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Overview of Neuro-ophthalmologic and Cranial Nerve Disorders

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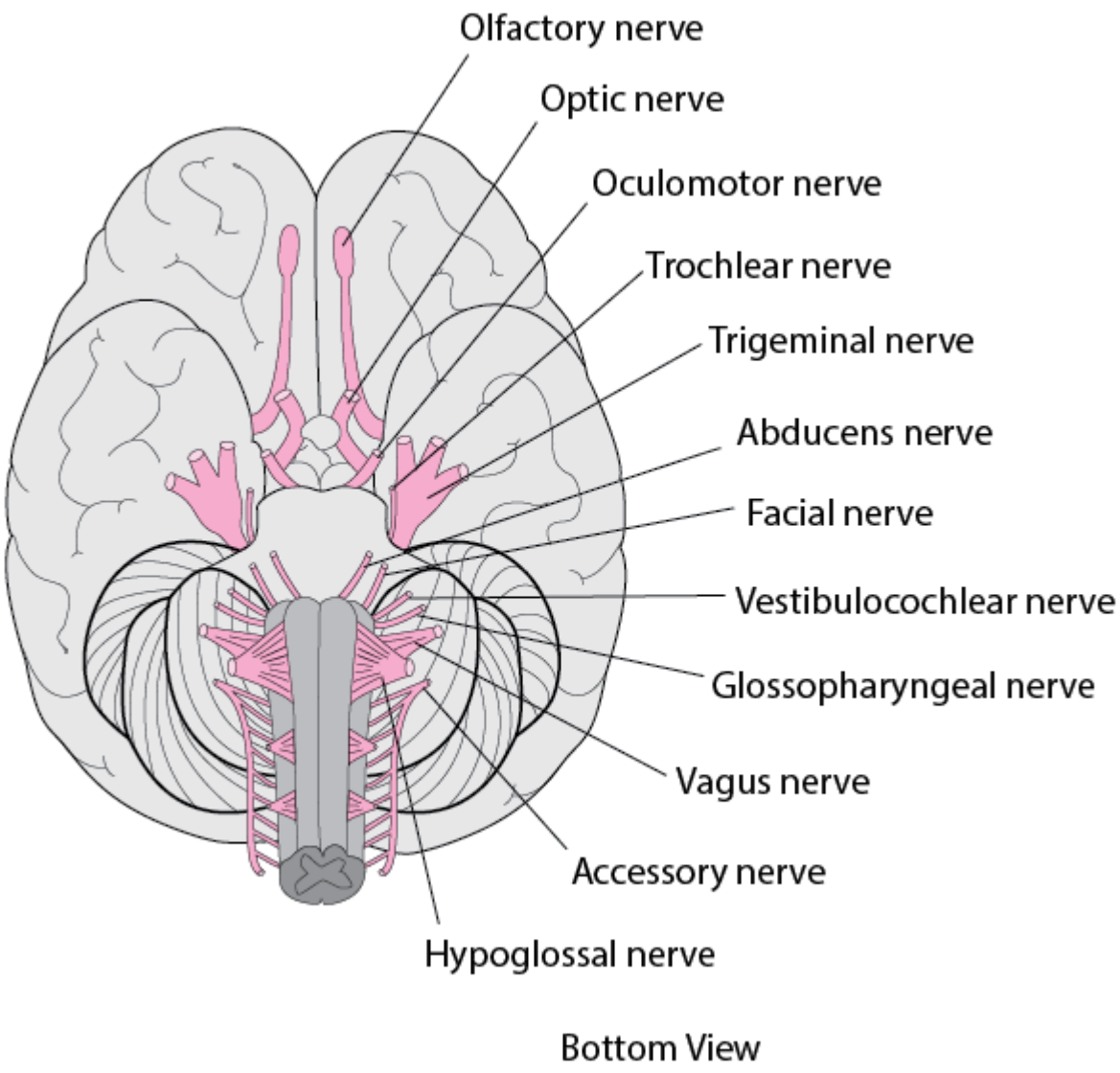
Dysfunction of certain cranial nerves may affect the eye, pupil, optic nerve, or extraocular muscles and their nerves; thus, they can be considered cranial nerve disorders, neuro-ophthalmologic disorders, or both.

Neuro-ophthalmologic disorders may also involve dysfunction of the central pathways that control and integrate ocular movement and vision.

