

NYSTAGMUS

Nystagmus describes a pattern of eye movements in which the eyes move to and fro, usually with alternating Slow and Fast phases. Nystagmus occurs normally in some conditions, but may also reflect a pathological condition. We name Nystagmus according to the direction of the fast phase (e.g. “jerk left”) because it is most visible. The key to understanding Pathological Nystagmus is the characteristics of the slow phase. Usually, the fast phase is a corrective movement which responds to the error accumulated during the slow phase. The slow phase thus indicates a problem with a Gaze Holding mechanism, usually either the Neural Integrator or the Vestibular System.

Normally Occuring Nystagmus

OptoKinetic Nystagmus (OKN) occurs during continuous motion of visual field.

OptoKinetic AfterNystagmus (OKAN) occurs after prolonged OKN.

Vestibular Nystagmus occurs during continuous head rotation in one direction.

Vestibular AfterNystagmus occurs after prolonged head rotation stops.

End-Point Nystagmus occurs in some individuals during attempts at extreme gaze positions.

Physiological Nystagmus refers to the small drifts and saccades which everyone makes during steady fixation. These movements occur in all directions, so it doesn't really resemble the other forms of nystagmus in which there is a drift in one particular direction and saccades in the opposite direction.

Pathological Nystagmus:

A variety of conditions can produce Nystagmus. Some forms of Nystagmus are well understood, some are ideopathic.

Gaze Evoked Nystagmus

Although normals may show nystagmus with extreme gaze deviations, in some cases a pathology can cause significant nystagmus with only moderate deviations. This form of nystagmus is associated with a deficiency in the Neural Integrator, which generates the constant firing rate needed to hold the eye in an eccentric posture. For Horizontal Gaze, this is the **Nucleus Prepositus Hypoglossi**. For Vertical Gaze, this is the **Interstitial Nucleus of Cajal**. Lesions of the **Cerebellum** can produce Gaze-Evoked Nystagmus in any direction, because the Cerebellum is involved in adjusting the gain of the step component of saccades.

Characteristics of Gaze Evoked Nystagmus:

Slow phase usually shows a decelerating profile. (For each cycle of Nystagmus, slow phase velocity is highest as gaze slips away from the desired gaze point and gets lower as gaze gets closer to primary until the point at which a return saccade is generated.)

Slow phase is always toward primary position.

Prolonged attempts to deviate gaze will often show a reduction in nystagmus amplitude.

When the patient then returns gaze to primary position, there may be a **Rebound Nystagmus** with fast phase in the opposite direction.

Vestibular Nystagmus:

When an imbalance exists in the vestibular system, the eyes behave as if the head were constantly rotating. The waveform is characterized by a constant velocity smooth phase and a jerk (saccadic) return. Often the nystagmus is made worse by sudden changes in head position.

Vestibular Nystagmus usually follows **Alexander's Law**, which states that the amplitude of Nystagmus is highest when gaze deviates in the direction of the fast phase. Thus, a downbeat nystagmus is biggest in downward gaze. This is most likely due to a combination of Vestibular Nystagmus and Gaze Evoked Nystagmus, as the oculomotor system uses adaptive control to produce

a Null point. If the Neural Integrator is allowed to “Leak” then the slip toward primary gaze will counteract the constant Vestibular pull.

If a Nystagmus only occurs in deviated gaze positions, it is referred to as a **first degree**, if it also occurs in primary gaze it is called **second degree**, and if it occurs in all positions of gaze it is **third degree**.

Vestibular Nystagmus can be further divided into **Peripheral** and **Central** types, based on the site of the lesion causing it.

Peripheral Vestibular Nystagmus is due to dysfunction of one or more of the semicircular canals or the peripheral nervous system which sends their signals to the brainstem.

Characteristics of Peripheral Vestibular Nystagmus

- usually has a mixture of horizontal and torsional components, not usually vertical. Extremely rare to get a pure vertical or torsional nystagmus from peripheral lesions.
- is suppressed by fixation.
- shows normal or low VOR gain, but not high VOR gain.
- has no associated abnormality in pursuits and saccades.

