Supranuclear Eye Movement Abnormalities

Eric R. Eggenberger, DO, MSEpi, FAAN

ABSTRACT

Purpose of Review: The components of the efferent ocular motor network include supranuclear, nuclear, internuclear, infranuclear, neuromuscular junction, and muscle. Within this schema, clinicians are often least acquainted with the supranuclear components; however, derangement of this system is a common cause of ocular dysmotility and diplopia. This article will provide the neurologist with an overview of the anatomy and clinical aspects of the supranuclear ocular motor control systems.

Recent Findings: Continued research moves us toward a more complete understanding of the anatomy and physiology of the complex networks providing supranuclear control of eye movements. This background serves as a framework for the application of clinical techniques, such as bedside assessment of the vestibuloocular reflex, localizing limitations of conjugate gaze (eg, midbrain lesions affecting vertical gaze), and derangements of specific classes of eye movements (pursuit and saccadic dissociation in conditions such as Parinaud dorsal midbrain syndrome).

Summary: The efferent neuro-ophthalmic system is a complex series of networks that function to provide accurate control of eye movements, visual stabilization, and ocular alignment. Disturbance within these networks can produce diplopia; impaired control of eye movement, such as gaze palsy; or unwanted eye movements, such as nystagmus.

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Address correspondence to Dr Eric Eggenberger, Michigan State University, A217 Clinical Center, 804 Service Road, East Lansing, MI 48824-1313, *eric.eggenberger@hc.msu.edu*.

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Definition of Terms

Comitant: An ocular deviation (misalignment) that is the same in all positions of gaze

Esophoria: One or both eyes are turned in (cross-eyed)

Exophoria: One or both eyes turning out (wall-eyed)

Hyperdeviation, hypertropia: One eye is higher than the other; by definition named for the higher eye (eg, right hypertropia, left hypertropia)

Incomitant: An ocular deviation that varies in amount in different positions of gaze

Phoria: Tendency for ocular misalignment; eg, most healthy patients have a small amount of esophoria or exophoria (not apparent under most binocular conditions)

Tropia: Manifest or overt ocular misalignment (eg, exotropia, esotropia)

KEY POINTS

- Supranuclear systems provide afferent direction to the oculomotor nuclei to effect distinct classes of eye movements, such as saccades and pursuits.
- Several distinct classes of eye movements (which are anatomically and functionally separate) subserve different ocular motor needs, including saccades, pursuit, optokinetic nystagmus, vergence, and gaze holding. These discrete eye movement classes are often selectively affected or spared in certain diseases.
- Saccades serve to place the fovea quickly on an object of interest; abnormalities of saccades may affect initiation, speed, suppression of unwanted saccades, and accuracy features.
- Normal saccades require a coordinated interplay between several different neuronal subtypes, including burst neurons (triggering saccadic bursts) and omnipause neurons (maintaining burst-neuron quiescence).

SUPRANUCLEAR ANATOMY AND CONTROL OF OCULAR MOTILITY

The supranuclear (ie, above the oculomotor nuclei) ocular motor system is principally concerned with bilateral eye movements and as such causes bilateral eye movement deficiencies such as gaze preference or palsy; however, supranuclear dysfunction is also a frequent cause of ocular misalignment and binocular diplopia. The supranuclear ocular motor system has rich afferent connections, including projections from the cerebral hemispheres (eg, frontal eye fields and basal ganglia), cerebellum (eg, calibration and modulation of vestibular and otolith systems), and all portions of the brainstem (eg, vestibular and otolith projections) that ultimately converge on the ocular motor nuclei and serve to govern the distinct classes of eye movements, including saccades, pursuit, the vestibuloocular reflex (VOR), gaze holding, fixation, optokinetic nystagmus, and vergence (convergence and divergence). The cerebellum performs critical coordination and calibration functions for the ocular motor system, particularly the vestibulocerebellum (flocculus, paraflocculus, nodulus, and uvula), vermis, and fastigial nuclei. The flocculus and paraflocculus are involved in smooth pursuit, gaze holding, and calibration of the VOR. The vermis and fastigial nuclei are involved in saccadic and pursuit control. The nodulus and uvula participate in modulation of the vestibular system.

Many of these eye movements are involuntary and serve to stabilize images on the retina during particular environmental or head movements.

SPECIFIC EYE MOVEMENT CLASSES

Saccades

Saccades are the primary eye movement used in the visual exploration of the environment, rapidly moving the eyes in a conjugate fashion to foveate targets of interest. Saccades may be volitional or triggered involuntarily by head (fast phases of VOR) or environmental movement (fast phases of optokinetic response). Saccades generally obey a defined relationship between saccadic amplitude and speed (the main sequence), whereby the larger the intended saccade, the greater the velocity, which may exceed 500 degrees per second for saccades of 30 degrees.[1] Saccades are thereby always of short duration, typically less than 100 milliseconds (in comparison, a blink lasts 200 milliseconds).

