Chapter 147: Evaluation of Eye Movements in the Diagnosis of Disease of the Vestibular System

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The accurate diagnosis and anatomic localization of the cause of a vestibular disorder usually requires a reliable assessment of general ocular motor function. This is especially necessary because the anatomic substrate underlying the generation of the slow and quick phases of vestibular nystagmus is intertwined with that of other, non-vestibular types of eye movements. This chapter therefore reviews the basic mechanisms underlying the generation of all types of eye movements, including patterns of eye-head coordination, the diagnostic significance of the more common ocular motor abnormalities, including various types of nystagmus, and some simple methods of bedside clinical examination of eye movements.

An approach to understanding eye movements should begin with a classification of eye movement types based on function (Table 147-1). All eye movements serve the needs of our visual sense and are aimed at ensuring optimal visual acuity. Vestibular and optokinetic eye movements work together to keep the image of the world stationary on the retina during head rotation. By producing compensatory slow phases in the orbit that are equal and opposite to head movements, eye position in space (or gaze) can be held constant - and consequently vision is clear - during head rotation. Saccadic, pursuit, and vergence eye movements change gaze so that images of objects of interest are brought to or kept on the fovea, where visual resolution is highest. Saccades rapidly bring onto the fovea the image of an object detected in the periphery; pursuit movements maintain on the fovea the image of an object that is already moving. Vergence movements cause the eyes to move in opposite directions so that the image of an object is placed simultaneously on both foveas.

Ocular Motor Control Signals

To interpret abnormal ocular motility, it is helpful to understand the way the central nervous system normally controls eye movements (Leigh and Zee, 1991). The physician must know the normal patterns of innervation (1) for appropriately moving the eyes so as to change gaze accurately and (2) for holding the eyes steady, to maintain gaze on a stationary object of interest. The major hindrance to rotation of the globe is orbital viscosity because the globe's movement of inertia is relatively small. For rapid eye movements (saccades, quick phases of nystagmus), a powerful contraction of the extraocular muscles is necessary to overcome viscous drag; a phasic increase in the frequency of neural discharge called the *pulse of innervation* accomplishes this. Once the eyes are brought to their new position, they must be held there against the elastic restoring forces of the orbital tissues, which tend to return the globe to its primary position. Preventing this centripetal drift requires a steady contraction of the extraocular muscles, which is produced by a constant, tonic level of neural activity called the *step of innervation.* The ocular motor control signal for saccadic eye movements is thus a pulse-step of innervation (Fig. 147-1). This pattern of activity is reflected in the characteristics of the discharge of both ocular motoneurons and the eye muscles themselves.

The saccadic pulse and step can be considered as eye velocity (phasic) and eye position (tonic) commands, respectively. For other types of conjugate (versional) eye movements (vestibular, optokinetic, pursuit), the ocular motoneurons also discharge according

to velocity and position. Thus all types of versional eye movement commands encode both eye velocity and eye position.

Table 147-1. Functional classes of human eye movements

Class of eye movement	Main function
Visual fixation	Holds the image of a stationary object on the fovea
Vestibular	Holds images of the seen world steady on the retina during brief head rotations
Optokinetic	Holds images of the seen world steady on the retina during sustained head rotations
Smooth pursuit	Holds the image of a moving target on the fovea
Nystagmus (quick phase)	Resets the eyes during prolonged rotation and directs gaze toward the oncoming visual scene
Saccades	Brings images of objects of interest onto the fovea
Vergence	Moves the eyes in opposite directions so that images of a single object are placed simultaneously on both foveas.

The immediate premotor command for the saccadic pulse is generated by burst neurons. For horizontal saccades, these lie within the pontine paramedian reticular formation (PPRF); for vertical saccades, they lie within a portion of the mesencephalon called the *rostral interstitial nucleus of the medial longitudinal fasciculus (riMLF).* Burst neurons discharge at high frequencies beginning just before the saccade and are time-locked to it. They are otherwise silent.

The step of innervation is thought to be created by a neural gaze-holding network, or neural integrator, that integrates (in the mathematic sense) the saccadic eye velocity command to produce the appropriate position-coded information for the ocular motoneurons. The neural integrator for horizontal movements is though to be located in the medial vestibular nucleus (MVN) and the nucleus prepositus hypoglossi (NPH) (Cannon and Robinson, 1987). The neural integrator for vertical eye movements probably includes NPH and MVN as well as the interstitial nucleus of Cajal (INC) (Fukushima et al, 1990).

Another class of neurons within the pons, called *pause cells,* also are related to saccadic eye movements. They discharge tonically except during saccades, when they pause. By inhibiting burst cells, pause cells prevent unwanted discharges of saccadic burst neurons, which might cause extraneous, unwanted saccades. Pause cells also ensure the synchronization of burst cells needed to produce the high-frequency discharge underlying the rapid speed of saccades. Fig. 147-2 schematizes the relationship among burst neurons, pause neurons, and the neural integrator.

