Nystagmus is an oscillation of one or both eyes. Nystagmus can be a physiological phenomenon such as optokinetic nystagmus (OKN) or induced vestibular nystagmus (which are normal oculomotor responses), or it can be a pathological phenomenon in which the eye(s) oscillate spontaneously. Nystagmus is usually involuntary, although a small percentage of individuals can oscillate their eyes at will (voluntary nystagmus), which is a normal human variation (like ear wiggling). This article describes OKN, with emphasis on its use for assessing visuomotor function from birth.

**Optokinetic nystagmus**

*Professor Chris Harris, PhD*

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**Learning objectives**
Understand the techniques for assessment of vision in infants with Optokinetic Nystagmus (Group 7.1.4)

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**About the author**

After studying physics and optics at Imperial College London, **Chris Harris** obtained his PhD from City University of New York, where he studied the development of human eye movements. In 1989 he set up an eye movement laboratory in Great Ormond Street hospital carrying out research into abnormal oculomotor development. In 2000, he was appointed professor of neuroscience at Plymouth University. He has published over 100 papers in the area and continues research into visual and motor development. He is honorary visiting professor at the School of Optometry and Vision Sciences in Cardiff University, where he collaborates on studies of nystagmus. He is scientific advisor to Nystagmus Network and co-edited their recent book on nystagmus. He teaches many aspects of vision and eye movements including visual perception on the new Plymouth University Optometry Programme.

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OKN was first described in 1823 by Purkinje as a response by spectators to a moving cavalry parade. It is a normal reflexive oscillation of the eyes comprising of cycles of alternating slow phases and quick (fast) phases induced by the movement of the whole or large part of the visual field.

OKN is usually considered as one of the canonical oculomotor subsystems, alongside the vestibulo-ocular reflex (VOR), the saccadic system, smooth pursuit/fixational eye movements, and vergence. However, this classification is questionable as OKN has direct or indirect links with all the other systems, and it is difficult to pinpoint a dedicated OKN circuit in the primate brain.

The natural (and evolutionary) OKN stimulus is the retinal image motion caused by self-motion. Indeed, with full-field immersive stimulus motion, there is a powerful illusion of self-motion (vection) and the stimulus is perceived as stationary. During head rotation, the visual world rotates giving rise to rotational optic flow that is independent of depth. During head translation (as caused by walking, for example) complex patterns of optic flow occur in depth, and depend on the distance of the local visual scene. Rotational and translational flow lead to different OKN responses (OKNd and OKNe). In the laboratory or clinic, however, OKN is induced by large displays of moving stripes, dots, or other patterns usually in the frontal parallel plane with negligible motion in depth. The limited stimulus size is usually insufficient to generate vection.

**OKNd versus OKNe**

All vertebrates with ocular motility (and many non-vertebrates) demonstrate an optokinetic response, but there are two types of OKN: delayed OKN (OKNd) (also known as slow, slow build-up or indirect OKN), and early OKN (OKNe) (also known as fast, fast build-up or direct OKN). OKNd supplements the rotational vestibular system and is seen in afoveate laterally eyed animals such as the rabbit, and has a low gain (gain = stimulus velocity divided by slow phase velocity). It takes seconds to build up to its final gain, with a time-constant similar to the vestibular time-constant, requiring a velocity storage mechanism. Although primates possess an OKNd system, they also have high gain OKNe which is an evolutionary, more recent, system closely allied to (if not the same as) the smooth pursuit system and, in humans, completely dominates OKNd. After stimulus onset, the slow phase OKNe velocity rapidly rises within half a second, but ceases in the dark (unmasking optokinetic nystagmus – OKAN – which is driven by underlying OKNd). In humans, OKNd and OKNe are driven cortically. A direct OKN pathway from the retina to the pretectum (nucleus of the optic tract) as seen in other animals is either weak or non-existent in humans. The OKNe pathway is the same as the smooth pursuit pathway, involving striate and extra-striate cortices with descending connections via the internal capsule to the brainstem pontine nuclei, cerebellum (floccular region), vestibular nuclei and the oculomotor nuclei (Figure 1).

**Figure 1** Simplified schematic to illustrate the different pathways for OKNd and OKNe. NOT = nucleus of the optic tract; VSM = velocity storage mechanism; Flocc = cerebellar flocculus region; VN = vestibular nuclei; VCX = visual cortex; MT/MST = area MT/MST.

