Ataxia

► Incoordination (clumsiness) of movements that is *not* the result of muscular weakness

► From Greek αν (used as a negative prefix) + τάξις (order), meaning "lack of order".

Ataxia may be caused by

► Cerebellar disorders
► Sensory disorders
► Vestibular disorders

Cerebellar ataxia

► lesions of the cerebellum or its afferent or efferent connections in
  ▪ the cerebellar pedunes,
  ▪ red nucleus,
  ▪ pons,
  ▪ spinal cord.
Frontal lobe ataxia

- Because of the crossed connection between the frontal cerebral cortex and the cerebellum, unilateral frontal disease can also occasionally mimic a disorder of the contralateral cerebellar hemisphere.
- Involvement of the frontopontocerebellar tract (Arnold's bundle)

Clinical signs of cerebellar dysfunction

- Nystagmus
- Dysarthria:
  - the muscles of voice production and speech lack coordination so that sudden irregular changes in volume and timing occur, i.e. scanning or staccato speech.
- Upper limbs:
  - ataxia and intention tremor, best seen in movement directed towards a restricted target, e.g. the finger–nose test;
  - dysdiadochokinesia, i.e. slow, inaccurate, rapid alternating movements.
- Lower limbs: ataxia → the heel–knee–shin test
- Gait and stance ataxia: heel-to-toe-walk or standing still on one leg
- Hypotonia - is not very useful in clinical practice.

Cerebellar representation is ipsilateral

- A left cerebellar hemisphere lesion will produce
  - nystagmus which is of greater amplitude when the patient looks to the left,
  - ataxia which is more evident in the left limbs,
  - a tendency to deviate or fall to the left when standing or walking.

Clinical patterns of cerebellar ataxia

- Midline
- Superior vermis
- Cerebellar hemisphere
- Pancerebellar
**Midline pattern**

- Lesion in the vermis and flocculonodular lobe and their associated subcortical (fastigial) nuclei
  - control of axial functions, including eye movements, head and trunk posture, stance, and gait.

- **Signs**
  - Nystagmus
  - Head & trunk *titubation* (oscillation of the head and trunk)
  - instability of stance, and gait ataxia

- **Causes**
  - Tumor
  - Multiple sclerosis

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**Superior vermis pattern**

- Selective involvement of the superior cerebellar vermis

- **Signs**
  - Gait ataxia

- **Causes**
  - alcoholic cerebellar degeneration
  - Wernicke’s encephalopathy
  - Tumor
  - Multiple sclerosis

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**Cerebellar hemisphere pattern**

- Cerebellar hemispheres coordinate movement and maintain tone in the ipsilateral limbs and regulate lateral gaze

- **Signs:**
  - Ipsilateral hemiataxia & hypotonia of limbs
  - Nystagmus
  - Transient lateral gaze paresis
  - Dysarthria (with left hemisphere lesions)

- **Causes:**
  - Infarction
  - Hemorrhage
  - Tumor
  - MS

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**Pancerebellar pattern**

- **Signs**
  - Nystagmus
  - Bilateral gaze paresis
  - Bilateral hypotonia
  - Bilateral limb ataxia
  - Gait ataxia

- **Causes**
  - Drug intoxications
  - Hypothyroidism
  - Hereditary cerebellar degeneration
  - Paraneoplastic cerebellar degeneration
  - Infections and parainfectious encephalomyelitis
  - Creutzfeld-Jakob disease
  - MS
Cerebellar ataxia treatment

- Treatment depends on the cause
- No efficacious pharmacologic symptomatic treatment in terms of controlling cerebellar ataxia
  - there are some early reports of a 5-HT1A agonist being of value (buspirone [Buspar, Spamilan])

Causes of cerebellar malfunction

- Common:
  1. drugs, especially anticonvulsant intoxication (phenytoin)
  2. alcohol, acute intoxication
  3. cerebrovascular disease
  4. multiple sclerosis
- Rare:
  1. cerebellar abscess, usually secondary to otitis media;
  2. cerebellar degeneration
    - hereditary (e.g. Friedreich's ataxia and autosomal dominant cerebellar ataxia),
    - alcohol induced
    - paraneoplastic;
  3. Arnold–Chiari malformation (the cerebellum and medulla are displaced unusually low in relation to the foramen magnum);
  4. Wernicke's encephalopathy
  5. Hypothyroidism
  6. Posterior fossa tumors;

Acute drug intoxication

- Pancerebellar syndrome
  - Ethanol
  - Barbiturates
  - Benzodiazepines
  - Meprobamat
  - Anticonvulsants (phenytoin)
  - Hallucinogens (phencyclidine [“angel dust”])
- Associated with a confusional state

Wernicke’s encephalopathy

- acute disorder
- the clinical triad of
  - ataxia,
  - ophthalmoplegia,
  - confusion
- thiamine (vitamin B1) deficiency
  - chronic alcoholics,
  - malnutrition from any cause.
Pathology

The medial thalamic nuclei, mammillary bodies, periaqueductal and periventricular brainstem nuclei (especially those of the oculomotor, abducens, and acoustic nerves), and superior cerebellar vermis.

