52. K. E. Van Holde and L. B. Cohen, *Biochemistry* **3**, 1803, 1809 (1964); *Brookhaven Symp. Biol.* **17**, 184 (1964).
53. V. Bloomfield, K. E. Van Holde, W. O. Dalton, *Biopolymers* **5**, 149 (1967).
54. L. W. Nichol, J. L. Bethune, G. Kegeles, E. L. Hess, in *The Proteins*, H. Neurath, Ed. (Academic Press, New York, ed. 2, 1964), vol. 2, p. 305.
55. G. A. Gilbert, *Proc. Roy. Soc. London Ser. A* **250**, 377 (1959).
56. K. E. Van Holde, *J. Chem. Phys.* **37**, 1922 (1962); G. G. Belford and R. L. Belford, *ibid.*, p. 1926.
57. R. Josephs and W. F. Harrington, *Proc. Nat. Acad. Sci. U.S.* **58**, 1587 (1967).
58. G. Kegeles, L. Rhodes, J. L. Bethune, *ibid.*, p. 45; L. F. Ten Eyck and W. Kauzmann, *ibid.*, p. 888.
59. J. C. Gerhart and H. K. Schachman, *Biochemistry* **7**, 538 (1968).
60. J. Eigner and P. Doty, *J. Mol. Biol.* **12**, 549 (1965).
61. D. M. Crothers and B. H. Zimm, *ibid.*, p. 525.
62. H. B. Gray, Jr., V. A. Bloomfield, J. E. Hearst, *J. Chem. Phys.* **46**, 1493 (1967); P. Sharp and V. A. Bloomfield, *ibid.* **48**, 2149 (1968).
63. O. Kratky and G. Porod, *Rec. Trav. Chim.* **68**, 1106 (1949).
64. R. J. Douthart and V. A. Bloomfield, *Biopolymers*, in press.
65. J. Harpst, A. Krasna, B. H. Zimm, *Biopolymers* **6**, 595 (1968); P. Sharp and V. A. Bloomfield, *ibid.*, in press; E. P. Geiduschek and A. Holtzer, *Advan. Biol. Med. Phys.* **6**, 431 (1958).
66. R. E. Harrington, *Biopolymers* **6**, 105 (1968).
67. For extensive references, see J. Vinograd and J. Lebowitz, *J. Gen. Physiol.* **49**, 103 (1966); V. A. Bloomfield, *Macromol. Rev.*, in press.
68. V. A. Bloomfield and B. H. Zimm, *J. Chem. Phys.* **44**, 315 (1966); M. Fukatsu and M. Kurata, *ibid.*, p. 4539.
69. J. Vinograd, J. Lebowitz, R. Radloff, R. Watson, P. Laipis, *Proc. Nat. Acad. Sci. U.S.* **53**, 1104 (1965).
70. H. B. Gray, Jr., *Biopolymers* **5**, 1009 (1967).
71. D. A. Clayton and J. Vinograd, *Nature* **216**, 652 (1967); I. B. Dawid and D. R. Wolstenholme, *J. Mol. Biol.* **28**, 233 (1967).
72. J. C. Wang, D. Baumgarten, B. M. Olivera, *Proc. Nat. Acad. Sci. U.S.* **58**, 1852 (1967).
73. S. Brenner, G. Streisinger, R. W. Horne, S. P. Champe, L. Barnett, S. Benzer, M. W. Rees, *J. Mol. Biol.* **1**, 281 (1959).
74. A. E. Hook, D. Beard, A. R. Taylor, D. G. Sharp, J. W. Beard, *J. Biol. Chem.* **165**, 241 (1946); D. G. Sharp, A. E. Hook, A. R. Taylor, D. Beard, J. W. Beard, *ibid.*, p. 259.
75. M. F. Maestre, *Polymer Preprints* **7**, 1163 (1966).
75. I. J. Bendet, J. L. Allison, M. A. Lauffer, *Virology* **6**, 571 (1958); I. J. Bendet, L. G. Swaby, M. A. Lauffer, *Biochim. Biophys. Acta* **25**, 252 (1957); M. A. Lauffer and I. J. Bendet, *ibid.* **55**, 211 (1962).
77. D. J. Cummings and L. M. Kozloff, *Biochim. Biophys. Acta* **44**, 445 (1960); *J. Mol. Biol.* **5**, 50 (1962); D. J. Cummings, *Biochim. Biophys. Acta* **68**, 472 (1963).
78. D. P. Filson and V. A. Bloomfield, *Biochemistry* **6**, 1650 (1967); D. P. Filson, thesis, University of Illinois (1967).
79. L. C. Kanner and L. M. Kozloff, *Biochemistry* **3**, 215 (1964).
80. R. J. Douthart and V. A. Bloomfield, unpublished results.
81. P. Pfuderer, P. Cammarano, D. R. Holladay, G. D. Novelli, *Biochim. Biophys. Acta* **109**, 595 (1965).
82. D. P. Filson and V. A. Bloomfield, *ibid.* **155**, 169 (1968).
83. Preparation of this article was supported in part by PHS research grant GM 12555-04.

