DISORDERS OF CEREBELLUM

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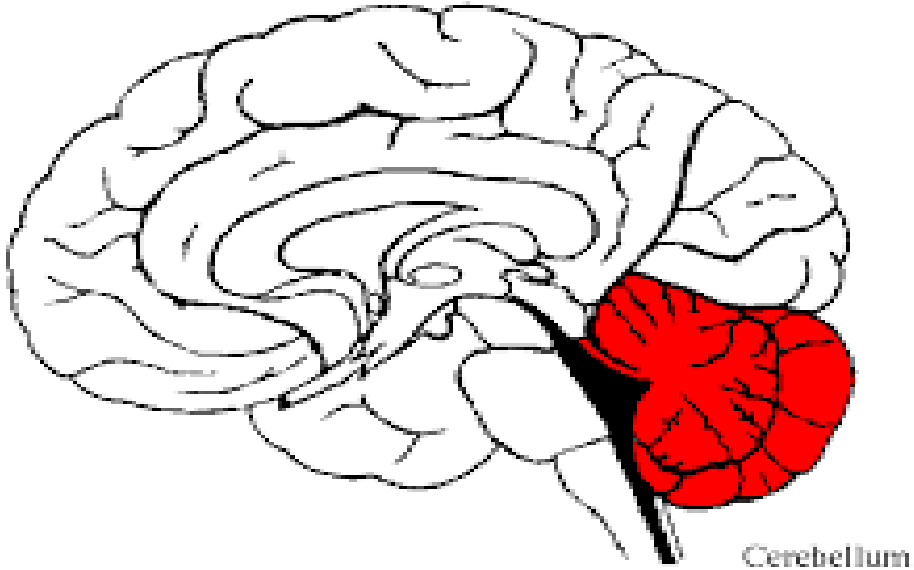