Ataxia in Wernicke’s encephalopathy

▶ Cerebellar and vestibular involvement
▶ Gait ataxia primarily or exclusively;
  ▪ the legs themselves are ataxic in only about one-fifth of patients, and the arms in one-tenth.
▶ Dysarthria rare.
▶ Amnestic syndrome or global confusional state,
▶ Nystagmus
  ▪ horizontal or combined horizontal-vertical,
▶ Bilateral lateral rectus palsy,
▶ Absent ankle jerks.
▶ Caloric testing reveals bilateral or unilateral vestibular dysfunction.

The diagnosis of WS

▶ Established by the response to administration of thiamine,
  ▪ usually given initially in a dose of 100 mg intravenously.

Recovery from Wernicke’s encephalopathy

▶ Ocular palsies improve first
▶ Ataxia, nystagmus, and acute confusion start to resolve within a few days
▶ Recovery may not be full
Infectious disorders

Fisher Variant of Guillain-Barré Syndrome

- Viral infection
  - St. Louis encephalitis
  - AIDS-dementia complex
  - Meningoencephalitis associated with Varicella, mumps, poliomyelitis, infectious mononucleosis

- Bacterial infection — less common
  - 10-20% cases of brain abscess

Other acute cerebellar disorders

- Vertebral-basilar ischemia

- Cerebellar hemorrhage

Other cerebellar disorders

- MS
- Alcoholic cerebellar degeneration
- Hypothyroidism
- Paraneoplastic cerebellar degeneration
- Friedreich ataxia
- Posterior fossa tumors
- Other
Alcoholic cerebellar degeneration

- in chronic alcoholics,
- result of nutritional deficiency
  - history of daily or binge drinking lasting 10+ yrs with associated dietary inadequacy.
- insidious in onset
- gradually progressive, eventually reaching a stable level of deficit
- No specific treatment
  - quit drinking
  - Thiamine supplementation

Degenerative changes restricted to the superior vermis

Spinocerebellar Ataxias

- Most of the spinocerebellar ataxias are hereditary disorders—i.e., spinocerebellar heredoataxias.
- Start in childhood or adolescence and progress slowly thereafter.
- They present with varying clinical syndromes
  - common manifestations include
  - ataxia,
  - gait impairment,
  - dysarthria,
  - and reflex abnormalities.

Friedreich’s Ataxia

- familial, progressive degeneration of the spinocerebellar and corticospinal tracts and the posterior columns, of *autosomal recessive* inheritance.
- due to an expanded GAA trinucleotide repeat in a *noncoding* region of the *frataxin* gene on chromosome 9.
Friedreich’s Ataxia

- Begins in childhood
- Progressive gait ataxia followed by ataxia of all limbs within 2 years
- Knee & achilles tendon reflexes lost
- Cerebellar dysartria
- Joint position & vibration sense impaired in legs
- Weakness develops later in the course
- Babinski sign appears in first 5 years

Additional features

- Pes cavus
- Kyphoscoliosis (can be severe)
- Cardiomyopathy

Paraneoplastic cerebellar degeneration

- a remote effect of systemic cancer.
- Associated neoplasms
  - Lung cancer (especially small-cell)
  - ovarian cancer,
  - Hodgkin’s disease,
  - and breast
- Pancerebellar syndrome
- The pathogenesis
  - antibodies to tumor cell antigens that cross-react with cerebellar Purkinje cells
    - anti-Yo (ovarian and breast cancer),
    - antinuclear antibodies, such as anti-Hu (small-cell lung cancer)
    - anti-Ri (breast cancer).
- symptoms before or after the diagnosis of systemic cancer and typically develop over months.
- Signs:
  - Gait and limb ataxia
dysarthria
  - the limbs may be affected asymmetrically.
  - Nystagmus rare.
Creutzfeldt-Jakob Disease

- A prion disease that causes dementia
- Cerebellar signs are present in about 60% of patients
- In 10% ataxia is a presenting sign
- There is also dementia, pyramidal and extrapyramidal signs, myoclonus
- Death in the 1st year

Posterior Fossa Tumors

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<th>Type</th>
<th>% of all</th>
<th>% in Adults (≥20)</th>
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<td>Metastases</td>
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<td>56</td>
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<td>Medulloblastoma</td>
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<td>Acoustic neuroma → Cerebello-pontine syndrome</td>
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<td>Hemangioblastoma</td>
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<td>Ependymomas</td>
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Sensory ataxia

- Due to the proprioception (position sense) loss
- Loss of touch sensation
  - Interferes with fine manipulative skills in the hands,
  - With standing and walking in the case of the feet.
- Compensatory use of the eyes (→ Romberg sign)
- Clumsiness and unsteadiness are worse in the dark, or at other times when his eyes are closed,
  - E.g. washing his face, having a shower, whilst putting clothes over his head in dressing.
Polyneuropathy and ataxia

Hemispheric lesion and sensory ataxia

Sensory tracts

Spinal cord disease and ataxia
Signs of SA in upper limbs

► Pseudoathetosis
  ▪ the patient is unable to keep his fingers still in the outstretched position.
  ▪ appears only when the eyes are closed

► Clumsiness of finger movement,
  ▪ e.g. when turning over the pages of a book singly, and when manipulating small objects in the hands, made much worse by eye closure.