Control of Horizontal Conjugate Gaze

The abducens nucleus itself is the assembly site of the final, horizontal versional command (Fig. 147-3). The nucleus contains two types of neurons: (1) abducens motoneurons, with axons that innervate the lateral rectus muscle; and (2) abducens internuclear neurons, with axons that project, via the contralateral medial longitudinal fasciculus (MLF), to the medial rectus subdivision of the contralateral oculomotor nucleus. Lesions of the abducens nucleus thus cause a conjugate gaze palsy, an inability to move the eyes beyond the midline with any type of ipsilaterally directed versional eye movement (saccadic, pursuit, optokinetic, or vestibular). Lesions of the MLF, on the other hand, deprive the ipsilateral medial rectus muscle of its innervation during versional eye movements. This leads to paresis of adduction except during convergence, or internuclear ophthalmoplegia (INO). If a "conjugate" gaze palsy is not perfectly conjugate, a coexisting abducens nerve lesion (abduction affected more than adduction) or contralateral MLF lesion (adduction affected more than abduction) is suggested. A brainstem lesion affecting one abducens nucleus and the adjacent MLF causes paralysis of both ipsilateral conjugate gaze and of adduction of the ipsilateral eye; the only remaining movement is abduction of the contralateral eye. This is called the *one-and-a-half syndrome.* A unilateral abducens nerve palsy combined with a bilateral INO also causes a one-and-a-half syndrome (Pierrot-Deseilligny, 1988).

How do saccadic, pursuit, and vestibular commands reach the abducens nucleus? The velocity commands for horizontal saccades come from burst cells located within the PPRF adjacent to the abducens nucleus. Lesions here impair ipsilateral saccades (Henn et al, 1984). Pursuit and vestibular commands also may traverse part of the caudal aspect of the PPRF because a unilateral lesion in the PPRF may create an ipsilateral pursuit palsy. Vestibular slow phases and pursuit, on the other hand, may be spared if the lesion is in the more rostral portions of the PPRF (Pierrot-Deseilligny et al, 1989).

The excitatory commands for the horizontal vestibuloocular reflex come from the contralateral vestibular nuclear complex. When the head is still, neurons in the right and left vestibular nuclei discharge tonically at the same rate. During horizontal head rotation, the horizontal semicircular canal is stimulated in one labyrinth and inhibited in the other. This creates an imbalance between the discharge rates of the right and left vestibular nuclei; activity increases on one side and decreases on the other. The difference encodes head velocity and provides the command that generates the slow phase of vestibular nystagmus. During sustained, constant-velocity head rotations, peripheral vestibular signals become inaccurate as the cupula slowly returns to its initial position. Visual (optikinetic) inputs, however, also reach the vestibular nuclei, and by supplanting the fading labyrinthine signal, they help to maintain an accurate internal representation of the head's velocity and the necessary compensatory nystagmus.

This tight relationship between optokinetic and vestibular eye movements is reflected in abnormalities of optokinetic responses that occur after peripheral or central vestibular lesions. Smooth-pursuit tracking movements, however, also contribute to the generation of the slow phases of optokinetic nystagmus and confound the assessment of the nystagmus response to optokinetic stimuli. To circumvent the pursuit contribution to optokinetic nystagmus, the physician can measure optokinetic afternystagmus (OKAN), a prolonged, slowly decaying nystagmus that occurs after the lights are turned off following full-field optokinetic stimulation. OKAN is the best measure of the action of the portion of the optokinetic responses generated via the vestibular nuclei. Its absence is a reliable sign of bilateral peripheral vestibular loss.

The eye position signal for all horizontal versional eye movements depends on the function of a common neural integrator, which is shared by each of the versional eye movement systems. It appears that the neural integrator is not confined to one anatomic locus; cells in the cerebellum (especially the flocculus), the perihypoglossal and vestibular nuclei of the rostral medulla, and perhaps the cell groups of the paramedian tracts near the medial longitudinal fascilus, all seem important (Büttner-Ennever et al, 1989; Cannon and Robinson, 1987; Zee et al, 1981).

Control of Vertical Conjugate Gaze

No "vertical gaze center" equivalent to the abducens nucleus has been identified. Certain mesencephalic structures, however, are important for vertical eye movements (Fig. 147-4) (Büttner-Ennever et al, 1982; Pierrot-Deseilligny et al, 1982).

The vertical premotor saccadic command arises in burst cells located within the riMLF. This structure is located ventral to the aqueduct in the prerubral fields at the junction of the midbrain and thalamus. Vertical burst neurons in the riMLF discharge for torsional as well as vertical eye movements (Vilis et al, 1989). Burst neurons for up-and-down saccades are intermingled on each dise, but each riMLF only encodes torsional movements that cause the eye on the side of the riMLF to extort and the eye on the opposite side to intort. The normal function of the vertical burst cells in the riMLF probably depends on ascending inputs from the caudal pons because bilateral pontine lesions may cause slow or absent vertical sacades (Henn et al, 1984). The riMLF probably projects both directly caudally, and via (posterior) commissural connections, to the oculomotor and trochlear (cranial nerves III and IV) nuclei. Axon collaterals impinge on the interstitial nucleus of Cajal (INC) where velocity-to-position integration takes place for vertical gaze-holding. The INC projects its downward commands directly to the ocular motor nuclei while upward commands must pass dorsally through the posterior commissure. Bilateral lesions of the riMLF in monkeys and in human beings either produce a predominant deficit of downward saccades or paralyze all vertical saccades. On the other hand, more dorsal lesions, in the posterior commissure, produce specific deficits in upward gaze (Parinaud's syndrome) (Ranalli et al, 1988).