Cranial nerve disorders can also involve dysfunction of smell, vision, chewing, facial sensation or expression, taste, hearing, balance, swallowing, phonation, head turning and shoulder elevation, or tongue movements (see table Cranial Nerves). One or more cranial nerves may be affected.

(See also Horner Syndrome, Optic Nerve Disorders, and Approach to the Neurologic Patient.)

Cranial nerves



Cranial Nerves

Nerve	Function	Possible Abnormal Findings	Possible Causes*,†
Olfactory (1st)	Provides sensory input for smell	Anosmia	Head trauma Nasal disorders (eg, allergic rhinitis) Neurodegenerative disorders (eg, Alzheimer disease, Parkinson disease) Paranasal sinusitis Tumors of the cranial fossa, nasal cavity, and paranasal sinuses Infections (eg, COVID-19 due to severe acute respiratory syndrome coronavirus 2 [SARS-CoV2])
Optic (2nd)	Provides sensory input for vision	Amaurosis fugax (transient monocular blindness), unilateral loss of superior or inferior visual field	Embolism of the ophthalmic artery Ipsilateral internal carotid disease Embolism of retinal arteries
		Anterior ischemic optic neuropathy	Crowded optic disk morphology (called disk at risk) Complications after cataract extraction Connective tissue disease that causes arteritis (eg, giant cell [temporal] arteritis, antiphospholipid antibody syndrome) Diabetes Hypotension or hypovolemia if severe Ipsilateral internal carotid artery obstruction Phosphodiesterase type 5 (PDE5) inhibitors (eg, sildenafil, tadalafil, vardenafil) Retinal artery embolism
		Optic neuritis (papillitis and retrobulbar)	Acute demyelinating disease (eg, multiple sclerosis, neuromyelitis optica) Bacterial infections (eg, TB, syphilis, Lyme disease) Postinfectious or disseminated encephalomyelitis Uveitis Viral infections (eg, HIV, herpes simplex, hepatitis B, cytomegalovirus)

* Disorders that cause diffuse motor paralysis (eg, myasthenia gravis,botulism, variant Guillain-Barré syndrome, poliomyelitis with bulbar involvement) often affect the motor part of the cranial nerves.

† Hypertension (microvascular disease) and infections (eg, postviral infections, tuberculosis, syphilis) can cause individual cranial nerve palsies.

Nerve	Function	Possible Abnormal Findings	Possible Causes*,†
		Toxic-nutritional optic neuropathy (toxic amblyopia)	Drugs (chloramphenicol, ethambutol, isoniazid, streptomycin, sulfonamides, digitalis, chlorpropamide, ergot, disulfiram) Methanol ingestion Nutritional deprivation if severe Organic mercury Vitamin B12 deficiency
		Hereditary optic neuropathies	Dominant optic atrophy Leber hereditary optic neuropathy
		Bitemporal hemianopia	Craniopharyngioma Meningioma of tuberculum sellae Saccular aneurysm in the cavernous sinus Suprasellar extension of pituitary adenoma
Oculomotor (3rd)	Raises eyelids Moves eyes up, down, and medially Adjusts amount of light entering eyes Focuses lenses	Palsies	Aneurysm of posterior communicating artery Ischemia of the 3rd cranial nerve (often due to small-vessel disease as occurs in diabetes) or its fascicle in the midbrain Transtentorial herniation due to intracranial mass (eg, subdural hematoma, tumor, abscess)
Trochlear (4th)	Moves eye in and down via the superior oblique muscle	Palsies	Often idiopathic Head trauma Infarction often due to small-vessel disease (eg, in diabetes) Tentorial meningioma Pinealoma
	Para	Myokymia of the superior oblique muscle (typically with brief episodic ocular movements that cause subjective visual shimmering, ocular trembling, and/or tilted vision)	Entrapment of the trochlear nerve by a vascular loop (similar to the pathophysiology of trigeminal neuralgia)
Trigeminal (5th)			
• Ophthalmic division	Provides sensory input from the eye surface, tear glands, scalp, forehead, and upper eyelids	Neuralgia	Vascular loop compressing the nerve root Multiple sclerosis (occasionally) Lesions of cavernous sinus or superior orbital fissure
• Maxillary and mandibular divisions	Provides sensory input from the teeth, gums, lip, lining of palate, and skin of the face	Neuralgia	Lesions of cavernous sinus or superior orbital fissure Multiple sclerosis (occasionally)

