BRAINSTEM SYNDROMES OF NEURO-OPHTHALMOLOGICAL INTEREST

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I. **Anatomical Considerations**

The brain stem is about the size of a fat forefinger and consists of three parts: the midbrain, pons and medulla **(Figs. 1-3)**.
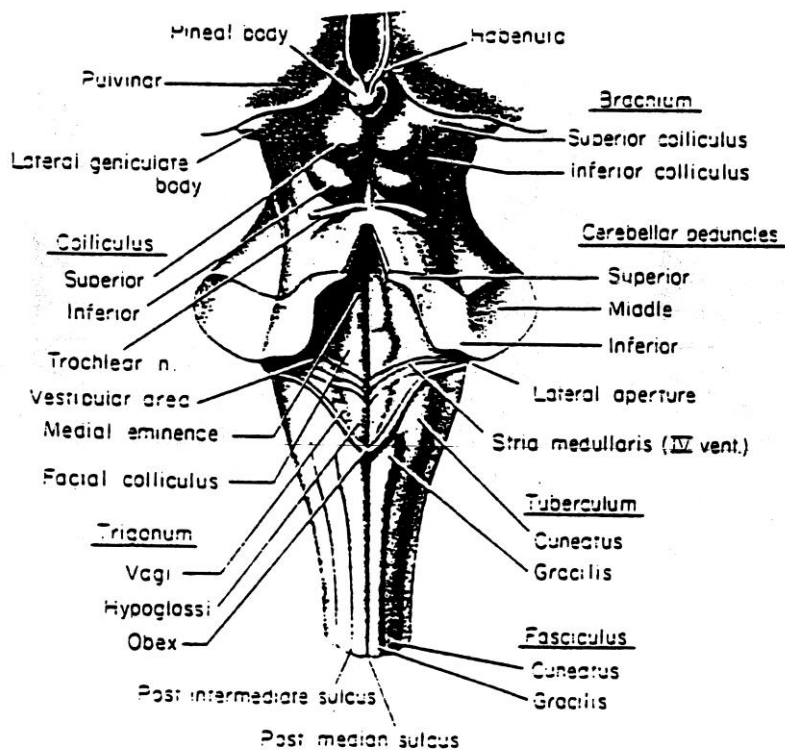

