ABNORMALITIES of eye movement are frequent manifestations of cerebrovascular disease. Several of these signs have characteristics which enable the clinician to localize the site as well as the probable nature of the underlying pathology. One may determine whether the motility disturbance is due to cerebral hemispheric or brainstem disease. Localization is aided by knowledge of central ocular motor anatomy and physiology which is extensively reviewed elsewhere.1,2 For the purpose of this discussion, it is important to recall that the cranial nerve ocular motor nuclei (III, IV, VI) are the final common pathways in the brainstem for information arising at several levels of the neuraxis. Disorders of ocular motility may, therefore, reflect pathological processes which do not directly involve these nuclear groups. We will review the clinical characteristics and anatomical substrates of a variety of supranuclear gaze disorders which are frequently, but not exclusively, associated with cerebrovascular disease.

**Horizontal Gaze**

Rapid horizontal eye movements (saccades) are generally believed to originate in the frontal lobes. The pathway for horizontal eye movement control (frontomesencephalic pathway) is probably polysynaptic, composed of many neurons, and passes near the internal capsule and basal ganglia to the midbrain. The pathway crosses at the junction of the midbrain and upper pons to terminate in the contralateral pontine paramedial reticular formation (PPRF) (fig. 1). The PPRF lies ventral to the sixth nerve nucleus and ventral and lateral to the medial longitudinal fasciculus (MLF) in the tegmentum of the pons (fig. 2). From the PPRF, horizontal eye movement commands are relayed to interneurons and motor neurons within the sixth nerve nucleus on the same side. The interneurons within the sixth nerve nucleus subsequently project to the contralateral medial rectus subdivision of the oculomotor nucleus via the medial longitudinal fasciculus (fig. 3). A fast eye movement “command” generated in the left frontal lobe will result in a horizontal saccade to the right with activation of the right lateral rectus and left medial rectus via the pathways described.

Smooth pursuit or “following” eye movements, which allow accurate visual tracking of moving targets, are initiated in the occipitoparietal region and presumably descend in a polysynaptic occipitomesencephalic pathway to the PPRF on the same side (fig. 1). A slow eye movement “command” generated in the right occipitoparietal region will result in horizontal pursuit to the right with activation of the right lateral rectus and left medial rectus (fig. 3). In addition to saccadic and pursuit eye movements, vestibuloocular reflexes are channeled through the PPRF, making it an important relay for several different modalities affecting ocular motor function (fig. 3).

An acute, destructive lesion involving the right frontal lobe will cause a left hemiparesis and leftward gaze palsy. The eyes, “driven” by the remaining normal left hemisphere, will be deviated to the right (i.e., the eyes look toward the side of the lesion). The patient will at first be unable to generate rapid eye movements to the left. Because the pursuit pathways originating in the occipitoparietal region may not be involved with a small frontal lesion, an alert patient will be able to follow slowly moving targets in either horizontal direction. In addition, appropriate tonic ocular deviations may be produced by either caloric irrigation or the oculocephalic (doll’s head) maneuver (the tendency of the eyes to maintain their direction of gaze when the head is passively rotated or flexed).

When the destructive lesion is isolated to one frontal lobe, the paralysis of horizontal saccades is transient, resolving in a matter of days, usually before any improvement is noted in the hemiparetic extremities. The role of making rapid eye movements is eventually taken over by the remaining intact hemisphere.4 If the
removing frontal lobe has been damaged previously, it will be unable to undertake this role, and a persistent bilateral saccadic palsy will ensue. An irritative lesion of the frontal lobe, such as that associated with a seizure focus, will drive the eyes to the opposite side and is accompanied by clonic movements of the opposite extremities. Tonic deviation of the eyes lasts only as long as the seizure, and once the patient becomes fully alert, a full range of horizontal extracocular movements returns.

A lesion in the brainstem which involves the PPRF will result in a pontine gaze palsy. These lesions are most often secondary to vascular occlusive or demyelinating disease and are often bilateral and asymmetrical, encompassing several brainstem nuclei and tracts. Since the PPRF is the final prenuclear substrate for ipsilateral gaze, a unilateral lesion involving this area will result in a loss of all horizontal movements (saccades and pursuit) to the affected side. A patient with a left-sided PPRF lesion will be unable to execute voluntary rapid eye movements or to pursue a slowly moving target to the left. In addition, cold caloric irrigation of the left ear, which normally causes a right bearing nystagmus, will evoke no response. Similar stimulation on the right will cause a slow tonic deviation of the eyes to the right with an absent fast phase of nystagmus to the left. An incomplete lesion of the PPRF will cause a gaze paralytic which may or may not be associated with abnormal caloric responses. Bilateral infarcts in the tegmentum of the brainstem involving the PPRF will result in complete paralysis of all voluntary and reflex horizontal eye movements. This condition is most commonly observed after massive hypertensive pontine hemorrhage, but it can be seen as an isolated acute sign in a small infarct of the PPRF. In contrast to the transient nature of gaze palsies caused by lesions of the cerebral hemispheres, a destructive lesion of the PPRF usually results in lasting paralysis of ipsilateral gaze.