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Nerve	Function	Possible Abnormal Findings	Possible Causes*,†
			Vascular loop compressing the nerve root
	Moves masticatory muscles (chewing, grinding the teeth)	Neuropathy	Carcinomatous or lymphomatous meningitis Connective tissue disorders Meningiomas, schwannomas, or metastatic tumors at the skull base
Abducens (6th)	Moves the eye outward (abduction) via the lateral rectus muscle	Palsies	Cavernous sinus thrombosis Often idiopathic Head trauma Increased intracranial pressure Infarction (may be mononeuritis multiplex) Infections or tumors affecting the meninges Multiple sclerosis Nasopharyngeal carcinoma Pontine or cerebellar tumors Pontine infarction Wernicke encephalopathy
Facial (7th)	Moves muscles of facial expression Proximal branches: Innervate tear glands and salivary glands and provide sensory input for taste on the anterior two thirds of the tongue	Palsies	Vestibular schwannoma Basilar skull fracture Bell palsy Guillain-Barré syndrome Infarcts and tumors of the pons Lyme disease Melkersson-Rosenthal syndrome Mobius syndrome Ramsay Hunt syndrome (herpes zoster oticus) Sarcoidosis Tumors that invade the temporal bone Uveoparotid fever (Heerfordt syndrome)
		Hemifacial spasm	Artery loop compressing the nerve root
Vestibulocochlear (8th)	Provides sensory input for equilibrium and hearing	Tinnitus, vertigo, sense of fullness in the ear, and hearing loss	Meniere disease Barotrauma
		Benign paroxysmal positional vertigo	Otolithic aggregation in the posterior or horizontal semicircular canal, related to aging and/or trauma Infection (occasionally)
		Vestibular neuronitis	Viral infection
		Hearing loss or disturbance	Acoustic neuromas Aging Barotrauma Cerebellopontine angle

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Nerve	Function	Possible Abnormal Findings	Possible Causes*,†
			tumors Congenital rubella infection Exposure to loud noises Hereditary disorders Meningitis Viral infection (possibly) Ototoxic drugs (eg, aminoglycosides)
Glossopharyngeal (9th)	Provides sensory input from the pharynx, tonsils, posterior tongue, and carotid arteries	Glossopharyngeal neuralgia	Ectatic artery or tumor (less common) compressing the nerve
	Moves muscles of swallowing and controls parotid gland secretion Helps regulate BP	Glossopharyngeal neuropathy	Tumor or aneurysm in the posterior fossa or jugular foramen (jugular foramen syndrome)
Vagus (10th)	Moves vocal cords and muscles for swallowing Transmits impulses to the heart (slows the heart rate) and smooth muscles of visceral organs (regulates peristalsis)	Hoarseness, dysphonia, and dysphagia Vasovagal syncope	Entrapment of recurrent laryngeal nerve by mediastinal tumor Herpes zoster Infectious or carcinomatous meningitis Medullary tumors or ischemia (eg, lateral medullary syndrome) Tumor or aneurysm in the posterior fossa or jugular foramen (jugular foramen syndrome)
Accessory (11th)	Turns the head Shrugs the shoulders	Partial or complete paralysis of the sternocleidomastoid and upper trapezius muscles	Iatrogenic (eg, due to lymph node biopsy in posterior triangle of the neck) Idiopathic Trauma Tumor or aneurysm in the posterior fossa or jugular foramen (jugular foramen syndrome)
Hypoglossal (12th)	Moves the tongue	Atrophy and fasciculation of tongue	Intramedullary lesions (eg, tumors) Lesions of the basal meninges or occipital bones (eg, platybasia, Paget disease of skull base) Surgical trauma (eg, due to endarterectomy) Motor neuron disease (eg, amyotrophic lateral sclerosis)

* Disorders that cause diffuse motor paralysis (eg, myasthenia gravis,botulism, variant Guillain-Barré syndrome, poliomyelitis with bulbar involvement) often affect the motor part of the cranial nerves.

† Hypertension (microvascular disease) and infections (eg, postviral infections, tuberculosis, syphilis) can cause individual cranial nerve palsies.

Causes and symptoms of neuro-ophthalmologic and cranial nerve disorders overlap. Both types of disorders can result from tumors, inflammation, trauma, systemic disorders, and degenerative or other processes, causing such symptoms as vision loss, diplopia, ptosis, pupillary abnormalities, periocular pain, facial pain, or headache.