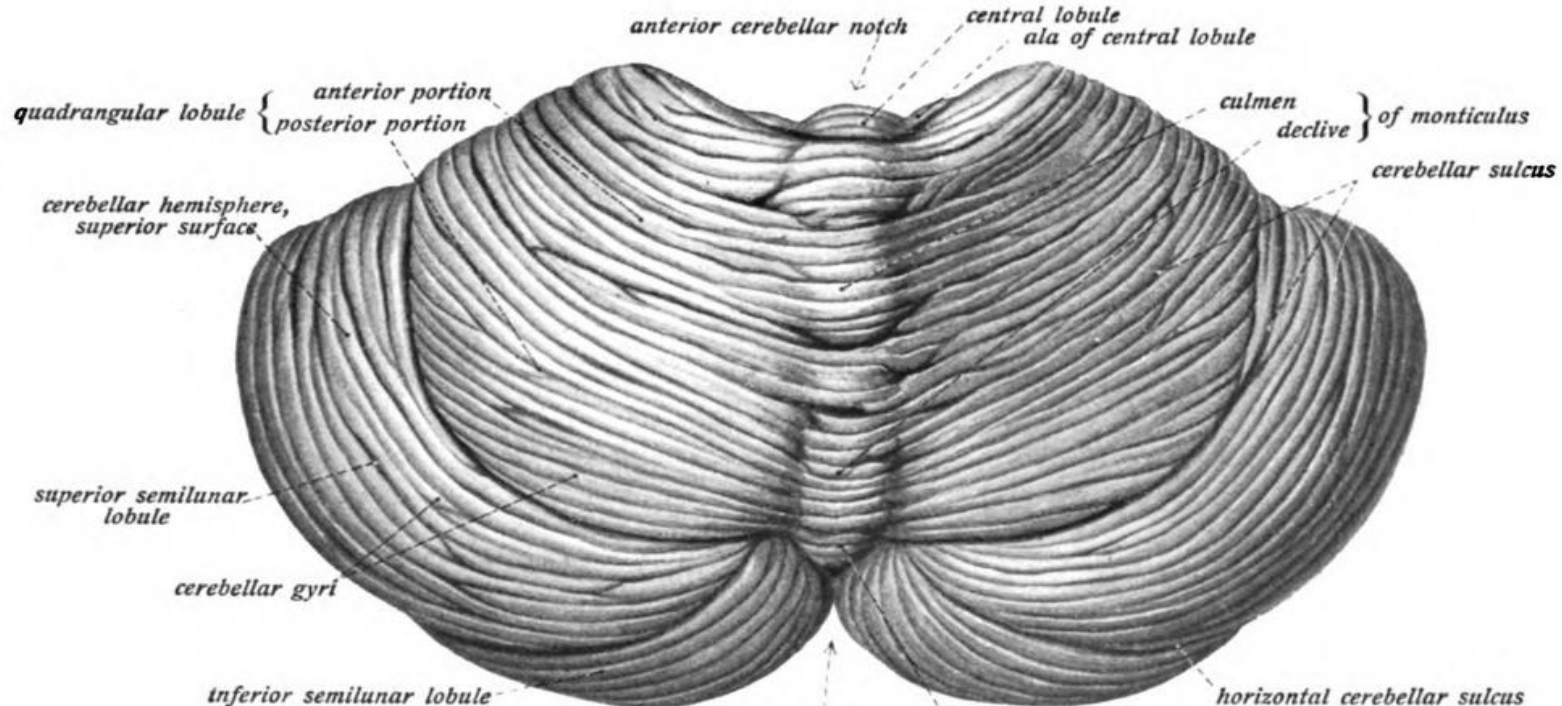
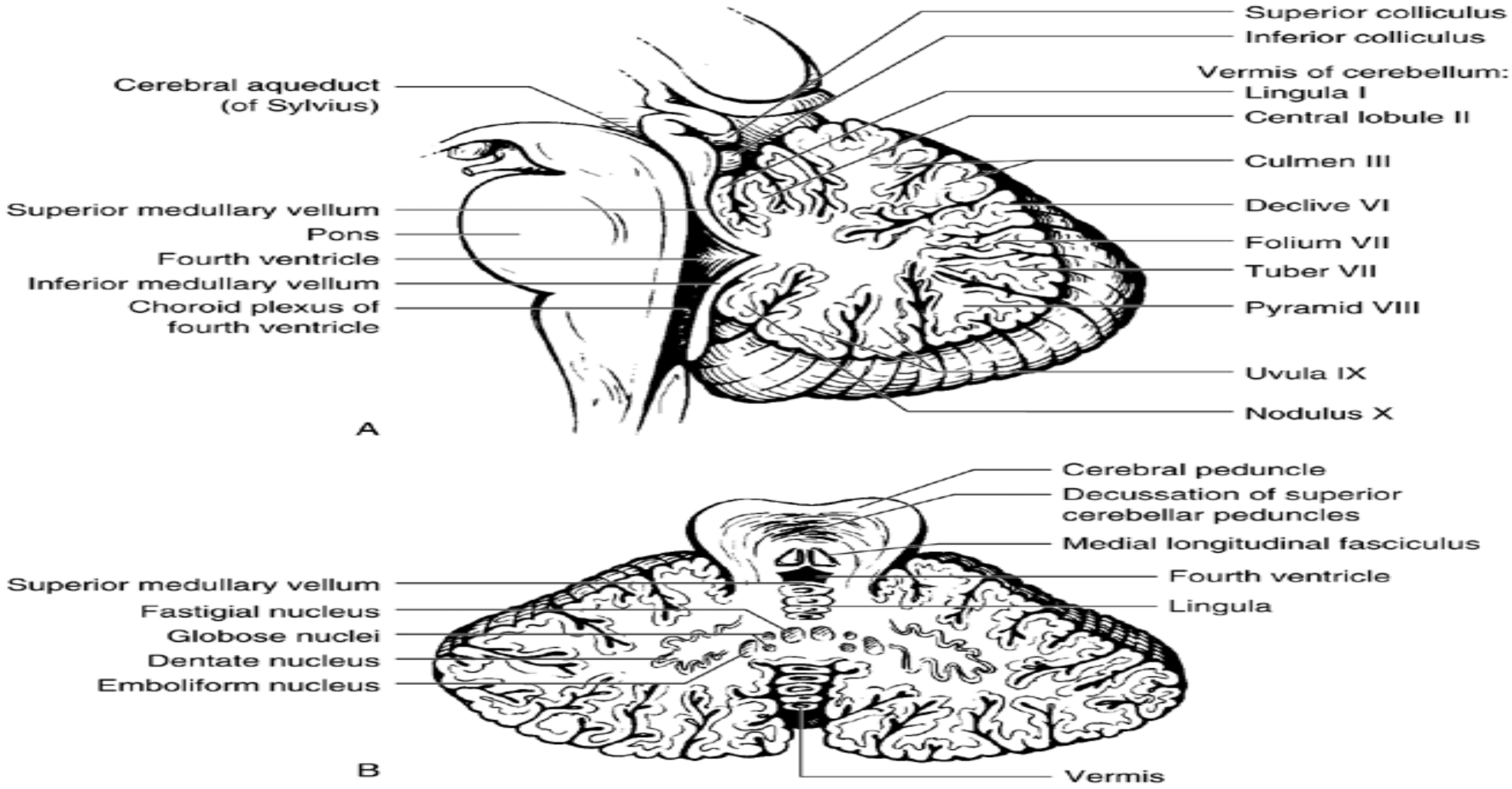