Fig. 1   Drawing of the posterior aspect of the brain stem with the cerebellum removed. (From Carpenter. *Human Neuroanatomy*. 1976; courtesy of The Williams & Wilkins Company.)
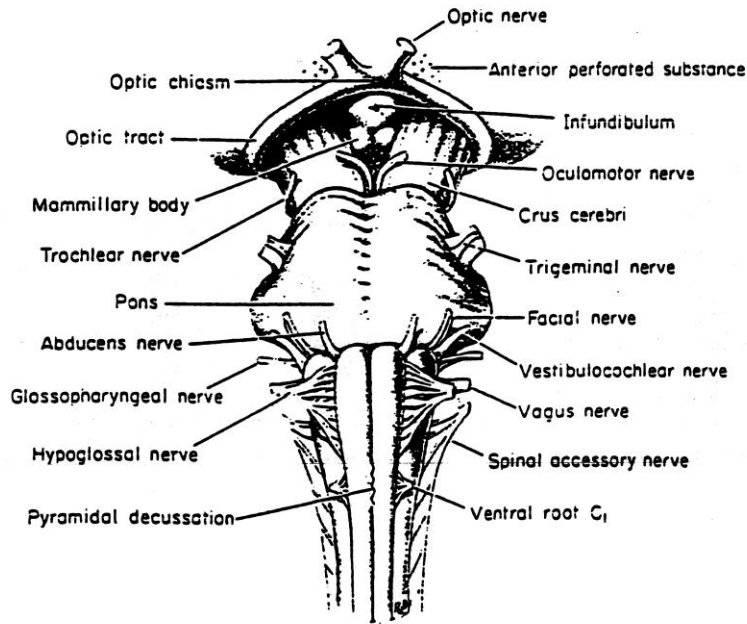
Fig. 2 Drawing of the anterior aspect of the medulla, pons and midbrain. (From Carpenter, *Human Neuroanatomy*, 1976; courtesy of the The Williams & Wilkins Company.)
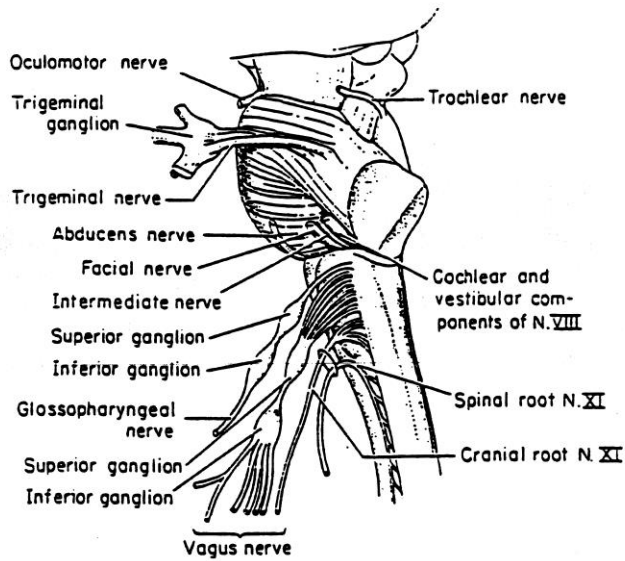
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CORE TEXT OF NEUROANATOMY

Fig. 3 Semidiagrammatic sketch of brain stem and cranial nerves showing the peripheral ganglia. (From Carpenter, *Human Neurocnatomy*, 1976; courtesy of The Williams & Wilkins Company.)

The midbrain surrounds the cerebral aqueduct and joins the posterior portion of the hypothalamus. Dorsal to the aqueduct is the quadrigeminal plate which contains the subcortical stations for hearing (inferior colliculi) and oculo-motor control (superior colliculi). The third nerve nuclei lie close to the midline, just ventral to the aqueduct. In the central portion of the midbrain lie the reticular formation, red nuclei and crossed cerebellar fibers on their way to the thalamus and frontal lobes. More laterally, are sensory pathways for pain and touch. Located posteriorly are some of the key nuclei involved in vertical gaze including the rostral interstitial nucleus of the medial longitudinal fasciculus(riMLF), the nucleus of Cajal (INC) and the nucleus of the posterior commissure (NPC). In the posterior midbrain, pupillary light fibers synapse on the pretectal nuclei before projecting to the third nerve nuclei. Since fibers for the near reflex synapse on the third nerve nucleus more anteriorly, injury to the dorsal midbrain result in pupillary-light dissociation. In this case, the pupils will respond poorly to light, but better to a near target.

The pons contains the nuclei of the sixth cranial nerves which are near the midline and immediately ventral to the fourth ventricle. More laterally are motor nuclei for the fifth and seventh nerves which control muscle activity of the jaw and face respectively. Far laterally and extending from the medulla are the cochlear and vestibular nuclei of the eighth nerve that subserve hearing and vestibular function respectively. The rest of the pons is packed with reticular substance (continuous with that in the midbrain and medulla), descending corticospinal and crossing corticobulbar fibers and connection from the frontal cortex to the cerebellum via the pontine nuclei and the middle cerebellar peduncle. Some of the key nuclei from a neuro-ophthalmological point of view include the posterior parapontine reticular formation (PPRF) which receives inputs from the cortex and is responsible horizontal saccedes. Lesion of the PPRF will cause an ipsilateral gaze palsy for saccades. The dorsolateral pontine nucleus (DLPN) is important in the generation of horizontal pursuit. The sixth nerve nucleus lies in the posterior part of the pons and it houses both the neurons that control the lateral rectus mucle and the interneurons that make up the medial longitudinal fasciculus Thus, a lesion of the abducens nucleus produces an ipsilateral gaze palsy. Lesions of the sixth nerve fascicle produce ipsilateral abduction failure only. Since the pursuit, saccade and vestibular pathways terminate at the sixth nerve nucleus, it essentially represents the horizontal gaze center.