Diagnosis

- Clinical evaluation
- Neuroimaging

(See also How to Assess the Cranial Nerves.)
Evaluation of neuro-ophthalmologic and cranial nerve disorders includes the following:

- Detailed questioning about symptoms
- Examination of the visual system
- Tests to detect nystagmus
- Examination of the cranial nerves

Visual system examination includes ophthalmoscopy and testing of visual acuity, visual fields, pupils, and eye movements (ocular motility). As part of this testing, the 2nd, 3rd, 4th, and 6th cranial nerves are examined.
Neuroimaging with CT or MRI is also usually required.
The following parts of the visual examination are of particular interest in diagnosing neuro-ophthalmologic and cranial nerve disorders.
Pupils are inspected for size, equality, and regularity. Normally, the pupils constrict promptly (within 1 sec) and equally during accommodation and during exposure to direct light and to light directed at the other pupil (consensual light reflex). Testing pupillary response to consensual light via a swinging flashlight test can determine whether a defect is present. Normally, the degree of pupillary constriction does not change as the flashlight is swung from eye to eye.

- If a **relative afferent defect** (deafferented pupil, afferent pupillary defect, or Marcus Gunn pupil) is present, the pupil paradoxically dilates when the flashlight swings to the side of the defect. A deafferented pupil constricts in response to consensual but not to direct light.
- If an **efferent defect** is present, the pupil responds sluggishly or does not respond to both direct and consensual light.

Common Pupillary Abnormalities

Finding	Explanation
Asymmetry of 1–2 mm between pupils, preserved light responses, and no symptoms	Normal variant (physiologic anisocoria)
Asymmetry, impaired light responses, and preserved response to accommodation (light-near dissociation or Argyll Robertson pupil)	Neurosyphilis (possibly)
Bilateral constriction	Opioids Miotic eye drops for glaucoma (most common; causing unilateral constriction if single eye is dosed) Pontine hemorrhage (damaging the central sympathetic pathways that dilate pupils) Organophosphate or cholinergic toxins
Bilateral dilation with preserved light reflexes	Hyperadrenergic states (eg, withdrawal syndromes, drugs such as sympathomimetics or cocaine, thyrotoxicosis)
Bilateral dilation with impaired direct light response	Mydriatic eye drops such as sympathomimetics (eg, phenylephrine) and cycloplegics (eg, cyclopentolate, tropicamide, homatropine, atropine) Brain herniation Hypoxic or ischemic encephalopathy
Unilateral dilation with afferent pupillary defect	Lesions of the eye, retina, or 2nd cranial (optic) nerve
Unilateral dilation with efferent pupillary defect	Third cranial (oculomotor) nerve palsies, often due to compression (eg, due to aneurysm of the posterior communicating artery or to transtentorial herniation) Iris trauma (also irregular pupil) Mydriatic eye drops*
Unilateral dilation with minimal or slow direct and consensual light reflexes and pupil constriction in response to accommodation	Tonic (Adie) pupil†

* Transtentorial herniation and use of mydriatic eye drops can often be distinguished by instilling a drop of pilocarpine ocular solution into the dilated pupil; no constriction in response suggests mydriatic eye drops.

† Tonic (Adie) pupil is permanent but nonprogressive abnormal dilation of the pupil due to damage of the ciliary ganglion. It typically occurs in women aged 20 to 40. Onset is usually sudden. The only findings are slight blurring of vision, impaired dark adaptation, and sometimes absent deep tendon reflexes.

Eye movements are checked by having the patient hold the head steady while tracking the examiner's finger as it moves to the far right, left, upward, downward, diagonally to either side, and inward toward the patient's nose (to assess accommodation). However, such examination may miss mild paresis of ocular movement sufficient to cause diplopia.

Diplopia may indicate a defect in bilateral coordination of eye movements (eg, in neural pathways) or in the 3rd (oculomotor), 4th (trochlear), or 6th (abducens) cranial nerve. If diplopia persists when one eye is closed (monocular diplopia), the cause is probably a nonneurologic eye disorder. If diplopia disappears when either eye is closed (binocular diplopia), the cause is probably a disorder of ocular motility. The two images are furthest apart when the patient looks in the direction served by the paretic eye muscle (eg, to the left when the left lateral rectus muscle is paretic). The eye that, when closed, eliminates the more peripheral image is paretic. Placing a red glass over one eye can help identify the paretic eye. When the red glass covers the paretic eye, the more peripheral image is red.