Cerebellar lesions involving the floccular region also reduce or eliminate OKNe towards the side of the lesion. However, this is often
associated with spontaneous nystagmus (gaze-evoked and/or downbeat and/or rebound nystagmus), which is distinct from cortical lesions. OKN can be preserved, indicating that it does not involve the floccular region.6,7

Although horizontal OKN has been extensively studied, less is known about vertical OKN. Most studies have reported a vertical asymmetry with higher gain for upward stimulus motion, as seen in other frontally eyed animals.8 Although other studies have reported idiosyncratic or no asymmetry, or velocity dependent asymmetry.9 OKAN has also been reported to have an upward preference.10

‘Stare’ versus ‘look’ OKN

Many investigators have made the distinction between ‘look’ and ‘stare’ OKN. Look OKN is elicited by asking the subject to follow a particular visual feature as it moves through the visual field. In stare OKN the subject is instructed not to follow any feature, but to stare at a region. Look OKN has high gain with few quick phases while stare OKN has lower gain with many quick phases.11 Both are OKNe responses12 and reflect the task at hand, as confirmed by functional MRI.13 Look OKNe is essentially a smooth pursuit task attending to a small visual target, while stare OKNe is equivalent to attending to a region at a fixed distance from the subject (perhaps useful when moving through the world).

Both stare and look OKNe cannot be driven solely by retinal slip because slow phase velocity can often match the stimulus velocity (unity gain) and would eliminate the retinal slip. Target motion in space is required, which is re-constructed with extra-retinal information. Cortical cells in MST with large receptive fields have this property.14

Human adult OKN

Figure 2 shows an excerpt of a typical human horizontal stare OKN eye position record. Here the stimulus was a large grating of vertical black-and-white stripes moving to the subject’s right at a constant speed of 10 deg/s with an abrupt onset. Slow phases represent the period where the eyes are following the stimulus as it moves across the visual field to the right, and are approximately linear.

Figure 2 Typical example of adult OKN showing alternating slow phases and quick phases in response to vertical black and white stripes moving rightward at 10 deg/s. Note: 1) rapid onset of OKN relative to stimulus onset at t=0; 2) variability of slow phase and quick phase amplitude and timing; 3) occasional quick phase in direction of stimulus motion (dot); 4) drift of mean gaze position towards opposite direction of stimulus motion (contraversion).

Figure 3 Infant OKN. (A) OKN recorded using dc-electro-oculography from a 10-week-old infant binocularly viewing a full-field curtain reversing rotation from rightward to leftward rotation at 30 deg/s. Note rapid build-up of OKN (B) The development of monocular OKN. OKN recorded longitudinally (1-6 months) from a healthy infant viewing a full-field curtain with her right eye. Curtain speed was 25 deg/s rightward (nasal-temporal) and -25 deg/s (temporal-nasal). Note poor nasal-temporal response at 1 month. (C): Change in OKN gain with age at 30, 45, 60 deg/s. Note lower nasal-temporal gain and reduction with stimulus speed even at seven months of age.29
(rightward OKN or left beating nystagmus). The build-up is rapid, reflecting OKNe. Quick phases are saccadic eye movements that tend to reset eye position and are mostly in the opposite direction – but not always (see dot). Note that most quick phases are triggered before the eyes have crossed the midline, and there is often a net shift in eye position opposite to the stimulus direction, called ‘contraversions’. The notion that quick-phases prevent the eyes from reaching the gaze limit is a common misconception (probably originated by Walls in 1962). There is much variability in slow phase duration and amplitude, and quick phases do not precisely reset eye position on each cycle. Yet there is little net drift of eye position overall, implying some adaptive corrective mechanism.

**Human OKN development**

OKN is present from birth, as are VOR and saccades (usually). In contrast, smooth pursuit develops post-natally. Only fast build-up OKN has ever been reported (Figure 3a). Infants produce stare OKN, which can be elicited even when there is no response to visual objects and no smooth pursuit movement, as seen in delayed visual maturation. Infants also possess an OKN system as testified by OKAN in the dark.

The discordance between OKN and smooth pursuit development is interesting. It is most extreme in delayed visual maturation. However, lesions of the cortex in infants lead to the same binocular OKN asymmetries as seen in adults, which in adults has similar effect on smooth pursuit. The simplest explanation is that smooth pursuit and OKN have the same pathways, but the former requires attention to small regions of space. Thus, smooth pursuit development reflects the (cortical) development of the ability to track increasingly smaller visual targets, which may involve parietal cortical areas. However, this might also be related to the development of foveal tracking of objects moving in depth requiring the development of binocularity (see below).