Central Vestibular Nystagmus is due to dysfunction in the brainstem or Cerebellar regions serving the VOR. It sometimes is indistinguishable from Peripheral Vestibular Nystagmus, but usually has distinguishing characteristics.

Characteristics of Central Vestibular Nystagmus

- Can sometimes show pure vertical, horizontal or torsional components.
- usually is not well suppressed by fixation.
- can show abnormally high VOR gain, as well as low or normal.
- often has an associated smooth pursuit abnormality.

See - Saw Nystagmus

This is an acquired, pendular form of nystagmus in which there is a combination of vertical and torsional oscillation. As one eye elevates and intorts, the other eye depresses and extorts.

Exact cause is not known, but it is usually associated with visual loss at the level of the optic chiasm (e.g. parasellar tumor). One theory is that the loss of vision to the Cerebellum leads to an inappropriate Ocular Tilt reaction due to problems in otolith signal processing.

A rare congenital form of See-Saw Nystagmus has the torsion in the opposite direction.

Periodic Alternating Nystagmus

In some patients with Vestibular Nystagmus, the direction of the nystagmus reverses every 2 minutes. During the period when the direction is switching, there may be no nystagmus or a slight DownBeat Nystagmus. This condition is easily missed if the patient isn't observed for several minutes.

PAN is usually suppressed by fixation, so it shows up more in darkness, or with fogging lenses (e.g. Fresnel Goggles) or after a loss of vision. If vision is restored, usually the nystagmus will disappear.

The direction of Nystagmus in primary gaze is reversing because the Null Point is shifting.

Current theory is that the reversal reflects the attempt by the normal adaptive control mechanisms to correct an imbalance in the vestibular system, so the time course is due to a very long feedback loop.

Congenital Nystagmus:

Some individuals show a fairly constant Nystagmus from early in life, without a known cause. It is associated with a number of visual abnormalities, particularly **albinism**, but also aniridia and congenital achromatopsia among others. Since albinism has been linked to miswiring in the visual

system, it has been suggested that this may be the cause of Congenital Nystagmus. No specific area of the oculomotor control system has been identified yet as the site of the miswiring.

Characteristics of Congenital Nystagmus

Can be **jerk** form or **pendular** (slow in both directions, like a pendulum)

Almost always is a combination of horizontal and torsional movement, with torsion **not** following Listing's Law.

Develops in first few weeks of life, with some change of waveform through the first months.

Has a **Null Point** where amplitude is minimized. Often patients will have a head turn to allow their gaze direction to coincide with the Null.

Often increased by stress or visual effort (e.g. reading an eye chart).

Jerk forms usually show an accelerating slow phase.

Response to OKN drum is often inverted, with fast phase in direction of drum. The cause of this is not well understood, but it is diagnostic of Congenital Nystagmus.

Often reduced by convergence. If convergence reduces the Nystagmus significantly, some patients will become Esotropic. This is sometimes called **Nystagmus Blocking Syndrome**, because the Esotropia reflects an attempt to block the Nystagmus at the expense of binocularity.

Vision in Congenital Nystagmus:

Visual acuity depends principally on the Foveation Periods in CN: the phase in which the eye has relatively small position error and relatively low slip velocity. Visual acuity can be normal, even in the presence of large amplitude nystagmus, if the Foveation Periods are reasonably long (>50ms). Conversely, a small nystagmus can disrupt acuity substantially if there are no Foveation Periods at all.

Oscillopsia is a condition in which the world seems to be moving during eye movements. When normal subjects make voluntary nystagmus, they almost always experience oscillopsia.

Congenital Nystagmus patients rarely experience oscillopsia, perhaps because they are simply insensitive to motion or perhaps because they are compensating somehow.

