

Involuntary Eye Movement Oscillations

Rhythmic or arrhythmic involuntary sustained and/or oscillations of the eyes are classified as either nystagmus or saccadic (rapid conjugate eye movements) oscillations. There is an important distinction between them. Saccadic oscillations are initiated by saccadic eye movements, whereas in nystagmus the oscillations are initiated by smooth eye drifts and the fast phase in jerk nystagmus is corrective and not primary (Table 1) (Figure 1). This short review will describe the commonest types of these ocular oscillations, their causation and management^{1,2,3,4}.

Nystagmus

Nystagmus is an oscillation initiated by a slow drift of the eye. This drift may be sinusoidal (pendular nystagmus) or be followed by a fast corrective (saccadic) eye movement (jerk nystagmus). Although the direction of the nystagmus is conventionally described by the direction of its quick phases (for example upbeat nystagmus) it is important to remember that it is the smooth eye movement imbalance which reflects the underlying disorder (Table 2). Nystagmus usually results from a disturbance in one of the three mechanisms which hold gaze still – visual fixation, vestibulo-ocular reflex and the eccentric gaze holding mechanism⁵.

The commonest form of jerk nystagmus is *peripheral vestibular nystagmus*, which most frequently results from labyrinth or vestibular nerve dysfunction. Tonic vestibular input from the intact side is unopposed by input from the affected side causing drift of the eyes to that side. This type of nystagmus is usually mixed i.e. various combinations of horizontal, vertical and torsional components; it is always unidirectional, the quick phases beating away from the underactive labyrinth; its intensity increases when the eyes are turned in the direction of the quick phases; it is markedly suppressed by visual fixation (by using Frenzel goggles); it is usually accompanied by vertigo, which is of limited duration due to central compensation. If nystagmus persists for more than a few weeks, it is usually due to an abnormality of the central vestibular pathways. Treatment with diphenhydramine, promethazine, or prochlorperazine is appropriate for relief of the accompanying nausea and should be stopped as soon as possible since they can impair the normal compensatory mechanisms.

Several different types of *central vestibular nystagmus* are described, all of which show no change in intensity with the removal of visual fixation in contrast to peripheral vestibular nystagmus. *Downbeat nystagmus* may or may not be present in the primary position. It beats directly downwards and is often accentuated in lateral gaze. When present in the primary position a disturbance of the vestibulocerebellum, drug intoxication or an abnormality at the cranio-cervical junction, such as a Type 1 Chiari malformation, are usually found⁶. These causes include cerebellar degenerations, anticonvulsant drugs, lithium intoxication and intra-axial brainstem lesions. In about half of the patients with downbeat nystagmus, no cause can be found. Treatment can be attempted with clonazepam, baclofen, trihexyphenidyl or acetazolamide for the nystagmus associated with episodic ataxia type II^{7,8}.

Upbeat nystagmus when present in the primary position, is usually associated with focal brain-stem lesions in the tegmental gray matter, either at the pontomesencephalic junction or at the pontomedullary junction, involving the nucleus prepositus hypoglossi or the ventral

tegmental pathway of the upward vestibulo-ocular reflex. Multiple sclerosis, tumour, infarction and cerebellar degeneration are the commonest causes⁹. This type of nystagmus is occasionally suppressed by clonazepam.

Torsional nystagmus is a jerk nystagmus around the anteroposterior axis. It is commonly associated with other types of nystagmus. However, when it is pure it indicates a lesion of the lateral medulla, involving the vestibular nuclei. Occasionally it may be due to a midbrain-thalamic lesion, involving the interstitial nucleus of Cajal (INC.)

Gaze-evoked nystagmus is a common clinical observation with limited localising value. It is a jerk nystagmus which is absent in the primary position and is only present on eccentric gaze. It is due to abnormal functioning of the gaze-holding integrator neurons in the paramedian pontine reticular formation (PPRF) region, resulting from impaired inputs from the cerebellar flocculus. Bilateral horizontal, together with vertical, gaze-evoked nystagmus commonly occurs with structural brainstem and cerebellar lesions, diffuse metabolic disorders and drug intoxication. Treatment is not required since this type of nystagmus rarely causes severe visual problems.

Periodic alternating nystagmus (PAN) is a primary position horizontal nystagmus that changes direction in a crescendo-decrescendo manner, characteristically approximately every 90 sec. Between each directional change there is a null period of 0 to 10 sec. It is usually associated with lesions affecting the nodulus or uvula of the cerebellum. There is a congenital form¹⁰, and acquired forms are due to Chiari malformations, multiple sclerosis, fourth ventricle tumours, spinocerebellar degenerations and anticonvulsant intoxication. Baclofen has been shown to be an effective treatment for the acquired form¹¹.