Eye Movement Control in Primates

The oculomotor system contains specialized subsystems for acquiring and tracking visual targets.

David A. Robinson

The retinas of most animals in which the eyes face forward have a special area, the fovea centralis, which has a high density of photoreceptors. To see an object with good visual acuity, these animals must move their eyes to place its image on each fovea. The eye movement system is especially well developed in primates. The purpose of this system is to acquire a visual target and then track it so that its image remains on the fovea. To do this, the oculomotor system overcomes, with nervous tissue and muscle, the same problems encountered in tracking systems designed by man. Current research in this field is directed not only toward diagnosis of eye movement disorders in man but also toward understanding how the central nervous system processes information and manipulates signals to achieve the regulation and coordination which this control system displays.

Four Oculomotor Subsystems

All tracking systems made by man or nature have at least two requirements: to acquire a given target rapidly, and then to follow it if it moves relative to the environment. The eye movement systems which perform these two functions are called the saccadic and smooth pursuit systems. When the tracking device is mounted on a moving platform (for example, a shipboard-mounted radar system) an additional requirement is that of stabilizing the tracking device automatically against movements of the platform. For eye movements, this function is fulfilled by the vestibular system. Finally, for depth perception (analogous to stereoscopic range-finding in some gunnery systems) the vergence system controls the degree of convergence of the visual axes of the eyes necessary to maintain the target image on each fovea. In short, the saccadic, smooth pursuit, vestibular, and vergence systems perform the four functions of acquiring targets, tracking them if they move in the environment, compensating for movements of the head in the environment, and tracking in depth.

Almost all eye movements in primates are combinations of the movements produced by each of these subsystems. The tasks are different from each other and appear to be performed by separate neurological control systems specializing in individual tasks. They can be excited independently, and their responses can be observed independently, so that each may be studied in isolation. Figure 1 illustrates this subdivision and the types of movements produced by each system. Except for the vestibular system, which obtains information about movement of the head in space from the semicircular canals, all the systems depend on visual information derived from the retina and carried centrally on the optic nerve. The outputs of the four systems converge on the motor nuclei whose motor cells relay the information along the motor nerves to the extraocular muscles. Each eye is equipped with three pairs of antagonist muscles that rotate the globe in three roughly mutually perpendicular planes: horizontal, vertical, and torsional. This arrange-

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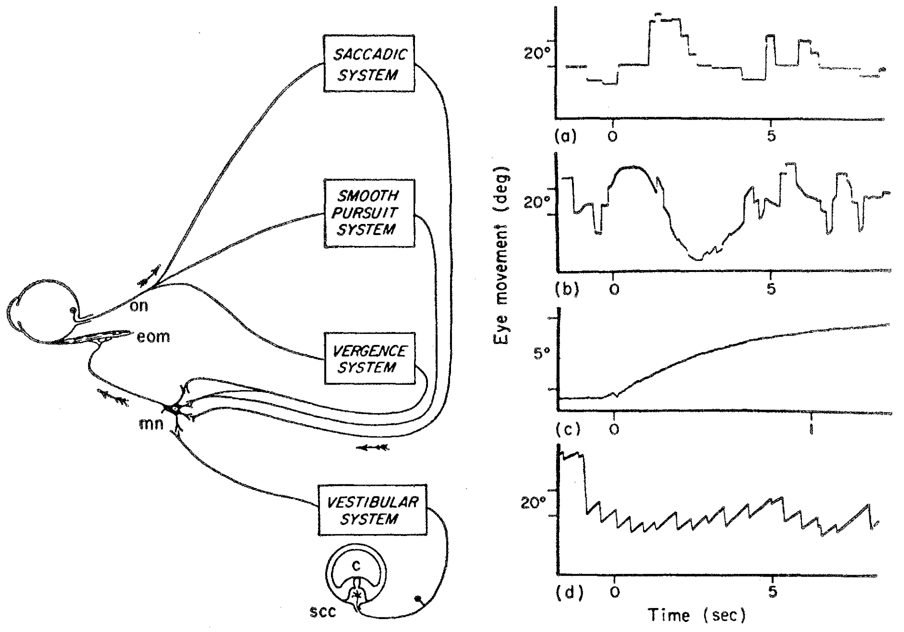

Fig. 1. A schematic representation of the primate eye movement system emphasizing the four subsystems involved in tracking visual targets. The saccadic system rapidly acquires new targets, the smooth pursuit system tracks the target if it moves in the environment, the vergence system performs binocular tracking in depth, and the vestibular system compensates for head movements. The types of eye movements made by each system are shown in a, b, c, and d, respectively. Each system converges on the motor nuclei (*mn*) which innervate the extraocular muscles (*eom*) and move the eyeball. Optic nerve, *on*; cupula, *c*; semicircular canal, *scc*.

ment gives full freedom to the oculomotor system in carrying out its various tasks. The behavioral characteristic of the four subsystems is described in the following sections with emphasis on their differences, which support the notion that they are neurologically distinct.

