# Chapter 7

## THE CONTROL OF EYE MOVEMENTS

Robert B. Daroff, M.D. and Louis F. Dell'Osso, Ph.D.

Dr. Daroff is Professor of Neurology at the University of Miami School of Medicine and Director of the Ocular Motor Neurophysiology Laboratory of the Miami Veterans Administration Hospital.

Dr. Dell'Osso is Associate Professor of Neurology at the University of Miami School of Medicine and Co-Director of the Ocular Motor Neurophysiology Laboratory, Miami Veterans Administration Hospital.

Eye movements subserve vision. The major functions of eye movements are the rapid acquisition of objects of interest in the peripheral field (peripheral retinal image) into the central field of vision (fovea) and the maintenance of this target foveation during movement. This movement may be target motion, subject motion, or both. In this chapter, we will discuss organization of the ocular motor system, followed by an anatomical overview and, lastly, some pertinent clinical considerations. We will cover only horizontal eye movements; vertical movements have not been as carefully studied but are presumed to have the same general characteristics.

### Physiological Organization

The ocular motor system is best conceptualized as two independent subsystems, version and vergence, acting synergistically (Fig. 1) (Dell'Osso & Daroff, 1974). The version subsystem mediates all conjugate, and the vergence subsystem all disconjugate, eye movements. Vestibulo-ocular outputs are in the version subsystem. Regardless of input, there are only three major categories of eye movement output: fast eye movements (FEM or saccades) and slow eye movements (SEM) from the version subsystem, and vergence eye movements (VEM) from its subsystem. All three outputs share a common pathway from the ocular motor neurons to the eye muscles (Fig. 2). The fast mode of the version subsystem mediates all conjugate saccades (FEM) and the slow mode all SEM. The latter includes, but is not limited to, the pursuit function. The different names attached to eye movements generally specify the eliciting input or the circumstance of occurence; all can be listed within one or more of the three outputs (FEM, SEM, VEM) of the ocular motor system (Table 1). A brief discussion of the different types of eye movements follows.

### Fast Eye Movements (Saccades)

The visual stimulus for FEM is target displacement. Following an instantaneous change in target position, the ocular motor system will respond with an FEM after a latency of 200-250 msec. Both the peak velocity and the duration of FEM are amplitude-dependent, varying from 30-700°/sec and 30-100 msec, respectively, for movements from 0.5°-40° in amplitude. FEM are conjugate and ballistic. The control system responsible for their generation is discrete (i.e., at discrete instants in time, control decisions are made based upon the continuous inflow of visual information; these decisions are essentially irrevocable). The control signal is retinal error which is reduced to zero

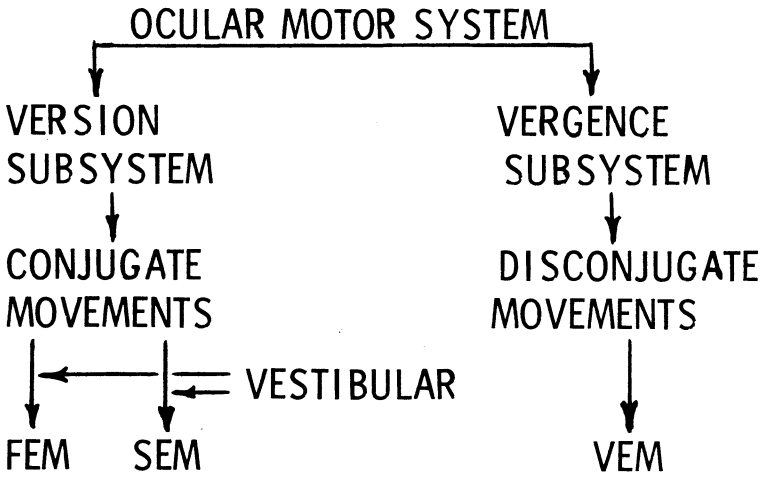


Figure 1. Basic organization of the ocular motor system emphasizing the division between the vergence and dual-mode version subsystems. The three basic motor outputs are: fast eye movements (FEM), slow eye movements (SEM), and vergence eye movements (VEM).

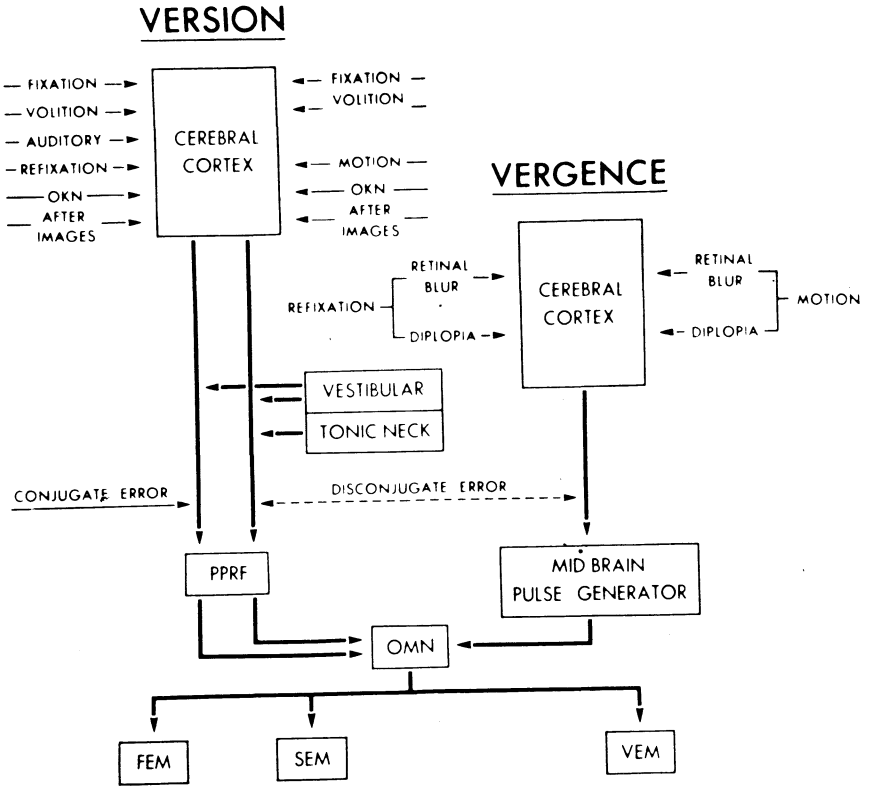


Figure 2. (From: Dell'Osso and Daroff, 1974) The ocular motor control system composed of the dual-mode version and the vergence subsystems. The output of the pontine paramedian reticular formation (PPRF) sums with that of the vergence neural pulse generator at the ocular motor nuclei (OMN) to produce the three basic types of eye movements: fast (FEM), slow (SEM), and vergence (VEM).

(From Dell'Osso and Daroff, Aerospace Med 45:873-875, 1974)

TABLE I. EYE MOVEMENT CLASSIFICATIONS

| Version | | Vergence |
|---|---|---|
| FEM | SEM | VEM |
| Saccade: Refixation | Pursuit (Tracking) | Refixation |
| Reflex | | |
| Voluntary | Voluntary | Tracking (Pursuit) |
| Microsaccade (Flick) | Microdrift | Microdrift |
| Corrective Saccade | Corrective Glissade (?) | Corrective Glissade (?) |
| Saccadic Pursuit (Cogwheel) | Compensatory | Voluntary |
| Fast Phase of Nystagmus (Jerk) | Slow Phase of Nystagmus | |
| Square Wave Jerk (Gegenrücke) | Pendular Nystagmus | |
| After-Image Induced | After-Image Induced | |
| REM | Slow Sleep Drifts | |
| Braking Saccades | Imaginary Tracking | Imaginary Tracking |
| | Proprioceptive Tracking | Proprioceptive Tracking |

(From: Dell'Osso and Daroff, 1974)
(Taken from Aerospace Med 45: 873-875)

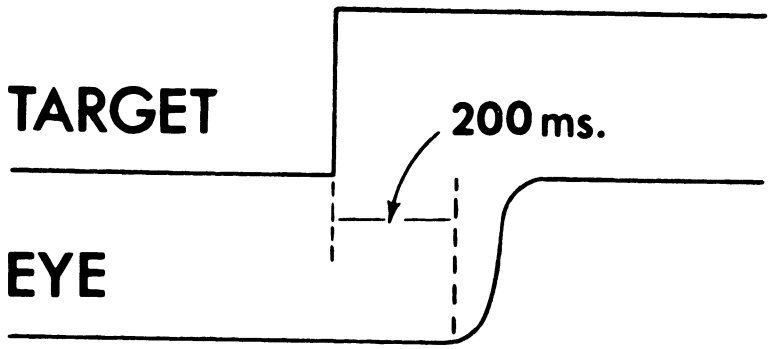


Figure 3. (From: Dell'Osso and Daroff, 1976) Fast eye movement (FEM) response to a rightward target displacement illustrating the latency and trajectory of the FEM (saccade.)

From Glaser J. (Editor): Clinical Ophthalmology - Hagerstown, MD, Harper & Row, Vol II, 1976.


Figure 4. (From: Dell'Osso and Daroff, 1976) Muscle activity of the agonistic left lateral rectus (LLR) and antagonistic left medial rectus (LMR) during a fast eye movement (FEM) to the left. Note the burst of LLR activity and total inhibition of the LMR during the FEM, and the absence of active braking activity in the LMR.

From Glaser J. (Editor): Clinical Ophthalmology - Hagerstown, MD, Harper & Row, Vol II, 1976.

by the essential negative feedback nature of the sub-system.

After the appropriate latency, an FEM response to a target displacement (Fig. 3) consists of a period of acceleration to a peak velocity and deceleration of the eyes onto the new target position. The muscular activity in the agonist-antagonist pair is characterized by a burst of maximal facilitation in the agonist and total inhibition in the antagonist during the movement (Fig. 4). Such recordings reveal that FEM deceleration is not consequent to active braking by the antagonist muscle. Rather, the two muscles merely assume the relative tensions necessary to hold the new target position. This is sufficient to accomplish the rapid deceleration because of the overdamped nature of the ocular motor plant (i.e. globe, muscles, and fatty supporting tissue).

The overdamped plant requires that the neural signal necessary to achieve the rapid FEM acceleration must be a high frequency burst of spikes which is followed by the tonic spike frequency required to stop and then hold the eyes at the new position. This combination of static and tonic firing patterns is designated the "pulse-step" of neural innervation (Fuchs and Luschei, 1970; Robinson, 1970 and 1975 a; Robinson and Keller, 1972). The relationship between the neural signals and resulting eye movements are illustrated in Figure 5. The eye movement in Figure 5a results from a step change in neural firing frequency and, reflecting the overdamped plant dynamics, is considerably slower than a normal FEM. A normal FEM trajectory occurs only when a pulse preceeds the step (Fig. 5b). A neural pulse generator and integrator combine to form the required pulse-step of innervation (Fig. 6). The generator and integrator are both located within the pontine paramedian reticular formation (PPRF) at the level of the abducens nuclei (Keller, 1974). The location of the summing junction for the pulse and step is uncertain but may be located in the nucleus prepositus hypoglossi (Graybiel and Hartwieg, 1974).

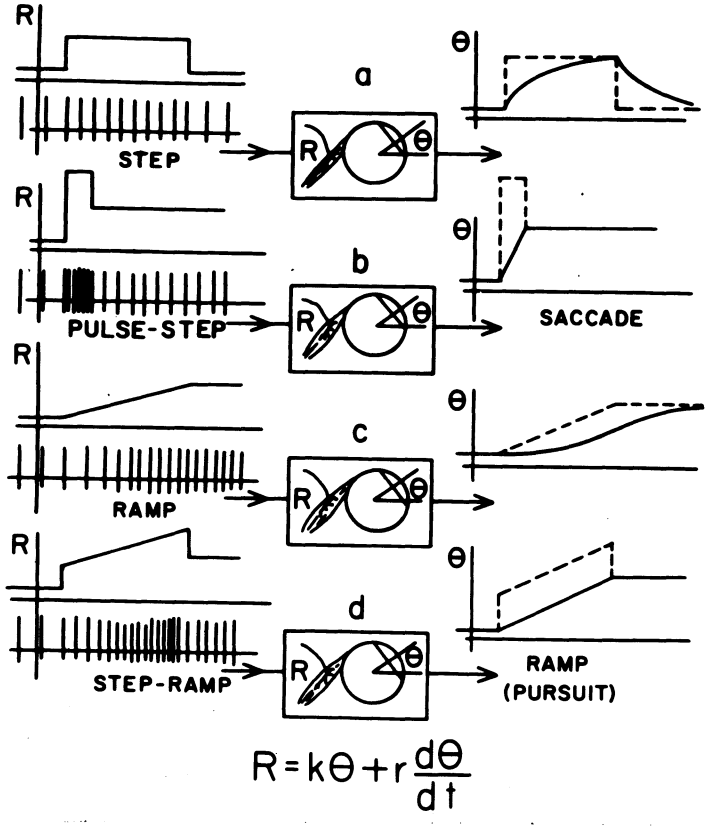


Figure 5. (From: Robinson, 1975 a) Illustration of the fast eye movement (FEM) responses (a and b) and slow eye movement (SEM) responses (c and d) which would result from the depicted neural innervation patterns. The top curves on the left and the dashed curves on the right are plots of instantaneous firing rate vs. time. The equation relates neural firing frequency (R) with eye position ($\theta$) and velocity ($\frac{d\theta}{dt}$). Note that the overdamped nature of the muscle and eyeball plant dynamics produces sluggish responses to a simple step (a) or ramp (c) change in firing frequency. To generate a proper FEM (saccade), a pulse-step is required (b). To generate a proper SEM (pursuit), a step-ramp is required (d).