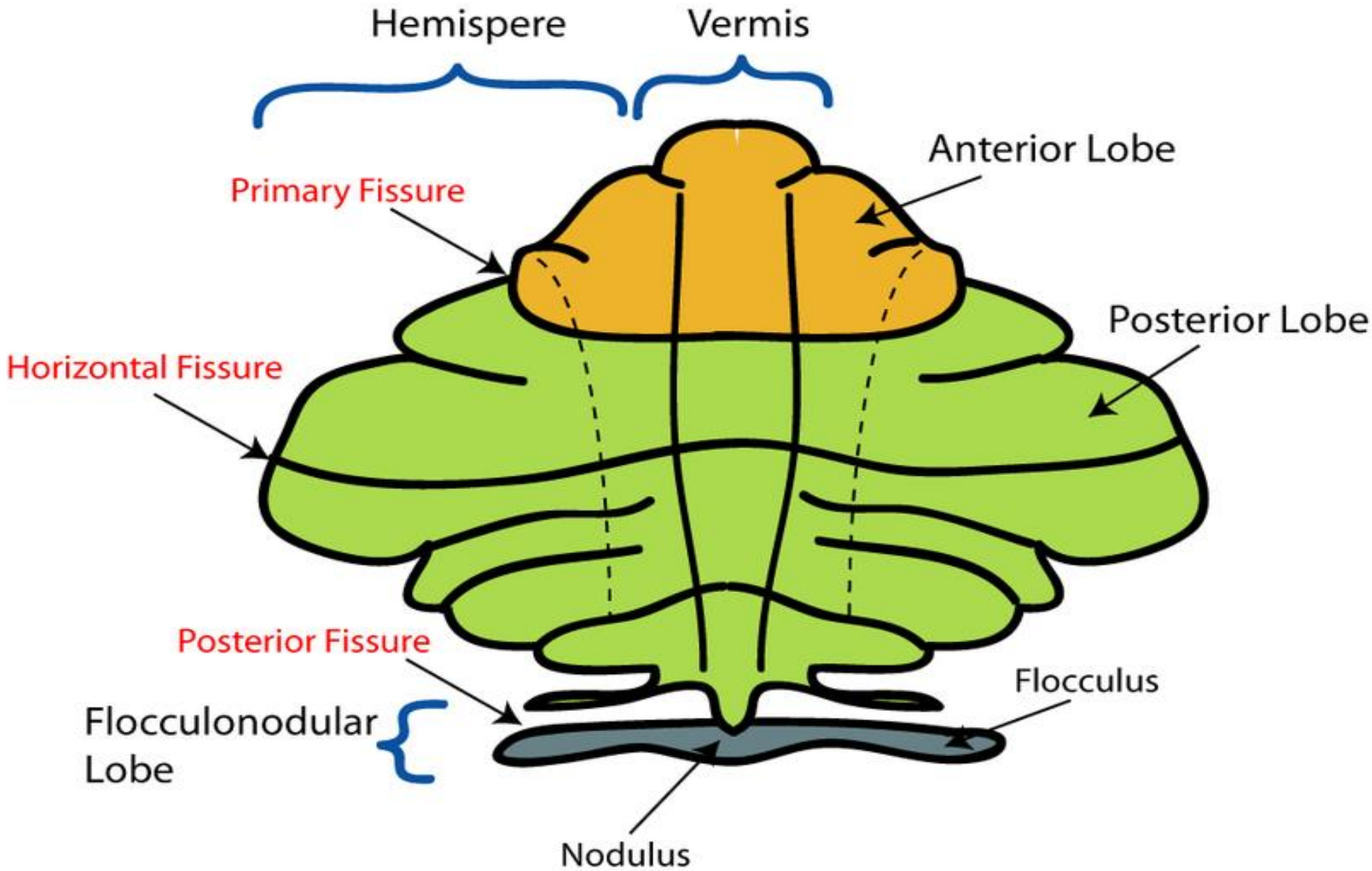
ANATOMY

- Lies just dorsal to the pons and medulla, consists of two highly convoluted lateral cerebellar hemispheres and a narrow medial portion, the vermis.
- It is connected to the brain by three pairs of dense fiber bundles called the peduncles
- Cortex folded into folia