Because of the proximity of the PPRF to other important ocular motor structures, there may be involvement of the adjacent sixth nerve nucleus and/or the medial longitudinal fasciculus (fig. 2). A lesion which involves the PPRF and ipsilateral MLF results in what has been designated a “one and a half” syndrome. In this disorder a right-sided lesion will cause a horizontal gaze palsy to the right and an internuclear ophthalmoplegia during gaze to the left. The ophthalmoplegia is characterized by failure or slowing of adduction of the right eye during leftward gaze as well as nystagmus of the abducting left eye. Thus, in a one and a half syndrome, the only remaining movement may be abduction of the eye on the side opposite

FIGURE 1. Schematic diagram of the course of the frontal saccade and occipital pursuit pathways. The saccade pathway crosses at the junction of the pons and midbrain; the pursuit pathway is uncrossed. Although depicted as direct projections to the brainstem, both pathways are, in fact, polysynaptic. III, oculomotor nucleus; IV, trochlear nucleus; VI, abducens nucleus; PPRF, paramedian pontine reticular formation; VN, vestibular nuclei. (Adapted from Medicine,11 by permission.)

FIGURE 2. Schematic cross-section of the brainstem at the level of the pons depicting the tegmental location of the PPRF and its relationship to the abducens nucleus (VI) and medial longitudinal fasciculus (MLF). The proximity of these structures explains the frequent clinical association of gaze paresis with internuclear ophthalmoplegia and sixth nerve palsies. (Adapted from Eye Movement Disorders,16 by permission.)
Pursuit to right or slow phase to right

FIGURE 3. Schematic representation of the ocular motor response to warm water caloric stimulation of the left ear. Impulses are transmitted via the vestibular division of the eighth nerve to the vestibular nuclei (VN), located in the floor of the fourth ventricle. Subsequent relay of these impulses to the contralateral PPRF leads to activation of the right lateral rectus (RLR) and left medial rectus (LMR) via the MLF, resulting in conjugate slow eye movement to the right. Fibers ascending in the MLF are derived from interneurons within the sixth nerve nucleus. Impulses descending in the right pursuit pathway will activate a similar conjugate ocular movement to the right. (Adapted from Medicine, by permission.)

Although a distinction has been made in the past between “anterior” (midbrain) and “posterior” (pons) involvement of fasciculus fibers in an internuclear ophthalmoplegia, it is often not possible clinically to localize the level at which the MLF is interrupted. Unilateral involvement of the MLF is secondary to vascular disease in approximately 70% of cases. The onset is often sudden in an older individual and associated with other brainstem symptoms, such as vertigo, ataxic gait, or diplopia. The deficit generally resolves over a period of two to three months. Bilateral internuclear ophthalmoplegia has been reported to occur more frequently in demyelinating disease, although other authors have found vertebrobasilar disease to be more common. Certain, any patient with a history of transient loss of consciousness who is found to have bilateral ophthalmoplegia should be suspected of having vascular disease since transient loss of consciousness is extremely rare in demyelinating disease. Disturbance of ocular motor function secondary to brainstem pathology may also include nystagmus with or without prominent symptoms of vertigo. The characteristics of nystagmus which help distinguish peripheral eighth nerve from central dysfunction have recently been reviewed.

Although nystagmus is considered to be one of the most reliable signs of posterior fossa pathology, it may also occur with vascular lesions of the cerebral hemisphere. During recovery from a gaze palsy secondary to a frontal lobe lesion, patients pass through a phase when they are able to make a gaze movement away from the side of the lesion but cannot sustain the deviated position. As the eyes drift back toward the side of the lesion, a corrective saccade may reposition them in an eccentric position. Repetition of this pattern results in nystagmus with the fast phase toward the side opposite the lesion, a pattern which has been termed “gaze paretic” nystagmus.

Vertical Gaze

Eye movements in the vertical plane are probably generated by simultaneous bilateral activation of the frontal or occipital cortex. The exact route taken by impulses involved in vertical gaze is not known in detail, although there is evidence that vertical gaze pathways converge on the periaqueductal region just ventral to the collicular plate.

Perhaps the most frequently encountered disorder of vertical gaze is the dorsal midbrain syndrome (Parinaud’s syndrome), a constellation of neuro-ophthalmological signs which include abnormalities of vertical gaze, pupillary responses, accommodation, and vergence. It is commonly seen in association with pineal, midbrain, or third ventricular tumors and midbrain infarction. Upward saccades and pursuit are affected first, then downward movements. Attempts at upward saccades may elicit convergence-retraction nystagmus which appears as rhythmic bilateral retraction and/or convergence of the eyes. The abnormality may be demonstrated to best advantage by utilizing downgoing optokinetic targets, each target providing a stimulus for an upward saccade. The pupils are often large in the dorsal midbrain syndrome and react better to near than to direct light (light-near dissociation). In addition, there may be pathological lid retraction (Collier’s sign). The paralysis of downgaze frequently observed in the dorsal midbrain syndrome may also be seen as an isolated ocular motility defect on rare occasion. The pathology in these cases is located bilaterally, dorsal and medial to the red nuclei near the ventral periaqueductal gray.

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