From Lennerstrand G. and Bach-Y-Rita P (Editors) Basic Mechanisms of Ocular Motility and Their Clinical Implications. Oxford and New York, Pergamon Press pp 435-443, 1975

The closed-loop nature of the FEM mode of the version subsystem can be depicted in a block diagram (Fig. 7). The retinal error signal, representing the difference between target and eye positions, is sensed in the cerebral cortex. Signals derived from this information are utilized in the brainstem to generate the neural command to the ocular motor neurons necessary for the FEM which moves the eye to its new position, thereby reducing the retinal error to zero.

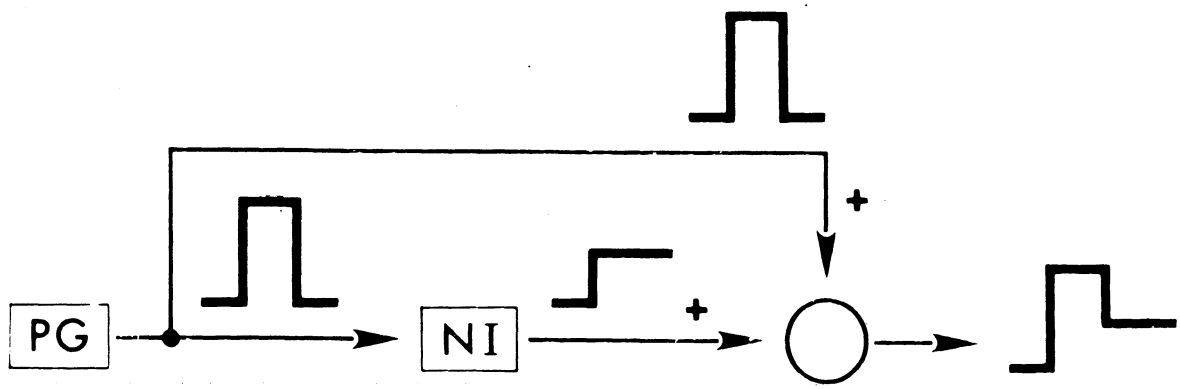


Figure 6. (From: Daroff, 1975) Schematic demonstrating how the pulse-step of neural innervations could be derived by summing the outputs of a neural pulse generator (PG) and a neural integrator (NI).
From Lennerstrand G. and Bach-Y-Rita P (Editors) Basic Mechanisms of Ocular Motility and Their Clinical Implications. Oxford and New York, Pergamon Press pp 435-443, 1975

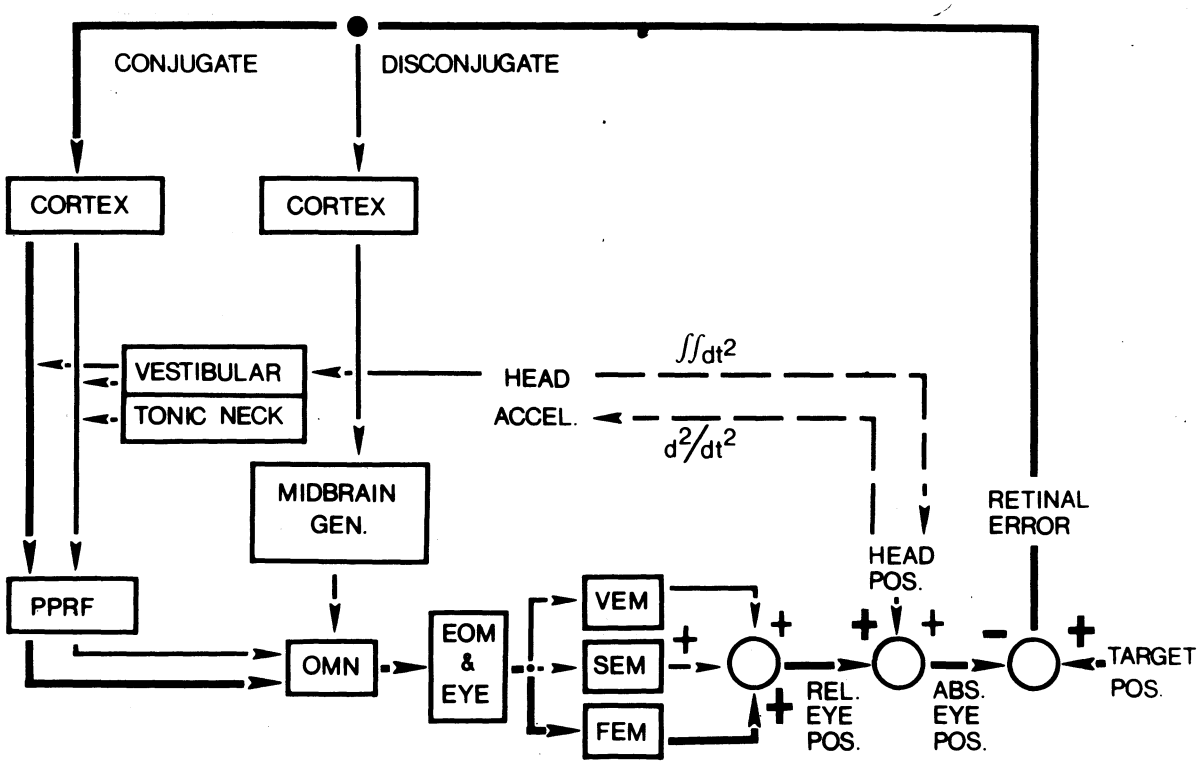


Figure 7. Basic closed-loop block diagram of the fast eye movement (FEM) mode of the version subsystem (heavy lines) super-imposed on the block diagram of the total ocular motor control system. The control signal, conjugate retinal error, is sent to the cortex and the decision to re-position the eyes forwarded to the pontine paramedian reticular formation (PPRF) where the motor commands are generated and passed on to the ocular motor nuclei (OMN). This innervation causes the extra-ocular muscles (EOM) to move the eye with a FEM and change relative eye position. Assuming no change in head position, the relative position constitutes the absolute eye position which sums with target position at the retina to produce zero retinal error.

## Slow Eye Movements: Pursuit

A major stimulus for SEM is a fixated target which moves; this evokes a pursuit SEM after a latency of 125 msec. The maximum pursuit velocities are only 30°-50°/sec, despite the fact that the SEM of the vestibulo-ocular reflex, optokinetic, and congenital nystagmus can be considerably faster. SEM are conjugate, smooth, and under a control system capable of continuous modification of motor output in response to visual input (in contrast to discrete FEM control). The input signal is retinal error ("slip") velocity which is reduced to zero when eye velocity matches target velocity. A moving target is usually required for a pursuit SEM, otherwise attempts to move the eyes smoothly result in a series of small saccades (Yarbus, 1967).

When a foveated target suddenly moves at a constant velocity, the pursuit response begins after a 125 msec latency (Fig. 8). The initial movement is at the same velocity as the target but, due to the latency, the eyes are behind the target and require a catch-up saccade for re-foveation before continuing the tracking with a pursuit SEM. The catch-up saccade follows the initiation of the pursuit movement because of the longer latency of the FEM subsystem. Plant dynamics prevent a linear increase (ramp) in neural firing frequency from rapidly accelerating the eyes to the velocity of a moving target (Fig. 5c). A "step-ramp" of innervation is necessitated (Fig. 5d). Thus, an instantaneous jump in firing frequency (the step) is followed by a linear increase in frequency (the ramp). The same neural integrator used in the formation of FEM may be utilized for the step-ramp of SEM--"final common integrator" (Robinson, 1975a). As with FEM, the SEM sub-system is closed loop with negative feedback (Fig. 9). The retinal error signal (slip velocity) is sensed at the cortex and this information is utilized in the brainstem to generate the required pursuit SEM which reduces the retinal error velocity to zero.

Since the FEM mode responds to position errors and the SEM mode to velocity errors, what would be the response to a sudden imposition of both types of error? Experiments using step-ramp target stimuli (i.e. the target simultaneously steps to a new position and assumes a constant velocity in the direction opposite to its step of displacement) have shown that the pursuit SEM mode is independent of, but synergistic with, the FEM mode of the dual-mode version subsystem (Rashbass, 1961).

## Slow Eye Movements: Vestibulo-Ocular

Head movement is the stimulus for vestibulo-ocular SEM. The latency between the onset of head movement and the resultant SEM has been reported to vary from 10 msec to 100 msec. The peak velocities of vestibulo-ocular SEM are also variable and may be as fast as 300°-400°/sec. The movements are conjugate and smooth, and the control system is continuous, but unlike the closed-loop saccadic and pursuit functions, the vestibulo-ocular system is open loop (Figs. 10 and 11). The control signal is head acceleration transduced by the

semicircular canals to a neural signal proportional to head velocity. The canals thus perform the integration step necessary to convert acceleration to velocity (Robinson, 1972). The velocity information enters the vestibular nuclei which projects to the pontine paramedian reticular formation (PPRF) where a final step of integration converts velocity to the position signal needed by the ocular motor neurons (Fig. 10). In Figure 11, the open-loop vestibulo-ocular function is diagramed such as would occur in darkness with no visual inputs. Final eye position is therefore equal to relative eye position plus head position. With the addition of vision (Fig. 12), a feedback loop is closed around the open-loop vestibulo-ocular function. Now the ability of the ocular motor system to relate eye position to target

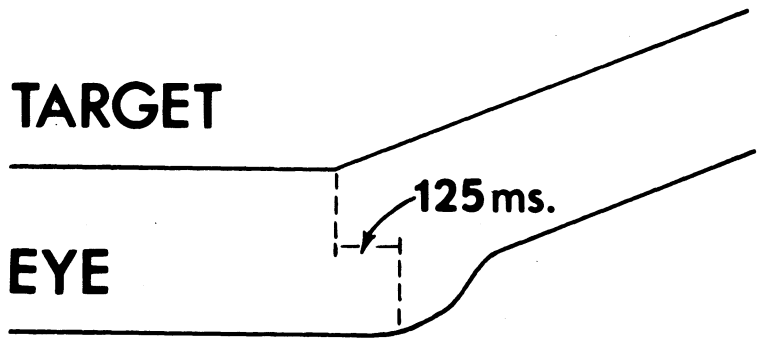


Figure 8. (From: Dell'Osso and Daroff, 1976) Slow eye movement (SEM) response to a target moving with a constant rightward velocity illustrating the latency of the SEM as well as the catch-up FEM. From Glaser J. (Editor): Clinical Ophthalmology - Hagerstown, MD, Harper & Row, Vol II, 1976.

position, in situations of head movement, is enhanced markedly.

With head on body movement, input from neck receptors sum with those from the vestibular end-organ to produce the compensatory eye movement (Rubin et al, 1975). For simplicity, we have not included a "tonic neck" function in our block diagrams.

## Vergence Eye Movements

The stimuli for VEM are target displacement or motion along the z-axis (towards or away from the observer). Vergence latency is approximately 160 msec, the maximum velocities are in the range of 20°/sec, and the movements are disconjugate and smooth. Their control is continuous and the inputs are retinal blur (open-loop) or diplopia (closed-loop) (Zuber, 1971). The VEM subsystem is uniquely capable of generating a uniocular eye movement and is asymmetrical (i.e., convergence movements are faster than divergence movements). The time course is similar to that depicted in Figure 5a for a step change in target position and Figure 5c for a constant target velocity. Thus, VEM outputs simply reflect innervational signals upon the overdamped plant dynamics. The VEM sub-system is a closed-loop when diplopia is the error signal (Fig. 13). The command from the midbrain generator to the ocular motor neurons executes the appropriate VEM to reduce diplopia to zero.

