	Tibialis anterior (foot dorsiflexor)
S1,2	Gastrocnemius (foot plantar flexor)

2. Pain symptoms

Radicular (root) pain is often described as lightning, stabbing, shooting or electrical pain in the dermatomal distribution of a dorsal root. Its presence indicates dorsal root inflammation or compression by an extramedullary lesion which arises outside the spinal cord. The extramedullary lesion itself, such as a herniated intervertebral disc or vertebral tumor, may also produce a more constant, dull, local pain. An intramedullary lesion arising inside the spinal cord creates a more diffuse pain or none at all.

3. Sensory signs and symptoms

A spinal cord lesion in the **spinothalamic tract** on one side creates a **pain (pin) and temperature** deficit in the **contralateral** body. The dermatomal level of loss only approximates the level of the lesion, since spinothalamic afferent fibers may ascend a few levels before decussating to the other side of the spinal cord. A **suspended** pattern of deficit with **sacral sparing** indicates an **intramedullary** lesion within the spinal cord itself. In other words, a lesion within or near the center of the spinal cord will disrupt the decussating spinothalamic fibers, and perhaps the medial portions of the spinothalamic tract. Since the sacral fibers of the spinothalamic tract are located most laterally or peripherally, they may be spared, and thus pain and temperature sensation over the sacral dermatomes is preserved (Fig. 1). On the other hand, a sensory deficit for pain and temperature **up to a level** with **sacral involvement** indicates an **extramedullary** lesion, arising from outside the spinal cord, and typically compressing it, as may occur with a tumor. These findings are summarized in Table 3. A spinal cord lesion on one side may produce **position sense and vibration deficits** in the **ipsilateral** body, since the dorsal (posterior) column pathways involved do not decussate in the spinal cord but more rostrally in the medulla.

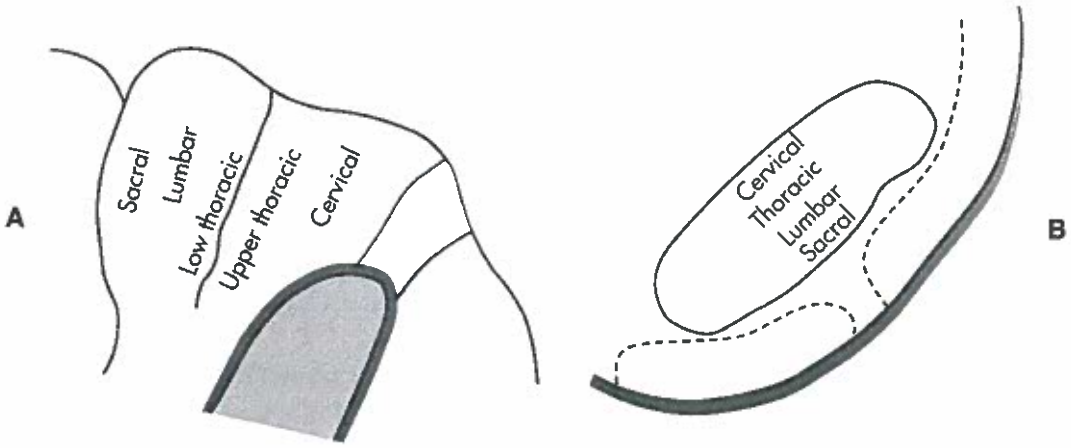


Fig. 1 Topographical localization within the dorsal columns (A) and the spinothalamic tract (B)

Table 3 Intramedullary vs. Extramedullary Lesions		
SYMPTOM	INTRAMEDULLARY	EXTRAMEDULLARY
Pain	Diffuse or none	Radicular
Sensory loss	Suspended	To a level or sacral
Sacral sparing	Present	Absent

Spinal cord syndromes

1. Clinical evaluation of patients

It must be understood that the signs and symptoms in patients often differ from what is expected in a hypothetical spinal cord lesion. For learning purposes, in order to begin to understand more complex concepts, a hypothetical spinal cord lesion at one level is thought of as a perfect "surgical slice" or "razor cut" there, which nearly never occurs in patients. Clinical spinal cord lesions often involve two or more adjacent levels, whether directly from the pathology itself, such as tumor or hemorrhage, or from the indirect effects of edema, ischemia and inflammation. Also, at any affected spinal cord level, some of the neurons, tracts, or roots may be severely affected, some may be partially or mildly affected, and others may be spared. Asymmetry also occurs, with greater involvement of the left or right side of a given spinal cord level. Nevertheless, knowledge of the hypothetical spinal cord lesion is the first step toward interpreting the more confusing array of signs and symptoms encountered in patients.