The machinery to generate saccade requires alertness; while slow phases may appear in coma, normal saccades are absent under these circumstances. The frontal eye fields in the lateral portion of the precentral sulcus (Brodmann areas 6 and 4) receive afferent input from the parietal eye fields (involved in reflexive saccades) and supplementary eye fields (frontal lobe area involved in planning saccades). The frontal eye fields project via the anterior limb of the internal capsule, decussating at the pontomesencephalic level to both the superior colliculus and the contralateral brainstem premotor reticular formations.[2] Although some models of saccadic control suggest that the superior colliculus is a necessary way station for most saccades, lesions in this area produce no disabling enduring saccadic defects, implying the existence of other pathways or adaptive mechanisms.[3] In addition to these pathways, numerous other areas contribute to saccades, as lesional data have shown (**Table 10-1**).

Several brainstem neurons discharge in coordinated sequence to produce normal saccades. The excitatory burst neurons (within the pons and midbrain) discharge 10 milliseconds to 12 milliseconds in anticipation of a saccade. Omnipause neurons, which have

TABLE 10-1 Specific Conditions and Lesions Causing Saccadic Dysfunction[a]

Lesion Site	Effect
Ocular motor nerves	Slow saccades, limited saccade range
Paramedian pontine reticular formation	Slowed horizontal saccades of normal or limited range
Rostral interstitial nucleus of the medial longitudinal fasciculus	Slowed vertical saccades of normal or limited range
Saccadic burst or omnipause neurons	Opsoclonus or flutter
Dorsal vermis	Hypometric saccades
Cerebellar fastigial nucleus	Hypermetric saccades
Superior colliculus	Loss of short-latency express saccades
Parietal eye fields	Increased saccadic latency, impaired visual search
Frontal eye fields	Increased saccadic latency to visual stimuli
Supplementary eye fields	Impaired remembered sequence of saccades
Basal ganglia	Difficulty with learned or predictive saccades

[a] Modified with permission from Leigh RJ, Zee DS, Oxford University Press.[2] © 2006 Oxford University Press, Inc.

KEY POINT

■ Saccadic dysfunction can involve latency, speed, accuracy, or unwanted saccadic intrusions.

a tonic firing rate and serve to maintain quiescence of burst neurons, cease to fire approximately 15 milliseconds before a saccade. Silence of omnipause neurons allows the excitatory burst neurons (within the paramedian pontine reticular formation [PPRF] of the pons for horizontal movements, and within the rostral interstitial nucleus of the medial longitudinal fasciculus [riMLF] of the midbrain for vertical movements) to fire, while inhibitory burst neurons suppress activation of the antagonist extraocular muscles (eg, inhibition of the medial rectus with lateral rectus firing).[4] The cerebellar vermis, fastigial nucleus, and flocculus are involved with calibrating and modulating saccadic responses.

The premotor reticular formation connects to the cranial nerve VI nucleus via the PPRF. The cranial nerve VI nucleus houses not only abducens neurons destined for the lateral rectus, but also internuclear neurons that join the medial longitudinal fasciculus (MLF) to innervate the contralateral cranial nerve III medial rectus subnuclei within the midbrain, thus effecting horizontal gaze. A consequence of this arrangement is that cranial nerve VI nuclear lesions produce ipsilateral gaze palsy (discussed later in this article).

Pathology of saccades can be divided into disorders of initiation (long latency), speed (slow saccades), absent or unwanted saccades, and accuracy (hypometric or hypermetric saccades). Saccadic initiation time (latency) is influenced by subject age, attention, and level of consciousness. Bilateral frontoparietal lesions may produce ocular motor apraxia, with dramatically impaired activation of volitional saccades while involuntary saccades are normal. Basal ganglia disease can produce increased latencies for saccadic initiation, notably in Huntington disease with lesser degrees of delay for Parkinson disease. Disorders of saccadic accuracy imply cerebellar system disease and typically

KEY POINT

- The vestibuloocular reflex is essential to maintain foveation (and thus clear vision) during head acceleration, and abnormalities in the vestibuloocular reflex can produce involuntary slow phases (eg, nystagmus with attendant oscillopsia), vertigo, and blur with head movements.

produce hypermetria (overshoot of saccades past the target). Slow saccades are always abnormal and may be caused by several diseases, including genetic (eg, spinocerebellar ataxia, Huntington disease, and Wilson disease), neurodegenerative (eg, progressive supranuclear palsy, advanced Alzheimer dementia, and, rarely, advanced ALS), infectious (eg, Whipple disease and tetanus), paraneoplastic conditions, PPRF lesions, ocular motor nerve, neuromuscular junction, or muscle disease.