The medulla contains the twelfth nerve nuclei ventral to the fourth ventricle, near the midline, homologous to the third, fourth and six cranial nerves above. Laterally, motor nuclei for the tenth nerve are homologous to nuclei of the fifth and seventh nerves in the pons. Vestibular nuclei extend well into the medullary region and receive input from both the semicircular canals and the otoliths. These structures further connect into the medial longitudinal fasciculus to connect to other nuclei to influence and stabilize vertical gaze with head movements that are up and down and with lateral head tilt. Lesions of this pathway may produce a skew deviation as will be discussed below. The spinal (sensory) nucleus of the fifth nerve extends though the medulla into the upper portion of the cervical cord and lies near the nucleus ambiguous. Corticospinal fibers cross in the lower medulla on their way to spinal anterior horn cells. Spinal sensory input converges on dorsally placed nuclei (cuneatus and gracilis) and through the medial lemniscus to the thalamus. Importantly, the sympathetic pathway has coalesced in the doral and lateral medullary area. The result is that a Horner's syndrome is quite common in lateral medullay lesions

II. Function
The functions of the brain stem may be grouped into the three groups: 1) specific functions of cranial nerves, 2) transmission of information to and from the cerebrum, cerebellum and spinal cord, and 3) general control of consciousness, respiration, cardiac activity and other visceral functions. Clinical disorders of the brain stem affect one or more of these categories.

III. Localization
The ability to localize lesions in the brain stem is enhanced by the great number and complexity of structures and connections which it contains. Longitudinal localization in the brain stem is based primarily on specific cranial nerve dysfunction. A 3rd nerve palsy suggests that a suspected bran stem lesion is located at the midbrain level while paralysis of the tongue on one side (12th nerve) would indicate involvement at the medullary level.
Transverse localization in the brain stem depends upon the knowledge of those structures which are near the midline (e.g., cranial nerve nuclei 3,4,6,12) and those structures which lie laterally (e.g., cranial nerve nuclei 5,7,8,10). Corticospinal pathways lie in a ventral position throughout the brain stem while sensory pathways are dorsal.
The concept of alternating hemiplegia is important to brain stem localization. This depends upon the fact that most cranial nerves (except the fourth nerve nucleus and superior rectus subnucleus of the third) are connected to peripheral structures which are located on the same side of the head as their nuclei in the brain stem. Corticospinal fibers passing nearby will cross at the junction of the medulla and the spinal cord

to reach the <u>opposite side</u> of the body. Thus, the findings of the third nerve palsy on one side and contralateral weakness with spasticity characteristic of corticospinal lesion on the opposite side of the body indicate a lesion at the level of the <u>midbrain</u>. A sixth nerve palsy on one side and spastic hemiparesis on the other indicate a lower pontine lesion. Weakness of the tongue on one side, associated with corticospinal involvement of the opposite side of the body indicate a <u>lower medullary</u> lesion.

A second feature of brain stem localization is the tendency to <u>involve bilateral</u> structures affecting both sides of the head and body not necessarily in the alternating pattern described above. This relates to the small size of the brain stem and the numerous structures which it contains. A third feature of brain stem localization is the tendency of lesions located outside the brain stem (extra-axial) to affect multiple cranial nerves on one side of the head and neck without sensory or motor signs involving the <u>extremities</u>. Tumors of the cranial nerves themselves, meningiomas and malignant tumors in the bone at the base of the skull can produce this finding. Thus, the appearance of a sixth nerve palsy, fifth nerve palsy and a seventh nerve palsy on one side without any sensory or weakness on the opposite side of the body would support a lesion in the cerebellopontine angle that is extramedullary.