It should also be noted that when a spinal cord lesion is localized to a certain level, this level refers to the spinal cord itself, and not the surrounding bony vertebral column. As humans develop and grow, the bony vertebral column lengthens, but the spinal cord does not (Fig. 2). For example, a severe fracture and displacement of the T12 vertebral body would approximately affect the L3 level of the spinal cord itself.

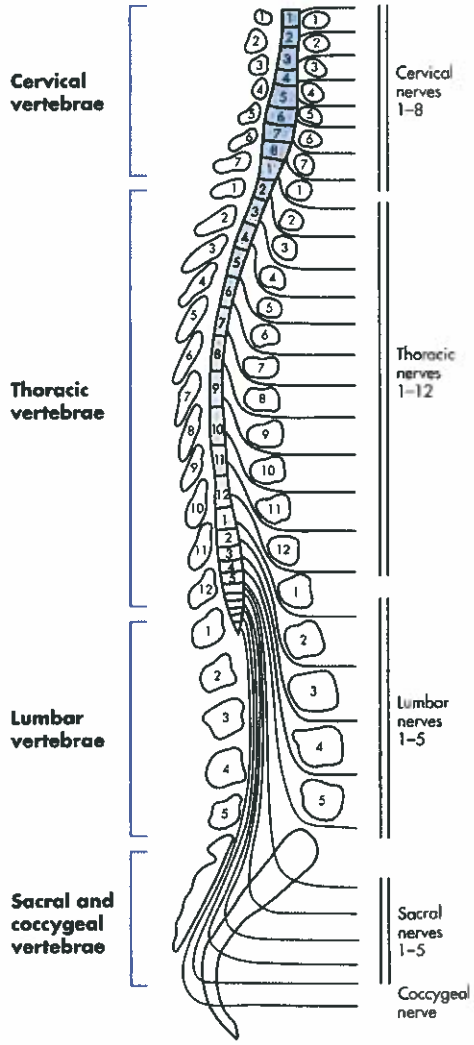


Fig. 2 Relation of spinal cord segments and spinal roots to the vertebral column

2. Spinal cord transection or transverse myelopathy (myelitis)

A **transection or transverse myelopathy** refers to a complete or nearly complete lesion encompassing the cross-sectional extent or breadth of the spinal cord at one, or a few adjacent, levels. It may be described as a transverse myelitis when the lesion is inflammatory or infectious in nature. The spinal cord level involved is suggested by the

dermatomal level of sensory loss and the presence of any lower motor neuron signs. Upper motor neuron signs may be present in limbs innervated by lower motor neurons caudal or inferior to the level of the spinal cord lesion. For example, a C8 transverse myelopathy may produce severely atrophic, weak hand muscles with fasciculations and spastic, hyper-reflexic, weak lower limbs with Babinski signs. Bladder and bowel dysfunction may occur from impairment of the descending motor tracts which control the sacral anterior horn cells that innervate the sphincter muscles.

However, when the transection is due to severe, acute **trauma**, the setting of spinal or neurogenic shock may be initially present. Weakness may be accompanied by decreased muscle tone and muscle stretch reflexes, with the expected upper motor neuron signs only gradually emerging weeks to even months later. Extensive involvement of anterior horn cells at levels C3, C4 and C5 may impair phrenic nerve function and cause respiratory failure.

Other causes of transverse myelopathy are extramedullary lesions such as **tumors** (especially vertebral metastases), **spinal stenosis** (spinal cord compression from degeneration of the bony spinal column and herniated intervertebral discs), extradural hemorrhage or abscess. On occasion, severe spinal cord ischemia (impaired blood circulation) could by itself create a transection at several levels. **Viral infections,** reactions to vaccines, **or autoimmune demyelination** of the spinal cord, such as from **multiple sclerosis**, cause inflammatory lesions of the spinal cord, or **transverse myelitis**.

3. Spinal cord hemisection (Brown-Sequard syndrome)

A lesion affecting approximately the left or right half of the spinal cord cross-section at one level creates a **hemisection or Brown-Sequard syndrome** (Fig. 3). Involvement of the spinothalamic tract produces a **contralateral deficit to pain and temperature sensation**, since spinothalamic sensory fibers decussate within the spinal cord, and then continue their ascending pathway. Involvement of the dorsal or posterior columns produces an **ipsilateral deficit of vibration and position sense**, since these sensory fibers ascend up the same side of the spinal cord, only decussating later in the medulla. Involvement of the anterior horn cells and corticospinal tract on one side would produce **ipsilateral weakness,** with lower motor neuron (LMN) and upper motor neuron (UMN) signs, respectively. As mentioned earlier, LMN signs are difficult to detect clinically in the case of a thoracic level lesion.