**Monocular OKN asymmetry**

Neonates exhibit a striking monocular OKN asymmetry. During monocular viewing, horizontal stimulus motion in the temporal-nasal or ‘nasalward’ direction of the viewing eye (leftward for the right eye, rightward for the left eye) elicits a strong fast build-up OKN response, whereas there is a weak or absent response to nasal-temporal or ‘temporalward’ stimulus motion for the viewing eye (Figure 3b). With both eyes open, there is a strong response in both directions because one eye always experiences temporal-nasal stimulation. During the first few months after birth, there is a rapid development of monocular symmetry, but even by six months there may be residual asymmetry at high speeds (Figure 3c).

A similar asymmetry occurs for monocular smooth pursuit. Studies with motion visual evoked potentials (VEPs) have demonstrated that this asymmetry is sensory. In the dark, OKAN is also asymmetric and, intriguingly, occurs only in the temporal-nasal direction even when the stimulus was nasal-temporal in the light.

The development of nasal-temporal OKN depends on visual experience, and is a prime example of developmental plasticity. In premature infants, the nasal-temporal gain depends on post-natal rather than conceptional age. Infants who experience unequal post-natal visual stimulation (for example strabismus, anisometropia and unilateral cataract), usually have a persistent and irreversible monocular OKN asymmetry which can be detected in adulthood. A similar asymmetry persists for smooth pursuit. Monocular asymmetry is more likely to persist the earlier the visual deficits occur, and affects both eyes for nasal-temporal OKN. Monocular asymmetry may not persist when onset is later, or might only persist in one eye. However, dating strabismus onset by the persistence of monocular OKN asymmetry later in life is not foolproof, since the monocular OKN asymmetry does not preclude early onset (less than six months), although persistent asymmetry strongly suggests that a squint had an early-onset.

The possibility that there may be a causal link between the developments of monocular OKN and stereopsis is a longstanding issue. As most visual functions are developing in the first few months post-natally, spurious correlations can emerge. Indeed the evidence points away from any direct causal relationship. The time course of nasal-temporal OKN and stereopsis developments are quite different. Lack of stereopsis can be associated with a wide range of levels of monocular OKN asymmetry, including symmetry even. Furthermore, in patients with surgery for infantile esotropia, monocular OKN asymmetry persists even though stereopsis has been preserved. Most convincingly, infants with unilateral blindness can have symmetrical monocular OKN. It appears that some kind of motion rivalry, rather than lack of stereopsis, leads to persistent monocular OKN asymmetry.

**Motion in depth**

In real life, objects move in depth as well as in the frontal parallel plane. There are two ways the brain could resolve the velocity of a small region of visual space. One would be to detect the change in positional disparity over time and the other would be to detect the difference in retinal motion from both eyes (interocular velocity difference). When an object moves in depth relative to the eyes, its images will have different velocity vectors in each retina. Provided the geometry of the eyes is known, the 3D velocity vector can be reconstructed precisely from the 2D image motions of each eye. Although mathematically equivalent, they are very different physiologically, since change in positional disparity over time requires...
neurological and/or developmental conditions. Preparedness for serious outcomes with onward referral pathways is essential.

In a clinical setting, the reflexive nature of OKN proves a useful test for some degree of vision in the visually unresponsive infant (or the older patient with functional blindness), but the crucial corollary is that any absence of OKN can be confidently interpreted as pathological, rather than a lack of attention or motivation. To this end, it is important to provide a moving stimulus that is as large as possible. Small hand-held striped drums are not useful in this respect. A large hand-held high-contrast cloth or tape that is manually swept past an infant is useful. Large TV monitors or (front/back) projection systems with pre-recorded or computer generated stimuli are now feasible. The ideal, but technically difficult, stimulus is a full-field rotating patterned drum or curtain that completely surrounds the patient.

The recent advent of numerous commercial video-based eye trackers now makes objective recording of OKN feasible (but the issue of stimulus size is still crucial). In principle, these could be used with infants, provided calibration can be achieved. However, OKN parameters depend on many factors including stimulus velocity and overall size, spatial frequency, contrast sensitivity, monocular/ binocular viewing, alertness, instructions and calibration precision. Also, technical issues are important, such as the recording instrument, sampling frequency, filtering and analysis software. Altogether, quantitative measures require normative data from each installation. Even so, the stochastic nature of OKN and considerable normal individual differences lead to difficulties in establishing useful clinical criteria.