ANATOMY


Superior colliculus
Inferior colliculus
Cerebral aqueduct (of Sylvius)
Vermis of cerebellum:
Lingula I
Central lobule II
Culmen III
Superior medullary vellum
Declive VI
Pons
Folium VII
Fourth ventricle
Tuber VII
Inferior medullary vellum
Pyramid VIII
Choroid plexus of fourth ventricle
Uvula IX
Nodulus X
A
Cerebral peduncle
Decussation of superior cerebellar peduncles
Medial longitudinal fasciculus
Superior medullary vellum
Fourth ventricle
Fastigial nucleus
Lingula
Globose nuclei
Dentate nucleus
Emboliform nucleus
B
Vermis


Hemispere
Vermis
Anterior Lobe
Primary Fissure
Posterior Lobe
Horizontal Fissure
Posterior Fissure
Flocculus
Flocculonodular Lobe
Nodulus

FUNCTIONAL ANATOMY

- Archicerebellum
  - flocculonodular lobe
  - helps maintain equilibrium and coordinate eye, head, and neck movements; it is closely interconnected with the vestibular nuclei.
- Paleocerebellum
  - vermis of the anterior lobe, the pyramid, the uvula, and the paraflocculus
  - It helps coordinate trunk and leg movements. Vermis lesions result in abnormalities of stance and gait.
- Neocerebellum
  - middle portion of the vermis and most of the cerebellar hemispheres
  - They control quick and finely coordinated limb movements, predominantly of the arms.

PHYSIOLOGY

- Receives a tremendous number of inputs from the spinal cord and from many regions of both the cortical and subcortical brain.
- Receives extensive information from somesthetic, vestibular, visual, and auditory sensory systems, as well as from motor and nonmotor areas of the cerebral cortex
- WHILE THE CEREBELLUM DOES NOT SERVE TO INITIATE MOST MOVEMENT, IT PROMOTES THE SYNCHRONY AND ACCURACY OF MOVEMENT REQUIRED FOR PURPOSEFUL MOTOR ACTIVITY

BASIC CHARACTERISTICS OF CEREBELLAR SIGNS & SYMPTOMS

- Lesions of the cerebellum produce errors in the planning and execution of movements, rather than paralysis or involuntary movements.
- In general, if symptoms predominate in the trunk and legs, the lesion is near the midline; if symptoms are more obvious in the arms, the lesion is in the lateral hemispheres.
- If only one side of the cerebellum is affected, the symptoms are unilateral and ipsilateral to the lesion.
- The most severe disturbances are produced by lesions in the superior cerebellar peduncle and the deep nuclei
- Many of the symptoms of cerebellar disease improve gradually with time if the underlying disease process does not itself progress.

BASIC CHARACTERISTICS OF CEREBELLAR SIGNS & SYMPTOMS

- Almost all patients with cerebellar lesions have some type of gait disturbance.
- Speech disturbances occur with bilateral damage
- Signs and symptoms similar to those produced by cerebellar lesions can appear with disorders that affect structures adjacent to the cerebellum or affect the afferent or efferent connections of the cerebellum

SIGNS OF CEREBELLAR DISORDERS

DEFICIT	MANIFESTATION
Ataxia	Reeling, wide-based gait
Decomposition of movement	Inability to correctly sequence fine, coordinated acts
Dysarthria	Inability to articulate words correctly, with slurring and inappropriate phrasing
Dysdiadochokinesia	Inability to perform rapid alternating movements
Dysmetria	Inability to control range of movement
Hypotonia	Decreased muscle tone
Nystagmus	Involuntary, rapid oscillation of the eyeballs in a horizontal, vertical, or rotary direction, with the fast component maximal toward the side of the cerebellar lesion
Scanning speech	Slow enunciation with a tendency to hesitate at the beginning of a word or syllable
Tremor	Rhythmic, alternating, oscillatory movement of a limb as it approaches a target (intention tremor) or of proximal musculature when fixed posture or weight bearing is attempted (postural tremor)

ATAXIA

- A term derived from the greek word meaning "lack of order."
- Most conspicuous and most common
- Incoordination or clumsiness of movement
- Difficulty regulating the force, range, direction, velocity, and rhythm of muscle contractions and in maintaining the synergy that normally exists among the various muscles involved in motor activities
- If the legs and trunk are affected, difficulty in maintaining posture and coordinating leg movements will result in ataxia of gait