The velocity commands for vertical vestibular and pursuit commands and, in part, the vertical eye position command ascend in the MLF and the superior cerebellar peduncle (brachium conjunctivum) to the midbrain. The INC receives these projections where the conversion of velocity to position signals for vertical gaze-holding takes place (Fukushima et al, 1990). Thus, bilateral INO causes not only bilateral failure of adduction but also

impairment of the vertical vestibuloocular reflex, vertical smooth pursuit, and vertical eccentric gaze-holding (Ranalli and Sharpe, 1988a).

Higher-Level Control of Saccades

The importance of the superior colliculus (SC) in the generation of saccades is supported by the observation in monkeys that acute lesions of the SC impair their ability to make any type of saccade. Normally, the SC mediates the saccadic commands emanating from the cerebral hemispheres that are destined for the premotor saccade staging areas in the paramedian reticular formation in the midbrain (vertical adn torsional) and pons (horizontal) (Fig. 147-5). After ablation of the SC, however, animals eventually recover the ability to generate saccades. This is probably mediated by direct pathways from the frontal lobes to the brain stem.

In intact subjects, more "reflexive" saccades, for example, saccades in response to the sudden appearance of a novel stimulus seen in the periphery, are probably triggered via direct projections from the parietal lobes (from the lateral intraparietal area (LIP) and area 7a) to the SC. More "voluntary" saccades, for example, a saccade in response to a verbal command, are probably generated from frontal structures (the frontal eye fields (FEF), the supplementary eye fields (SEF) and other prefrontal areas), either directly or via the basal ganglia, to the SC>The caudate nucleus (CN) and the substantia nigra pars reticulata (SNpr) are presumably the structures in the basal ganglia that influence saccade generation by the SC. More specifically, by exerting a tonic inhibitory influence on the SC, the SNpr probably gates reflexive and volitional saccades that are generated by the SC. By an inhibitory projection to SNpr, the CN can phasically inhibit SNpr and thereby lead to disinhibition of the SC, "permitting" a saccade to occur. A projection from the frontal lobes to the CN presumably carries the signal that phasically excites caudate neurons and leads to inhibition in the SNpr and then facilitation of the generation of voluntary saccade. At other times, the SNpr tonically inhibits the SC and prevents uncalled-for reflexive saccades. Finally, the internal medullary lamina (IML) of the thalamus is a structure with connections to the CN, SC, and cerebral hemispheral structures. Its function is unknown.

It must be emphasized that the frontal and parietal lobes are reciprocally connected, allowing for each structure to influence the other and also to have common subcortical projection sites. This anatomic complexity precludes a strict separation of function between the posited "voluntary" and "reflexive" pathways for initiation of saccades, but nevertheless the hypothetical scheme shown in Fig. 147-5 is useful (Tian et al, 1991).

Cerebellar Influence on Eye Movements

The cerebellum plays an important role in both immediate on-line and long-term adaptive ocular motor control (Zee and Optican, 1985). The long-term control refers to the mechanisms that ensure that eye movements remain appropriate to their stimulus during normal development and aging as well as in disease. The vestibulocerebellum, especially the flocculus, contains a group of Purkinje cells that discharge according to the velocity of the eyes moving in space (gaze velocity) during smooth-pursuit tracking, with the head either still or moving. Other cells discharge in relation to saccades or to the position of the eyes in the orbit.

Lesions of the flocculus impair smooth visual tracking: both smooth pursuit with the head still and steady fixation of a target rotating with the head (Zee et al, 1981). The latter, called vestibulo-ocular reflex (VOR) *cancellation,* is comparable to fixation suppression of caloric-induced nystagmus. Floccular lesions also cause horizontal gaze-evoked nystagmus, a finding that implicates the vestibulocerebellum in the normal function of the neural integrator. Other signs of flocculectomy are downbeat nystagmus; rebound nystagmus; increased or decreased amplitude (gain) of the vestibuloocular reflex; and postsaccadic drift or glissades (see next section on saccade disorders). Lesions of the nodulus produce disorders of the control of the duration of vestibular responses (Hain et al, 1989; Waespe et al, 1985). After nodulus lesions, the duration of vestibular responses is increased, habituation to repetitive stimulation no longer occurs, tilt suppression of postrotatory nystagmus does not occur, and periodic alternating nystagmus, a horizontal jerk nystagmus that changes direction every few minutes, may appear.

The vestibulocerebellum also participates in the long-term prevention of ocular motor dysmetria. Floccular lesions interfere with the adaptive capability for maintaining the accuracy of vestibular eye movements as well as with the prevention of postsaccadic drift. For example, when normal subjects wear reversing prisms, which make the seen world move in the same direction as head rotation, they undergo an adaptive reprogramming of their vestibuloocular relfex. They learn to generate slow phases in the same direction as head rotation, even when the head is being rotated in complete darkness. Patients with cerebellar lesions and animals with floccular lesions show deficits in this adaptive capability (Lisberger et al, 1984; Yagi et al, 1981).