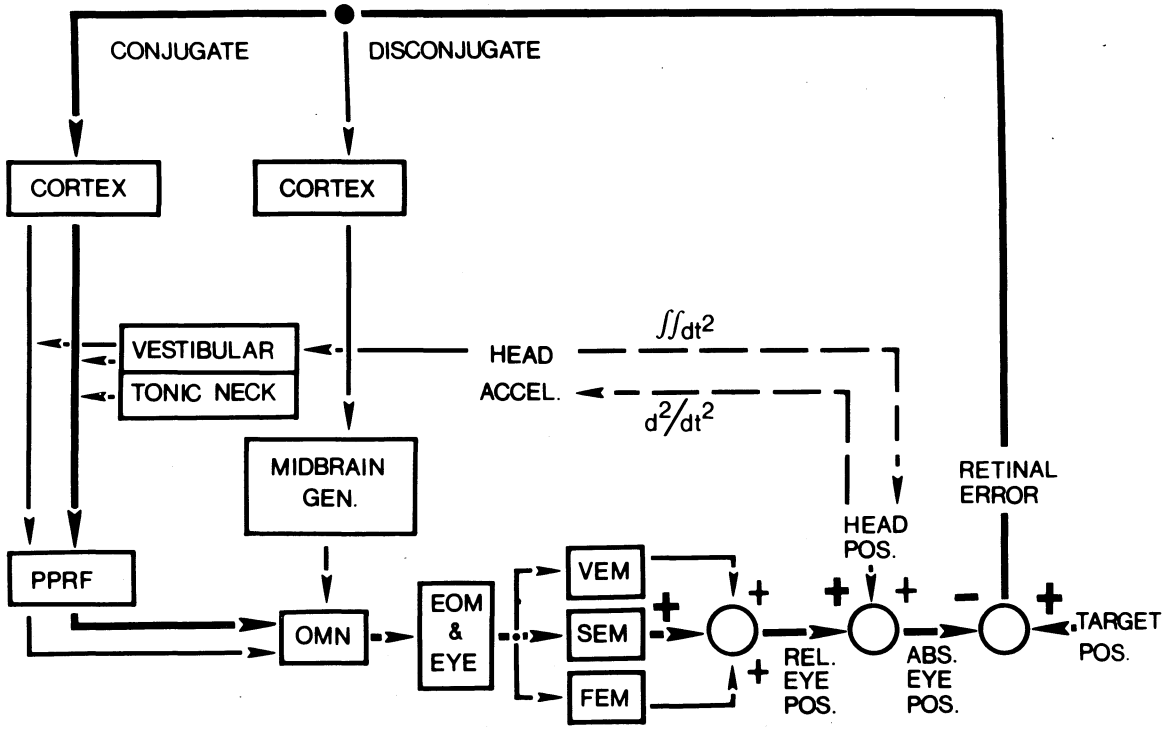


Figure 9. Basic closed-loop block diagram of the slow eye movement (SEM) mode of the version subsystem (heavy lines) super-imposed on the block diagram of the total ocular motor control system. The control signal, conjugate retinal error velocity, is sent to the cortex and the decision to move the eyes is forwarded to the pontine para-median reticular formation (PPRF) where the motor commands are generated. They are then passed on to the ocular motor nuclei (OMN). This innervation causes the extra-ocular muscles (EOM) to move the eye with a SEM and change relative eye velocity. Assuming no change in head position, this new absolute eye velocity sums with target velocity at the retina to produce zero retinal error velocity.

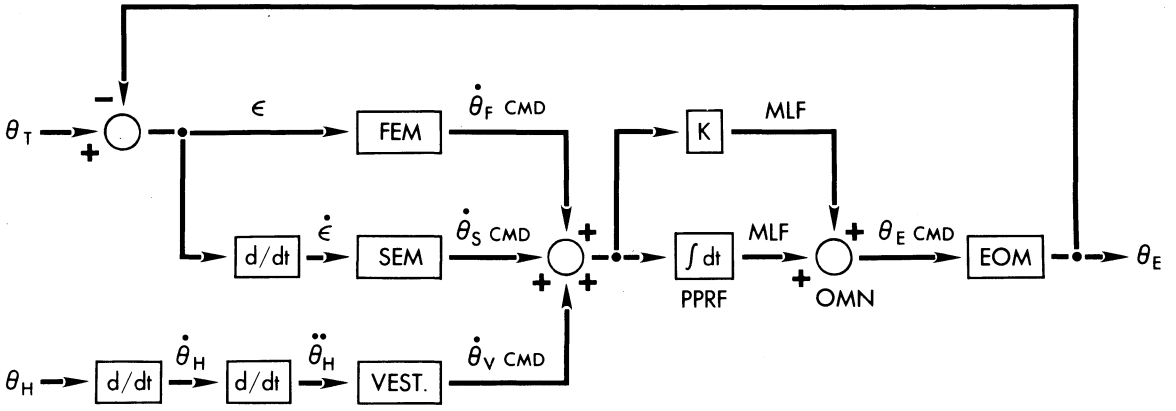


Figure 10. Block diagram of the dual-mode version subsystem with vestibular input which illustrates the difference between the closed-loop fast eye movement (FEM) and slow eye movement (SEM) mechanisms and the open-loop vestibulo-ocular apparatus. For simplicity the velocity commands of the FEM ($\dot{\theta}_F$ CMD), SEM ($\dot{\theta}_S$ CMD), and vestibular eye movements ($\dot{\theta}_V$ CMD) are shown summing and utilizing a final common integrator ($\int$ dt) located in the PPRF. Its output and the velocity outputs travel to the oculomotor nuclei (OMN) via the medial longitudinal fasciculus (MLF). The eye position command ($\theta_E$ CMD) is sent to the extra-ocular muscles (EOM) to effect the required eye position ($\theta_E$). $\theta_T$ is the target position. In this way, the position error, $\epsilon=\theta_T-\theta_E$, and the velocity error, $\dot{\epsilon}=\frac{d}{dt}(\theta_T-\theta_E)$, are driven to zero; there is no feedback to the vestibular system, which responds to head acceleration ($\ddot{\theta}_H$). Head position ($\theta_H$) and velocity ($\dot{\theta}_H$) are also shown along with their relationship to $\ddot{\theta}_H$.

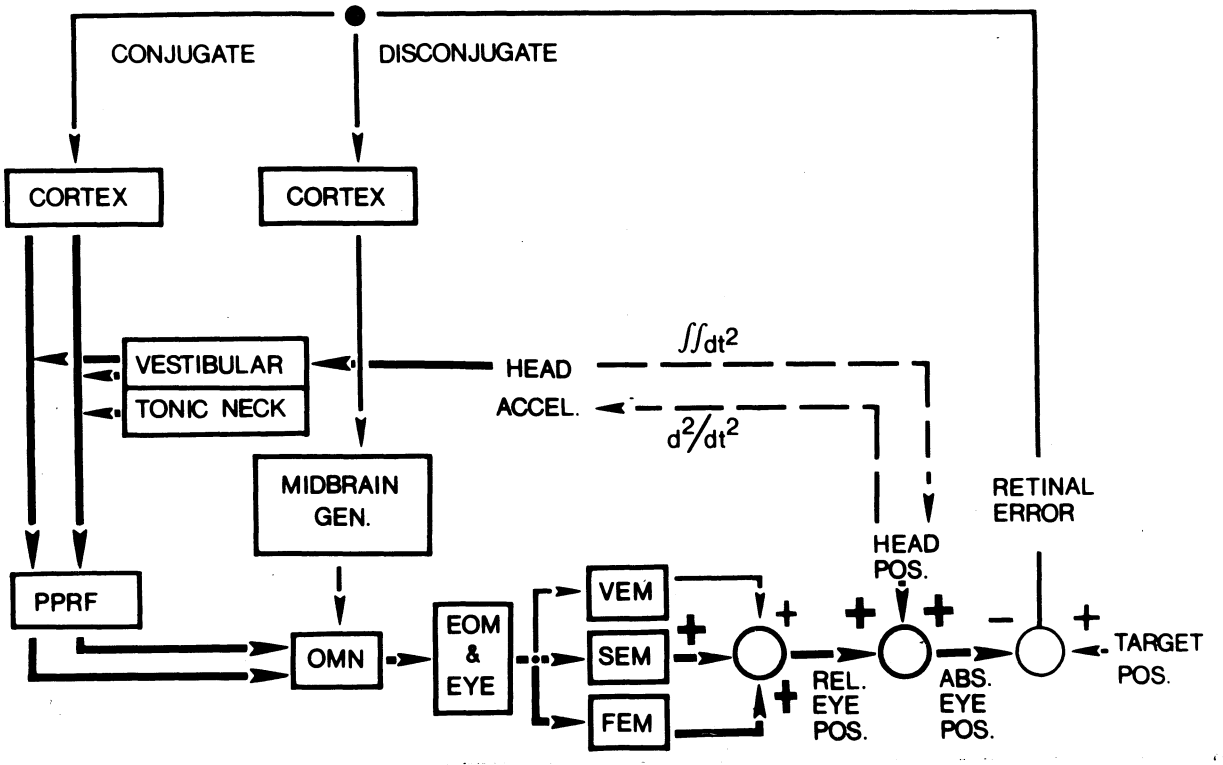


Figure 11. Basic open-loop block diagram of the vestibulo-ocular mechanism (heavy lines) super-imposed on the block diagram of the total ocular motor control system. The input is head acceleration which is converted to a neural signal proportional to head velocity by the semi-circular canals and sent to the pontine paramedian reticular formation (PPRF) via the vestibular nuclei. Here the motor commands are generated and passed on to the ocular motor nuclei (OMN). This innervation causes the extra-ocular muscles (EOM) to move the eye with a SEM in an attempt to match head velocity and a FEM if eye position requires change consequent to an internal centering mechanism. Absolute eye position is the sum of relative eye position and the now non-zero head position. The dashed lines show the mathematical relationships between head position and acceleration; they are not signal paths.

## Sub-system Synergism

When eye movements are studied in the laboratory or evoked in clinical examinations, individual types are isolated by the fixation of the head and/or providing a simple appropriate stimulus. However, most naturally occurring eye movements are a combination of different versional admixed with vergence eye movements reflecting the synergistic operation of all the sub-systems (Fig. 14).

Under- or over-activity in any subsystem may result in dynamic eye movement disturbances (Fig. 15). These constitute the abnormal ocular oscillations of which nystagmus is the most common (Daroff and Troost, 1976a).