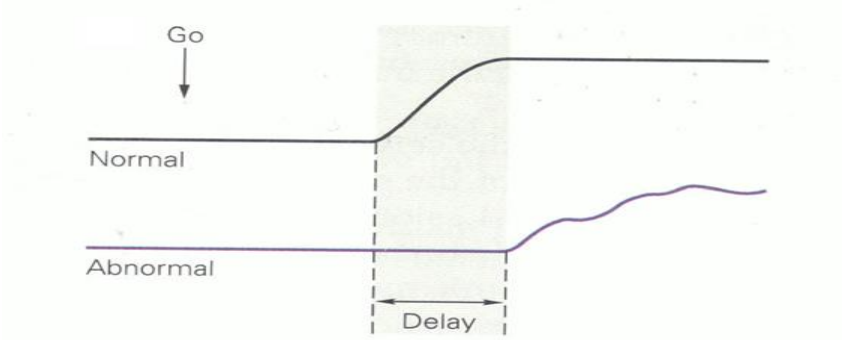
ATAXIA

- Ataxia of the arms (limb ataxia) creates its own specific clinical signs
- Difficulty in bringing a limb smoothly and accurately to a specific target in space is called dysmetria
- An involved limb may either overshoot (hypermetria) or undershoot (hypometria) its target
- Complex movements, because of errors in the timing and sequencing of their component parts, may deteriorate into a series of successive simple movements, rather than one smooth, coordinated movement. This is termed decomposition of movement and is most evident in movements involving multiple joints.

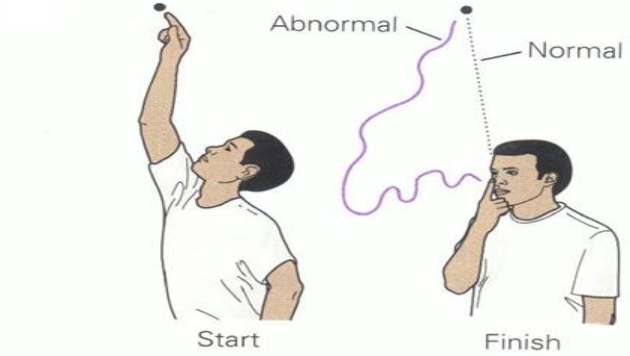
ATAXIA

- At the end of such movements, when the patient is attempting to achieve the greatest precision, a coarse tremor may develop called an intention tremor
- Dysmetria, decomposition, and tremor all can be demonstrated by simply asking the patient to point from one stationary target to another, such as in bringing the tip of the finger of the extended upper extremity to the nose
- Limb ataxia may also be manifested as an impairment of the ability to perform rapidly alternating movements, dysdiadochokinesia.

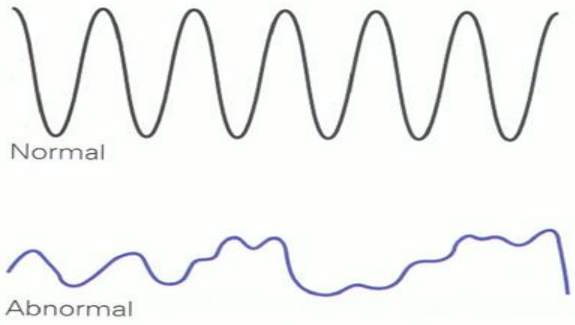
SIGNS OF CEREBELLAR DISORDERS



Hypometria &
Response delays



Ataxia



Incoordination/
rapid alternating
movements
(dysdiadocho-
kinesia)

ATAXIA

- Persistent incoordination of axial muscles may lead to reversible abnormalities of stance and posture, such as head or body tilt,or to more permanent skeletal abnormalities, such as scoliosis.
- Truncal ataxia may result in swaying of the trunk, staggering gait, and difficulty in sitting unsupported
- Bulbar muscles may also be affected, leading to slurred speech (dysarthria) and numerous disturbances of oculomotor activity, including nystagmus.