Similarly, the vestibulocerebellum is important for ensuring that the eyes rotate in a plane parallel to that in which the head rotates so that images can be stabilized appropriately on the retina (Schultheis and Robinson, 1981). An example of a clinical disorder of such a mechanism is *perverted nystagmus,* an induced vestibular response with inappropriately directed slow and quick phases of nystagmus.

The dorsal vermis and underlying fastigial nuclei are important in the control of saccadic amplitude; lesions here produce saccadic inaccuracy (dysmetria) and impair the ability to make long-term adaptive adjustments in sacadic accuracy (Optican and Robinson, 1980). Pursuit deficits have also been reported after lesions in the cerebellar vermis (Pierrot-Deseilligny et al, 1990). Other "cerebellar eye signs", which cannot be localized precisely, include square-wave jerks (see next section), defective convergence, divergence nystagmus, and alternating hyperdeviation (skew) on lateral gaze.

Disorders of Saccadic Eye Movements

Abnormalities of saccades can be divided into disorders of accuracy, velocity, latency, and stability. Furthermore, they can be analyzed as disorders of the saccadic innervational commands: the pulse, the step, and the match between pulse and step (Robinson, 1978) (Fig. 147-6). For optimal performance the saccadic pulse must have (1) the appropriate amplitude (approximately height times width), to ensure that the saccade is accurate; and (2) the appropriate height, to ensure that the saccade is of high velocity. The saccadic pulse and step must be perfectly matched to prevent drift of the eyes after the saccade. A change in the pulse amplitude creates saccadic overshoot or undershoot - saccadic dysmetria. This is characteristic

of disoders of the dorsal vermis or the fastigial nuclei of the cerebellum, although it apears with lesions in other parts of the nervous system. In Wallenberg's syndrome, for example, a specific pattern of saccadic dysmetria occurs: saccades overshoot to the side of the lesion, undershoot away from the side of the lesion, and with attempted purely vertical saccades there is an inappropriate horizontal component toward the side of the lesion. Lesions of the superior cerebellar peduncle produce just the opposite - saccades overshoot when directed away from the side of the lesion (Ranalli and Sharpe, 1986).

A decrease in the height of the saccadic pulse causes slow saccades. Normally saccades follow a relatively invariant relationship between peak velocity and amplitude. Slow horizontal saccades usually imply disease affecting the horizontal burst cells in the pons caused by, for example, olivopontocerebellar atrophy. Slow vertical saccades usually imply disease affecting the vertical burst cells of the midbrain, caused by progressive supranuclear palsy, Huntington's disease, or Niemann-Pick disease, for example. A mismatch between the size of the pulse and step produces brief (several hundred milliseconds) postsaccadic drift or glissades. Postsaccadic drift occurs with disease of the cerebellar flocculus. The combination of slow, hypometric saccades and postsaccadic drift also occurs with INO, oculomotor nerve palsies, myasthenia gravis, and ocular myopathies. In ocular myasthenia gravis the combination of an adaptive increase in saccadic innervation, intrasaccadic fatigue, and pulse-step mismatches leads to characteristic "quiver movements" - saccades in which the eyes start out fast, slow down, and transiently reverse direction. Administration of edrophonium to patients with myasthenic ophthalmoparesis may cause saccades to overshoot the target transiently; the drug unmasks the central adaptive changes that have been made in an attempt to overcome the ocular muscle weakness.

Disorders of saccadic initiation lead to an increase in saccadic latency; the normal saccadic latency is about 200 milliseconds. Often an associated head movement or a blink is needed to help initiate the saccade. Impaired saccadic initiation has been reported in patients with a variety of conditions, including frontal lobe lesions, congenital or acquired oculomotor apraxia, Huntington's disease, progressive supranuclear palsy, and Alzheimer's disease. Patients with bilateral frontal lobe lesions or Parkinson's disease also have difficulty in rapidly alternating gaze between two stationary targets. Patioents with Huntington's disease show a characteristic defect in initiating more voluntary, as opposed to more reflexive saccades. They have particular difficulty in predictive tracking and in the antisaccade task (ie, looking opposite to the appearance of a target). They are unable to suppress inappropriate saccades to the visual target (Tian et al, 1991).

Inappropriate saccades disrupt steady fixation (Sharpe and Fletcher, 1984) (Fig. 147-7). They include square-wave jerks: small amplitude (up to 5 degrees) saccades that take the eyes off target and are followed within 200 milliseconds by a corrective saccade. Square-wave jerks may occur in normal elderly subjects or in patients with cerebral hemisphere lesions but are especially prominent in patients with progressive supranuclear palsy and cerebellar disease. Square-wave jerks may be an exaggeration of the micro-saccades that occur in normal individuals during fixation and can be detected most easily by ophthalmoscopy when the patient is instructed to fixate a target seen with the other eye. Macrosquare-wave jerks (10 to 40 degrees in amplitude, with a short intersaccadic interval) have been observed in patients with multiple sclerosis and olivopontocerebellar atrophy.