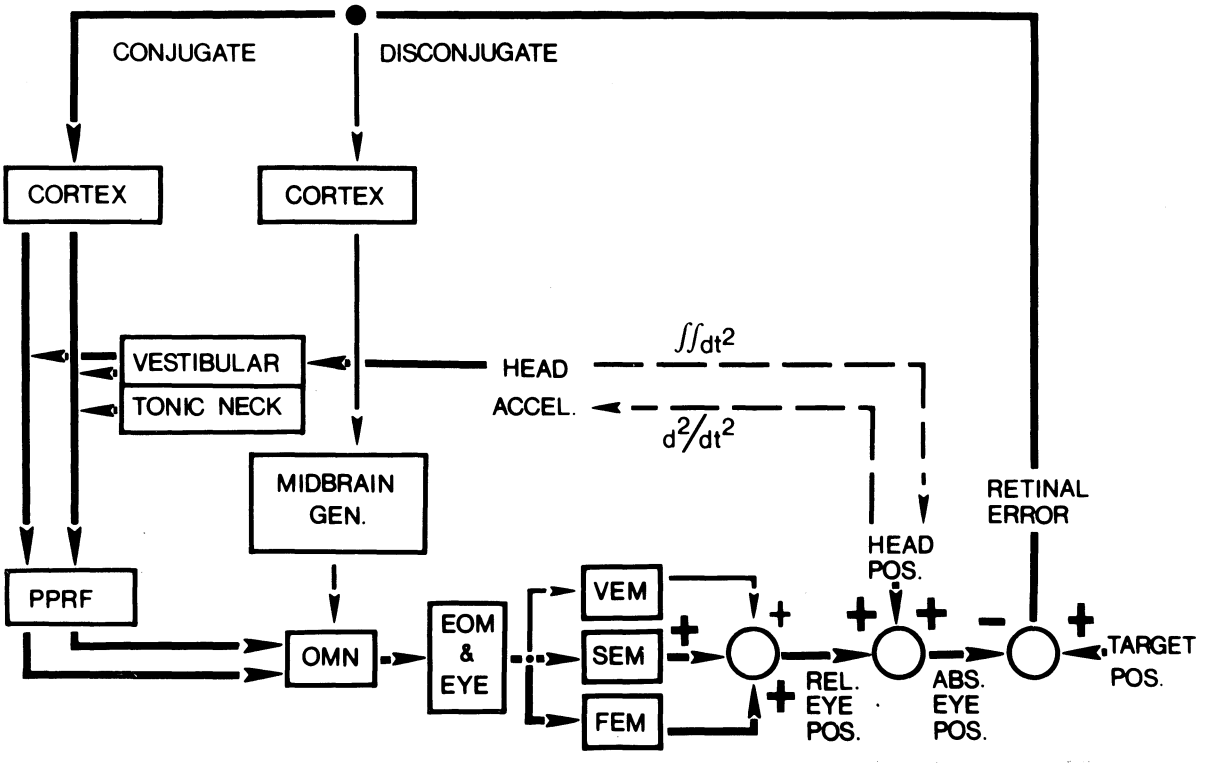


Figure 12. Basic closed-loop block diagram of the dual-mode version subsystem (heavy lines) with open-loop vestibular inputs (heavy lines) super-imposed on the block diagram of the total ocular motor control system. The retinal error inputs combine with head acceleration and position inputs to create all version outputs (FEM, SEM, and FEM plus SEM). See Figures 7, 9, and 11 for explanation of the individual components of the version subsystem.

## Anatomic and Clinical Correlations

We aim ultimately to conceptionalize all abnormal ocular motor phenomena within the physiological and control system frame work outlined above. Presently, lack of critical pathophysiological information ofttimes impedes our goal. Despite such limitations, clinicians are obliged to correlate eye movement disorders with pathological lesions and disease states. Expediency compels the utilization of pragmatic operational schemata which are knowingly simplistic. We will discuss the operational approaches which, in our judgement, have distinct proven utility in evaluating gaze disorders. Our discussion will be restricted to static (paralytic) as opposed to dynamic (oscillatory) disturbances of the horizontal versional subsystem and will commence with anatomical considerations.

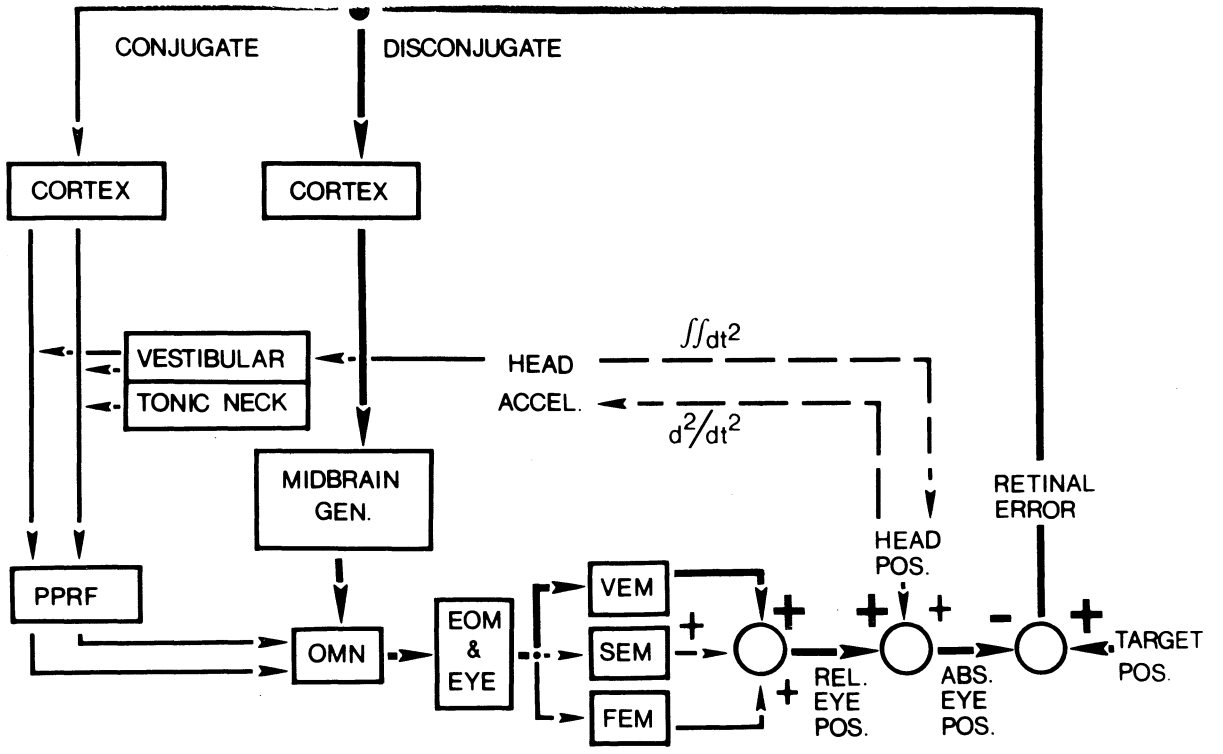


Figure 13. Basic closed-loop block diagram of the vergence subsystem (heavy lines) super-imposed on the block diagram of the total ocular motor control system. The control signal, disconjugate retinal error (static diplopia) and/or error velocity (changing diplopia), is sensed by the cortex. The decision to move the eyes is forwarded to a mid-grain structure where the motor commands are generated and passed to the ocular motor nuclei (OMN). This innervation causes the extra-ocular muscles (EOM) to move the eye with a VEM and change relative eye position and/or velocity. Assuming no change in head position, this new absolute eye position and/or velocity sums with target position and/or velocity to produce zero disconjugate retinal error(s).

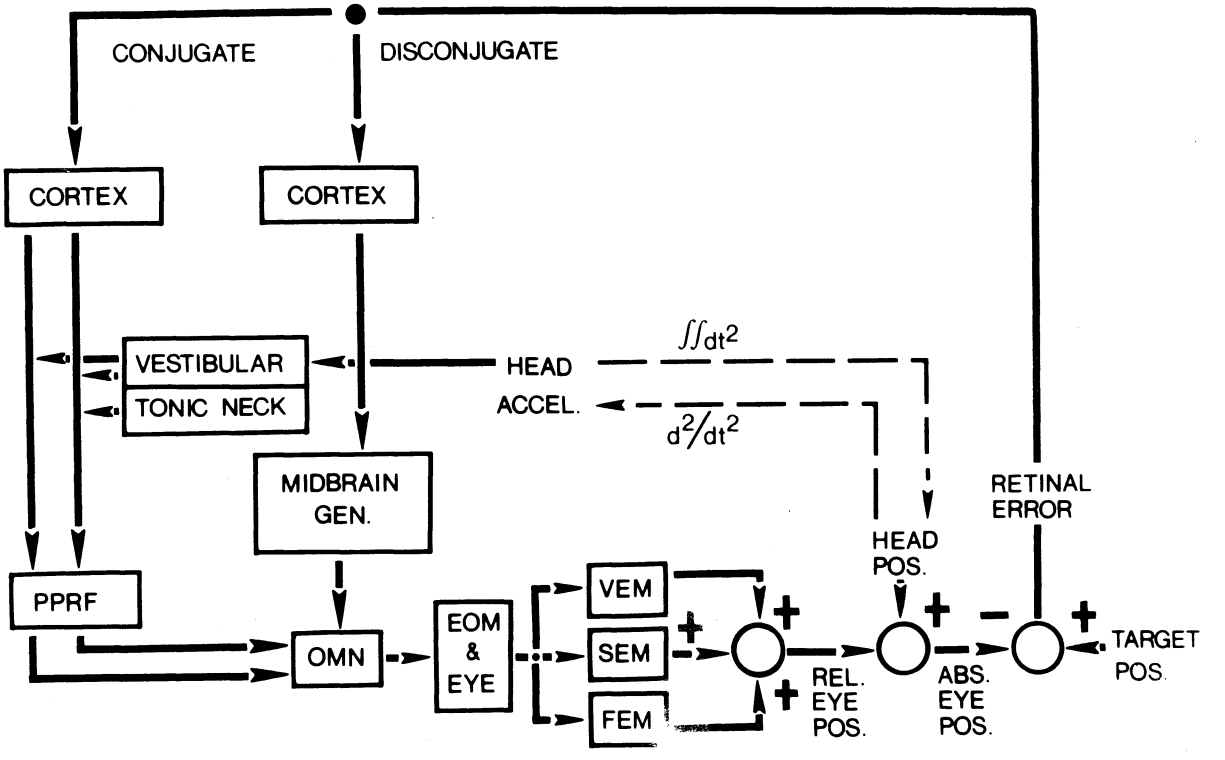


Figure 14. Basic block diagram of the ocular motor system with vergence and dual-mode version subsystems. Explanation of the various componants are provided in preceeding Figures.

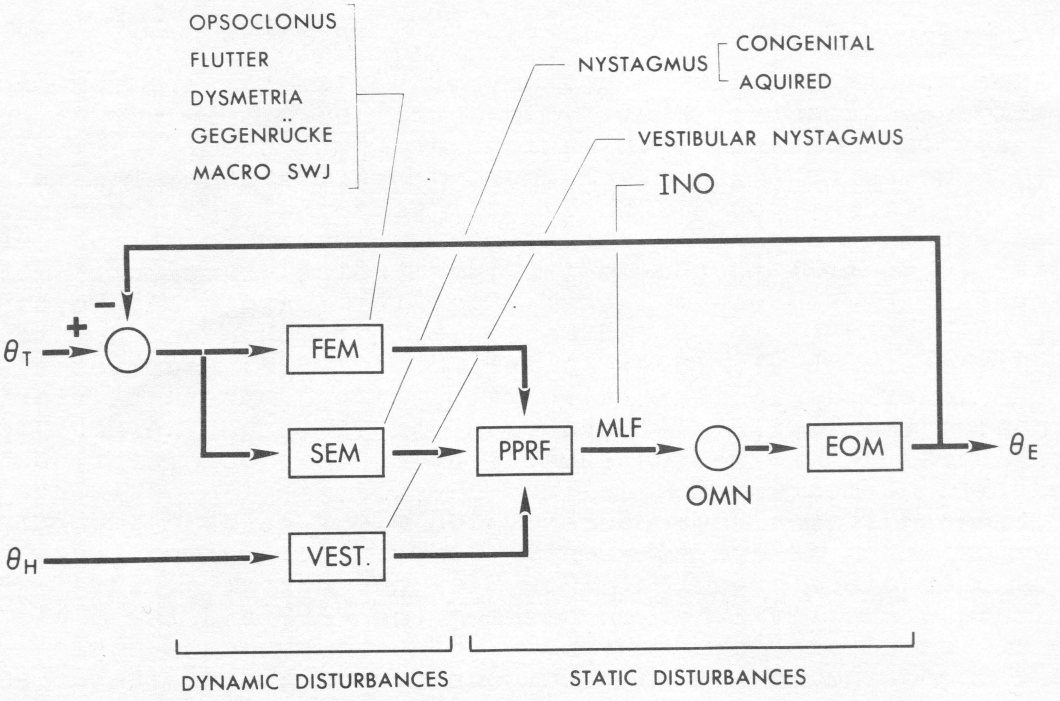


Figure 15. Simplified block diagram of the dual-mode version sub-system and vestibular input with various ocular motor disorders related to disturbances in specific sub-systems. $\theta_T$ is target position, $\theta_H$ is head position, and $\theta_E$ is eye position.