Treatment of Congenital Nystagmus:

There are no pharmaceutical or surgical treatments that are effective in alleviating Congenital Nystagmus. In some cases, surgery (**Kestenbaum Procedure**) may be used to realign the null point to primary gaze by resecting extraocular muscles. Prisms can be prescribed to align forward gaze with the Null point or to allow convergence without diplopia so that the amplitude of the nystagmus is reduced. In addition, Biofeedback can be used to teach patients to reduce the amplitude and increase the foveation periods.

Latent Nystagmus

This was discussed previously in the context of OKN asymmetries. Latent Nystagmus is one part of **Infantile Squint Syndrome**, a collection of eye movement abnormalities associated with Infantile Esotropia. In Latent Nystagmus, when either eye is covered, both eyes show slow phase drift toward the covered eye. With both eyes viewing, there is no nystagmus, or very small amplitude nystagmus. If vision in one eye is suppressed, the nystagmus may appear with binocular viewing, referred to as **Manifest Latent Nystagmus**.

Latent Nystagmus follows Alexander's Law and sometimes produces a head turn so that the non-amblyopic or dominant eye is adducted.

In addition to Latent Nystagmus, the Infantile Squint Syndrome includes **Dissociated Vertical Deviation**. In this condition, when either eye is covered the covered eye drifts upward while the viewing eye remains fixed. When the deviated eye is uncovered, it returns to primary gaze with a single downward saccade.

The third component to the syndrome is an **asymmetry in monocular OKN** responses, such that OKN is more robust for movement toward the nose than away.

GENERALIZED DISORDERS AFFECTING OCULAR MOTILITY

Neuromuscular Junction Disorders

Some diseases which weaken muscles can give oculomotor symptoms similar to those associated with brainstem disease. The most common of these is Myasthenia Gravis.

Myasthenia Gravis is a disease in which the immune system generates antibodies to Acetylcholine receptors, reducing their number and thereby reducing the effectiveness of the neuromuscular junction.

Oculomotor signs are often the first indication of Myasthenia, with involvement of the levator palpebrae and extraocular muscles. These muscles may be affected together, or in isolation. Symptoms may include

- ptosis, due to levator weakness
- exotropia, due to medial rectus weakness
- very rapid but hypometric saccades, due to mid-saccadic fatigue
- “Peek” sign, due to fatigue of the Orbicularis Oculi.

Myasthenia can mimic a variety of brainstem disorders, but has certain unique features which occasionally show up: Superfast Saccades, and simultaneous involvement of extraocular, levator and orbicularis muscles.

Finally, administration of Tensilon (a short acting anti-Cholinesterase, blocking the enzyme which normally breaks down Ach) will temporarily reverse the symptoms, confirming the diagnosis of Myasthenia.

Treatment of Myasthenia involves drugs to block Cholinesterase activity, surgical removal of thymus gland to reduce immune response, or addition of a lid crutch on spectacles to reduce ptosis.

Sympathetic/ Parasympathetic Disorders:

Disorders affecting either the Sympathetic or Parasympathetic Nervous Systems can have effects on the pupils, lenses and lids, in isolation or in combination.

EX: **Horner’s Syndrome**: This is a loss of sympathetic innervation to the eye, caused by damage at central levels (e.g. Hypothalamus), ganglion levels or in the nerve itself. It can be unilateral or bilateral. Horner’s Syndrome is often the first sign of a malignant tumor, and so early diagnosis is important.

The most prominent symptom is a pupil which constricts normally under bright light or near viewing, but won’t dilate or dilates slowly to dim light or emotional stimulation.

A secondary symptom is slight ptosis caused by denervation of Muller’s Muscle, a smooth muscle which works to maintain lid elevation. Muller’s Muscle plays a minor role, and the ptosis is often hard to detect.

Another symptom is an increase in accommodative amplitude such that the near point is “1-4 cm closer” (an increase of 2 or more diopters?). This could be due to loss of Sympathetic inhibition of accommodation, but also consider that depth of field may be greater with a smaller pupil.

Synkinesis Disorders:

These occur when the normal pattern of innervation is disrupted, and a single nerve innervates normally distinct muscles. This can be acquired, in which case it is called **aberrant regeneration**. A variety of congenital conditions exist which are due to misdirected innervation.