The saccadic system. This system is specialized in moving both eyes from one position to another very rapidly. Vision is impaired during a saccade so that it is desirable that little time be lost in the movement to maximize the amount of time in seeing. Figure 1a is a record of the horizontal position of a subject's eye in "looking about." Most of the time is spent in periods of steady fixation of different parts of the visual field which are interrupted by quick changes of fixation. Saccades are used for reading or the examination of any object or picture when it and the observer are stationary. The extraocular muscles are among the fastest in the body, and saccades are their fastest product. A 10-degree human saccade lasts 45 milliseconds, and the eye velocity reaches a peak of about 400 degrees per second. During a saccade, the agonist muscle contracts almost maximally, and the antagonist is inhibited completely, so that almost the full reserve of force of the muscles is called upon to make the movement as rapid as possible.

The saccadic system behaves like a sampled-data system. Such systems are unique in that they do not receive information continuously but only at discrete time intervals. When a subject is asked to watch a target that suddenly jumps to one side he will follow it by a saccade after a reaction time of about 200 milliseconds. However if the target jumps back to its starting place after 100 milliseconds the subject will still make a saccade, wholly inappropriate by then, 200 milliseconds after the first target jump to where the target was, and then another 200 milliseconds will pass before he returns his eyes to the starting point (*1*). The system behaves as though, when the target moves, it samples the error and then ceases to take in any new information. After one reaction time it responds with a saccade appropriate to the position error as it existed 200 milliseconds ago. This sampling behavior has been investigated rather thoroughly for the eye movement system (*2*), and is of current interest in other neuromuscular systems involved when man is an operator in a man-machine task (for example, control of jet aircraft and space capsules). The concept of sampled data does appear appropriate to the gross behavior of the saccadic system, although closer scrutiny reveals that during the 200-millisecond period after the initial error sampling takes place, all visual information is not blocked. Subsequent changes in both target velocity and position influence the amplitude of the impending saccade, but the probability that they will do so diminishes with increasing time between the initial sample and the final motor act (*3*, *4*).

Saccadic eye movements are, in general, voluntary acts based on visual information, but they can also be made with eyes closed or in total darkness. They also occur during certain periods of sleep (*5*), and are thought to be associated with "watching" the visual imagery of dreams (*6*). There is probably an involuntary side to saccades. When one suddenly perceives movement in the periphery, one's eyes are drawn to it (by a saccade) almost automatically. Thus saccades may be initiated involuntarily by visual stimuli, and voluntarily with or without visual stimuli.

The smooth pursuit system. This system, on the other hand, is almost entirely automatic and requires a visual stimulus. Smooth-pursuit eye movements cannot be made in the absence of a moving visual stimulus, and they are involuntary in situations where the entire visual field is in motion. This occurs when looking into a rotating mirror or out the window of a moving train, when the eyes smoothly follow an object until it becomes uncomfortable to continue without a head movement. At that time, the eyes saccade the other way to pick up and track another object. The resulting sawtoothed movement is called optokinetic nystagmus. More commonly the smooth pursuit system tracks only one object moving in a stationary environment. Figure 1b shows the eye movements of a subject watching a person walk about. The saccadic system still scans over the person's body, but within each intersaccadic interval the eye velocity matches the velocity of the moving objects being observed. Clearly, the value of this pursuit is that it is easier for the visual system to perceive the form and pattern of images if they are stationary on the retina rather than moving. The smooth pursuit system appears to be not concerned with the error itself between target and fovea (which is corrected by the saccadic system), but only with matching the eye velocity to target velocity (*7*). To do this it apparently extracts from the visual system information concerning the direction and rate of movement of images on the retina and then supplies a signal to the extraocular muscles designed to reduce this rate of movement to zero. Although the smooth pursuit system can produce eye velocities up to 100 degrees per second, it cannot correctly match the velocity of visual stimuli above about 30 degrees per second.

The smooth pursuit system differs from the saccadic system in a number of ways. Two have already been mentioned: its involuntary nature and the fact that target velocity rather than target position is its appropriate stimulus. Experiments in which the target velocity is changed twice in rapid succession indicate that the smooth pursuit system is a continuous rather than a sampled system (*3*). Its reaction time is only 125 milliseconds. It is slower than the saccadic system and requires 130 milliseconds to effect a step change in eye velocity compared to 20 to 70 milliseconds required by most saccades (*8*). Barbiturates, alcohol (*7*), and some disease processes (*9*) selectively attack the smooth pursuit system before the saccadic system. Another difference appears when the two systems are made to oscillate by external visual feedback. This can be brought about by measuring the subject's eye position and allowing it to change the target position by some electrical or optical scheme. Normally, an eye movement will produce an equal and opposite change in the retinal error between target image and fovea. In the terminology of control theory, the oculomotor system is thus said to have a negative feedback gain of 1.0. External feedback can add or subtract from this value and change the net feedback gain. Almost all control systems oscillate if the negative feedback gain is sufficiently increased, and the oculomotor system is no exception. All three systems—saccadic, smooth pursuit, and vergence—oscillate under increased visual feedback. The vestibular system is not included because it is not a feedback system. The saccadic system oscillates when the net feedback gain is 5.0 at a frequency of about 2 hertz, whereas the smooth pursuit system oscillates at a gain of 8.0 at a frequency of 3.3 hertz (*3*).