IV. <u>**Brain Stem Disorders**</u>

Midbrain- As discussed above, one of the hallmarks of a brainstem lesion is the occurrence of cranial nerve palsy and a neurological deficit such as weakness, sensory dysfunction and cerebellar dysfunction that occurs on the opposite side of the body. For instance, a right third nerve palsy and a left hemiparesis designates a right midbrain lesion. The cranial palsy tells us the side of the lesion and the level of the lesion. One of the more common and classic midbrain disorders occurs with injury to the posterior part of the midbrain . The **dorsal midbrain syndrome** is characterized by 4 hallmark features. 1. Upgaze palsy, 2. Eyelid retraction, 3. Convergence retraction saccades and 4. pupillary light dissociation. There are several nuclei that are important in vertical gaze control including the rostral interstitial nucleus of the medial longitudinal fasciculus(riMLF), the nucleus of Cajal (INC) and the nucleus of the posterior commissure (NPC). In particular, the riMLF is important in vertical saccades while the INC is important in controlling vertical pursuit and vertical gaze holding. Finally, the NPC is important in coordinating vertical gaze and eyelid movement. Because fibers dedicated for upgaze cross in the posterior commissure, it is not uncommon for dorsal midbrain lesions to produce predominantly an upgaze palsy. Eyelid retraction may ensue as the NPC becomes disconnected from the levator subnucleus of the third nerve. . Since fibers for the near reflex synapse on the third nerve nucleus more anteriorly, injury to the dorsal midbrain result in pupillary-light dissociation. In this case, the pupils will respond poorly to light, but better to a near target.