Macrosaccadic oscillations consist of sequences of markedly hypermetric saccades, separated by a normal intersaccadic interval (several hundred milliseconds), which continually overshoot the target. This causes a prominent, back-and-forth oscillation about the point of fixation. Macrosaccadic oscillations reflext an increase in saccadic system gain (the saccade amplitude - target displacement relationship). They are typically found in patients with lesions in the midline deep cerebellar nuclei (Selhorst et al, 1976).

Saccadic oscillations without an intersaccadic interval (back-to-back, to-and-fro saccades) are called *ocular flutter* when they are limited to the horizontal plane and *opsoclonus* when they are multidirectional (horizontal, vertical, torsional). Either type of oscillation may occur in patients with various types of encephalitis, as a remote effect of neuroblastoma or other tumors, and in association with toxins. Such oscillations are often brought out by a change in gaze or eye closure. Flutter and opsoclonus may reflect a disorder of saccadic pause neurons, although some patients with opsoclonus do not show abnormalities in the region of the brain stem where pause cells are located (Ridley et al, 1987). Some otherwise normal patients have a small-amplitude, intermittent, microsaccadic flutter, only observed with the ophthalmoscope (Ashe et al, 1991). Voluntary nystagmus is another example of a saccadic oscillation without an intersaccadic interval. It often causes difficulties in diagnosis of abnormalities on the electronystagmogram.

Disorders of Smooth Pursuit

A pathway for smooth pursuit, which runs from visual cortical areas to the brain stem via the cerebellum, is summarized in Fig. 147-8 (Pierrot-Deseilligny, 1988). Although certain neurons in the primary visual cortex respond to moving visual stimuli, they are unable to provide the pursuit system with precise information about the speed and direction of the target. In rhesus monkeys, striate cortex projects to the middle temporal visual area (MT, which contains neurons that encode the spped and direction of a moving target (Maunsell and Van Essen, 1983). Restricted, experimental lesions in MT cause a selective defect of vision: a "scotoma for motion" (Dürsteler and Wurtz, 1988). Human patients with lesions affecting the temporooccipital region have been reported to have selective defects in motion detection (Zihl et al, 1983) and are unable to make accurate smooth pursuit or accurate saccadic eye movements because of this deficit (Leigh, 1989; Thurston et al, 1988). In monkeys, the area MT projects to the adjacent medial superior temporal visual area (MST), where cells respond to moving visual stimuli but also necode eye movement signals (Newsome et al, 1988). Experimental lesions of MST produce a unidirectional (ipsilateral) deficit for smooth pursuit and also a defect of motion detection in the contralateral hemifield (Leigh, 1989; Thurston et al, 1988). Area MST projects through the posterior internal capsule and posterior aspect of the cerebral peduncle to the dorsolateral pontine nuclei (DLPN) (Tusa and Ungerlieder, 1988). Experimental lesions of DLPN also cause an ipsilateral deficit of smooth pursuit tracking (May et al, 1988). DLPN and other pontine nuclei may also receive projections from the frontal eye fields (FEF) that are concerned with smooth pursuit (Leichnetz, 1989); experimental lesions of FEF impair pursuit eye movements (MacAvoy and Bruce, 1989). DLPN projects principally to the contralateral cerebellar flocculus, but also to the vermis. Purkinje cells within the flocculus encode gaze velocity during smooth pursuit or combined eye-head trracking (Miles and Fuller, 1975). Lesions here impair smooth pursuit, more so for ipsilateral tracking. The flocculus projects to the ipsilateral vestibular nuclei, and lesions of this area, including those associated with Wallenberg's syndrome, mainly impair contralateral

smooth pursuit (Waespe and Wichmann, 1990). The medial vestibular nucleus and adjacent nucleus prepositus hypoglossi (NPH) are important for integration of the smooth pursuit signal (Cannon and Robinson, 1987), which is subsequently passed to the ocular motoneurons.

In addition to the asymmetric deficits of pursuit that may occur with focal lesions of the pathway described in Fig. 147-8, a wide variety of conditions may bilaterally impair smooth pursuit. Perhaps the commonest cause of impaired smooth pursuit is as a side effect of medications such as anticonvulsants and sedatives. Smooth pursuit is performed less well by elderly subjects, and is impaired in a variety of neurologic conditions such as Parkinson's disease, progressive supranuclear palsy, Alzheimer's disease, and in schizophrenia.

In individuals with congenital nystagmus, smoot pursuit appears to be "reversed"; the slow phases of nystagmus may be directed opposite to the motion of the target (Halmagyi et al, 1980a). The pathogenesis for this apparent "reversal" of smooth pursuit is controversial (DellžOsso, 1986; Kommerell and Mehdorn, 1982).