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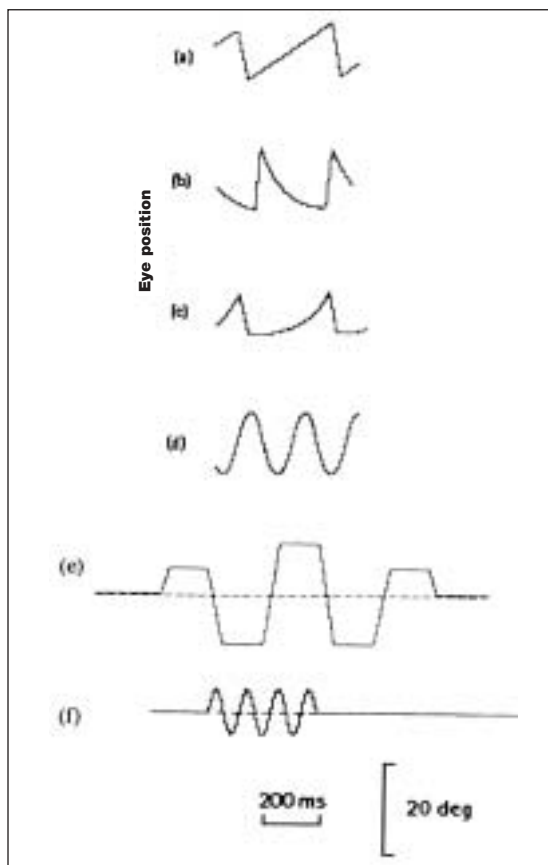


Figure 1. Wave forms and saccadic oscillations of nystagmus. (a) Constant velocity drift of the eyes. This occurs in nystagmus caused by peripheral or central vestibular disease and also with lesions of the cerebral hemispheres. The added quick phases give a sawtooth appearance. (b) Drift of the eyes back from an eccentric orbital position toward the midline (gaze-evoked nystagmus). The drift shows a negative exponential time-course with decreasing velocity. This waveform reflects an unsustained eye position signal caused by an impaired neural integrator. (c) Drift of the eyes away from the primary position with a positive exponential time-course (increasing velocity). This waveform suggests an unstable neural integrator and is encountered horizontally in congenital nystagmus and vertically in cerebellar disease. (d) Pendular nystagmus, which is encountered as a type of congenital nystagmus and with acquired disease. (e) Macro-saccadic oscillations: hypermetric saccades about the position of the target. (f) Ocular flutter: to-and-fro, back-to-back saccades without an intersaccadic interval. (Redrawn from Leigh and Zee. *The Neurology of Eye Movements*. Oxford University Press, 1999²⁸).

Pendular nystagmus is either congenital or acquired due to cerebellar and brainstem disease, usually multiple sclerosis¹². Acquired pendular nystagmus may have both horizontal and vertical components, and the amplitude and phase relationships of the two sinewaves determine the trajectory of the eyes e.g. oblique, circular or elliptical¹³. It can affect one eye or both, equally or unequally, and is often symptomatic resulting in oscillopsia. It may be associated with oscillations of other structures such as the palate, head or limbs¹⁴. In some patients gabapentin or memantine may reduce the amplitude of nystagmus and relieve oscillopsia¹⁵.

Congenital nystagmus is almost invariably a horizontal conjugate nystagmus, which is unaltered by vertical position. It is generally of jerk type with accelerating slow phases, and has an eccentric null position often leading to a head turn or occasionally a head oscillation¹⁶. Fixation effort enhances congenital nystagmus. Less commonly the nystagmus is of a pendular type. Reversed optokinetic nystagmus, beating in the direction of the target motion, is a feature of congenital nystagmus¹⁷.

Latent nystagmus is a type of congenital nystagmus that is only present on monocular viewing and which then beats toward the viewing eye¹⁸. It is absent on binocular viewing. If the patient has amblyopia in one eye latent nystagmus is present with both eyes viewing, when it is called manifest latent nystagmus.

Saccadic oscillations

Saccadic oscillations are bursts of saccades, which may be intermittent or continuous, causing a disruption of fixation. Two main types can be identified, those with brief periods of fixation between saccades (intersaccadic interval approximately 200 msec) and those composed of back-to-back saccades (Table 3).