Pons- Pontine syndromes often involve the sixth nerve nucleus, sixth nerve fascicle or the medial longitudinal fasiculus. As discussed above, a lesion of the sixth nucleus will produce an ipsilateral gaze palsy. Since the seventh nerve winds around the sixth nerve nucleus, it may be involved by lesions that arise in fourth ventricle region. The combination of an ipsilateral facial palsy with an ipsilateral gaze palsy is sometimes referred to as the **facial collicular syndrome.** Multiple sclerosis (MS) commonly produces symptoms of brain stem involvement. One particular neurological finding is especially common. That is internuclear ophthalmoplegia. This is characterized by weakness of medial rectus function of one eye associated with nystagmus in lateral movement of the other. This type of finding indicates movement of the medial longitudinal fasciculus that connects the third nerve and sixth nerve areas **(Fig. 7)**. While MS is the commonest cause of this finding in patients aged 20-40 years, other lesions in the same area rarely can produce the same finding. In MS, there may be bilateral internuclear ophthalmoplegia in which each eye fails to adduct properly. Above the age of 50, the most common cause of this finding is a small infarction.
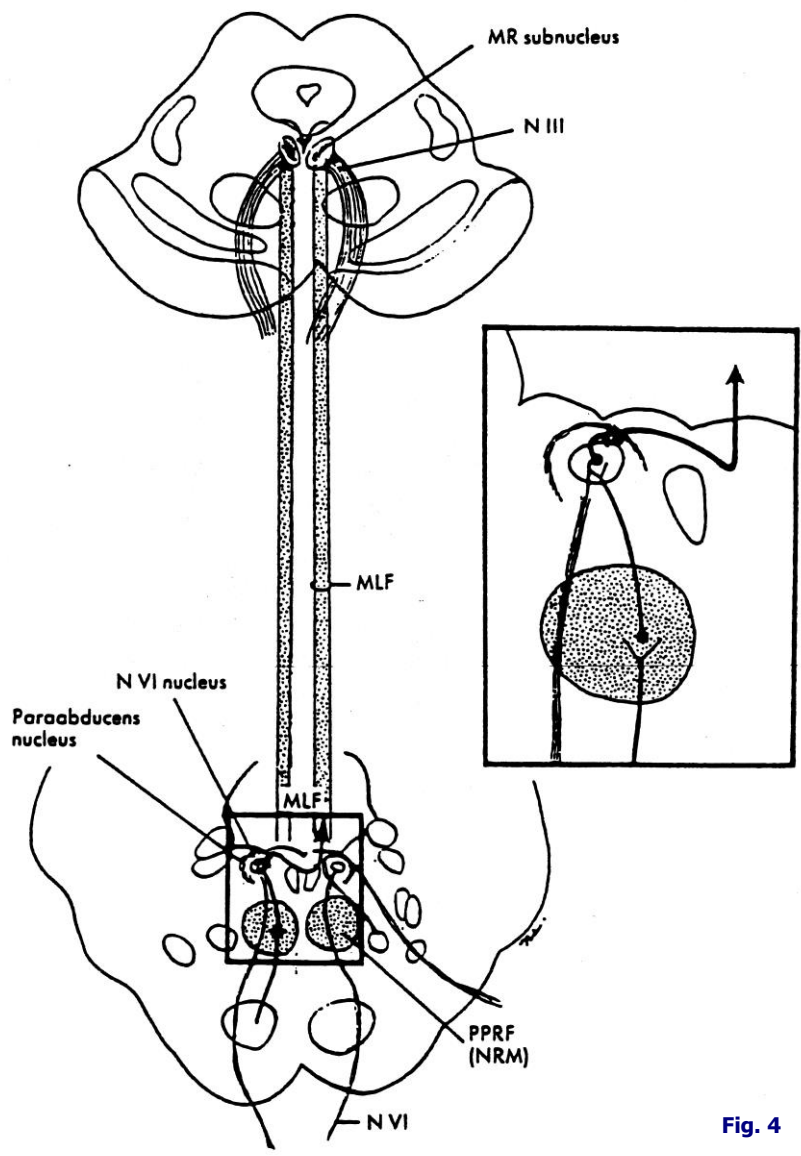
MR subnucleus

N III

MLF

N VI nucleus

Paraabducens
nucleus

MLF

PPRF
(NRM)

N VI

Fig. 4

Another unusal pontine lesion produces what is called the **one and half syndrome.** This results from injury to the horizonital gaze center and the ipsilateral MLF. The patient will have ipsilateral gaze palsy and an interuclear ophthalmoplegia (INO). For instance, a left sided pontine lesion would result in a left gaze palsy and a left INO. The only normal eye movement is abduction of the right eye. Stroke and MS are common causes.

Medullary Lesions- Occlusion of the posterior inferior cerebellar artery produces a highly variable combination of dizziness, nystagmus, cerebellar disturbance, facial numbness, Horner's syndrome, and weakness of the palate on the side of involvement with contralateral loss of pain and temperature over the body. This is the full-blown lateral medullary infarction of Wallenberg's Syndrome which is well known. Partial syndromes are more common with only mild dizziness, perhaps associated with hiccoughing. On examination there may be a mild ipsilateral Horner's Syndrome, ipsilateral facial numbness, and contralateral numbness of the body. One of the common ocular motility findings is a skew deviation. **Skew deviation** is a vertical separation of the eyes that can not be explained by a fourth or third nerve palsy. It oftens results from injury of the otolith pathways that help balance our eyes with lateral head tilt. In essence, if the pathway is injured before its decussates to join the longitudinal