Pursuit

The pursuit system functions to maintain foveation of a moving object. This system may have evolved out of or in concert with systems to hold gaze steady during head and body motion. The primary stimulus for smooth pursuit is target motion across the retina. This information is conveyed from the retina to the magnocellular layers of the lateral geniculate, then to the striate cortex in addition to middle temporal and medial superior temporal visual areas (the human analogue to these primate structures appears to reside in the parieto-occipital-temporal junction).[2] Diffuse brainstem regions, including the dorsolateral pontine nuclei, cerebellum, reticular formation, ocular motor, and vestibular nuclei, play a role in normal smooth pursuit. The system contains largely ipsilateral connections (in comparison to the saccadic system with crossed hemisphere to brainstem connections), and lesions typically produce defects in ipsilesional smooth pursuit (typically low gain, or saccadic pursuit); however, the diffuse anatomy involved in pursuit renders precise localization of a defect difficult. Additionally, pursuit is influenced by individual characteristics, such as level of alertness, age, and medications.

Vestibuloocular Reflex

The VOR serves to maintain foveation during head acceleration. This reflex is essential for clear vision during many common activities, such as walking or riding in a car. Even sitting still with the head stable involves a small amount of vertical head displacement during cardiac systole, and in the absence of the VOR bilaterally, this small movement produces vertical oscillopsia. The semicircular canals sense angular head acceleration, while the otolith organs encode translational head acceleration; the otoliths also sense gravitational pull. These inputs are combined with visual and proprioceptive information within the vestibular nuclei to generate a sense of head orientation and motion. Perturbation of inputs producing conflicting information concerning these parameters can lead to a sense of dizziness.

The semicircular canal system includes a horizontal, anterior, and posterior canal in both the right and left labyrinth such that head acceleration in any plane is detected. The vestibular system has a resting tonic discharge rate that is modulated up (with acceleration toward the sensing ear) or down (for acceleration away from the sensing ear) comprising a push-pull system. The semicircular canals project to the ocular motor nuclei to achieve eye motion that compensates for head acceleration, thus serving to maintain foveation as the head moves (akin to a gimbal mechanism).

This action is easiest to understand in the horizontal plane. While viewing a target, head acceleration to the right increases the right horizontal (lateral) semicircular canal input while decreasing the left lateral semicircular canal input. Excitatory connections from the stimulated right horizontal canal synapse within the right vestibular nucleus to project to the left abducens nucleus to drive the left abducens nerve and lateral rectus; in addition, the MLF transmits the impulse to the right oculomotor nucleus to activate the right medial rectus, thus turning the eyes conjugately to the left.

Simultaneously, the decreased output from the left horizontal canal through connection within the vestibular nucleus serves to inhibit the antagonist yoke pair (right lateral rectus and left medial rectus). The VOR requires precise control, such that a 10-degree head movement induces an exactly 10-degree conjugate eye movement in order to maintain clear vision; any error in this reflex results in significant blur with head acceleration. This anatomy and physiology underlie the oculocephalic response commonly assessed in coma and the slow phases of caloric-induced response. The reflex can be adapted to different conditions, such as refractive error whereby spectacles minify (myopic) or magnify (hyperopic) the world, thus requiring an appropriate adjustment in ocular movements for a given head movement. This underlies the oft-reported dizzy sensation precipitated by a change in spectacle correction, and resolves in hours in most normal subjects via cerebellar control. Modulation of the VOR gain is largely under control of the cerebellar nodulus and uvula. The reflex is also influenced by level of alertness and several classes of medication. Lesions of the vestibular system are numerous and can be divided into unilateral or bilateral hypofunction. Unilateral vestibular lesions typically produce nystagmus and vertigo and are beyond the scope of this article. Bilateral vestibular lesions often produce no vertigo, as the vestibular hypofunction is symmetric. Patients with bilateral lesions present with head movement-induced oscillopsia (**Case 10-1**), but no nystagmus.

The examination hallmark of VOR hypofunction is an abnormal head impulse test. To perform the head impulse test, the examiner moves the patient's head rapidly (but only small amplitude) while the patient is viewing a stationary target and assesses the ocular response. If the VOR is intact, the patient's eyes will remain on the target, while VOR impairment moves the eyes off the target and requires a subsequent catch-up saccade to refoveate the target. Several potential causes of bilateral vestibular hypofunction have been identified, but toxicity (especially related to prolonged aminoglycoside antibiotics) is the most common identifiable cause.

KEY POINT

- The head impulse test provides clinical assessment of the vestibuloocular reflex integrity.