Common Disturbances of Ocular Motility

Clinical Finding	Syndrome	Common Causes
Pareses		
Paresis of horizontal gaze in one direction	Conjugate horizontal gaze palsy	Lesion in the ipsilateral pontine horizontal gaze center or in the contralateral frontal cortex Wernicke encephalopathy
Paresis of horizontal gaze in both directions	Complete (bilateral) horizontal gaze palsy	Large bilateral pontine lesion affecting both horizontal gaze centers
Bilateral paresis of all horizontal eye movements except for abduction of the eye contralateral to the lesion; convergence unaffected	One-and-a-half syndrome	Lesion in the medial longitudinal fasciculus and ipsilateral pontine horizontal gaze center
Unilateral or bilateral paresis of eye adduction in horizontal lateral gaze but not in convergence	Internuclear ophthalmoplegia	Lesion in the medial longitudinal fasciculus
Bilateral paresis of upward eye movement with dilated pupils, loss of the pupillary light response despite preservation of pupillary accommodation and constriction with convergence, downward gaze preference, and downbeating nystagmus	Parinaud syndrome (a type of conjugate vertical gaze palsy)	Pineal tumor Dorsal midbrain infarct
Bilateral paresis of downward eye movements	Conjugate downward gaze palsy	Progressive supranuclear palsy
Unilateral eye deviation (resting position is down and out); unilateral paresis of eye adduction, elevation, and depression; ptosis; and often a dilated pupil	3rd cranial nerve palsy	Aneurysms Oculomotor nerve or midbrain ischemia Trauma Transtentorial herniation
Unilateral paresis of downward and inward (nasal) eye movement, which may be subtle, causing symptoms (difficulty looking down and inward) Head tilt sign (patient tilts the head to the side opposite the affected eye)	4th cranial nerve palsy	Idiopathic Head trauma Ischemia Congenital
Unilateral paresis of eye abduction	6th cranial nerve palsy	Idiopathic Infarct Vasculitis Increased intracranial pressure Wernicke encephalopathy Multiple sclerosis
Skew deviation (vertical misalignment of the eyes)	Partial and unequal involvement of 3rd cranial nerve nuclei, vertical gaze center, or median longitudinal fasciculus	Brain stem lesion anywhere from midbrain to medulla
Weakness or restriction of all extraocular muscles	External ophthalmoplegia	Dysfunction of eye muscles or of neuromuscular junction Usually caused by the following: • Myasthenia gravis • Graves disease • Botulism • Mitochondrial myopathies (eg, Kearn-Sayre syndrome)

Clinical Finding	Syndrome	Common Causes
		• Oculopharyngeal dystrophy • Myotonic dystrophy • Orbital mass (eg, tumor, pseudotumor)
Involuntary or abnormal movements		
Rhythmic involuntary movements, usually bilateral	Nystagmus	Many causes: • Vestibular disorders (eg, Meniere disease, vestibular neuronitis) • Multiple sclerosis • Head trauma • Drugs (eg, antiseizure drugs, anxiolytics, and sedatives)
Fast downward jerk and slow upward return to midposition	Ocular bobbing	Extensive pontine destruction or dysfunction
Gaze overshoot followed by several oscillations	Ocular dysmetria	Cerebellar pathway disorders
Burst of rapid horizontal oscillations about a point of fixation	Ocular flutter	Many causes: • Postanoxic encephalopathy • Occult neuroblastoma • Paraneoplastic effects • Ataxia-telangiectasia • Viral encephalitis • Toxic effects of drugs
Rapid, conjugate, multidirectional, chaotic movements, often with widespread myoclonus	Opsoclonus	Many causes (same as for ocular flutter, above)

Treatment

- Treatment of the cause

Treatment of neuro-ophthalmologic and cranial disorders depends on the cause.

Drugs Mentioned In This Article

Drug Name	Select Trade
chloramphenicol	No US brand name
cyclopentolate	AKPENTOLATE, CYCLOGYL
chlorpropamide	DIABINESE

Drug Name	Select Trade
pilocarpine	ISOPTO CARPINE, PILOPINE HS, SALAGEN
tropicamide	MYDRIACYL, TROPICACYL
homatropine	TUSSIGON
disulfiram	ANTABUSE
vardenafil	LEVITRA
ethambutol	MYAMBUTOL
sildenafil	VIAGRA
tadalafil	CIALIS
isoniazid	LANIAZID
atropine	ATROPEN