In the infant that has poor or absent behavioural visual responsiveness without spontaneous nystagmus, and which cannot be explained by ophthalmoscopy, the differential diagnoses are delayed visual maturation, cerebral visual impairment, and saccade initiation failure (oculomotor apraxia). OKN is very useful in this context because it is present in delayed visual maturation provided the stimulus is large. It is absent with bilateral cortical damage and present but with missing quick phases in saccade initiation failure (see below). Absent OKN can reflect genuine blindness, but also cortical damage to both hemispheres. Electrophysiology (VEPs and

<table>
<thead>
<tr>
<th>Stimulus direction</th>
<th>Both eyes viewing</th>
<th>Left eye viewing</th>
<th>Right eye viewing</th>
<th>Spontaneous nystagmus</th>
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<tbody>
<tr>
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<td>2 Blindness or no cortical vision</td>
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<td>5 R cortical lesion + MOA</td>
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Table 1 Typical OKN Responses: p strong response; º weak or absent response; ¬ usually absent response. Arrows indicate direction from patient perspective. MOA = monocular OKN asymmetry; R / L GEN right/left beating gaze evoked nystagmus.
electroretinography (ERGs) are therefore useful in distinguishing between these possibilities. Also note that horizontal infantile nystagmus (congenital nystagmus) can completely disrupt horizontal OKN (but not vertical OKN).

Useful information can be gleaned by looking for within-individual asymmetries in OKN, where directional differences (usually leftward vs. rightward) are demonstrable (see Table 1). A cortical lesion affecting the temporo-occipitoparietal region or descending smooth pursuit pathway reduces slow phase velocity (that is, gain) towards the side of the lesion, with a similar effect on smooth pursuit. If the lesion is large, a hemianopic visual field defect might also be present in the contralateral field; for this reason, gross assessment of the visual field by confrontation methods can be useful. Note that OKN is driven in both directions from the intact side via inter-hemispheric connections (corpus callosum).

Monocular OKN asymmetry is present in all very young infants as part of physiological development, but persists with early onset visual disorders such as infantile esotropia (with or without latent nystagmus). Obvious monocular asymmetry after three months of age requires further examination for persistent asymmetry including visual acuity and cover test. Considerable care is needed to disentangle monocular from binocular asymmetries (see Table 1). Both can co-exist at any age, but are more likely in the premature infant with cortical damage (such as periventricular leukomalacia). Also note the further complication that temporal-nasal OKN can be reduced in an amblyopic eye. Cerebellar lesions (especially the flocculus/paraflocculus) also give rise to OKN and smooth pursuit deficits towards the same side. However such deficits are usually accompanied by other cerebellar signs including gaze-evoked, and/or downbeat and rebound nystagmus. Such lesions might also reveal the underlying OKNd with its slow build-up if the stimulus is maintained for some 20 seconds or so. Thus, it is important to identify the type of any underlying spontaneous nystagmus.

Quick Phases
Quick phases have a similar main sequence to saccades (peak velocity versus amplitude and duration versus amplitude relationships), albeit perhaps not identical. Diseases that reduce the speed of saccades also similarly affect quick phases. OKN is also a particularly convenient way to test for saccade speed in infants.

Although most OKN studies have focussed on slow phase gain, quick phases are nevertheless an integral part of stare OKN. Mean quick phase amplitude and beat frequency increase approximately linearly with stimulus velocity. From cycle to cycle, quick phase and slow phase amplitudes may only be weakly correlated, but mean quick phase amplitude is equal and opposite to mean slow phase amplitude, thus keeping mean eye position constant. This process breaks down in children with saccade initiation failure (also known as ‘ocular motor apraxia’ or ‘supranuclear gaze palsy’), who intermittently fail to generate quick phases, thus allowing the eyes to deviate to the mechanical limit of gaze. It is important to recognise that this is not absent OKN, but a failure of quick phases. Saccade initiation failure is associated with a wide range of disorders, but is especially associated with congenital or acquired cerebellar vermis abnormalities. It is often associated with delayed motor development. OKN provides a reliable method for detecting this disorder, even without recording eye movements. A similar phenomenon occurs in adults with progressive supranuclear gaze palsy. Because of the wide clinical associations of saccade initiation failure, beat frequency (OKN cycles per second) is an unreliable measure of afferent vision. The focus must be on slow phase velocity.

Conclusion
Eliciting OKN is a very useful clinical neuro-ophthalmological test because of its reflexive nature and ease of use, particularly in paediatrics. This apparent simplicity, however, hides a highly complex system. OKN depends on many visual parameters including stimulus speed, direction and area, contrast, spatial frequency content, but also depends on the integrity of numerous neural pathways in the brain, particularly extrastriate cortical pathways. Unfortunately, the groups of patients that would benefit most from non-subjective visual assessment are also the most likely to have covert neurological lesions, such as the premature and/or strabismic infant, and the cognitively impaired elderly. In the author’s experience, abnormal OKN usually reflects neurology not ophthalmology.