Signs of SA in lower limbs

► Marked Rombergism.
  ▪ The patient immediately becomes unsteady in the standing position when the eyes are closed.

► When walking the patient looks at the ground and at his feet.

► Loss of touch and joint position sense in the feet and toes.

Vitamin B₁₂ deficiency

► impaired absorption by the gastrointestinal tract such as occurs in pernicious anemia

► gastrointestinal surgery,

► Sprue

► infection with fish tapeworm;

► strictly vegetarian diet

SCD - course

At onset – weakness and paresthesias of the hands and feet.

vibration and position sense lost

Ataxia of gait.

Weakness gets worse and spasticity of the limbs appears.

Time course vary from weeks to months
Vitamin B\textsubscript{12} deficiency pathology

- Neurologic signs caused by impaired myelin production

Subacute combined degeneration of the spinal cord – myelene lesions

- Posterior funiculus
- Pyramidal tracts

Macrocytic megaloblastic anemia in B\textsubscript{12} deficiency

- May not be present!

- Optic nerve atrophy and centrocecal scotoma
- Peripheral neuropathy
- Behavioral and psychiatric changes

Oval Macrocytes and Hypersegmented Neutrophils in Vitamin B12 Deficiency
**B12 deficiency treatment**

- Treatment with vitamin B12 *im*
  - daily (1000ug) for 2 weeks,
  - then weekly 100 ug for 2 months
  - Then 100 ug monthly

**Polyneuropathies**

- Involving thick myelinated sensory fibers
  - Diabetes
  - Paraneoplastic sensory neuropathy
  - Immune-mediated PN
  - Taxol
  - Pyridoxine
  - Isoniasid

**Myelopathy involving posterior columns**

- Acute transverse myelitis
- AIDS
- MS
- Compresion due to
  - Tumor
  - Spondylosis (ostheophits)
- Vascular malformations

**Spinal stenosis &spinal cord compression**
Tabes dorsalis

- Fibrosis & Inflammation
  - Posterior roots & meninges
  - Especially lumbosacral
- Sensory ganglia: Degeneration of neurons
- Posterior columns of spinal cord: Axonal loss

Onset

- 10 to 30 years after initial, often untreated, infection
- May occur in adults or children

Clinical features I

- Lightning pains:
  - Especially lower extremity & abdomen
- Sensory
  - Joint position & Vibration sense: Reduced
- Hitzig zones
  - Regions of reduced sensation
  - Locations: Central face; Nipples; Ulnar forearms; Peroneal legs
- Analgesia:
  - Leads to painless ulcers & Joint damage (Charcot's joints - Neurogenic osteoarthropathy)

Clinical features II

- Hyporeflexia
- Pupil disorder:
  - Argyll Robertson pupils Irregular (Light: Poor contraction; Accomodation: Good contraction)
- Autonomic:
  - Impotence; blader dysfunction (flaccid bladder)
- Optic atrophy
- Systemic: Aortitis
Testing

► Serum
  ▪ USR – unheated reagin test
  ▪ Microhemagglutination assay (MHA-TP) positive;
  ▪ VDRL may be normal
► Also test for HIV!
► CSF
  ▪ Early & Active disease
    ► Cells: 10 to 200/µl
    ► Protein: ~100 mg/dl
    ► IgG: High
  ▪ Late: May be normal

Treatment

► Penicillin for active neurosyphilis

Ataxia in vestibular disease

► Vestibular inputs are vital to cerebellar function,
► disorders of the vestibular system can produce ataxia, especially of gait.

► recognized by
  ▪ the presence of prominent vestibular symptoms and signs like vertigo and rotatory nystagmus
  ▪ by the absence of other cerebellar, brainstem and sensory signs
► acute and unilateral
  ▪ associated with prominent vertigo, nausea and vomiting.
► In slow-onset, chronic bilateral cases of vestibular dysfunction,
  ▪ Above characteristic manifestations may be absent,
  ▪ and dysequilibrium may be the sole presentation.
**Ataxia in frontal lobe lesion**

- Due to lesion of cortico-cerebellar tracts (eg. Fronto-ponto-cerebellar tract)
- Ataxic gait (frontal lobe gait)
  - Neoplasms of frontal lobe
  - Anterior cerebral artery syndrome
  - Hydrocephalus
    - Gait ataxia +
    - Memory disturbance
    - Urinary incontinence
- Frontal release signs (deliberation signs)

**Subcortical lesions**

- Status lacunaris (lacuna state)
  - Multiinfarct
  - Ataxia
  - Emotional instability
  - Increased jaw reflex & other reflexes
- Ataxic hemiparesis
  - Lacunar stroke of internal capsule or pons