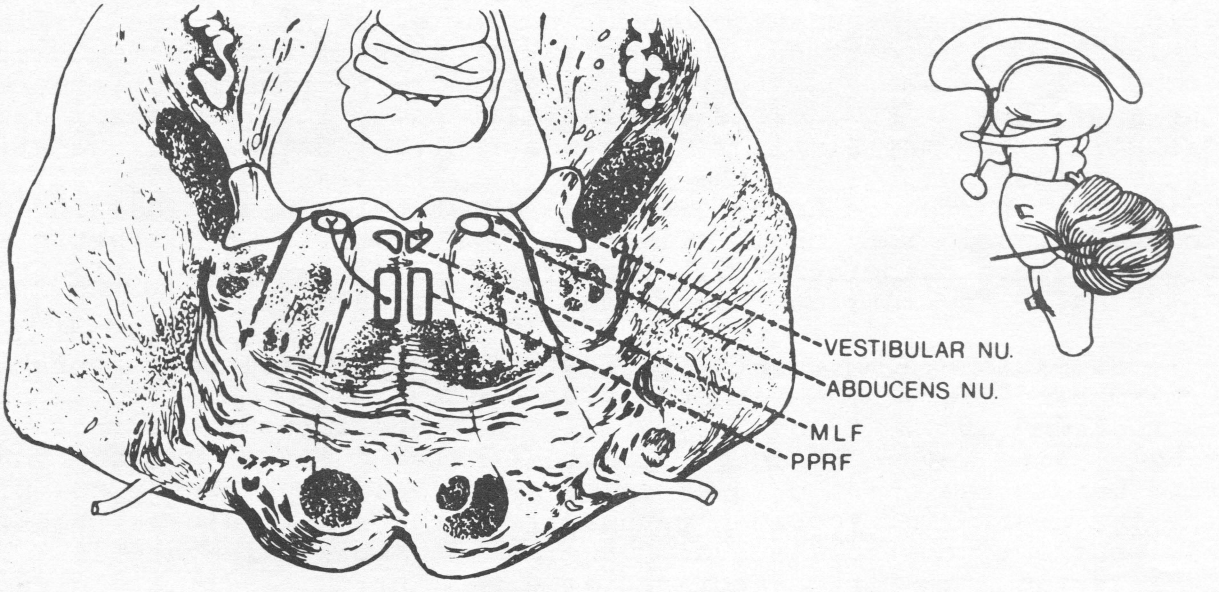


Figure 16. (From: Sharpe et al, 1974) Schematic cross section through caudal pons showing postulated projections from pontine paramedian reticular formation (PPRF) to the ipsilateral abducens nucleus and opposite medial longitudinal fasciculus (MLF). The possible synapses between these projections in the nucleus prepositus hypoglossi and abducens interneurons are not shown.

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Precise details of the anatomy of horizontal eye movements are presently unavailable. What follows will be simple operational constructs not incompatable with basic anatomical studies. These have usually lead us to the correct lesion localization. The major prenuclear structures for all horizontal versional eye movements are located within the pontine paramedian reticular formation (PPRF) immediately ventral to the medial longitudinal fasciculi (MLF) at the level of the abducens nuclei (Fig. 16) (Daroff and Hoyt, 1971; Goebel et al, 1971; Cohen and Henn, 1972ab; Cohen and Komatsuzuki, 1972; Highstein et al, 1974; Keller, 1974; Sharpe et al, 1974). The PPRF generates ipsilateral horizontal eye movements via its projections to the ipsilateral abducens and, through the MLF, to the contralateral medial rectus subnucleus of the oculomotor nuclei (Figs. 16 and 17). Recent anatomical and physiological experiments have identified additional structures which might have an important role in the mediation of eye movement. Of particular importance is the nucleus prepositus hypoglosi (Graybiel and Hartwieg, 1974) which may constitute a summing junction between the PPRF and the ocular motoneurons. There are interneurons within the abducens nuclei which project to motoneurons within the oculomotor nuclei (Baker and Highstein, 1975). Conversely, interneurons within the oculomotor nuclei project to motoneurons in the abducens nuclei (Maciewicz et al, 1975). The functional significance of these neurons and their connections are presently unknown.

Unilateral pursuit SEM abnormalities consequent to cerebral hemispheric lesions are ipsilateral to the diseased hemisphere (Daroff, 1970a; Daroff and Hoyt, 1971; Troost et al, 1972; Daroff and Troost, 1976b). Thus, our anatomical schematic of pursuit pathways (Fig. 18) depicts the eye movement as "originating" in the ipsilateral hemisphere. The cardinal abnormality of pursuit eye movements is "cogwheel" or "saccadic" pursuit. Instead of a smooth SEM, there is the admixture of FEM. This occurs bilaterally in a number of clinical situations and may simply reflect inattention, fatigue, or sedating drugs. When unilateral, the pathology is ipsilateral (Fig. 19). Unilateral pursuit abnormalities are practically never isolated neurological signs. They occur primarily with posterior hemispheric lesions and are associated with contralateral visual field defects and optokinetic asymmetrics (Daroff and Troost, 1976b).

Saccadic eye movements originate in the contralateral cerebral hemisphere (Fig. 20). Although area eight of Brodmann traditionally is regarded as the frontal eye field, intracellular recordings from single units have not, to date, demonstrated cortical neurons that fire before the onset of a saccade; such cells have been found within the thalamus. The saccadic pathway from the contralateral cerebral hemisphere to the ipsilateral PPRF is presumably polysynaptic. This is inferred from both anatomical studies (Astruc, 1971) and clinical observations in patients with Progressive Supranuclear Palsy. This condition is associated with eye movement paralysis (David et al, 1968), yet the pathology is limited to neurons within the basal ganglia and to midbrain. Axons are essentially spared. In the caudal midgrain, the descending saccadic pathway undergoes a decussation and

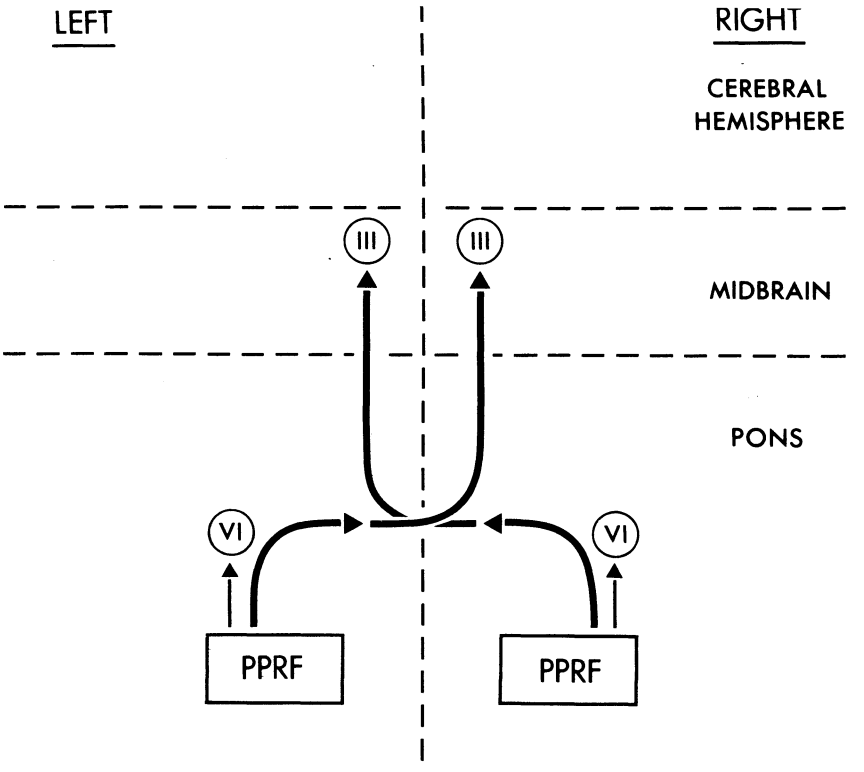



Figure 17. (From: Daroff and Troost, 1976 b) Operational schematic showing output of PPRF to ipsilateral VI and opposite III nuclei. Crossing to the latter is at level of VI and pathway ascends to midbrain in MLF. From Glaser J. (Editor): Clinical Ophthalmology - Hagerstown, MD, Harper & Row, Vol II, 1976.

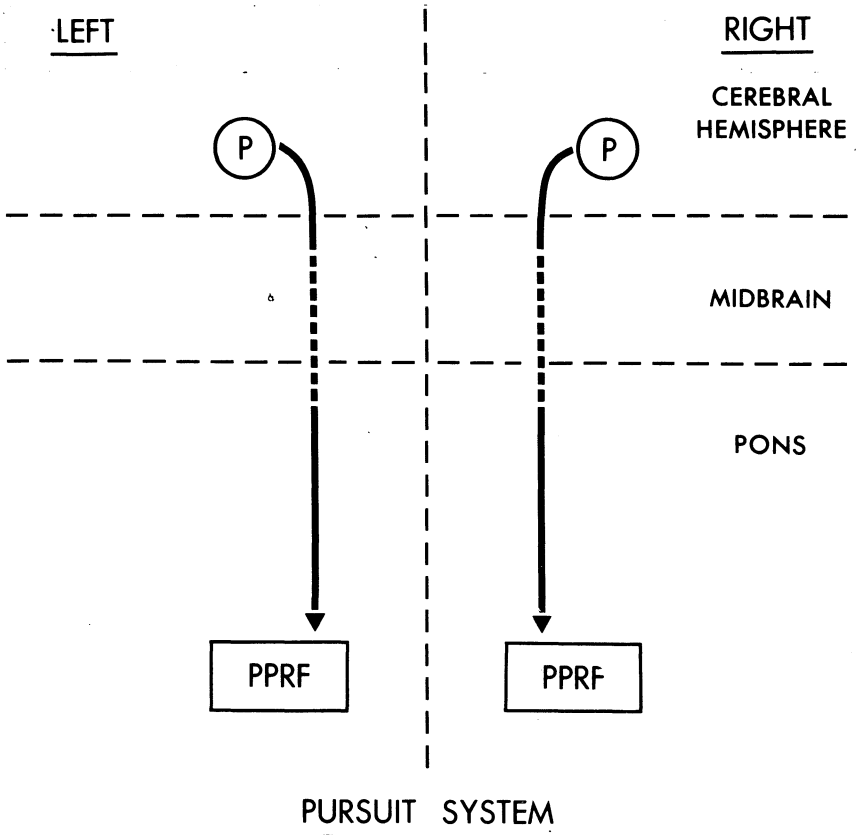



Figure 18. (From: Daroff and Troost, 1976 b) Operational schematic of pursuit anatomy which, for clinical purposes, is ipsilateral. Dashed lines indicate location of possible double decussation. From Glaser J. (Editor): Clinical Ophthalmology - Hagerstown, MD, Harper & Row, Vol II, 1976.

descends through the PPRF until reaching the anatomical level of the abducens nuclei. Here at the caudal 1/3 of the pons (Fig. 16) the PPRF functions as a pre-nuclear aggregate ("pontine center") for all ipsilateral versional eye movements.

The projections of the saccadic, pursuit, and vestibular inputs to the PPRF are shown in Figure 21 and these are combined with the PPRF outputs in Figure 22, the last of these schemata. An outline of supranuclear phenomenology (Table 2) can be supplemented with more detailed descriptions provided elsewhere (Daroff and Hoyt, 1971; Daroff and Troost, 1976b)

The cerebellum is omitted from the diagrams although we recognize its strong influence upon all the ocular motor subsystems (Daroff, 1970b and 1975; Daroff and Hoyt, 1971; Robinson, 1975abc; Westheimer and Blair, 1974; Hoyt and Frisen, 1975).

The terms "palsy" and "paresis" are applied to eye movement disorders in a manner analogous to that of extremity motor impairment. Thus, palsy (paralysis) implies complete disruption of the motor pathway and paresis (weakness) implies an incomplete or subtotal disruption. However, whereas extremity strength can be graded in a simple fashion, eye movement "pareses" are considerably more complicated. At least five different clinical phenomena are regarded, perhaps loosely, as examples of saccadic paresis (Table 3). Each represents a specific abnormality in the neuronal firing pattern for FEM. The normal pattern, as described previously, consists of a pulse-step (Fig. 5b) increase in firing frequency within the appropriate mononeurons (3rd, 4th, and 6th cranial nerve nuclei). There is overwhelming evidence that the pulse is generated within the PPRF and its intergration to form the step also occurs within the PPRF (Keller, 1974). Thus, the entire operation depicted in Figure 6 (except for the summing of the pulse and step) occurs in the PPRF at the level of the abducens nuclei.

A defective neural integrator would cause the motoneurons to receive only pulse signals. In such a situation, a saccadic refixation will be of normal speed and amplitude, but, without the tonic step pattern, the eyes will not be held in the new deviated position. They will drift back toward primary position with a decelerating exponential time course. If the subject maintains an effort to refoveate the eccentric target, the slow drift will be countered by a FEM back to the target. The phasic patterning of the FEM and slow exponential drifts constitute "gaze-paretic" nystagmus (Fig. 23) (Kommerell, 1975). This form of nystagmus thus represents a stepless eccentric saccade consequent to defective neural integration within the PPRF in a patient who maintains the gaze effort. If the latter is not maintained, the eyes would continue the decellerating exponential drift until coming to rest at primary position.