Optokinetic Nystagmus

Optokinetic nystagmus is stimulated by self-rotation in light or constant velocity environmental movements (eg, scanning out the side window of a moving car). It serves to maintain foveation on a

Case 10-1

A 60-year-old man developed osteomyelitis, requiring 6 weeks of antibiotics, including gentamycin. Nearing completion of the antibiotic regiment, he noted blurred vision with head movements or while riding in the car, especially on uneven pavement (''my vision lags''). Examination revealed decreased vestibuloocular reflex gain by head impulse testing bilaterally. Although he could read 20/20 print, his acuity dropped to 20/60 during 1-Hz to 2-Hz head shaking. Vestibular physical therapy helped diminish these symptoms and improved functional abilities.

Comment. Aminoglycoside antibiotics are a common ototoxic agent, and with absent or diminished vestibuloocular reflex bilaterally, patients note oscillopsia and blur with any head acceleration. If severe, this can produce vertical oscillopsia even when sitting still because of the minimal vertical head translation related to cardiac systole.

KEY POINTS

- The vergence system facilitates binocular foveation as an object of regard moves closer or farther from the observer, through convergence and divergence eye movements.
- Vergence dysfunction is common in neurodegenerative and many other conditions, typically producing binocular horizontal diplopia at distance (divergence paresis) or near (convergence insufficiency).

portion of the moving object or scene as it travels across the retina, and consists of smooth pursuits and fast phases (saccades). Optokinetic nystagmus appears to have evolved to enhance foveation during self-rotation once the VOR has acclimated (the cupula, which serves as the transducer of physical rotation to electric impulses within the semicircular canal, returns to baseline position quickly once constant velocity is attained and ceases to signal change in vestibular input during sustained self-rotation). Optokinetic nystagmus asymmetries have traditionally been used to assist in the localization of visual field defects. Although any postchiasmal lesion may produce a complete homonymous hemianopia, an occipital lesion leaves optokinetic nystagmus intact, while a parietal lesion (affecting the optic radiations) produces an optokinetic nystagmus defect with stimuli rotated in an ipsilesional direction. Testing for optokinetic nystagmus also has a small role in clinical assessment of the patient with functional visual loss. The presence of optokinetic nystagmus implies some level of intact afferent visual function, but does not correspond with a specific acuity or field amount.

Gaze Holding and the Pulse-Step

When shifting gaze to a peripheral target of interest, one must generate an accurate saccade to the target, then supply appropriate innervation to maintain foveation on that target. Saccadic movements achieve this through a pulse and step: the pulse of innervation rapidly moves the eyes to the target of interest; then a lower level of innervation, the step, is involved in maintaining gaze on the target. The step is mathematically related to the pulse via integration, a function that is calculated by a brainstem network involving the nucleus prepositus hypoglossi, the medial vestibular nucleus, and parts of the cerebellum (flocculus).[5] Any mismatch in this calculation results in faulty gaze holding, with a pathologic slow phase back toward primary position driven by the elastic forces of the extraocular muscles within the orbit (gaze-evoked nystagmus).

Vergence

The vergence system serves to keep both foveas on a target that is changing distance from the observer (eg, convergence when fixating a target approaching the nose). Dysfunction of the vergence system results in horizontal ocular misalignment at a particular distance, producing binocular horizontal diplopia at distance or near viewing. The patient may actually experience a slight oblique orientation to the images, although the predominant misalignment will be horizontal. Both divergence and convergence dysfunction exist in the form of paresis or spasm, producing differing horizontal misalignment at distance versus near viewing. In addition, supranuclear circuitry is responsible for fusion of any phorias. Most healthy patients have small horizontal phorias (esophoria or exophoria); however, these are asymptomatic due to proper functioning of the vergence networks, which serve to fuse small amounts of misalignment. A key distinguishing feature of vergence-related horizontal diplopia versus the horizontal diplopia related to cranial nerve VI palsy is the examination findings. A cranial nerve VI palsy will demonstrate incomitant measurements (impaired abduction of one eye produces an esotropia that increases in gaze toward the paretic side), while vergence dysfunction creates a comitant (the same in all positions of gaze) misalignment for a given viewing distance. Occasionally dysfunction of these pathways from medications, structural origin, fatigue, or idiopathic causes produces intermittent binocular horizontal diplopia because of manifestation of a baseline horizontal phoria. Convergence insufficiency

is perhaps the most common of the vergence dysfunction patterns, producing a larger exophoria at near than distance and horizontal diplopia at near.