ATAXIA TYPES

	Cerebellar	Vestibular	Sensory
Dysarthria	May be present	Absent	Absent
Nystagmus	Often present	Present	Absent
Vertigo	May be present	Present	Absent
Limb ataxia	Usually present	Absent	Present(only in the legs)
Stance	Unable to stand with feet together	May be able to stand with feet together	Able to stand with feet together and eyes open, but unable with eyes closed
Vibratory and position sense	Normal	Normal	Impaired
Ankle reflexes	Normal	Normal	Depressed or absent

HYPOTONIA

- Hypotonia refers to a decreased resistance to passive stretch as might occur with passive limb movement
- Normal cerebellum contributes to the maintenance of muscle tone through facilitatory influences on skeletal muscle stretch reflexes
- most evident shortly after acute cerebellar injury and tends to decrease with time
- Decreased muscle tone may result in a pendular limb, with pendular deep tendon reflexes

HYPOTONIA

- it can exacerbate the symptoms produced by ataxia.
- Decreased tone in postural muscles, for example, contributes to gait disturbances and postural asymmetry.
- Hypotonia in the muscles of speech promotes abnormalities in pitch and loudness, and in oculomotor muscles results in difficulty in maintaining the gaze

DYSEQUILIBRIUM & VERTIGO

- The floccolonodular lobes have extensive connections with both the vestibular nuclei and the vestibular apparatus
- Unsteadiness of gait or an inability to sit or stand without swaying or falling, as well as abnormalities of head posture and eye movement (nystagmus)
- Cerebellar infarction and hemorrhage (stroke) have been shown to induce signs and symptoms such as vertigo, nausea, vomiting, and nystagmus

EXTRACEREBELLAR CAUSES OF CEREBELLAR SYMPTOMS

- Conditions that disrupt the spinocerebellar tracts can cause dysmetria and ataxia by depriving the cerebellum of proprioceptive input. These kinds of defects underlie Friedreich's ataxia and many of the cerebellar findings of multiple sclerosis
- Disruption of somatosensory nerves in the peripheral nervous system can impair the proprioceptive sense enough to cause a sensory ataxia e.g. alcoholic or other types of peripheral neuropathy
- Disorders of the vestibular system, by interfering with balance and equilibrium, can mimic and exacerbate the gait problems associated with cerebellar damage

ETIOLOGY

- Congenital malformations
- Hereditary ataxias
- Acquired conditions

CONGENITAL MALFORMATIONS

- Almost always sporadic
- Manifest early in life
- Non-progressive
- Although ataxia, hypotonia, tremor, and abnormal eye movements may be present, marked cerebellar hypoplasia has been shown by imaging studies and autopsy to be present in totally asymptomatic individuals
- Often occurring as part of complex malformation syndromes (eg, Dandy-Walker malformation) that affect other parts of the CNS

CONGENITAL MALFORMATIONS

- The Dandy-Walker malformation consists of a ballooning of the posterior half of the fourth ventricle and hypoplasia of the cerebellar vermis
- Hydrocephalus almost always develops and accounts for many of the accompanying clinical manifestations
- The Chiari malformations (the most common developmental abnormality of the posterior fossa) encompass a group of anomalies of the brainstem and cerebellum, in which there is a herniation of part of the cerebellum, medulla, and sometimes the pons through the foramen magnum into the upper cervical spinal canal

HEREDITARY ATAXIAS

- Autosomal recessive or autosomal dominant
- Autosomal recessive ataxias include:
  - Friedreich ataxia (the most prevalent)
  - Ataxia-telangiectasia
  - Abetalipoproteinemia
  - Ataxia with isolated vitamin E deficiency
  - Cerebrotendinous xanthomatosis

FRIEDREICH ATAXIA

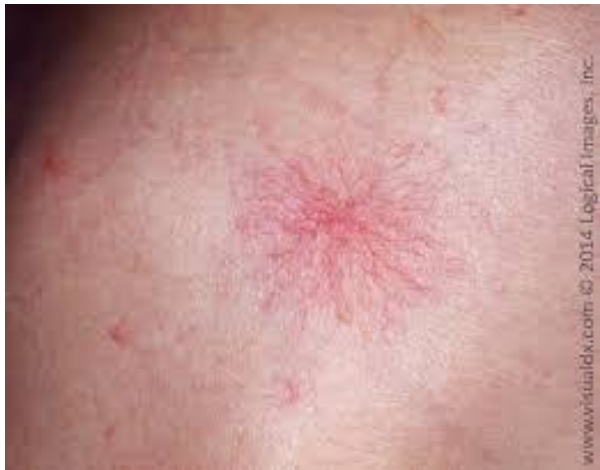
- The most common of the early-onset hereditary spinal ataxias, accounting for at least 50% of these disorders.
- Gene mutation causing abnormal repetition of the DNA sequence GAA in the gene that codes for the mitochondrial protein frataxin
- Autosomal recessive.
- Decreased frataxin levels lead to mitochondrial iron overload and impaired mitochondrial function
- Gait unsteadiness begins between ages 5 and 15; it is followed by upper-extremity ataxia, dysarthria, and paresis, particularly of the lower extremities.
- RELENTLESSLY PROGRESSIVE ATAXIA