The vestibular system. This system measures the motion of the head in space and moves the eyes in the head to compensate and maintain the visual axis stable in the environment. Information about head orientation is obtained from the semicircular canals lying in the vestibule of the inner ear. Each is a fluid-filled circular tube with a hinged fluid-tight vane, the cupula (*c* in Fig. 1), lying across its lumen. Angular acceleration of the head causes the fluid to be "left behind" which deflects the cupula. Nerve cells beneath it sense its deflection, and alter their rate of discharge proportionately. The elements determining the dynamic behavior of the canals (*10*) are the moment of inertia of the ring of fluid, the viscous drag of the fluid as it flows through the canal, and the spring stiffness of the gelatinous cupula which always returns to a neutral position in the absence of applied forces. Because the viscosity is the predominate reacting force, the velocity of the fluid flow is approximately proportional to the angular acceleration of the head. Consequently cupula position (the integral of fluid velocity) is proportional to the angular velocity of the head. Thus, this sense organ behaves like an integrating accelerometer, and in its normal mode of action the neural discharge to the central nervous system is proportional to head velocity (*11*). If the head movements are of too short or too long duration, the viscous reaction force no longer predominates over the inertial or spring forces, and the canal ceases to integrate head acceleration properly. The range of frequencies of head movements over which the semicircular canals behave as integrating accelerometers is approximately 0.017 to 17 hertz.

To stabilize eye position, the incoming vestibular velocity signal must be integrated once more by the nervous system before being translated into eye position by the extraocular muscles. There are three semicircular canals (on each side of the head) lying in three roughly mutually perpendicular planes. They can resolve angular head velocity about any axis in space into three components which are applied in the correct combination to the three pairs of antagonist muscles of each eye to counterrotate them about the same axis. If rotation continues for more than 10 or 15 degrees in the same direction a saccade resets the eyes rapidly in the opposite direction and stabilization then continues to take place for a new visual axis position. If rotation persists it creates the alternating saw-toothed pattern of fast and slow phases (Fig. 1d) called vestibular nystagmus. If rotation at a constant velocity is sustained beyond about 10 seconds, nystagmus will cease because such stimulation lies below the physiological bandwidth of the system.

Although the smooth pursuit system can compensate for retinal image movement caused by head movement, it cannot do so accurately above 30 degrees per second; yet head movements can easily exceed 300 degrees per second. The vestibular system can compensate for these large velocities, and its short direct path through the brain stem insures an almost immediate reaction.

The vergence system. This is the only system which moves the eyes in opposite directions. It is the slowest of all the systems. In Fig. 1c a single vergence movement made by a subject looking from a far to a near target is illustrated. The movement lasts for about 800 milliseconds. The reaction time is about 160 milliseconds. It does not appear to be a sampled system (*12*). It oscillates at 2.5 hertz when placed under external negative visual feedback (*12*). The stimulus for this system is the difference between the retinal errors seen by each eye, and it applies to the extraocular muscles a signal that causes the eyes to converge or diverge at 10 degrees per second for each degree of interretinal error (*13*). When a subject looks from some point A to another, B, which lies at a different angle and depth in his visual field, he first makes a saccade from A to a point in space which allows his two visual axes to just straddle B, and this is followed by a pure vergence movement until both eyes are directed at B (*8*). This sequence illustrates that the vergence system is a separate neurological system that can only create equal and opposite eye movements that summate with the conjugate movements of the other systems.

The Final Common Path

The motor nerves and muscles form a unit called the final common path because it is shared by all four subsystems. It is useful to know the way nervous activity in the final common path is converted through the tension developed in the muscles to eye position. The scheme describing the mechanics of the globe and one antagonist pair of extraocular muscles is shown in Fig. 2. The globe is held in the bony orbit by many passive tissues such as the optic nerve, fat pad, suspensory