COMMON SUPRANUCLEAR LESIONS

Skew

Skew deviation is among the most common supranuclear causes of diplopia and is frequently encountered in clinical practice. Skew is related to dysfunction of otolith fibers and produces a vertical misalignment of the eyes (hypertropia). As a supranuclear lesion, ocular ductions are full (in contrast to cranial nerve III palsy, for example, an infranuclear process producing limitations of ductions in one eye, eg, adduction, supraduction, and infraduction limitations). The vertical misalignment with skew may be comitant or incomitant. Uncrossed hypertropia is a relatively common pattern (right hypertropia in right gaze with left hypertropia in left gaze). The vertical misalignment with skew tends to be similar in upgaze or downgaze for any given horizontal eye position (eg, right and upgaze similar to right and downgaze). This range of expression explains why skew may at times be difficult to separate from infranuclear dysfunction with vertical misalignment, such as trochlear neuropathy, although associated torsion assists in this regard (extorsion with hypertropic cranial nerve IV palsy versus intorsion with hypertropic eye in skew). Torsion may be suspected if the history includes diplopic images with tilt of one or both images, and can be shown clinically through specialized testing with double Maddox rods or fundus photography.

Skew deviation may be difficult to precisely localize within the posterior fossa, with connections from the vestibular organ and nerve to the vestibular nuclei (medulla), the MLF, connecting pathways involving the cerebellum, and interstitial nucleus of Cajal (midbrain) all implicated.[6,7] With lesions above the level of the pontine vestibular decussation, the ipsilesional eye is often hypertropic (eg, skew with internuclear ophthalmoplegia often with ipsilateral hypertropia), while lesions below this decussation more often produce a contralesional hypertropia (eg, Wallenberg lateral medullary syndrome with contralateral hypertropia). Associated features of skew acutely commonly include central vestibular nystagmus such as downbeat or torsional nystagmus. The ocular tilt reaction is a special circumstance of skew deviation with the added features of head tilt and torsion of both eyes such that the head tilts toward the lower eye and the hypertropic eye intorts while the hypotropic eye extorts.

Parinaud Dorsal Midbrain Syndrome

Parinaud dorsal midbrain syndrome is one of the most common and distinct supranuclear causes of ocular motor dysfunction. Diplopia with Parinaud syndrome may be related to skew deviation or vergence dysfunction; skew produces vertical separation, while convergence dysfunction results in horizontal diplopia. Lesions within the dorsal midbrain (often infarction, neoplasm [pineal origin], hydrocephalus, or demyelination), typically affecting the posterior commissure and neighboring structures, produce combinations of the following (**Figure 10-1**):

1. Vertical gaze palsy
2. Vergence dysfunction (convergence spasm or paresis)
3. Light-near dissociation of the pupils
4. Eyelid retraction
5. Square-wave jerks
6. Convergence-retraction nystagmus
7. Skew deviation

Although most patients do not have all seven features, constellations of these

KEY POINTS

- Skew deviation is a supranuclear vertical misalignment of the eyes.
- Parinaud dorsal midbrain syndrome produces a distinct and localizing constellation of signs including convergence retraction nystagmus, vertical gaze palsy, pupillary light-near dissociation, and skew deviation.

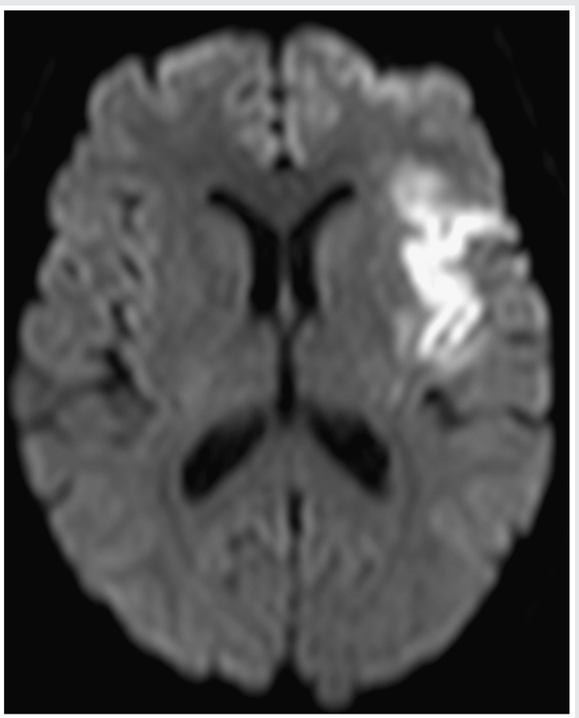

FIGURE 10-1 Diffusion-weighted MRI in patient with left gaze preference demonstrates left middle cerebral artery territory infarct.

KEY POINTS

- Horizontal gaze defects most commonly result from pontine lesions, while vertical gaze deficits typically indicate midbrain dysfunction.
- Lesions of the abducens (cranial nerve VI) nucleus produce an ipsilateral gaze palsy.

features are very useful in localization. The presence of convergence-retraction nystagmus is pathognomonic for dorsal midbrain localization, while bilateral light-near dissociation (poor pupillary response to light with retained brisk pupil response to a near target; see "Diagnostic Approach to Pupillary Abnormalities" by Dr. Aki K. Kawasaki, MD, in this issue of CONTINUUM) is associated with a very limited differential diagnosis (Parinaud dorsal midbrain syndrome, Argyll Robertson pupils, peripheral neuropathy with autonomic nerve involvement, severe afferent visual loss, or cranial nerve III aberrancy).