Eye-Head Movements

During normal behavior we use a combination of eye and head movements to stabilize gaze in response to perturbations of the body or to acquire and track a target of interest. During locomotion, our heads undergo rotational perturbations caused by transmitted vibrations from heel strike. Studies of head stability during locomotion have shown that the peak velocity of these rotational head perturbations generally does not exceed 150 degrees per second, but their predominant frequency can be as high as 5 Hz (Grossman et al, 1988; Grossman et al, 1989; King et al, 1991); these findings are summarized in Fig. 147-9. Studies of head movements in patients who have lost vestibular function indicate that head stability is largely due to the mechanical properties of head and neck muscles, rather than to neural reflexive factors (Gresty, 1987; Grossman and Leigh, 1990). Thus, the vestibulocollic reflex probably contributes little to head stability for natural (high-frequency) head movements. Moreover, the cervicoocular reflex (compensatory eye movements during head-on-body rotation due to neck proprioception) contributes little to gaze stability in normal individuals, although it may become more important if labyrinthine function is lost (Bronstein and Hood, 1986; Kasai and Zee, 1978).

Voluntary eye-head movements can be thought of as being saccadic or pursuit. During small eye-head saccades (less than 30 degrees, approximately), the shift of gaze may be achieved by superposition of an internal saccadic command and the vestibuloocular reflex (Guitton and Volle, 1987). For larger eye-head saccades (over 40 degrees, approximately), it appears that the vestibuloocular reflex is "disconnected". Nevertheless, the vestibular signal due to the head movement is still available to saccadic burst neurons so that an accurate gaze change may be achieved (Laurutis and Robinson, 1986).

During smooth eye-head tracking, more than one mechanism may operate to override the vestibuloocular reflex so that gaze follows the moving target smoothly. Evidence suggests that an internal smooth pursuit signal is partly used to *cancel* the vestibuloocular reflex; an addtional mechanism may be a reduction in the activity or partial *suppression* of the vestibuloocular reflex during such eye-head tracking (Leigh et al, 1987, 1989; Lisberger, 1990; Robinson, 1982). In general, the dynamic properties of smooth eye-head tracking

parallel those of smooth-pursuit eye movements; if they do not, the vestibuloocular reflex may be deficient (Leigh et al, 1987).

Disorders of Eye-Head Coordination

As noted earlier, bilateral loss of function from the semicircular canals probably does not cause head instability. On the other hand, unilateral labyrinthine loss may lead to a head tilt, which is part of the ocular tilt reaction - skew deviation, counterrolling of the eyes, and head tilt (Brandt and Dieterich, 1987). Other disorders causing instability of the head include tremors such as those caused by Parkinson's diseae, and abnormal postures caused by dystonia and torticollis, for example (Gresty, 1989).

Patients with congenital nystagmus may also have a head tremor. Such head tremors do not compensate for the ocular oscillations, and both are likely to be caused by a common underlying disorder (Dell'Osso and Daroff, 1986). Intermittent head tremor is also a feature of spasmus nutans, which affects infants and young children. Other features of this condition include head tilts and turns and nystagmus. The nystagmus is characteristically intermittent, of small amplitude and high frequency, and is typically asymmetric in the two eyes (Weissman et al, 1987). Any child presenting with a monocular form of nystagmus reqires a complete ophthalmologic examination and consideration of imaging studies to exclude a tumor of the anterior visual pathways.

Disorders of eye-head saccades include the involuntary head-turning associated with focal epileptic seizures (Wyllie et al, 1986), and paresis of voluntary head-turning associated with conjugate gaze palsy following an acute lesion of one cerebral hemisphere. Ocular motor apraxia, which is characterized by impaired ability to make voluntary eye movements, is often characterized by thrusting head movements by which the patient is able to shift gace. These head movements are much more conspicuous in the congenital form of ocular motor apraxia, which exclusively affects horizontal eye movements (Fielder et al, 1986; Zee et al, 1977). Acquired ocular motor apraxia is associated with bilateral frontoparietal hemispheral deficits, and both horizontal and vertical head movements are affected (Pierrot-Deseilligny et al, 1989).

Disorders causing impairment of smooth pursuit (discussed earlier) usually, but not always, also cause commensurate deficits of smooth, combined, eye-head tracking (Chambers and Gresty, 1983). Patients who have lost vestibular function, on the other hand, often show combined eye-head tracking that is superior to smooth pursuit (Leigh et al, 1987).

Mechanisms of Nystagmus

Nystagmus is a repetitive, to-and-from movement of the eyes. When pathologic, it reflects abnormalities in the mechanisms that hold images on the retina: the vestibular, optokinetic, and pursuit systems and the neural integrator. A disturbance of any of these mechanisms may cause drifts of the eyes - the slow phases of nystagmus during attempted steady fixation. Corrective quick phases or saccades then reset the eyes.

Constant velocity drifts of the eyes with corrective quick phases produce jerk nystagmus, which usually is caused by an imbalance of vestibular or possibly optokinetic or pursuit drives. Most lesions of the peripheral vestibular apparatus (labyrinth or CN VIII) cause a mixed horizontal-torsional nystagmus, with slow phases directed toward the side of the lesion. Some acute peripheral vestibular lesions initially evoke nystagmus with slow phases directed away from the side of the lesion. Because smooth pursuit is preserved, peripheral vestibular nystagmus is suppressed during fixation. The physician may evaluate this at the bedside using the ophthalmoscope; when the fixating eye is transiently covered, drifts of the optic disk and retinal vessels may appear or may increase in velocity if an underlying vestibular imbalance exists. Frenzel glasses also can be used to remove fixation and bring out nystagmus.