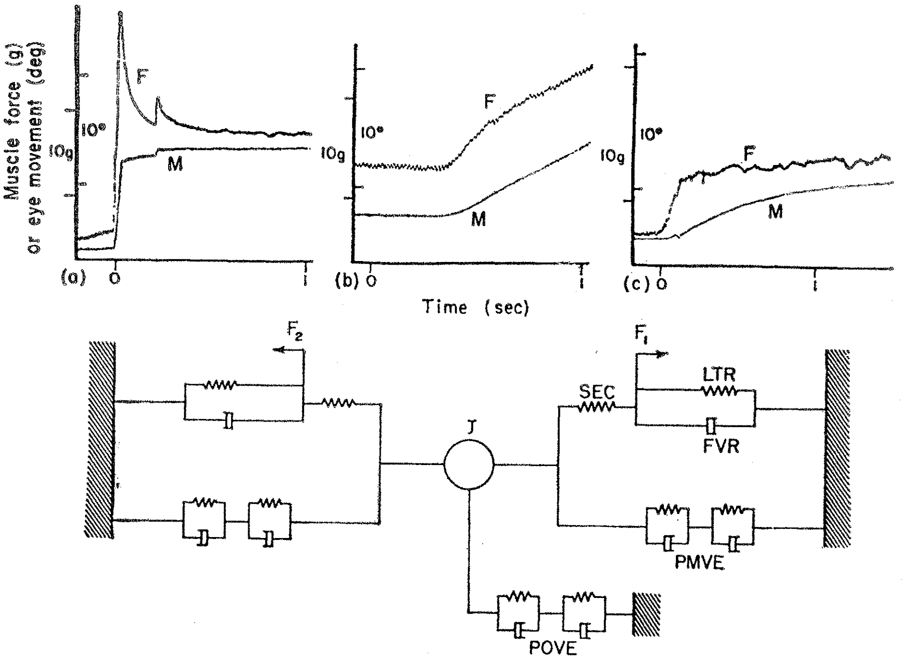

Fig. 2. A model of the mechanics of the extraocular muscles, globe, and suspensory tissues. The globe, of moment of inertia *J*, is held in the bony orbit by passive orbital viscoelastic elements (*POVE*). Each muscle has passive viscoelastic elements (*PMVE*) and an active portion composed of a series elastic component (*SEC*) and a contractile component subdivided into an element with a force-velocity relationship (*FVR*) and an active state tension generator (F_1, F_2) which displays a length-tension relationship (*LTR*). The recordings represent net isometric muscle force (*F*) and eye movement (*M*) for saccadic (a), smooth pursuit (b), and vergence (c) movements.

ligaments, and conjunctiva, whose viscoelastic properties are represented by the springs and dashpots of the passive orbital viscoelastic elements. Each muscle also has its passive elements. Electrical activity in the nerves, which may be thought of as the control signal, is converted to active state tension (F_1 and F_2) in the two muscles. This force is transmitted to the globe through the mechanical elements of the active portion of muscle.

If a subject fixates straight ahead and one eye is drawn aside (by pulling on an opaque suction contact lens firmly seated on the eye), the static spring stiffness of all the elements (Fig. 2) is found to be 1.2 grams per degree (*14*, *15*). The detachment of the two muscles from the globe during corrective surgery reveals that about 20 percent of this figure lies in the passive orbital elastic elements and 30 percent in the two passive muscle elastic elements combined (*16*). The remaining 50 percent resides in the length-tension relation of muscle and indicates that as the muscles are lengthened they are capable of generating more tension. Such studies (*16*) also indicate that when the eye looks straight ahead both muscles exert a tonic force of about 14 grams. During steady deviations the force increases in the agonist (up to 50 grams) and decreases in the antagonist until the difference just balances the restraining force of the passive tissues. The maximum force of human extraocular muscles is estimated at 150 grams. If the eye, drawn aside by the contact lens, is suddenly released, it returns with a small initial rapid motion followed by a slower motion that lasts over 700 milliseconds and constitutes 75 percent of the total movement. This step response indicates that the system appears to be largely overdamped. The small fast motion has been investigated by applying sinusoidal forces to a contact lens on the eye (*17*) and demonstrating that the inertia *J* resonates with a stiff spring (thought to be the series elastic component) at 35 hertz with a damping factor of 0.5. Theoretical studies (*18*) suggest that the principal source of viscosity, which constitutes the greatest mechanical impedance to rapid movements, resides in the force-velocity relationship of muscle itself.

From what is now known about the mechanics of the system in Fig. 2, it is almost possible to predict the control signals needed to produce saccadic, smooth pursuit, and vergence movements. Even so, it is desirable to observe these signals more directly by fastening the contact lens to a strain gauge which prevents the eye from moving but measures the net force which the isometric muscles exert in their efforts to rotate the globe (*3*, *14*, *19*). Figure 2 (a–c) illustrates the net isometric force measured in one eye and the movement of the other eye during saccadic, smooth pursuit, and vergence movements. The vergence movement is slow because the tension is only a slightly rounded step function. The smooth pursuit movement is more rapid, because the eye is initially accelerated by a rate of rise of force twice as large as that needed to maintain velocity in the steady state. The saccade is the most rapid movement, because a large pulse of force is applied to overcome the viscous impedance of the mechanical system and maintain a high velocity during the movement. At the end of the movement the pulse of force is removed and replaced by a lower holding force. The 150-gram force of which human extraocular muscles are capable is not used to hold the eye in steady deviation but is held in reserve for the pulse of force associated with saccades.