An inoperative generator is associated with complete versional paralysis in the appropriate direction. However, if the pulse is generated but blocked from summing with the step (Fig. 6), a pulse-less

TABLE II. DIFFERENTIAL LOCALIZATION OF HORIZONTAL SACCADIC PALSY

| Anatomic Location of Lesions | FRONTO-MESENCEPHALIC | | PONTINE PARAMEDIAN RETICULAR FORMATION | |
|---|---|---|---|---|
| | Hemisphere | Midbrain Pre-decussation | PPRF Rostral to VI | PPRF Level of VI |
| Direction of Palsy | Contralateral to lesion. | | Ipsilateral to lesion. | |
| Duration of Palsy with Fixed Lesion | Transient | Intermediate. May clear. | Permanent | |
| Smooth Pursuit Function | May be spared | | Always impaired | |
| Conjugate Deviation | Ipsilateral. Invariable. | Ipsilateral. Variable. | Contralateral. only when acute | |
| Associated Paralysis | Extremities and lower face, contralateral to lesion; ipsilateral to gaze palsy. | | Extremity paralysis contralateral to lesion and gaze palsy. Facial paralysis ipsilateral to gaze palsy. | |
| Cold Caloric Irrigation on Side of Palsy | Tonic ocular deviation to side of stimulus with normal fast phase in opposite direction. | | Tonic ocular deviation to side of stimulus with normal fast phase in opposite direction. | No response |
| Cold Caloric Irrigation on Side Opposite Palsy | Tonic deviation with variable fast phase; normal, impaired, absent. | Tonic deviation. Variable fast phase. | Tonic deviation. Occasional small amplitude fast phases. | |

(From: Daroff and Troost, 1976 b)



From Glaser J. (Editor): Clinical Ophthalmology - Hagerstown, MD, Harper & Row, Vol II, 1976.

TABLE III. OPERATIONAL DEFINITIONS OF SUPRANUCLEAR EYE MOVEMENT DISORDERS

I. Palsy or Paralysis (Total loss of function in a given direction beyond primary position)

   A. Saccade Palsy (normal pursuit)

   B. Pursuit Palsy (normal saccades; exceedingly rare)

   C. Gaze Palsy (both saccades and pursuit paralyzed)

II. Paresis (incomplete or subtotal involvement)

   A. Saccade Paresis (normal pursuit co-existing with any of the following:)

      1. Slow saccades

      2. Gaze-paretic nystagmus

      3. Limited eccentric excursion

      4. Inability to maintain eccentric fixation

      5. Unilateral hypometric saccades

   B. Pursuit Paresis (normal saccades)

      1. Unidirectional "saccadic" pursuit

   C. Gaze Paresis (combination of saccadic paresis with pursuit palsy or paresis)

(From: Daroff and Troost, 1976 b)

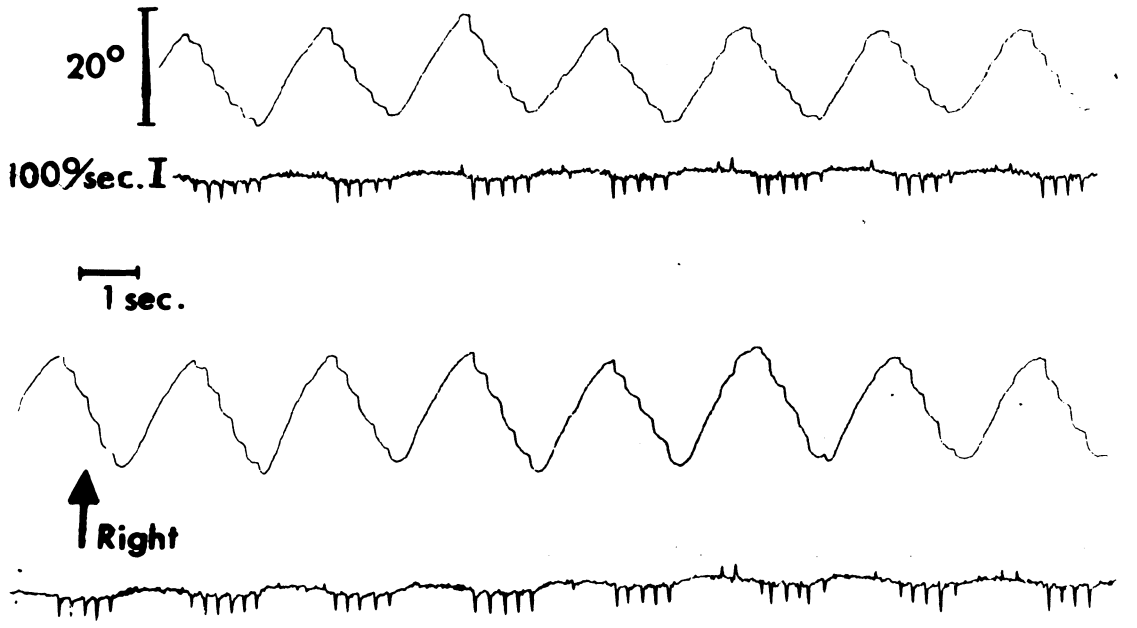



Figure 19. Unilateral cogwheel (saccadic) pursuit to the left during sinusoidal tracking in patient with previous left cerebral hemispherectomy. Upper two tracings represent eye position and velocity, respectively, from right eye. Lower tracings are from left eye. The pursuit movements to the right are smooth with only occasional saccades intersperced. Those to the left are slower than the target and require repetative catch-up saccades to re-achieve target fixation. These leftward saccades are particularly distinct in the velocity tracings.

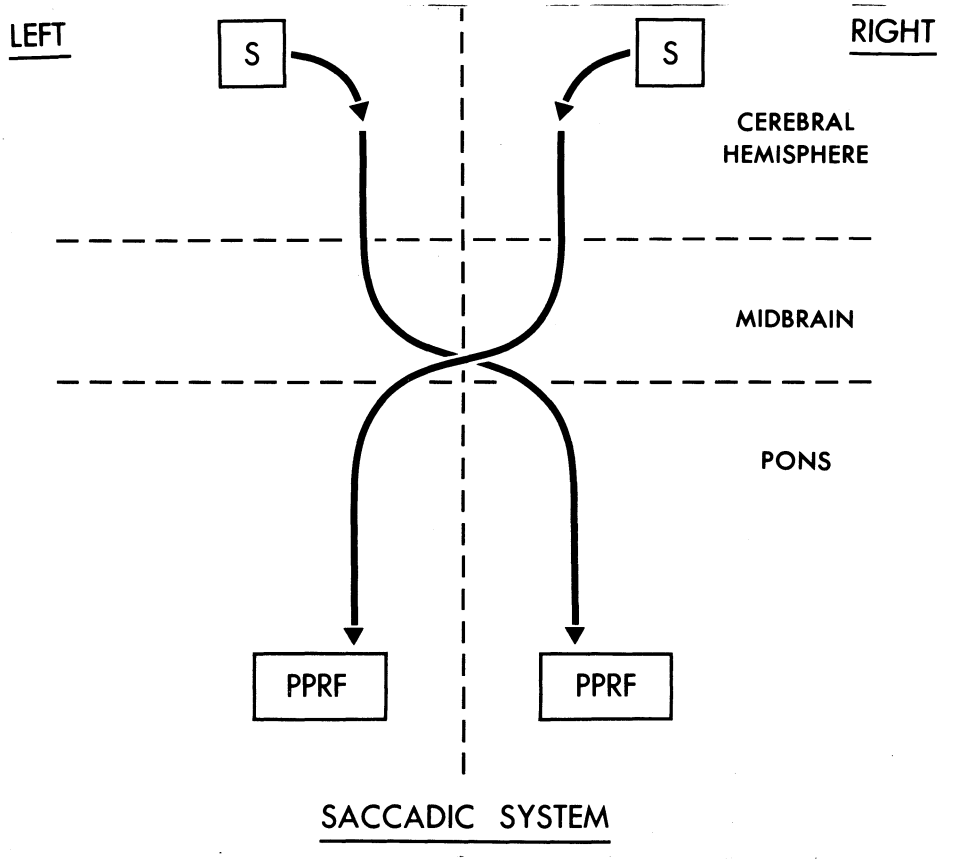



Figure 20. (From: Daroff and Troost, 1976 b) Operational schematic of saccadic anatomy. Saccades originate in contralateral cerebral hemisphere. The pathway descends through the hemisphere with multiple synapses and decussates at the midbrain-pontine junction. It then descends in the PPRF to the caudal pons at the level of the abducens nuclei.From Glaser J. (Editor): Clinical Ophthalmology - Hagerstown, MD, Harper & Row, Vol II, 1976.

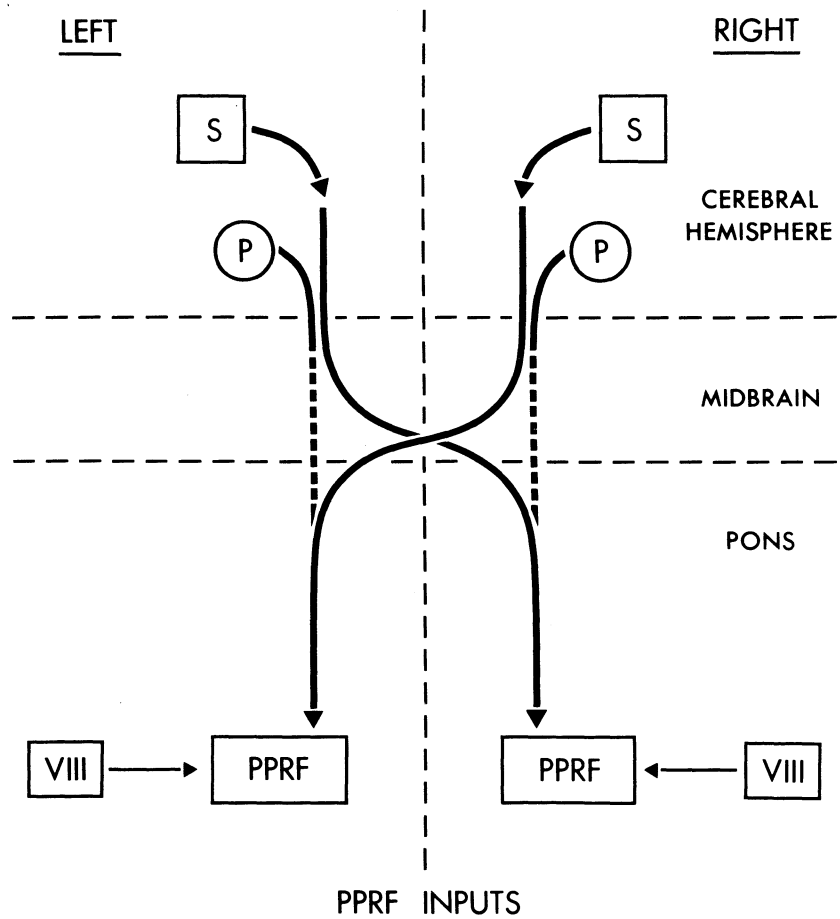
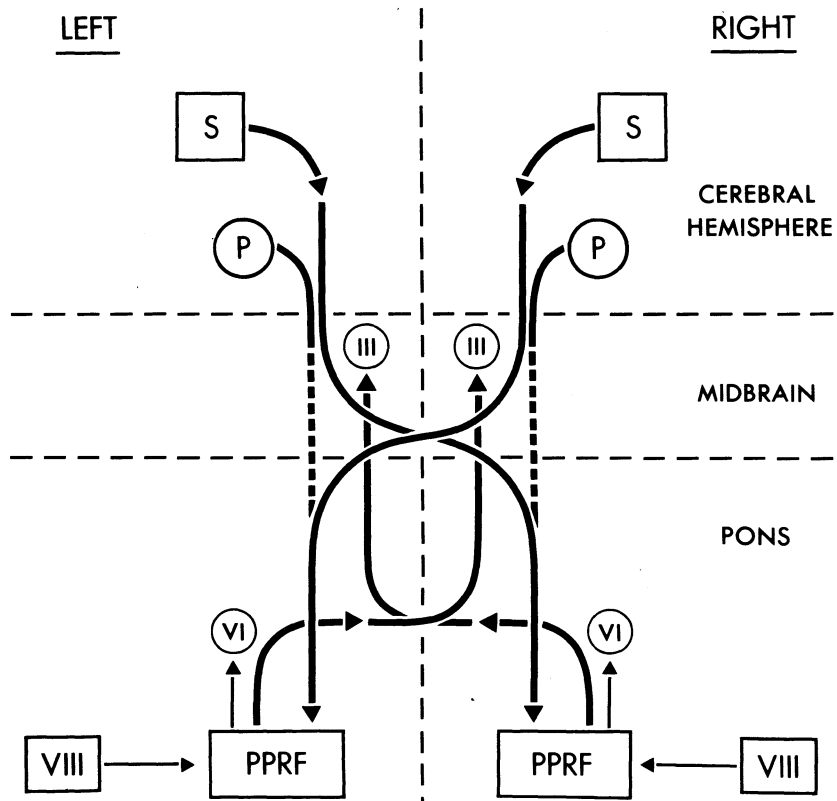



Figure 21. (From: Daroff and Troost, 1976 b) Schematic combining Figures 18 and 20 with addition of vestibular input to the PPRF. From Glaser J. (Editor): Clinical Ophthalmology - Hagerstown, MD, Harper & Row, Vol II, 1976.