Nystagmus induced by a change in head position frequently results from degenerative changes in the labyrinth (Brandt, 1990). These cause the posterior semicircular canal to become sensitive to gravity. Positioning the patient in a head-hanging posture (below a plane parallel to the ground), with the head turned toward the involved side, may induce nystagmus and vertigo. The nystagmus can take up to 30 seconds to commence and has predominant vertical and torsional components that move the eyes in a plane parallel to that of the posterior semicircular canal being stimulated. Nystagmus usually abates after 10 to 15 seconds. When the patient sits up, the nystagmus may transiently reapper, but with the slow phases directed to the opposite direction observed in the head-hanging position. Repeating the postural testing may induce further episodes, but these usually become progressively less severe with repetitive testing. When this typical clinical picture is present, the patient's nystagmus and vertigo probably are caused by benign labyrinthine disease. A few days of physical therapy, consisting of repetitive movement of the head into the offending position with eyes closed, or sometimes a single maneuver to dislodge the abnormal debris, usually abolishes the vertigo. When posturally induced nystagmus does not have these features, disease of the central nervous system and especially the posterior fossa must be considered. In particular, purely vertical positional nystagmus is suggestive of a posterior fossa lesion.

Eye nystagmus induced by head-shaking is a useful clinical sign. There is a characteristic pattern associated with a unilateral loss of labyrinthine function (slow phases toward the affected ear after horizontal head-shaking and slow phases away from the affected ear after vertical head-shaking) (Hain et al, 1987). Central lesions may also produce head-shaking-induced nystagmus if the velocity-storage mechanism is imbalanced (Fetter et al, 1990).

Nystagmus caused by disease of central vestibular connections may be purely torsional, purely vertical (down-beat or up-beat), or purely horizontal, or it may have a pattern that mimics peripheral vestibular lesions. Smooth pursuit usually is affected as well, so the velocity of the slow-phase drift of central vestibular nystagmus does not diminish with fixation. Purely torsional nystagmus usually reflects intrinsic brainstem involvement within the vestibular nuclei and suggests syringomyelia (Noseworthy et al, 1988). Down-beat nystagmus in primary position usually reflects disease at the craniocervical junction, such as the Arnold-Chiarri deformity or degenerative lesions of the cerebellum (Baloh and Yee, 1989). Up-beat nystagmus in primary position occurs with lesions at the pontomedullary or pontomesencephalic junction or within the fourth ventricle (Ranalli and Sharpe, 1988b). Down-beat and sometimes up-beat nystagmus are increased by convergence or lateral gaze.

Periodic alternating nystagmus - horizontal jerk nystagmus that changes direction every 2 minutes - is a form of central vestibular nystagmus and usually is caused by lesions in the nodulus of the cerebellum (Leigh et al, 1981; Waespe et al, 1985). It can be treated successfully with baclofen (Halmagyi et al, 1980b).

Disease of the cerebral hemisphere may produce horizontal nystagmus in primary position with constant-velocity slow phases directed toward the intact hemisphere. Slow-phase velocity is not diminished by fixation. This nystagmus may result from an imbalance of pursuit tone.

Nystagmus on attempted eccentric gaze and with slow phases that show a declining exponential time course results from an unsustained eye position command. This gaze-evoked nystagmus commonly occurs are a side effect of certain medications, especially anticonvulsants, hypnotics, and tranquilizers, and with disease of the vestibulocerebellum or its brainstem connections in the medial vestibular nucleus and nucleus prepositus hypoglossi. Gaze-evoked nystagmus also may explain Alexander's law (Robinson et al, 1984). With prolonged eccentric gaze, gaze-evoked nystagmus may dampen and actually change direction. Gaze nystagmus that increases with prolonged eccentric gaze is usually a sign of ocular myasthenia gravis. It is then called *centripetal nystagmus* (Leech et al, 1977) and is often followed by rebound nystagmus when the eyes return to the primary position; slow phases are directed toward the prior position of eccentric gaze. Rebound nystagmus usually coexists with other cerebellar eye signs (Hood, 1973).

Latent nystagmus consists of slow phases that often have an exponentially declining velocity (Dell'Osso et al, 1979). Some otolaryngologists have used the term *latent nystagmus* to refer to spontaneous nystagmus recorded by electronystagmography with the eyes closed. This nystagmus appears when one eye is occluded; then both eyes drift conjugately so that the slow phases of the viewing eye are directed toward the nose. Latent nystagmus usually is associated with strabismus and is acquired early in life; it rarely implies any underlying neurologic disease but rather is related to a loss of cortical binocular function.