Horizontal Gaze

Gaze preference. Acute hemispheric lesions may produce conjugate deviation of the eyes (and head) toward the side of the lesion (patient looks toward the hemispheric stroke). This supranuclear ocular motor lesion is more common with right-sided, relatively smaller deficits involving the frontoparietal regions, but requires a larger lesion of the left hemisphere (often fronto-temporal-parietal).[8] This right-left disparity is hypothesized to result from the predominant role of the right hemisphere in spatial orientation functions. The supranuclear nature of these lesions is borne out by the ability to conjugately drive the eyes contralaterally past midline with the oculocephalic or caloric-induced VOR. Such supranuclear gaze preferences typically spontaneously resolve within days to 1 week (**Figure 10-2**).

Gaze palsy. In contrast to a gaze preference, horizontal gaze palsy implies a lesion of the abducens nucleus within the pons that produces an ipsilesional gaze palsy that cannot be overcome by supranuclear activation such as the oculocephalic maneuver (the patient looks away from the brainstem). Based on neighboring anatomy, several variations on the gaze palsy theme exist. Inclusion of the adjacent MLF produces a concomitant internuclear ophthalmoplegia, constituting the one-and-one-half syndrome (abduction of the contralesional eye is the only preserved horizontal eye movement). Addition of the encircling facial nerve adds cranial nerve VII palsy, comprising the eight-and-one-half syndrome (one-and-one-half plus 7).[9] Knowledge of these lesions reinforces details of pontine anatomy and provides exquisite localizing value.

Vertical Gaze

Burst neurons facilitating vertical saccades reside within the riMLF, which is situated rostral to the oculomotor nucleus; dysfunction of the riMLF produces slow or absent vertical saccades, and may result from infarction, demyelination, neoplasm, or neurodegenerative processes. Given that the deficit is supranuclear, intact vertical eye movements may be

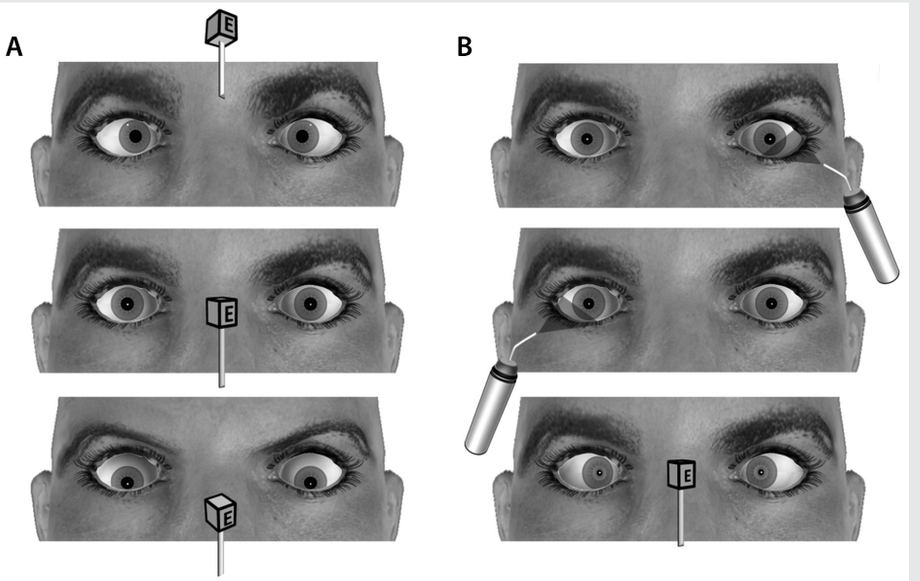

FIGURE 10-2 Parinaud dorsal midbrain syndrome. *A*, Impaired supraduction (*top panel*) greater than infraduction (*bottom panel*) is present. Note eyelid retraction in *bottom panel*. *B,* Light-near dissociation with impaired light reaction in both eyes, but retained near-induced miosis (sans tonic pupil response).

Courtesy of Joao Lemos, MD.

possible when bypassing volitional pathways (such as the oculocephalic reflex: eye movements in response to head movement when foveating).