Duane’s Retraction Syndrome

This is a condition in which the abducens nerve is virtually absent and the lateral rectus muscle is innervated instead by the oculomotor nerve. The problem is bilateral in only 15-20% of cases. It is

either genetic or may be acquired during the 2nd month of gestation when the oculomotor nerves are developing.

Basic symptoms are a paralysis of horizontal gaze on the affected side. Abduction is often completely absent, and adduction may be limited. When patients try to adduct the affected eye, there is a retraction of the globe due to simultaneous innervation of the lateral and medial rectus muscles.

Marcus-Gunn Jaw Winking phenomenon

This congenital condition results from a synkinesis of the levator portion of the oculomotor nerve and the trigeminal nerve. The levator is partially innervated by the trigeminal nerve, so that effort to move the jaw or stick out the tongue causes the lid to elevate.

Degenerative diseases of the Midbrain.

A variety of diseases which affect the midbrain show oculomotor signs, particularly in vertical gaze control. Some conditions are treatable, such as **Whipple's disease**, while others are not.

Progressive Supranuclear Palsy is a degenerative disorder affecting the Midbrain particularly. Symptoms include

Vertical Gaze palsy, particularly downgaze, leading eventually to total ophthalmoplegia.

Insufficiency of eye opening (levator apraxia)

difficulty with swallowing and speech

mental slowing (subcortical Dementia)

stiff neck (nuchal dystonia)

poor posture control

Oculomotor signs are often among the first to appear, with patient complaints hinting at difficulty with downgaze (reading, descending stairs, eating.) Even in advanced cases, the VOR will be intact, localizing the deficit to a supranuclear gaze control site. The stiffness of the neck may make this diagnosis difficult.

Diseases of the Cerebellum:

The **Cerebellum** plays a crucial role in coordinating movement and particularly in adjusting the gain of eye movements in response to visual feedback. Some Cerebellar dysfunction may be congenital, such as Chiari Malformation, others may be acquired as by stroke, for example.

The oculomotor areas of the Cerebellum are partitioned into (a) the dorsal vermis and fastigial nuclei, which control saccade accuracy, and (b) the "vestibulo-cerebellum" (flocculus, paraflocculus, nodulus and uvula) which affect smooth pursuit, OKN and VOR. Lesions or diseases of the cerebellum can affect almost every category of eye movement, but particularly look for gaze instability, saccade dysmetria, and high gain in the pursuit, VOR or saccadic system.

Diseases of the Basal Ganglia.

The **Basal Ganglia**- The Striatum (caudate, putamen) and the Substantia Nigra play an important role in communicating cortical saccade control to the Superior Colliculus.

Huntington's Disease (aka HD, or Huntington's Chorea) is an inherited disorder which particularly affects the basal ganglia, particularly the corpus striatum, but can also affect the cortex, brainstem and cerebellum. Symptoms are a progressive motor disturbance, including chorea (jerky, involuntary movements) and eventually dementia, usually appearing first between ages 30 to 50. Every aspect of motor behavior is eventually affected and patients usually end up institutionalized for many years. Death often comes from pneumonia, because patients cannot cough effectively to clear their lungs.

Patients with HD show an inability to initiate saccades, particularly to remembered or imagined targets. Often they will use blinks and head turns to aid voluntary saccades. They also show excessive distractibility, in that they have difficulty holding fixation without making saccades to peripheral

targets. Sometimes they show slow saccades, as well. Often their chorea will include the orbicularis muscle, resulting in blepharospasm.

Parkinson's Disease also affects the basal ganglia, particularly the substantia nigra. Major symptoms include tremor, particularly in the hands, rigidity and postural instability.

The effects on the oculomotor system are similar to HD, with difficulty initiating movement and particularly with vertical gaze. Head/eye coordination is also impaired and lid control may be sluggish.

Parkinson's Disease, Huntington's Disease and Progressive Supranuclear Palsy have many oculomotor signs in common, and it may be difficult to differentiate them based on eye signs alone.