FRIEDREICH ATAXIA

- Mental function often declines
- Tremor, if present, is slight
- Lost reflexes and vibration and position senses
- Talipes equinovarus (clubfoot), scoliosis, and progressive cardiomyopathy are common.
- By their late 20s, patients may be confined to a wheelchair
- Cardiomyopathy with abnormal electrocardiogram (ECG) findings is present in most patients
- Death, often due to arrhythmia or heart failure, usually occurs by middle age

ATAXIA TELANGIECTASIA

- Most common cerebellar ataxia of infancy and childhood
- Cerebellar deficits are accompanied by characteristic vascular lesions (telangiectasia) and recurrent pulmonary infections
- First motor symptom is usually truncal ataxia, which is noted when the child first begins to walk, resulting in an awkward, unsteady gait.
- When the child reaches 4 or 5 years of age, the limbs become ataxic and dysarthria may be evident
- For reasons unknown, telangiectasias develop in the skin or conjunctiva of the eye in this disorder



SPINOCEREBELLAR ATAXIAS

- SCAs are the main autosomal dominant ataxias.
- Classification of these ataxias has been revised many times recently as knowledge about genetics increases.
- Currently, at least 43 different gene loci are recognized; about 10 involve expanded DNA sequence repeats.
- Some involve a repetition of the DNA sequence CAG that codes for the amino acid glutamine, similar to that in Huntington disease.

SPINOCEREBELLAR ATAXIAS

- Manifestations vary.
- Some of the most common SCAs affect multiple areas in the central and peripheral nervous systems; neuropathy, pyramidal signs, and restless leg syndrome, as well as ataxia, are common
- Some SCAs usually cause only cerebellar ataxia
- SCA type 3, formerly known as Machado-Joseph disease, may be the most common dominantly inherited SCA worldwide.
- Symptoms include ataxia, parkinsonism, and possibly dystonia, facial twitching, ophthalmoplegia, and peculiar bulging eyes

ACQUIRED CONDITIONS

- Nonhereditary neurodegenerative disorders (e.g., Multiple system atrophy)
- Systemic disorders:
  - Alcoholism (alcoholic cerebellar degeneration)
  - Celiac disease
  - Heatstroke
  - Hypothyroidism
  - Vitamin E deficiency
- Multiple sclerosis
- Cerebellar strokes
- Idiopathic
- Repeated traumatic brain injury
- Toxin exposure: carbon monoxide, heavy metals, lithium, phenytoin, and certain solvents
- Drugs: anticonvulsants
- Primary brain tumors (medulloblastoma, cystic astrocytoma) in children
- Infections

ALCOHOLIC CEREBELLAR DEGENERATION

- Chronic alcoholics frequently develop a condition termed the Wernicke-Korsakoff syndrome
- Wernicke's disease is characterized by oculomotor abnormalities, altered mental status, and ataxia of stance and gait
- Prominent cerebellar dysfunction occurs in about one third of all alcoholics, and is prominent among those with Wernicke's disease
- Stance and gait are primarily affected
- Legs >> arms, trunk

ALCOHOLIC CEREBELLAR DEGENERATION

- Despite the well-known acute affects of alcohol directly on the cerebellum, it is generally thought that the chronic cerebellar syndrome observed in alcoholics is caused by thiamine deficiency rather than toxicity of the alcohol itself
- Almost always malnourished
- Symptoms can be relieved by administration of thiamine

VITAMIN E DEFICIENCY

- Vit E is essential for normal neurologic function
- Severe and prolonged vitamin E deficiency produces spinocerebellar degeneration
- Occurs due to an inherited failure to synthesize apoprotein B, which is necessary for the intestinal absorption of fat
- Extremely low levels of circulating lipids and fat-soluble vitamins
- Present in adolescence with progressive ataxia, areflexia, and proprioceptive loss, reflecting the degeneration of posterior column and spinocerebellar tracts

DEMYELINATING DISORDERS

- Both the spinocerebellar pathways and the cerebellum contain abundant myelin and may be damaged by these types of disorders
- The most common of the demyelinating diseases of the CNS is multiple sclerosis, which is characterized by multisystem demyelination and clinical features encompassing spasticity, visual and oculomotor disturbances, urinary dysfunction, and cerebellar deficits