Common causes of a hemisection include trauma, extramedullary tumors, and herniated discs with degenerative disease of the bony spine.

4. Syringomyelia or syrinx

Syringomyelia refers to a spinal cord lesion from a **syrinx**, or cavity, within or near the center of the spinal cord. It is thus an **intramedullary** lesion, arising from within the spinal cord itself, and primarily affects the gray matter there. The syrinx usually occurs in the cervical or thoracic spinal cord, and may extend over several segments or levels in a longitudinal or rostral-caudal direction, enlarging slowly over time. Involvement of the central gray matter at cervical or thoracic levels selectively interrupts the decussating spinothalamic fibers there, creating a deficit of pain and

temperature over these dermatomes, but sparing the sacral dermatomes (Fig. 3). This would be described as a **suspended sensory level with sacral sparing,** and the area of sensory impairment would approximate the area covered by wearing a cape or shawl. If the syrinx later slowly expands laterally into the spinothalamic tracts, the outermost sacral fibers would still be spared. Weakness may occur later on, if the anterior horn cells or corticospinal tract are involved by the syrinx expanding into the ventral gray or lateral white matter. The posterior or dorsal columns are generally spared, with **preservation of vibration and position sense**.

Syringomyelia may be a late residual of severe spinal cord injury. A traumatic cervical spinal cord hemorrhage will resorb if the patient survives, leaving a cavity or syrinx in its place. Other causes include intramedullary spinal cord tumors or impaired cerebrospinal fluid flow, typically from a congenital abnormality in the posterior fossa (Chiari malformation). Although rarely encountered, syringomyelia is a "classic" example of an intramedullary spinal cord lesion.

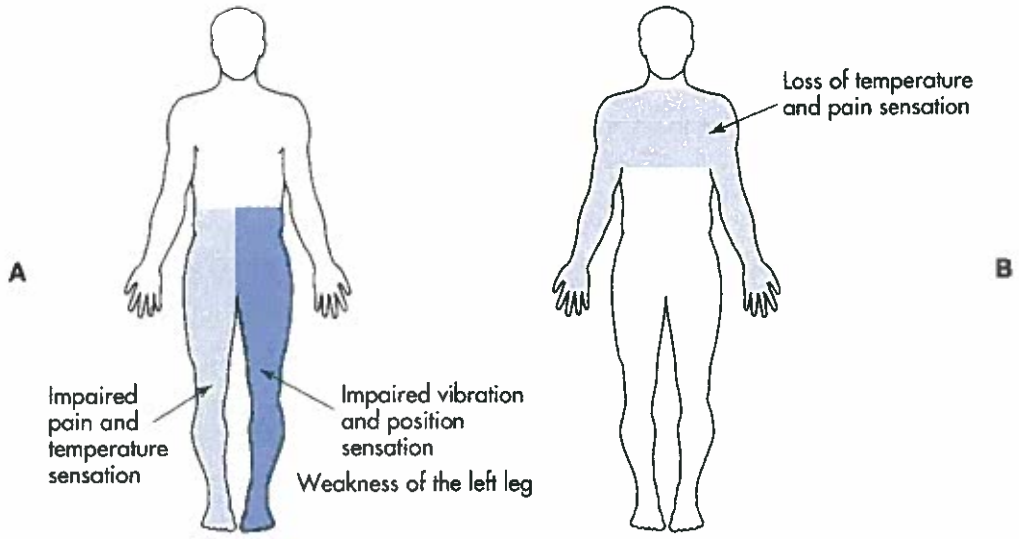


Fig. 3 Sensory deficits from spinal cord hemisection (A) and syringomyelia (B)

5. Anterior spinal artery occlusion

The anterior spinal artery is supplied by several radicular branches of the aorta and has a midline, longitudinal orientation. It supplies the anterior or ventral 2/3 of the spinal cord, where an ischemic lesion, a "spinal cord stroke," would occur if it were blocked or occluded. Occlusion may occur due to atherosclerotic disease of the aorta or as a complication of surgery for an aortic aneurysm. It may also be caused by an aortic dissection in a hypertensive patient, where aortic intima is torn, inciting thrombosis and occlusion of its arterial branches. Although severe spinal cord ischemia may also result in a transverse myelopathy, the anterior spinal artery occlusion is another "classic" syndrome to recognize.