Deficits of vertical gaze. Vertical gaze defects come in several varieties, involving upgaze or downgaze, and various classes of eye movements (saccades or pursuits). Patients with acute vertical gaze palsies typically have midbrain lesions. Selective loss of downgaze saccades implies bilateral riMLF lesions, while loss of all downward eye movements suggests interstitial nucleus of Cajal or posterior commissure lesions. Acute paralysis of upgaze for all classes of eye movements implies a lesion of the posterior commissure of the interstitial nucleus of Cajal. Selective loss of all vertical saccadic eye movements may occur in bilateral riMLF lesions, while paralysis of all vertical eye movements occurs in interstitial nucleus of Cajal or posterior commissure lesions.[2]

Progressive Supranuclear Palsy

Progressive supranuclear palsy (PSP) is a neurodegenerative disease characterized by ocular dysmotility, cognitive decline, and parkinsonism. The prevalence of PSP is less than 5 per 100,000[10,11] with an average age at onset in the sixties, and median survival of 6 to 7 years from onset. Core features for the clinical diagnosis of PSP include gradually progressive symptoms, onset age older than 40 years, vertical supranuclear palsy or slowing of vertical saccades and prominent postural instability with falls in the first year of onset, and no evidence of another disease explanation. Supportive features include symmetric proximal greater than distal akinesia or rigidity; abnormal neck posture, especially retrocollis; poor or absent response to levodopa; early dysphagia and dysarthria; and early cognitive impairment, often with apathy, impaired abstract thought, and decreased fluency (**Case 10-2**). The

Case 10-2

A 65-year-old man presented with imbalance-related frequent falls. Examination showed mildly hypophonic monotone dysarthria, bradykinesia with diminished blink rate, and nearly continuous square-wave jerks. Vertical saccades appeared slow and hypometric.

Comment. A diagnosis of progressive supranuclear palsy was made. Treatment consisted of patient education and physical therapy for gait stability.

disease is pathologically characterized by an abnormal accumulation of tau protein within the brain.

Although eye movement abnormalities are the most distinct feature of PSP and often present early, ocular motility abnormalities may appear late or be absent. The classic ocular motor finding is a supranuclear paresis, initially for vertical but ultimately involving horizontal eye movements over time. Slow saccades are often the initial ocular motor abnormality, and vertical saccades may take an oblique course (vertical saccades may trace an arc pattern including a horizontal trajectory rather than the intended purely vertical movement, the round-the-house sign) perhaps due to coincident square-wave jerks (horizontal saccadic intrusions less than 5 degrees in amplitude that take the eyes off the target, then return the eyes to the target after a saccadic interval of 180 milliseconds to 200 milliseconds). Horizontal saccades tend to be hypometric early, with slowing appearing later in the course (after vertical saccade involvement). Frequent or continuous square-wave jerks are a characteristic PSP finding, which in combination with the parkinsonism feature of bradykinesia and decreased blink rate constitute a useful clinical sign, as the ratio of square-wave jerks to blink rates may help to distinguish PSP from idiopathic Parkinson disease (PSP is generally associated with a lower blink rate and a higher rate of square wave jerks than Parkinson disease).[12] Impaired smooth pursuit is common in PSP, and eventually both smooth pursuit and saccades (ie, all volitional eye movements) are lost. Initially, the impaired ductions can be overcome with the oculocephalic maneuver; however, with time, ophthalmoplegia resistant to all modes of activation ensues. Fusional amplitudes (the amount of ocular misalignment that can be overcome to produce fusion, or a single binocular image) tend to be markedly reduced, and at times even small horizontal deviations related to vergence dysfunction are unable to be fused, producing persistent diplopia. Such diplopia is typically resistant to prism as the fusional mechanisms fail to alleviate even miniscule residual ocular misalignment.

In addition to the characteristic eye movement dysfunction, impaired postural reflexes may lead to early fall-related morbidity and cognitive decline (milder degrees of dementia compared with Alzheimer disease). MRI is typically normal, especially early, but in advanced disease may reveal midbrain atrophy manifest as flattening of the normal convex midbrain appearance on sagittal imaging.

Post–Cardiovascular Surgery

A very small minority of patients undergoing cardiac procedures (often coronary artery bypass grafting or aortic valve procedures) will awaken with enduring ocular motor deficits characterized by various combinations of impaired volitional gaze. Two relatively distinct forms are most commonly reported. In one form, volitional saccades, pursuits, and vergence are lost (**Case 10-3**), while in a

Case 10-3

A 78-year-old man underwent scheduled aortic valve replacement with postoperative complications of atrial fibrillation and cardiac tamponade. Following extubation, he demonstrated a supranuclear ophthalmoparesis with absent voluntary saccades and pursuits. His speech was sparse and dysarthric, and he required assistance to walk. These defects persisted unchanged during follow-up examination.

Comment. This is a typical case of post–cardiovascular surgery ocular motor deficiency with loss of fast phases and pursuits.

second form, selective loss of saccadic and quick phases is evidenced. Imaging is typically normal, and scant pathology (few cases and little pathologic findings) has involved pontine areas or appears normal.[13,14] The defects typically remain indefinitely.