Nystagmus with slow phases that show an increasing exponential time course are typical of congenital nystagmus and may also be caused by instability of smooth-pursuit or gaze-holding mechanisms (Optican and Zee, 1984). Congenital nystagmus usually is primarily horizontal, accentuated by attempted fixation, diminished by convergence or active eyelid closure, associated with a head turn, and sometimes accompanied by "reversed" smooth pursuit. Occasionally, acquired lesions of the cerebellum produce nystagmus with slow phases that have increasing exponential waveforms. In patients with congenital nystagmus and achromatopsia, or cone deficiency, the slow phases of nystagmus have an exponentially decaying waveform without any latent component.

Pendular nystagmus consists of a slow phase that is a sinusoidal oscillation rather than a unidirectional drift. Quick phases may be superimposed. Congenital nystagmus often appears pendular, although the slow-phase waveform of the nystagmus is usually not a true sinusoid. Congenital nystagmus may appear more jerky on extremes of horizontal gaze. Acquired pendular nystagmus may be a manifestation of multiple sclerosis, toluene intoxication, or a sequel to brainstem infarction with inferior olivary hypertrophy (the syndrome of palatomyoclonus) (Gresty et al, 1982; Nakada and Kwee, 1986). Acquired

pendular nystagmus may have both horizontal and vertical components, and the amplitude and phase relationships of the two sine waves determine the trajectory taken by the eyes, for example, oblique if the sine waves are in phase, or more commonlyu elliptic (or circular) if the waves are 90 degrees out of phase. Acquired pendular nystagmus frequently is disconjugate and may even be horizontal in one eye and vertical in the other.

Other forms of nystagmus include convergence-retraction nystagmus, which occurs with midbrain lesions and usually coexists with upgaze paralysis (Parinaud's syndrome). In some cases convergence nystagmus may consist of asynchronous adducting saccades (Ochs et al, 1979). It is unknown whether adducting saccades alone can account for retraction or whether co-contraction must occur as well. Seesaw nystagmus, when one eye goes up and the other goes down, also occurs with midbrain lesions and may be related to an imabalance of activity in structures that receive projections from the labyrinthine otolith organs (Nakada and Kwee, 1988). Skew deviation and the ocular tilt reaction (one-half cycle of seesaw nystagmus) may be other manifestations of otolith and especially utricular imbalance (Brandt and Dieterich, 1987). Skew deviation occurs with peripheral lesions as well as with lesions in the medulla, the pons, and the midbrain.

Dissociated nystagmus, which is greater or present only in the abducing eye, commonly occurs in INO. The mechanism of abducting nystagmus in INO is unknown, although several hypotheses have been proposed (Zee et al, 1987). One hypothesis suggests that convergence is used to help adduct the weak eye, leading to abducting nystagmus in the other. Alternatively, an adaptive increase in saccadic innervation might help adduct the weak eye but, because of Hering's law of equal innervation, also would lead to abduction overshoot and nystagmus in the other. Others have suggested that the abducting nystagmus occurs because the MLF lesion interrupts either an ascending inhibitory pathway to contralateral medial rectus motoneurons or a descending excitatory pathway to contralateral abducens motoneurons. Finally, dissociated nystagmus in INO may reflect asymmetric gaze nystagmus because of involvement of structures outside but adjacent to the MLF. In any patient with INO, one or more of these mechanisms may be responsible for the dissociated nystagmus.

Adaptive Capabilities of Ocular Motor System

A major focus of recent ocular motor research, which has direct bearing on vestibular diagnosis and treatment, has been on the adaptive processes by which the brain "repairs" itself in the face of disease and trauma (Zee and Optican, 1985; Zee, 1990). A consequence of such an adaptive capability is that an ocular motor disorder reflects the "pure" effects of a lesion only when a patient is examined immediately after the neurologic insult. Otherwise the physician must also take into account the added effects of attempts to compensate for the dysmetria created by the lesions.

A practical implication of this adaptive capability is the effects of wearing corrective glasses (but not contact lenses) on the vestibuloocular reflex. The magnification factor of such glasses acts as a stimulus to a change in the amplitude of the vestibuloocular response. Thus, for example, people who wear minus lenses for nearsightedness will have a lower-than-normal amplitude of vestibular responses, whereas those who wear plus lenses for farisghtedness will have higher-than-normal amplitude responses (Cannon et al, 1985). The physician must consider these changes when evaluating the results of vestibular testing.

The adaptive repair process itself can be disturbed by lesions that involve the structures that subserve adaptive control of their input or output pathways. Lesions within the adaptive networks actually may create ocular motor abnormalities such as macrosaccadic oscillations with cerebellar disease. Such lesions also may reveal past neurologic damage that had been well compensated before more recent lesions.

Recent investigations have emphasized the importance of visual experience in correcting dynamic vestibular performance (gain) after a unilateral loss of labyrinthine function (Fetter et al, 1988). On the other hand, the static disturbance (spontaneous nystagmus) is repaired independently of visual inputs.

Finally, tests of ocular motor adaptive capability eventually may become important clinical diagnostic aids in patients with obscure or complicated neurootologic symptoms. For example, patients with cerebellar lesions have defects in the ability to modulate adaptively their vestibuloocular reflex in response to wearing reversing prisms (Yagi et al, 1981).