It usually occurs in the lower thoracic or upper lumbar spinal cord, so involvement of the corticospinal tract there leads to **paraplegia** with UMN signs in the lower limbs, and a **thoracic level of sensory loss, without sacral sparing, to pain and temperature**. Since the posterior or dorsal columns are preserved, **vibration and position sense remain normal** (Fig. 4). Back pain or radicular pain are common initial symptoms. As expected of a "stroke," this syndrome occurs suddenly and progresses over hours.

6. Posterolateral syndrome or subacute combined degeneration

This syndrome is "classically" due to **vitamin B12 deficiency** and is thus potentially treatable or reversible if diagnosed early. Vitamin B12 deficiency may also cause a polyneuropathy, optic neuropathy, and dementia, which will be discussed later. In the spinal cord, demyelination and degeneration of the white matter takes place, usually at **thoracic** levels. "Combined degeneration" refers to the combined involvement of the posterior (dorsal) and lateral columns. Another old term for this syndrome is "posterolateral sclerosis." **Vibration and position sense are reduced or lost** in the lower limbs, leading to unsteadiness and falling if the patient stands or walks in the dark, or with eyes closed. This is further exacerbated by a **spastic paraparesis** from involvement of the corticospinal tract. **Pain and temperature sensation are not affected** by this spinal cord syndrome (Fig. 4). The posterolateral syndrome may also be caused by copper deficiency or the human immunodeficiency virus (HIV).

7. Amyotrophic lateral sclerosis (ALS)

ALS is a degenerative disease where upper and lower motor neurons are selectively and progressively destroyed, for unknown reasons. Motor neuron lesions therefore occur diffusely, in the cerebral cortex and brain stem, as well as in the spinal cord. ALS will be discussed again later, but is mentioned here since it initially may appear to be only a spinal cord lesion. If LMN signs developed in the upper limbs, and UMN signs were found in the lower limbs, a cervical myelopathy would be suspected. A cervical spine MRI (magnetic resonance imaging) scan would be appropriately ordered to explore the possibility of cervical spinal cord compression by a herniated disc, tumor, or other extramedullary lesion. In ALS, however, **sensory pathways are not affected**, bowel and bladder functions remain normal, and radicular pain is not present. **Fasciculations** are often prominent in ALS and may soon be found in many muscles, including the limbs, tongue, neck, and trunk. In other instances, weakness may begin focally, as with impaired speech and swallowing, or asymmetrically, as in one shoulder. The diagnosis becomes apparent when **diffuse weakness with UMN and LMN signs progresses** without any better explanation or obvious cause (Fig. 4).

8. Tabes dorsalis

The term "tabes" refers to nervous system involvement by infection with **syphilis**. Syphilis is a sexually transmitted treponemal infection, which was more common decades ago. Syphilis causes several neurological syndromes, and **tabes dorsalis** is worth

knowing as a "classic" example of neurosyphilis affecting the spinal cord. If genital syphilis is treated at its onset, neurosyphilis syndromes like tabes dorsalis would be prevented from developing months to years later. "Dorsalis" refers to lesions of the dorsal roots and dorsal spinal cord. At first, lumbosacral dorsal roots become infected and inflamed, producing severe **radicular pains** in the lower limbs, described as lightning, electrical, or shocklike. The dorsal or posterior columns secondarily degenerate, so **impairment of vibration and position sense** in the lower limbs is noted. Eventually, most sensory fibers degenerate at these dorsal roots, creating **loss of all sensation in the lower limbs, where reflexes are lost** since the afferent reflex arcs are disrupted. Significant injury to the feet may go unnoticed since pain perception there is impaired. **Strength remains intact**, however, since the motor neurons and corticospinal tract are spared (Fig 4).

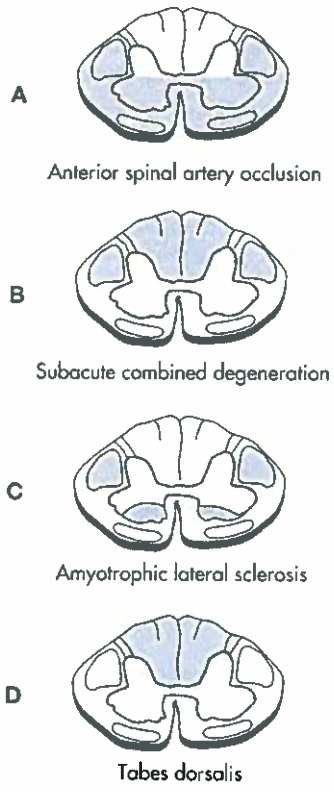


Fig. 4 Spinal cord disorders (lesions are shaded)