The control signals during eye movements may also be observed by thrusting needle electrodes into the extraocular muscles to observe their electrical activity (*20*, *21*), and by placing microelectrodes into the motor nuclei of animals and recording the action potentials of single motor nerve cells (*22*). Both methods reveal that when a muscle increases its force, more muscle fibers are recruited into the pool of those already active, and the rate of discharge of active units increases to as high as 400 impulses per second. These methods also confirm that during a saccade, the agonist muscle is excited by a pulse of intense activity and the antagonist is completely inhibited. The duration of the pulse of activity is equal to the duration of the movement. Since the agonist is almost maximally excited, larger saccades cannot be made by the application of much more force so they must have a larger duration (*14*).

Although a detailed description of the elements in Fig. 2 is still not available, the research of the last 5 years has provided a general understanding of the way in which activity in the final common path is related to eye position and eye movement. Work remains to be done on improving the description of the mechanics of extraocular muscles and their fiber types, and especially in using these analytic descriptions in problems of eye movement disorders in man.

Central Nervous System Organization

Most fish have no foveas and little visual overlap between their eyes. Consequently they have no saccadic or vergence systems. However, they have very well-developed smooth pursuit and vestibular systems. Visual perception takes place in the optic tectum of the fish, which is more simply organized than the visual cortex of primates; therefore it is important for survival that fish have retinal images that are stabilized by these two velocity compensating systems. However, since the activity of these systems can carry the eye to its mechanical limits, a fast resetting mechanism had to develop simultaneously with both systems. This system, responsible for the fast phase of vestibular and optokinetic nystagmus, appears to be the forerunner of the saccadic system. As the central nervous system evolved, the cortex developed, the fovea came into existence, and eye movement came under cortical control. The cortex appears to have used the fast-phase brainstem system for its own purposes to form the saccadic system. As encephalization progressed, the primary visual area shifted from the optic tectum (the homologue of the mammalian superior colliculi) which subserved smooth pursuit movements to the visual cortex and this function has gone with it. In primates it is not clear what visual or eye movement function remains in the superior colliculi (*23*). Figure 3 presents a simplified picture of those portions of the nervous system involved in eye movements.

The vestibular system. This is the most localized system. Information concerning head velocity enters the vestibular nuclei and is immediately relayed along the medial longitudinal fasciculus, which distributes the information from the six canals appropriately among the motor nuclei and so to the 12 extraocular muscles. This three-neuron arc (*24*) is inadquate to perform the temporal integration known to take place in the pathway, but multisynaptic pathways exits in the pontine reticular formation and the cerebellum which may perform this function. What generates the fast phase of vestibular nystagmus in unknown, but it depends on the integrity of the brain stem between the vestibular and the oculomotor nuclei (*25*). The pulse of activity that produces the resetting saccade must be distributed in the right proportion to the motor nuclei, so that the direction of the fast-phase movement is opposite to the slow phase. It is likely that the same pulse erases the information stored in the brain-stem integrators so that they may be ready to generate the next slow phase. Since eye and head movements in the same direction are common, the voluntary saccadic system must be capable of completely blocking the action of the vestibular system. These are only a few of the functions executed by this system in ways that are not understood at the nerve cell level.

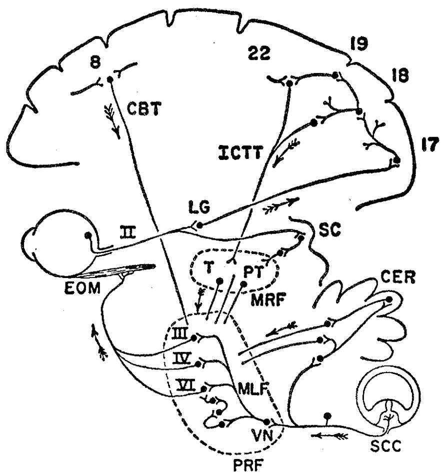

Fig. 3. A schematic of the major oculomotor pathways in the central nervous system. *CBT*, corticobulbar tract; *CER*, cerebellum; *EOM*, extraocular muscles; *ICTT*, internal corticotectal tract; *LG*, lateral geniculate body; *MLF*, medial longitudinal fasciculus; *MRF*, mesencephalic reticular formation; *PRF*, pontine reticular formation; *PT*, pretectal nuclei; *SC*, superior colliculi; *SCC*, semicircular canals; *T*, tegmentum; *VN*, vestibular nuclei; II, optic nerve; III, IV, VI, oculomotor, trochlear and abducens nuclei and cranial nerves; 17, 18, 19, 22, Brodmann's areas of occipital and parietal visual and association areas; 8, Brodmann's premotor area in the frontal lobes.