The oscillations with intersaccadic intervals include square wave oscillations consisting of sequences of square wave jerks (SWJ), which can occur in Alzheimer's disease and progressive supranuclear palsy. *Macrosaccadic oscillations* (up to 40 deg) straddle the intended fixation position and show a crescendo-decrescendo pattern. This type of oscillation is usually observed in acute damage to the dorsal cerebellum involving the deep cerebellar nuclei, as in demyelination, tumour or haematoma¹⁹.

Table 1 – Definitions of types of ocular oscillation

Nystagmus – a sustained to and fro oscillation initiated by a smooth eye movement

Saccadic oscillations – sustained oscillations initiated by fast (saccadic) eye movements

Table 2 - Types of nystagmus and their mechanism

Impaired vestibulo-ocular reflex
 Peripheral vestibular
 Central vestibular – downbeat, upbeat, torsional, periodic alternating nystagmus

Impaired gaze-holding mechanism
 Gaze-evoked nystagmus

Visual fixation
 Congenital nystagmus
 See-saw nystagmus

Unknown mechanism
 Pendular nystagmus

Oscillations without any intersaccadic interval (back-to-back) include opsoclonus, ocular flutter and convergence-retraction saccadic pulses. *Opsoclonus* consists of multidirectional (including oblique and torsional) back-to-back saccades of varying amplitude. It has been suggested that the disorder arises due to disordered pause cell function in the PPRF²⁰. A variety of posterior fossa disorders can give rise to the condition, including parainfectious brain stem encephalitis, metabolic-toxic states or as a paraneoplastic (non-metastatic) disorder; in children it is associated with occult neuroblastoma and in adults with small cell carcinoma of the lung and carcinoma of the breast and uterus^{22,23}. Both anti-Ri and anti-Hu antibodies have been identified in paraneoplastic opsoclonus in adults. It can also occur in neonates associated with myoclonus - 'dancing eyes and dancing feet.'²⁴ This appears to be a maturational deficit which usually resolves over approximately 6 weeks. Treatment may be with plasmapheresis or intravenous immunoglobulins²¹ and drug treatments have included corticosteroids, propranolol, verapamil, clonazepam and gabapentin. *Ocular flutter* consists of bursts of back-to-back saccades in the horizontal plane only, observed in patients with multiple sclerosis and signs of cerebellar disease²⁵. It can also be observed in patients recovering from opsoclonus. A voluntary form of flutter (voluntary flutter) can be induced by about 8% of the population, usually by convergence. It consists of salvoes of horizontal back-to-back saccades. Lesions of the dorsal midbrain are often associated with upward gaze palsies and *convergence-retraction nystagmus* (Parinaud's syndrome). This is incorrectly termed a nystagmus since it actually consists of asynchronous adducting saccades and should be redesignated convergence-retraction saccadic pulses²⁶. It may alternatively be due to opposed vergence movements²⁷.

References

1. Kaminski HJ and Leigh RJ. (2002) *The neurobiology of eye movements: from molecules to behaviour*. Ann NY Acad Sci 956: 1-615.
2. Leigh RJ and Zee DS. (1999) *The neurology of eye movements*. New York: Oxford University Press.
3. Buttner U and Fuhry L. (1999) *Drug therapy of nystagmus and saccadic intrusions*. Adv Otorhinolaryngol 55: 195-227.
4. Leigh RJ and Tomsak RL. (2003) *Drug treatments for eye movement disorders*. J Neurol Neurosurg Psychiatry 74: 1-4.
5. Serra A and Leigh RJ. (2002) *Diagnostic value of nystagmus: spontaneous and induced ocular oscillations*. J Neurol Neurosurg Psychiatry 73: 615-618.
6. Halmagyi GM, Rudge P, Gresty MA, and Sanders MD. (1983) *Downbeating nystagmus. A review of 62 cases*. Arch Neurol 40: 777-784.
7. Averbuch-Heller L, Tusa RJ, Fuhry L, Rottach KG, Ganser GL, Heide W, Buttner U, and Leigh RJ. (1997) *A double-blind controlled study of gabapentin and baclofen as treatment for acquired nystagmus*. Ann Neurol 41: 818-825.