Figures 22. (From: Daroff and Troost, 1976 b) Schematic combining Figures 17 and 21. This contains major inputs to and outputs from PPRF. From Glaser J. (Editor): Clinical Ophthalmology - Hagerstown, MD, Harper & Row, Vol II, 1976.

FEM results (Fig. 24) (Daroff, 1975; Kommerell, 1975). The configuration of the slow pulse-less FEM is in sharp contrast to the normal FEM waveform (Fig. 3). A defective generator may produce sub-optinal firing frequencies which could explain limitations in amplitude excursions. Pulse-step impairments may explain the wave form of internuclear ophthalmoparesis (Dell'Osso et al, 1974).

## Ocular Motor Gain

Gain is an important concept warranting particular attention. Despite the repetition, we must re-emphasize that all types of eye movements are motor outputs in response to sensory inputs (Fig. 25). This Figure (from Robinson, 1968) shows that the inputs for saccadic, smooth pursuit, and vergence eye movements are visual, whereas the input to the vestibular sub-system is acceleration. The outputs of all the subsystems converge upon the motoneurons. This figure also demonstrates graphically the closed-loop nature of the saccadic, pursuit and vergence subsystems, as opposed to the open-loop vestibular subsystem.

The relationship between the sensory input (visual or head movement) and motor output (eye movement) is the Gain. Specifically,

$$\text{Gain} = \frac{\text{Output}}{\text{Input}} \qquad G = \frac{O}{I}$$

When the output equals the input, the gain is unity (1.0) and the eye movement is deemed "normal". We shall examine defective gains for pursuit, saccadic, and vestibular eye movements (Table 4).

A pursuit gain greater than 1.0 has not been recognized. When eye velocity does not match target velocity (gain <1.0), the eyes lag behind the target. This produces a retinal positional error signal which generates a catch-up saccade. Repetition of the slow pursuit and catch-up saccades constitute cog-wheel or saccadic pursuit (Fig. 19). This reflection of decreased pursuit velocity gain (Troost et al, 1972) is the most common acquired ocular motor abnormality encountered in clinical practice.

Dysmetria occurs with abnormal gains in the FEM sub-system. When the gain exceeds 1.0, the eyes overshoot the target; with gains less than 1.0, the eyes undershoot (Weber and Daroff, 1971). Slight decreases in gain are extremely common in large amplitude refixations and result in small undershoots, followed by a corrective saccade (Weber and Daroff, 1972). When the gain is markedly low, a multiple-step hypometric saccade results (Fig. 26) (Troost et al, 1974). In this Figure, the individual saccades are of normal velocity. However, in some disease states, particularly Progressive Supranuclear Palsy, the individual small saccades are slow, reflecting a defect in pulse firing rate as well as duration. Whereas depression of pursuit gain tends to be relatively stable, intra-subject saccadic gains are exceedingly variable and rarely fixed. Thus orthometric may alternate with multiple-step hypometric saccades.

TABLE IV.

| $G=\frac{O}{I}$ | Saccades<br>Saccade Amplitude / Target Amplitude | Pursuit<br>Pursuit Velocity / Target Velocity | Vestibular<br>Eye Velocity / Head Velocity |
|---|---|---|---|
| | >1 overshoot | >1 ----- | >1 ----- |
| | <1 undershoot | <1 cogwheel saccadic | <1 oscillopsia |

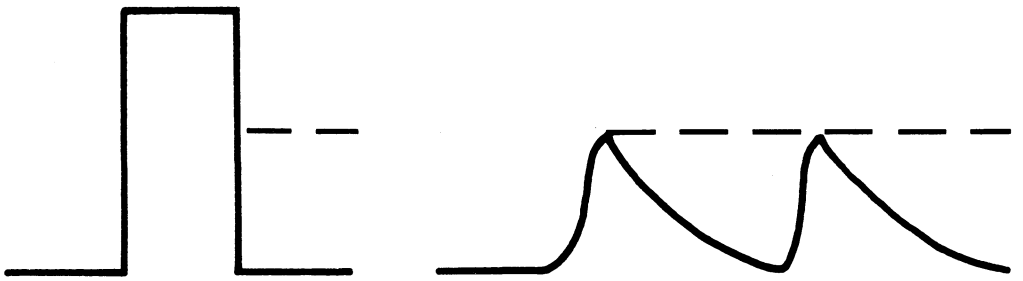


Figure 23. Illustration (left) of pulse increase of neural firing without step (dashed line) and resultant eye movement (right.) The eye makes normal eccentric FEM, but absence of step causes inability to maintain deviated gaze position (dashed lines.) The eye thus drifts back toward primary position in decellerating exponential trajectory. Step-less FEMs (saccades) are mechanism for gaze-paretic nystagmus.

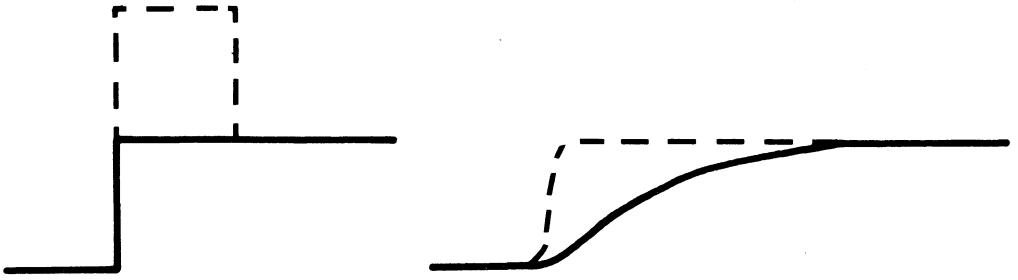
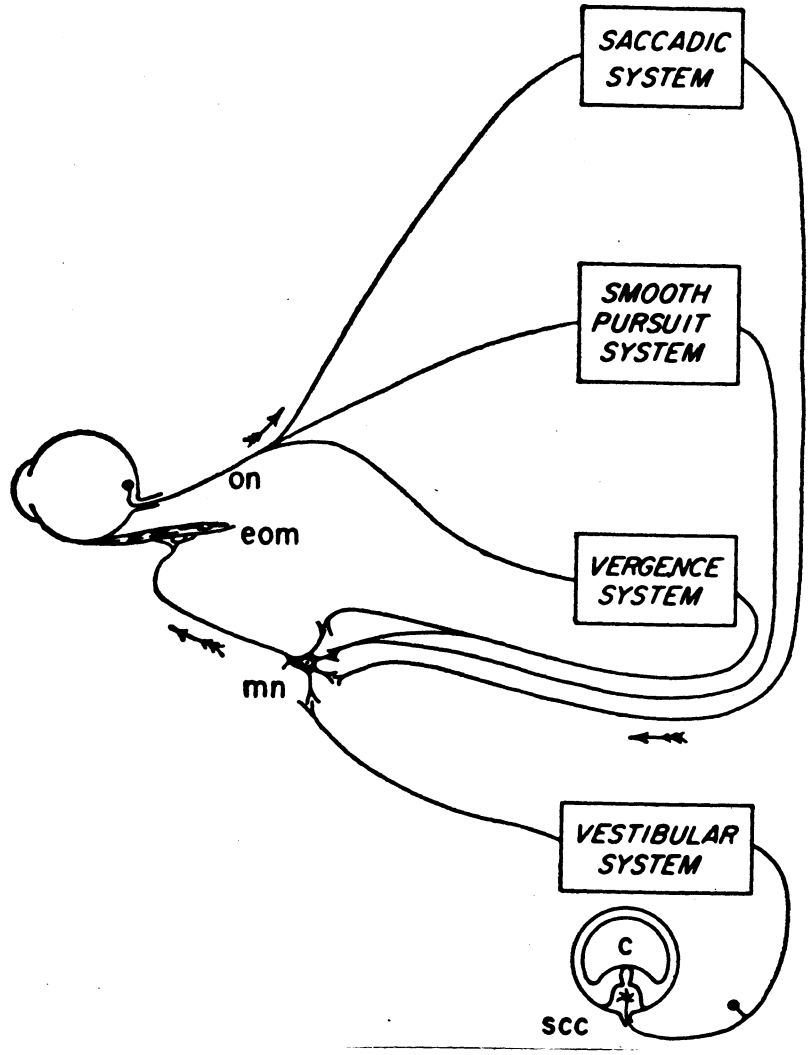


Figure 24. Illustration (right) of a slow pulse-less fast eye movement (FEM) and the underlying step of innervation (left). The dashed lines show the normal pulse-step of innervation and the correspondingly normal FEM.

The vestibulo-ocular gain in complete darkness is approximately 0.6. The eyes, therefore, lag behind the head. With a visible fixation target, the gain increases to 1.0 for all but exceedingly fast head movements. The increase in gain from 0.6 to 1.0 represents the summation of the pursuit function in illuminated conditions upon the vestibulo-ocular reflex (Barr et al, in press; Troost et al, in press). When the gain is 1.0, the eyes move in the head at a speed equal to that of the head but in the opposite direction (Fig. 27). Although the eyes deviates within the head (E) they do not deviate in space (E+H) and hence are able to maintain steady fixation upon a target. If the eye velocity becomes less than head velocity (Fig. 27 at higher frequencies), the eyes will deviate in space (E+H) and oscillopsia (illusory movement of the environment) results. Vestibulo-ocular gains in excess of 1.0 would also induce oscillopsia but have not been encountered as a spontaneous occurence. It does develop as an adaptation to prisms spectacles however (Robinson, 1975bc).

We have attempted to explain certain clinical eye movement disturbances in terms of their patho-physiological mechanisms. The past decade has witnessed a remarkable burgeoning of basic eye movement research and quantitative clinical studies. As such endeavors continue, our understanding of clinical phenomenology will increase accordingly.




From Robinson DA: Science 161:1219-1224, 1968
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Figure 25. (From: Robinson, 1968) Diagram of ocular motor system showing visual inputs (on) to the closed loop saccadic, pursuit, and vergence sub-systems, and head movement input from semi-circular canals (scc) to open loop vestibular sub-system. All sub-systems converge on ocular motoneurons (mn) which innervate extra-ocular muscles (EOM) to move the eye.