NEOPLASTIC DISORDERS

- Neoplastic disease, whether located within or near the cerebellum, or at some distant site, can adversely affect cerebellar function.
- Paraneoplastic cerebellar degeneration occurs most often in association with lung, breast, or ovarian cancer or Hodgkin's disease
- Posterior fossa tumors: one third of all intracranial tumors in adults and about two thirds in children
- Tumors of the cerebellopontine angle: acoustic neuromas

VASCULAR DISORDERS

- The cerebellum is supplied by distal branches of the posterior inferior cerebellar artery, the anterior inferior cerebellar artery, and the superior cerebellar artery, all of which are supplied by the basilar artery.
- Ischemic disease and hemorrhage in the posterior fossa seldom give rise to cerebellar signs alone
- Cerebellar deficits are usually accompanied by brainstem and cranial nerve findings, including nausea, vomiting, vertigo, and visual disturbances, which may dominate the clinical picture
- Cerebellar hemorrhage typically manifests as an acute onset of headache, repeated vomiting, vertigo and dizziness, and an inability to walk or stand.
- Coma develops over hours or days in about 50% of these patients

VASCULAR DISORDERS

- In many cases, cerebellar hemorrhage is not suspected until neuroimaging or autopsy
- The typical patient is hypertensive and older than 60 years of age, and frequently has a prior history of transient neurologic symptoms
- Cerebellar infarction is more common than cerebellar hemorrhage, it represents only about 1% of all strokes
- However, has one of the highest mortality rates, estimated to be 20% to 50%
- Cerebellar infarction with edema formation can lead to sudden respiratory arrest due to increased intracranial pressure in the posterior fossa.

INTOXICATIONS

- Toxins, include drugs, solvents, and heavy metals
- Practically all drugs given at high enough doses can cause neurologic signs and symptoms, including those indicating cerebellar dysfunction
- The *drug-induced cerebellar syndrome* is characterized by transient gait ataxia, dysarthria, and nystagmus.
- Symptoms usually subside with discontinuation of the offending agent.
- The most common form of this syndrome is that associated with anticonvulsant medications
- Others include certain cardiac agents, antineoplastic agents, and lithium

INTOXICATIONS

- Volatile solvents found in many products, such as adhesives, solvents, aerosols, and fire extinguishers may cause ataxia along with other neurologic problems, including psychoses, cognitive impairment, and pyramidal signs
- Heavy metals: mercury, manganese, bismuth, thallium, and lead

INFECTIONS

- Both slow and conventional viruses may produce a cerebellar syndrome
- Creutzfeldt-Jakob disease, for example, is an encephalopathy resulting from infection with a so-called slow virus. It is now thought that almost 50% of affected patients may have a cerebellar form of this disease, in which cerebellar deficits dominate the clinical picture for the first several months
- Encephalitis
- Viral cerebellitis: polio, mumps, rubella, chickenpox, and herpes viruses; occurs in young children

INJURY DUE TO PHYSICAL OR MECHANICAL TRAUMA

- Direct mechanical trauma to the head, particularly in the area of the occiput, can produce cerebellar hemorrhage and tissue disruption
- As some patients emerge from the acute phase of closed-head injury, cerebellar deficits may become more prominent.
- Cerebellar dysfunction is known to occur following thermal injury, whether it is due to heat stroke or prolonged fever
- Radiation-induced injury to the cerebellum can result from both therapeutic and accidental exposure to ionizing radiation, manifested as diffuse atrophy and various functional deficits

METABOLIC DISORDERS

- Disorders of lipids, the urea cycle, pyruvate and lactate metabolism, and some aminoacidurias are associated with cerebellar symptoms
- Genetically determined metabolic disorders may give rise to either intermittent bouts of ataxia, due to the accumulation of circulating neurotoxic substances such as ammonia, or to persistent progressive ataxia
- Acquired disturbances of liver function, electrolyte balance (e.g., hyponatremia), and endocrine activity (e.g. hypothyroidism) may also produce cerebellar findings.

DIAGNOSIS

- Diagnosis of cerebellar disorders is clinical and includes a thorough family history and search for acquired systemic disorders
- Neuroimaging, typically MRI, is done
- Genetic testing is done if family history is suggestive

TREATMENT

- Treatment of the cause if possible
- Usually only supportive
- Some systemic disorders (eg, hypothyroidism, celiac disease) and toxin exposure can be treated
- Occasionally, surgery for structural lesions (tumor, hydrocephalus) is beneficial

THANK YOU