Table 3 – Types of saccadic oscillations

1. With an intersaccadic interval
 Square wave oscillation
 Macrosaccadic oscillation
 Convergence-retraction pulses (nystagmus)
 Ocular bobbing
2. Back-to-back saccades
 Opsoclonus
 Ocular flutter
 Voluntary flutter (nystagmus)

8. Barton JJ, Huaman AG, and Sharpe JA. (1994) *Muscarinic antagonists in the treatment of acquired pendular and downbeat nystagmus: a double-blind, randomised trial of three intravenous drugs*. *Ann Neurol* 35: 319-325.
9. Fisher A, Gresty M, Chambers B, and Rudge P. (1983) *Primary position upbeating nystagmus. A variety of central positional nystagmus*. *Brain* 106 (Pt 4): 949-964.
10. Gradstein L, Reinecke RD, Wizov SS, and Goldstein HP. (1997) *Congenital periodic alternating nystagmus. Diagnosis and Management*. *Ophthalmology* 104: 918-928; discussion 928-919.
11. Halmagyi GM, Rudge P, Gresty MA, Leigh RJ, and Zee DS. (1980) *Treatment of periodic alternating nystagmus*. *Ann Neurol* 8: 609-611.
12. Lopez LI, Bronstein AM, Gresty MA, Du Boulay EP, and Rudge P. (1996) *Clinical and MRI correlates in 27 patients with acquired pendular nystagmus*. *Brain* 119 (Pt 2): 465-472.
13. Averbuch-Heller L, Zivotofsky AZ, Das VE, DiScenna AO, and Leigh RJ. (1995) *Investigations of the pathogenesis of acquired pendular nystagmus*. *Brain* 118 (Pt 2): 369-378.
14. Schwartz MA, Selhorst JB, Ochs AL, Beck RW, Campbell WW, Harris JK, Waters B, and Velasco ME. (1986) *Oculomasticatory myorhythmia: a unique movement disorder occurring in Whipple's disease*. *Ann Neurol* 20: 677-683.
15. Bandini F, Castello E, Mazzella L, Mancardi GL, and Solaro C. (2001) *Gabapentin but not vigabatrin is effective in the treatment of acquired nystagmus in multiple sclerosis: How valid is the GABAergic hypothesis?* *J Neurol Neurosurg Psychiatry* 71: 107-110.
16. Gresty M, Page N, and Barratt H. (1984) *The differential diagnosis of congenital nystagmus*. *J Neurol Neurosurg Psychiatry* 47: 936-942.
17. Halmagyi GM, Gresty MA, and Leech J. (1980) *Reversed optokinetic nystagmus (OKN): mechanism and clinical significance*. *Ann Neurol* 7: 429-435.
18. Gresty MA, Metcalfe T, Timms C, Elston J, Lee J, and Liu C. (1992) *Neurology of latent nystagmus*. *Brain* 115 (Pt 5): 1303-1321.
19. Dell'Osso LF and Daroff RB. *Nystagmus and saccadic intrusions and oscillations*. 1999 In: *Neuro-ophthalmology* (3 ed.), edited by Glaser JS. Philadelphia: Lippincott, Williams & Wilkins, 1999, p. 369-401.
20. Averbuch-Heller L and Remler B. (1996) *Opsoclonus*. *Semin Neurol* 16: 21-26.
21. Bataller L, Graus F, Saiz A, and Vilchez JJ. (2001) *Clinical outcome in adult onset idiopathic or paraneoplastic opsoclonus-myoclonus*. *Brain* 124: 437-443.
22. Hersh B, Dalmau J, Dangond F, Gultekin S, Geller E, and Wen PY. (1994) *Paraneoplastic opsoclonus-myoclonus associated with anti-Hu antibody*. *Neurology* 44: 1754-1755.
23. Luque FA, Furneaux HM, Ferziger R, Rosenblum MK, Wray SH, Schold SC, Jr., Glantz MJ, Jaeckle KA, Biran H, Lesser M, and et al. (1991) *Anti-Ri: an antibody associated with paraneoplastic opsoclonus and breast cancer*. *Ann Neurol* 29: 241-251.
24. Hoyt CS, Mousel DK, and Weber AA. (1980) *Transient supranuclear disturbances of gaze in healthy neonates*. *Am J Ophthalmol* 89: 708-713.
25. Schon F, Hodgson TL, Mort D, and Kennard C. (2001) *Ocular flutter associated with a localised lesion in the paramedian pontine reticular formation*. *Ann Neurol* 50: 413-416.
26. Ochs AL, Stark L, Hoyt WF, and D'Amico D. (1979) *Opposed adducting saccades in convergence-retraction nystagmus: a patient with sylvian aqueduct syndrome*. *Brain* 102: 497-508.
27. Rambold H, Kompf D, and Helmchen C. (2001) *Convergence retraction nystagmus: a disorder of vergence?* *Ann Neurol* 50: 677-681.

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