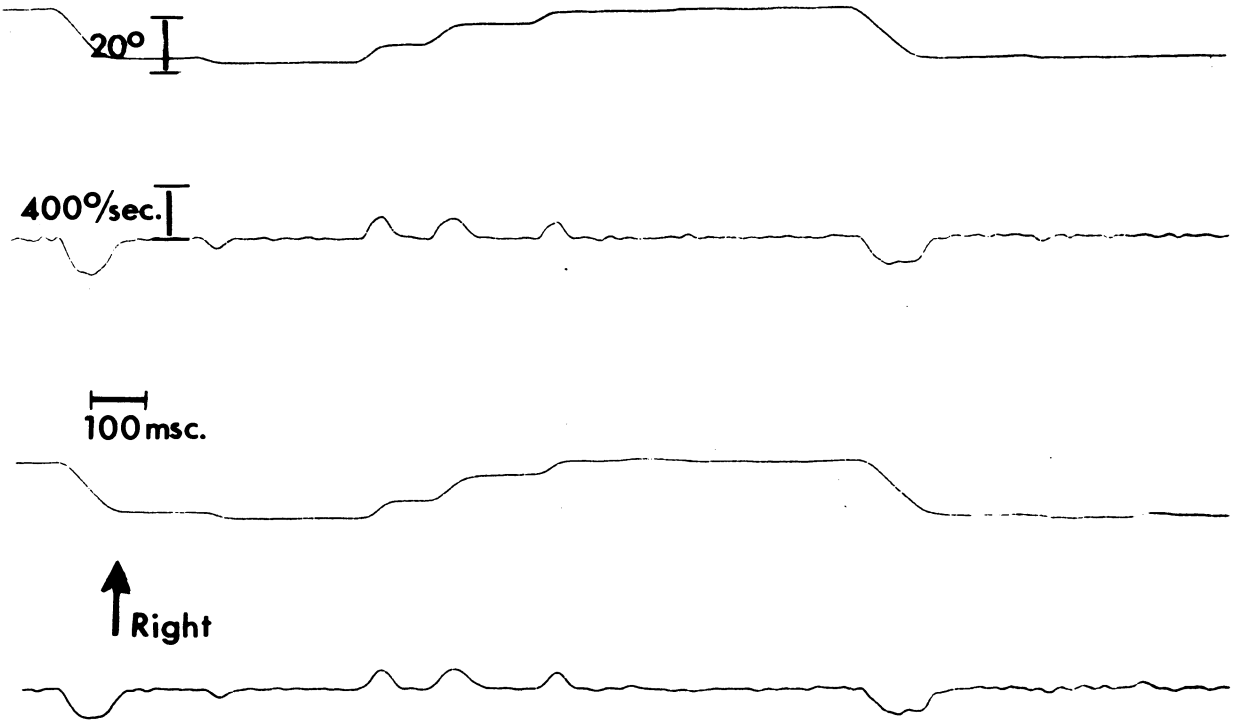


Figure 26. Oculogram of multiple-step hypometric saccade to right and orthometric (single-step) saccade to left. Upper two tracings are position and velocity singles, respectively, from right eye; lower two tracings are from left eye. Hypometric saccades reflect markedly lowered gain. A slight lowering of gain below 1.0 would cause a small undershoot followed by a corrective FEM after a latency of 125 msc. Such a movement is shown in the leftward saccade of the left eye at the first portion of the tracing.

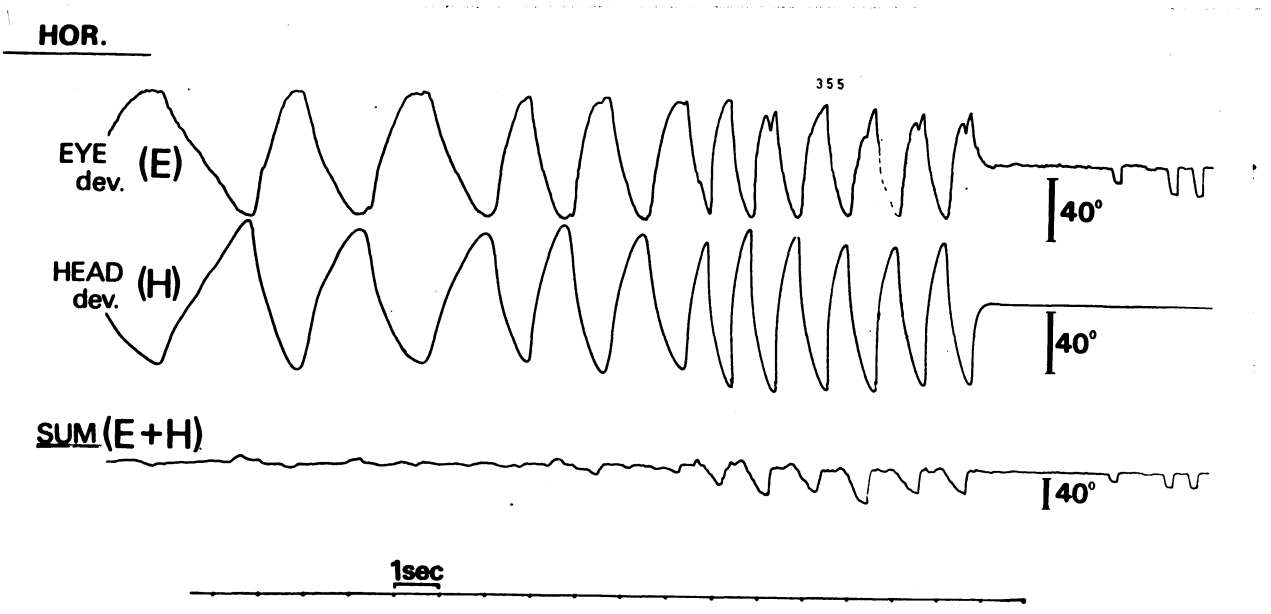


Figure 27. (From: Bender and Feldman, 1967) Recording of vestibulo-ocular reflex in subject fixating on visible target. At slow sinusoidal oscillations, the relative eye position (E; eye in head) was equal in velocity and opposite in direction to the head movement (H) resulting in no change in absolute eye position (E+H; eye in space.) The gain of the reflex was 1.0 and the subject was free of oscillopsia. At higher frequency oscillations (right side of tracing), the gain dropped below 1.0, the eyes moved in space (E+H) and oscillopsia developed. Arch Neurol 17:354, 1967

## References


Astruc, J. (1971). Corticofugal connections of area 8 (frontal eye field) in Macaca Mulatta. Brain Res. **33**: 241-256.

Baker, R. and Highstein, S. M. (1975). Physiological identification of interneurons and motoneurons in the abducens nucleus. Brain Res. 91: 292-298.

Barr, C. C., Schultheis, L. W., and Robinson, D. A. (in press). Voluntary, non-visual control of the human vestibuloocular reflex. Acta Oto-Laryng.

Bender, M. B. and Feldman, M. (1967). Visual illusions during head movement in lesions of the brain stem. Arch. Neurol. 17: 354-364.

Cohen, B. and Henn V. (1972a). Unit activity in the pontine reticular formation associated with eye movements. Brain Res. 46: 403-410.

Cohen, B. and Henn, V. (1972b). The origin of quick phases of nystagmus in the horizontal plane. Bibl. Ophthal. 82: 36-55.

Cohen, B. and Komatsuzaki, A. (1972). Eye movements induced by stimulation of the pontine reticular formation: evidence for integration in oculomotor pathways. Exp. Neurol. 36: 101-117.

Daroff, R. B. (1970a). Physiologic, anatomic and pathophysiologic considerations of eye movements. Trans. Ophth. Soc. U. K. 90: 409-416.

Daroff, R. B. (1970b). Ocular motor manifestations of brain stem and cerebellar dysfunction. In "Neuro-Ophthamology, Vol. V" ed. J. L. Smith, Huffman Publishing Co., Hallandale, Florida, pp. 104-118.

Daroff, R. B. (1975). Concluding remarks: summary of clinical presentations. In "Basic Mechanisms of Ocular Motility and Their Clinical Implications", ed. G. Lennerstrand and P. Bach-Y-Rita, Pergamon Press, Oxford and New York, pp. 435-443.

Daroff, R. B. and Troost, B. T. (1976a). Nystagmus and other ocular oscillations. In "Clinical Ophthalmology", Vol. II, ed. J. Glaser, Harper and Row, Hagerstown, Maryland.

Daroff, R. B. and Troost, B. T. (1976b). Supranuclear disorders of eye movements. In "Clinical Ophthalmology", Op. Cit.

Daroff, R. B. and Hoyt, W. F. (1971). Supranuclear disorders of ocular control systems in man: clinical, anatomical and physiological correlations, 1969. In "The Control of Eye Movements", ed. P. Bach-Y-Rita, C. C. Collins, and J. E. Hyde, American Press, New York, pp. 175-235.

David, N. J., Mackey, E. A., and Smith, J. L. (1968). Further observations in progressive supranuclear palsy. Neurology. 18: 349-356.

Dell'Osso, L. F. and Daroff, R. B. (1974). Functional organization of the ocular motor system. Aerospace Med. 45: 873-875.

Dell'Osso, L. F. and Daroff, R. B. (1976). Eye movement characteristics and recording techniques. In "Clinical Ophthalmology", Op. Cit.

Dell'Osso, L. F., Robinson, D. A., and Daroff, R. B. (1974). Optokinetic asymmetry and internuclear ophthalmoplegia. Arch. Neurol. 31: 138-139.

Fuchs, A. F. and Luschei, E. S. (1970). Firing patterns of abducens neurons of alert monkeys in relationship to horizontal eye movement. J. Neurophys. 33: 382-392.
Goebel, H. H., Komatsuzaki, A., Bender, M. B., and Cohen, B. (1971). Lesions of the pontine tegmentum and conjugate gaze paralysis. Arch. Neurol. 24: 431-440.
Graybiel, A. M. and Hartwieg, E. A. (1974). Some afferent connections of the oculomotor complex in the cat: an experimental study with tracer techniques. Brain Res. 81: 543-551.
Highstein, S. M., Cohen, B., and Matsunami, K. (1974). Monosynaptic projections from the pontine reticular formation to the IIIrd nucleus in the cat. Brain Res. 75: 340-344.
Hoyt, W. F. and Frisen, L. (1975). Supranuclear ocular motor control and its disorders. In "Basic Mechanisms of Ocular Motility and Their Clinical Implications", Op. Cit.
Keller, E. L. (1974). Participation of medial pontine reticular formation in eye movement generation in monkey. J. Neurophys. 37: 316-332.
Kommerell, G. (1975). Activity in eye motoneurons and brain stem units during eye movements. In "Basic Mechanisms of Ocular Motility and Their Clinical Implications", Op. Cit.
Maciewicz, R. J., Kaneko, C. R. S., Highstein, S. M., and Baker, R. (1975). Morphophysiological identification of interneurons in the oculomotor nucleus that project to the abducens nucleus in the cat. Brain Res. 96: 60-65.
Rashbass, C. (1961). The relationship between saccadic and smooth tracking eye movements. J. Physiol. 159: 326-338.
Robinson, D. A. (1968). Eye movement control in primates. Science. 161: 1219-1224.
Robinson, D. A. (1970). Oculomotor unit behavior in the monkey. J. Neurophys. 33: 393-404.
Robinson, D. A. (1972). On the nature of visual-oculomotor connections. Invest. Ophthal. 11: 497-503.
Robinson, D. A. (1975a). Oculomotor control signals. In "Basic Mechanisms of Ocular Motility and Their Clinical Implications", Op. Cit.
Robinson, D. A. (1975b). The neural basis for pontine and cerebellar control of eye movement. Jap. J. Ophthal. 19: 25-38.
Robinson, D. A. (1975c). How the oculomotor system repairs itself. Invest. Ophthal. 14: 413-415.
Robinson, D. A. and Keller E. L. (1972). The behavior of eye movement motoneurons in the alert monkey. Bibl. Ophthal. 82: 7-16.
Rubin, A. M., Young, J. H., Milne, A. C., Schwarts, D. W. F., and Fredrickson, J. M. (1975). Vestibular-neck integration in the vestibular nuclei. Brain Res. 96: 99-102.
Sharpe, J. A., Rosenberg, M. A., Hoyt, W. F., and Daroff, R. B. (1974). Paralytic pontine exotropia. Neurology. 24: 1076-1081.
Troost, B. T., Daroff, R. B., Weber, R. B., and Dell'Osso, L. F. (1972). Hemispheric control of eye movements. II. Quantitative analysis of smooth pursuit in a hemispherectomy patient. Arch. Neurol. 27: 449-452.

Troost, B. T., Dell'Osso, L. F., and Daroff, R. B. (in press). Effects of visual pursuit deficit on the human vestibulo-ocular reflex. Neurology.
Troost, B. T., Weber, R. B., and Daroff, R. B. (1974). Hypometric saccades. Amer. J. Ophthal. 78: 1002-1005.
Weber, R. B. and Daroff, R. B. (1971). The metrics of horizontal saccadic eye movements in normal humans. Vision Research. 11: 921-928.
Weber, R. B. and Daroff, R. B. (1972). Corective movements following refixation saccades: type and control system analysis. Vision Research. 12: 467-475.
Westheimer, G. and Blair, S. M. (1974). Functional organization of primate oculomotor system revealed by cerebellectomy. Exp. Brain Res. 21: 463-472.
Yarbus, A. L. (1967). Eye movements and vision. Plenum Press, New York.
Zuber, B. L. (1971). Control of vergence eye movements. In "The Control of Eye Movements", Op. Cit., pp. 447-471.

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