The smooth pursuit system. This system uses information extracted from the visual system, presumably from areas 17, 18, and 19 (Fig. 3) in the cortex and from the superior colliculi. The information needed is the direction and velocity of image movement on the retina and single cells have been observed in the visual cortex (*26*), the retina (*27*), and the superior colliculi (*28*) which seem to provide this information. If the superior colliculi are vestiges of the optic tectum of the fish, they presumably have access to structures, possibly in the tegmental area, organized to move the eyes at various velocities in different directions to keep the retinal image velocity at or near zero. This region (*T*) is known to be intimately involved with eye movements (*29*) but its function is still unclear. Velocity information from the cortex is believed to descend in the internal corticotectal tract (*30*) and may mix with velocity information from the superior colliculi in the tegmental and pretectal areas of the mesencephalic reticular formation. The relative use of these two sources of velocity information is probably species-dependent. One may speculate that since the vestibular system contains a mechanism (the integrators) for driving the eyes at a velocity that is proportional to an input signal and the smooth pursuit system has the same requirement, they may share the same neural networks. Vestibular and optokinetic nystagmus certainly can compete with each other, but it is not known whether they do this at the input to the integrators or at the motor nuclei. Electrical stimulation of areas 18 and 19 (Fig. 3) produce conjugate eye movements to the opposite side (*31*), but most investigations have been carried out in the lightly anesthetized monkey in which all movements are smooth, and no one has yet demonstrated smooth pursuit movements by stimulation of the cortex of the unanesthetized monkey.

The vergence system. Electrical stimulation of cortical areas 19 and 22 (Fig. 3) produces vergence movements in the lightly anesthetized monkey (*32*). Although this needs verification in the absence of anesthesia, it suggests that here the vergence system extracts visual information of the difference in retinal error between the eyes and sends it, also by the internal corticotectal tract, to the brain stem. This system is not only responsible for movements of convergence and divergence but must also actively maintain fusion of the two retinal images by controlling vertical and torsional muscle balance, so it must have access to all the motor nuclei.

The saccadic system. Saccades can be evoked by stimulation of cortical area 8 (Fig. 3), known as the frontal eye fields. The movements produced by a brief (30-millisecond) stimulus train in the unanesthetized monkey are conjugate contralateral saccades indistinguishable from the animal's spontaneous saccades (*33*). Stimulation of many sites in the frontal eye fields shows that no other types of eye movement are evoked. At each site, the saccade occurs above a certain stimulus threshold in an all-or-nothing fashion, and the size and direction of the saccade depends not so much on how the cortex is stimulated (above threshold) as on where it is stimulated. Stimulation of different subdivisions of the frontal eye fields produces saccades which range from 2 to 60 degrees in amplitude depending only on stimulus location. These observations support the hypothesis of neurology that the frontal eye fields are the cortical outlet for the voluntary saccadic system. It also suggests that all sizes and directions of saccades required by the animal to look anywhere in his visual field are coded by location in this area of the cortex.

Fibers leave this area and descend in the corticobulbar tract to the pontine reticular formation (the ill-defined region marked *PRF* in Fig. 3) where so much of the oculomotor signal processing takes place and the pulse of activity associated with saccades is generated. It appears that cortical stimulation has access to these pulse generators and sets in motion an irreversible stereotyped chain of neural events in the brain stem that leads to a saccade. If the first stimulus is followed by a second test stimulus it appears that the pulsatile system has a refractory period of about 25 milliseconds during which it cannot be reexcited and a relative refractory period of 40 milliseconds during which it can be reexcited only by an increased stimulus intensity. The combination of threshold, all-or-nothing response, and a refractory period are characteristics which often occur together in pulse generator devices either made by man (for example, the one-shot multivibrator) or nature (for example, the nerve action potential). However, if the second test stimulus is delivered to the opposite cortex, there is no refractoriness and it produces a second saccade in the opposite direction which can occur so soon after the first that it mechanically interferes with it. When this happens the first saccade appears to be canceled in midflight and replaced by the second. This suggests that horizontal saccades are created by two pulse generators, one for left gaze triggered from the right cortex, and the other for right gaze triggered from the left, each of which is post-stimulus refractory and which mutually interact so that only one pulse generator can be on at any one time.

When two cortical points are stimulated simultaneously either on the same or opposite sides, the resulting saccade is a weighted mixture of the two movements evoked by each stimulus separately with the weightings determined by stimulus intensity. For example if the left and right cortices are stimulated together the resulting saccade amplitude can be continuously varied from a right movement through zero to a left movement by varying the ratio of stimulus intensities. Since saccade amplitude is largely determined by the pulse duration of the pulse generators, it appears that some neural network must control this pulse width on the basis of which fibers from the cortex carry the activity rather than the temporal nature of the activity itself. When two sets of fibers are excited at once this network must reach a compromise between them and control the pulse width accordingly.