fasciclus, the ispilateral eye will be hypotropic. This is common in medullary lesions. So, in a left lateral medullary lesion, the left eye will be relatively down. This happens because, there is less input to the right inferior rectus muscle and the left superior rectus muscle. It is helpful to know that the otolith pathway projects to the contralateral vertically acting muscles which include the inferior rectus, inferior oblique, superior rectus and superior oblique muscles. Since the nuclei that control the superior rectus and superior oblique muscles cross back both eyes are affected by such lesion. See diagram below. Once the pathway has crossed to become part of the MLF, the lesion is on the side of the higher eye. You will notice that many patients with INO's will have an ipsilateral hyper Skew deviations from midbrain lesions also produce an ipsilateral hypertropia
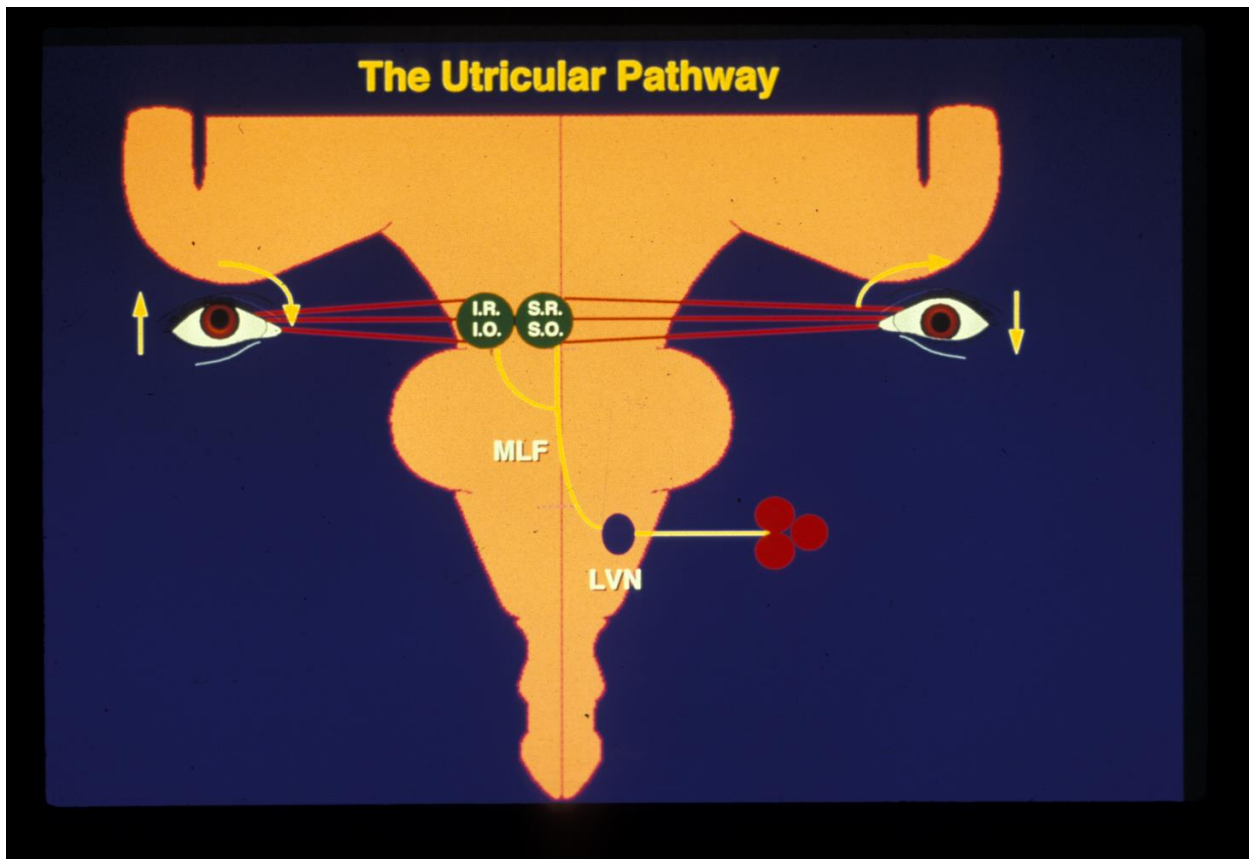
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