Parkinson Disease

Idiopathic Parkinson disease is characterized by the clinical tetrad of tremor, bradykinesia, cogwheel rigidity, and later impairment of postural reflexes. Vergence dysfunction is the primary ocular difficulty evidenced in Parkinson disease, producing convergence-insufficiency–related binocular horizontal diplopia at near distances (**Case 10-4**). Additional ocular features may include square-wave jerks (typically lower rates than found in PSP), hypometric saccades, and impaired smooth pursuit.[15]

Oculogyric Crisis

Oculogyric crisis is a dystonic reaction first described in relationship to the 1917 epidemic of encephalitis lethargica (also known as von Economo encephalitis) as part of the postencephalitis parkinsonism feature, but, given the rarity of this condition presently, it is almost exclusively now seen in relationship to medications (most often dopamine antagonists, such as antipsychotic agents or metoclopramide, but also anticonvulsant toxicity [eg, phenytoin, carbamazepine, lamotrigine]). These abnormal eye movements are often preceded by a sense of fear, which is followed most commonly by conjugate upward deviation of the eyes (lateral deviation is much less common). Associated features include eye pain, jaw spasm, retrocollis, and impaired communication. The duration of the crisis is related to the presence of the offending agent and can be aborted by anticholinergic medications.

CONCLUSIONS

The supranuclear system involves diffuse and extensive portions of the CNS requiring cortical, subcortical, brainstem, and cerebellar coordination. Although supranuclear dysfunction often produces conjugate limitation of eye movements,

KEY POINT

- Parkinson disease may produce convergence dysfunction with binocular horizontal diplopia at near.

Case 10-4

A 62-year-old woman with Parkinson disease for 7 years presented with binocular horizontal diplopia while reading. Examination showed visual acuity 20/20 in both eyes, a 1-prism to 2-prism diopter exotropia at distance, and 12-prism diopter exotropia at near consistent with convergence insufficiency.

Comment. Vergence dysfunction is common in extrapyramidal disease. Convergence exercises diminished the frequency of diplopia, and reading glasses with base-in prism resolved her symptoms.

skew deviation and vergence dysfunction result in ocular misalignment and diplopia. An understanding of the supranuclear anatomy and physiology governing ocular motility is essential to diagnose these common disorders in clinical practice.

REFERENCES

1. Boghen D, Troost BT, Daroff RB, et al. Velocity characteristics of normal human saccades. Invest Ophthalmol 1974;13(8):619–623.
2. Leigh RJ, Zee DS. The neurology of eye movements. 4th ed. New York: Oxford University Press, 2006.
3. Hanes DP, Smith MK, Optican LM, Wurtz RH. Recovery of saccadic dysmetria following localized lesions in monkey superior colliculus. Exp Brain Res 2005;160(3):312–325.
4. Buttner-Ennever JA, Buttner U. The reticular formation. In: Buttner JA, ed. Neuroanatomy of the oculomotor system. New York: Elsevier, 1988.
5. Arnold DB, Robinson DA. The oculomotor integrator: testing of a neural network model. Exp Brain Res 1997;113(1):57–74.
6. Dieterich M, Brandt T. Wallenberg's syndrome: lateropulsion, cyclorotation and subjective visual vertical in thirty-six patients. Ann Neurol 1992;31(4):399–408.
7. Keane JR. Ocular skew deviation. Analysis of 100 cases. Arch Neurol 1975;32(3):185–190.
8. Tijssen CC, Van Gisbergen JA, Schulte BP. Conjugate eye deviation: side, site, and size of the hemispheric lesion. Neurology 1991;41(6):846–850.
9. Eggenberger E. Eight-and-a-half syndrome: one-and-a-half syndrome plus cranial nerve VII palsy. J Neuroophthalmol 1998;18(2):114–116.
10. Schrag A, Ben-Shlomo Y, Quinn NP. Prevalence of progressive supranuclear palsy and multiple system atrophy: a cross-sectional study. Lancet 1999;354(9192):1771–1775.
11. Nath U, Burn DJ. The epidemiology of progressive supranuclear palsy (Steele-Richardson-Olszewski syndrome). Parkinsonism Relat Disord 2000;6(3):145–153.
12. Altiparmak U, Eggenberger E, Coleman A, Condon K. The ratio of square wave jerk rates to blink rates distinguishes progressive supranuclear palsy from Parkinson disease. J Neuroophthalmol 2006;26(4):257–259.
13. Devere TR, Lee AG, Hamill MB, et al. Acquired supranuclear ocular motor paresis following cardiovascular surgery. J Neuroophthalmol 1997;17(3):189–193.
14. Leigh RJ, Tomsak RL. Syndrome resembling PSP after surgical repair of ascending aorta dissection or aneurysm. Neurology 2004;63(6):1141–1142.
15. Lepore FL. Parkinson's disease and diplopia. Neuroophthalmology 2006;30(2–3):37–40.