Summary

The neural organization of the oculomotor system is much more complex than that suggested by Fig. 3 and the foregoing descriptions. The final picture of this system must explain a great variety of signal manipulation and coordination. The electrical stimulation of the frontal eye fields just discussed is an example of how functional descriptions of the organization and interaction of elements of the subsystems can be built up. The areas where future research will no doubt concentrate are the mesencephalic and pontine reticular formations into which information flows from many sources. In and through this small volume of neural tissue, a vast amount of information processing and transmission takes place, only a small part of which is concerned with eye movements. However, it is here that the four oculomotor subsystems perform their final transformations on the incoming signals and establish the interactions required between them before passing the total output to the final common path. Stimulation and single nerve cell recording with microelectrodes in animals will probably be the methods used in future research, coupled with techniques to avoid the use of anesthesia and to measure eye movement accurately.

I have tried here to emphasize the importance of function in oculomotor research. A discussion of the evolution of eye movements by Walls (*34*) also puts strong emphasis on function. The oculomotor system is one of the few control systems in physiology where function can be stated with such clarity and the function of each of its subsystems can be stated with equal clarity. With our knowledge about the final common path and an appreciation of the simple task each subsystem must perform it is possible to state what information each system needs, how it must process it, and what form of control signal it must present to the final common path in order to accomplish its goal. This knowledge should help in interpreting the data that will emerge when we seek to discover how all this is accomplished at the nuclear and cellular level.

References and Notes

1. G. Westheimer, *Arch. Ophthalmol.* **52**, 932 (1954).
2. L. R. Young and L. Stark, *IEEE (Inst. Elec. Electron. Eng.) Trans. Human Factors Electron.* **HFE-4**, 38 (1963).
3. D. A. Robinson, *J. Physiol.* **180**, 569 (1965).
4. L. L. Wheeless, Jr., R. M. Boynton, G. H. Cohen, *J. Opt. Soc. Amer.* **56**, 956 (1966).
5. A. F. Fuchs and S. Ron, *Electroencephalogr. Clin. Neurophysiol.* **23**, 244 (1968).
6. W. Dement, in *The Oculomotor System*, M. B. Bender, Ed. (Harper and Row, New York, 1964), p. 366.
7. C. Rashbass, *J. Physiol.* **159**, 326 (1961).
8. A. L. Yarbus, *Eye Movements and Vision* (Plenum, New York, 1967).
9. G. K. von Noorden and T. J. Preziosi, *Arch. Ophthalmol.* **76**, 167 (1966).
10. A. J. Van Egmond, J. J. Groen, L. B. W. Jongkees, *J. Physiol.* **110**, 1 (1949).
11. G. M. Jones and J. H. Milsum, *IEEE (Inst. Elec. Electron. Eng.) Trans. Bio-Med. Eng.* **BME-12**, 54 (1965).
12. B. L. Zuber and L. Stark, *IEEE (Inst. Elec. Electron. Eng.) Trans. Syst. Sci. Cyb.* **SSC-4**, 72 (1968).
13. C. Rashbass and G. Westheimer, *J. Physiol.* **159**, 339 (1961).
14. D. A. Robinson, *ibid.* **174**, 245 (1964).
15. D. S. Childress and R. W. Jones, *ibid.* **188**, 273 (1967).
16. D. A. Robinson, D. M. O'Meara, A. B. Scott, C. C. Collins, in preparation.
17. J. G. Thomas, *Kybernetik* **3**, 254 (1967).
18. G. Cook and L. Stark, *Commun. Behav. Biol.* **1**, 197 (1968).
19. D. A. Robinson, *J. Pediat. Ophthalmol.* (31 Aug. 1966), p. 31.
20. Å. Björk and E. Kugelberg, *Electroencephalogr. Clin. Neurophysiol.* **5**, 595 (1953).
21. J. E. Miller, *Amer. J. Ophthalmol.* **46**, 183 (1958).
22. K. P. Schaefer, *Pflüger's Arch.* **284**, 31 (1965).
23. P. Pasik and T. Pasik, in *The Oculomotor System*, M. B. Bender, Ed. (Harper and Row, New York, 1964), p. 40.
24. J. Szentágothai, *J. Neurophysiol.* **13**, 395 (1950).
25. R. Lorente de Nó, *Ergeb. Physiol.* **32**, 73 (1931).
26. D. H. Hubel and T. N. Wiesel, *J. Neurophysiol.* **28**, 229 (1965).
27. H. B. Barlow, R. M. Hill, W. R. Levick, *J. Physiol.* **173**, 377 (1964).
28. R. M. Hill, *Nature* **211**, 1407 (1966).
29. J. E. Hyde and R. C. Eason, *J. Neurophysiol.* **22**, 666 (1959).
30. E. C. Crosby and J. W. Henderson, *J. Comp. Neurol.* **88**, 53 (1948).
31. I. H. Wagman, H. P. Krieger, M. B. Bender, *ibid.* **109**, 169 (1958).
32. R. S. Jampel, *Amer. J. Ophthalmol.* **48**, 573 (1959).
33. D. A. Robinson and A. F. Fuchs, in preparation.
34. G. L. Walls, *Vision Res.* **2**, 69 (1962).
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